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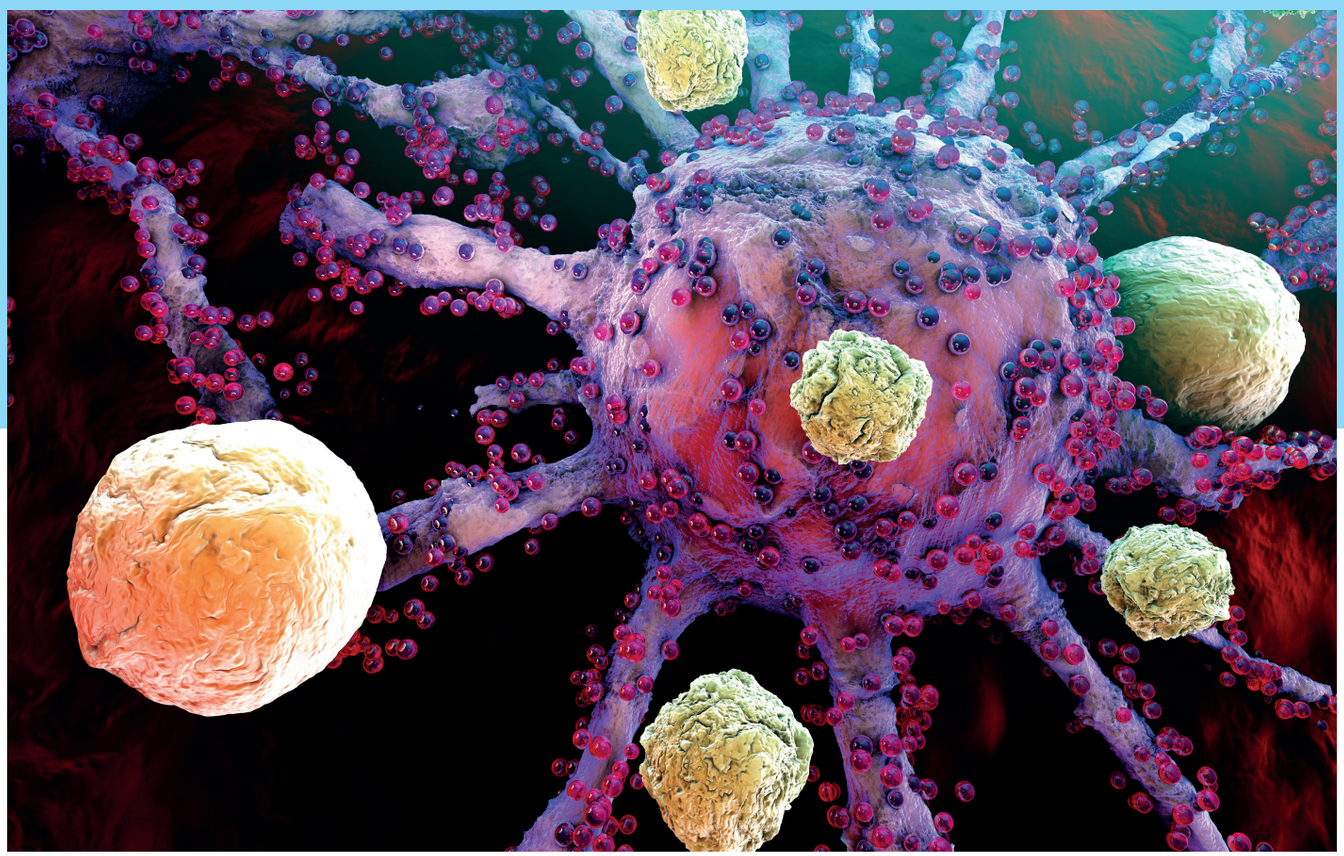

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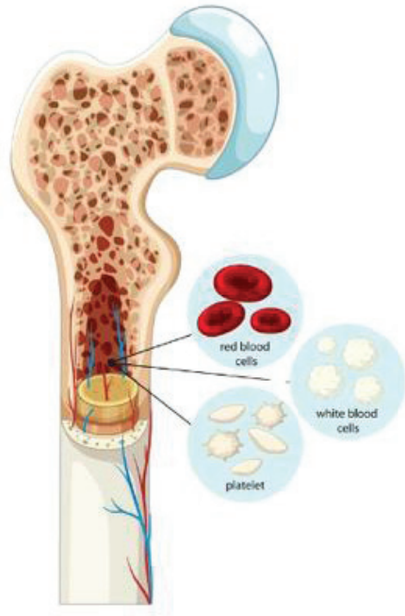

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A001. Clinical Outcomes and Toxicity Profile of Cetuximab-Containing Regimen in Locoregional Recurrent and Distant Metastatic Head and Neck Squamous Cell Carcinoma: A Single-Institution Retrospective Audit

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[1]Omega Hospitals, Hyderabad, India

Keywords:
- cetuximab-based chemotherapy
- locoregional recurrence
- distant metastasis
- recurrent/metastatic squamous cell carcinoma of head and neck

Aim and Objectives: To investigate the treatment outcomes of a regimen comprising cetuximab in groups of patients with locoregionally recurrent and metastatic squamous cell carcinoma of the head and neck (R/M SCCHN).

Materials and Methods: Between January 2013 and May 2023, we included 100 patients with R/M SCCHN who were treated with cetuximab-based chemotherapy. Clinical outcomes, viz. OS, PFS, ORR, DCR, and toxicity profile were evaluated.

Results: Median age of study group was 56.5 (29–84). 85% were male. 13% had multiple comorbidities. 52% had metastatic disease, and 48% recurrent disease. 49% accounted for Ca oral cavity as the primary site, followed by less common sites. ECOG PS was 1 in 56%, 2 in 34%, and 3 in 10% of patients. Median duration of follow-up was 33.5 months (10–390). mOS was 19 months (95% CI: 17.1–20.9). 1 year OS rate was 77.9%, while 2-year OS rate was 33%. mPFS was 3 months (95% CI: 2.7–3.3). 3-month PFS rate was 34.7%, while 6-month PFS rate was 12.6%. 37% showed PR, 18% SD, and 45% PD as initial response. Thus, for the entire study population, ORR was 37% and DCR 55%. On subgroup analysis, mOS for patients with recurrent disease was 23 months (18.2–27.8), and 17 months (14.8–19.1) for patients in the metastatic stage ($p = 0.01$). mPFS was 3 months in both the groups. Patients with recurrent disease showed better response rates with ORR of 43.8% and DCR of 60.5% as against ORR and DCR of 30.8 and 50% in metastatic setting, respectively. No patients died of severe adverse reactions during treatment. Grade III and above toxicities were noted in 27% showing rash, 12% diarrhea, 15% mucositis, 21% fatigue, and 5% febrile neutropenia.

Conclusion: When treated with a cetuximab-containing regimen, locoregional recurrence of SCCHN is associated with superior disease control and survival results compared to distant metastatic SCCHN.

A002. Real-World Data of Nonmetastatic Carcinoma Esophagus Patients Treated with Multimodality Treatment in a Resource-Constrained Setting from South India Under PMJAY/AROGYASREE Scheme

Matta Venkata Ravi Teja[1]
[1]GSL Medical College, Andhra Pradesh, India

Keywords:
- esophagus
- NACRT
- surgery
- survival
- clinic-demographic profile
- immunotherapy

Aim and Objectives: The aim was to analyze the clinico-demographic profiles and survival outcomes of nonmetastatic esophageal cancer treated with multimodality treatment at our institute where most patients are from rural and low socio economic backgrounds.

Materials and Methods: Data of non-metastatic carcinoma esophagus patients were taken from medical records from January 2020 to December 2023. Clinico-demographic data and survival patterns with multimodality approaches were analyzed.

Results: A total of 47 patients were included in our study. The mean age at presentation is 55 years. Male to female ratio is 2:3. 18 (38.3%) were smokers and 12 (25.5%) were alcoholics. The commonest site is the middle thoracic esophagus in 22 patients (46.8%), 5 (31.9%) had a lower third. Squamous cell carcinoma is the most common histology (82%). Stage 2 is the most common stage of presentation in 22 (46.8%) followed by stage 3 (36.2%). 20 received neo-adjuvant chemo-radiotherapy (NACRT), 13 (65%) received

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paclitaxel + carboplatin (weekly), 7 (35%) received CAPEOX regimen along with radiation (41.4–45 Gray). Of these, only 8 (40%) underwent surgery, while 12 (60%) could not. 5 (62.5%) who underwent surgery achieved pathological complete response. 24 received definitive CRT with 14 (58.3%) achieving complete response and 10 (41.6%) having partial response. Three patients defaulted without treatment. The median overall survival of the analyzed population is 10.5 months. In a subset analysis, the survival of patients who underwent surgery was 12 months, and without surgery was 8 months.

Conclusion: Outcomes of esophageal cancer despite the advances in the multimodality treatment are still dismal. Our study also shows that patients who are not able to undergo surgery after NACRT have the lowest survival. We need to critically analyze the reasons for not able to perform radical surgery despite NACRT in a resource-constrained setting like ours, in order to improve survival rates, where use of immunotherapy is still not feasible.

A003. Efficacy of Low-Dose Nivolumab in Advanced Carcinomas

Abhishek Tiwari[1], Soumya Surath Panda[1], Ghanshyam Biswas[1], Lalatendu Moharana[1], Lipsita Samantaray[1], Santhosh Meedimale[1], Susheel Kumar Yeshala[1], Antara Sanyal[1]

[1]Department of Medical Oncology, IMS & SUM Hospital, Bhubaneswar, Odisha, India

Keywords:

- low-dose immunotherapy
- low-dose Nivolumab

Aims and Objectives: Immunotherapy with PD-1/PDL1 blocking monoclonal antibodies has improved survival compared to the standard-of-care chemotherapy for several malignancies at different stages of these malignancies. Due to financial constraints, many cancer patients in medical need have no access to these drugs. In this study, we aimed to investigate whether a low dose of nivolumab could also lead to an effective therapeutic response.

Materials and Methods: A retrospective analysis was conducted at IMS and SUM Hospital, Bhubaneswar, India, focusing on advanced cancer patients unable to afford standard immunotherapy. Patients received a flat low dose of nivolumab (40 mg every 28 days), with treatment continued until disease progression or intolerable toxicity. Data were gathered from electronic medical records, including demographics, treatment details, and adverse events.

Results: A total of 46 patients received low-dose nivolumab for different malignancies. The mean age of the participants was 52 years. The median follow-up time for all patients was 5.8 months. The median OS was 7.6 (range, 4.1–16.0) months. The overall response rate (ORR) was found to be 28.5%, with the disease control rate (DCR) being 52%. In metastatic renal cell carcinoma patients, the ORR and DCR were higher than the overall population, at 37.5 and 75%, respectively. One patient achieved complete remission, and one had prolonged partial remission.

Conclusion: A low dose of nivolumab is a cheap and effective therapeutic option for patients in medical need for whom standard-dose immune checkpoint inhibitors are not accessible for any reason.

A004. Experience of Next-Generation Sequencing in a Tier-III City in India: A Prospective Study at Kanpur

Vikas Tulsidas Talreja[1]

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Keywords:

- next-generation sequencing
- Tier-III city
- broad gene panel
- Illumina
- Thermo Fisher
- precision medicine
- Kanpur
- oncology
- genetic diagnostics

Aim: This study aims to evaluate the implementation and outcomes of next-generation sequencing (NGS) using a broad gene panel in a tier-III city in India, specifically focusing on 150 patient samples processed at a medical facility in Kanpur.

Background: The application of NGS in oncology and genetic diagnostics has revolutionized precision medicine. However, the literature documenting the use of NGS in tier-III cities in India is limited. This study is the first of its kind to prospectively assess the feasibility, challenges, and clinical impact of using NGS in such a setting. The study uses platforms from Illumina and Thermo Fisher to analyze genetic mutations and variations in a broad spectrum of genes.

Materials and Methods: A total of 150 samples from patients with various oncological and genetic conditions were collected and analyzed using Illumina and Thermo Fisher NGS platforms. The gene panel included a comprehensive set of genes associated with the conditions under investigation. Data analysis focused on identifying actionable genetic variants and their implications for patient management.

Results: The findings will be presented, highlighting the spectrum of genetic alterations detected, the proportion of actionable mutations, and the clinical decisions influenced by the NGS results. The study also examines the logistical and infrastructural challenges encountered, as well as the overall feasibility of conducting advanced genomic testing in a tier-III city setting.

Conclusion: This pioneering prospective study in Kanpur provides valuable insights into the application of NGS in resource-limited settings, demonstrating its potential to enhance diagnostic accuracy and treatment personalization. The results underline the importance of expanding genomic testing capabilities beyond metropolitan areas to improve health care equity and outcomes.

A005. Clinicopathological Features and Pathological Complete Response to Neoadjuvant Chemotherapy in Young Breast Cancer Patients Treated Under a State-Funded Free Health Care Program at a Tertiary Care Center in South India

Niveditha Gajjala[1], Deepak Y. C.[1], Sindhusha K.[1], Ravi Mohan P.[1]

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Keywords:

- breast cancer
- NACT
- young
- pCR

Aim and Objectives: To assess the clinicopathological features and pathological complete response (pCR) rates with neoadjuvant chemotherapy (NACT) in young breast cancer patients.

Materials and Methods: This is an ambi-directional, single-institution study. It assessed the clinicopathological features of 45 young (≤39) women with breast cancer and pCR rates after NACT from 2021 to 2023. Data were analyzed using descriptive statistics.

Results: The youngest was 19 years, with mean of 34 ± 4.6 years. Risk factors included 9 with nulliparity, overweight in 13, Class I obesity in 11 women, and Class II obesity in 3 women. A family history of any other cancers was present in 9 women. The TNM stage distribution was as follows: stage I: 0, stage-II: 6, stage-III: 33, stage-IV (oligometastatic): 6. Locally advanced cancer constituted 84%. Triple-negative breast cancer constituted majority of subtype (53%), Luminal A (22%), Luminal B (6%), HER-2 over-expression (16%). NACT with sequential doxorubicin and cyclophosphamide followed by paclitaxel regimen was used. Where appropriate dose dense regimen was given and of eligible patients where HER-2 positive trastuzumab was added. Complete pathological response seen was in 4 (8.8%) patients, partial response, with down staging of tumor seen in 33 (73%) patients, and no response in 8 (16%) patients.

Conclusion: Majority of the young women had locally advanced triple-negative cancer. The pathological complete response rate was 8.8% and the partial response, with down staging of tumor was 73%, similar to Western studies. The results observed prove that treatment under a government funded cancer treatment scheme are not inferior to the West.

A006. Limited Methotrexate Levels with Fixed Leucovorin Rescue during High-Dose Methotrexate in Children with Cancer: A Perspective from Tertiary Cancer Care Hospital in South India

Vasudeva Bhat K.[1], Nishitha Thalamati[1], Krishna Satish Kumar[1], Shreya Saha[1], Archana M. V.[1], Harish Varma T.[1], Emine A. Rahiman[1], Swathi P. M.[1], Aditya Prabhu M.[1], Roshan Rajan George[1], Chaithra Venkatesh[1], Vijetha Shenoy Belle[1]

[1]*Division of Pediatric Hematology and Oncology, Kasturba Medical College, Manipal, Karnataka, India*

Keywords:

- ALL
- HDMTX
- mucositis
- MTX levels

Aim and Objectives: Methotrexate (Mtx) is a key drug for the treatment of high-risk acute lymphoblastic leukemia (ALL) and has no late effects secondary to its use. However, acute toxicities post Mtx infusion remains a concern especially when levels are not monitored or not available. Glucarpidase availability is a challenge, hence we present the data of using limited mtx levels for children with high risk ALL while receiving high-dose methotrexate (HDMTX) during interim maintenance.

Materials and Methods: Retrospective data were collected for children with high risk ALL <18 years who received HDMTX from November 2019 till December 2023. Baseline organ function tests, complete blood count, mtx levels, and presence/absence of mucositis were collected in predesigned proforma. Mtx levels were available at 24 and 42 hours for all patients while any patient with MTX levels at 42 hours ≥1.0 micromol/L had repeated levels every 12 hourly till levels dropped to ≤0.2 micromol/L. Leucovorin 3 doses were administered at 42, 48, and 54 hours for all patients and additional doses only to those who had higher 42-hour level or previous mucositis.

Results: A total of 90 patients with median age of 9.5 years (range: 1–18 years) with male:female ratio of 1.72:1 received a total 350 courses of HDMTX. The mean 24-hour and 42-hour mtx levels for the first course were 145 and 0.67 micromol/L respectively; however, 39 (43%) and 11(12.2%) had levels above the desired threshold of 150 and 1 micromol/L at the end of 24 and 42 hours, respectively. There was no correlation of higher baseline creatinine levels or acute kidney injury with higher mtx levels ($r = 0.1$). There was no significant difference in mtx levels in subsequent courses ($p = 0.5$). Grade 3 and above mucositis occurred in 14 (15.5%) patients; however, there was no correlation between Mtx levels and mucositis ($r = 0.3$). None of the patients developed methotrexate-induced renal dysfunction/seizures or expired due to mucositis.

Conclusion: Limited mtx level monitoring especially during the first course of HDMTX at time points 24 hours and 42 hours is critical and can predict the tolerance of further courses of HDMTX if further levels cannot be monitored. Limited dose leucovorin rescue has lower rates of Grade 3 and above mucositis compared to historical cohorts.

A007. Clinical and Molecular Profiling of Myeloproliferative Neoplasms in a Tertiary Care Center in South India

Rekabtala Bhaskar[1]

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In 2022 the World Health Organization (WHO) revised the classification of myeloid neoplasms. PV, ET, and PMF are characterized by overlapping features and have been grouped into the category of Philadelphia-negative classical MPNs. They are associated with a higher risk of transforming into acute myeloid leukemia. Therefore, the diagnosis and evaluation play a significant role in the prognosis and outcome of patients.

To estimate the incidence of BCR-ABL negative myeloproliferative neoplasms with diagnosis based on the molecular work up and record the clinico-pathological outcomes of these patients from a single-institute data.

The study population consisted of 74 patients who were diagnosed with BCR::ABL1 negative myeloproliferative neoplasm, of which 46 patients who were not willing for further evaluation or who did not follow-up after a single visit and who were previously treated were excluded.

Consequently, 28 patients were included, and all were ≥18 years old, with clinical picture and/or lab parameters with molecular work-up suggestive of a diagnosis of MPN and previously untreated. Patients who were evaluated with molecular work-up suggestive of chronic myeloid leukemia were excluded.

Statistical Analysis: To answer the objectives of this observational study, data were collected with no formal sample size calculation. The inclusion period was from January 2015 to September 2023, with a duration of 8 years and 9 months.

Descriptive statistics were used to represent summary and dispersion measures of demographic, clinical, and disease characteristics of the cohort of patients.

Results: Over a period of 8 years and 9 months, a total of 28 cases were observed.

The median age at diagnosis for MPN is 50 years. In this study 23 patients (82%) were above the age of 50. Median age is 55 years (23–75 years). No significant gender preponderance was observed. 15 patients were males (54%) and 13 (46%) were females (1.1:1).

The most recognized symptoms of MPN disorders include fatigue, early satiety, abdominal discomfort.

The presenting complaints represented in these data include weakness in 6 patients (21.4%), fever in 5 (17.9%),

abdominal pain in 10 (35.7%), reduced appetite in 9 (32.2%), dyspnea in 1 (3. 6%), orthopnea in 1 (3.6%), melaena in 1 (3. 6%), hematemesis in 1 (3. 6%), and weight loss in 3 patients (10.7%).

Clinical examination findings revealed splenomegaly at presentation in 15 patients (53.6%), and 4 patients (14.3%) had hepatomegaly.

The most common comorbidities seen in MPN are hypertension, diabetes, and dyslipidemia. In our study the most common comorbidity was hypertension seen in 9 patients (32.1%), 3 (10.7) were diabetic, and 1 patient (3.6) had COPD. 54% of the patients had no known comorbidities.

The most frequently identified MPN in our study group was essential thrombocytosis, 46.3% (13), closely followed by polycythemia vera, 39.3% (11), and less common subset of patients were diagnosed with primary myelofibrosis, i.e., 14.3% (4).

Molecular analyses were conducted in 96.4% of our cases. All were positive for JAK2 mutations, which is inclusive of JAK2 V617F mutation and JAK2 exon 12–15 mutation.

None of the patients tested positive for MPL mutation and for CALR.

The incidence of arterial and veinous thrombosis in PMF is about the same as in ET and is significantly lower than in polycythemia vera. In this study, 11 patients (39%) had a history of vascular events including infarction causing CVA and arterial or venous thrombosis.

The most common causes of death in myelofibrosis include the progression of leukemia in about 20% of patients. None of the patients in this study transformed to acute leukemia.

MPNs are a group of disorders characterized by diversity of presentation and can be prognosticated based on mutational work up. The incorporation of molecular alteration in one of the driver genes as a major WHO criterion underscores the importance of evaluation of these markers and this study represents the real-world molecular analysis and incidence from a single-center data.

A008. Comprehensive Clinicopathological and Treatment Analysis of Lung Cancer Patients: Insights from the AIIMS Rishikesh Prospective Cancer Registry

Amit Sehrawat[1], Anusha M.[1], Monika Chaudhary[1], Sathya Natarajan[2], Ravi Kumar[1], Udit Chauhan[1], Mayank Mishra[1], Deepak Sundriyal[1]

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Keywords:

- lung cancer
- AIIMS Rishikesh
- prospective study
- treatment outcomes

Aim and Objectives: Lung cancer is a significant global health challenge, with 2.5 million new cases in 2022. In India, lung cancer ranks among the top five cancers, comprising 81,748 cases (5.8% of all cancers), with 75,031 deaths recorded in 2022. This study aims to provide insights into lung cancer patients' demographic profile, clinical characteristics, management strategies, and outcomes at AIIMS Rishikesh, India.

Materials and Methods: Data were prospectively collected from the Cancer Registry at AIIMS Rishikesh from July 2022 to January 2024. Demographic, clinical, and treatment-related information was recorded and analyzed using descriptive statistics. Statistical analysis was conducted using SPSS ver. 24.

Results: A total of 186 lung cancer cases were included, with a mean age of 59 years. The male-to-female ratio was approximately 3.22:1, with most cases from Uttarakhand and Uttar Pradesh. Smoking history was prevalent in 80.65% of patients. The most prevalent symptoms were cough (70.3%), chest pain (56.0%), dyspnea (46.7%), hemoptysis (20.3%), and anorexia (13.1%). Non-small cell lung cancer (NSCLC) constituted 79.03% of cases, with squamous cell carcinoma (51.7%) and adenocarcinoma (47.6%) being the most common subtypes. Neuroendocrine tumors/small cell carcinoma accounted for 15.05% of cases. Immunohistochemistry (IHC) was performed in 53.8% of cases. Financial constraints limited mutation analysis to 52.6% of cases, revealing EGFR mutations in 33.6%, predominantly exon 19 deletions (54.5%). ALK mutations were detected in 4.08%, and ROS1 mutations in 2.04%. Most patients presented at advanced stages, with therapy primarily directed towards palliation. Chemotherapy was the most common treatment, with paclitaxel + carboplatin being the predominant regimen. Delays in therapy and dose modifications were observed due to toxicity, with a high proportion of deceased cases during follow-up.

Conclusion: This prospective analysis provides comprehensive insights into the management and outcomes of lung cancer patients at AIIMS Rishikesh. The findings underscore the challenges and complexities in managing lung cancer, emphasizing the need for tailored approaches to improve patient outcomes.

A009. Prospective Study to Evaluate Clinical Features and Treatment Outcome of First-Line Therapy in Unresectable Locally Advanced and Metastatic Pancreatic Carcinoma

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Objectives: We aimed to evaluate the clinical features and treatment outcomes of first-line therapy in unresectable locally advanced and metastatic pancreatic cancer.

Materials and Methods: We enrolled and followed up 60 patients meeting inclusion criteria, in a prospective observational study from May 2021 to March 2023 in a tertiary cancer center.

Results: The median age at presentation was 58 years with male to female ratio of 1.3:1. The most common symptom at presentation was abdominal pain, followed by generalized weakness, weight loss, jaundice, and anorexia. CA19-9 level was increased in 79.3% patients. Most (53.33%) common location of tumor was head of pancreas with liver being most common site of metastasis. Modified FOLFIRINOX and gemcitabine + nabpaclitaxel were the two most common regimens received by almost half of study participants in each group. After the first line chemotherapy, 1.7% had complete response, 28.3% had partial response, 43.3% had stable disease, and 26.7% had progressive disease. The overall response rate was 30% and disease control rate was 73.3%. Grade III/IV toxicities were 10% anemia, 15% neutropenia, 3.33% thrombocytopenia, 1.67% nausea/vomiting, 16.67% diarrhea, and 1.67% neuropathy. Modified FOLFIRINOX and gemcitabine + nabpaclitaxel had similar outcomes in terms of toxicity, response, and survival. With the median follow-up of 12.59 months, median PFS was 7.8 months and OS was 12.16 months.

Conclusion: Pancreatic cancer is one of the aggressive malignancies with limited treatment options. Modified FOLFIRINOX and gemcitabine + nabpaclitaxel had similar outcomes in terms of toxicity, response, and survival in

advanced stages. Pancreatic malignancies must be managed in a multidisciplinary clinic.

A010. An Indian Perspective on PD-L1 Expression in Metastatic Non-Small Cell Lung Carcinoma and Its Correlation with Clinicopathologic Parameters

Barnini Ghosh[1], Indranil Ghosh[1], Amit Dutt Dwary[1], Prabrajya Narayan Mohapatra[1]
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Objectives: The most widely accepted predictive biomarker for immune-oncology in metastatic non-small cell lung carcinoma (NSCLC) is the programmed death ligand 1 (PD-L1) assay by immunohistochemistry (IHC). Its importance lies in optimizing treatment with immune checkpoint inhibitors, reducing unnecessary toxicities and expenses from the use of such drugs. The aim of this study was to evaluate the prevalence and quantification of PD-L1 expression among metastatic NSCLC patients. It also aimed to identify any possible subgroup of patients who are more likely to express PD-L1, based on their clinico-pathological and driver mutation profile. In a resource-constrained setting, this might help to identify a subgroup with higher likelihood of PD-L1 expression.

Materials and Methods: Data of 125 histopathologically proven metastatic NSCLC patients, who had undergone PD-L1 testing, were analyzed retrospectively. PD-L1 assay by IHC was done using rabbit monoclonal antibody (Clone SP 263) on Ventana Benchmark XT autostainer and tumor proportion score (TPS) was calculated. Clinico-pathologic parameters taken into consideration were age, gender, histologic type, histologic grade, family history of cancer, addiction status (with respect to smoking, alcohol, smokeless tobacco), previous treatment received (radiotherapy, chemotherapy), and driver mutations (EGFR mutation, ALK rearrangement, ROS1 rearrangement, BRAF mutation, MET exon 14 skipping mutation, and Her2 mutation).

Results: Of the total 125 patients, adenocarcinoma was observed to be the most common histology (71%), followed by squamous cell carcinoma (21%). 52% tested positive for PD-L1 expression, with 22.4% having high expression (TPS $\geq$ 50). No correlation of PD-L1 expression was observed with gender, histological subtype or grade, family history, addiction status, or previous treatment received. No statistically significant correlation was observed between driver mutations and PD-L1 expression.

Conclusions: PD-L1 expression was found in 52% of metastatic NSCLC but was not significantly correlated with any of the clinicopathologic parameters or driver mutations tested.

A011. Breast Cancer in Patients Aged 80 and Above: A Retrospective Study from Western India

Kunal Jobanputra[1], Pritam Kalaskar[1], Udip Maheshwari[1], Ashish Joshi[1], Vashishth Maniar[1], Kshitij Joshi[1], Disha Morzaria[1], Akash Pawar[1], Akshay Shivchhand[1], Krushna Chaudhari[1], C. Bose[1], Ravi Wategaonkar[1], Pradip Kendre[1], Chandrashekhar. Pethe[1], Makarand Randive[1], Pravin Khandare[1], Mangesh Mekha[1], Devendra Pal[1], Nitin Bayas[1], Sonal Dhande[1]
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Objectives: We aimed to study the clinical characteristics, treatment patterns, and survival outcomes of elderly patients (aged $\geq$80 years) diagnosed with breast cancer.

Materials and Methods: We conducted a retrospective study of consecutive patients aged $\geq$80 years who were newly diagnosed with breast cancer between January 2018 and December 2023. The study included patients from community oncology centers located in western India.

Results: A total of 1,696 patients were diagnosed with breast cancer during the above period, of which 106 patients (6.3%) aged $\geq$80 years were included in the study (102 females, 4 males). The median age was 82 years (IQR: 81–85) with a median follow-up of 17.7 months (95% CI: 13.7–21.6). Eastern Cooperative Oncology Group Performance Status (ECOG-PS) at presentation was 0–1 in 92 patients (86.8%) and $\geq$2 in 14 patients (13.2%). Two-thirds of patients had comorbidities ($n = 69$, 65.0%), with most common being hypertension ($n = 58$, 54.7%), diabetes mellitus ($n = 37$, 34.9%), and ischemic heart disease ($n = 14$, 13.2%).

The most common histology was invasive ductal carcinoma ($n = 82$, 77.3%). Hormone receptor (HR) and HER2 status were available for 96 of the 106 patients, where 68 (70.8%) were HR+, 17 (17.7%) were HER2+, and 20 (20.8%) had triple-negative breast cancer (TNBC). Two-thirds of patients ($n = 70$, 66.0%) had nonmetastatic disease, while 36 (34.0%) had metastatic disease.

Only 33 out of the 70 patients (47.1%) with nonmetastatic disease underwent surgery. Among these patients, 9 received chemotherapy (12.6%) and 3 received adjuvant radiotherapy. Hormonal therapy was received by 42 of the 49 patients (85.8%) with HR+ nonmetastatic disease. The median overall survival (OS) for patients with nonmetastatic disease was 52.1 months (95% CI: 45.8–58.5).

The most common sites of metastases were the lung (58.3%), bone (44.4%), and liver (16.7%). Only 22 out of 36 patients (61.1%) received systemic therapy for metastatic disease. The median OS for patients with metastatic disease was 28.6 months (95% CI: 14.4–42.8).

Conclusion: There is a need to increase the utilization of treatment options to improve outcomes for breast cancer in octogenarians. The proportion of TNBC among elderly patients in India appears to be higher compared to global data.

A012. Exceptional Response to Relapsed Urothelial Cancer with Enfortumab Vedotin and Low-Dose Nivolumab

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Keywords:

- urothelial carcinoma
- Enfortumab vedotin
- Nivolumab
- relapsed cancer
- immunotherapy

Background: Urothelial carcinoma is a challenging malignancy with high rates of recurrence and progression. Standard treatments often provide limited efficacy in relapsed cases. This case report highlights an exceptional therapeutic response to a combination of enfortumab vedotin and low-dose nivolumab in a patient with relapsed urothelial carcinoma.

Case Summary: A 54-year-old male initially presented with hematuria and burning micturition in 2020. Following a transurethral resection of bladder tumor (TURBT) on November 18, 2020, histopathology revealed high-grade solid urothelial carcinoma with focal lamina propria invasion, presence in prostatic ducts, and lymphovascular invasion. Subsequent imaging and procedures identified recurrent disease and the involvement of vesicoureteric junctions,

leading to several treatments including intravesical mitomycin-C, systemic docetaxel, dendritic cell therapy, gemcitabine, and carboplatin.

After experiencing progression of symptoms and evidence of residual disease on imaging, the patient commenced treatment with enfortumab vedotin 120 mg monthly starting February 15, 2023, in combination with low-dose nivolumab 40 mg IV every 3 weeks. Despite initial combination with gemcitabine, this was discontinued, and enfortumab vedotin and nivolumab were continued.

To date, the patient has received 13 cycles of enfortumab vedotin and 15 cycles of nivolumab, with the most recent cycle on July 17, 2024. Follow-up imaging and clinical assessments have shown significant reduction in disease activity, normalization of bladder structure, and resolution of symptoms. The patient currently exhibits normal renal function with a creatinine level of 0.68 mg/dL.

Review of Literature: Recent studies have demonstrated the efficacy of enfortumab vedotin, an antibody–drug conjugate targeting Nectin-4, in urothelial carcinoma, particularly in relapsed settings. Nivolumab, a PD-1 inhibitor, has shown promise in enhancing antitumor immunity. The combination of these agents aims to exploit complementary mechanisms of action to achieve superior therapeutic outcomes. However, data on the combined use in high-risk relapsed urothelial cancer remains sparse, highlighting the significance of this case report.

Conclusion: This case demonstrates an exceptional response to the combination of enfortumab vedotin and low-dose nivolumab in a patient with relapsed high-grade urothelial carcinoma. The patient's significant clinical improvement and normalization of renal function underscore the potential of this combination therapy as an effective treatment option in similar clinical scenarios. Further studies are warranted to validate these findings and explore the broader applicability of this regimen.

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A013. A Rare Neoplasm of Stomach

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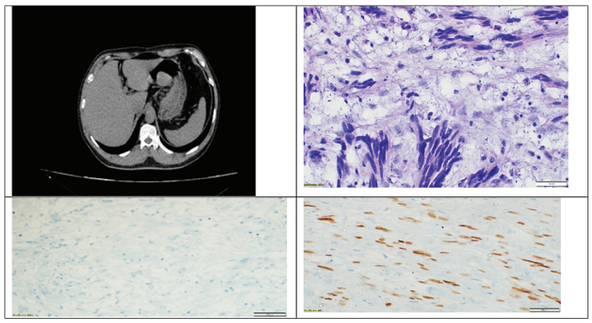
Introduction: Gastric schwannomas are an extremely rare type of GI mesenchymal tumor that should be considered in the differential diagnosis when encountering gastric masses.

Case Report Here we had a 60-year-old female with diabetes, hypertension, and cerebrovascular disease presenting with upper abdominal pain. OGD scopy showed large submucosal lesion with central ulceration in distal stomach. Imaging showed an exophytic lesion in mid body of stomach most probably GIST. She underwent distal gastrectomy from elsewhere and was started in imatinib as per histopathology report of gastric GIST.



After 2 weeks of imatinib therapy, she developed generalized edema and hence drug was stopped. She came to our center for further management. Slide review at our center was suggestive of schwannoma, IHC positive for S100 and Sox 10. Postoperative imaging did not reveal any residual disease. Hence, she is put on follow-up and is currently doing well.

Conclusion: Gastric schwannomas often mimic the physical features of GIST but can be easily distinguished with S-100 immunohistochemical staining. It is crucial to correctly identify these lesions as they carry an excellent prognosis and surgical resection is generally curative.

A014. Evaluation of Low-Dose Nivolumab with Neoadjuvant Chemotherapy in Non-Small Cell Lung Cancer: A Phase II Open Label Randomized Clinical Trial (ELON)

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Keywords:

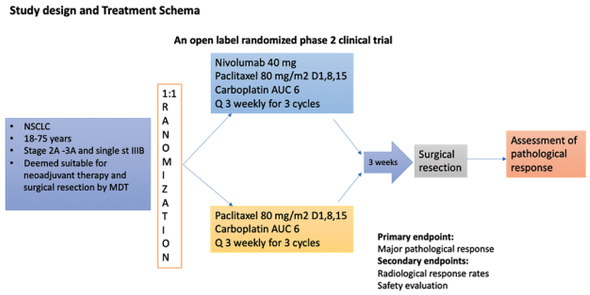
- low-dose Nivolumab
- neoadjuvant chemoimmunotherapy
- major pathological response

Introduction: Immune checkpoint inhibitors (ICIs) have become integral part of lung cancer treatment. However, high cost limits accessibility in low and middle income countries. Flat dose- response relation, high receptor occupancy (PD1) at 1/10th of recommended dose as shown in phase 1 trials and preliminary clinical experience showing responses at low doses, set a background to further explore the low dose strategies for ICIs. In this study we intend to evaluate efficacy of low dose nivolumab in combination with chemotherapy as neoadjuvant treatment in potentially resectable non-small cell lung cancer in terms of major pathological response.

Materials and Methods: This is being continued as a single center, phase II randomized clinical trial. Potentially resectable non-small cell lung cancer of stage IIA to stage IIIA and Stage IIIB with single station N2 lymph node as per AJCC 8th edition) patients, with ECOG PS 0–1, age 18–75 years, preserved vital organ functions, are being enrolled. Eligible patients are being randomized in 1:1 ratio to receive either neoadjuvant chemo-immunotherapy using low dose

nivolumab (at 40 mg flat dose every 3 weekly) or chemotherapy alone for 3 cycles. After a gap of at least 3 weeks, patients in both treatment arms are evaluated radiologically and undergo surgery. Primary end point is major pathological response rate (MPR) and secondary endpoints are radiological response rates and safety. Post-surgery adjuvant treatment will be as per clinician discretion based on histopathology report. Assuming MPR rates of 45% with chemo-immunotherapy and 10% with chemotherapy alone, with power of 80% and alpha error of 5%, we will **randomize 25 patients in each group (total 50)**. Additional patients will be recruited to compensate for consent withdrawal, protocol violations and loss of follow-up. This trial is approved by the Institute Ethics committee and registered with clinical trial registry of India (CTRI no. …..)

Conclusion: If we could demonstrate that low dose nivolumab has clinically meaningful activity, it would pave the way to redefine the optimum dose of ICIs. This would have a substantial financial implication and make these treatments affordable to a large majority of patients in LMICs.



A015. Clinical and Molecular Prognostic Markers of Survival in Metastatic Gastric Cancer: An Institutional Observation Study

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Keywords:
- gastric cancer
- prognosis
- metastasis
- Her2 neu and trastuzumab

Background: Gastric cancer is the 5th most common cancer and the fourth leading cause of cancer death worldwide. Despite the progress in the field of cancer treatments, clinical outcomes of patient affected by gastric cancer are not encouraging. The 5 years survival rate is <30% in locally advanced and 6% in metastatic disease. Patients of same TNM stage often shows very differential clinical outcomes, which implies there must be other factors responsible for those differences. A deep understanding of clinical and molecular factors may help to identify prognostic and therapeutic biomarkers, which in turn helps in the management of patients.

Aim: This study was aimed at prediction of prognostic value of various clinical and molecular factors with the help of survival outcomes.

Materials and Methods: This is a retrospective and descriptive single-center study. Baseline demographics, PS, co-morbidities, location of tumor, histological subtype, tumor markers, site and number of metastasis, molecular profile (Her2, MSI, and PDL1) and treatment data of metastatic gastric cancer patients registered between January 2020 and May 2023 were analyzed. Kaplan–Meier curves were used to identify overall survival. Multivariate cox regression analysis was used to predict clinical and molecular factors that affect the survival outcome.

Results: This study analyzed data of 105 patients of which 79 (75.24%) were men, and 26 (24.76%) were women. Median OS is 7.9 months (95% CI: 5.1–9.5) and PFS is 5.1 months (95% CI: 3.9–6.0). The factors that determined survival were age, performance status, hemoglobin, albumin, Ca19.9 levels, histological type, number of metastatic sites, Her 2 neu and MSI status. The histological subtype, PS, Her2 neu status, and no. of metastatic sites were determined as independent prognostic factors after performing multivariate analysis.

Conclusion: Several studies have defined numerous prognostic factors for gastric cancer. In concordance with the literature, this study also showed the important prognostic markers. HER2 remains an important biomarker in the management of gastric cancer and the addition of trastuzumab prolonged the overall survival.

Practice changing points:

•Identifying and validating prognostic markers are important for patient counselling, risk stratification, and treatment optimization.

•Testing for molecular markers like HER2, PDL1, and MSI allows identifying a patient who will benefit from targeted therapy.

A016. Experience with Triplet Therapy in De Novo Metastatic Hormone-Sensitive Prostate Cancer: A Single-Center Study from India

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Objective: Study treatment outcomes with triplet therapy in de-novo mHSPC from a high-volume institution in India.

Materials and Methods: Single-institute retrospective chart review study at Tata Medical Center, Kolkata, India between 2021 and 2024. Data collected from hospital electronic medical records till June 2024. Patients fulfilling eligibility-criteria with triplet therapy (ADT plus Docetaxel plus ARSi) included STATA statistical software used for analysis.

Results: 93 patients with high volume mHSPC disease were analyzed. Median age: 67 years (range 48–78 years). 73 patients (78%) had bone with/without nodal metastasis. 20 (22%) had visceral with/without bone metastasis. 77 patients (83%) presented with ECOG 0–1. 52 (56%) had Gleason score of 8 or above. Baseline prostate specific antigen (PSA) ranged from 1.44 to 10,000 ng/mL with mean PSA 719.43 ng/mL. 27% patients underwent bilateral orchiectomy, 73% received medical castration. 79 (85%) patients received 6–8 cycles of docetaxel in the triplet therapy. ADT plus ARSi was then continued till progression or unacceptable toxicities. At median follow-up of 18 months two years' predicted PSA progression free survival (PFS) was 80% and radiological PFS was 84%. No difference in PFS between bone versus visceral metastasis (log rank $p = 0.16$). Two years' overall survival rate was 80%. 14 (15%) had grade 2 and above adverse effects mainly anemia, neutropenia and hypertension.

Conclusions: This study from Indian cohort shows comparable survival outcomes with acceptable toxicities; reported in the index trials with triple therapy. It should be

offered as first line therapy among eligible patients with mHSPC. Further prospective larger scale studies are required from Indian subcontinent.

A017. Low-Dose Nivolumab 6 Weekly Plus Triple Metronomic Chemotherapy in Advanced Head and Neck Cancer: A prospective, Open-Label Single-Center Study from Eastern India

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Keywords:
- low
- Nivolumab
- OMCT
- DCR
- PFS
- six weekly

Aims and Objectives: Primary endpoint was 1-year PFS. Secondary end points were OS, response rate, and duration of response.

Materials and Methods: This was a phase 3 open level single arm study. Recurrent metastatic or unresectable head and neck non-nasopharyngeal squamous cell carcinoma patients received oral methotrexate 9 mg/m^2 once a week, celecoxib 200 mg twice daily, and erlotinib 150 mg once daily (TMC) with intravenous nivolumab (N) 40 mg flat dose once every 6 weeks. Primary endpoint was 1-year PFS, secondary end points were OS, response rate, and duration of response.

Results: Thirty-two patients received N + TMC regimen. 14 (43.7%) were previously exposed to cisplatin. Median PFS was 7 months (95% CI: 6.82–7. 17). ORR (CR + PR`) at 6 months was 56%, with 25% achieving CR. No significant differences in PFS or OS between platinum naive and refractory disease. OS at 1 year was 37.5% % with median OS of 10.2 months. 9 (28.1%) had grade 3 or above mucositis, 5 (15.6%) had grade 3 skin rashes, none had any immunologic adverse events. There was no treatment-related mortality.

Conclusion: Low-dose Nivolumab 6 weekly 40 mg along with TMC results in comparable OS and PFS with 3 weekly Nivolumab + TMC or Pembrolizumab and chemotherapy, in recurrent metastatic or unresectable HN non-nasopharyngeal Sq cell ca. It is associated with favorable toxicity profile, and is more affordable.

A018. A Phase 3 Prospective Randomized Trial of Two-Weekly TPF(Taxane/Platinum/5FU) versus Three-Weekly TPF as Induction Chemotherapy in Locally Advanced Squamous Cell Carcinoma of Head and Neck—An Interim Analysis

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Objective: Three-weekly TPF has been an effective chemotherapy regimen for locally advanced head and neck squamous cell carcinoma (HNSCC). However, it is associated with a high incidence of neutropenia (77–80%) and febrile neutropenia (5–12%). To address this, we conducted a phase 3 prospective trial comparing the efficacy and safety of two-weekly TPF (2wTPF) with three-weekly TPF (3wTPF).

Materials and Methods: Patients with locally advanced HNSCC, with primary tumors in the oral cavity, oropharynx, or hypopharynx, classified as stage III, IVA, or IVB, were randomized in a 1:1 ratio into two arms. The two-weekly arm received Docetaxel 50 mg/m^2, Cisplatin 50 mg/m^2, 5-fluorouracil (5-FU) 2,500 mg/m^2 (24-hour infusion), and leucovorin 250 mg/m^2 for four cycles. The three-weekly arm received Docetaxel 75 mg/m^2, Cisplatin 75 mg/m^2, and 5-FU 750 mg/m^2 over 6 hours (day 1–day 4) for three cycles. The primary endpoints were overall response rate and toxicity profile. This was followed by definitive treatment with either chemo-radiotherapy or surgery.

Results: In this interim analysis, 102 patients were recruited from December 2023 to June 2024. Of these, 22 were still on chemotherapy, and 5 were lost to follow-up. Among the 75 patients analyzed (2wTPF: 38, 3wTPF: 37), the overall response rate (ORR) was 76% with 2wTPF (CR = 5%, PR = 71%, SD = 5%) compared to 48% with 3wTPF (CR = 0%, PR = 48%, SD = 18%) ($p = 0.013$). Seven patients (18%) progressed on 2wTPF, while 12 (32%) progressed on 3wTPF ($p = 0.02$). The three-weekly regimen had higher grade 3/4 neutropenia ($p = 0.03$), diarrhea ($p = 0.03$), and infections ($p = 0.04$), with more dose reductions (43 vs. 21%, $p = 0.05$) and delays in chemotherapy (32 vs. 13%, $p = 0.04$). More patients in the 2wTPF arm underwent surgery (23 vs. 13%, $p = 0.5$). Three patients died in each arm, with one death per arm due to treatment-related causes. PFS and OS data remain immature.

Conclusion: The two-weekly TPF regimen demonstrated significantly better response rates and lower toxicity compared to the three-weekly TPF regimen, making it a viable alternative in high-prevalence countries like India.

A019. αKlotho: A Potential Protector Against Aggressive Tumor Biology

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Keywords:
- αKlotho
- breast cancer
- biomarkers

Aim: To assess the role of serum alpha Klotho level in patients with carcinoma breast and to see whether serum alpha Klotho can be used as a biomarker for pathological complete response.

Objectives: (1) To estimate serum Klotho level in all patients with biopsy-proven carcinoma breast who are previously untreated. (2) To correlate serum alpha Klotho level with various parameters like TNM stage, grade, hormone, and Her2Neu status. (3) To assess the role of serum klotho level as a biomarker for pathological complete response in neoadjuvant chemotherapy setting. *Hypothesis:* As Klotho is identified as a novel tumor suppressor gene, patients with low serum alpha Klotho level will have a more aggressive disease and may have a poor pathological complete response.

Materials and Methods: This prospective cross-sectional study enrolled 84 previously untreated patients with biopsy-proven breast carcinoma and no significant history. Serum αKlotho levels were measured before initiating treatment and its association with various clinicopathological characteristics was studied.

Results: Among our patients, 65% were estrogen receptor (ER)+, 41.6% were HER2+, and 11.9% had triple-negative breast cancer. Tumor stages varied with 11.9% at T1,

29.8% at T2, 19% at T3, and 39.3% at T4. Nodal involvement was 16.7% at N0, 48.8% at N1, 14.3% at N2, and 20.2% at N3, and 20.2% were metastatic breast cancer (MBC). Most tumors were of grade 2 (56%), followed by grade 3 (33.3%) and grade 1. 61.9% of the patients received neoadjuvant chemotherapy (NACT). The mean serum αKlotho level was 1.81 ng/mL (range 0–5.15 ng/mL). Significant findings were higher αKlotho levels in ER+ tumors (2.04 vs. 1.37 ng/mL in ER-negative, $p = 0.011$), decreasing αKlotho levels with increasing tumor grade (3.54 ng/mL in grade 1, 1.71 ng/mL in grade 2, 1.42 ng/mL in grade 3, $p = 0.001$), decreasing levels with advancing T stage (2.6 ng/mL in T1 to 1.61 ng/mL in T4), decreasing levels with advancing N stage (2.92 ng/mL in N0, 1.31 ng/mL in N3, $p = 0.001$), and were lower in MBC (1.47 ng/mL) compared to nonmetastatic disease (1.9 ng/mL). αKlotho levels negatively correlated with Ki67 expression and positively correlated with TILs. Patients with PNI and LVI had a lower Klotho level. Among 53 patients who received NACT, there was no significant difference in αKlotho levels between those who achieved PCR (1.46 ng/mL) and those who did not (1.53 ng/mL).

Conclusion: αKlotho may have protective roles in breast carcinoma. Higher αKlotho levels were associated with lower histological grade ($p = 0.001$) and node-negative disease ($p = 0.001$). Patients who had higher αKlotho had a lower T stage, more TILs, lesser LVI and PNI. These associations make αKlotho a potential target for further therapeutic interventions.

A020. Significance of Vitamin D Levels in Post-Menopausal Hormone Receptor-Positive Breast Cancer Patients

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Keywords:

- breast cancer
- post-menopausal
- vitamin D
- hormone receptor positive

Aims and Objectives: To determine the correlation between Vitamin D (Vit D) levels in post-menopausal breast cancer (PMBC) patients and other clinicopathological (CP) factors.

Materials and Methods: This is a retrospective study of 259 newly diagnosed and treated PMBC patients at Regional Cancer Centre Trivandrum, from January 1, 2019 to December 31, 2022. Patients with renal dysfunction, bone disease, and Paget's disease were excluded. Routine investigations and Vit D and dual energy X-ray absorptiometry (DEXA) scan were assessed at baseline. The chemiluminescent assay (Elecsys Vit D assay) is used at our center and a value of more than 30 ng/mL is considered normal. DEXA scan with a T-score of 1 or higher indicated a healthy bone and less than −2.5 indicated osteoporosis, rest as osteopenia.

Results: A total of 259 PMBC patients were included in the study. Age, comorbidities, sidedness of cancer, stage, histology, grade, estrogen receptor/progesterone receptor/Her-2-neu status, and pathological complete response rates were correlated. The mean age group of the study population was 58.65 years (SD: 7.4). The mean Vit D level was 18.8 ng/mL (SD: 8.6). Normal Vit D levels were recorded in 11.2% of patients while 25.5 and 63.3% had borderline or deficient Vit D, respectively. Osteopenia and osteoporosis in DEXA scan were 43.6 and 37.8% of patients, respectively. Early stage BC was noted in 72.4, 57.6, and 61% of patients with normal, borderline, and deficient Vit D levels, respectively. The most common stage was stage IIA (29.7%). HER2 positivity was seen in 17% of patients. None of the CP factors had a significant correlation with Vit D levels.

Conclusion: More than three-fourths of PMBC patients had either deficient or borderline Vit D levels. There was no association with other CP factors. More prospective studies are required to find the association between Vit D deficiency and the development of BC in post-menopausal patients.

A021. Genomic Profiling of Driver Gene Alterations in Patients with Non-Small Cell Lung Cancer, Patterns of Treatment, and Impact on Survival Outcomes: A Single-Center Experience of More Than 1,200 Patients

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Keywords:

- next generation sequencing
- NSCLC
- targeted therapy
- immunotherapy

Aims and Objectives:

The utility of Next-Generation-Sequencing (NGS) in patients of non-small cell lung cancer (NSCLC) has led to an exponential increase in the identification of targetable gene alterations. 60-65% of NSCLC patients from western datasets and 80% of patients from Asian datasets report identification of driver-gene alterations, however, Indian NGS data were lacking. We present the largest Indian NGS data reporting the frequency of driver-gene alterations, treatment pattern, and survival outcomes in patients of NSCLC.

Materials and Methods: This retrospective single-center study conducted between May 2019 and December 2023 included histologically confirmed NSCLC cases with NGS testing done on tissue or liquid biopsy samples at the time of diagnosis. All cases were discussed in the thoracic medical-oncology disease-management group, and the study was approved by the Institutional Ethics Committee.

Results: Data of 1,230 patients was analyzed. Median age was 59 years (IQR, 51–66), 65.3% ($n = 803$) were males, 34.6% ($n = 426$) had a history of smoking, and 78.1% ($n = 961$) had an adenocarcinoma histology. NCCN approved driver-gene alterations were picked up in 64.8% ($n = 797$) cases. EGFR, ALK, ROS1, ERBB2, MET, RET, NTRK, BRAF, and KRAS gene alterations were seen in 33.7% ($n = 414$), 7.6% ($n = 94$), 2.4% ($n = 29$), 6.1% ($n = 75$), 1.9% ($n = 23$), 2.2% ($n = 22$), 0.7% ($n = 8$), 3.3% ($n = 40$), and 9.6% ($n = 118$) cases, respectively. 62.1% ($n = 495/797$) driver-positive patients could receive targeted therapy, and 21.7% ($n = 94/433$) driver-negative patients could receive immunotherapy. With the receipt of targeted therapy, median OS of driver-positive patients was 31.9 months (95% CI: 26.7–37.2) versus 8.3 months (95% CI: 6.5–10.2, $p < 0.001$) without. Similarly, in driver-negative patients, median OS with the receipt of immunotherapy was 16.4 months (95% CI: 12.5–20.4) versus 11.4 months (95% CI: 9.2–13.6, $p = 0.003$) without.

Conclusion: NGS testing is imperative in patients of NSCLC due to high rates of detection of targetable gene alterations. Indian NSCLC NGS data are unique compared to Western and Asian counterparts. Adequate efforts must be undertaken to increase the utility of targeted and immunotherapy agents.

A022. Treatment Outcomes of All-trans-Retinoic Acid (ATRA), Arsenic trioxide (ASO), and Daunorubicin (DNR) in High-Risk Pediatric Acute Promyelocytic leukemia (APL) a Single-Center Study at Quaternary Care Center in South India

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Keywords:

- all-*trans*-retinoic acid
- arsenic trioxide
- daunorubicin
- pediatric acute promyelocytic leukemia

Aims and Objectives: Treatment outcomes of all-*trans*-retinoic acid (ATRA), arsenic trioxide (ASO), and daunorubicin (DNR) in high-risk pediatric acute promyelocytic leukemia (APL) a single-center study at quaternary care center in South India.

Materials and Methods: In this retrospective study, we included 19 of 30 children up to 18 years with newly diagnosed high risk (11 low risk) acute promyelocytic leukemia from a quaternary care center in South India (Vijayawada) between January 2015 to December 2023 treated with ATRA, ATO and DNR in induction followed by ATRA and ATO consolidation.

Results: Among 19 high risk APML children included in this study, there were 10 boys and 9 girls. 11 achieved complete remission with a median duration of 24 days, 7 patients died (6 IC bleed, 1 renal failure) before starting ATRA, ATO, and DNR, 1 patient died (ileal bleed) during induction. No differentiation syndrome occurred in high-risk patients. One patient had QT prolongation requiring treatment modification. On long-term follow-up of patients who achieved complete remission, none developed relapse, on follow-up of 8-year, relapse rates were zero.

Conclusion: This study demonstrated that the combination of all-*trans*-retinoic acid, arsenic trioxide, and variable doses of daunorubicin for induction, followed by all-*trans*-retinoic acid and arsenic trioxide for consolidation in high-risk pediatric acute promyelocytic leukemia, yielded favorable outcomes. The translation of adult data to the pediatric population has been successful in pediatric acute promyelocytic leukemia (APL).

A023. A Study to Identify Patterns of Care among Gall Bladder Carcinoma Patients in Real-World Setting Presenting at a Tertiary Cancer Care Center in North India

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Keywords:

- carcinoma gall bladder
- immunotherapy

Aims and Objectives: The study was conducted to evaluate the patterns of care in treatment of carcinoma gall bladder in a tertiary care center.

Materials and Methods: A total of 50 biopsy proven patients of carcinoma gall bladder registered between July 2022 and July 2024 were treated with either single or multiple treatment modality including surgery, postoperative radiation therapy, and chemotherapy with or without immunotherapy.

Results: Among 50 patients about 1/5th (22%) were administered immunotherapy. A 36.4% (4/11) showed near CR. A group of 26% (13) patients who underwent radical surgery, 84.6% (11/13) achieved CR. A total of 40% (20/50) patient had progressive disease out of which 45% (9/20) switched to salvage therapy whereas 55% (11/20) expired. The NGS incorporated in majority of patients (60%, 30/50) out of which 30% revealed positive "driver mutations" including MSH, TP53, PDL1, Her2neu.

Conclusion: The patterns of care in tertiary care center revealed integration of immunotherapy in 22% patients. Gemcitabine–Cisplatin doublet chemotherapy was used in majority (70%) among total of 44 (88%) who received chemotherapy with or without IO. Radical surgery was possible in 26% and yielded maximum percentage of CR likely due to less advanced and resectable disease.

A024. Right-Sided versus Left-Sided Colon Cancer: Does the Location Matter?

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Keywords:

- right sided versus left colon cancer
- CEA
- MSI

Aim: To compare right-sided and left-sided colon cancers in terms of clinical presentation, prognosis, molecular biology, and response to treatment in patients treated at our center.

Objectives: (1) To evaluate the difference in pattern of spread, progression free survival, overall survival, response to therapy, and molecular biology between left-sided and right-sided colon cancer in metastatic setting.

(2) To assess the difference in disease free survival, overall survival, response to therapy and molecular biology between left-sided and right-sided colon cancer in curative (adjuvant) setting.

(3) To assess the prognostic significance of serum levels of carcino-embryonic antigen in patients at presentation.

Study Design: Single-center retrospective study.

The study sample will be drawn from a database of patients treated in the Department of Medical oncology, at our center between January 2019 to January 2024. We will be using the database to identify all the patients diagnosed with histologically proven carcinoma colon and who were treated at our center.

Results: There were a total of 150 colorectal patients diagnosed and treated at our center during the study time. Out of this, 83 patients were treated with a curative intent and 67 patients had metastatic disease at presentation with a median age at presentation of 59.41 years. In the curative setting we compared the disease- free survival (DFS) between the two sides. We observed that the median DFS was 24.47 months in the right sided tumors and 37.6 in the left sided ones with a *p*-value of 0.96. This disparity was more pronounced in the Stage III tumors. We also analyzed the prognostic significance of CEA value at presentation with a cut-off of 100 ng/mL and it was found that a higher CEA value was associated with a poor prognosis—median DFS of 9.3 months versus 30.83 months with a *p*-value of <0.005.

In the metastatic setting we observed a median PFS of 10 months across the groups (95% CI; 6.0–11.0 months) with left sided tumors having a median PFS of 11.0 months while the right-sided ones had a median PFS of 7 months (*p*-value

0.83). According to our analysis CEA value at presentation has a prognostic significance with a median PFS of 6 months versus 18 months (p-value <0.005).

Coming to the prevalence of micro satellite instability between the two sides it was observed that right sided tumors had more incidence of MSI compared to the left-sided ones with a p-value of <0.05.

Conclusion: To conclude across all stages of colon cancers right sided tumors are associated with a worse prognosis compared to left sided ones. These cancers differ significantly in the molecular biology also. It was observed that the CEA value at presentation carried significant prognostic importance across all sub-groups. The large CI observed in some results can be explained by the small sample size. The data were analyzed by Cox-regression model also which indicated a strong overall model significance.

This study has shown that right sided and left sided colon cancers behave as two different entities in terms of prognosis and molecular biology. However, further studies with a larger study population and longer follow-up are necessary to look into the clinical implications of these findings.

A025. Cytogenetic and Clinical Profile of CML Patients Presenting in Blast Crisis: Prospective Study from a Regional Cancer Center in South India

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Objectives: This study analyses array of additional cytogenetic abnormalities (ACA) in CML Blast Phase (CML BP) patients, with their clinical presentation, prevalence, complexity and lineage specificity.

Materials and Methods: 58 subjects in CML Blast phase were prospectively studies from January 2023 to July 2024. The demographic data, presentation, lineage assessment, ACA and survival were evaluated. Conventional cytogenetic study and karyotypic analysis was performed for all cases.

Results: Among the 58 subjects 67.24% were males, and the median age of presentation was 41 years. Fever (72.4%), fatigue (41.3%) and abdominal pain (25.86%) were the most common symptoms. 22.4% cases presented as de-novo blast phase and 77.5% progressed from chronic phase. Extramedullary involvement was seen in 6.89%. Immunophenotype indicated myeloid (65.51%), lymphoid (32.75%) and biphenotypic (1.72%) lineage specificity. Cytogenetics revealed ACAs in 74.13% cases, most common abnormalities were double Ph (44.18%), trisomy 8 (25.58%), trisomy 19 (13.95%) and inversion 3 (11.6%). Among all cases, 53.48% had complex ACAs ($\geq$2 ACA), while 46.51% has single ACA. Double Ph was the most common ACA among myeloid and lymphoid lineage. Median survival in this study was 14 months at 95% confidence interval (10.955–17.045). No significant prognostic difference was observed between complex versus single ACA ($p = 0.147$) and major versus minor route abnormality ($p = 0.815$).

Conclusions: Myeloid lineage is most common in CML-BP patients. Common ACAs observed are Double Ph, Trisomy 8, Trisomy 19 and inversion 3. Fever is the most common presenting complaint. Complex ACA has trend towards poorer outcome. Inversion 3, typical of AML and MDS, may suggest poor response to TKI. Due to relatively small sample size, further studies with larger cohorts are warranted.

A026. Real-World Data on Biomarker-Driven Treatment of Lung Cancer in Our Center with or without Chemotherapy

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Background: Lung cancer remains a major cause of cancer mortality worldwide. The integration of biomarker-driven targeted therapies has transformed treatment strategies, particularly when combined with chemotherapy. This report examines real-world data from lung cancer patients at our center who received biomarker-driven targeted therapies, with or without sequential chemotherapy.

Materials and Methods: This retrospective study includes lung cancer patients treated at our center from January 2015 to April 2024 who have undergone comprehensive genetic testing for actionable mutations and were treated with targeted therapies based on identified biomarkers. Data were collected on whether the patient received chemotherapy, treatment response and progression-free survival (PFS).

Results:

Patient Demographics:

• Total number of patients: 91

Biomarker Distribution:

• EGFR mutations: 67

• ALK rearrangements: 21

• ROS1 rearrangements: 3

Treatment Regimens:

• EGFR TKIs: Erlotinib, Gefitinib, Afatinib, Osimertinib

• ALK inhibitors: Crizotinib, Ceritinib, Alectinib, Lorlatinib

• ROS1 inhibitors: Crizotinib

• PD-L1 inhibitors: Pembrolizumab, Nivolumab

• Chemotherapy: Pemetrexed, Cisplatin, Carboplatin, Docetaxel

With/without Chemotherapy:

Without chemotherapy (TKI alone): 24

With chemotherapy: 67

Treatment Outcomes:

1. EGFR-Positive Patients ($n = 67$):

• Partial Response (PR): 28

• Complete Response (CR): 11

• Stable disease (SD): 20

• Progressive Disease (PD): 7

• mPFS: 30 months (targeted therapy alone)

2. ALK-Positive Patients ($n = 21$):

• Partial Response (PR): 3

• Complete Response (CR): 3

• Stable disease (SD): 15

• Progressive Disease (PD): 0

• Median PFS: 32 months

3. ROS1-Positive Patients ($n = 3$):

• Partial Response (PR): 1

• Complete Response (CR): 0

• Stable disease (SD): 1

• Progressive Disease (PD): 1

• mPFS: 9 months (targeted therapy alone)

Discussion: The real-world data from our center underscore the efficacy of biomarker-driven targeted therapies in lung cancer treatment. The data also highlight the potential for improved outcomes with concurrent therapy in selected patients.

Conclusion: Biomarker-driven targeted therapies offer significant clinical benefits in the management of lung cancer with or without chemotherapy. Our center's real-world data support the continued use of comprehensive biomarker testing and personalized treatment approaches. Further research is needed to optimize sequencing strategies and manage resistance mechanisms.

A027. Novel Economically Feasible Oral Capecitabine and Cyclophosphamide Combination for Recurrent or Metastatic Head and Neck Cancers

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Aim: To assess the feasibility, efficacy, and safety of a combination drug regimen in patients with advanced and metastatic HNSCC.

Primary objective

- To observe the progression-free survival.

Secondary objective

- To observe the overall survival, toxicity profile and quality of life.

Materials and Methods: This prospective observational study was carried out at our facility between June 2023 and June 2024 on patients with metastatic and recurrent locally advanced head and neck squamous cell malignancies. The drug combination tablets were administered orally within 30 minutes after a meal for 14 days in 3-weekly cycles for up to 6 cycles. Drug combination consisted capecitabine 2000 mg plus cyclophosphamide 100 mg.

Results: During the study period, a total of 101 patients were enrolled, with 2 patients lost to follow-up. The Eastern Cooperative Oncology Group (ECOG) performance status ranged from 0 to 1. The median age of the patients was 55 years (range: 27-80 years). The male-to-female ratio was 3.3:1. Most patients, 62.6%, were smokers, and 88.9% were tobacco consumers. Regarding tumor origin, the primary sites were as follows: oral cavity in 63 patients (63.6%), oropharynx in 13 patients (13.13%), larynx in 16 patients (16.16%), and hypopharynx in 7 patients (7.07%). Previous treatment was received by 69 patients (69.6%). Previous platinum was received by 57 patients that 57.5% of total patients and 82.6% of previously treated patients. The median progression free survival (PFS) was 179 days. The median overall survival (OS) was 302 days. No documented grade 3 or 4 adverse reaction. Majority of patients had self-limiting Grade 1 mucositis.

Conclusion: Our study is the first report on the feasibility-safety and efficacy of a drug combination of two chemotherapeutic agents, cyclophosphamide and capecitabine. The drug combination is affordable, widely accessible, and suitable for outpatient treatment of patients in remote rural areas

A028. Clinical Impact of Comprehensive Genomic Profiling in Advanced Cancer—A Real-World Single-Institution Retrospective Study

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Introduction: Next generation sequencing based comprehensive genomic profiling is becoming common practice to detect clinically relevant genomic alterations however its clinical impact as part of routine management remains uncertain.

Objectives: To determine the proportion of patients with advanced cancer, who received targeted therapy based on the NGS based comprehensive genomic analysis and degree of clinical benefit.

Materials and Methods: Single institution retrospective study of all adult patients with solid tumor who underwent CGP analysis during January 2020 to august 2023. Clinical benefit rate was defined as the proportion of patients receiving CGP directed therapy for 6 months or longer.

Results: 108 NGS was attempted during study protocol; 70 met the inclusion criteria. Male 48.5% with median age of 57, female 51.5% with median age of 56. The most common cancers were Lung cancer 28.5% followed by Pancreas 10%. CGP identified targeted therapy in 24% of patients and out of that 6% patients received targeted therapy.in the overall cohort of 70 patients, clinical benefit was seen in 3% patients. Most common reason for patients not receiving CGP directed therapy was because of availability of a standard of care treatment or rapid progressing disease and poor performance status.

Conclusion: We demonstrate that Clinical genomic profiling has been increasingly used into routine clinical practice in the management of advanced cancers; however, 6% of patients received targeted therapy based on CGP assay. clinical benefit was seen in 3% patients in the overall cohort.

A029. Lung Cancer in Adolescent and Young Adults: Unveiling Challenges and Outcomes—A Report from the Network of Oncology Clinical Trials India

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Background: Adolescent and Young Adult (AYA) cancers (age 18-39) present with unique subset of challenges with regards to their management and outcomes. Network of Oncology Clinical Trials (NOCI) is a collaborative group developed with an academic grant from the Biotechnology Industry Research Assistance Council (BIRAC).This study aimed to determine the clinicopathological features and outcomes of AYA lung cancer patients from the network.

Materials and Methods: Data were collected retrospectively from the records from January 1, 2015 to December 31, 2020, after ethics committee approval from each of the six centers in the NOCI network. The data were analyzed for demographic details, baseline characteristics, disease patterns, treatment modalities, and treatment outcomes. Descriptive statistics was used in the form of means/medians for continuous variables and frequencies/percentages for

categorical variables. Time to event analysis was done on Kaplan-Meier curves and OS and PFS calculated.

Univariate and multivariate analysis was done using log-rank test and cox regression respectively.

Results: Total of 51 patients [median age:37 years (23–39), females: 54.9%] were identified. Adenocarcinoma ($n = 34$) 66% was the most common histology and 68.6% ($n = 35$) were non-smokers. In the majority ($n = 47$), 92% of the patients presented with metastatic disease. Exposure to smoking was documented in ($n = 12$) 23.5% of subjects. Targeted therapy [EGFR ($n = 5$) 42%, ALK ($n = 5$) 42%, ROS ($n = 2$) 16% was administered in 23.4% of cases. Radiological response of complete response, partial response, and stable disease was observed in 41.3% of patients. The median progression-free survival (PFS) was 8.8 months (95% CI: 5–12.4), and the median overall survival (OS) was 23.8 months (95% CI: 15.6–31.8).The median PFS and OS were superior among those receiving targeted therapy as compared to those receiving chemotherapy (PFS 8 vs. 19 mo, $p = 0.72$; OS 8 vs. 26 mo, $p = 0.15$).

Conclusions: Unlike what is reported in older individuals, younger lung cancer patients are likely to be non-smokers, and a significant proportion present with targetable mutations. However, the majority have advanced disease and poor survival outcomes.

Clinical trial identification

CTRI/2022/01/039233

A030. Prevalence of Multi-drug Resistant Bacteria among Neutropenic Cancer Patients and Its Association with 30-day Mortality: A Single-Center Study from a Regional Cancer Center

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Background: Neutropenia is one of the most frequent complications of cytotoxic chemotherapy induced myelosuppression. It impacts cancer treatment in several ways, including increased mortality from infection and treatment cost, frequent hospitalizations, reduction in dose intensity, treatment discontinuation.

Materials and Methods: This is a single-center observational study of 220 neutropenic cancer patients from March to May 2024. Baseline blood reports noted, appropriate culture samples were sent based on patients' symptoms, before starting broad spectrum empirical antibiotics. Antibiotics were later modified according to culture and sensitivity reports, if an organism was isolated. Others were continued on empirical regimen and antibiotics escalated based on clinical condition and 30-day mortality was measured.

Results:

1. Culture positivity rate among neutropenic patients was 30.9%.

2. The 30-day mortality among neutropenic patients was18.18%.

3. The most common organism isolated was *Klebsiella pneumoniae* [MDRO] (26.47%), followed by *Escherichia coli* (CRE, 19.11%).

4. The 30-day mortality amongst culture positive neutropenic patients was 13.23%.

5. The most common cancer among neutropenic patients that expired was acute lymphoblastic leukemia (relapsed/ high-risk cases) post-HR block, followed by AML post 3 + 7 chemotherapy regimen.

6. Among the culture positives, prevalence of MDR (multi drug resistant) bacteria was 41.17%.

7. Percentage of patients who expired due to MDR infection versus sensitive isolate among culture positive was 77.77 and 22.22%.

8. Patients with MDR infection were more likely to die compared to those infected with a sensitive isolate. The result was statistically significant [$p < 0.05$].

9. Majority of the MDR isolates were resistant to meropenem, teicoplanin, vancomycin, colistin retaining sensitivity to tigecycline.

10. Five of the MDR isolates were resistant to all available antibiotics at our tertiary center.

Conclusions: Neutropenia remains a major cause of morbidity, mortality, cost burden in cancer patients. Patients with MDR infection had worse outcomes as compared to those with a sensitive isolate. Antibiotic prophylaxis has been a complimentary strategy toward reduction of infections but has also led to emergence of multidrug resistant organisms (MDRO). An appropriate culture and sensitivity report helps in antibiotic stewardship and better outcomes while also preventing development of resistant organisms.

A031. Prevalence of Depression Among Children Diagnosed with Cancer at a Regional Cancer Hospital in India

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Background: An estimated four lakh children (aged 0 to 19 years) are diagnosed with cancer every year. Children and adolescent with cancer are at risk of developing depression due to physical symptoms, disturbance in the development, frequent hospitalization, prolong treatment and related complications. The purpose of this study is to estimate the prevalence of depression among children and adolescents diagnosed with cancer.

Materials and Methods: This study was conducted at tertiary hospital between April 2024 to June 2024. 50 patients aged between 7 to 17 years were included in the study. The children's depression, inventory scale was used to assess the depression, which was developed by Kovacs and Beck.

Results: out of 50 participants, five (10%) were found to have depression with cut-off score of above 15 and 20 for boys and girls, respectively. All five subjects were boys. Among them three belong to mild depression two belong to severe depression. They belong to 9 to 12 age group. Cancer patients above twelve years old had higher odds of been depressed (OR 2.13) as compared to patients less than twelve years. Three of them had hematological malignancies, one with osteosarcoma with amputated leg and one with sinonasal carcinoma with progressive disease.

Conclusion: The prevalence of depression among study participants is 10%. There is need to integrate psychotherapy into routine care of pediatric population. This can help them to improve their quality of life, compliance to treatment and thereby increase the survival rate.

A032. Clinical Profile and Survival Outcomes in Wilms Tumor Patient Treated by SIOP Protocol at a Regional Cancer Center

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Background: Wilms tumor is the most common treatment responsive pediatric solid tumor. The outcome of wilms tumor has improved due to the evolution of treatment approach. The purpose of this study was to analyze the clinical outcome of children with wilms tumor treated by SIOP protocol in a regional cancer center.

Materials and Methods: In total 30 patients treated by SIOP protocol were analyzed from a duration of June 2018 to June 2024.

Results: Gender distribution showed male to female ratio of 6:1 with median age at diagnosis was 48 months with youngest being 7 months to oldest being 8 years. The abdominal lump was the dominant clinical presentation with a mean duration of 35 days (15 days to 2 months). Radiological staging work up shows that stage 1, 2, 3, 4, 5 were 23.34, 13.3, 40, 20, 3.3%, respectively. Neoadjuvant chemotherapy was received by all patients. In addition, 20% has metastasis at presentation with lung as most common site and 46.4% of patients have high-risk histology. Disease relapse was seen 20% of patients. Out of 24 alive patients 23 patients are without disease (15–69 months) and one patient is alive with disease and 6 patients died due to disease. The mean DFS and OS were 33.8 months (6–69 months) and 34.7 months (7–69 months), respectively.

Conclusion: Majority of patients presented to our center are in advanced stage. Though the clinicopathological profile was more in line with western data but survival of patients with wilms tumor is lower compared to high income countries due to delay in presentation and poor adherence to treatment.

A033. Bridging Gaps in Awareness of Cancer-Associated Lifestyle Factors in Adolescents and Young Adults (AYAs): An Interventional Study in Kanpur

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Keywords:

- lifestyle behavior
- cancer
- adolescents
- young adults
- awareness
- prevention

Objectives: Cancer is a major public health concern, and its incidence is growing worldwide. The adolescent and young adult (AYA) age group bridges pediatric and adult age groups. AYAs have unique lifestyle patterns that may contribute to cancer risk. This study sought to assess the awareness and educate AYAs of Regency Hospital, Kanpur, about cancer risk-associated lifestyle factors.

Materials and Methods: This cross-sectional interventional study was conducted from March to June 2023. A predesigned, pretested, validated questionnaire was used for data collection. Descriptive and analytical analysis was performed using SPSS. Analytical analysis was conducted using the Chi-square test to find the relationship between different lifestyle factors and demographic characteristics such as age and gender.

Results: The study included a total of 360 participants consisting of 170 (47.2%) males and 190 (52.8%) females aged between 15 and 39 years from Regency Hospital, Kanpur. Among them, 92.5% had awareness of smoking as a risk factor for cancer. However, there were lower levels of awareness regarding lifestyle behaviors associated with cancer risk, including inadequate consumption of fruits and vegetables, regular intake of sweets and sugary drinks, following a high-fat diet (28.3%); insufficient physical activity (38.3%), and obesity (36.1%).

Conclusion: The current study indicated a disparity in knowledge levels among adolescents and young adults (AYAs) at Regency Hospital, Kanpur. It is crucial to address these gaps in knowledge and promote healthy behaviors related to cancer prevention through targeted education campaigns among adolescents and young adults.

A034. Addressing the Challenges of Ewing Sarcoma in Resource-Limited Settings: Analysis of Patient Demographics, Treatment Approaches, and Outcomes in a Tertiary Care Center in LMIC

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Objectives: Ewing's sarcoma (ES) is a rare malignant neoplasm, accounting for 10 to 15% of bone sarcomas, with an annual incidence 2.93 per 1,000,000 children.

Advances in multimodal therapy have improved survival rates from 20% to over 70%. Subclinical metastatic disease is common, and approximately 25% of initially localized cases eventually relapse. Data regarding second-line management is limited, with dismal survival rates.

Materials and Methods: We conducted a retrospective review of medical records for 29 patients with ES who were diagnosed and treated at our institution between 2018 and 2023. We compiled data on demographics, symptoms, radiological and histopathological findings, treatment strategies, and outcomes in the first- and second-line setting.

Results: 17 (59%) were male, with median age 14 years (range 2–60). Symptoms included swelling (55%), pain (41.4%), and fever (3.4%). t (11;22) translocation was seen in 75%. Tumor location included femur (31%), pelvis (17.2%), tibia (10.3%), humerus (10.3%), fibula (6.9%), and others (10.2%). Extraosseous sites included kidneys (7%) and lungs (3.4%). 18 (62%) had metastatic disease, sites included bone (17.3%), lungs (13.8%), and bone marrow (12%). IHC revealed CD99 (93.3%), FLI-1 (58.6%), synaptophysin (31%), and vimentin (6.9%) positivity. First-line chemotherapy predominantly utilized the ddVAC-IE regimen (82.8%). Responses included complete remission (13.7%), partial remission (41.3%), stable disease (13.7%), and progressive disease (13.7%). Definitive treatment included surgery (36%) and radiotherapy (64%). Recurrence occurred in 18 (62%), sites included CNS (46.1%), original site (38.4%), viscera (30%), and bone (23%). For second-line chemotherapy ($n = 5$), four received VIT and one VDC. 2 progressed, 2 were lost to follow-up, and 1 died. The median PFS1 was 9 months, PFS2 3 months, and OS 14 months.

Conclusion: This study offers valuable insights into the demographics, clinicopathological characteristics, and treatment outcomes of ES in an LMIC setting. The findings underscore the dismal outcomes and the need for continued research to develop more effective treatment strategies.

A035. Understanding the Mosaic of Dual Primary Malignancies through Real-World Data at a Tertiary Care Center in Urban India

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Keywords:
- dual primary malignancy
- multiple malignancy

Aims and Objectives: Portrayal of real world data of patients presenting with multiple primary malignancies at a tertiary care center in urban India.

Materials and Methods: This is a retrospective analysis of data collected over a period of 10 years, from 2014 to 2024. Data were extracted from electronic medical records, including demographics, family history, clinical presentation, types and stages of cancers, genetic testing, treatment regimens, and follow-up outcomes.

Results: The study included 4,500 patients of which 13 patients (0.28%) were found to have more than one primary malignancy. Of these cases, 4 were males, and 9 females; with an average age of presentation being 55 years for the first malignancy. Significant family history was observed in 3 cases—with unrelated malignancies between generations observed in one of the them. The average time interval was 56 months between the first and second, and 40 months between second and third malignancies. Four of the malignancies were synchronous (diagnosed within a period of 6 months from each other), while nine were metachronous.

Conclusion: We noticed a variability in the incidence of dual malignancies globally (2–17%), as well as among different regions in India—Northern India (0.67%), Western India (1.51%) and Southern India (0.08%). The limited availability of genetic and treatment data highlights the need for diagnostic approaches and personalized treatment plans, along with comprehensive data collection across India.

A036. A Study of Molecular Classification of Gastric Adenocarcinoma and Correlation with Clinicopathological Response

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Keywords:
- molecular classification
- gastric carcinoma
- clinico-pathologic correlation

Aims and Objectives:

To study the various clinicopathological factors of gastric adenocarcinoma (Ca).

To determine the IHC expression of various molecular markers in gastric Ca and their correlation with known prognostic factors.

Correlation of different molecular subtypes with treatment response and survival.

Materials and Methods:

1. Sample size of 104 patients.
2. Study period: December 2020 to January 2023.
3. E-Cadherin, p53,HER2-neu,MSI,PDL-1 by IHC and EBER by in situ hybridization.
4. Patients were then grouped into 5 molecular subtypes—microsatellite instable, EBV associated, epithelioid mesenchymal type, p53 mutated, and p53-proficient types (combining TCGS and ACRG classification).
5. Treatment: NACT/upfront surgery/chemotherapy.
6. Correlation of clinicopathological response of the different molecular subtypes.

Results: Of the 104 cases in our study population, 54% of the tumors were poorly differentiated. 81.73% of patients had LVI and 55.77% of patients had PNI. In post-op staging, pT3 and pN2 were the most common. Of the 36 post-NACT cases, 49.31% cases had partial treatment response. None of the patients had EBV expression, 9.62% of cases had MSI instability, 55% of cases had abnormal p53 expression, 17% of tumors had reduced E-Cadherin expression. Her-2/neu was positive in 7.69% of tumors and 10.58% of tumors had PDL1 expression. On follow-up to 4 to 20 months, 80 were alive and 18 were dead, 6 were lost to follow-up. Of those alive 16 had metastasis with liver as the most common metastatic site and 6 patients had recurrence at the surgical site. Correlation of the molecular subtypes with post op stage, DFS, OS, and PFS till August 2024 is still ongoing.

Conclusion: In this study we have divided gastric carcinoma into five molecular subtypes. 20% of GC cases exhibited markers that can serve as an indication for known immunotherapy (11 PDL1+ cases and 10 MSI-H cases) 7.69% cases for anti-Her 2 therapy. Further data regarding DFS, OS, PFS till August 2024 are awaited. Further studies in Asian population are essential for a better understanding on the prognostic value of these molecular markers.

A037. Clinicopathological Features and Treatment Outcomes of Adolescents and Adults Rhabdomyosarcoma: A Single-Institution Experience

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Background: Adolescent and adult rhabdomyosarcoma is a rare entity with a reported poor prognosis compared to its pediatric counterpart; hence, it needs further exploration of clinicopathological features and treatment outcomes.

Materials and Methods: This is a retrospective analysis of the data of histopathologically confirmed RMS patients over the age of 14 who registered at our institute between 2014 and 2021. They analyzed age, histopathological subtype, site of primary, IRSG stage, IRSG grade, COG risk group, PAX-FKHR gene fusion status, type of treatment (operative vs. nonoperative), response to primary therapy, overall survival (OS), event-free survival (EFS), and treatment-related toxicities.

Results: The median age of 57 patients was 23 years, including 38 (66.7%) males. 27 (47.4%) patients had distant metastasis at diagnosis, 44 (77.2%) had primary at an unfavorable site, majority from head and neck region 27 (47.4%). Distribution of histopathological subtypes were ARMS in19 (33.9%) patients, ERMS in 11 (19.3%) patients, undifferentiated RMS 8 (14%) in patients, PRMS and Spindle Cell RMS in 7 (12.2%) patients each and sclerosing RMS in 5 (8.7%) patients.

PAX-FKHR gene fusion was found in 9 (50%) out of 18 evaluable patients. Of the 45 patients treated with curative intent, 23 (51.1%) patients could undergo surgical resection of the primary tumor, and 18 (40%) patients were treated with definitive radiation therapy. 35 (75.8%) patients were offered neoadjuvant chemotherapy, with an overall response rate of 29 (64.4%). 32 (88.8%) patients had grade 3/4 toxicity in perioperative chemotherapy, mostly hematological, including febrile neutropenia in 28 (77.7%) patients. 26 (72.2%) of patients required dose modification in perioperative therapy. After a median follow-up of 24 months and 38 events, the median event-free survival (EFS) was 18 (95% CI: 14.8–21.2) months, while the median overall survival (OS) was 24 (95% CI: 18.7–29.2) months.

Conclusion: Adolescent and adult RMS patients need a risk-based multimodality treatment approach with proper dose modification as required as they develop significant toxicity. Further prospective collaborative studies are required to improve outcomes in this cohort.

A038. Real-Life Clinico-pathological Profile of Neuroendocrine Tumor (NET): An Experience from a Tertiary Care Hospital in Mumbai

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Keyword:

- neuroendocrine tumors

Aims and Objectives: To study real-world clinical-pathological profile of neuroendocrine tumors (NETs) at a tertiary care hospital.

Materials and Methods: This is a retrospective observational study of all patients with NETs registered at tertiary care cancer institute from 2016 to 2024. A total of 27 patients' data were collected. Clinicopathological features of all these 27 patients were studied and analyzed.

Results: The median age was 53 years (29–79 years) with male preponderance (male: 70.3%, $N = 19$). Diagnosis was made by either biopsy (n: 21) or pos- surgery with histopathological diagnosis at time of surgery. 18 out of 27 patients had histology grade 1 followed by grade 2 seen in 7 patients and 2 patients had grade 3. The most common primary site of origin was small intestine ($10/27 = 37\%$), followed by pancreas (7/27), lung (3/27), gastric (2/27), and other included liver, ovary appendix and mediastinal mass. The most common presenting symptom was weight loss, followed by pain. 11 out of 27 were metastatic at presentation). Long acting Octreotide analogue was the most common primary therapy (13/27), followed by Chemotherapy (9/27) followed by PRRT therapy (4/27), PRRT was used as second-line treatment in all 4 patients either due to disease progression on treatment or relapse, followed by watchful monitoring.

Conclusion: The clinicopathological profile of NETs in the Indian population differs from Western countries. Patients present with metastatic disease, GI NET being more common, diverse clinical profile, thus represents a need for creating awareness among patients and medical fraternity and formulating Indian guidelines for optimized treatment.

A039. Young and Vulnerable: The Alarming Trends of Lung Cancer in Young Adults—A Single-Center Experience from South India

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Keywords:

- lung cancer
- young adult
- driver mutation
- targeted therapy

Aims and Objectives: There is limited data on the epidemiology and outcomes in lung cancer in young adults in low and middle income countries (LMICs). The following is a single center, retrospective real-world experience on managing young adults with lung cancer.

Materials and Methods: Data on lung cancer patients aged 40 years or younger, presenting to Cancer Institute (WIA) in Chennai between 2017 and 2022 were extracted from medical records. Progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan–Meier method.

Results: Study included 73 patients. Majority of them were females ($n = 42$; 57.5%). Median age was 36 years (range 23–40 years). Only 15 (20.5%) of patients were ever-smokers. Commonest histology was adenocarcinoma ($n = 62$; 85%). Fifty-four patients (74%) had driver mutation testing reports available; of which 23 (42.6%) were EGFR mutation positive, 7 (13%) were ALK and 1 was ROS fusion positive. Most patients were stage-IV at presentation ($n = 61$; 83.6%).

First line of therapy was palliative chemotherapy ($n = 37$; 50.7%) and/or TKIs ($n = 29$; 39.7%). Commonest first line TKIs used was Gefitinib ($n = 29$), including empirical initiation in 18 patients. No patient received Osimertinib in first line.

Median PFS was 11.6 months (95% CI: 8.5–14.5 months). Amongst the 41 patients who progressed, 16 did not receive and further therapy, 18 received second-line chemotherapy, and only 6 received Osimertinib.

Median follow-up was 26.5 months (95% CI: 12.9–40.1 months). The median OS was 19.2 months (95% CI: 12.7–25.7 months). For patients with a driver mutation, median OS was 22 months (95% CI: 16.5–27.6 months). Median OS was better for patients who received TKIs with palliative chemotherapy (29.5 months), than only TKI (8.1 months) or only chemotherapy (16.8 months)

Conclusion: Lung cancer in young adults often presents at advanced stage and is associated with a poor survival, making it a significant societal challenge as it affects individuals in their most productive years. Management in a LMICs is furthered hampered by lack of universal availability of life-saving therapy like Osimertinib, and a significant proportion of patients not receiving any therapy on progression, highlighting the urgent need for better social support and access to care.

A040. Golden Years, Grim Realities: Lung Cancer in Geriatric Patients—A Real-World Experience from South India

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Keywords:

- lung cancer
- geriatric oncology

► driver mutation
► targeted therapy

Aims and Objectives: Management of Lung cancer in the geriatric population is met with numerous challenges in view of underlying co-morbid conditions and ageing associated frailty. The following is a real world experience of managing geriatric lung cancer patients from a standalone cancer center in South India

Materials and Methods: Data on lung cancer patients aged 65 years or older, presenting to Cancer Institute (WIA) in Chennai between 2017 and 2021 were extracted from medical records. Overall survival (OS) was calculated using the Kaplan–Meier method.

Results: Our study included 229 patients. The median age was 70 years (range 65–86). Majority were males ($n = 171$; 74.7%). Ever smokers were 129 patients (56.3%). Common comorbidities were diabetes ($n = 75$; 32.8%), hypertension ($n = 94$; 41%), coronary artery disease ($n = 26$; 11.4%). Common histology was adenocarcinoma ($n = 150$; 65.5%), small cell carcinoma ($n = 37$; 16.2%) and squamous cell carcinoma ($n = 27$; 11.8%). Driver mutation testing reports were available for 112 patients, of which EGFR mutation in 65 (58%), and ALK fusion in 4 (3.5%). Most patients presented with stage-IV ($n = 155$; 67.7%) and stage-III ($n = 58$; 25.3%) disease. 24 patients did not receive any treatment (10.5%). Gefitinib was used as first line TKI in 75 (37.1%), and Osimertinib in 7 (3%). 58 patients (28.3%) defaulted treatment before planned completion of first line therapy. Of the 91 patients with documented progression during/after first line therapy, 35 (38%) did not receive any further treatment. Common second line options were Osimertinib ($n = 14$; 15.4%) and OMCT ($n = 3$; 14.3%). Only two patients received Immune check point inhibitors.

Median follow-up was 43.7 months. Median OS was 8.5 months (95% CI: 6.7–10.3 months), and was better in patients with a positive driver mutation (16.7 months) and with adenocarcinoma (10.8 months), compared to patients without a driver mutation (9.6 months), small cell (3.1 months) and squamous cell carcinoma (5.5 months).

Conclusion: Lung cancer in the elderly is compounded by a high incidence of comorbidities, alarming dropout rates, and a limited number of patients receiving second-line therapy. Additionally, restricted access to expensive targeted therapy like Osimertinib and immune checkpoint inhibitors contributes to poor survival outcomes.

A041. MicroRNAs as Therapeutic and Prognostic Markers for Resistance to Therapy in HER2/neu-Positive Breast Cancers

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Background: Despite the clear benefits of Anti HER2 therapies, many patients demonstrate resistance, primary or adaptive, mechanisms that are not fully understood. Current studies have shown that miRNAs are essential for both expressions of HER2 and the action of trastuzumab/pertuzumab in breast cancer. Heterodimerization of HER2 with other HER family members under the regulation of miRNAs could induce various intracellular signaling pathways and resistance in breast cancer. Based on this, miRNAs not only can be utilized as significant predictors of drug resistance in HER2-positive breast cancer but can also be targeted. In the current study, we aim to demonstrate miRNA mediated resistance to therapy in anti-HER2 treated patients by correlating miRNA levels to response to NACT.

Materials and Methods: This study was conducted at Sri Shankara Cancer Hospital and Research Centre, Bangalore after obtaining Institutional Ethical Committee approval. Patients enrolled were during the time period June 2022 to Jan 2024. FFPE blocks from 100 confirmed primary HER2 positive BCs, treated with standard NACT were collected. Responders and non-responders were classified based on residual cancer burden (RCB) post-surgery and followed prospectively. The levels of miR were estimated using Taqman q-RT-PCR technique and correlated with RCB. Choice of specific MIRs was guided by meta-analysis from TCGA.

Results: The median age of our cohort was 49 y. Following standard of care NACT, 55% of patients achieved pCR. The highest pCR rates (65%) were seen in the subgroup which received dual anti HER2 therapy. The pCR rates were higher for the HR −ve, HER2 +ve subgroup when compared to HR+ve HER2 +ve BC. (73.1 vs. 44.9%, $p < 0.05$). Top MIRs Mir21, 193a, 15b, 98, and 187 associated with disease-free survival were used to generate a score to correlate with response to NACT. More work to complete q-PCR analysis and analyze specific downstream pathways that contribute to resistance and also functional elucidation in-vitro for mechanism is underway

Conclusions: Our work demonstrates a possible mechanism for primary resistance to anti HER2 therapy and pave the way for application of microRNA as a tool for predicting and targeting against resistance to trastuzumab in breast cancer.

A042. Audit of CSF Testing for Leptomeningeal Disease Across Solid Tumors in a Tertiary Care Hospital

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Keywords:
► leptomeningeal disease
► cerebrospinal fluid
► solid tumors
► diagnostic accuracy
► leptomeningeal tumor spread
► tertiary care hospital
► audit

Background: Leptomeningeal disease (LMD) is a critical and challenging complication arising from the leptomeningeal spread of malignant cells from solid tumors. The incidence of LMD varies by tumor type, with higher rates observed in cancers such as breast cancer, lung cancer, and melanoma. The clinical presentation can be diverse, often leading to delays in diagnosis. Literature suggests that early detection and accurate diagnosis through CSF analysis and neuroimaging are crucial for effective management, as LMD significantly affects prognosis and quality of life. However, diagnostic sensitivity remains a challenge, with variations in the yield of cytological and molecular testing. This audit examines the effectiveness and efficiency of CSF testing protocols in diagnosing LMD in a tertiary care hospital setting.

Aim: The primary aim of this audit is to evaluate the diagnostic accuracy, timeliness, and clinical impact of cerebrospinal fluid (CSF) testing for leptomeningeal disease (LMD) in patients with solid tumors. The audit seeks to identify areas for improvement in current practices and to enhance patient management and outcomes.

Materials and Methods: A retrospective analysis was performed on patients with solid tumors who underwent CSF testing for suspected LMD on MRI brain between 01.01.2023 and 30.06.2024. Data were collected from medical record register, including patient demographics, primary tumor types, CSF analysis results, imaging findings, and subsequent management strategies. CSF cytology was done to look for malignant cells. The primary outcomes included the diagnostic yield of CSF analysis, time to diagnosis, and the influence of CSF findings on clinical management.

Results: The audit included 36 patients who were suspected to have leptomeningeal disease on the basis of MRI brain report. The most frequently observed primary tumors were carcinoma breast (47.2%) followed by carcinoma lung (38.8%). Among carcinoma lung adenocarcinoma were most common histopathology (57%). Out of total 36 patients CSF cytology (malignant cell) were detected in 10 cases (27.7%). Among carcinoma breast patient CSF positivity was 35.2% and among carcinoma lung patient CSF positivity was 28.5%. These patients were started on intrathecal chemotherapy for control of leptomeningeal disease.

Conclusion: This audit underscores the pivotal role of combining MRI brain imaging with cerebrospinal fluid (CSF) cytology in diagnosing leptomeningeal disease (LMD) in patients with solid tumors. The dual approach enhances diagnostic accuracy and provides complementary information that is critical for clinical decision-making. MRI brain imaging serves as a noninvasive, highly sensitive tool for detecting leptomeningeal enhancement or nodular deposits. CSF cytology, on the other hand, involves the microscopic examination of cerebrospinal fluid to detect malignant cells. While it is considered the gold standard for confirming LMD, its sensitivity can be limited, with detection rates varying widely. In cases where MRI findings are suggestive of LMD but CSF cytology is negative, clinicians may consider additional tests, such as CSF flow cytometry or molecular diagnostics, to increase the sensitivity of detection.

A043. Audit of HER2Neu Testing Across Solid Tumors in a Tertiary Care Hospital

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Background: HER2Neu (human epidermal growth factor receptor 2) is a protein that affects the growth of cancer cells and a critical biomarker in the management of various solid tumors, particularly breast and gastric cancers. Accurate HER2Neu testing is pivotal for guiding targeted therapies and improving patient outcomes. This study audits the HER2Neu testing practices across different solid tumors in a tertiary care hospital to understand the prevalence and implications of HER2 positivity in different cancer type.

Aims:

This audit aims to

• Assess the prevalence of HER2 positivity across multiple solid tumor types.

• Compare these findings with existing literature, particularly focusing on Indian data.

• Provide insight into the clinical implications of HER2 testing for patient management and therapeutic decisions.

Materials and Methods: The study was conducted at a tertiary care hospital and included patients diagnosed with various solid tumors, specifically pancreatico-biliary, lung, breast, colorectal, and esophago-gastric cancers. Formalin-fixed paraffin-embedded (FFPE) tissue samples were collected from these patients were subjected to HER2 testing using immunohistochemistry (IHC) and, where necessary, fluorescence in situ hybridization (FISH). The HER2 status was categorized based on established scoring criteria, and the prevalence of HER2 positivity was calculated for each cancer type

Result: We audited data of 122 patients with various tumor sites on whom HER2Neu immunohistochemistry (IHC) was performed. 53.28% ($n=65$) cases were of carcinoma breast, 18.85% ($n=23$) case were of carcinoma gall bladder, 5.74% ($n=7$) cases were of colon cancer, 5.74% ($n=7$) cases were of gastric carcinoma, 4.92% ($n=6$) cases belonged to lung cancer, carcinoma rectum was 4.1% ($n=5$) and others were 7.37% ($n=9$). Among all examined samples, 45.9% ($n=56$) were negative for HER2 with IHC score 0. 19.67% ($n=24$) were having IHC score 1+, 15.57% ($n=19$) had IHC score 2+ and IHC score 3+ was in 18.85% ($n=23$) cases. In breast cancer patients, HER2 positivity with IHC score 3+ was 24.61%, while in gastric carcinoma it was 28.57%. 17.39% cases of carcinoma gall bladder were found to have IHC score 3+ and in lung cancers with all histology it was 16.67%. Treatment decisions were significantly influenced by HER2-Neu status in 28% of patients, leading to the administration of targeted therapies such as trastuzumab.

Review of literature with Indian data

HER2 overexpression or amplification has been extensively studied in breast cancer, with approximately 15–20% of breast cancers reported to be HER2-positive. However, HER2 positivity is also observed in other solid tumors, such as gastroesophageal, colorectal, lung, and pancreatic cancers, though with varying prevalence rates. Indian studies on HER2 positivity in non-breast cancers are cited, but available data suggest a lower prevalence compared to Western populations. This audit contributes to the growing body of Indian data on HER2 testing across diverse solid tumors emphasizing the need for comprehensive testing and reporting.

This study contributes valuable data to the limited existing literature on HER2 testing in Indian populations and reinforces the importance of robust HER2 testing practices in guiding cancer treatment and improving cancer care outcomes. The prevalence of HER2 positivity varied significantly across different cancer types, with breast cancer showing the highest rates, consistent with global and Indian data. However, HER2 positivity was also identified in other solid tumors, including gastroesophageal, colorectal, lung, and pancreatic-biliary cancers, underscoring the importance of comprehensive testing beyond breast cancer. The relatively lower prevalence of HER2 positivity in non-breast cancers within the Indian population, compared to Western counterparts, highlights potential geographical and ethnic differences that warrant further investigation.

A044. The PD-L1 Testing Across Different Solid Tumors in a Tertiary Care Hospital to Assess Prevalence of PD-L1 Positivity, and Its Impact on Clinical Decision-Making

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Background: PD-L1 (programmed death-ligand 1) is an immune checkpoint protein that promote tumor immune evasion and a critical biomarker used to guide immunotherapy in various solid tumors. PD-L1 testing is essential for identifying patients who are likely to benefit from PD-1/PD-L1 inhibitors, thereby improving treatment outcomes. This study audits the PD-L1 testing across different solid tumors in a tertiary care hospital to assess prevalence of PD-L1 positivity, and its impact on clinical decision-making.

Aims: This audit aims to:

• Assess the prevalence of PD-L1 positivity across multiple solid tumor types.

• Compare these findings with existing literature, with a focus on Indian data.

• Provide insights into the clinical implications of PD-L1 testing for patient management and therapeutic decisions.

Materials and Methods: The study was conducted at a tertiary care hospital and included patients diagnosed with various solid tumors, specifically lung, breast, colorectal, esophago-gastric, and pancreatico-biliary cancers. Formalin-fixed paraffin-embedded (FFPE) tissue samples from these patients were subjected to PD-L1 testing using immunohistochemistry (IHC). The PD-L1 status was categorized based on established scoring criteria, and the prevalence of PD-L1 positivity was calculated for each cancer type.

Result: Total of 74 patients were included in this audit who needed and under gone PDL1 testing. 21.62% ($n = 16$) patients were having lung cancer, mostly non-small cell lung cancer. Patients having pancreatico-biliary carcinoma were 27% ($n = 20$), colorectal carcinoma was 14.86% ($n = 11$), esophago-gastric cancer was 9.46% ($n = 7$), head and neck cancer was 6.75% ($n = 5$), breast cancer was 2.7% ($n = 2$) and others solid tumors tested were 17.61% ($n = 13$). Overall, 29.73% ($n = 22$) cases were having PDL1 <1%, 54.05% ($n = 40$) having PDL1 1–49% and 16.22% ($n = 12$) were having PDL1 >49%. Amongst tumor having PDL1 <1%, pancreatico-biliary carcinoma was 31.82%, carcinoma lung was 22.73%, colorectal carcinoma was 9.1%, esophago-gastric cancer was 9.1% and others were 27.25%. tumor having PDL1 score between 1–49% were 25% pancreatico-biliary carcinoma, 20% lung cancer, 17.5% colorectal carcinoma, 10% head and neck cancer 7.5% esophago-gastric cancer and rest was others. In lung cancer, 31.25%, 50%, and 18.75% case were having PDL1 <1%, 1–49%, and >49%, respectively. In pancreatico-biliary carcinoma, 35%, 50%, and 15% case were having PDL1 <1%, 1–49%, and >49% respectively. In colorectal carcinoma, 18.18%, 63.64%, and 18.18% case were having PDL1 <1%, 1–49%, and >49%, respectively. 80% of head and neck cancer was having PDL1 score between 1–49% and 20% was having >49%. PDL1 score in 42.86% esophago-gastric cancer was between 1–49% and 28.57% was having >49%.

Review of literature with Indian data:

PD-L1 expression has been widely studied in various cancers, with significant implications for the use of immune checkpoint inhibitors. In lung cancer, particularly non-small cell lung cancer (NSCLC), PD-L1 testing is now standard practice to guide immunotherapy. Studies in breast cancer, colorectal cancer and head and neck cancers have shown variable PD-L1 expression, influencing treatment strategies. Existing studies on PD-L1 expression in Indian populations have reported varying prevalence rates across different tumor types, with higher rates generally observed in lung and esophago-gastric cancers, similar to global trends. This audit contributes to the limited Indian data on PD-L1 testing across diverse solid tumors, emphasizing the need for comprehensive testing and consistent reporting to guide immunotherapy use effectively.

Conclusion: This audit seeks to provide a detailed overview of PD-L1 positivity across a range of solid tumors in a tertiary care hospital. By comparing the findings with existing literature, especially from India, the study highlights the significance of PD-L1 testing in guiding immunotherapy and improving patient outcomes. The completion of the data section will offer valuable insights into the prevalence of PD-L1 positivity in these cancer types and its clinical implications.

A045. Epithelioid Angiosarcoma Presenting as Massive Peritoneal Bleed: A Case Report of Continuous Draining and Hypertransfusion Management

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Keywords:

- epithelioid angiosarcoma
- hemoperitoneum
- hyper transfusion
- coagulopathy
- multidisciplinary approach
- neoadjuvant chemotherapy
- palliative care

Aims and Objectives:

• To present a rare case of epithelioid angiosarcoma with massive peritoneal bleeding.

• To highlight the diagnostic challenges and management strategies for such a presentation.

• To discuss the approach to continuous draining, hypertransfusion, and management of coagulopathy.

• To emphasize the importance of a multidisciplinary approach in treatment.

Materials and Methods: The patient's clinical history, presenting symptoms, physical examination findings, diagnostic workup including imaging studies (e.g., MRI, CT scan), histopathological examination of biopsy specimens, and treatment modalities (surgery, chemotherapy, radiation) are comprehensively reviewed and discussed. Follow-up data including response to treatment and any complications are also included.

Results: The patient presented with hemorrhagic intramuscular lesions and was diagnosed with epithelioid angiosarcoma. Despite initial chemotherapy, she developed severe anemia and hemoperitoneum requiring continuous abdominal drainage and multiple transfusions. Hemostatic radiotherapy and further palliative chemotherapy were administered, but the patient's condition continued to deteriorate, highlighting the aggressive nature of the disease and the complexity of managing such cases.

Conclusion: Epithelioid angiosarcoma of the thigh is an exceedingly rare and aggressive malignancy with a challenging diagnosis. A multidisciplinary approach, including surgical resection, radiotherapy, and chemotherapy, can lead to favorable outcomes. Early detection and comprehensive treatment are crucial for improving prognosis and survival rates in patients with this rare neoplasm.

A046. Clinico-epidemiological Profile and Treatment Outcome of Breast Carcinoma: A Retrospective Study from a Tertiary Cancer Center of North-East India

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Keywords:

- breast carcinoma
- TNBC
- HR+
- HER2+ve
- survival

Aims and Objectives: This study was undertaken to know the clinico-epidemiological profile and outcome of breast carcinoma in North-East Indian population.

Materials and Methods: A retrospective analysis was performed on medical records of patients with breast carcinoma, diagnosed, treated and followed up in the Department of Medical Oncology, Dr. B. Borooah Cancer Institute during January 2020 to December 2021.

Results: A total of 1,500 patients were evaluated with median age of 47.6 years. Out of 1197 histopathologically proven patients with breast carcinoma, 29.5% patients presented in early stage, 44% presented in locally advanced stage and 25.9% presented with de-novo metastasis. Among all 36.7% patients were hormone receptor (HR) positive while 18.9% were HER2-enriched, 27% were triple negative and 17% patients expressed both HR and HER2. Doxorubicin-cyclophosphamide followed by taxane was the most common regimen used in curative intent. Pathological CR rate was 27.5%. The overall survival has got significant correlation with pathological CR ($p < 0.001$). Among the patients presented with de-novo metastasis liver was the most common organ involved in HER2-enriched group while it was bone in other subtypes. The most common chemotherapy regimen used in palliative intent was taxane ± trastuzumab, followed by 5-flourouracil-epirubicin-cyclophposphamide. The survival rate at 6-months, 1-year, 2-years and 3-years are 92%, 82%, 87.9%, 41.5% respectively for TNBC subset; 92%, 79.6%, 64.8%, 36.7% respectively for HER2-enriched; 93%, 86.4%, 79.48%, 55.4% respectively for HR positive subgroup; and 93.9%, 85.2%, 78.2%, 48.7% respectively for those expressing both HR and HER2.

Conclusion: Advanced stage of presentation is the most important factor associated with poor survival amongst the patients with breast cancer. Although several novel therapeutic agents have shown promising results in clinical trials, many patients from developing countries like India are not able to avail the benefit from these therapeutic agents due to high cost, resulting poor outcome in HER2-enriched and TNBC subtypes.

A047. Real-World Data on Biomarker-Driven Treatment of Lung Cancer in Our Center with or without Chemotherapy

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Background: Lung cancer remains a major cause of cancer mortality worldwide. The integration of biomarker-driven targeted therapies has transformed treatment strategies, particularly when combined with chemotherapy. This report examines real-world data from lung cancer patients at our center who received biomarker-driven targeted therapies, with or without sequential chemotherapy.

Materials and Methods: This retrospective study includes lung cancer patients treated at our center from January 2015 to April 2024 who have undergone comprehensive genetic testing for actionable mutations and were treated with targeted therapies based on identified biomarkers. Data were collected on whether the patient received chemotherapy, treatment response and progression-free survival (PFS).

Results

Patient demographics:

• Total number of patients: 91

Biomarker distribution:

• EGFR mutations: 67

• ALK rearrangements: 21

• ROS1 rearrangements: 3

Treatment regimens:

• EGFR TKIs: Erlotinib, Gefitinib, Afatinib, Osimertinib

• ALK inhibitors: Crizotinib, Ceritinib, Alectinib, Lorlatinib

• ROS1 inhibitors: Crizotinib

• PD-L1 inhibitors: Pembrolizumab, Nivolumab

• Chemotherapy: Pemetrexed, Cisplatin, Carboplatin, Docetaxel

With/without chemotherapy:

Without chemotherapy (TKI alone): 24

With chemotherapy: 67

Treatment outcomes:

1. EGFR-positive patients ($n = 67$):

• Partial response (PR): 28

• Complete response (CR): 11

• Stable disease (SD): 20

• Progressive disease (PD): 7

• mPFS: 30 months (targeted therapy alone)

2. ALK-Positive Patients ($n = 21$):

• Partial Response (PR): 3

• Complete Response (CR): 3

• Stable disease (SD): 15

• Progressive Disease (PD): 0

• Median PFS: 32 months

3. ROS1-Positive Patients ($n = 3$):

• Partial Response (PR): 1

• Complete Response (CR): 0

• Stable disease (SD): 1

• Progressive Disease (PD): 1

• mPFS: 9 months (targeted therapy alone)

Discussion: The real-world data from our center underscore the efficacy of biomarker-driven targeted therapies in lung cancer treatment. The study showed that patient who received upfront chemotherapy with targeted therapy had a statistically significant PFS of 22 months versus 12 months with targeted therapy without chemotherapy HR 3.48 (1.86–6.52, $p < 0.001$). The response rates were also found to be better in patient who received chemotherapy along with targeted therapy compared to monotherapy alone. The data also highlight the potential for improved outcomes with concurrent therapy in selected patients.

Conclusion: Biomarker-driven targeted therapies offer significant clinical benefits in the management of lung cancer with or without chemotherapy. Our center's real-world data support the continued use of comprehensive biomarker testing and personalized treatment approaches. Further research is needed to optimize sequencing strategies and manage resistance mechanisms.

A048. Molecular Profiling and Treatment Patterns of Salivary Gland Cancers in Head and Neck Region

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Keywords:

- salivary gland tumor
- drug therapy
- molecular: mutation

Aims and Objectives:

The Aims and objective of this study was to determine the molecular profile of malignant salivary gland tumors and to evaluate the impact of systemic therapy.

Materials and Methods:

• We did a SNaPshot Molecular Profile of all patients with real time PCR looking for 21 hotspot mutation sites in nine cancer genes:

• (EGFR, HER2, KRAS, NRAS, PI3KCA, BRAF, MEK1, PTEN, AKT1-) and studied the expression of ER/PR/Her2-Neu/AR/Ckit via IHC.

• Depending on the molecular profile and symptomatic burden, patients were offered either observation, targeted therapy or chemotherapy.

Results: Out of the 69 evaluable patients, 55% ($n = 38$) had actionable target. Androgen Receptor (AR) expression was present in a predominant number of patients ($n = 23$, 34%), with it alone being expressed in 17% ($n = 12$) of patients, and along with other actionable targets in the other. 60 (87%) patients received systemic therapy either in form of chemotherapy (35, 58.3%) or targeted therapy (25, 41.7%). The strategy of observation in asymptomatic status led to a median OS of 32.27 (3.03–NA) which was similar to that of patients receiving systemic therapy ($p = 0.992$). In patients with visceral crisis, the median OS was higher in patients receiving chemotherapy than targeted therapy (19.07 (14.20–23.8) versus 6.07 (2.23–NA), $p < 0.001$).

Conclusion: Actionable targets are seen in salivary gland tumors and treatment strategies should be based on these and symptomatic status

A049. To Study the Response of Neoadjuvant Chemotherapy in Patients with Locally Advanced Carcinoma Breast with and without Metabolic Syndrome

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Keywords:

- locally advanced breast cancer
- metabolic syndrome
- neo-adjuvant chemotherapy

Aims and Objectives: Metabolic syndrome and its related components exert a significant impact on the initiation, progression, treatment response, and prognosis of breast cancer. This study is done to correlate the relationship between metabolic syndrome (metS) with pathological complete response (pCR) to neoadjuvant chemotherapy (NACT) among patients with locally advanced breast cancer (LABC).

Materials and Methods: 212 LABC were recruited to this prospective observational study. Patients were randomized into two arms, arm A (MetS group) with requirements as per NCEP ATP III Criteria and rest all are grouped to arm B (non-MetS). All patients received NACT followed by surgery, radiation and hormonal therapy as per hormonal status. Chi square test was performed to know association between the parameters. Univariate and multivariate analyses were performed to evaluate the parameters predicting pCR between the two groups.

Results: 188 patients were included for final interim analysis after excluding 24 patients with arm A comprising 90 and arm B comprising 98 patients. pCR was achieved in 19 (21%) and 30(36%) of arm A and arm B respectively ($p = 0.024$). On univariate analysis, HER2neu+ve patients in arm A have 81% lower odds of getting non pCR ($p = 0.005$) compared to HER2neu+ve patients in arm B who have 42% lower odds of getting non pCR after NACT ($p = 0.224$). HR+ve patients have observed value of 88% higher odds of having non pCR in arm A ($p = 0.23$) as compared to that of 10% in arm B ($p = 0.846$). Post-menopausal women have 70% lower odds of having non pCR in arm A ($p = 0.078$) compared to 8% higher odds in arm B ($p = 0.867$).

Conclusion: LABC patients with MetS reported low pCR to NACT. ER+ve breast cancer patients reported lower pCR and Her2neu+ve patients reported higher pCR to NACT in MetS group. Pre-menopausal with metabolic syndrome have shown lower response to NACT

A050. A Rare Case Report of EML4-ALK-Positive Lung Adenocarcinoma Presenting with Bone Metastasis

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Introduction: The fusion between echinoderm microtubule-associated protein-like 4 (EML4) and anaplastic lymphoma kinase (ALK) have been recently identified in a few subsets of non-small cell lung cancers (NSCLCs). EML4-ALK is most often detected in never smokers with lung cancer and has unique pathologic features. EML4-ALK is oncogenic both in vitro and in vivo and ALK kinase inhibitors are quite effective. This ALK fusion was identified in 2007 in Japanese non-small cell lung cancers (NSCLC). The majority of ALK-rearranged tumors (>60%) demonstrate a solid growth pattern with >10% signet-ring cells. In contrast only a small minority of EML4- ALK wild type tumors, including those with EGFR mutations, demonstrate a solid growth pattern with >10% signet ring cells.

Case Report: 41 years old male, ECOG PS- 2, non-smoker, nil family history presented to the outpatient department with complaints of backpain on October 2023. He was given symptomatic treatment but the pain did not subside and after four months the patient presented with sudden onset weakness of bilateral lower limbs with bladder and bowel involvement. Contrast enhanced MRI screening of the whole spine was performed which revealed altered signal intensity lesion in D3 and D4 vertebral body and its posterior element. The height of the vertebral body was decreased suggestive of pathological fracture. Contrast enhanced CT scan of thorax was done which revealed a 4.4*3.9*3.9 cm lesion in superior segment of left lower lobe abutting major fissure and abrupt cut off superior lobar branch of left lower lobar bronchus. The lesion had encased left pulmonary artery extending to left main bronchus with encasing the descending thoracic aorta with enlarged subcarinal lymph nodes. Decompression surgery of D3-D4 was done and the histopathology report was suggestive of metastatic poorly differentiated invasive mucinous adenocarcinoma with signet ring or goblet cells. Immunohistochemistry suggested cells are positive for CK 7 AND 20, TTF1, Napsin A, vimentin and negative for p40, PAX 8, CD 2, villin. NGS panel with circulating tumor cells was done for the same and the fusion detected was ALK-EML4. PDL1 testing was done on tissue which was negative. The circulating tumor cell count was 2 CTCs/1.5 mL. The patient was started ALK inhibitor ceritinib. After 3 months a reevaluation PET CT scan was done which revealed near complete metabolic and morphological response noted in left lung lesions and mediastinal nodes. There was complete metabolic response with sclerotic changes noted in bones and no new lesion.

Discussion: Anaplastic lymphoma kinase (ALK)-rearrangements are oncogenic drivers that occur in 3–7% of patients with non-small-cell lung cancer (NSCLC). Most patients with ALK-rearranged NSCLC are usually younger, are never smokers or have a light smoking history, and have adenocarcinoma histology. Ceritinib is a next-generation, selective oral ALK inhibitor with a 20 times greater potency than crizotinib. ASCEND-4 is the first randomized, global, phase 3 study to evaluate the efficacy safety, and patient-reported outcomes of ceritinib versus platinum-pemetrexed doublet followed by pemetrexed maintenance in untreated patients with advanced ALK-rearranged NSCLC. It has been shown that treatment-naive patients with ALK rearranged NSCLC in the ceritinib group had a statistically significant and clinically meaningful improvement in progression-free

survival compared with those in the chemotherapy group that included pemetrexed maintenance.

A051. Analysis of Primary CNS Lymphoma and Its Overall Survival, Assessment of Response Rate, and Its Toxicity Profile (Grade III/IV Toxicity) with High-Dose Methotrexate-Based Chemotherapy in Tertiary Care Hospital

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Keywords:
- ECOG
- PD
- CR
- CNS lymphoma
- Methotrexate

Aims and Objectives:

Primary Objective:

Analysis of primary CNS lymphoma and its clinical feature and outcome of treatment at FMRI since January 2014.

Secondary Objective:

Assessment of response rate
Overall survival
Pattern of failure
Grade V toxicity due to treatment

Materials and Methods: Single center ambispective analysis of histopathologically proven patients of primary CNS lymphoma attending the Department of Medical oncology, FMRI. These patients were treated with chemotherapy from January 2013 to November 2025. Adverse events during chemotherapy were documented and graded using CTCAE v.5 (Common terminology criteria for adverse events).

Results: Till now 40 patients enrolled since January 2013 to January 2023 who were registered at our institute and received high-dose methotrexate (HDMTX)-based chemotherapy with sufficient medical records were analyzed. The median age was 58 years (range, 22–82 years), and the ratio of male to female was 3:1. Multiple intracranial lesions were present in 47.5% of patients. The CR was 20 (50%), PR was 4 (10%), PD was 2 (5%), expired 14 (35%). The ORR = CR + PR (overall response rate) was 60%. Mortality rate 14 (35%). Overall survival 26 (65%). Significant grade IV toxicities were neutropenic sepsis 9 (22.5%), grade IV pancytopenia 2 (5%), SIADH 2.5% and grade III anemia in 1 (2.5%). 67.5% patients did not show any toxicity.

Conclusion: All our patients were immunocompetent and with good performance status (ECOG). The prognosis of patients with high dose methotrexate based chemotherapy has improved during the last decades and appears safe. This analysis is still ongoing.

A052. Efficacy of Scalp Cooling in Prevention of Chemotherapy-Induced Alopecia in Children with Acute Lymphoblastic Leukemia: A Nonrandomized Trial with Ultrasonographic and Electron Microscopic Correlation

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Keywords:
- scalp cooling
- chemotherapy-induced alopecia
- acute lymphoblastic leukemia
- ALL
- CIA

Background and Objectives: Chemotherapy-induced alopecia (CIA) is a common adverse event in children undergoing chemotherapy. Scalp cooling (SC), although effective in adults in preventing CIA, has not been investigated in children. The primary objective was to evaluate the efficacy of SC in achieving successful hair preservation (HP), defined as NCI-CTCAEv5.0 alopecia grade 1 at the end of induction (EOI), in children under 15 years old with intermediate-(IR) and high-risk (HR) acute lymphoblastic leukemia (ALL). Secondary outcomes included changes in scalp ultrasonographic and scanning electron microscopic parameters (SEM) along with trichoscopy and trichogram findings at EOI.

Materials and Methods: It was a non-randomized trial conducted between June 2023 -June 2024. Participants were sequentially assigned to either SC or non-cooling group. SC was done using a pre-cooled Elasto-Gel cap (scalp temperature maintained $<25°C$), from 30 minutes before to 30 minutes after chemotherapy infusion (daunorubicin + vincristine).

Results: Twenty-two children (median age: 72 months) were enrolled (13 IR-ALL, 9 HR-ALL). One child in SC and two in non-cooling group out of 11 in each died before EOI. Successful HP was achieved in 9/10 in SC group versus 2/9 in non-cooling group ($p = 0.005$). Amongst sonographic parameters, there was a significantly lesser decrease in dermal thickness in SC group (-0.03 vs. -0.3 mm, $p = 0.049$). Amongst SEM parameters, there were smaller declines in shaft diameter (-7.9 vs. -21.6 µm, $p = 0.005$) and cuticular scale density (-3.5 vs. -12 scales/100µm, $p = 0.0004$) in SC group. Trichoscopic and trichogram findings associated with CIA were observed in both groups, but they were more pronounced in the non-cooling group. No subjects reported headaches or dizziness during SC.

Conclusion: SC was associated with a higher likelihood of successful HP in children with ALL undergoing induction chemotherapy. Further studies investigating the long-term safety outcomes of scalp cooling are needed.

A053. Neoadjuvant Carboplatin, Nab-Paclitaxel, Oral Metronomic Therapy and Low-Dose Nivolumab for "Borderline Resectable" Oral Cavity Carcinoma: A Prospective Phase II Single Arm Trial (NeoLOCUS)

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Keywords:
- oral cancer
- nivolumab

► immunotherapy
► metronomic drug therapy
► head and neck cancer

Aims and Objectives:

Aim- To assess the safety and efficacy of the study regimen for "Borderline Resectable" Oral cavity squamous cell carcinoma (OCSCC).

Primary Objective: To assess the Proportion of patients undergoing R0 resection after 2 cycles of planned therapy.

Secondary Objectives: To assess the Objective response rates (ORR) and adverse events (AE)

Materials and Methods:

Study Design: Prospective, Phase II, Single Arm Interventional Study.

Population: Eligible patients deemed as 'Borderline Resectable' OCSCC after Tumor Board discussion per predefined criteria:

1. Oral tongue primary with extension to posterior one-third of tongue or floor of mouth.

2. Buccal mucosa primary with diffuse margins and peritumoral edema going up to level of sigmoid notch of mandible but not above.

Intervention: Nab-paclitaxel 175 mg/m^2 + Carboplatin AUC 5 + Low-dose Nivolumab (20 mg/40 mg based on weight) + Triple OMT-Erlotinib 100 mg OD, Celecoxib 200 mg BD and 9 mg/m^2 weekly Methotrexate × 2 cycles (3-weekly)

Results: 33 patients (M-30,F-3) with median age 44.5 years enrolled between March 2023 and May 2024. 32/33 completed planned induction therapy. ORR was 65.6% (PR-21, SD-11). None had PD. 31/32 pts (96.8%) deemed eligible for surgery after Induction.

28 patients (90.3%) underwent surgery (24 had surgery after 2 cycles, i.e., 75%). Three patients (10.7%) had pathological CR. Two underwent definitive CTRT, one chose maintenance OMT and one defaulted.

One patient had Grade 4 Acute Kidney Injury and dropped out after cycle 1. Grade 3 AE were Hematological (24.2%), Infections (9%), Acneiform rash (6%) and Diarrhea (6%). Two patients had grade 2 Immune-mediated hypothyroidism, one had Grade 2 Immune-mediated polyarthritis and one had Reactivation of latent tuberculosis.

Conclusion: Neoadjuvant multi-agent chemotherapy and low-dose Nivolumab for OCSCC is safe and feasible. Response rates are encouraging, resulting in excellent conversion rates to surgery. Early usage of immunotherapy appears to produce better results, warranting validation in a randomized trial.

A054. Clinical Profile and Outcomes of Hepatocellular Carcinoma in HbsAg-Positive Patients: Single-Institute Experience

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Keywords:
► chronic HBV infection
► HBV DNA level
► dynamic changes
► hepatocellular Carcinoma (HCC)

Aims and Objectives: To study the serum HBV DNA levels in HCC patients and its relation to disease severity and outcome.

Materials and Methods: This retrospective prognostic study included 98 patients with HCC admitted at our institute from January 2022 to January 2024. Presence of locally advanced or metastatic HCC not amenable to locoregional treatment confirmed by biopsy or imaging. Exclusion criteria were associated HCV infection or other viral infection and other concurrent cancer. Pretreatment HBV DNA levels were measured by real time quantitative polymerase Chain reaction.

Results: Mean age of patients was 55.02 ± 9.57 years, with majority being male (90.8%). HBV DNA was not detected in 19 (19.4%), <10,000 in 45 (45.9%) and >10,000 in 34 (34.7%) patients. Child–Pugh score was significantly lower in those with HBV DNA was not detected (5.89 ± 1.32), followed by HBV DNA <10,000 IU/mL (6.29 ± 1.42) and highest in those with HBV DNA >10,000 IU/mL (7.56 ± 2.44; $p = 0.002$). Median overall survival was 108 (99.7, 116.3) months in all patients. Overall Survival was higher in those with HBV DNA was not detected (130 months; 95% CI: 86.3, 173.7), followed by HBV DNA <10,000 IU/mL (110 months; 95% CI:103.8, 116.2) and lowest in those with HBV DNA >10,000 IU/mL (95 months; 95% CI: 83.57, 106.4), $p = 0.205$.

Conclusion: Baseline HBV DNA levels can be used as a marker for disease severity in HCC and can also be prognostic marker for predicting survival.

A055. Multi-Institutional Study on Breast Cancer Among Adolescent and Young Adults in NOCI Affiliated Centers Across India

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Keywords:
► breast cancer
► AYA
► clinicopathological profile
► Network of Oncology Clinical Trials in India (NOCI)

Background: Adolescent and Young Adults (AYA) group includes patients aged between 15 and 39 years. Breast cancer is the 3rd most common cancer among AYA in India. Breast cancer burden and their clinicopathological status in AYA group is unknown in India.

Objective: To understand the demographic and clinicopathological profile of AYA patients with breast cancer.

Materials and Methods: This is a retrospective observational study conducted across six tertiary care NOCI centers in India; the clinicopathological and survival data of AYA breast cancer patients diagnosed and treated in the period of January 2015 to June 2021.

Results: Data from 199 breast cancer patients were collected. Two-third of the patients were in the 30 to 34 age group. Half of them had grade 2 histology. Hormone positive patients were 51.25%, TNBC 30.15% and Her2neu enriched 15%. Most of the patients belonged to either Stage II (43.2%) or III (43.7%). Upfront treatment was surgery in 149 patients and neo-adjuvant chemotherapy in 40 patients. Median follow-up was 37 months. Three year OS and PFS were 82% and 78% respectively. Among hormone positive group, 3 year OS and

PFS were 84% and 80% respectively. In Her2neu enriched group, 3-year OS and PFS were 77% and 70% respectively. In TNBC group, 3-year OS and PFS were 80% and 75%, respectively.

Conclusion: Breast cancer profile of AYA patients in India is different from western world data; with more hormone positive, Her2neu negative and intermediate grade tumors.

A056. To Study the Neutrophil–Lymphocyte Ratio as a Predictive Marker of Response to Neoadjuvant Chemotherapy in Locally Advanced Triple-Negative Breast Cancer

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Keywords:

- neoadjuvant chemotherapy
- triple negative breast cancer
- pathological complete response
- neutrophil lymphocyte ratio

Aims and Objectives: Inflammation is key driver of cancer development and progression. Neutrophil is an important component of tumor induced inflammatory response whereas lymphocyte is related to antitumor immune response. The neutrophil–lymphocyte ratio (NLR) is a cost-effective and simple inflammatory parameter. The present study is designed to explore the predictive value of NLR for predicting pathological complete response (pCR) after NACT in locally advanced TNBC.

Materials and Methods: Total of 120 patients with locally advanced TNBC planned for NACT and subsequent breast surgery are recruited for this prospective observational study. All clinicopathological characteristics noted and a baseline peripheral complete blood count is performed. NLR calculated as the ratio between absolute neutrophil and lymphocyte counts. ROC curve is used to predict the relationship between pCR and NLR. Correlations between clinicopathologic variables, NLR and the response to NACT will be assessed using the chi-square test. A binary logistic regression model will be used for prediction.

Results: A total 101 patients were included for the final analysis after excluding 19 patients (16 defaulters and 3 progressive disease). pCR was seen in 30.7% (31/101) patients. Optimal NLR cutoff value of 2.185 was identified and was associated with sensitivity of 67.7% and specificity of 67.1%. Mean NLR ratio in patients with pCR was 2.29 ± 1.21. We found that higher NLR were significantly associated with non-pCR. Area under the curve for the resultant predictive scoring model was 0.672 (95% CI: 0.554–0.791).

Conclusion: Our study underscores the utility of NLR as a non-invasive biomarker for predicting treatment response in triple negative LABC patients undergoing NACT. Lower baseline NLR are more likely to exhibit pCR.

A057. Hypopharyngeal Primary Small Cell Carcinoma–A Case Report of a Rare Tumor and Its Chemotherapeutic Management

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Keywords:

- hypopharynx
- small cell carcinoma
- chemotherapy
- cancer

Aims and Objectives: A subtype of neuroendocrine malignancies, small cell carcinoma (SMCC) primarily affects the lungs. 2.5% to 5% of all SMCCs are extrapulmonary. SMCC can develop in extra-pulmonary locations all over the body, most frequently in the larynx, large intestines, esophagus, and bladder. This type of tumor is aggressive in nature, spreading quickly both locally and regionally as well as far and wide. Only 6% of SMCCs are extra-pulmonary, which is a far lower incidence of SMCC than small cell lung cancer. For extra-pulmonary SMCCs, the function of local and systemic therapeutic approaches is still unclear [3, 4].

Materials and Methods: The E.N.T. Department at VMMC and Safdarjung Hospital received a 54-year-old patient from the Dwarka neighborhood of Delhi who had been experiencing significant shortness of breath and neck swelling for the previous four months. Following emergency tracheostomy, bilateral pyriform sinus development was seen by fiberoptic laryngoscopy in the operating room. Both true vocal cords were movable, and the chink was likewise sufficient. Following the growth's identification of small cell carcinoma using fiberoptic laryngoscopy-guided biopsy, the patient was referred to the Department of Radiation Oncology for additional care. There was no prior history of co-morbid conditions such as diabetes, hypertension, TB, or chronic obstructive pulmonary disease in the patient. The patient disclosed that for over 30 years, they had smoked one pack of cigarettes per day.

A FDG avid mass (SUV-11.6) measuring $5.7 \times 7.5 \times 8.9$ cm was seen in the hypopharynx on PET-CT, completely obliterating the airway and involving the left thyroid lobe. There was a clinically left level III–IV hard fixed node that was about 4×4 cm, and there were subcentrimetric, enlarged bilateral cervical level II–IV lymph nodes. Additionally, a PET-CT scan of the proximal left humerus showed an intramedullary lesion (SUV-12.6) that may indicate hematogenous metastases to bone. In order to look for brain metastases, an NCCT of the brain was also performed, and the results showed normal study.

Results: The patient was finally planned for palliative systemic chemotherapy with Cisplatin and Etoposide with zoledronate for bone metastases and palliative radiation therapy to left humerus lesion whenever required. Currently the patient is doing well with chemotherapy showing signs of good response clinically and subjectively.

Conclusion: Because EPSMCC cancers have a high potential for metastatic dissemination, even in patients with clinically confined tumors, systemic chemotherapy is the cornerstone of treatment for these patients. EPSMCC has traditionally been treated similarly to small cell lung cancer because there is no established treatment protocol. A maximum of four to six cycles of etoposide and platinum-based therapy are recommended for limited stage illness, according to the most recent evidence-based clinical guidelines for small cell lung cancer published by the National Comprehensive Cancer Network (http://www.nccn.org). But in order to achieve a strong result, we require additional innovative medications such immune checkpoint inhibitors that can have a substantial impact on patients' survival.

A058. Clinicopathological Characteristics and Outcomes of Patients with HER2-Low Breast Cancer: 6-Year Ambispective Cohort Study from India

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Keywords:
- HER2-Low
- breast cancer
- survival outcomes

Aims and Objectives:

1. To analyze the clinical and pathological features of HER2-Low breast cancers.

2. To assess the treatment outcome in HER2-Low breast cancers.

3. To analyze the clinicopathological differences separately in HER2neu 1+ and 2+ cohorts, in Hormone positive versus negative cohorts, and in metastatic versus non-metastatic cohorts.

4. To estimate the progression free survival (PFS) and overall survival (OS) in HER2-Low breast cancer in different cohorts.

Materials and Methods: This was an ambispective cohort study where we analyzed the patients with carcinoma breast who were treated at our institute in the last 6 years. Out of 1,845 patients, 243 were identified to have low HER2 expression. Patients were classified as Low HER2 positive if they had HER2 1+ or 2+ by IHC and negative by FISH. The clinical and pathological characteristics, PFS and OS of HER2 low subset, Estrogen Receptor (ER) positive and negative HER2 low cohorts and Metastatic (MBC) HER2 low patients were analyzed separately.

Results: A total of 243 patients were analyzed. Of which 157 had HER2 2+ and 86 had 1+ expression. 240 were females. 79.8% were ER+ and 20.2% were ER negative among the total patients. 76.7% and 81.5% were ER+ in HER2 1+ and 2+ cohorts respectively. 78.2% were non-metastatic and 21.8% had MBC. 34.6% were treated with Neoadjuvant chemotherapy (NACT) and 42.4% with adjuvant chemotherapy (CT). 4.5% of patients treated with NACT attained PCR. 53.1% had T2, 16.8% had T4 disease. Most of the patients had N0 (35.4%) and N1 (37%) disease. The OS of all low HER2+ patients were 4.97 years 95% CI (4.72–5.22). The OS in HER1+ and 2+ cohorts were 4.08 years and 5.04 years respectively. The PFS in low HER2+ patients was 5.01 years 95% CI (4.74–5.27) and 4.29 years and 4.89 years in HER2 1+ and 2+ cohorts.

In the ER+ and negative cohorts, 31.4% of ER+ were treated with NACT and 45.4% of ER+ patients were treated with adjuvant CT. Most of ER+ low HER2 patients were of T2 stage (53.6%, $p = 0.037$). 36.6% were N0 and 34% were N1. 14.4% of ER+ low HER2 were MBC and 16.3% ER negative low HER2 were MBC. The OS of ER+ lowHER2+ cohort was 4.44 years and ER- HER2+ cohort was 4.43 years.

Patients with MBC had a larger tumor size and nodal positivity (T4 43.4%, N1 37.8%, $p = 0.001$). The PFS and OS in MBC were 3.42 and 3.07 years compared to 5.29 years and 5.37 years in non-metastatic patients. Patients who were treated with NACT had an OS and PFS of 4.24 and 4.20 years and those who were treated with adjuvant CT had an OS of 5.39 years.

Conclusion: The data on low HER2-positive patients is scarce in the Indian population. The low HER2+ patients had a PFS of 4.97 years and an OS of 5.01 years. Most of the patients had a T2 and N1 disease. The research gap low HER2+ subset is significant, especially considering the recent approval of trastuzumab deruxtecan in India. With ongoing trials in MBC and non-metastatic settings, the benefit from this newer option may become clearer, particularly in ER+ low HER2 subset.

A059. Computational Insights into Cancer Therapy: The Power of Molecular Docking

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Keywords:
- lung cancer
- rare mutations
- molecular docking
- computational methods drug–target interactions

Aims and Objectives: To evaluate and implement personalized treatment strategies for lung cancer patients with rare resistant mutations by utilizing molecular docking techniques to predict drug efficacy and optimize therapeutic outcomes in the absence of standard treatment guidelines.

Materials and Methods: Two lung cancer patients who presented to our outpatient department with rare resistant mutations.

First patient: Sixty-year-old male with Stage IIIB lung adenocarcinoma was initially treated with Cisplatin and Pemetrexed but progressed. Molecular testing revealed ALK-positivity, and he was subsequently treated with Crizotinib, resulting in clinical improvement. After 66 months, he experienced disease progression and was found to have the ALK C1156Y resistant mutation.

Second patient: 68-year-old man was diagnosed with metastatic adenocarcinoma lung at presentation (oligo metastases to bone and brain) in 2023. Molecular testing revealed the rare EGFR mutations S768I and G719D.

Since both mutations were rare, we performed docking studies to determine best drug for treatment

Results: Through in silico drug response prediction, for case 1 we found that alectinib showed better binding with ALK wild-type and mutant proteins than lorlatinib did. Hence, we initiated treatment with alectinib 600 mg BD. The patient responded exceptionally well; PET CT after 7 months showed a complete metabolic response. The latest CXR showed a good response with a progression-free interval of 15 months.

For case 2 through molecular docking analysis, Osimertinib showed slight better binding affinity towards EGFR mutants than afatinib. Interestingly, both the drugs showed good binding affinity towards the EGFR mutant's active sites. Further due to logistics, he was started on afatinib 40 mg orally daily from August 2023. He received radiotherapy to the L4 vertebra and brain metastases and consolidation RT to the lung lesion. The Latest PET CT done after one year (July 2024) showed a complete metabolic response.

Conclusion: In cases where standard treatment guidelines are lacking due to the rarity of specific mutations, and where the low incidence hinders the observation of treatment responses, clinicians may employ molecular docking techniques. These computational methods can predict the efficacy of potential treatments by simulating drug-target

interactions at the molecular level by understanding the mode of action of these drugs towards the druggable target.

A060. Tolerance and Dose Titration of Tepotinib in MET Exon 14 Skipping Mutation in Non-Small-Cell Lung Cancer (NSCLC): Case Report

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Background: The MET Exon 14 (METex14) skipping mutation is the result of genetic changes that impede MET protein degradation, resulting in prolonged activation and possible oncogenic transformation. These skipping mutations affect around 3–4% of non-small-cell lung cancer (NSCLC) patients.

Materials and Methods: A 74-year-old gentleman diagnosed with Metastatic NSCLC. He received a combination 1 cycles of 750 mg Pemetrexed plus 380 mg carboplatin. Following which he developed complication and chemotherapy dose was reduced. PET showed a partial response with a positive METex 14 driver mutation. Patient was switched to Capmatinib 400 mg twice daily for 1.5 months. On 1.5-month follow-up, he demonstrated deterioration in ECOG status from 2 to 3, with an increase in amylase and lipase enzymes, with a weight loss of 3 kg. Capmatinib was terminated and the patient was started on Tepotinib 225 mg once daily.

Results: The patient was administered Tepotinib 225 mg for 18 months. After 2 months, though the symptoms improved, the patient developed grade 3 pedal edema. Tepotinib was switched from once daily to 5 days a week (Monday to Friday) and torsemide was added twice a day (5 mg) as an add-on therapy. The severity of pedal edema decreased (grade 3 to grade 2), and all enzyme levels returned to normal, with improvement in weight. For persistent pedal edema, Tepotinib 225 mg was recommended thrice a week (Monday, Wednesday, Friday) and the torsemide increased to 10 mg twice daily. Improvements in weight and edema were observed after five months. The PET scan revealed a mediastinal node but reduction of previous metastatic sites. The patient was continued to Tepotinib 225 mg three days per week and complete remission was observed on PETCT scan after two weeks. Till date PET scan showed complete response with improvement of quality of life.

Conclusions: Tepotinib therapy leads to complete remission of metastatic NSCLC. The dose titration essential for continue therapy; however, this has to be evaluated in large-scale clinical studies.

A061. Real-World Outcomes in Indian Patients with Recurrent or Metastatic Head and Neck Cancer Treated with Erbitux and Chemotherapy: Impact of CPS Score (RACE-Head Neck India)

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Background: The current guidelines for recurrent/metastatic head and neck cancer (R/M SCCHN) recommend evaluating PD-L1 (combined positive score (CPS) to predict the efficacy of 1st-line immune therapy with/without chemotherapy, as per KEYNOTE-048 (KN-048). Cetuximab had no bearing on efficacy based on CPS score (as KN-048), but real-world data is lacking. In the current analysis, we evaluate the impact of CPS score on the efficacy and safety of cetuximab.

Materials and Methods: In this multicenter, retrospective, real-world data analysis of 139 R/M SCCHN patients (collected between May 2018 to Sept 2023 from 3 Indian centers.) The efficacy endpoints evaluated were response rate (RR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS) for overall population and based on CPS scores (<20, ≥ 20).

Results: Data from 139 patients (median age: 53 years, range: 32–80). Most were males (91.4%) with performance scores of 1 (71.9%) and 2 (23%). The primary tumor site was the oral cavity in 59% of patients. Cetuximab with taxane-based chemotherapy was given to 95%. CPS scores <20 and ≥ 20 was 53.2% and 46.8%. The overall RR was 80.57%, with 75.67% for CPS <20 and 86.15% for CPS ≥ 20. DCR was 97.84% overall, 98.64% for CPS <20, and 96.92% for CPS ≥ 20. In overall population, mPFS was 9.0 months, and mOS was 20.0 months. PFS and OS did not differ significantly between CPS groups ($p = 0.70$ and $p = 0.35$). Of 139 patients, 113 received immunotherapy (Nivolumab and Pembrolizumab) after progression on cetuximab, while 26 received chemotherapy. Adverse effects included skin toxicity and immune reactions.

Conclusions: The current real-world retrospective data analysis reaffirms the efficacy of cetuximab in patients with R/M SCCHN. Analysis according to CPS scores (<20 and ≥ 20) did not impact any of the efficacy parameters, including similar outcomes in patients with CPS ≥ 20.

A062. Health-Related Quality of Life (HRQoL) with Tepotinib in Patients with MET Exon 14 (METex14) Skipping Non-Small Cell Lung Cancer (NSCLC) with Brain, Liver, Adrenal, or Bone Metastases in the Phase II VISION Trial

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Keywords:
- HRQoL
- tepotinib
- *MET*ex14
- NSCLC

Aims and Objectives: Tepotinib, a highly selective MET inhibitor, showed robust and durable activity in patients with *MET*ex14 skipping NSCLC in the VISION trial (NCT02864992). Systemic and intracranial activity was seen in patients with brain metastases. We analyzed HRQoL in patients with brain, liver, adrenal or bone metastases.

Materials and Methods: Eligible patients (including patients with brain metastases if asymptomatic or neurologically stable on a stable steroid dose) received oral tepotinib 500 mg (450 mg active moiety) once daily. HRQoL was assessed at baseline and during follow-up using the EORTC QLQ-C30 Global Health Score (GHS), EQ-5D-5L visual analog scale (VAS), and EORTC QLQ-LC13 cough, dyspnea, and chest pain scores. Subgroup analyses evaluated patients with brain, liver, adrenal or bone metastases at baseline per independent review (data cut-off: November 20, 2022). Mean change from baseline across all visits was evaluated by linear mixed model regression in patients with baseline and $\geq$1 post-baseline score.

Results: Of 313 enrolled patients, change from baseline in HRQoL was evaluable in 52 patients with brain, 56 with liver, 54 with adrenal, and 86 with bone metastases. At baseline, among evaluable patients, mean $\pm$ standard error (SE) EORTC QLQ-C30 GHS was worst in patients with bone metastases (49.90 ± 2.03), followed by patients with adrenal (51.85 ± 2.51), liver (58.33 ± 2.77), or brain metastases (59.94 ± 2.53). A similar pattern was observed for baseline EQ-5D-5L VAS (bone: 60.42 ± 1.94; adrenal: 63.06 ± 2.45; liver: 65.30 ± 2.46; brain: 66.75 ± 2.57). During tepotinib treatment, patients with metastases maintained HRQoL and showed trends for symptom improvement in cough, with stability in dyspnea and chest pain.

Conclusion: In the VISION trial in *MET*ex14 skipping NSCLC, patients with brain, liver, adrenal or bone metastases maintained overall HRQoL during tepotinib treatment, with trends for improvement in cough, consistent with results for the overall population.

A063. A Physiotherapist's Perspective of Geriatric Clinic in a Tertiary Oncology Center

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Keywords:
- geriatric oncology
- elderly
- falls
- balance

Aims and Objectives:

Aim:

To describe Comprehensive Geriatric Assessment (CGA) results of Indian geriatric oncology patients

Objective:

Analyze various domains amongst elderly and find correlation between outcome measures used

Materials and Methods: Retrospective analysis of data collected in geriatric clinic at tertiary oncology center, Varanasi. Baseline demographics and diseases details of patients aged 60 years and above with malignancies were evaluated using various validated tools which included Performance Oriented Mobility Assessment (POMA), Short Physical Performance Battery (SPPB), 6 Minute- Walk test (6MWT) and Fatigue Numeric rating scale (NRS). Based on results, patients were referred to various specialists and advised methods to address any identified vulnerabilities

Results: 100 patients were assessed. Almost equal number of males and females, and equal distribution amongst age groups. Nearly 56% had a normal BMI. Highest number of GI cancers and most common co morbidity was hypertension. Majorly no walking aid was required. Correlation between SPPB and POMA was assessed using Spearman's rank correlation method which showed a correlation coefficient of 0.79; implies a strong positive association between SPPB and POMA

Conclusion: Commonly deranged domains included fatigue (97%), risk of fall (80%), reduced aerobic capacity (75%) and comorbidities (73%). Also, a strong association was found between outcome measures used.

A064. Effect of Early Pelvic Floor Muscle Exercises (Kegel's) After Robotic Prostatectomy in Prostate Cancer Patients

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Keywords:
- Kegel's
- exercise
- pelvic floor rehabilitation
- quality of life
- robotic prostatectomy
- urinary incontinence

Aims and Objectives:

1. To study the effect of Kegel's exercise after prostatectomy in patients with prostate cancer.
2. To study the duration required for the pelvic floor muscles to gain strength and endurance, thereby leading to urinary continence.

Materials and Methods: In this study, 69 patients who underwent robotic prostatectomy were included. These patients were assessed on day 3 of the surgery, catheter removal day, at 3 weeks, and at 6 weeks. Patients who had metastasis were excluded from the study.

Inclusion:

1. Patients who underwent Robotic prostatectomy.
2. Male patients.
3. No previous urology related surgery.
4. Severe urinary Incontinence before surgery.

Exclusion:

1. Metastatic diseases.
2. Other co-morbidities which included chronic kidney diseases or cardiac issues.

ACI protocol for post-prostatectomy patients:

According to the protocol followed at Asian Cancer Hospital: Patients were mobilized out of bed with an abdominal binder and ambulated on immediate postoperative day 1 [1]. Later, Kegel's exercise was taught on day 3 which comprised contraction of the PFM in which a patient was advised to draw in the perineal muscles (in case of fast- twitch contract and relax) which was taught on day 3 (with a

catheter in situ). A rest pause of approximately 5 s was maintained between two consecutive repetitions. On day 10 (after catheter removal), the patient was advised to draw in the perineal muscles (in case of slow-twitch contract and hold for 10 s, and progress to 20 s on attaining comfort for performing contractions, for which patients were asked to perform the contraction in case they had an episode of the urgency of urination and could not urinate due to social reasons) and also perform four exercises namely: a posterior pelvic tilt, a pelvic bridge, static adductors, and pelvic rotation. The patient was advised to perform the exercises five times a day, with ten repetitions with a rest pause of 5 s between each repetition of the exercise was suggested. In the 3rd week, progressions of exercise were carried on in the form of a hold which progressed from 10–20 s to 30 s hold time (slow-twitch fibers' recruitment). During this tenure, a few patients had issues comprehending commands or understanding the technique of the PFM contraction. The relatives and patients were therefore instructed to place their hand over the lower abdomen of the patient to attain feedback on the contraction. The patients were thereby expected to continue with the exercises for 6 weeks and note down the reduction in the level of incontinence over this period. Compliance with Kegel exercises was not a major issue, since the feedback of the same was taken via telephonic conversations with the patient themselves. The patients and relatives were found to cooperate and comply with the prescribed protocol.

Outcome measures:

Pelvic floor muscle grading, a 24 h pad test, and an International Prostate symptom scoring were incorporated to assess the reduction in incontinence at 3 weeks and 6 weeks postoperatively.

Pelvic floor muscle grading:

Laycock developed the Modified Oxford Grading System to evaluate the strength of pelvic floor muscles. This is a method used to manually check pelvic floor muscle strength. It is a six-point scale: 0 = no contraction, 1 = flicker, 2 = weak, 3 = moderate, 4 = good (with lift), and 5 = strong. This testing is done in the semi-fowlers position.

24 h pad test (in grams):

The patients were instructed to wear a pad for 24 h. Later, this pad was weighed and the weight was noted in terms of grams.

International Prostate Symptom Score (I-PSS):

The International Prostate Symptom Score (I-PSS) is based on 7 questions concerning urinary incontinence and 1 question concerning quality of life. The urinary symptoms scoring is from 0 to 5 and can range from 0 to 35 (asymptomatic to symptomatic), whereas the quality of life scoring is from 0 to 6.

Questions under urinary symptoms:

1. Incomplete emptying.
2. Frequency.
3. Intermittency.
4. Urgency.
5. Weak stream.
6. Straining.
7. Nocturia.

The scoring is therefore divided as—1–7: Mild, 8–19: Moderate, and 20–35: Severe by the American Urology Association (AUA).

The Who Health Organization (WHO) and the International Union against Cancer (UICC) recommends a single question for the quality of life which states 0 as delighted and 6 as terrible.

Results: A total 69 patients were screened between the duration of 1 year, i.e., 2017–2018, and it was observed that 4 patients had incontinence 3 months post-surgery. On the contrary, 65 patients gained continence.

It was evident that total 69 patients were included in the study, out of which 65 gained continence and 4 patients remained incontinent after the duration of the 6 weeks protocol period.

It is evident that the patients showcased a pelvic floor muscle grading of 2, 3, 4 at the point of catheter removal, 3 weeks and 6 weeks follow-up post-robotic prostatectomy, respectively. Therefore, it was seen that at 6 weeks, the patient has a significant improvement in pelvic floor muscle strength.

it states that the loss of urine due to incontinence using 24 h pad test (in g) was 72, 34, and 12 g at the time of catheter removal, 3 weeks, and 6 weeks follow-up post-robotic prostatectomy, respectively. This means that there was a reduction in the dribbling of urine which was achieved at 6 weeks and came down from 72 to 12 g.

It is seen that the symptom scoring and quality using an International Prostatectomy Symptom Score (IPSS) was found to be 27, 12, and 6 at the time of catheter removal, 3 weeks, and 6 weeks, respectively. Therefore, it was seen, there was an improvement in the quality of life and a reduction in the symptoms related to urinary incontinence.

Conclusion: This study states that there is a definitive effect of early pelvic floor muscle exercises (Kegel's exercises) post-Robotic Prostatectomy in Prostate cancer patients after a span of 6 weeks. The patient regained good pelvic floor muscle strength, a reduction in dribbling, or leakage of urine, and there is an improvement in the quality of life post 6 weeks of robotic prostatectomy. It is also evident that 94.20% of the patients have shown a full recovery or have gained continence by 3 months post-robotic prostatectomy following a regular exercise regime of pelvic floor muscle (Kegel's exercises).

A065. Exploring the New Cancer Care Vital Signs in Geriatric Oncology—An Institutional Pilot Study

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Keywords:

- G8
- geriatric
- oncology
- fatigue
- signs

Aims and Objectives: The present study attempted to identify the new cancer care vital signs among geriatric patients on chemotherapy and the need of framing streamlined screening questionnaires which could be easy to interpret in resource limited set ups.

• *Primary*

1. Prevalence of fatigue and depression among geriatric patients on chemotherapy.

2. Facilitate to construct screening scale swifter and streamlined along with the vital signs in day-to-day practice regularly.

• Secondary

3. Impact of fatigue and depression on WHO -5 wellbeing scale

4. Correlation between fatigue and depression.

Materials and Methods: The present study conducted from July -August 2024 in the Dept. of Medical Oncology at tertiary cancer care academic institution. The study was undertaken as a pilot study to explore the new vital signs among geriatric patients on chemotherapy reported to Medical Oncologist. Based on the eligible criteria, 40 patients were recruited in the study. Descriptive cross sectional study design utilized and the tools used for quantification and evaluation were G8, FACIT-F, GDS and WHO-5 WBS.

Results: The mean age group was 67 years. The most common sites were GI [30%] f/b GY [25%] and Breast/Thoracic [12.5% each]. Males and females constituted in the study were 45% and 55% respectively. The prevalence of severe fatigue as per FACIT-F found to be 77.5% [$n = 31$]. Among the participants, 62.5%{ $n = 25$] found to be depressed on GDS. Prevalence of depression and fatigue were considerably high in female patients compared to males.

Conclusion: Fatigue and Depression are the two most tip of the ice berg symptoms which were primarily missed owing to HCPs or patient barriers. The need to develop screening questionnaires which could be swifter and efficient in resource limited setups.

A066. Clinical Profile and Response to Induction Chemotherapy in Unresectable Head and Neck Cancer Patients Treated Under Arogyasree/PMJAY Scheme in a Tertiary Cancer Center from South India: A Real-World Evidence

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Keywords:
- head and neck cancers
- induction chemotherapy
- response
- toxicity
- radiotherapy
- curative intent

Aims and Objectives: To evaluate the clinical profile and response to induction chemotherapy in unresectable head and cancer patients.

Materials and Methods: Head and neck cancer patients deemed unresectable by MDT with PS:01 were given DCF regimen for 3 cycles and response evaluation was done by RECIST 1.1,toxicity grading by CTCAE 5.0 from the year 2022 to 2024 along with collection of clinicopathological profile data.

Results: Our study population is 36 with a median age of 49 years. Hypopharynx (52.7%) is the common site followed by Oral cavity (41.6%). Stage 4A (50%) is the common stage of presentation followed by stage 4B (47.2%).Statistically significant reduction both T and N size noted after induction chemotherapy, with 18 (50%) patients had partial response, 4 (11.2%) had complete response, 7 (19.4%) had stable disease, 4 (11.2%) had progressive disease, 2 (5.6%) patients died, 1 (2.8%) lost to follow-up. Grade 3 and grade 4 febrile neutropenia is 11.1%. In our study, 78.7% completed planned radiotherapy post-induction chemotherapy.

Conclusion: Hypopharynx had the maximum response, least response rates with oral cavity with manageable toxicities. We had evidenced that with use of induction chemotherapy, patients deemed unfit for curative intent at presentation can be converted to curative treatment.

A067. Oral Metronomic Chemotherapy in Unresectable Locally Advanced or Metastatic Head and Neck Cancers

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Keywords:
- head neck cancer
- metronomic chemotherapy
- quality of life

Background: Metronomic chemotherapy (MC) is an emerging therapeutic option in patients with metastatic and locally advanced head and neck squamous cell carcinoma (HNSCC) patients, who have progressed or are intolerable to Conventional platinum based chemotherapy. The response to platinum-based chemotherapy is minimal with worsened quality of life (QOL). Recently targeted and immunotherapies have been approved in these subgroups, but in resource limited settings MC could be an effective treatment option.

Objective: The aim of the study was to assess the effect of oral MC on changes in quality of life (QOL) in advanced/recurrent HNSCC patients.

Materials and Methods: Patients with advanced, metastatic, and recurrent HNSCC who presented to the Department of Medical Oncology, Government Kilpauk Medical College, Chennai over a span of 1 year were included in the study. QOL assessed with the European organization for research and treatment of cancer (EORTC) QLQ-C30 and QLQ-H&N 35 questionnaires.

Results: In this study, 54 patients were included, while 50% patients had grade 3 or more pain at the time of enrolment, only 5% patients had grade 3 or more pain at the end of 6 months. Mean QLQ-C 30 score at the time of presentation was 68.4. With oral MC, there was a steady increase in QOL score QLQ-C30; 75.35 at 2 months, 81.26 at 4 months, and 85.38 at the end of 6 months. Mean QLQ-H&N 35 score at the time of presentation was 62.50. QLQ-H&N score steadily increases with oral MC; 71.16 at 2 months, 75.43 at 4 months, and 80.69 at the end of 6 months. In subgroup analysis, both QLQ-C30 and QLQ-H&N 35 significantly correlated with disease progression.

Conclusion: The use of oral metronomic therapy with methotrexate, erlotinib and celecoxib significantly improves the QOL and improves pain control in patients with advanced/recurrent HNSCC.

A068. Clinical Application of Circulating Tumor Cells (CTC) in Continuation/Discontinuation of Systemic Treatments in Metastatic Solid Organ Malignancies in Complete Remission: A Single-Center Experience

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Keywords:
- CTC
- NED
- MRD

Aims and Objectives: To evaluate the clinical utility of CTC in decision making for continuation or discontinuation of systemic treatments in metastatic solid organ malignancies with no evidence of disease on serial scans.

Materials and Methods: Patients with metastatic solid organ malignancies with NED on 2 subsequent scans at least 6 months apart, good PS and no disease related symptoms were evaluated with CTC on blood using the CDCSO (Central Drugs Standard Control Organisation, New Delhi) validated Oncodiscover CTC platform (One cell diagnostics labs, Pune). All patients had expressed a wish to discontinue treatment due to concerns related to cost, side effects and QOL. Patients having more than or equal to 1 CTC/1.5 mL blood continued to receive treatment and patients with CTC 0 on 2 subsequent follow-ups 3 to 6 months apart were given the option to stop systemic treatment after informed consent.

Results: 10 patients of metastatic solid organ malignancies (*N*: 10) were analyzed, 5 males and 5 females. Mean age was 55 years (range 36–83 years.) Malignancies identified were breast (5: 4 her 2 positive and 1 TNBC), RCC (2), HNSCC (2), salivary gland (1- her 2 positive). Median duration of NED on subsequent scans 6 months apart before discussion of CTC was 1.5 years. Systemic targeted/immunotherapy types identified were trastuzumab 3 patients (all her 2 positive breast), Pembrolizumab + TKI - 2 patients (both RCC), Pembrolizumab -2 (1 HNSCC, 1 TNBC), TDM-1 (1 Breast and 1 salivary gland), OMCT + Nivolumab -1 (HNSCC). Median number of cycles of therapy received was 29 (range 26-64). CTC clearance led to treatment discontinuation in 1 (10%) patient of HNSCC on OMCT and low dose IO after an informed consent. CTC persistence led to treatment continuation in 8 (80%) patients. Therapy was changed with subsequent progression in 1 patient (10%).

Conclusion: Despite NED and no disease related symptoms, MRD in the form of CTCs were detected in 90% of patients. CTC is an emerging biomarker in precision oncology to counsel patients in need of continuation or discontinuation of systemic treatments having NED on serial scans when there are issues related to cost of treatment and therapy related toxicity. It can identify super responders who are actually in a MRD like state. It has potential to be a sensitive marker in early detection of resistance, disease relapse, and treatment monitoring in future.

A069. Clinical Spectrum of BCR-ABL-Negative (Non-CML) Chronic Myeloproliferative Neoplasms

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Keywords:

- polycythemia vera
- essential thrombocytosis
- primary myelofibrosis
- chronic myeloproliferative neoplasms

Aims and Objectives:

Aim: To study the clinical spectrum of patients diagnosed with BCR-ABL negative (non cml) chronic myeloproliferative neoplasms in a tertiary care center in India.

OBJECTIVE:

To study:

• Clinical.

• Hematological profile in patients with BCR-ABL negative chronic myeloproliferative neoplasms including bone marrow studies.

• Molecular mutations associated with these malignancies.

Materials and Methods:

Study Population: A cross-sectional study was done over a period of 1 year on 30 patients who were admitted in our institute with a confirmed diagnosis of BCR-ABL negative chronic myeloproliferative neoplasms including polycythemia vera (PV), essential thrombocytosis (ET), primary myelofibrosis (PMF), and myelodysplastic syndromes (aCML, CMML, JMML) diagnosed as per their criteria. An informed consent was taken from all the participants.

Inclusion criteria

1. Already diagnosed BCR-ABL negative chronic myeloproliferative neoplasm patients.
2. Age above 18 years.

Exclusion criteria

1. Patients with other co-morbid conditions, histopathological investigations could not be done because of their morbid illness.
2. Patients who fail to give informed consent.

Results: In our study, the most commonly seen malignancy was polycythemia vera. Usual age of presentation between the 5th–6th decade with male predominance. Abdominal discomfort with early satiety was the most common symptom. The proportion of patients having polycythemia were found most commonly in PV followed by ET, whereas the proportion of patients having anemia were more commonly seen in MF compared to other neoplasms. Mutational analysis revealed that JAK2 V617F was the most common mutation that occurred in patients with PV, ET, and MF, followed by JAK EXON 14 and CAL R, the latter occurred more commonly in ET.

Conclusion: Our study outlines the common clinical presentations, hematological profile and mutational analysis in patients with BCR ABL negative chronic myeloproliferative neoplasms.

A070. Clinicopathological Spectrum of a Rare Uterine Malignancy—Uterine Leiomyosarcoma—A Tertiary Care Experience

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Keywords:

- uterine leiomyosarcoma
- spindle cell variant
- myxoid variant

Aims and Objectives: To study the clinicopathological spectrum of uterine leiomyosarcoma at tertiary care center.

Materials and Methods:

Study Population: It is a retrospective study, where data were collected over the span of 8 years from 2016 to 2024 from the available records in our institute and was compiled and processed. During this period, we have had retrieved 15 patients of biopsy proven uterine leiomyosarcoma and their data set was analyzed and has been presented.

Results: The mean age of presentation of uterine leiomyosarcoma in our patient population is 48.7 years and the median is 50 years.

All patients are multiparous women.

About 53% of patients are postmenopausal women.

The most common symptom of presentation is abnormal uterine bleeding which was seen in 9 patients (60%) followed by excessive white discharge per vaginum in 4 patients (26%) and abdominal pain in 2 patients (13.4%).

Upfront metastasis was in seen in 8 patients (53%) and all patients have lung metastasis. One patient had both Lung and bone metastasis.

14 patients had Spindle cell type of leiomyosarcoma and 1 of our patients had Myxoid type of leiomyosarcoma.

Conclusion: Uterine leiomyosarcoma is a rare aggressive uterine neoplasm, more common in multiparous, older patients (>45 years). Since paucity of data on leiomyosarcoma, we are reporting this study, but we need further larger studies to know the disease characteristics and hence aiding timely management to improve the survival.

A071. Outcome and Toxicity with the Use of L-Asparaginase-Free Regimen in Adult Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Prospective Study from a Tertiary Care Hospital in South India

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Keywords:

- adult Philadelphia chromosome-positive acute lymphoblastic leukemia
- L-asparaginase
- Imatinib
- Dasatinib
- thrombosis
- adverse events
- overall survival

Aims and Objectives: To study complete remission rates, event free survival, overall survival and toxicity with the use of L-asparaginase free regimen in adult Ph-positive ALL patients.

Materials and Methods: Patients between the age 15-55 years with Ph-positive ALL (ALL carrying t (9;22) on conventional karyotype, FISH or BCR-ABL positivity on RT-PCR) who were fit and gave consent for intensive chemotherapy were considered for the study. They were treated with BFM-95 protocol with omission of L-Asparaginase and addition of a BCR-ABL TKI: Imatinib/Dasatinib. CR was defined by absence of circulating blasts and <5% blasts on BM examination at end of induction. Failure to achieve CR, Adverse event leading to discontinuation/change of therapy, relapse and death due to any cause were considered as event.

Results: There were 45 Ph-positive ALL patients out of 208 Adult ALL cases (21.6%). Median age was 39 years (15-55 years). 51% of patients were male. 33 patients (73.3%) received Dasatinib, 12 (26.7%) received Imatinib. 34 (75.5%) patients achieved CR, 6 (13.3%) died during induction, 3 (6.7%) had persistence of disease, 2 (4.4%) defaulted treatment. Grade 3-4 adverse events typically associated with L-Asparaginase (Thrombosis, Pancreatitis, Hypersensitivity-reactions) were seen in 1 (2.2%) patient and Hepatic dysfunction was seen in 3 (6.67%) patients. Median duration of follow-up was 18.4 months. 8 patients (17.8%) had relapse. Median EFS and OS were 16.4 and 29.7 months respectively. 2-year EFS and OS were 39% and 54% respectively. 16 (35.6%) patients are in MMR at 2 years and are on TKI maintenance. No patients underwent allogenic HSCT.

Conclusion: The study reveals poor outcomes of Ph-positive ALL patients as compared to western data. However, L-asparaginase omission was not associated with poor survival when compared to published data from India. Achieving MMR earlier was associated with better survival. Utilization of allogenic HSCT could improve outcomes.

A072. Safety Profile of Palbociclib in Geriatric Population (Hormone-Positive, HER2neu-Negative) Metastatic Breast Cancer—Our Institute's Experience

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Aims and Objectives: Advanced breast cancer more prevalent in older patients, very few were included in pivotal trials. This study evaluated the safety of palbociclib in geriatric population group with metastatic breast cancer (Hormone-positive and Her2neu-negative patients)

Materials and Methods: Patients age more than 65 years treated with (Palbociclib 125 mg OD for days 1–21 of each 28-day cycle till disease progression/unacceptable toxicity) plus Endocrine therapy (T. letrozole) for Hormone-positive and Her2neu-negative metastatic breast cancers in our institute, from May 2022 to October 2023. Number of patients was 25. We analyzed safety data with (CTCAEv4.0 criteria) and quality of life using EORTC scale QLQ-C30.

Results: Patient data analyzed from January 2023 to June 2024. Number of patients: 36.

Median age 70.4, of whom 70% presented on adverse events. Most common grade 3–4 neutropenia (56%).

25% patients needed drug dose modifications. No drug-related death.

Conclusion: Palbociclib is well tolerated in geriatric patient comparable to that in younger patients. However, addition of Palbociclib to endocrine therapy shall be evaluated individually in this older and frailer sub groups.

A073. Clinicopathological Profile and Survival Outcomes of Her-2 Low versus Her-2 Negative subsets of Breast Cancer from a Tertiary Care Center in South India

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Keywords:

- breast cancer
- Her-2 Low
- Her-2 Negative

Aims and Objectives: Expansion of Her-2 negative breast cancer into Her-2 low (Her-2 IHC 1+; or 2+ with FISH negative) and Her-2 negative subgroups has unraveled new perspectives in prognostic outlooks and therapeutic options. We have made an effort to look into our experience retrospectively; whether the clinicopathological profile and Survival among Indian patients is the same as in Western literature.

Primary Objective: Clinicopathological profile of Her-2 low and Her-2 negative breast cancer patients in relation to HR status.

Secondary Objective: Survival outcomes of Her-2 low and Her-2 negative breast cancer patients in relation to HR status.

Materials and Methods: Retrospective analysis of Her-2 Low (IHC 0, 1+; or 2+ with FISH Negative) and Her-2 Negative Breast cancer patients treated in our clinic; diagnosed between February 2017 till September 2021. Data cutoff for Survival analysis was till January 2024.

Results: Of the 227 patients; 101 (44%) were Her-2 Low and 126 (56%) were Her-2 Negative. 146 (64%) were HR +ve and 81 (36%) were HR −ve. Median age was 52 years (25-89). Her-2 low patients among HR +ve subgroup were comparatively younger. More of early stage at presentation for Her-2 Negative group. There was no difference for Her-2

status with menopausal status, side of tumor or histological type. Higher grade tumors were observed in the Her-2 Negative group. More Node +ve patients were there in Her-2 Low group. Her-2 Negative status was more associated with HR −ve status as well. Median duration of follow-up was 43 months. Four-year EFS for the entire population was 82% and OS was 95%. Among the HR +ve population, 4 year OS for Her-2 Low subset was 89.8% and Her-2 Negative subset was 100%. Among the HR -ve population, 4 year OS for Her-2 Low subset was 88.9% and Her-2 Negative subset was 100% (*p*-value 0.021).

Conclusion: Her-2 Low subtype is associated with younger population, higher T and N-stage as well as higher grade of tumors. More studies are required to verify this finding and formulate personalized therapeutic algorithms to improve clinical outcomes in these patients.

A074. MicroRNA Expression Profiles in Non-Small Cell Lung Cancer Related Pleural Effusion and Its Prognostic Significance in Treatment Response and Survival Outcome

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Keywords:
- miRNA
- NSCLC
- survival

Aims and Objectives: To study the miRNAs expression pattern in the pleural effusion of non-small cell lung cancer (NSCLC) and to predict the association of baseline miRNA expression pattern with treatment response and survival outcome in patients with stage IV NSCLC.

Primary Objectives: (1) To study the expression pattern of miRNA (miRNA-93, miRNA-100, miRNA-134, miRNA-151, and miRNA-345) in pleural effusion associated with stage IV NSCLC. (2) To study role of above miRNA expression in predicting treatment response.

Secondary Objectives: (1) To study the correlation between the expression of miRNA in pleural effusion with baseline clinicopathological features. (2) To correlate the overall survival (OS) with miRNA expression pattern.

Materials and Methods: This is a prospective study of 29 patients with treatment naive stage IV NSCLC with pleural effusion diagnosed and treated in our center. 10 mL of pleural fluid samples were collected before starting systemic therapy. miRNA expression pattern was analyzed quantitatively in pleural fluid samples using RTPCR method. The data were analyzed using appropriate descriptive statistics.

Results: Of the 29 patients included in the study, 17 were females and 12 were males. Median duration of symptoms were two months. Eight patients were chronic smokers and six were chronic alcoholic. 55% patients were in ECOG PS2 at presentation. Eight patients expired during the study period. Median expression values were miRNA 93–9.4, miRNA 100–11.34, miRNA 134–9.28, miRNA 151– 8.2, miRNA 345–11.15, with maximum expression for miRNA 100 and minimal for miRNA 151. Mirna expression levels at the time of presentation were highly sensitive in predicting mortality with maximum sensitivity of 100% (miRNA 345) and minimum of 62.5% (miRNA 93 and miRNA 151).

Conclusion: Expression patterns of miRNAs are systematically altered in malignant pleural effusion of patients with NSCLC. The five miRNA signature from the effusion may serve as a predictor for the survival of such patients.

A075. Avelumab First-Line (1L) Maintenance for Advanced Urothelial Carcinoma (aUC): Long-Term Outcomes from the JAVELIN Bladder 100 Phase 3 Trial in Patients (pts) with Histological Subtypes

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Aims and Objectives: Avelumab 1L maintenance is the standard-of-care treatment for pts with aUC without progression after 1L platinum-based chemotherapy (PBC) based on results from the JAVELIN Bladder 100 trial (NCT02603432). Approximately 20% of UCs are mixed with other histological subtypes/variants. We report post hoc analyses from JAVELIN Bladder 100 in pts with histological subtypes.

Materials and Methods: Eligible pts with unresectable locally advanced or metastatic UC without progression after 1L PBC were randomized 1:1 to receive avelumab + best supportive care (BSC) or BSC alone. The primary endpoint was overall survival (OS) measured from randomization; secondary endpoints included progression-free survival (PFS) and safety. This post hoc analysis included pts with predominantly UC mixed with <50% histological subtype component.

Results: In the avelumab + BSC and BSC alone arms, respectively, 44/350 and 57/350 pts had histological subtypes. Median follow-up in both arms was ≥38.0 mo (efficacy cutoff, June 4, 2021). In pts with histological subtypes, OS and PFS were prolonged with avelumab + BSC versus BSC alone; median OS (95% CI) was 19.3 (13.6–36.8) versus 14.1 (9.3–24.3) mo (stratified HR, 0.74 [95% CI: 0.44–1.24]), and median PFS by investigator (95% CI) was 4.2 (2.0–7.2) versus 2.0 (1.9–3.5) mo (stratified HR, 0.52 [95% CI: 0.33–0.83]), respectively. Long-term safety (cutoff, April 6, 2023) was generally consistent with results from the overall safety population. In the avelumab + BSC and BSC alone arms, any-grade treatment-related adverse events occurred in 36 (83.7%) versus 1 (1.8%), and were grade ≥3 in 9 (20.9%) and 0, respectively.

Conclusion: Exploratory analyses from JAVELIN Bladder 100 show long-term efficacy and safety of avelumab 1L maintenance in pts with histological subtypes, consistent

with the overall population, supporting the use of avelumab 1L maintenance in this population.

[298/300 words including main body; excludes title and authors]

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A076. Avelumab First-Line Maintenance (1LM) in Advanced Urothelial Carcinoma (aUC): Conditional Survival and Long-Term Safety in Patients (pts) Treated for ≥1 or ≥2 Years in the JAVELIN Bladder 100 Phase 3 Trial

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Aims and Objectives: In the JAVELIN Bladder 100 trial (NCT02603432), avelumab 1LM + best supportive care (BSC) significantly prolonged overall survival (OS) and progression-free survival (PFS) versus BSC alone in pts with aUC without progression after 1L platinum-based chemotherapy (PBC). We report conditional survival estimates and safety in pts treated with avelumab for ≥1 or ≥2 years.

Materials and Methods: Pts with unresectable locally advanced or metastatic UC without progression after 1L PBC were randomized 1:1 to receive avelumab + BSC or BSC alone. The primary endpoint was OS; secondary endpoints included PFS and safety.

Results: Among 350 pts randomized to avelumab + BSC, treatment duration was ≥1 year in 118 (33.7%) and ≥2 years in 68 (19.4%). Pts treated for ≥2 years versus the overall avelumab + BSC arm had higher proportions with prior 1L gemcitabine + cisplatin (64.7 vs. 52.3%), nonvisceral metastases (58.8 vs. 45.4%), and PD-L1+ tumors (64.7 vs. 54.0%). In pts treated for ≥1 year, the probability of an additional 1/1.5 years of OS was 93.2%/86.8%; the probability of an additional 6 months/1 year of PFS was 77.9%/66.7%. In pts treated for ≥2 years, the probability of an additional 1/1.5 years of OS was 95.8%/90.3%; the probability of an additional 6 months/1 year of PFS was 82.9%/66.7%. Among pts treated for ≥1 or ≥2 years, any-grade treatment-related adverse events (TRAEs) occurred after ≥1 or ≥2 years in 50.0% and 35.3%, including grade ≥3 TRAEs in 11.9% and 5.9%, respectively.

Conclusions: Pts with aUC who received ≥1 or ≥2 years of avelumab 1LM had a high probability of surviving for an additional 1 year or more. No new safety concerns were identified. These results further support avelumab 1LM as a standard of care in this population.

Legal entity responsible for the study: Merck (CrossRef Funder ID: 10.13039/100009945)

Funding Statement: This trial was sponsored by Pfizer and was previously conducted under an alliance between Merck (CrossRef Funder ID: 10.13039/100009945) and Pfizer. This analysis was sponsored by Merck. Medical writing support was provided by Katherine Quiroz-Figueroa of Nucleus Global and was funded by Merck.

A077. Avelumab First-Line Maintenance (1LM) for Advanced Urothelial Carcinoma (aUC): Long-Term Patient-Reported Outcomes (PROs) in the Phase 3 JAVELIN Bladder 100 Trial

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Objectives: In the JAVELIN Bladder 100 trial, avelumab 1LM + best supportive care (BSC) significantly prolonged overall survival versus BSC alone in patients with aUC without disease progression after 1L platinum-based chemotherapy, and health-related quality of life was maintained. We report long-term exploratory PRO analyses in the overall avelumab + BSC arm and in patients receiving ≥12 months of avelumab.

Materials and Methods: PROs (secondary endpoint) were assessed at baseline, day 1 of each 4-week cycle, end of treatment/withdrawal, and up to 90 days post treatment. PRO instruments used were National Comprehensive Cancer Network/Functional Assessment of Cancer Therapy Bladder Symptom Index-18 and EuroQol 5 Dimensions 5 Levels. Data were not evaluated in the BSC alone arm because few patients remained on study treatment at later time points.

Results: At data cutoff (June 4, 2021), median follow-up in the overall avelumab arm ($n = 350$) was 38.0 months, and median duration of treatment was 5.8 months. Baseline characteristics in patients treated for ≥12 months ($n = 118$ [33.7%]) were similar to those in the overall avelumab arm, except for a higher proportion with ECOG performance status 0 (70.3 vs. 60.9%) and lower proportion with visceral metastases (47.5 vs. 54.6%). In both populations, completion rates for both PRO instruments among evaluable patients were >80% during treatment. PRO scores generally remained stable; no clinically relevant changes from baseline were reported. Among evaluable patients treated for ≥12 months, ≈75% reported no change or a decrease in being bothered by treatment side effects throughout 24 months of treatment.

Conclusions: Prolonged avelumab 1LM treatment (≥12 months) was associated with stable PROs, indicating preservation in quality of life, further supporting the use of avelumab 1LM until progression or unacceptable toxicity in patients with aUC who are progression-free after platinum-based chemotherapy.

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A078. Avelumab First-Line Maintenance (1LM) for Advanced Urothelial Carcinoma (aUC): Long-Term Outcomes from JAVELIN Bladder 100 in Patients with Low Tumor Burden

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Aims and Objectives: In the JAVELIN Bladder 100 phase 3 trial (NCT02603432), avelumab 1LM + best supportive care (BSC) significantly prolonged overall survival (OS) and progression-free survival (PFS) versus BSC alone in patients with aUC without progression after 1L platinum-based chemotherapy (PBC). Low tumor burden (e.g., non-visceral metastases or lymph node [LN]-only disease) has been associated with better outcomes in patients with aUC receiving immune checkpoint inhibitors. We report exploratory analyses of efficacy and safety in patient subgroups with low tumor burden from JAVELIN Bladder 100.

Materials and Methods: Patients with unresectable locally advanced or metastatic UC without progression after 1L PBC were randomized to receive avelumab + BSC or BSC alone. The primary endpoint was OS; secondary endpoints included PFS and safety. Subgroups included patients with nonvisceral metastases at start of PBC (including bone metastasis) or LN-only disease at randomization.

Results: In the avelumab + BSC and BSC alone arms, 159 patients each had nonvisceral metastases and 51 patients each had LN-only disease, of whom 42 and 35 patients had pelvic/retroperitoneal LN-only disease. At the efficacy data cutoff (June 4, 2021), median follow-up was ≥38 months in both arms. In patients with nonvisceral metastases, LN-only disease, or pelvic/retroperitoneal LN-only disease, median OS with avelumab + BSC versus BSC alone was 31.4 versus 17.1 months (HR, 0.60 [95% CI: 0.45–0.79]), 31.9 versus 22.7 months (HR, 0.86 [95% CI: 0.51–1.47]), and 31.2 versus 20.2 months (HR, 0.72 [95% CI: 0.39–1.31]), respectively. PFS was also prolonged with avelumab + BSC versus BSC alone in all subgroups. Incidences of treatment-related adverse events were similar across subgroups.

Conclusion: Exploratory analyses suggest that avelumab 1LM has pronounced efficacy and a manageable safety profile in patients with aUC who have low tumor burden.

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A079. Right Sided Versus Left-Sided Colon Cancer: Does the Location Matter?

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Keywords:

- right-sided versus left colon cancer
- CEA
- MSI

Aims and Objectives:

Aim: To compare right sided and left sided colon cancers in terms of clinical presentation, prognosis, molecular biology and response to treatment in patients treated at our center.

Objectives: (1) To evaluate the difference in pattern of spread, progression free survival, overall survival, response to therapy and molecular biology between left sided and right sided colon cancer in metastatic setting.

2) To assess the difference in disease free survival, overall survival, response to therapy and molecular biology between left-sided and right-sided colon cancer in curative (adjuvant) setting.

3) To assess the prognostic significance of serum levels of carcino-embryonic antigen in patients at presentation.

Materials and Methods:

Study Design: Single-center retrospective study.

The study sample will be drawn from a database of patients treated in the Department of Medical oncology, at our center between January 2019 to January 2024. We will be using the database to identify all the patients diagnosed with histologically proven carcinoma colon and who were treated at our center.

Results: There were a total of 150 colorectal patients diagnosed and treated at our center during the study time. Out of this, 83 patients were treated with a curative intent and 67 patients had metastatic disease at presentation with a median age at presentation of 59.41 years. In the curative setting we compared the disease- free survival (DFS) between the two sides. We observed that the median DFS was 24.47 months in the right sided tumors and 37.6 in the left sided ones with a *p*-value of 0.96. This disparity was more pronounced in the Stage III tumors. We also analyzed the prognostic significance of CEA value at presentation with a cut-off of 100 ng/mL and it was found that a higher CEA value was associated with a poor prognosis—median DFS of 9.3 months versus 30.83 months with a *p*-value of <0.005.

In the metastatic setting we observed a median PFS of 10 months across the groups (95% CI: 6.0–11.0 months) with left-sided tumors having a median PFS of 11.0 months while the right-sided ones had a median PFS of 7 months (*p*-value 0.83). According to our analysis CEA value at presentation has a prognostic significance with a median PFS of 6 months versus 18 months (*p*-value < 0.005).

Coming to the prevalence of micro satellite instability between the two sides it was observed that right-sided tumors had more incidence of MSI compared to the left-sided ones with a *p*-value of <0.05.

Conclusion: To conclude across all stages of colon cancers right sided tumors are associated with a worse prognosis compared to left sided ones. These cancers differ significantly in the molecular biology also. It was observed that the CEA value at presentation carried significant prognostic importance across all sub-groups. The large CI observed in some results can be explained by the small sample size. The data were analyzed by Cox-regression model also which indicated a strong overall model significance.

This study has shown that right sided and left sided colon cancers behave as two different entities in terms of prognosis and molecular biology. However, further studies with a larger study population and longer follow-up are necessary to look into the clinical implications of these findings.

A080. Toxicity Profile of High-Dose Methotrexate in Adult All Patients and Its Correlation with Serum Methotrexate Levels: A Prospective Observational Study

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Keywords:

- Methotrexate
- toxicities
- serum Methotrexate

Aims and Objectives: To evaluate different toxicities associated with HDMTX and to correlate between serum methotrexate level and toxicities associated with HDMTX at 24, 48 and 72 hours of Methotrexate infusion. To assess the need for serum methotrexate level estimation at 24, 48, and 72 hours, in-patient burden and delay in subsequent treatment due to toxicities.

Materials and Methods: In this prospective observational study, we analyzed 200 cycles of high dose methotrexate in adult ALL patients who received Methotrexate at 5 g/m^2. Acute and delayed toxicities were noted and correlated with serum Methotrexate levels at 24, 48, and 72 hours. We also looked for extended hospital stay and delay in initiation of next cycle due to Methotrexate toxicity.

Results: We observed 77 (34.5%) out of 200 cycles resulted in one or other type of toxicity leading to reduction of doses in 47 (23.5%) cycles. Myelosuppression (20%) and deranged LFT (27%) were the frequent toxicities. Vomiting was the most common GI toxicity (18%) irrespective of dose of methotrexate. Analysis of serum methotrexate levels at 24, 48, and 72 hours was correlated with the toxicities associated with MTX and it was statistically significant. The patients who had Methotrexate-induced toxicities and toxic levels of serum methotrexate had prolonged hospital stay with mean 11.48 days and next cycle was delayed by mean 17.39 days due to delayed ANC recovery.

Conclusion: We concluded toxicities such as myelosuppression, elevation of liver enzymes and direct bilirubin were common, more so in cycles with toxic levels of Methotrexate. Toxicities led to treatment delay, dose reduction and increased length of hospital stay. Early recognition of toxicity can be achieved by measuring serum methotrexate levels and escalation of Leucovorin rescue.

A081. A Novel Cetuximab-Based Quadruplet Regimen Post-DCF Progression in Boderline Resectable Head and Neck Squamous Cell Carcinoma: A Single-Center Experience from India

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Keywords:

- locally advanced head and neck cancer
- cetuximab
- resectable

Aims and Objectives:

Aim: To assess operability in borderline resectable head and neck squamous cell carcinoma post DCF local progression by use of Cetuximab based quadruplet regimen.

Objective: To assess disease response of given/to assess toxicity of quadruplet regimen.

Materials and Methods: This case series involved seven patients with locally advanced HNSCC affecting the oral cavity and soft palate from November 2022 to April2024. Initially, these patients underwent three cycles of docetaxel, cisplatin, and 5-FU, but exhibited disease progression. Subsequently, they were administered Cetuximab 400 mg/m^2 loading dose followed by 250 mg/m^2 weekly, Irinotecan 100 mg day 1 and day 8, Cisplatin 50 mg Day 1 and day 8, Methotrexate 50 mg Day 1, 8 and day 15 of 21 days regimen weekly for 6 to 9 cycles. At the end of treatment PET CT with MRI fusion was done to assess response and patient underwent definitive local treatment.

Results: All patients received locoregional treatment 6 patients in form of surgery with negative margins, tumor downstaging, while 1 patient received definitive CT + RT. We did not observe any Grade 3/4 side effects, most of side effects were of Grade 1 and 2 skin reaction.

Conclusion: With use of this novel Cetuximab-based regimen post-DCF progression, we managed to convert borderline resectable disease to resectable disease, make patient undergo definitive treatment with no adverse grade 3 or 4 effects, only side effects being skin rash which is common is patients receiving Cetuximab. In our experience the above regimen yields positive results. Limitation is retrospective nature and lack of any prospective data of use of Cetuximab in neoadjuvant setting hence larger study is needed.

A082. Efficacy and Toxicities Profile of Cyclin-Dependent Kinase 4/6 Inhibitors in Hormone-Positive, HER2NEU-Negative Metastatic Breast Cancer

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Keywords:

- CDK4/6 inhibitors
- real world
- PIK3CA
- Indian study
- breast cancer

Background: Recently, CDK 4/6 inhibitors such as Palbociclib, Ribociclib, and Abemaciclib have revolutionized the treatment of hormone positive and Her2neu negative metastatic breast cancer. This study evaluated the efficacy and toxicity of these CDK 4/6 inhibitors in such patients at a tertiary center in Gurugram, India.

Objective: The primary objectives were to assess the overall response rate at 3, 6, and 12 months, PFS, and toxicity. The secondary objective was to evaluate OS.

Materials and Methods: This ambispective study at Paras Hospital, Gurugram (India) included patients with hormone-positive, HER2-negative metastatic breast cancer receiving CDK 4/6 inhibitors from September 1, 2022 to June 30, 2024, and retrospectively followed back to January 2017.

Results: In this study of 63 patients, abemaciclib was the most used CDK 4/6 inhibitor (42.9%), followed by palbociclib (36.5%) and ribociclib (20.6%). The mean follow-up was 27.6 months for abemaciclib, 39.3 months for palbociclib, and 43.4 months for ribociclib. Median PFS was 37.9 months overall, 21.9 months for palbociclib, 37.9 months for ribociclib, and not reached for abemaciclib. Median OS was not reached in any group. Better PFS was linked to age >60, postmenopausal status, Ki-67 < 20%, and PR > 70%. Median PFS was 38.6 months for de novo metastasis, 29.8 months for relapsed metastasis, 38.6 months for bone-only, and 34.5 months for visceral metastasis.

In this study, 30 patients (47.6%) progressed after CDK 4/6 inhibitor therapy. Of these, 20 (66.6%) switched to fulvestrant while continuing CDK 4/6 inhibitors, and 10 (33.3%) switched to chemotherapy. The second PFS was unreached in the fulvestrant but was 4.8 months in the chemotherapy. Of the 30 patients with progression, 7 (23%) had PIK3CA mutations, showing a median PFS of 9.1 months, with median OS still unreached.

The three CDK 4/6 inhibitors were generally well tolerated. Among patients on abemaciclib, 70% had anemia (18.5% grade 3–4), 37% had neutropenia, and 25.9% had diarrhea (3.7% grade 3–4). In the palbociclib group, 56.5% had anemia, with 39.1% having neutropenia and 4.3% thrombocytopenia. Ribociclib caused anemia in 53.8%, neutropenia in 69.2%, and grade 3–4 hepatotoxicity in 7.7%. Portal vein thrombosis occurred in 3.7% (abemaciclib) and 7.7% (ribociclib). Dose reductions were needed for 34.9% of patients, including 4.8% due to age over 80.

After 3 months of CDK 4/6 inhibitor treatment, 95.2% had a partial response and 3.2% progressed. At 6 months, 4.9% achieved complete response, 80.3% partial response, and 9.8% progressed. By 12 months, 32.7% had a complete response, 16.3% partial response, and 14.3% showed progression.

Conclusion: In hormone-positive, HER2-negative metastatic breast cancer (MBC), all three CDK 4/6 inhibitors have demonstrated improvements in PFS and OS when combined with hormonal therapy, consistent with pivotal trials. Better PFS was linked to postmenopausal status, age >60, high PR expression (>70%), and low Ki-67 (<20%), while PIK3CA mutations correlated with worse PFS. Continuing CDK 4/6 inhibitors with fulvestrant after progression further improved PFS. Hematological toxicities were manageable, with abemaciclib causing more anemia but less diarrhea compared to findings from the pivotal trials.

A083. Progression from T-Cell Lymphoma to MPAL in MLN-Eo with ETV6-FLT3 Fusion: A Complex Clinical Entity

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Introduction: T-cell lymphoblastic lymphoma is an aggressive hematological malignancy primarily affecting young adults. The potential for transformation to acute lymphoblastic leukemia or mixed phenotypic acute leukemia poses significant challenges in management. This report presents a case of a patient diagnosed with T-LBL who progressed to MPAL, complicating her clinical course.

Case Presentation: A 52-year-old female patient presented with neck swelling, and imaging studies revealed lymphadenopathy above and below the diaphragm. Biopsy results indicated immunoreactivity for CD34, Tdt, CD3, CD5, CD79a, and CD43, along with a high MiB-1 index (95–98%), supporting the diagnosis of stage 3 T-LBL. Bone marrow examination showed no signs of malignancy, and initial hematological parameters were within normal ranges (CBC: 13.5 g/dL, WBC:15,000/µL, platelets: 189,000/µL).

Treatment: The patient was initiated on MCP841 induction therapy, to which she responded favorably. Progression of disease during the first maintenance cycle, the patient presented with increased lymph node size and associated symptoms. CECT imaging revealed significant lymph node enlargement. Hematological investigations indicated a severe alteration in the blood profile: CBC: 5.6 g/dL, 171,000

WBC, 28,000 platelets; PBS: 6% blasts, MDC: 6% blast cells, 50% myelocytes, 18% metamyelocytes,12% polymorphs,6% monocytes, and 8% eosinophils. Bone marrow examination demonstrated strong MPO positivity, with C-Kit (CD117) positivity in myeloid immature cells. Notably, Tdt and CD34 were negative, raising suspicion for acute myeloid leukemia (AML). Lymph node biopsy and immunohistochemistry (IHC) revealed: CD3: Positive CD34: Positive C-Kit (CD117): Negative MPO: Positive CD13: Positive CD10: Negative CD20: Negative CD2: Negative CD4: Positive CD8: Negative Tdt: Negative. These findings were consistent with a diagnosis of Mixed Phenotypic Acute Leukemia (MPAL) with T/myeloid infiltration. Genetic analysis revealed complex chromosomal rearrangements involving chromosomes 1, 11, 12, and 13. Notably, Next Generation Sequencing (NGS) results indicated the presence of the ETV6-FLT3 fusion.

Discussion: The progression from T-cell lymphoma to MPAL is a rare phenomenon, complicated by genetic mutations such as the ETV6-FLT3 fusion, which has implications for the pathogenesis and treatment of the disease. Such transformations highlight the necessity for continuous monitoring and reevaluation of treatment strategies. The presence of the ETV6-FLT3 mutation suggests a common pathway for leukemogenesis, linking the initial T-cell malignancy with evolving myeloid characteristics. The therapeutic implications of this finding remain to be fully elucidated.

Conclusion: This case illustrates the intricate nature of hematological malignancies, showcasing the transition from T-cell lymphoblastic lymphoma to mixed phenotypic acute leukemia characterized by an ETV6-FLT3 fusion. This report serves as a reminder of the complexities involved in diagnosis and management, urging clinicians to adopt vigilant monitoring and comprehensive treatment approaches tailored to the evolving landscape of the disease.

A084. Demographic Profile, Treatment Pattern, and Outcome of Recurrent/ Metastatic Soft Tissue Sarcoma: A Single-Center Experience from Eastern India

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Keywords:

- soft tissue sarcoma
- liposarcoma
- leiomyosarcoma
- outcome

Background: Soft tissue Sarcomas (STSs) heterogeneous group of aggressive malignancy with diverse histology. Although large scale prospective data are lacking, several histology and molecular driven approaches reported in literature. Here we aim to report the pattern of care, response and survival outcome of recurrent/ metastatic STSs treated at our institute.

Materials and Methods: This is a single-center retrospective study at Tata Medical Center, Kolkata. Consecutive patients with recurrent/metastatic STSs treated between 2018 and 2024 were included. Demographic profiles, treatment details and outcomes data were captured from electronic medical records of hospital till July 2024. Those who were treated with curative intent initially and later developed recurrent/ metastatic were also included in this study.

Results: Out of 83 screened patients, 49 patients were eligible for analysis with a median age of 67 years (range 24–72), majority being males (51%) with advanced/metastatic (57%) diseases. Most common site was axial (83.7%) compared to extremities (6.3%). Leiomyosarcoma (65.3%) followed by Liposarcoma (34.7%) was common histology, 18% having grade 3 tumor with 26% positive for MDM2 mutation. Most common site of distant metastases was lung (59.2%). Debulking surgery was performed in 51% of cases. Adriamycin was most commonly (41%) used systemic therapy followed by pazopanib (25%) and palbociclib (20%). The best response to first line therapy was stable disease (41%) followed by partial response (12%). The most common second and subsequent lines of therapies were pazopanib and adriamycin. With a median follow-up of 22 months; median progression free survival was 29 months (95% CI: 5.5–52.41) with median overall survival of 91 months (95% CI: 22.37–159.62).

Conclusions: Although retrospective in nature with small sample size, this study demonstrated potential therapeutic implication and remarkable survival outcome of recurrent/ metastatic STSs treated at a single center from eastern India.

A085. Prostate-Specific Antigen Response with Apalutamide and Its Correlation with Clinical Outcomes in Metastatic Castration Sensitive Prostate Cancer: A Review

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Keywords:

- apalutamide
- metastatic castration-sensitive prostate cancer (mCSPC)
- prostate-specific antigen (PSA) response

Aims and Objectives: To review clinical evidence on PSA response with apalutamide and its correlation with clinical outcomes in metastatic castration-sensitive prostate cancer (mCSPC).

Materials and Methods: An extensive search of clinical studies was conducted through PubMed and Google scholar published in English language between 2021 and 2024 with emphasis on studies that examined PSA response and clinical outcomes with apalutamide in mCSPC.

Results: Total 11 [1 phase-III RCT/10 retrospective (7 abstracts)] studies of apalutamide were included. Post-hoc analysis of phase-III trial demonstrated higher percentage of patients achieving PSA90 (decline $\geq$90%) response and ultra-low PSA ($\leq$0.02 ng/mL) at 3m with apalutamide + ADT (59% and 23%) compared to placebo (13% and 5%). Patients achieving PSA90 response and ultra-low PSA with apalutamide + ADT had longer radiographic progression-free survival (rPFS; HR: 0.44 and 0.28), overall survival (OS; HR: 0.35 and 0.24) and time-to-development castration-resistance (TTCRPC; HR: 0.38 and 0.20). Seven retrospective studies comparing PSA90 response with apalutamide + ADT, abiraterone + ADT and enzalutamide + ADT showed higher percentage of patients achieving PSA90 response with apalutamide + ADT at 3 m and/or 6 m. Difference in PSA90 response between apalutamide + ADT and comparator ranged 7 to 22.8% at 3 m or 6 m. Five (5/7) studies showed median time range of 3.1 to

3.6 m to achieve PSA90 response and two (2/7) studies demonstrated lower risk of death and TTCRPC with apalutamide + ADT at 24 m. Two retrospective studies demonstrated significantly better 24 m survival rate with apalutamide + ADT compared to enzalutamide + ADT and abiraterone + ADT. One retrospective study of apalutamide + ADT showed better OS and rPFS rate in patients achieving PSA levels ≤0.2 ng/mL than patients with PSA >0.2 ng/mL.

Conclusion: Available clinical evidences show that apalutamide + ADT is associated with early rapid and deep PSA decline in mCSPC patients. PSA90 response with apalutamide + ADT seems to be associated with better clinical outcomes compared to abiraterone or enzalutamide in management of mCSPC.

A086. Clinical Profile of Patients with Cancer and Human Immuno-Deficiency Infection, Cross-Sectional Observation Study from a Tertiary Care Cancer Center

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Keywords:
- HIV
- ADC
- NADC
- Cancer
- CD4 count

Introduction: Anti-retroviral therapy has transformed human Immunodeficiency virus infection (HIV) into a manageable chronic condition. The overall profile of cancers in HIV patients evolved with AIDS-defining cancers (ADC) declining and non-ADC remaining constant.

Aims and Objectives: We undertook a prospective cross-sectional observational study with the primary objective to identify the proportion of ADC among total cancers in HIV-infected patients. The secondary objectives were to describe the mean duration of HIV before cancer diagnosis and mean CD4 count in ADC and NADC.

Materials and Methods: Study subjects included a successive series of HIV-positive patients diagnosed with cancer at our center between Jan 2023 and Aug 2024. Relevant clinical information was extracted from electronic medical records.

Results: In the study period, 151 patients were diagnosed with HIV and cancer. The median age was 48 years (SD: 10.1, 19–75). Majority were female (72.19%). Most common cancers were cervix (30.4%), hematolymphoid (17.2%), and breast (17.2%). ADC contributed to 45% of all cancers (68 total, 46 cervical and 22 NHL). Among the NADC, common cancers were breast (17.2%), lung (7.9%), and rectum (3.3%). At diagnosis, 31.1% were metastatic. At cancer diagnosis 21.1% were newly diagnosed with HIV infection. Among those with a prior history of HIV, 86.5% were on HAART and the median duration of HIV infection prior to cancer diagnoses was 6 years (SD 6.49, range 0.08–22). CD4 count was available at cancer diagnosis for 36%. Mean CD4 count at cancer diagnoses in ADC and NADC were 392 and 449 cells/µL, respectively

Conclusion: Cervical cancer was the most common overall and breast cancer was the most common NADC among HIV infected patients. In our single center cohort, ADCs still represent a significant portion of overall cancers among HIV patients.

A087. A Multicentric, Noninterventional, Cross-Sectional Analytical Survey to Understand the Current Practices and Challenges Associated with Graft-versus-Host Disease in India

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Keywords:
- graft-versus-host disease (GvHD)
- treatment guidelines
- adherence to guidelines

Aims and Objectives: Graft-versus-host disease (GvHD) causes substantial social, physical, and psychological burden for patients undergoing allogenic hematopoietic stem cell transplantation (HSCT).[1] While existing guidelines suggest a structured approach, real-world GvHD management practices may vary significantly.[2] The lack of extensive literature underscores the need for further research. This cross-sectional survey was designed to understand the variable management practices in India and adherence to guideline-based recommendations.

Materials and Methods: A multicentric survey (Oct–Nov 2022) using a structured questionnaire was carried out with bone marrow transplant physicians ($n = 33$) from 33

Table 1 Commonly used recommendations in GvHD management

	Acute GvHD		Chronic GvHD	
	Criteria/ recommendations	% Respondents	Criteria/ recommendations	% Respondents
Grading GvHD	Glucksberg	77	NIH 2014	35
	Clinical judgement	20	Clinical judgement	49
	MAGIC	20		
Definition of steroid refractoriness	Guideline	87	Guideline	30
	Clinical judgement	13	Clinical judgement	70

Abbreviations: GvHD, graft-versus-host disease; MAGIC, Mount Sinai Acute GvHD International Consortium, NIH, National Institutes of Health.

Indian centers to understand current treatment practices and guideline adherence in GvHD.

Results: The respondents performed annually an average of 23 allogenic transplants, with a split of 52 and 48% of acute (a) and chronic (c) GvHD, respectively. Only 60% of respondents involved other specialists in co-management of GVHD.

Most respondents (77%) used the Glucksberg methodology, despite Mount Sinai Acute GvHD International Consortium (MAGIC) criteria being more current and detailed for scoring aGvHD severity.[2] Nearly half (49%) used clinical judgment for cGvHD severity, though National Institutes of Health (NIH) 2014 criteria are the widely accepted standard for diagnosis and scoring (**Table 1**).[2]

About 58% of aGvHD and 48% of cGvHD patients responded to steroids, while rest were refractory, dependent, or intolerant to side effects. There was notable reliance (70%) on clinical judgement in cGvHD in defining steroid refractoriness (**Table 1**).

Conclusion: This study underscores the lack of adherence to treatment guidelines. Non-adherence was more common in cGvHD, highlighting the need to simplify complex algorithms for adoption of internationally vetted guidelines in clinical practice.

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A088. Real-World Experience with Immunotherapy in Solid Tumors: A Single-Center Experience from Eastern India

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Keywords:

- immunotherapy
- immune related adverse effects (irAE)
- lung cancer

Aims and Objectives: In the era of immuno-oncology, real-world experience with immune checkpoint inhibitors (ICIs) in solid tumors is an unmet need. We aim to report patterns of care, objective response, immune-related adverse events (irAEs), and survival outcomes in different solid tumors treated with ICIs at our center.

Materials and Methods: This is a single-center retrospective chart review study at Tata Medical Center, Kolkata. Consecutive patients fulfilling eligibility criteria and treated with ICIs as a standard of care between 2020 and 2024 were analyzed. All data collected from electronic medical records of hospitals till July 2024. Histologically confirmed malignancy of solid organs treated with different ICIs (nivolumab, pembrolizumab, durvalumab, atezolizumab, and avelumab) as a standard of practice either in a neoadjuvant, adjuvant, or metastatic setting plus or minus chemotherapy or tyrosine kinase inhibitors were included.

Results: Out of 145 screened patients, 99 patients were eligible for analysis with a median age of 63 years (range 25–86), with the majority being male (81%) with advanced/metastatic (74%) diseases. Lung cancer (56.6%) with adenocarcinoma histology (39.4%) was most common. Among ICIs, the majority of the patients received pembrolizumab (45.5%) followed by nivolumab (26%) in the metastatic setting. 65% received monotherapy, and 30% had PDL1 expression >1%. These ICIs were used mainly in first-line and second-line (82%) settings with an objective response rate of 60%. irAEs was seen in 52% of patients, with the majority being grades 1 and 2. The most common grade 3 irAE was endocrine dysfunction. (8%), colitis (6%) and hematological (4%). With a median follow-up of 49 months, the median PFS of the cohort was 15 months (95% CI: 10.68–19.31) and 32 months (95% CI: 4.3–59.6), with PDL1 >1%. Median OS was 53 months (95% CI: 44.27–61.72).

Conclusion: In developing countries like India, where routine use of ICIs is a major challenge due to cost, access barrier, poor coverage of health insurance, etc., this study showed efficacy, safety, and survival outcomes of ICIs in real-world settings from eastern India.

A089. Updated Results from AVENANCE: Real-World Effectiveness of Avelumab First-Line Maintenance (1LM) in Patients with Advanced Urothelial Carcinoma (aUC) and Analysis of Second-Line Treatment

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Aims and Objectives: Previous results from the non-interventional, ambispective AVENANCE study (NCT04822350) showed the effectiveness and safety of avelumab 1LM in patients with aUC in France. We report updated data and analyses by second-line treatment.

Materials and Methods: Eligible patients had aUC without progression after 1L platinum-based chemotherapy and previous, ongoing, or planned avelumab 1LM treatment. The primary endpoint is overall survival (OS). Additional follow-up and analysis are ongoing.

Results: 595 patients were analyzed. At data cutoff (December 7, 2023), median follow-up was 26.3 months (range, 0.6–43.7); 125 patients (21.0%) remained on avelumab. Reasons for discontinuation were disease progression in 340 patients (72.5%), adverse event in 53 (11.3%), death in 44 (9.4%), and other reasons in 32 (6.8%). 330 patients (55.5%) received second-line treatment after avelumab: chemotherapy in 244 (73.9%), antibody–drug conjugate (ADC) in 62 (18.8%; including enfortumab vedotin, 56 [17.0%]). Characteristics of patients who received second-line ADC or chemotherapy were generally similar; most patients had received 1L carboplatin + gemcitabine (62.3 vs. 63.6%), and had an ECOG performance status of 0/1 (81.6 vs. 82.3%) and metastatic disease at start of 1L chemotherapy (96.8 vs. 95.0%). In the overall population, median OS from start of avelumab 1LM was 21.3 months (95% CI: 17.6–24.6), and 1- and 2-year OS rates (95% CI) were 66.52% (62.53–70.19%) and 45.89% (41.55–50.12%), respectively. In patients who received second-line ADC or chemotherapy, median OS (95% CI) from start of avelumab 1LM was 31.3 months (29.1–not estimable) and 14.4 months (13.2–15.9).

Conclusion: Updated results from the AVENANCE study confirm the effectiveness of avelumab 1LM in a real-world population. In patients with second-line treatment (≈70% of patients who discontinued), a contemporary sequence of ADC after 1L platinum-based chemotherapy and avelumab 1LM treatment showed encouraging OS.

Funding Source: This trial was sponsored by Pfizer and was previously conducted under an alliance between Merck (CrossRef Funder ID: 10.13039/100009945) and Pfizer. This analysis was sponsored by Merck. Medical writing support was provided by Amy Davidson of Nucleus Global and was funded by Merck.

A090. DPyD Polymorphism: Are Indians Different? A Single-Center Experience

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Keywords:
- DpYD
- GI cancer
- gene polymorphism
- chemotherapy toxicity

Aims and Objectives: Mutations of DPyD can result in severe adverse reactions and even death in patients receiving fluoropyrimidines, a common chemotherapeutic agent. The spectrum of mutations and their clinical significance in Indians is not well characterized to date; resulting in unexpected toxicity in many patients.

To describe the spectrum of DPyD mutations in the screened population.

To find causal associations between mutations and possible Treatment Related Adverse Events (TRAE).

Materials and Methods: A Prospective analysis of GI cancer patients who were tested for DPyD deficiency between January 1, 2023 to July 30, 2024, for a period of 4 chemotherapy cycles. The incidence of TRAEs were noted and correlated with DPyD screening result.

Results: Of the 169 cases screened, 150 were analyzed of whom toxicity (any grade) was seen in 54 (36%) patients [Grade III/IV toxicity-20 (13.3%), death-5 (3 in DPD wild type and 2 mutation positive)]. Twenty required hospitalization. Pre-emptive testing was done in 133 and for 17 after toxicity. Mutations were detected in 109 cases (64.4%) of which 34 (22.6%) patients had TRAEs -any grade and 12 - grade III/IV - including 2 deaths (both were poor metabolizers with loos of function mutation). In the remaining 41 wild-type patients, 20 (13.3%) had toxicity (any grade) and 8 (5.3%) - grade III/IV- including 3 deaths. The most common mutation was c. 85T>C DPYD*9A p.C29R ($n = 50$) followed by c.2194G>A DPYD*6 p. V732I ($n = 22$) of whom 40% and 50% had toxicity which did not correlate with CPIC recommendations except in 2 cases. Two patients had non-functional mutations causing death in both.

Conclusion: The spectrum of DPyD mutations in our study seemed different from the Dutch and CPIC databases. The toxicity did not correlate with CPIC recommendations, needing an entirely different dose modification guideline for Indian population.

A091. Clinical Profile and Treatment Outcome of Peripheral T Cell Lymphoma at a Tertiary Care Institute in Western India

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Keywords:
- non-Hodgkin lymphoma
- peripheral T cell lymphomas
- CHOP-based chemotherapy

Aims and Objectives: This study was undertaken to assess the demographics, clinic-pathological characteristics and outcomes of patients with peripheral T cell lymphoma (PTCL) at a tertiary care center in western India.

Materials and Methods: This mixed design cohort study included all patients diagnosed with PTCL from 2021 to 2024 at our study site. The diagnosis of PTCL was made according to the WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues.

Results: A total of 28 patients were diagnosed with PTCL. The median age was 46 years (range 19–76 years) with male predominance (78.6%). The most common subtype was PTCL-not otherwise specified (39.2%), followed by angioimmunoblastic T-cell lymphoma (AITL: 32.1%), and anaplastic large cell lymphoma (ALCL: 25%). One case had Subcutaneous panniculitis like T cell lymphoma. Majority of the patients had Stage III/IV disease (71%). The median overall survival (OS) and event-free survival (EFS) were 32.2 ± 5.1 months and 28.1 ± 5.1 months, respectively. Older age, anaplastic type, higher IPI grading were associated with poor survival.

Conclusion: PTCL is a diverse group of NHL with poor overall outcome compared to their B cell counterparts. Failure

of CHOP-based chemotherapy warrants search for novel and affordable agents for treatment.

A092. Pathological Response Rates after Neoadjuvant Docetaxel, Cisplatin, and 5-Fluorouracil-Based Regimen in Squamous Cell Carcinoma of Esophagus: Experience from a Tertiary Cancer Center in North-East India

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Keywords:
- pathological response rates
- neoadjuvant chemotherapy
- docetaxel
- cisplatin
- 5-fluorouracil
- esophageal cancer

Aims and Objectives:

Primary Objective

To evaluate complete pathological response rate after neoadjuvant chemotherapy in patients with squamous cell carcinoma esophagus.

Materials and Methods:

Study Design: Prospective single arm observational study.

Selection of patients: Histologically confirmed cases of squamous cell carcinoma esophagus planned for neoadjuvant docetaxel, cisplatin, and 5-fluorouracil (DCF) based chemotherapy.

Results: An interim analysis was performed on 22 patients fulfilling the criteria between November 2020 to August 2021. These patients were planned for docetaxel, cisplatin, and 5-fluorouracil (DCF) based neoadjuvant chemotherapy. Eventually 17 patients who underwent surgery were included in the analysis for pCR rates.

Pathological response rates are analyzed according to modified Ryan score.

Complete response is seen in four ($n = 4/17$; 23.5%) patients, one patient ($n = 1/17$; 5.7%) had near complete response, partial response in eight ($n = 8/17$; 47.05%) patients and poor response in four ($n = 4/17$; 23.5%) patients.

The correlation of pathological response with the clinicodemographic profile of patients and various risk factors associated with esophageal cancer have been studied.

Conclusion: Esophageal cancer is the fifth leading cause of cancer deaths in India and majority of esophageal carcinoma in developing countries are of squamous cell carcinoma histology.

Improvement in R0 resection rates and pathological complete response rates with the addition of taxane to cisplatin and 5- fluorouracil has made the NACT with triplet DCF-based regimen an acceptable option in preoperative setting in locally advanced SCC of esophagus.

A093. ROS-1 Rearrangements in Non-Small Cell Lung Cancer: Biology, Diagnostics and Therapeutics: A Case Series

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Keywords:
- lung
- adenocarcinoma
- ROS-1
- FISH
- immunohistochemistry
- NGS
- rearrangement

Aims and Objectives: *ROS-1* rearrangement is found in 0.9–2.6% of non-small-cell lung cancers (NSCLCs). Many methods have been utilized for the detection of *ROS1* rearrangements, including IHC, FISH, RT-PCR, and NGS. This review is a discussion on the present and futuristic diagnostic scenario of *ROS1* identification in lung cancer along with its management.

Materials and Methods: This is a retrospective analysis of all advanced NSCLC patients who were >18 years at the age of diagnosis, ECOG 0-2 and had ROS1 rearrangement. Patients registered at State Cancer Institute, Guwahati from January 1, 2021 to December 31, 2023 were included. Prior history of malignancy or treatment for malignancy, synchronous malignancies were not exclusion criteria.

Results: Seven patients, with stage IV non-small cell lung cancer, were included. One patient presented with synchronous malignancy of ovary with ROS1 positive lung cancer. Median age at presentation was 52 years, 5 out of 7 patients (71.4%) were females; all the patients were nonsmokers. Three patients were diagnosed by IHC which was later confirmed by FISH, one was diagnosed by FISH upfront, and the rest of the three patients were diagnosed by NGS (two patients had CD 74 fusion partner and one had SDC4 fusion partner). Most common histopathology was adenocarcinoma ($n = 5$, 71.4%). Most common site of metastasis was pleura (31.3%) followed by brain (25%) and skeleton (18.8%). Targeted therapy (crizotinib) was given in six patients, out of which two patients progressed ; seventh patient (patient with synchronous carcinoma ovary) was started on chemotherapy. Four out of seven patients expired, fifth patient defaulted; sixth patient is continuing crizotinib and seventh patient is on chemotherapy.

Conclusion: Currently, crizotinib, repotrectinib, and entrectinib are approved for ROS1 tumors; however, ceritinib and lolartinib have already showed good clinical efficacy too. The molecular characterization of individual ROS1-positive NSCLC patients may offer a unique tool for the development of therapies adapted to the molecular profile of each of these patients.

A094. Outcome of Neo-adjuvant Chemotherapy in Locally Advanced Gall Bladder Cancer: An Overview from a North-Eastern Cancer Care Center

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Keywords:
- locally advanced gall bladder cancer
- pathological complete response
- neo-adjuvant chemotherapy
- R0 resection

Aims and Objectives:

Primary Objective: To estimate R0 resection rate after neo-adjuvant chemotherapy (NACT) in locally advanced gall bladder cancer (GBC).

Secondary Objectives: To determine pathological complete response (pCR) rate and disease-free survival (DFS) rate at 1 year.

Materials and Methods: Study Design: retrospective observational study conducted between January 1, 2022 to December 31, 2023.

Selection of patients: histologically proven cases of locally advanced gall bladder cancers (T2-4, N0-1, M0) who received at least 3 cycles of neo-adjuvant chemotherapy were selected.

Results: Majority patients belonged to age group of 40 to 58 years with M: F ratio 2:3. Most common histopathological type was adenocarcinoma (95%). Most common chemotherapy regimen used was Gemcitabine plus Cisplatin (GC). Compliance to chemotherapy was 100%. Radiological response was observed in 84% of patients. Overall resection rate was 79% with R0 resection achieved in 93% of patients, while 21% patients were inoperable post-NACT. Pathological complete response was observed in 27% of patients, whereas partial response was seen in 40% patients. One-year DFS rate was 60%. Twenty percent patients each had local and distal recurrences.

Conclusion: NACT in locally advanced GBCs is feasible which benefited at-least 2/3rd of the patients who eventually had a R0 resection. In absence of the sufficient data to support routine use of NACT in advanced GBC, further research in the form of RCT should be conducted to quantify the benefit of NACT in this subset of patients.

A095. The Role of Molecular Tumor Boards in Establishing Precision Oncology Services in a Tertiary Care Center in India

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Keywords:

- medical tumor board (MBT)
- germline
- somatic

Backgrounds: Precision oncology, which tailors' cancer treatment based on individual genetic and molecular profiles, has emerged as a transformative approach in modern cancer care. However, the implementation of precision oncology in community-based cancer centers, particularly in low- and middle-income countries like India, remains limited due to a lack of specialized expertise and resources. This study aimed to assess the impact of establishing a precision oncology service through the implementation of Molecular Tumor Boards (MTBs) on cancer care outcomes in a tertiary care center in India. Precision oncology, which tailors' cancer treatment based on individual genetic and molecular profiles, has emerged as a transformative approach in modern cancer care. However, the implementation of precision oncology in community-based cancer centers, particularly in low- and middle-income countries like India, remains limited due to a lack of specialized expertise and resources.

Aims and Objectives: This study aimed to assess the impact of establishing a precision oncology service through the implementation of Molecular Tumor Boards (MTBs) on cancer care outcomes in a tertiary care center in India.

Materials and Methods: A prospective observational study was conducted over eight months at a tertiary care center in India. All cancer patients aged 18 years and above who underwent genetic testing during the study period were included, while those with incomplete clinical histories were excluded. MTBs were conducted monthly, with meeting times scheduled based on the availability of patient genetic reports. The MTBs consisted of multidisciplinary teams, including oncologists, pathologists, and geneticists, who reviewed genetic profiles and provided personalized treatment recommendations.

Patient confidentiality was maintained throughout, and informed consent was obtained from all patients prior to MTB discussions.

Results: A total of seven MTBs were organized over the eight-month period, during which genetic reports from 68 patients were reviewed. The average age of the patients was 51 years, with 82.4% female and 17.6% male. Breast cancer was the most common diagnosis (58.8%), followed by lung, ovarian, colon, and endometrial cancers. Of the 68 patients, 31 underwent germline testing and 37underwent somatic testing. Actionable outcomes, defined as treatment changes or the initiation of targeted therapies, were identified in 13 of the 31 patients with germline testing, while 18 were recommended for further testing or treatment. Among the 37 patients with somatic testing, actionable outcomes were identified in 17 cases, and 20 patients were recommended for additional testing or treatments. Most recommendations focused on altering treatment regimens, with a smaller number of patients advised to pursue further genetic testing or continue observation.

Conclusion: The implementation of MTBs in a tertiary care center in India significantly contributed to the delivery of personalized cancer care, resulting in actionable treatment changes for a substantial proportion of patients. These findings underscore the potential of MTBs to bridge the gap between advanced molecular diagnostics and routine clinical practice, promoting the broader adoption of precision oncology in community-based cancer centers.

A096. NLR as a Prognostic Indicator for Outcomes in Head and Neck Cancer Patients: A Retrospective Record-Based Cohort Study

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Keywords:

- head and neck neoplasms
- lymphocytes
- neutrophils
- prognosis
- survival analysis

Aims and Objectives: (1) To assess the threshold for NLR among patients with primary head and neck cancer. (2) To identify factors associated with high NLR. (3) To evaluate survival outcomes of the study cohort and the associated variables.

Materials and Methods: This retrospective record-based cohort study includes 1,471 primary head and neck cancer patients with pre-treatment NLR values and follow-up data. The primary end point is overall survival (OS). Threshold for NLR was determined using an outcome-based method by maximizing log-rank test statistic and survival differences. Chi-square test of independence was used to study the associations. Logistic MVA identified factors associated

with high NLR. The Kaplan–Meier method and log-rank tests were performed to evaluate survival outcomes. Cox multivariate analysis (MVA) identified the variables associated with survival outcomes.

Results: 58.9% patients had high NLR, among which the proportion of males was larger. Among high NLR patients, the following variables show a significant difference in proportion: gender, smoking status, site of cancer and "N" stage. The median survival for NLR strata is 63.4 months (low) and 61.07 months (high). The difference in survival rate was significant for the factors: high NLR, smoking, age, site, CT regimen, metastasis, and recurrence.

Conclusion: Patients with substantial disease burden were likely to have high NLR, and this marker was associated with bad survival. Further evidence on NLR as a prognostic marker, will enable delineating at-risk patients and tailoring of interventions.

A097. A Retrospective Study of Pegaspargase in Pediatric Patients with Acute Lymphoblastic Leukemia

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Keywords:

- acute lymphoblastic leukemia
- pediatric ALL
- pegaspargase
- side effects

Aims and Objectives: To evaluate the clinical profile of pegylated *Escherichia coli* asparaginase (pegaspargase) in terms of treatment-related side effects in pediatric patients with ALL.

Materials and Methods: This retrospective study included pediatric patients with ALL who were treated at the Pediatric Hemato-Oncology Center in Hyderabad from January 2019 to December 2022. The medical records of patients aged 18 years and below, with a diagnosis and treatment for ALL, were accessed. Patients treated with intramuscular/intravenous pegaspargase (2,500 IU/m^2) for ALL were included in the study. Patient demographic characteristics and disease status were documented. The adverse events with the use of pegaspargase were also noted.

Results: A total of 300 patients with ALL were included in the study. The majority of patients were aged <10 years (65.7%). Most of the patients were male (58%). B-cell ALL was the predominant immunophenotype in 253 patients. As per the National Cancer Institute (NCI) criteria, 192 patients had standard-risk ALL. Bacterial/fungal infection was the most common manifestation in 25.7% of patients. Allergic reactions were observed in 15% of patients. Thrombosis was noted in 19 patients, while 18 patients experienced fatigue. Other side effects included hypertension ($n = 13$), hyperglycemia ($n = 11$), and pancreatitis ($n = 8$).

Conclusion: Pegaspargase holds promise as a vital therapeutic agent in the treatment of pediatric ALL, with most adverse events being manageable and reversible.

A098. Real-World Outcomes of Induction Chemotherapy with Cetuximab (Erbitux) in Indian Patients with Locoregionally Advanced Head and Neck Cancer

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Aims and Objectives: Locoregionally advanced squamous cell carcinoma of head and neck (LA SCCHN) are often aggressive. Induction chemotherapy (ICT) with Docetaxel/cisplatin/5-FU (TPF) is the current preferred regimen but is associated with toxicities including hematological and cardiovascular. With this real-world data (RWD) analysis, we evaluated the efficacy and safety of cetuximab with chemotherapy as ICT for LA SCCHN.

Materials and Methods: In this single-center (HCG Aastha Cancer Institute, Ahmedabad, India), retrospective, RWD; LA SCCHN patients receiving induction cetuximab based regimens was collected from February 2023 to June 2024. We evaluated efficacy (response rates [ORR]) and safety.

Results: Data from 46 patients with median age of 54.5 years (range 24–83 years) was analyzed. Majority of patients were males (89.1%), with a performance score of 0 (10.8%), 1 (84.78%), and 2 (4.34%). The sites included: oral cavity (76.08%), oropharynx (8.69%), hypopharynx (10.87%), and larynx (2.34%). TPE regimen included docetaxel + cisplatin + cetuximab (54.34%) or paclitaxel + carboplatin + cetuximab (4.34%). Other regimen combinations included cetuximab + methotrexate (19.56%), cisplatin + irinotecan + methotrexate + cetuximab (19.56%) and irinotecan + methotrexate + cetuximab (2.17%). Treatment was given as (1) upfront cetuximab regimen ($n = 24$), or (2) Cetuximab post-TPF progression ($n = 14$), or (3) recurrent (amenable to curative treatment) with/without prior platinum exposure ($n = 8$). ORR was 89.13% in overall population, 87.5% in upfront cetuximab regimen, 92.3% in cetuximab post TPF, and 8 (100%) in recurrent patients (amenable to curative treatment). The adverse events noted were, mucositis (71.73%), skin reactions (67.39%), diarrhea (26.08%), febrile neutropenia (6.52%) and IRR (infusion-related reaction) (2.17%). Patients achieving a response were amenable to receive curative surgery or CTRT.

Conclusion: Our RWD shows that ICT with cetuximab when administered before surgery/radiotherapy induces high primary site response and is tolerable in LA SCCHN patients.

A099. Germ Cell Tumor in AYA: An Institutional Experience

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[2]*Institutional Ethics Committee*

Keywords:

- AYA
- GCT

Aims and Objectives: Germ cell tumor (GCT) is a common cancer among adolescents and young adults (AYAs) with high cure rate but with significant long-term morbidity like fertility issue. This study reviews the experience of GCT in AYA group treated at a single center of South Tamil Nadu.

Materials and Methods: Patients diagnosed as of GCT in the age group of 15 to 39 years during the year 2021 to 2022 were included in the study. Clinical presentation, stage, treatment details and outcome at 2 years of follow-up we recorded by reviewing the medical records.

Results: The study included 27 AYA GCT cases, representing 7.35% (27/367) of all AYA cancers during that

period, out of which 92.59% (25) were males and 7.41% ($n = 2$) were females. Median age was 28 years (range 17- 39 years). 2 female GCT patients had dysgerminoma of ovary presented in the stage III. 88% ($n = 22$) of male GCT cases presented with testicular mass while 2 patients presented with mediastinal GCT (8%) and 1 patient presented with retroperitoneal GCT. NSGCT was the most common histology ($n = 21$) followed by pure seminoma ($n = 4$). Among the male GCT cases, 72% ($n = 18$) presented in stage III while 20% ($n = 5$) in stage II and 8% ($n = 2$) in stage I GCT. Most common 1st line chemotherapy used was BEP regimen followed by EP. All patients were counselled for semen analysis and sperm banking before the start of chemotherapy, however only 45% ($n = 12$) patients underwent semen analysis, all of the had oligospermia and 16% ($n = 4$) of them underwent sperm banking. The 2 years OS was 91.4% for seminoma while it 75.3% for NSGCT.

Conclusion: Advanced stage of the disease is more common in our center which may be related to lack of awareness of the disease and ignorance among AYA due to various socioeconomic issues.

A100. Observational Study of Synchronous Oligometastatic Lung Cancer Presenting in Our Tertiary Care Hospital and Their Outcome

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Background: The treatment of oligometastatic lung cancer is evolving post the emergence of local therapies like surgery and local ablative therapies. But a number of patient and disease related factors influence the treatment patterns and decision making. The responses for various approaches and treatment related toxicities are not extensively studied. In this study we attempted to study these aspects of care.

Aims: The aim of our study is to analyze the incidence, prevalence, progression-free and overall survival of patient of oligometastatic disease at our center. To study the pattern of care given at our center.

Materials and Methods: We did a retrospective, single-center, non-interventional study at the thoracic department in tata memorial center, Mumbai. We enrolled patients aged 18 years or older with oligometastatic non-small cell carcinoma lung. We have done a systematic review of the clinical histories of patients diagnosed between January 2023 and December 2023. The responses were evaluated using Response Evaluation Criteria in Solid Tumors, version 1.1 and efficacy and safety analyses were done in all the patients.

Statistical Analysis: Descriptive statistics was performed. Progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan–Meier survival analysis.

Results: Between January 2023 and December 2023, 62 patients were enrolled into the study. Of the 62 patients, 29 had brain metastasis. Of these 29 patients, 18 received brain directed therapy with 8 receiving it in curative intent and 10 received it in palliative intent. In total 14 patients were treated with curative intent. At the time of the primary analysis (median follow-up: 10.9 months), 32 of 62 patients with measurable disease at baseline had a confirmed partial response; thus, the proportion of patients achieving an objective response was 51.6% and 7 patients had stable disease while 8 had progressive. Adverse events were predominantly grade 1 or 2, with an overall good tolerance profile. The most common severe (grade 3/4 events) adverse event is hyponatremia in 8 patients followed by neutropenia in 7 patients. But febrile neutropenia was noted in only 2 patients. The median OS at the time of final analysis was 19.95 months while the PFS is 15.47 months

Conclusion: The pattern of care in oligometastatic disease can be curative but this depends on multiple patient and disease related factors. With emerging data and the advent of immunotherapy and targeted therapy better outcomes can be seen.

A101. Analysis of Delay in Initiation of Chemotherapy after Admission to Day Care Unit of Tertiary Cancer Institute

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Keywords:
- chemotherapy
- daycare unit
- delay in initiation of chemotherapy

Aims and Objectives: To perform a survey to identify the causes for delay in initiation of chemotherapy after admission in a day care unit at National Cancer Institute

Materials and Methods: A survey of admitted patients for elective chemotherapy was conducted for three months 1/1/2021 to 31/3/2021 in day care chemotherapy units in National Cancer Institute, Nagpur. Time taken for various processes from the time of patient's arrival in the ward till the time of initiation of chemotherapy was noted. The difference in time between process was analyzed.

Results: 16% chemotherapy were started within one hour of admission, 37% within 2 hours, 25% within 3 hours, and 22% chemotherapy were initiated after 3 hours.

Conclusion: Reducing waiting time between patient admission and initiation of chemotherapy is a big challenge in any cancer institute due to involvement of multiple processes, department, and people. It directly affects operations, bed occupancy and turnaround time daycare center, and ultimately patient satisfaction.

Identifying the causes for delay and application of lean techniques will optimize the time taken for initiation of chemotherapy and improve patient satisfaction.

A102. Study: Role of Lenvatinib Multitargeted Tyrosine Kinase Inhibitor as Neoadjuvant Therapy in Locally Advance Invasive Thyroid Cancer

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Keywords:
- lenvatinib
- differentiated thyroid cancer
- poorly differentiated thyroid cancer
- head and neck cancer

Aims and Objectives: Role of lenvatinib multiple tyrosine kinase inhibitor as neoadjuvant therapy in locally advance invasive thyroid cancer to reduce tumor burden, enabling previously impossible surgeries and reduced the surgical morbidity.

Materials and Methods: Lenvatinib instituted in patients of DTC and PDTC. Intent: Neoadjuvant, palliative in recurrent and metastatic unresectable DTC, systemic induction prior to nonsurgical local therapy/RAI—continue as maintenance therapy. Do not include recurrent or residual

disease who receive lenvatinib. Exclude the anaplastic thyroid carcinoma and medullary thyroid carcinoma.

Results: $N = 5$, starting dose: 24 mg, had to be stepped down to 14 to 18 mg in 3 patients. Pediatric patient started on 8 mg dose. Response rate: treatment with neoadjuvant intent shows 5/6 patients had PR. 4 have received surgery. Common toxicities (all grades): diarrhea, mucositis, fatigue. Hypertension in 2. Pediatric patient had hand foot syndrome. Duration: 8 to 12 weeks (median: 10 weeks). Change in Surgical Morbidity Complexity Score (SMCS): decrease in SMCS score from 3 to 1 in 4 patients and 4 to 1 in 1 patient. Survivals: in neoadjuvant group, 1 nodal recurrence—salvage surgery done. Estimated 18 month PFS. Induction followed by maintenance group—2 disease progression/new-onset met. 1 death.

Conclusion: As we all know thyroid malignancy is chemotherapy and radiotherapy insensitive. Neoadjuvant Lenvatinib is a promising option in those DTC/PDTC who have no specific mutations. Improves resectability and decreases morbidity. Results from the ongoing Phase II trial might pave way for a paradigm change in management of these cancers or disprove its rationale. Neoadjuvant Lenvatinib is not an escape route for lesser resections.

A103. Assessment of Cell-Free DNA (cfDNA) as a Biomarker in Colorectal Malignancies: A Longitudinal Observational Cohort Study

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Keywords:
- cell-free DNA
- colorectal malignancies
- cfDNA dynamics

Aims and Objectives: Globally, cfDNA and circulating tumor DNA (ct-DNA) have gained recognition in colorectal malignancies, for prognostic evaluation, MRD assessment, and guiding therapy decisions. However, data on cfDNA from India remain limited. We aimed to quantify baseline cfDNA and understand the association of their clinicopathological features and survival with cfDNA and its dynamics.

Materials and Methods: We recruited 51 patients with newly diagnosed CRC. Cohort A had patients with curative intent ($n = 29$), while Cohort B included patients with palliative intent ($n = 22$). 5 mL blood was collected in EDTA tubes at two-time points: baseline (Sample 1) and post-therapy (Sample 2). Sample 2 was collected either at the end of neoadjuvant therapy or 24 hours post-surgery in cohort A. In cohort B, sample 2 was collected after 3 months of first-line therapy. cfDNA was isolated using the Maxwell-RSC-ccfDNA isolation kit and quantified using SYBR-Green real-time-PCR of the beta-globin gene. No intervention was planned on cfDNA levels

Results: Baseline characteristics of all 51 patients are shown in **Table 1**. Mean baseline cfDNA levels were 1.63 × 2.91 ng/µL. No significant association was observed between TNM stage, node positivity, histology, CEA, and baseline cfDNA levels. Baseline cfDNA levels did not show a significant association with clinical response (**Table 2A, B**), progression-free survival (PFS), or overall survival (OS).

Longitudinal samples (1 and 2) were available for 15 patients. We found fair concordance between cfDNA dynamics (rise or fall) and clinical response except for 4 discordant responses (**Table 3**). The possible reason for discordant responses could be attributed to analytical failures. cfDNA responders had a trend toward improved PFS and OS ($p = \text{NS}$).

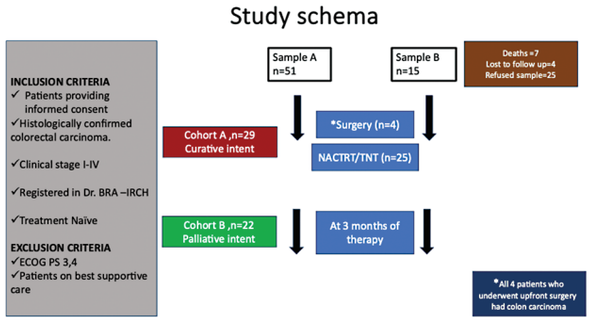

Fig. 1 Study schema.

Table 1 Baseline characteristics

Characteristics	*n* (%)
Total patients (*n*)	51
Age (years), median (IQR)	44 (18–71)
Gender	
Males	31 (60.8%)
Females	20 (39.2%)
TNM stage	
I and II	7 (13.7%)
III	19 (37.2%)
IVA	9 (17.6%)
IVB and IVC	16 (31.3%)
Tumor (T) stage	
T1/T2	7 (13.7%)
T3	20 (39.2%)
T4	24 (47.1%)
Node (N) stage	
N0	9 (17.6%)
N1	18 (35.3%)
N2	21 (41.2%)
N3	3 (5.9%)
Metastasis (M) stage	
M0	26 (51%)
M1	25 (49%)
Histology	
Well-differentiated	4 (7.8%)
Moderately differentiated	23 (45.1%)
Poorly differentiated	24 (47.1%)
dMMR	3 (5.8%)
RAS/RAF mutation	2 (3.9%)
Her2 expression	1 (2%)
CEA (ng/mL), median (IQR)	34 (3.8–94)

Table 2A Clinical response versus baseline cfDNA: cohort A[a]

(Response evaluated in 23 patients)			
	Baseline cfDNA < 1.63 ng/μL ($n = 19$)	Baseline cfDNA ≥ 1.63 ng/μL ($n = 4$)	
CR/PR/SD ($n = 17$)	13	4	$p = 0.26$ (Fisher's exact)
PD ($n = 6$)	6	0	

[a]4 patients of ca colon who underwent upfront surgery are not included in this analysis.

Table 2B Clinical response versus baseline cfDNA: cohort B

(Response evaluated in 20 patients)			
	Baseline cfDNA < 1.63 ng/μL ($n = 15$)	Baseline cfDNA ≥ 1.63 ng/ μL ($n = 5$)	
PR/SD ($n = 9$)	8	1	$p = 0.22$ (Fisher's exact)
PD ($n = 11$)	7	4	

Table 3 Clinical response versus cfDNA dynamics[a]

	Fall in cfDNA ($n = 7$)	Rise in cfDNA ($n = 7$)	
PR/SD ($n = 9$)	6	3	$p = 0.26$ (Fisher's exact)
PD ($n = 5$)	1	4	

[a]1 longitudinal sample post-surgery is excluded from this analysis.

Conclusion: There was no significant association between baseline cfDNA and clinicopathological profile. cfDNA dynamics were concordant with clinical response in colorectal malignancies, with the exception of four discordant responses.

A104. Case Report: First Use of Lutetium 177 FAPI 2286 Therapy in Relapse Refractory Ewings Sarcoma.

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Keywords:

- Ewings sarcoma
- PNET

Aims and Objectives: First use of Lutetium 177 FAPI 2286 therapy in relapse refractory Ewings sarcoma.

Materials and Methods: The patient's clinical history, presenting symptoms, physical examination findings, diagnostic workup including imaging studies (e.g., MRI, CT scan), histopathological examination of biopsy specimens, and treatment modalities (surgery, chemotherapy, radiation, PRRT) are comprehensively reviewed and discussed. Follow-up data including response to treatment and any complications are also included.

Conclusion: We describe a rare case of relapse refractory Ewings Sarcoma after 6 years of remission and first use of PRRT (first use of Lutetium 177 FAPI 2286 therapy) in metastatic Ewings sarcoma post multiple lines of chemotherapy.

A105. Limited Duration of Brentuximab Vedotin in Relapsed Refractory Hodgkin's Lymphoma: A Long-Term Single-Center Experience

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Keywords:

- Brentuximab vedotin
- limited dosing
- Hodgkin lymphoma

Aims and Objectives: Brentuximab vedotin (BV) has shown better outcomes compared to chemotherapy in relapsed/refractory Hodgkin's lymphoma (r/rHL) with all international trials using a 16 or more dosing schedule. The financial toxicity of this dosing schedule in Indian setting has limited its use in this setting.

With this study we aim to analyze long-term outcomes of r/rHL treated with limited duration BV.

Materials and Methods: Patients from January 2013 till December 2023 with r/r HL who received BV from a single center were included, to study survival outcomes and toxicities.

Results: 11 patients received single agent BV at 1.8 mg/kg/dose every 3 weeks. Median age was 32 years (16–57 years) with 6 females (54.5%) and 5 males. All were pretreated with multiple lines of chemotherapy, immunotherapy ($n = 2$), and prior autologous BMT history ($n = 3$).

All patients received maximum of 6 cycles of BV. Overall response rate was 100% with all achieving complete remission (CR) in 3 cycles. 4 patients underwent autologous BMT while in CR. 2 patients relapsed after BV at 15 and 32 months, respectively.

At a median follow-up of 5 years in the entire cohort, mPFS was not reached. 5-year PFS rate was 75%, and 5-year OS rate 100%. The longest duration of response is 126 months with this patient still in CR till date.

Common toxicities were neutropenia, peripheral neuropathy and fatigue (grade 1 or 2). No dose reductions were required.

Conclusion: Our long-term analysis showed that in r/r HL, just 6 cycles of BV showed remarkable and durable response, translating into prolonged survival. Limited dosing would bridge the cost benefit gap, especially in our financial constraint settings. BV has become our preferred regimen in r/r HL at our center. Future studies to define the ideal sequence of BV versus immunotherapy in Indian patients are needed.

A106. The Power of HER in Lung Cancer

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Keywords:

- Her2neu mutation
- lung cancer
- trastuzumab deruxtecan

Aims and Objectives: Her2neu alteration (which includes mutation, amplification, overexpression) is an upcoming target of interest in metastatic non-small cell lung cancer (mNSCLC), especially with the remarkable results seen with trastuzumab deruxtecan.

In this study we aim to analyze her2neu alterations in mNSCLC from a single center and study their outcomes.

Materials and Methods: Patients with her2neu alterations on NGS testing (blood/tumor) were analyzed from March 2019 till December 2023. Median DoR (duration of response) with each her2neu agent and OS (overall survival) was calculated.

Results: 10 patients (3.12%) from a total of 320 mNSCLC were identified. The median age was 63 years (46–93 years) with majority male (6, 60%). 9 had adenocarcinoma subtype and 1 adenosquamous.

All Her2neu alterations were detected on comprehensive NGS testing. Tumor NGS was used in 7, and blood NGS in 3 patients. Her2neu mutation at exon20 was seen in 7 (70%), Her2neu amplification in 3 (30%), and 2 had both.

All patients received at least one Her2neu directed therapy—trastuzumab, trastuzumab emtansine (TDM1) and trastuzumab deruxtecan (TDxd). 8 patients received trastuzumab + chemotherapy in first line, with all patients achieving partial response. This led to a DoR of 8 months (95% CI: 0.98–15.0). 3 patients received TDM1 as second-line therapy with a DoR of 3 months (95% CI: 1.4–4.6). TDxd was given in later lines for 3 patients (all with her2neu mutation) and gave a DoR of 5, 17, and 28 months.

Median OS of entire cohort was 20 months (95% CI: 12.8–27.2).

Conclusion: Her2neu alterations are seen in 3 to 4% of mNSCLC and targeting this with anti-her2neu therapy has shown benefit. Our analysis showed that sequential use of anti-her2neu therapy led to a significant OS of 20 months. Trastuzumab + chemotherapy in first line gave a better DoR compared to historical cohorts with chemotherapy alone. The remarkable efficacy of TDxd even in refractory setting is exciting and warrants a search for Her2neu by comprehensive NGS testing in mNSCLC.

A107. Analysis of Mechanisms of Resistance in Patients Progressed on EGFR-Directed Therapy in Metastatic NSCLC in Indian Population

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Background: *EGFR* (epidermal growth factor receptor) mutations are noted in about 30% cases of non-small cell carcinoma lung (NSCLC) in the Indian population. EGFR directed targeted therapy is effective in the metastatic NSCLC leading a prolonged progression free survival and overall survival. But emergence of resistance in these cases is seen over the period. The pattern of resistance and the difference in the pattern between targeted therapy alone setting and in combination with chemotherapy was not well studied.

Aims: The aim of the present study was to analyze the pattern of resistance in EGFR mutated NSCLC in Indian population. We also studied the difference in the pattern of resistance between patients treated with EGFR directed TKIs alone and when combined with chemotherapy.

Materials and Methods: This was a *post hoc* analysis of the randomized, open-label, phase III study that compared Gefitinib with Gefitinib plus chemotherapy in patients with advanced NSCLC with activating *EGFR* mutations in the first-line setting. These patients were regularly followed up. In patients having progression, either biopsy, if not possible, cell block if any tappable fluid or liquid biopsy were done. Then histopathological analysis and EGFR RTPCR were done.

Statistical Analysis: Descriptive statistical analyses were used. Fisher's exact probability test was done to note the significance in the difference of T790M mutation between the two arms.

Results: 275 patients had disease progression out of the 350 patients and 206 of these 275 patients were available for final analysis. Following the analysis, T790M was noted to be the most common mode of resistance being noted in 30% of the patients followed by loss of sensitizing mutation in about 28%. When the patterns of resistance in the individual arms were analyzed separately, the emergence of T790M as a pattern of resistance was more in the gefitinib alone arm compared to the chemotherapy plus gefitinib arm, 38% versus 19% (Fisher's exact probability test, p =0.008). The analysis of the Gefitinib arm revealed new resistant mutation in 44 patients with T790M being seen in 43 and S768I in 1 patient. New sensitizing mutation was noted in 5, loss of prior sensitizing mutation was seen in 21 patients. Rest 49 available for analysis in this arm retained the prior *EGFR* mutation. In the Gefitinib arm, 17 patients had new resistance mutation all being T790M, 1 had new sensitizing mutation, 29 had loss of previous sensitizing mutation, and rest 40 retained their original mutations. Histological transformation was noted as a pattern of resistance in 6% with transformation to small cell carcinoma being noted in 4.5%.

Conclusion: The emergence of T790M was lesser compared to the prior studies, but the prior studies predominantly used EGFR TKI alone. When analyzed separately T790M was more in the TKI alone arm compared to combination of TKI and chemotherapy. More over histological transformation and the loss of sensitizing mutations highlight the importance of repeat biopsy and molecular analysis in guiding further therapy.

A108. Real-World Experience with Immunotherapy in Stomach and GE Junction Cancers

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Keywords:

- immunotherapy
- metastatic gastric/GE junction tumors
- biomarkers

Aims and Objectives: Introduction of immunotherapy (IO) in metastatic G/GE junction (mG/GE) cancer improves PFS and OS as per internation trial data.

Aim: To analyze outcomes with IO in mG/GE adenocarcinoma.

Materials and Methods: An analysis of all mG/GE Adenocarcinoma patients who received nivolumab/pembrolizumab in any line between January 2019 and June 2023 was done. The end points for this study were PFS, OS, and safety.

Results: 39 patients received IO (nivolumab 79.5%, pembrolizumab 20.5) with majority males (30, 76.9%) and median age of 68 years. Molecular profile showed 20.5% ($n=8$) were MMR deficient (dMMR), 51.3% ($n=20$) PDL1 positive and 2 Her2neu positive.

64.1% ($n=25$) received IO in first-line and in later lines in the rest ($\pm$ chemotherapy). Average IO doses were 10. At a median follow-up of 18 months, PFS was 12 (95% CI: 2.6–21.4) and OS 17 months (95% CI: 5.4–28.5).

In dMMR patients ($n=8$), median PFS and OS were not reached, with PFS and OS rates at 24 months being 56 and 62%, respectively. MMR proficient ($n=31$) population showed PFS of 12 (95% CI: 2.6–21.4) and OS of 17 months (95% CI: 0.1–35.1). PDL1+ve patients ($n=20$) showed a PFS of 12 months (95% CI: 14.1–19.8) with OS not reached.

Most common adverse effects were hypothyroidism, fatigue, and skin toxicity; with three patients having grade 3 side effects (pneumonitis and hepatitis).

Conclusion: Our experience with IO is similar to clinical trial data and better than historical datasets. Remarkable survivals in dMMR subgroup emphasizes importance of looking for MMR deficiency. PDL1-positive subgroup fared better than PDL1 negative, highlighting its importance. Better biomarker selection is essential for maximum benefit with immunotherapy in G/GE cancers

A109. Case Report and Literature Review: Long Clinical Remission with Nivolumab and Nivolumab beyond Progression in a Heavily Pretreated Case of Relapsed Refractory Classical Hodgkin's Lymphoma

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Keywords:
- relapsed Hodgkin's lymphoma
- refractory Hodgkin's lymphoma
- immunotherapy
- nivolumab
- brentuximab vedotin
- salvage chemotherapy
- PD-1 inhibitor
- classical Hodgkin's lymphoma
- autologous stem cell transplantation (ASCT)
- complete metabolic remission

Aims and Objectives: To report a case of successful treatment in a patient with relapsed/refractory classical Hodgkin's lymphoma (CHL) using immunotherapy after failure of multiple lines of chemotherapy and to review relevant literature on reinduction regimens in and prognostic factors.

Materials and Methods: We described the treatment course of a case with primary refractory classic Hodgkin lymphoma and discussed different options for salvage therapy, with an emphasis on immunotherapy. We searched PubMed for all published clinical trials investigating immunotherapy in classic Hodgkin lymphoma. The reference list of each identified paper was searched for additional publications.

Results: Our patient was salvaged with anti-programmed cell death 1 (PD-1) antibody with brentuximab vedotin (BV), a CD30-directed antibody–drug conjugate. We identified five one-armed phase II trials investigating anti-PD-1 therapy in first relapse/refractory disease in a total of 254 patients aged 9 to 71 years, of which one included 31 children. The complete remission rate before high-dose chemotherapy was 59 to 95% overall and 67 to 89% among those with refractory disease.

Conclusion: Although it remains to be proven in randomized trials, anti-PD-1 therapy may provide higher complete response rates than traditional chemotherapy. Anti-PD-1 therapy has the potential to increase the chance of cure while decreasing the risk of late effects from chemotherapy and radiotherapy.

A110. A Retrospective Analysis of Tolerance and Survival Outcomes with Perioperative FLOT in Gastric and GE Junction Tumors

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Keywords:
- FLOT chemotherapy
- gastric cancer
- pCR
- toxicities

Aims and Objectives: Aim of this study was to evaluate the efficacy, safety, and outcomes of FLOT chemotherapy in gastric and GEJ cancer patients, focusing on treatment response, adverse effects, and survival rates.

Materials and Methods: This retrospective study examined 65 patients with gastric or gastroesophageal junction cancer treated with FLOT chemotherapy from 2016 to 2023. Clinical data were collected from EMR. The study assessed adverse effects, surgery rates, pathologic complete response (pCR), recurrence, and survival.

Results: In this study of 65 patients, 53 (81.5%) were male, and 12 females (18.5%). Majority (63.1%) were PS 1. 63% had comorbidities, with diabetes (60.9%) and hypertension (46.3%) being the most common. Majority were stage III disease (72.3%), with 55.4% had T4 tumors. Tumor locations included proximal involvement (52.3%), body of the stomach (21.5%), and distal involvement (26.2%). Adenocarcinoma was the primary histology (70.8%), 17 patients had poorly cohesive, including signet cell histology (26.2%).

DPD mutation testing showed high risk in 16.9%. 92.3% completed four cycles of neoadjuvant chemotherapy (NACT). Adverse effects of any grade were experienced by 75.4%, fatigue (55.4%) and anemia (52.3%) being the most frequent, Grade 3–4 were 46.1%. Radiological responses showed partial response in 47.7%, while 10.8% had a complete response. Surgery was performed on 84.6% of patients, with 15.4% achieving pCR. Two patients died due to postoperative complications. Adjuvant chemotherapy within 4 weeks of surgery was administered to 60% of the patients. Overall, 53.8% of the cohort completed 8 cycles of FLOT. The median follow-up was 45 months. 3-year median overall survival (OS) rate was 81.5%, and the median progression-free survival (PFS) rate was 61.5% at 2 years. Recurrence rates were 16.9% for local recurrence and 26.2% for distant metastasis. 12 patients (18.5%) died during the study period, while 11 were lost to follow-up.

Conclusion: In comparison to other FLOT studies, this study showed similar pCR rates and improved tolerability with lower Grade 3–4 adverse effects. Recurrence, death, and postoperative mortality rates were consistent with other trials. The higher OS and PFS in this study likely reflect differences in patient demographics and follow-up duration,

affirming FLOT's efficacy. This study demonstrates that FLOT chemotherapy provides effective outcomes in gastric and gastroesophageal cancers.

A111. To Evaluate Outcomes and Tolerability of Triple Metronomic Chemotherapy with Low-Dose Immunotherapy and Axitinib in Resource-Constraint Settings in Cases of Unresectable, Recurrent, and Metastatic Head and Neck Squamous Cell Carcinomas

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Aims and Objectives: To compare outcomes of combination of triple oral metronomic chemotherapy and Axitinib with low-dose nivolumab in patients of locally advanced unresectable, recurrent, and metastatic carcinoma of the oral cavity in resource constraint situations. Primary end point of the analysis is PFS. Secondary end points were OS and response rates. Adverse events during the course of treatment were monitored as per CTCAE v5.

Materials and Methods: 167 patients with unresectable advanced, recurrent, or metastatic oral cavity cancers were retrospectively studied from April 2022 till August 2023 who received a combination of triple oral metronomic chemotherapy with Axitinib and low dose nivolumab until disease progression or unacceptable toxicity. Out of 167 patients, 132 patients actually received OMCT IA.

Results: With median follow-up period of 20 m, 6 m PFS, and 7 m OS was observed in this study with ORR rates of 37.9% (50 patients). Most common grade 3 or more adverse events noted were skin rash, hyponatremia, and transaminitis. 36% of the patients required dose gap or modification in view of adverse events. Most common grade 1 and 2 adverse events were anemia, hyponatremia, skin rash, mucositis, and transaminitis. 21% patients who initially received low-dose immunotherapy later stopped in view of resource constraints. In 5 (3.8%) patients, immunotherapy was stopped in view of adverse events.

Conclusion: OMCT IA is relatively well tolerated with fair survival outcomes in cases of unresectable, recurrent, or metastatic head and neck squamous cell carcinomas. Further prospective studies are required to further evaluate any benefit with the addition of oral VEGF inhibitor.

A112. The Role of Molecular Tumor Boards in Establishing Precision Oncology Services in a Tertiary Care Center in India

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Keywords:
- medical tumor board (MBT)
- germline
- somatic

Aims and Objectives: This study aimed to assess the impact of establishing a precision oncology service through the implementation of molecular tumor boards (MTBs) on cancer care outcomes in a tertiary care center in India.

Materials and Methods: An 8-month prospective observational study at a tertiary care center in India included cancer patients aged 18 and older who underwent genetic testing. Monthly Molecular Tumor Boards, featuring oncologists, pathologists, and geneticists, reviewed genetic profiles to offer personalized treatment recommendations. Patient confidentiality and informed consent were maintained, and all recommendations were documented.

Results: Over an 8-month period, seven multidisciplinary tumor boards (MTBs) reviewed genetic reports for 68 patients with an average age of 51 years (82.4% female, 17.6% male). Breast cancer was the most prevalent diagnosis (58.8%), followed by lung, ovarian, colon, and endometrial cancers. Of the 68 patients, 31 received germline testing and 37 underwent somatic testing. Actionable outcomes, such as treatment changes or the initiation of targeted therapies, were identified in 13 of the 31 patients with germline testing, with 18 recommended for further testing or treatment. Among the 37 patients with somatic testing, actionable outcomes were found in 17 cases, and 20 were advised to pursue additional testing or treatments. Most recommendations involved altering treatment regimens, while a smaller number suggested further genetic testing or continued observation.

Conclusion: Implementing MTBs in a tertiary care center in India notably enhanced personalized cancer care, leading to actionable treatment changes for many patients. This underscores MTBs' potential to integrate advanced molecular diagnostics into routine practice and supports broader adoption of precision oncology in community-based centers.

A113. A Tiger Man in Disguise: A Case Report

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Keywords:
- extramedullary plasmablastic transformation (EPT)
- multiple myeloma
- tiger man appearance

Aims and Objectives: Extramedullary plasmablastic transformation (EPT) is an aggressive form of multiple myeloma which occurs due to hematogenous spread. It can be seen in 10% of patients with myeloma. Discordant EPT in a patient with bone marrow in morphological remission is rare occurrence. We are reporting a case in view of its rarity and diagnostical dilemma it triggered.

Materials and Methods: A 71-year-old male with IHD presented with renal failure in February 2022. On evaluation, he was diagnosed with multiple myeloma. M band was positive, IgG was elevated to 2426. PETCT revealed only a single lesion in pubis and cytogenetics came out as deletion of chromosome 13. He was treated with VTD chemotherapy and once in remission he was continued on Thalidomide and Dexamethasone maintenance. 8 months later he presented with right epididymo-orchitis and b/l hip pain. His infection improved with antibiotics, but he had persistent b/l hip pain with generalized body ache. He was suspected of having myeloma relapse and a SPEP along with immunoglobulin and light chain assays were done, all of which came back negative. Bone marrow aspiration showed that marrow is in morphological remission.

Results: PETCT revealed diffuse uptake at multiple sites. There was interval resolution in the lytic lesion in the old sites; however, multiple new onset bony lytic lesions and multiple soft tissue deposits were noted involving various organs, skin and skeletal muscle—showing a tiger man appearance on PETCT. To solve the diagnostic dilemma, a biopsy was taken from the pectoral lesion which had the maximum SUV which was p53 and C-MYC positive and Ki 67 of 90%.

Thus, a diagnosis of extramedullary plasmablastic transformation in a known case of myeloma was made on histopathology

Conclusion: EPT in myeloma is rare entity. Extramedullary involvement in conjunction with prior or concurrent multiple myeloma, albeit uncommon, is often associated with poor clinical outcome. Multiple genetic mutations have been linked to its development. It has an aggressive clinical course and a median survival of 4.5 months after survival.

Tiger man appearance in PETCT is classically described in muscular sarcoidosis. But EMD presenting in this manner has not been reported in literature so far.

A114. Clinicopathological and Survival Outcome in Male Primary Mediastinal Germ Cell Tumors: A Decade Experience

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Keywords:

- PMGCT
- mediastinal seminoma
- mediastinal NSGCT

Aims and Objectives: To analyze the clinicopathological characteristics and survival outcomes of primary mediastinal germ cell tumor treated at our center.

Materials and Methods: It was a single-center, retrospective, observational study of patients with PMGCT, treated at our institute from January 2011 to December 2021. After obtaining approval from the Ethics committee, patient demographics, tumor characteristics, and details of treatment and survival were retrieved from case records. A total of 25 PMGCT cases were analyzed. Kaplan–Meier method was used to estimate progression-free survival (PFS) and overall survival (OS).

Results: Out of 855 male patients diagnosed with GCT in the study period, 25 had PMGCT (2.9%). The median age was 26 years (13–40). 56% had ECOG performance status (PS) $\geq$3. Superior vena caval obstruction syndrome (SVCS) was the presenting symptoms in 9 (36%) patients. Seminoma and nonseminomatous GCT were seen in 10 (40%) and 15 (60%) patients, respectively. Among mediastinal seminoma, 3 (30%) patients were good risk and 7 (70%) patients were intermediate risk. 50% received Bleomycin, Etoposide, Cisplatin (BEP) and 30% received Etoposide, Ifosfamide, Cisplatin (VIP) chemotherapy. Post-chemotherapy 30% patients had partial response (PR) and at 5 years overall survival is 100%. Among mediastinal nonseminomas all were high risk. The most common histology was mixed GCT (40%), followed by teratoma (30%) and yolk sac histology (25%). 70% received BEP and 30% received VIP. After chemotherapy 25% had progressive disease and 67% had partial response. At 5 years of follow-up, 55% patients were alive. Peripheral neuropathy has been seen in 32% patients, while 8% had fertility issues and 1 patient had a bleomycin induced pulmonary toxicity.

Conclusion: Primary mediastinal germ cell tumor is a rarer entity comprising nonseminomatous histology predominantly. When compared to testicular counterpart, mediastinal seminoma has a similar outcome. However mediastinal nonseminomatous GCT presented in advanced stage and had a poor response to therapy as well as poor prognosis. There is a need for further research to improve outcomes in nonseminomatous PMGCT.

A115. Primary Pulmonary Choriocarcinoma: A Case Report

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Keywords:

- choriocarcinoma
- primary pulmonary choriocarcinoma
- lung neoplasms
- lung cancer
- chemotherapy

Aims and Objectives: Primary pulmonary choriocarcinoma (PPC) is an extremely rare and aggressive form of malignancy that originates within the lung parenchyma, rather than metastasizing from a primary site such as the reproductive organs. These tumors are characterized by the production of β-hCG and often present with non-specific respiratory symptoms.

The non-specific symptoms and rarity of this condition can lead to significant delays in diagnosis and initiation of appropriate treatment. While there is no standard treatment, PPC is typically managed according to choriocarcinoma guidelines. However, PPC has lower response to therapy and poorer prognosis as compared to gestational choriocarcinoma.

Materials and Methods: A case reported in Safdarjung Hospital, Delhi of a **38-year-old female**, gravida 2 para 2 (G2P2), with no history of smoking presented with sudden-onset, progressive chest pain radiating to the axilla. The pain was associated with intermittent breathing difficulty. Initial evaluation with a chest X-ray revealed a lung mass.

Subsequent serum tumor marker assessment showed an elevated LDH level of 443 U/L and a markedly elevated βhCG level of 198,898 mIU/mL. A PET-CT scan performed at the time of diagnosis demonstrated a large ($10.4 \times 9 \times 12.7$ cm) hypermetabolic ($SUV_{max} = 9$) mass in the upper lobe of the right lung. The mass extended into the posterior mediastinum, abutting the trachea, right main bronchus, right pulmonary artery, and superior vena cava. It also abutted the paravertebral structures posteromedially. Additionally, multiple FDG-avid mediastinal lymph nodes were observed, with the largest in the anterior mediastinum measuring 1.5×1.4 cm ($SUV_{max} = 2.8$). Right supraclavicular and infraclavicular lymph nodes measuring 1.5×1 cm ($SUV_{max} = 1.6$) were also noted.

A **biopsy** of the lung mass confirmed the diagnosis of choriocarcinoma. Immunohistochemical staining showed tumor cells positive for CK7 and βhCG, and negative for CK20, Napsin, MUC5AC, and Oct3/4.

The patient received four cycles of cisplatin and etoposide chemotherapy.

A repeat PET-CT scan performed after the completion of chemotherapy revealed a **partial response** to treatment. The right upper lobe lung mass had decreased in size to $6.3 \times 4.2 \times 8.3$ cm ($SUV_{max} = 1.4$). Notably, no enlarged FDG-avid mediastinal lymph nodes were observed. Serum tumor marker assessment showed a decrease in LDH to 201 U/L and a significant reduction in βhCG to 3.47 mIU/mL. The patient is currently continuing chemotherapy in view of partial response.

Results: Comparison of serum markers and tumor characteristics before and after administration of four cycles of chemotherapy.

Comparison of pre- and posttreatment PET scan suggestive of partial response.

	Pretreatment	Posttreatment
S. LDH	443 U/L	201 U/L
βhCG	198,898 mIU/mL	3.47 mIU/mL
Size of primary	10.4 × 9 × 12.7 cm	6.3 × 4.2 × 8.3 cm
SUV_{max} of primary	9	1.4
Mediastinal lymph nodes	Multiple	None

This case highlights the diagnostic and therapeutic dilemmas posed by PPC, emphasizing the need for a high index of suspicion and a multidisciplinary approach.

Conclusion: Primary pulmonary choriocarcinoma is a rare and challenging malignancy with a dismal prognosis. Early diagnosis, prompt initiation of multimodality treatment, and exploration of novel therapeutic strategies are crucial for improving patient outcomes. Further research is imperative to enhance our understanding of the disease biology, identify prognostic markers, and develop more effective treatment modalities for this aggressive malignancy.

A116. Effects of TP53 Mutation on Tumor Biology of Triple-Negative Breast Cancer

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Keywords:
- TP53 mutation
- tumor grade
- Ki67 proliferation index
- clinical stage
- pathological prognostic stage
- nodal involvement
- retrospective study

Aims and Objectives: To assess association between TP53 mutation and various disease parameters in TNBC, including tumor grade, Ki67 index, clinical (cT and cN) and anatomic stages, pathological and clinical prognostic stages.

Materials and Methods: We conducted a retrospective analysis of 27 TNBC patients. Biopsy slides and blocks were examined for TP53 mutation using immunohistochemistry.

Results: TP53 mutations were found in 19 patients (70.4%), suggesting higher prevalence in TNBC.

• Tumor Grade: TP53-mutated patients had significantly higher percentage of high-grade tumors (88.9% with grade 3) than mutation-negative patients (50.0%, $p = 0.030$).

• Ki67 Proliferation Index: Higher percentage of TP53 mutation-positive patients had Ki67 >30% (73.7%) compared to mutation-negative patients (50.0%) ($p = 0.482$).

• cT Stage: TP53-mutated cases had higher percentage of advanced cT stages (21.1% in stages 3 and 4) than unmutated (12.5%), suggesting more advanced disease in TP53 mutation-positive cases.

• cN Stage: TP53 mutation-positive patients had lower percentage of cN stage 0 (47.4%) and higher percentage of cN stages 2 and 3 (15.8%) compared to those without TP53 mutations (62.5 and 12.5%, respectively) ($p = 0.769$) indicating more advanced nodal involvement in TP53 mutation-positive patients.

• Pathological Prognostic Stage: TP53-mutated patients had higher percentage in stage 3 (36.4%) compared to mutation-negative patients (100% in stages 1 and 2) ($p = 0.119$), suggesting potential association with more aggressive disease.

• Clinical Prognostic Stage: TP53-mutated patients had higher percentage in advanced stages (57.9% in stages 3 and 4) compared to mutation-negative patients (37.5%) ($p = 0.333$).

• Anatomic Stage at Diagnosis: TP53-mutated patients had higher percentage in stages 3 and 4 (36.8%) compared to mutation-negative patients (25.0%) ($p = 0.551$).

Conclusion: TP53 mutations are significantly associated with higher tumor grades, trend towards increased Ki67 proliferation, more extensive nodal involvement and higher stages. These findings highlight TP53 mutations' role in influencing tumor aggressiveness and disease progression, underscoring need for further research.

A117. Real-World Outcomes for Maintenance Avelumab Treatment in Indian Patients with Locally Advanced/Metastatic Urothelial Cancer

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Keywords:
- Avelumab
- real-world data
- urothelial carcinoma

Aims and Objectives: Avelumab maintenance after first-line platinum-based chemotherapy (1L PBC) in locally advanced/metastatic urothelial cancer (UC) has shown overall and progression free survival benefit in the JAVELIN Bladder 100 trial. We analyzed demographics and real-world outcomes from Indian patients receiving avelumab maintenance.

Materials and Methods: Retrospective patient record review was carried out for patients treated with avelumab maintenance. Survival outcomes were established using the Kaplan–Meier method.

Results: In total 42 patients (median age 64 years, range 33–83) were included, of which 81% were male and 19% were female. Lower tract UC was documented in 24 (57.1%), upper tract UC in 7 (16.7%), and 11 patients had missing data for site of UC. The 1L PBC given to the patients was: gemcitabine-cisplatin 17 (40.5%), gemcitabine-carboplatin 22 (52.4%), and ddMVAC 3 (7.1%). After 1L PBC, 11.9% had a complete response, and 59.5% had a partial response. Patients then proceeded to maintenance avelumab treatment with 4 to 6 weeks of completion of 1L PBC 23 (54.5%) and <4 weeks in 11 (26.2%) patients. The median duration of avelumab maintenance was 6 months; with an ORR of 16.7%, 4 patients had a complete response and 3 had a partial response. The median OS was not reached; the 12-month OS rate was 82.1%. The median PFS was 5 months (95% CI: 2.3–7.6) and in patients who received avelumab for >6 months the mPFS was 11 months (95% CI: 6.2–15.8). At the data cut-off 7 patients had expired and 20 patients were still ongoing treatment with avelumab maintenance. Physician determined tolerability to was considered good in 60% of the patients.

Conclusion: Our multi-center Indian real-world data confirms that avelumab maintenance treatment is well tolerated, and its efficacy data are consistent with previously reported clinical studies.

A118. Adoption of Biosimilars in Clinical Practice: A Survey

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Keywords:

- biosimilars
- data
- prescriber perspectives

Aims and Objectives: Biosimilars have made treatment accessible for patients globally and in India. Simultaneously concerns have been identified regarding the data released by biosimilars. We wanted to understand the prescriber perspectives on biosimilar adoption.

Materials and Methods: An online survey, regarding the adoption and biosimilar prescription in India was conducted from July to August 2024.

Results: We received 52 responses (Medical Oncologists, 46; Radiation Oncologists, 5; and Surgical Oncologist, 1). Most utilized biosimilars in practice; responses to the percentage of patients who received biosimilars in their clinics—0–20% patients, 20–40% patients, 40–60% patients, and >60% patients had 9, 12, 13, and 18 respondents, respectively. Reasons determining the use of biosimilars was similar efficacy (36%), similar safety (27%), similar pharmacokinetics (PK, 21%) and studies in all indications (16%). Respondents emphasized on the presence of endpoints such as overall survival, response rates, progression free survival, safety, and PK as decision-making factors before considering biosimilars. With reference to a noninferiority study design, 24 respondents (46%) stated that a biosimilar should not be considered if they do not report efficacy as per the per-protocol and intention to treat analyses; while 17 respondents (33%) were unsure. Most respondents mentioned that the biosimilar adoption will be impacted if its efficacy parameters barely fell with the predefined noninferiority range of ±20% (33 respondents, 63%) or crossed predefined range for PK (36 respondents, 69%); and that they will not extrapolate indications in the absence of trial data (34 respondents, 65%). The confidence of using a biosimilar before the release of full-text publication was documented as low (40 respondents, 77%). Most respondents mentioned low adoption of biosimilars in the presence of differences observed in physico-chemical structure and/or impurities (40 respondents, 77%) and clinical data (39 respondents, 75%).

Conclusion: Our survey has revealed prescriber perspectives on the adoption of biosimilars in clinical practice.

A119. Indian Real-World Data of Avelumab + Axitinib (A + Ax) in Advanced Renal Cell Carcinoma (aRCC)

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Keywords:

- axitinib
- avelumab
- immunotherapy
- renal cell carcinoma
- retrospective study

Aims and Objectives: In the phase 3 JAVELIN Renal 101 trial in patients with advanced renal cell carcinoma (aRCC), objective response rate (ORR) and progression-free survival (PFS) were significantly improved in patients treated with first-line avelumab plus axitinib (A + Ax) versus sunitinib. Here we evaluate real-world outcomes with first-line A + Ax in Indian patients with aRCC.

Materials and Methods: In this multicenter, noninterventional, retrospective study, clinical chart data from patients with aRCC treated with first-line A + Ax were reviewed. Endpoints included ORR and PFS per investigator assessment.

Results: Data from 20 patients (16 males; median age, 57 years) were analyzed. Median duration of treatment was 8.9 months (range, 3.2–29.7) and the median follow-up was 12 months. The most common metastatic site was the lung (14 patients) followed by bone (10 patients). International Metastatic RCC Database Consortium (IMDC) risk category was favorable, intermediate, or poor in four, 10, and four of patients, respectively—with missing data for two patients. The ORR was 55%, including complete response in one patient. Eight patients had disease progression or died, and median PFS was 12.5 months (95% CI: 12 months–NA). The median PFS in patients favorable, intermediate, or poor IMDC risk group were NA, 12.0 months (95% CI: 11.21–NA) and 12.5 months (95% CI: 8.84–NA), respectively. Single agent TKIs were the second-line therapies given to patients (cabozantinib in three patients, pazopanib in two patients, lenvatinib and sunitinib in one patient each).

Conclusion: We report the first real-world evidence of the effectiveness of first-line A + Ax in Indian patients with aRCC. Results were comparable with the JAVELIN Renal 101 trial.

A120. Genetic Threads of Hope: Unraveling Germline Mutations in Ovarian Cancer and Their Impact on Clinical Outcomes and Empowering Ovarian Cancer Defense with Cascade Genetic Testing—Indian Perspective

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Keywords:

- BRCA mutated
- non-BRCA mutated
- cascade testing

Aims and Objectives: (1) To compare the demographics, disease characteristics, overall survival (OS), progression-free survival (PFS) for BRCA-mutated and non-BRCA-mutated groups. (2) To assess the acceptance of cascade genetic testing among first-degree at-risk relatives.

Materials and Methods: Patients with high-grade epithelial ovarian/fallopian/primary peritoneal cancers tested for germline mutations from 2017 till 2023 were included. Patients were grouped into BRCA-mutated and non-BRCA-mutated but positive for other germline mutations. Clinical details and treatment details were noted individually for each group and analyzed separately. Proportion of at-risk first-degree relatives who had accepted cascade testing was evaluated.

Results: We had 72 patients with mean age of 48 years. BRCA mutations were seen in 81.7% and non-BRCA mutations in 18.3%. Commonest mutation was BRCA 1 (72%) followed by BRCA 2 (9.7%), while the rest were non-BRCA mutations. VUS contributed to 5% in BRCA mutated group and 69% in the non-BRCA mutated group. 12% of patients had prior history of breast cancer (77.5% BRCA mutations and 22.5% non-BRCA mutations with *p*-value of 0.661). Patients with history of breast cancer had no difference in PFS (*p*-value: 0.889) but less OS when compared to patients without history of breast cancer (*p*-value: 0.614). Family history of malignancy was present in 51% (BRCA mutations 92% and non-BRCA mutations 8% with *p*-value: 0.028). PFS was similar in both cohorts (*p*-value: 0.177) but the OS was higher in the BRCA-mutated group (*p*-value: 0.302). PARP inhibitors usage beyond 12 months did increase the PFS, but there was no difference in OS. Cascade testing was counselled for all family members, 35 at risk relatives of 24 patients underwent testing contributing to 33.3%.

Conclusion: There was no statistically significant difference in clinical characteristics of the carcinoma ovary among BRCA mutated and non-BRCA-mutated groups except for family history. Cascade genetic testing should be strengthened as a strategy to prevent ovarian cancer in LMICs.

A121. Efficacy of First-Line Nivolumab Plus Ipilimumab in Metastatic/Inoperable Malignant Pleural Mesothelioma

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Keywords:

- Nivolumab
- Ipilimumab
- pleural mesothelioma

Aims and Objectives: To study efficacy of first-line nivolumab plus ipilimumab in metastatic/inoperable malignant pleural mesothelioma.

Materials and Methods: We conducted a retrospective study at our institute on patients diagnosed as metastatic/inoperable malignant pleural mesothelioma from January 2021 to august 2023. We studied the epidemiological profile and the outcome of the treatment (first-line nivolumab plus ipilimumab) in terms of safety, response rates, and survival. Nivolumab dose given was 240 mg or 3 mg/kg every 2 weeks and the dose of Ipilimumab was 1 mg/kg every 6 weeks till progression. Overall survival analysis was done at the end of 6 months from the first dose.

Results: Total 15 patients were diagnosed with metastatic pleural mesothelioma among which 8 (54%) were males and 7 (46%) were females. Median age at diagnosis was 65 years (range 40–76 years). Median number of nivolumab cycles given was 7 cycles (range 2–26 cycles) and the median number of ipilimumab cycles was 3 cycles (range 1–10 cycles). Out of 15, 9 patients (60%) showed a partial response after the first reassessment done at 3 months and these patients continued to show a good response at the end of 12 months follow-up. One patient lost to follow-up after 2 cycles of nivolumab. At the end of 12 months of follow-up, 9 patients (60%) were alive and were continuing immunotherapy. Grade 3 treatment-related adverse effects were seen in 4 (27%) patients which were hepatitis and hypothyroidism.

Conclusion: We conclude that the combination of Nivolumab and Ipilimumab is safe and effective as first-line treatment in metastatic pleural mesothelioma and randomized trials from India are needed to evaluate the role of these agents in malignant mesothelioma.

A122. Observational Study of Synchronous Oligometastatic Lung Cancer Presenting in Our Tertiary Care Hospital and Their Outcome

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Background: The treatment of oligometastatic lung cancer is evolving post the emergence of local therapies like surgery and local ablative therapies. But a number of patient and disease-related factors influence the treatment patterns and decision making.

Objectives: The aim of our study is to analyze the incidence, prevalence, progression-free and overall survival of patient of oligometastatic disease at our center. To study the pattern of care given at our center.

Materials and Methods: We did a retrospective, single-center, non-interventional study at the thoracic department in Tata Memorial Center, Mumbai. We enrolled patients aged 18 years or older with oligometastatic non-small cell carcinoma lung. We have done a systematic review of the clinical histories of patients diagnosed between January 2023 to December 2023. Descriptive statistics was performed. Progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan–Meier survival analysis.

Results: Between January 2023 and December, 2023, 62 patients were enrolled into the study. Of the 62 patients, 29 had brain metastasis. Of these 29 patients, 18 received brain directed therapy with 8 receiving it in curative intent and 10 received it in palliative intent. In total 14 patients were treated with curative intent. At the time of the primary analysis (median follow-up 10.9 months), 32 of 62 patients with measurable disease at baseline had a confirmed partial response; thus, the proportion of patients achieving an objective response was 51.6% and 7 patients had stable disease while 8 had progressive. Adverse events were predominantly grade 1 or 2, with an overall good tolerance profile. The most common severe (grade 3/4 events) adverse event is hyponatremia in 8 patients followed by neutropenia in 7 patients. But febrile neutropenia was noted in only 2 patients. The median OS at the time of final analysis was 19.95 months while the PFS is 15.47 months

Conclusion: The pattern of care in oligometastatic disease can be curative but this depends on multiple patient and disease related factors. With emerging data and the advent of immunotherapy and targeted therapy better outcomes can be seen.

A123. NIVO-ALTER Study: Assessing Nivolumab's Altered Dosing in Non-Small Cell Lung Cancer

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Objectives: In countries with economic burdens, altered dose immunotherapy is increasingly used in cancer management. Low-dose Nivolumab in combination with oral metronomic therapy has demonstrated improved survival outcomes in recurrent/metastatic head and neck cancer. However, limited data are available on the use of altered-dose Nivolumab in lung cancer.

Materials and Methods: Retrospectively analysis 96 patients with NSCLC, tested negative for EGFR and ALK mutations and had received at least one dose of Nivolumab. The standard dose (Std. D) of Nivolumab, administered at 3 mg/kg intravenously every 2 weeks, was compared with altered dose (Alt. D) included 100 mg biweekly (24%), 40 mg biweekly (35%), and 40 mg every 4 weeks (10%). The primary objective was to assess efficacy, including overall survival (OS), progression-free survival (PFS), and safety.

Results: The median age of the population is 62 years, with 91.7% being Males. ECOG score was 1 in 66.7% and 2 in 30.2%. The PFS in the SD group was 5.0 ± 0.9 months, and 3.0 ± 0.4 months in AD group. The PFS of SD versus AD was statistically significant ($p = 0.002$). The SD and AD group's OS was 10.0 ± 1.4 and 5.0 ± 1.1 months, respectively. There was no statistical significance in the OS of SD versus AD (0.075). The SD showed a better RR at 49% compared to 39% in the AD group. Altered doses were associated with fewer adverse events. In the PDL-1 positive subgroup receiving second-line treatment, median OS and PFS changes were insignificant.

Conclusion: Among NSCLC patients in the second line and beyond, altered-dose Nivolumab resulted in shorter OS and PFS, though there was no change in the PDL-1-positive subgroup. Therefore, low-dose Nivolumab can be considered a less toxic and reasonably effective option for patients without access to standard doses, particularly in PDL-1-positive patients.

A124. Analysis of Mechanisms of Resistance in Patients Progressed on EGFR-Directed Therapy in Metastatic NSCLC in Indian Population

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Objectives: The aim of the present study was to analyze the pattern of resistance in EGFR mutated NSCLC in Indian population and the difference in the pattern of resistance between patients treated with EGFR TKIs and when combined with chemotherapy.

Materials and Methods: This was a *post hoc* analysis of the randomized, open-label, phase III study that compared Gefitinib with Gefitinib plus chemotherapy in patients with advanced NSCLC with activating *EGFR* mutations in the first-line setting. These patients were regularly followed up. In patients having progression, mutational and histological analysis was done. Descriptive statistical analysis was used and Fisher's exact probability test was done.

Results: 275 patients had disease progression out of the 350 patients and 206 of these 275 patients were available for final analysis. T790M was the most common mode of resistance being noted in 30%. When the individual arms were analyzed separately, the emergence of T790M was more in the gefitinib arm compared to the chemotherapy plus gefitinib arm, 38 versus 19% (Fisher's exact probability test, $p = 0.008$). The analysis of the Gefitinib arm revealed new resistant mutation in 44 patients with T790M being seen in 43 and S768I in 1 patient. New sensitizing mutation was noted in 5, loss of prior sensitizing mutation was seen in 21 patients. Rest 49 available for analysis in this arm retained the prior *EGFR* mutation. In the Gefitinib arm, 17 patients had new resistance mutation all being T790M, 1 had new sensitizing mutation, 29 had loss of previous sensitizing mutation and rest 40 retained their original mutations. Histological transformation was noted in 6% with transformation to small cell carcinoma being 4.5%.

Conclusion: The emergence of T790M was lesser compared to the prior studies, but the prior studies predominantly used EGFR TKI alone. T790M was more in the TKI alone arm compared to combination of TKI and chemotherapy. More over histological transformation and the loss of sensitizing mutations highlight the importance of repeat biopsy and molecular analysis in guiding further therapy.

A125. COMBAT Study: Comparative Real-World Evaluation of CDK 4/6 Inhibitors in HR+/Her2− Metastatic Breast Cancer

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Objectives: CDK 4/6 inhibitors have revolutionized HR-positive/Her2-negative metastatic breast cancer

Table 1 ORR

First line	Overall	Palbociclib	Ribociclib	Abemaciclib	*p-Value (Sig. < 0.01)*
ORR	66%	62%	65%	73%	0.53
CR (complete response)	6.9%	3.8%	2.3%	13.4%	0.22

Table 2 PFS

PFS -months	Overall	Palbociclib	Ribociclib	Abemaciclib	*p-Value (Sig. < 0.01)*
First line	25	24.2	27.8	29	0.395
Second line	15	11.2	17.3	15.9	0.397
Third and beyond	6	5.5	6.3	7.0	0.374
Liver mets second line	–	7.8	9.8	10.2	0.392

treatment, with Palbociclib, Ribociclib, and Abemaciclib all approved. However, prospective comparisons are lacking. This study provides retrospective comparative data on their efficacy.

Materials and Methods: We enrolled metastatic HR+/Her2− breast cancer patients from two tertiary cancer centers in India, who had previously received CDK 4/6 inhibitors and were unsuitable for curative treatment. The primary goal was to assess efficacy through progression-free survival (PFS) and overall response rates (ORR) using KM curves. Safety was a secondary endpoint.

Results: Out of 145 eligible patients with a median age of 53, 54% were in first-line treatment, 36% in second-line, and 10% in third-line or beyond. 16% had bone-only metastases, while the rest had visceral involvement. The median follow-up was 29 months. Of the patients, 52 received Palbociclib, 44 Ribociclib, and 49 Abemaciclib.

At the 3-year mark, 8.3% of the patients remained progression-free in the entire population. Specifically, 3.8% were progression-free with Palbociclib, 9% with Ribociclib, and 12% with Abemaciclib.

PIK3CA mutation was prognostic, with a median PFS of 8.2 for positive and 20 months for negative patients, showing a significant difference.

Conclusion: All three CDK 4/6 inhibitors (Palbociclib, Ribociclib, and Abemaciclib) demonstrated comparable ORR and PFS in HR+/Her2− metastatic breast cancer patients. However, the complete response rates were higher in the first-line setting for patients on Abemaciclib. The presence of the PIK3CA mutation correlated with shorter PFS.

A126. Impact of CPS on Indian Recurrent/Metastasis Oral Cavity Patients Treated with Cetuximab Plus Chemotherapy: A Real-World Study

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Objective: The current treatment guidelines recommend the options of using pembrolizumab or, cetuximab with chemotherapy. PD-L1 combined positive score (CPS) is an important biomarker, which may predict the benefits of pembrolizumab in recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC) patients. CPS score is not expected to affect the efficacy of Cetuximab, though no real-world data are available to confirm the same. In this study, we evaluated the impact of CPS score on the efficacy of cetuximab.

Materials and Methods: This retrospective real-world study included patients of oral cavity cancers, treated at three cancers of India between May 2018 and September 2023. Efficacy endpoints evaluated included response rate (RR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS) for the overall population and based on CPS scores <20 and ≥ 20.

Results: A total of 82 oral cavity cancer (including subsites buccal mucosa, tongue, and floor of the mouth) were included in this analysis. Median age was 53 years (range: 32–80 years). Majority were males (92.7%), with a performance score of 1 (76.8%) and 2 (17.1%). Patients with <20 and ≥ 20 CPS scores were 46.3 and 53.7%, respectively. The RR was 81.7%, with CPS <20 at 81.6% and CPS ≥ 20 at 81.8%. DCR for the entire population was 97.6%, with CPS <20 at 100% and CPS ≥ 20 at 95.4%. The overall PFS and OS were 8.0 (95% CI: 6.7–9.2) months and 20.0 (95% CI: 17.2–22.7) months, respectively. Based on CPS scores <20 and ≥ 20, PFS and OS showed no significant difference ($p = 0.835$ and $p = 0.149$, respectively).

Conclusions: This is the first real-world retrospective subset study of oral cavity patients reaffirming the efficacy of cetuximab in R/M SCCHN patients. Analysis based on CPS scores (<20 and ≥ 20) did not impact efficacy outcomes.

A127. Clinical Profile and Treatment Outcomes of Hepatocellular Carcinoma from a Tertiary Care Hospital in South India: A Retrospective Study

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Keywords:

- hepatocellular carcinoma
- HCC

Aims and Objectives: The prevalence of hepatocellular carcinoma (HCC) is increasing worldwide, and it is now the 6th most common cancer and the 3rd most common cause of cancer-related death. Survival data for patients with hepatocellular carcinoma are very sparse in India. We performed this study to understand the clinical profile and survival outcomes of HCC patients treated at our hospital. We also tried to identify the prognostic factors for survival.

Materials and Methods: This is a retrospective study of 107 patients with hepatocellular carcinoma treated at our institute from January 2017 to December 2019.

HCC was diagnosed according to EASL criteria-triple phase contrast multidetector computed tomography (MDCT)/magnetic resonance imaging (MRI) and/or histology (where indicated).

BCLC stage was used to guide treatment decisions.

The collected data were analyzed with IBM SPSS Statistics for Windows, Version 23.0.

Results: The mean age at presentation was 60 years. The patients were predominantly males. The most common presenting symptoms were loss of weight and loss of appetite. The most common etiology of HCC was alcoholic liver disease. 91% patients were newly diagnosed to have cirrhosis and

HCC, none of the patients were diagnosed on routine surveillance.

Majority of the patients were BCLC stage C. A significant association was seen between BCLC stage and OS ($p = 0.002$). The mean OS was significantly associated with CTP class ($p = 0.001$). There was no association between AFP and OS ($p = 0.215$)

Conclusion:

•Alcoholic liver disease was the most common cause of HCC.

•BCLC stage and CTP were found to be prognostic in terms of OS.

•No correlation could be identified between serum AFP levels and OS.

•Most of the patients are detected at a late stage (BCLC C being most common), precluding curative therapies.

•Improving the awareness among public about the harms of alcohol consumption, and improving access to primary health care, to detect cirrhosis at an early stage, may help reduce the disease burden.

A128. Identification and Characterization of Germline Mutations in Indian Females with Cancers

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Keywords:

- next-generation sequencing
- hereditary cancer
- pathogenic variants
- VUS
- genetic screening
- Indian population
- breast cancer
- ovarian cancer
- multigene panel
- Illumina Nextseq 2000
- Ion Gene Studio S5 Plus
- germline mutations

Aims and Objectives: This study aims to identify and characterize germline mutations in Indian females with breast, ovarian, endometrial, and other cancers using Next-Generation Sequencing.

Materials and Methods: NGS was performed using two sequencing platforms: the Illumina Nextseq 2000 and Ion Gene Studio S5 Plus System. Two multigene hereditary cancer panels were used: the 146-gene Nonacus panel and the 28-gene Oncomine HRR panel. DNA target enrichment for the Illumina platform was conducted using the GALEAS Hereditary Plus Kit, with libraries prepared from 50 ng of DNA and quality checked using Qubit and Tape-Station before sequencing. The HRR libraries were prepared using the ION AmpliSeq Library Kit Plus and sequenced on the Ion S5™ Plus instrument. Data analysis was conducted using Nonacus' cloud-based software and the Ion Reporter platform, respectively.

Results: A total of 178 patients (42 males and 136 females) were analyzed. Among females, the mean age for various cancers was 48.4 years for breast cancer (range: 32–75), 53.86 years for ovarian cancer (range: 30–77), 57.55 years for endometrial cancer (range: 31–73), and 51.15 years for other cancers (range: 23–76). Pathogenic variants were identified in 32 of 136 females (23.52%). The most common pathogenic mutations were in *BRCA1* (12/136; 8.82%), *BRCA2* (7/136; 5.14%), *MLH1* (3/136; 2.20%), and *MSH6* (3/136; 2.20%). Mutations in other genes, such as *MSH2*, *NBN*, *POLE*, *PTEN*, *RB1*, and *TP53*, each had a frequency of 0.73%. Pathogenic variants were detected in breast (9/136; 6.61%), ovarian (8/136; 5.88%), endometrial (9/136; 6.61%), and other cancers (4/136; 2.94%). Variants of uncertain significance (VUS) were found in 24 of 136 females (17.64%), with *BRCA1*, *BRCA2, CHEK2, POLD1*, and *RAD50* being the most frequent, each detected in 2.20% of the cohort. No pathogenic variants or VUS were found in 56 patients (41%).

Conclusion: These findings highlight the importance of comprehensive genetic screening for cancer risk assessment, enabling personalized treatment and preventive measures to improve patient outcomes

A129. Experience of Cancer Genomic Profiling in a Tertiary Care Center

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Keywords:

- next generation sequencing
- cancer
- tumor mutation burden
- CGP

Aims and Objectives: Comprehensive genomic profiling of stage IV tumors to identify diagnostic, prognostic and therapeutic markers.

Materials and Methods: Tumor samples from 50 patients were collected for targeted panel sequencing using Oncomine Comprehensive assay plus by ThermoFisher Scientific. Five samples were rejected due to inadequate tumor cell content. Genomic alterations, including single nucleotide variations, insertions/deletions, copy number variations, and gene rearrangements, were assessed and Tumor mutation burden (TMB) was computed. TMB-high (TMB-H) was defined as $\geq$10 mutations/Mb. Genomic Instability Metric (GIM) score was also computed in ovarian cancers with a threshold of 16%.

Results: Mean age was 57.4 ranging from 7 to 84. Average tumor cell content 59.4% (ranging 25–90%). Tumor site included ovary (27%), lung (13%), breast (11%,) brain (11%), endometrial (11%), head and neck (7%), gastrointestinal (7%), prostate (4%), and others (5%). 129 oncogenic variants were detected out of which 27 were therapeutic (*BRCA1/2, PALB2, BRAF, MYD88, PIK3CA, IDH1, NBN, ARID1A,* etc.). 9 prognostic, 12 related, and 6 unrelated variants to the cancer type were found. Microsatellite instability-high was detected in one case which was orthogonally confirmed using fragment length analysis, TMB-H in 3 cases. In patients with ovarian cancer high Genomic Instability Metric (GIM) score was observed in 3 cases which included *NBN, BRCA2, ATM and CHEK1* mutations. Loss of heterozygosity was not called in 10 cases.

Conclusion: Our analysis uncovered critical oncogenic variants which hold therapeutic potential especially in advanced staged cancers. Furthermore, this underscores the value of genomic profiling in understanding tumor biology and personalizing treatment strategies for advanced cancer patients.

A130. A Case Series on Early Onset Colorectal Cancer: A Single-Center Experience

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Background: Early onset colorectal cancer (EO CRC) is colorectal cancer diagnosed less than 50 years of age and contributes to 10% of all diagnosed cases of CRC.[1] 70 percent of the cases are left sided.[2] 30% of the cases have a family history of cancer.[3] 3 to 5% are associated with hereditary cancer syndromes of which Lynch syndrome is the most common.[4] Other causes include obesity, sedentary lifestyle, alcohol use, etc. Gut microbiome also plays a role in the pathogenesis.[5,6] Screening for CRC is thus recommended from 45 years of age.[7] Even then, people are reluctant to perform this due to lack of awareness, financial constraints, and lack of access to health care especially in developing nations. This study aims to bring to light the increasing incidence of EO CRC and need to strengthen screening programs and to understand the importance of genetic testing.

Materials and Methods: This is a retrospective study of seven patients treated at GG Hospital, Thiruvananthapuram, Kerala, India from June 2023 to May 2024 with EO CRC.

Results: The median age of the study population is 35 years. The female to male ratio is 4:3. All the cases had left sided adenocarcinoma with sigmoid colon affected in four cases and rectum in three cases. Constipation and bleeding per rectum were the presenting features. All the patients were non vegetarians, had no addictions and lead a sedentary life style. Significant family history was present in only two patients, both having history of GI Cancers in first- and second-degree relatives. Molecular analysis for mutations was done in four patients. One had APC gene mutation. Another patient was found to have microsatellite instability (MSI) high status and another had KRAS G12D mutation. All the patients received fluoropyrimidine based chemotherapy. Three patients could not do mutation analysis due to financial constraints. Stage 4 patients received targeted treatment also. The details are given in the below table.

Conclusion: The incidence of EO CRC is steadily increasing. This calls for greater awareness, strict implementation of screening practices and education of primary health care providers. Genetic testing is also a must as we might miss an opportunity to identify hereditary CRC. More trials are needed to investigate the different aspects of EO CRC, especially the causes so that we can provide better health care.

Table 1 Characteristics of patients with EO CRC in this case series

Age	Site	BMI	Family history	Stage	Priortreatment	Mutation analysis	Treatmentplan
32	Sigmoid	13.33	Nil	III, local recurrence	FOLFOX, RT for Local Recurrence	MSI High	FOLFIRI+Bevacizumab (Bev)
33	Sigmoid	22.3	Colon Ca for father	III	Nil	APC+	CapeOx
47	Rectum	22.86	Nil	III	Nil	MSS	CapeOx f/b chemoRT and TME
47	Rectum	26.04	Nil	III	Nil	Not done	NACTRT followed by TME and adjuvant
35	sigmoid	20.76	Nil	II	Nil	KRAS G12D	CapeOx
39	Rectum	26.02	GI Ca in 1st, 2nd degree	II, margin +	no	Not done	CapeOx and long course chemoRT
34	Sigmoid	25.95	Nil	IV	CapeOx	Not done	FOLFIRI+Bev

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A131. Real-World Data of Radioiodine Refractory Thyroid Cancer Treated with Lenvatinib: A Single-Center Experience from Eastern India

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Keywords:
- radioiodine refractory thyroid cancer
- lenvatinib

Aims and Objectives: Treatment of differentiated thyroid cancer consists of surgery with or without radioiodine (RAI) therapy. For patients who develop radioiodine refractory disease, without any targetable

mutation, the use of oral tyrosine kinase inhibitors (TKI) like Lenvatinib and Sorafenib is standard practice.

The primary aim of this study is to assess the response, progression free survival (PFS) of patients of Radioiodine Refractory Thyroid Cancer on Lenvatinib; overall survival (OS) and toxicity were secondary endpoints.

Materials and Methods: This was a retrospective study from Tata Medical Center Kolkata, India, which included patients with RAI refractory differentiated thyroid cancer between 2012 and 2024. Data were captured from hospital electronic medical records till June 2024. Standard or lower doses of lenvatinib was offered as first-line therapy after RAI therapy completion.

Results: Consecutive 32 eligible patients (male:female:15:17) were analyzed, with median age at diagnosis 55 years (range 12–70). The mean cumulative dose of RAI was 333 mCi (interquartile range: 161). The median starting dose of lenvatinib was 16 mg (range: 8–24). With a median follow-up of 17 months, disease control rate (CR + PR + SD) was 90%. 3 patients developed progression at first response assessment. Dose modification of lenvatinib was done in 26 patients as per guidelines, with a minimum dose level of 4 mg. Cabozantinib was offered as second-line therapy to 10 patients. Median PFS was 23 months (95% CI: 15–30) and median OS was 137 months (95% CI: 93–180). The most common adverse effects (CTCAE version 5) were Grade 2 skin rash (12), HFS-hand-foot syndrome (5); whereas Grade 3 were HFS (7) and proteinuria (2).

Conclusion: This study shows that even lower doses of lenvatinib were equally efficacious in terms of response and outcome in RAI refractory thyroid cancer as compared to standard dose reported in landmark trials and can be offered among patients where full dose cannot be attempted.

A132. DPYD Mutation Testing and Toxicity Profile among Patients Receiving Fluoropyrimidine-Based Chemotherapy

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Keywords:

- DPYD mutation
- pharmacogenomics
- chemotherapy toxicity

Aims and Objectives: To correlate DPYD gene mutation and toxicity profile among patients receiving fluoropyrimidine-based chemotherapy.

Materials and Methods: Data of cancer patients who had toxicity while on fluoropyrimidine-based chemotherapy (for both adjuvant and palliative settings) tested for DPYD gene mutation were extracted from our center's electronic records from December 2018 to January 2022 and evaluated. We collected demographics of the patients, genotypes of DPYD gene, disease status, chemotherapy type, and the associated toxicities.

Results: Total 90 patients who were treated with 5-FU (13%) and Capecitabine (83%) were tested for DPYD gene with median age of 55 years. 63 (70%) patients were found to have some DPYD mutation. Exon2 (85T>C) was the commonest mutation seen in 43 (68%) and 9 of them had homozygous mutation for the same. 16 (17%) patients had double heterozygous mutation for Exon2 (85T>C) and Exon 6 (496 A>C) experienced severe myelosuppression. Myelosuppression and diarrhea were most common adverse effects seen with 15 (23%) of them have >grade 3 diarrhea.

Conclusion: The search for DPD deficiency by phenotypic study allows early modification of 5-FU and capecitabine doses to avoid major toxicity. We observed higher prevalence of DPYD gene mutation in our population. Phenotypically normal metabolizers were found to have significant toxicity (≥grade 3). There is an unmet need for estimating prevalence of DPD mutations and variants of significance among Indians.

A133. Paradox of Perioperative Chemotherapies FLOT (Fluorouracil Plus Leucovorin, Oxaliplatin, and Docetaxel) versus EOX (Epirubicin, Oxaliplatin, and Capecitabine) in Nonmetastatic Gastric Carcinoma Survival—A Retrospective Analysis

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Keywords:

- progression-free survival
- overall survival
- FLOT
- EOX

Aim: To compare FLOT (fluorouracil plus leucovorin, oxaliplatin and docetaxel) versus EOX regimen (epirubicin, oxaliplatin, and capecitabine) in the perioperative setting in nonmetastatic gastric carcinoma.

Objective: To analyze progression-free survival (PFS) and overall survival (OS) in patients receiving FLOT versus EOX chemotherapies in the perioperative setting in nonmetastatic gastric carcinoma.

Materials and Methods: This is a descriptive study with retrospective analysis. Patient's clinical data were retrieved from the Tumor registry from Jan 2017 to May 2023 after Institute Ethics approval. Only details of patients with stage II–III gastric carcinoma were used for analyses. The PFS was calculated from the date of diagnosis till progression/recurrence or death due to disease or any cause and OS was calculated from the date of diagnosis till death due to any cause.

Statistical analysis was performed using SPSS software v22.0. The univariate analysis was done by log-rank analysis. The survival was defined as per Kaplan–Meier curves.

Results: 348 patients were analyzed in a perioperative setting, 205 in the FLOT regimen and 143 in the EOX regimen. The median follow-up was 35.8 months. The median OS between FLOT and EOX was not reached versus 25.6 months, respectively ($p = 0.167$). The median PFS was 20.4 months versus 17.1 months between FLOT versus EOX regimens ($p = 0.465$). The pCR rate was 3.9% versus 4.2% between FLOT versus EOX. Tumor downstaging (35.6 versus 22.4%) and R0 resection rates (63.4 versus 51%) were better with FLOT compared to EOX. The pCR, downstaging, and R0 resection rates showed a significant impact on OS and PFS benefits in both these regimens.

Conclusion: FLOT regimen showed nonsignificant favorable survival outcomes and tumor downstaging. The OS/PFS outcomes are less compared to randomized studies. Need prospective study comparing EOX versus FLOT as well as molecular exploratory research.

Editorial

Significance and Implications of BRAF-V600E mutation in Thyroid Neoplasm

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The incidence of thyroid cancer has increased worldwide over last few decades and it accounts for the most common endocrine tumor. This increased incidence of thyroid cancer is attributed to radiological detection of small thyroid lesions. In the last decade, there has been an unprecedented advancement in the molecular information of thyroid neoplasms, which has revolutionized the histological classification, prognostication, and evidence-based management of thyroid neoplasm.[1–3]

The recent World Health Organization classification of thyroid neoplasm has enlisted new categories based on histological features, molecular classification, and biological behavior. Overall follicular cell-derived neoplasms have been classified into benign tumors, low-risk neoplasm, and malignant neoplasm. Malignancies derived from thyroid follicular cells are categorized at the molecular level and majority of well differentiated thyroid carcinoma are grouped into two categories. The first, with predominantly expansile pattern of growth, often with clear encapsulation and follicular architecture are classified as RAS-like tumors due to associated high incidence of RAS mutations. These are the most differentiated carcinoma based on histomorphology, iodine metabolism, and functional thyroid differentiation expression profiles. The second important group with histological abnormalities including papillary architecture, infiltrative growth pattern have associated high frequency of BRAF-V600E mutation like tumors.[1]

Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy (~85%). BRAF-V600E mutation is the most common underlying genetic alteration which leads to activation of downstream mitogen-activated protein kinase pathway, which eventually upregulates extracellular signal-regulated kinases pathway, causing tumorigenesis. This mutation is not only involved in tumorigenesis but also involved in transformation to aggressive high-grade differentiated and nondifferentiated cancer. The frequency of BRAF-V600E mutation varies among the histological subtypes of PTC with highest frequency (80%) seen in tall cell variant. Some other subtypes of PTC also show BRAF-V600E mutations, like infiltrating follicular variant [FV-PTC], oncocytic variant, and some cases of warthin-like PTC. Hobnail PTC is clinically aggressive subtype of PTC that also shows BRAF-V600E mutation with concomitant TP53 mutations, TERT promoter mutations, and PIK3CA mutation, attributing to aggressive clinical course.[1,4–6]

The prognostic significance of BRAF-V600E mutations in PTC is still contentious. Many published studies have reported aggressive clinical outcome associated with this mutation, but this was predicted in univariate analysis. Moreover, high prevalence of this mutation is seen in papillary thyroid microcarcinoma (PTMC), which is associated with excellent prognosis.[3–5,7,8]

Silver et al[9] underscores the prognostic significance of BRAF-V600E mutation in determining the aggressiveness of PTC measuring $\leq$1.5cm. In a retrospective study of 121 patients who were subjected to thyroid surgery for small PTC (1–1.5cm) or PTMC ($\leq$1 cm), BRAF-V600E mutations were detected in 42.4 and 43.6% of small PTC and PTMC, respectively. Among the PTMC cases with detected mutation, 54.1% demonstrated aggressive characteristics (extrathyroid extension, lymph node metastasis) in comparison to 19.4% of the nonmutated tumors. In the category of small PTC, aggressive pathological features were seen in 82.1% of mutated and 28.9% of non-mutated tumors. The authors suggested that performing the molecular testing for BRAF-V600E mutation can guide for appropriate patient care and management.[9]

Studies have shown that PTC with coexistent BRAF-V600E and TERT genetic mutations have poor disease-specific survival than those with either individual mutation alone.[1,9]

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The significance of detecting BRAF-V600E mutation in clinical management of thyroid lesion is more established as a diagnostic modality, especially in the fine-needle aspiration cytology (FNAC) of thyroid lesion under evaluation.[2,6]

Qi et al[2] retrospectively analyzed 252 patient who underwent thyroid surgery. All these patients underwent preoperative cytological examination, and thyroid puncture cell fluid was also analyzed for BRAF-V600E mutation by molecular testing: polymerase chain reaction (PCR). Postoperatively, 242 cases were diagnosed as PTC on histopathology examination that was used as gold standard diagnostic modality. In FNAC sample reporting, 57% of benign, 80% of indeterminate, and 88.9% of malignant cases shows BRAF-V600E mutation. The diagnostic sensitivity of BRAF-V600E mutation in samples from FNAC for diagnosing PTC was 91.7% in benign, 82.8% in indeterminate, and 89.4% in malignant cases; while the specificity was 100% in all the three categories. The authors found BRAF-V600E mutation analysis in samples from FNAC procedures as a highly effective supplementary diagnostic modality. However, prognostic significance of the mutation was not established.

Several other studies found BRAF-V600E mutation analysis as a useful adjuvant for detecting malignancy (PTC) in the cytological specimens of the thyroid lesion undergoing evaluation preoperatively, which helps in guiding the extent of operative procedure including regional lymph node dissection. Regarding the testing modality for detection of BRAF-V600E mutations, there has been a good concordance among gene sequencing, PCR, and IHC. In a study by Zhao et al,[6] the concordance for all the above mentioned three methods was seen in 92.4% of cases. The sensitivity and specificity for IHC was 98.6 and 97.6%, respectively. Hence, it can be utilized as the most convenient and reliable method in routine clinical workup of the cases. Immunostaining for BRAF-V600E using the clone VE1 is highly specific and sensitive for the detection of mutation in PTC. The staining should be diffuse and cytoplasmic ($\geq$90% of tumor cells) to be considered as positive test.

For the diagnosis of noninvasive follicular thyroid neoplasm with papillary-like-nuclear features (NIFTP), which is considered as low-risk thyroid neoplasm as per the recent WHO Classification (5th edition), the detection of BRAF-V600E mutation precludes the diagnosis of NIFTP. In the recent WHO classification of thyroid tumors update, molecular profiling data have revealed that infiltrative–FVPTC is a BRAF-like tumor (PTC family tumor), whereas encapsulated–FVPTC being a RAS-like neoplasm, aligns toward follicular thyroid carcinoma instead of PTC.[1]

In the recent WHO classification, two groups of high grade, nonanaplastic follicular derived carcinoma have emerged, that carries intermediate prognostic risk: poorly differentiated thyroid carcinoma (PDTC) and differentiated high-grade thyroid carcinoma (DHGTC). These tumors are large widely invasive and are associated with lymph node metastasis in about 30 to 50% of cases. Substantial proportion of DHGTC are BRAF-V600E driven and exhibit high proclivity for regional lymph node metastasis, while PDTC are enriched in RAS mutations, and are commonly associated with regional and distant metastasis. In addition, both of these entities are associated with secondary mutations, of which TERT mutations are most frequent.[1]

Another diagnostic important implication of BRAF-V600E is in the correct categorization of squamous cell carcinoma of thyroid as a subtype of anaplastic thyroid carcinoma (ATC), which was considered as separate entity in previous WHO classification (4th edition).[1,10,11] Chen et al[12] has done analysis of multi-institutional data and found pure squamous cell carcinoma of thyroid with or without associated differentiated component, were associated with BRAF-V600E mutation in 87% of cases and had clinical outcome parallel to that of ATC. The diagnostic utility is more critical at the metastatic site like lung in which presence of squamous cell carcinoma with BRAF V600E mutation rules out a second primary etiology in lung and confirms it to be a metastasis from ATC with squamous morphology.

From a therapeutic point of view recently it has been emphasized to do prompt testing for BRAF-V600E in all ATC cases, as those with mutation associated ATC will respond to therapeutic target (BRAF plus MEK inhibitors).[1]

To conclude, BRAF-V600E mutation is the most common mutation seen in PTC, DHGTC, and ATC. IHC is an efficient and reliable modality for detection of this mutation. The clinical utility of detecting this mutation caries mainly diagnostic and therapeutic implications. In cytology specimen, the detection of this mutation is confirmatory of malignancy; whereas in ATC, this mutation offers a therapeutic avenue for targeted therapy.

Conflict of Interest
None declared.

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Optimization of Tissue Handling and Processing in the Era of Precision Medicine: A Practical Recommendation from a Multidisciplinary Panel of Indian Experts

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Abstract

Molecular analysis of biospecimens is the key to diagnostic and therapeutic decisions in clinical practice. However, there is a lack of consolidated guidelines for biospecimen collection, tissue handling, and storage in India. Therefore, this study aims to generate expert recommendations for the optimization of tissue handling and processing practices in India in the era of precision medicine. This study aimed to evaluate the clinical gaps related to tissue handling for molecular analysis and develop expert recommendations to mitigate preanalytical issues associated with biospecimen processing. These expert recommendations will help in increasing the diagnostic yield and accuracy of biomarker testing in clinical practice. A virtual advisory board meeting was convened with 19 experts, including pathologists, molecular biologists, medical oncologists, surgical oncologists, interventional radiologists, and a senior histology technician from 10 hospitals in India, along with an accreditation officer for testing and calibration of laboratory procedures. The scientific coordinators developed specific questions to address the salient issues associated with the preanalytic phase of tissue specimen preparation. The experts discussed each question until a complete set of

Keywords
- biospecimens
- cold ischemia time
- fixation
- tissue processing
- paraffin blocks

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recommendations was obtained. The expert panel provided recommendations for tissue collection, processing, fixation, and block preparation to ensure high-quality biospecimens. As per the expert panel recommendations, tissue sampling can be performed from any easily accessible site, regardless of the primary or metastatic locations. In addition, the cold ischemia time should be <1 hour, 10% neutral-buffered formalin should be used as the fixative, isopropyl alcohol should be used as the dehydrating agent, the volume of tissue to fixative ratio should be 1:10, and all the paraffin blocks should be archived in dry, pest-free conditions at room temperature. The experts suggested that the formalin used for fixation should be freshly prepared and its pH should be checked daily; moreover, the pH and date of formalin preparation should be mentioned on the containers. The experts highlighted the need to educate multidisciplinary teams on the optimization of tissue handling practices and emphasized that a pathologist should always check the tissue for adequate quality and quantity for biomarker testing. The existing routine clinical procedures for collecting and handling biospecimens adversely affect their quality. The expert recommendations for preanalytical quality control would ensure high-quality biospecimens for molecular analysis and precision medicine.

Introduction

Biospecimens play a crucial role in the current era of precision medicine and translational research as they are a primary source of molecular information on a patient's disease in clinical practice.[1] These biospecimens are processed in multiple steps that begin with morphological diagnosis by immunohistochemistry to evaluate the histological type, followed by suitable molecular profiling of the tumor.[2,3] The importance of biospecimens for molecular diagnosis has been highlighted in several reports from different countries.[4] However, the success rate of molecular diagnoses based on biospecimens differs across institutions and depends on the institutes' acquisition and processing practices, in addition to the testing methodologies used.[4] Although single-gene assays are more commonly used in clinical practice, they provide limited information.[5] With the advent of multiple clinical biomarkers and the availability of potential targeted therapies, massive parallel sequencing platforms using next-generation sequencing (NGS) technology have been adopted by several laboratories in recent times. NGS assays are conducted with a more extensive deoxyribonucleic acid (DNA)/ribonucleic acid (RNA) input, where the optimal quality and quantity of the nucleic acid is extremely important, which is usually challenging to obtain when small tissues are not appropriately handled.[4] Amplicon-based NGS assays require minimal input material compared with hybrid capture technology-based assays.[4,6]

High-quality biospecimens are essential for personalized medicine.[7] To ensure the same, tissue samples should be collected and handled according to standard protocols that minimize chemical, mechanical, and thermal degradation and protect the molecular composition and consistency of the samples.[8] Several variables can affect the molecular integrity of the biospecimens, and result in potential errors during the determination of molecular and physical characteristics of biospecimens.[9,10] The variables affecting the quality of the biospecimens can be divided into three general categories: "preanalytical factors," "analytical factors," and "postanalytical factors."[11] The preanalytical phase involves the handling of specimens by a multidisciplinary team and is based on several processes that might introduce errors at different levels and hamper the biomarker testing results.[11] As per a recent study, approximately 60 to 70% of laboratory-associated errors in tissue specimen handling occur in the preanalytical phase.[1,12] Therefore, the preanalytical phase plays a vital role in the evaluation of cellular pathology.[11] Some preanalytical variables that affect the quality of biospecimens are the acquisition of adequate samples and processing of samples, including specimen fixation, temperature, fixation time, pH of the fixative, postfixation processing, and methodology of testing.[2,13]

There are many challenges associated with tissue handling and processing in India, which include a lack of awareness among the surgical fraternity during the collection of samples, poor tissue fixation practices, and climatic conditions/changes that adversely affect the quality of specimens.[11] There are several published international and national guidelines for the preanalytical steps that ensure valid and reliable molecular testing.[1,14–17] However, the existing guidelines for biospecimen collection and handling are not applied consistently.[1,18] Adherence to guidelines is further impacted because many guidelines are patented, which limits their accessibility to all members of the biomedical fraternity, particularly in India.[1] Hence, due to diverse existing clinical practices for biospecimen handling and preparation, differences in results can occur between different laboratories, making molecular diagnosis challenging.[19] Moreover, as multiple stakeholders are involved in tissue handling, including interventional radiologists, surgeons,

pathologists, molecular scientists, technologists, hospital administration staff, and researchers, increasing awareness regarding biospecimen handling and associated guidelines are crucial.[20] Thus, there is an unmet need to frame expert recommendations that serve as a consistent and up-to-date reference for multidisciplinary teams for the optimization of tissue handling and processing for precision medicine. This white paper aims to highlight the challenges in the field of biospecimen handling and provide recommendations on the standardization of variables in the preanalytical phase of tissue processing for optimal biomarker testing.

Methodology

A virtual advisory board meeting was conducted in August 2021 to develop recommendations for the optimization of tissue handling and processing for precision medicine. The panel comprised 19 experts including pathologists ($n = 10$), molecular biologists ($n = 2$), medical oncologists ($n = 4$), a surgical oncologist ($n = 1$), an interventional radiologist ($n = 1$), and a senior histology technician ($n = 1$) from 10 hospitals in India. The expert panel also included an accreditation officer for testing and calibration of laboratory procedures in India. The meeting was conducted in two sessions. In the first session, the experts acknowledged and recognized the challenges in the tissue journey from acquisition to storage (►**Table 1**). The experts discussed and provided recommendations to overcome those challenges in the second session.

To better align the discussion, the lead scientific coordinators independently developed relevant questions addressing important issues on the subject, such as practical issues with biomarker testing and different steps involved in the preanalytic phase of tissue specimen preparation, for the panel to address. The questionnaires are summarized in ►**Table 2**. During the advisory board meeting, each question was discussed and edited by the entire group through rounds of discussion and drafts until a complete set of recommendations was obtained. Based on the available literature and experts' clinical experience, recommendations for optimizing tissue handling were proposed. The workflow of the expert recommendation development is presented as an illustration in ►**Fig. 1**.

Table 1 Key challenges according to the expert panel for biomarker testing in India

1. Challenges in tissue acquisition and handling • Adequate quantity of tissue to permit morphologic diagnosis and ancillary biomarker profiling • Lack of uniform and standardized protocols for tissue management and processing across laboratories (no benchmark in histopathology) • Assays and platforms to assimilate data from the same pathology specimen
2. Excessive reliability on cytology specimens in the diagnostic workup
3. Lack of multidisciplinary approach: Local practices and ancillary analyses affect the tissue journey
4. Quality- and quantity-related issues of the tissue for biomarker testing
5. Lack of facilities for multiplex/next-generation sequencing testing
6. High turnaround time
7. Testing in the referral laboratories
8. Cost
9. Challenges with rebiopsy
10. Lack of training facilities for molecular diagnostics
11. Lack of appropriate archival facilities

Results

The preanalytical handling of the biospecimen from acquisition to storage is based on several successive procedures, such as tissue collection, fixation, processing, embedding, and storage. Additional factors affecting the integrity and molecular structure of the tumor include the quantity of the tumor within the collected tissues, tissue quality, and the characteristics of the genomic material depending on the test and diagnostic modality used.

The following are the practice recommendations based on evidence from current literature and the experts' clinical experience to control preanalytical determinants and variables.

Clinical Requirements of Biomarker Testing/NGS Testing

Present diagnostic and prognostic classifications, based on clinical and pathologic factors, are insufficient to accurately characterize tumors due to their clinical heterogeneity.[21] This is more relevant in cases of metastatic cancers wherein multiple lines of standard chemotherapy have been utilized and/or have failed. Testing such metastatic tissues for targets has become imperative, given the availability of various approved biomolecules.[2,22,23] Therefore, NGS has emerged as a technique that can be used to screen and diagnose both germline (inherited) and somatic (acquired) genomic mutations and is mainly used for genomic and transcriptomic analyses.[2] The novel and rare somatic mutations can accurately be detected by NGS technology (►**Box 1**).[24]

Tissue Acquisition

Issues Impacting the Tissue Journey

A key barrier to implementing biomarker testing is ensuring adequate tissue acquisition to provide sufficient material not only to permit morphologic diagnosis but also downstream ancillary biomarker profiling.[2] Obtaining an adequate tumor sample can be clinically challenging due to an inaccessible tumor location or late presentation with metastatic disease at diagnosis.[2]

The quality of one-third of core biopsy specimens was not found to be appropriate for novel immune biomarker discovery, NGS, and histopathologic testing.[25] It is now imperative that, whenever possible, the aim of any diagnostic

Table 2 Questions provided to the expert panel

A: Clinical requirements (questions specific to a medical oncologist)
1. Who are the candidates for biomarker testing?
2. How often do they need biomarker testing in routine oncology practice?
3. What are the common site-specific molecular tests performed?
4. What type of tissue sample should be sent for molecular testing? Fresh tissue/RNAlater/snap-freeze on or only paraffin blocks
5. In what type of patients do you suggest high-end genomic tests such as NGS in the course of their disease? Are the medical oncology community and colleagues aware of these tests? Do you counsel patients at the beginning of treatment regarding these issues?
6. What is the preferred testing modality while referring your patients for oncology biomarker testing? Germline or somatic?
7. What are the key challenges from the clinician's perspective while requesting these tests?
8. What is the reliability of small gene NGS panels?
B: Tissue acquisition (questions specific to an intervention radiologist/surgeon)
1. How easy/difficult is it to approach deep-seated tissues?
2. How do you assess the quality of the obtained tissue? How often do you take multiple passes? Do you take help from any surgeon? Any advice to be given at the outset to the clinician with regard to obtaining tissues?
3. Should touch imprint (ROSE) be practiced in evaluating tissue yield? How feasible is it to practice it commonly?
4. What is the ideal cold ischemia time to be followed with regard to small and big specimens? Is there any constant interaction on this among pathologists and surgeons? What is the experience of its impact on breast cancer specimens and predictive biomarker expression?
C: Tissue processing and handling (questions specific to a pathologist and laboratory personnel)
1. What are the critical factors for consideration for fixation—a type of fixative or time to fixation? a. Which is better—immediate fixing in the operating room or the frozen section room/pathology department? b. What is the size of the tissue bit to be processed? c. Shelf life: How frequently should the fixative be replaced? d. What should be the ratio of the fixative volume to tissue volume? e. Do you check these with your technical colleagues?
2. What is the optimum tissue processing protocol to process FFPE tissues?
3. How can the step of paraffin infiltration be standardized? What is the recommended melting temperature of paraffin used? What is the quality of paraffin, or any other parameters related to it?
4. How do you segregate a tissue block for molecular testing, especially in the case of lung cancer or GI malignancies if you have multiple bits?
5. Is there a dilemma on how much IHC testing is to be done for fear of losing out on tissue for molecular testing?
6. Tissue block selection: Which block is to be selected? What about tissue tumor content? When do you want to do the test? Do you want this test to be done on treatment naïve vs. post-NACT biopsy samples and whether to use the primary vs. metastatic site tissue? Are some guidelines available, or is it based on your practice?
7. How to ensure adequate storage conditions so that the RNA and DNA retain their integrity in FFPE tissue?
8. What is the best procedure to get maximum yield and accurate results in NGS?
9. Comment on various preanalytical and analytical aspects of NGS: The platform to be looked at, the reagent that is specific for the platform or usage of in-house reagents, the quality control EQA, troubleshooting, repeats, when to call inadequate/equivocal/when to give up on this test
10. How often do you face issues with the yield of DNA/RNA during the genomic test?

Abbreviations: DNA, deoxyribonucleic acid; EQA, external quality assessment; FFPE, formalin-fixed paraffin-embedded; GI, gastrointestinal; IHC, immunohistochemistry; NGS, next-generation sequencing; NACT, neoadjuvant chemotherapy; RNA, ribonucleic acid; ROSE, rapid on-site evaluation.

biopsy/tissue sampling procedure performed should be to maximize the amount of tissue acquired without compromising patient safety.[26] The quality of the biospecimens depends on the expertise of the surgeons and interventional radiologists in tissue collection. The best approach for individual patients can be determined by involving a multidisciplinary team comprising pathologists, radiologists, surgeons, and oncologists.[26] Usually, patient safety, accessibility of the site, and probable tissue yield determine the choice of the site to be sampled.[2,20,26] This will reduce the number of repeat biopsies and prevent unnecessary delays in treatment.[2] Surgeons and interventional radiologists need to

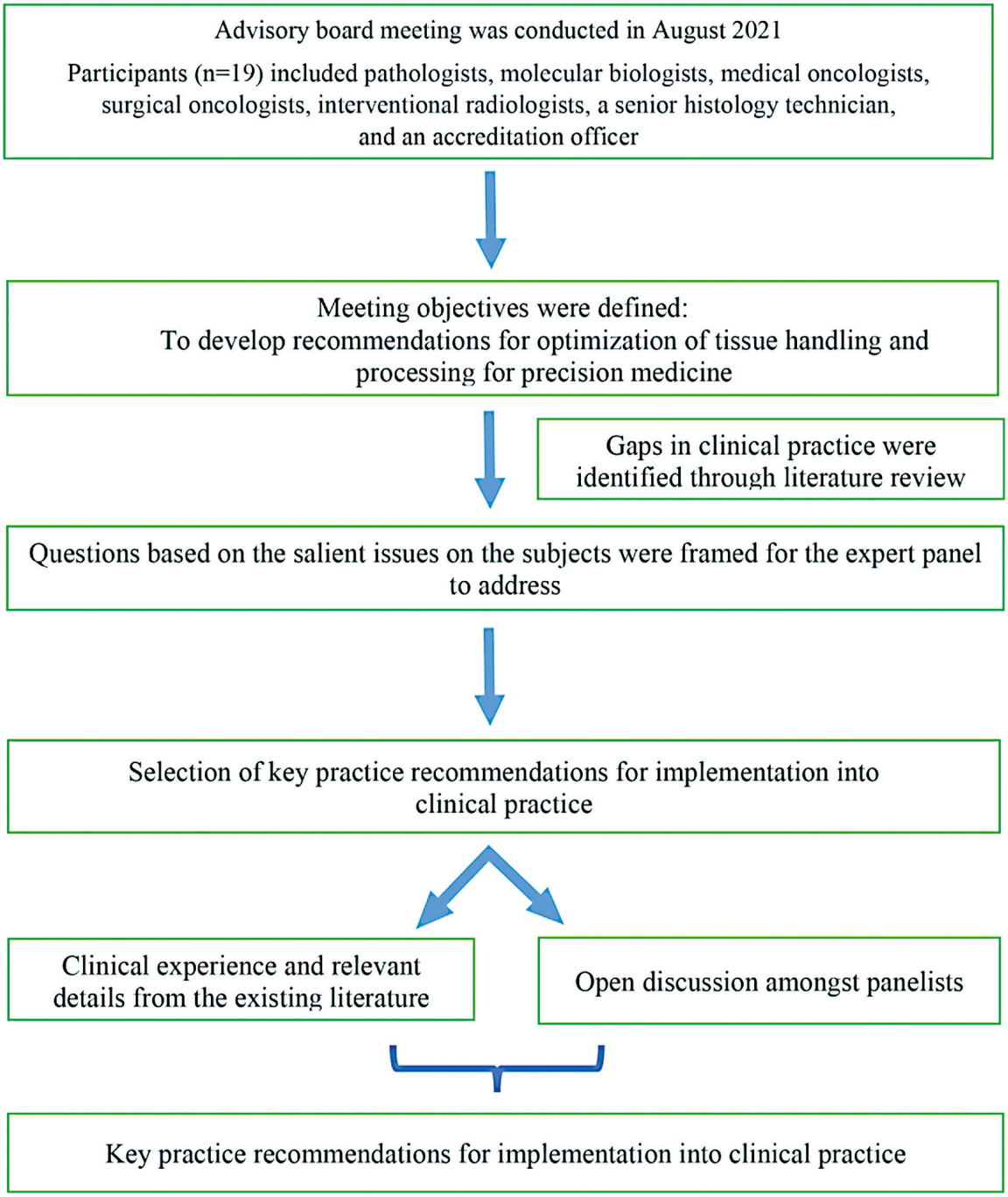

Fig. 1 Flowchart representation of expert recommendation development.

be trained to obtain adequate samples, especially from deep-seated tumors. A minimum of three tumor cores of different viable areas, avoiding necrotic regions of the tumor, should be obtained.[27] Rebiopsy for molecular workup may be required if diagnostic samples are inadequate for mutation analysis or the patient has disease progression (►**Box 2).**[28]

Tissue Handling: Cold Ischemia Time

Ischemia time is defined as the duration between specimen removal and proper fixation. Ischemia time is important as this allows activation of tissue enzymes, protein, and nucleic acid degradation, especially RNA, and autolysis. Ischemia time includes warm ischemia time and cold ischemia time.[29]

Box 1 Expert opinion on clinical requirements of biomarker testing/NGS testing

- Genetic testing can be performed to identify any actionable mutation for solid tumors whenever all the lines of standard therapy have been exhausted.
- A minimal panel of biomarkers should be performed depending on the tumor type and site (e.g., *EGFR*, *ALK*, *ROS1*, *BRAF*, and *PD-L1* for lung cancer).
- Multiplex testing should be preferred over single-gene assays whenever feasible, especially in cases showing progression on initial therapy (through repeat biopsies).
- NGS should be utilized for tumors when multiple genes need to be tested in cancers such as ovarian cancer, lung cancer, uncommon tumors such as tumors of the salivary gland, thyroid, colon, and rare tumor neurotrophic tyrosine receptor kinase fusion cancer; thus, the judicious use of tissues as well as reduced turnaround time is essential.
- Liquid biopsy can be considered for molecular testing when tissue diagnosis is not feasible.
- Germline testing should be done depending on the clinical requirement, considering their utility pertaining to the specific tumor type.
- Appropriate consent and genetic counseling should be done before and after germline testing as they have implications for the patient and family members.
- Small gene hotspots are of practical utility, cost-effective, and reliable. At the same time, the issues of interlaboratory quality assurance need to be addressed.

Abbreviations: ALK, anaplastic lymphoma kinase; BRAF, B-Raf proto-oncogene serine/threonine kinase; EGFR, epidermal growth factor receptor; NGS, next-generation sequencing; PD-L1, programmed death ligand 1; ROS1, receptor tyrosine kinase 1.

Box 2 Expert opinion on tissue acquisition

- Tissue sampling can be done from easily accessible sites irrespective of primary and metastatic sites.
- Choose less invasive technology or modality for the patient's diagnostic procedures. The collected tissue should be sufficient for both diagnosis and molecular testing.
- Image-guided biopsy is recommended for sampling small or extremely small tumors and deep-seated tumors, preferably by expert interventional radiologists trained in such procedures.
- A minimum of three, 1–2 cm biopsy cores per tumor, and sampling from different areas of the same tumor are recommended. A single-core biopsy is not recommended for deep-seated tumors.
- Rapid on-site evaluation may be used for adequacy assessment, wherever feasible.
- Cell blocks should be prepared for cytology specimens whenever possible, which aid in molecular testing.

Warm ischemia time is the interval between vessel ligation and specimen removal, whereas cold ischemia time starts from specimen removal to fixation.[1,29,30] Warm ischemia time can vary significantly, from a few minutes to several hours, and depends on the complexity of the surgical procedure, the expertise of the surgeon, the organ in question, and the modality of intervention. Cold ischemia time, which can take a few minutes or several hours, depends on the type of tissue, tumor size, collection method, surgeon, nursing staff, and procedures followed in various institutions.[19,29] Previous reports suggest that the changes occur in the RNA and protein of the tissue during this interval.[29,31] Recent literature suggests that a cold ischemia time of 1 hour can minimize the rate of biomolecular degradation (►**Box 3**).[1]

Specimen Type for Biomarker Testing

Both tissue biopsy (fresh and formalin-fixed, paraffin-embedded [FFPE]) and cytology specimens can be used for diagnosis and molecular testing.[2] Biospecimens should be preserved in a way that they will remain reliable for both expected and unforeseen uses.[9] The removed tissue specimen can be used in three ways for molecular evaluation: by freezing the tissue, keeping it fresh, or stabilizing the tissue in a fixative.[32] Fresh frozen specimens (FFSs) (−80 to −190°C) and FFPE specimens

Box 3 Expert opinion on cold ischemia time

- Tissues must be fixed immediately to avoid the rapid deterioration of DNA, RNA, and proteins.
- Cold ischemia time should be as minimal as possible and not exceed 1 hour.
- Ensure the training of nurses, trainees, and technologists on proper and prompt fixation of tissues and maintaining cold ischemia time below 1 hour.
- Maintaining a record of the time of administration of anesthesia and removal of the specimen may be submitted to the pathology department as a part of the details of the specimen.
- Timing of the beginning of fixation should be recorded.

Box 4 Expert opinion on the type of biospecimens

- Formalin-fixed paraffin-embedded specimens are the most preferred specimens for biomarker testing and tissue storage as it increases the shelf life of the tissues to several years.
- Separate standardization and validation need to be done for cytology specimens.
- Cell blocks should be prepared whenever feasible.

may be used as sample archival methods after surgical removal of biopsy for the preservation of nucleic acids and proteins.[2,33] FFS is considered the gold standard for molecular analysis as it provides high-quality nucleic acid yield and facilitates superior preservation.[34] However, FFS disrupts the features of the tissues morphologically and hinders the assessment of tumor fraction; it requires highly controlled conditions and expensive infrastructure for proper handling and storing of the frozen samples.[33,35] FFPE tissues are easy to handle logistically as many biomarker assays are now standardized using these samples; however, it can cause adulteration in molecular tests, resulting in false-positive or false-negative results.[27,36]

Cytology samples (fine-needle aspiration cytology, fluid samples, direct stained smears, or liquid-based preparations) can be used reliably for molecular testing,[26,37] provided upfront planning is done at the time of sample acquisition. The protocol for the testing needs to be separately validated for the cytology specimens. Cell blocks should be prepared for cytology specimens whenever feasible, as the same protocols can be used for histology (►**Box 4).**[26]

Tissue Processing and Handling

Tissue Fixation: Tissue Thickness, Time, and Volume of Fixative

Fixation is the preservation of cells, tissue structures, and their chemical constituents through chemicals.[19,29] This process involves submerging the tissue into a fluid called the fixative.[29] Fixation prevents decay or autolysis of cells and preserves tissue morphology. Poor fixation can lead to the generation of inappropriate and false-positive results that might preclude optimal diagnosis and further treatment.[27,38] Most biopsy specimens are small and are fixed quickly when placed in 10% neutral-buffered formalin (NBF) of pH 6.8 to 7.4 at 25°C; however, larger surgical specimens necessitate controlled fixation for a longer duration.[39,40]

The fixation process is predominantly dependent on three components: tissue thickness, time, and volume of fixative.[19] Inadequate compliance to any of these components will result in either under-fixation or over-fixation of the tissue.[19] Both over-fixation and under-fixation can adversely affect the molecular profile of the tumor. The rate of penetration of formalin in the tissue is variable depending on the type of tissue but is approximately 1 mm/h[19]; hence, a minimum dedicated time for fixation should be given. The infiltration of the fixative solution in the tissues occurs at varying speeds as it depends on the thickness of the sample. If the thickness is increased twice, the time allowed for the penetration of the fixative solution should be increased by four times.[41]

The duration for which the tissue is immersed in the fixative plays a crucial role in tissue processing in surgical pathology. The fixation time may vary depending on the size of surgical specimens.[35] The standard time duration required for the complete fixation process varies from a minimum of 6 hours for needle core and endoscopic biopsy specimens to more than 12 hours for sections derived from larger specimens.[19] The ratio between the volume of the tissue to the volume of fixative can vary from 1:10 to 1:20; generally, 1:10 is accepted as an optimum ratio for good fixation.[41]

The temperature and pH of the fixative can also impact the DNA yield. Fixation at room temperature triggers higher DNA degradation than at lower temperatures.[2] Therefore, it is recommended to initiate an immediate fixation at a low temperature of 4°C.[42] This may, however, take more time than fixation at room temperature and might decrease the staining intensity of the specimen.[2] A tissue fixed in formalin at low pH can cause extensive damage to DNA compared with tissue fixed at a neutral pH (►**Box 5).**[2]

Tissue Processing from Fixative to Paraffin

The tissue processing protocols must be standardized, which largely depends on the thickness of the tissue.[43] Suboptimal processing of tissues can adversely affect the recovery of biomolecules from the tissue specimen. The tissue processing after fixation is crucial for maintaining the quality of the biospecimen.[19] For fixed tissues, the biospecimens are processed across several steps, including sequential dehydration with ethanol, successive replacement by xylene in a process called clearing, and the process of replacement of xylene with paraffin, which is known as impregnation.[19] The quality of reagents, time, and temperature affect tissue quality. The time taken for this whole process may vary from 4 to 12 hours. Freshly prepared and high-quality reagents should be used in the process.[19] A delay in tissue processing could lead to incomplete dehydration of the tissue because of diluted alcohols and xylenes that are carried over from previous steps. Complete dehydration during processing is crucial, as the remaining water will not be replaced by paraffin and may cause tissue degradation. Inadequate dehydration of tissue is generally associated with improper fixation. Poor fixation leads to incomplete coagulation of proteins, which leads to the trapping of water within the tissue (►**Box 6).**[19]

The Impact of Paraffin on Fixed Tissues

Tissue fixation is followed by infiltrating the tissue through an embedding medium, usually wax. After infiltration, the tissue is embedded into a mold with the same medium to

Box 5 Expert opinion on tissue fixation

- Fixative: 10% neutral-buffered formalin at a pH of 6.8–7.4 is the recommended fixative of choice.
- The date of preparation of formalin should be recorded.
- Freshly prepared formalin is always preferred, and it is recommended to mention the expiry date on the containers used for biopsy sample collection (within 5 days of preparation) (►**Supplementary Fig. S1**, available in the online version).
- Fixation time should be recorded and controlled.
- Recommended time in formalin: At least 6 hours (for small biopsies) and 12–18 hours (for large specimens). Fixation beyond 24–36 hours should be discouraged. Tissue with high-fat content may require 48 hours.
- Particular care should be taken regarding fixation timing for procedures conducted before a weekend or public holiday, as over-fixation can impact the molecular testing results.
- Special care should be taken for transportation time if the sample is to be transported to the referral laboratory (especially for samples collected on the weekend) for further testing as the likelihood of over-fixation increases.
- The pH of formalin should be mandatorily checked daily, and if it is less than 6.8, it should be discarded.
- Formalin fixation of tissue specimens at 4°C leads to better nucleic acid preservation (but this may be difficult to implement in clinical practice). If fixation is done at 4°C, in-house standardization and validation are recommended not only for routine histopathology and immunohistochemistry evaluation but also for molecular diagnostic assays.
- Acidic or heavy metal fixatives or decalcified specimens should be avoided for biomarker testing.
- Specimen dimensions: Tissue section thickness should not be more than 4 mm (cassette size $3.5 \times 2.5 \times 0.5$ cm).
- Volume to mass ratio: Volume to mass ratio of 4:1 at a minimum, preferably 10:1, with tissue completely submerged.

Box 6 Expert opinion on tissue processing

- Optimum processing time for core biopsies should be not less than 3 hours for smaller tissues and 8–16 hours for large tissues.
- Preferred dehydrating agent: Isopropyl alcohol.
- Standardized, automated processing protocols are preferred over manual tissue processing.
- Details of tissue processing conditions should be recorded.
- The solutions in the automated tissue processors must be changed periodically as per the manufacturer's recommendation and the record of the same must be kept in the laboratory.
- The tissue processing quality should be evaluated by checking the histomorphological features, in addition to optimal DNA/RNA yield.

form a block that is stored at room temperature.[39,44] Ideal characteristics for the embedding material are inertness, ability to repel moisture and readily penetrate the tissue, and reliability at room temperature.[39] Several types of paraffin wax can be used as the embedding material.[39] Different kinds of paraffin have different melting points and textures and are affected by the characteristics of the sections of the final blocks.[19] The use of high-melting point paraffin leads to inadequate deparaffinization, reducing the recovery of biomolecules from the tissue, and in the intensity and extent of immunostaining.[1]

Tissue Quality and Quantity: How to Improve the Diagnostic Yield of Molecular Testing

It is pertinent to manage tissue specimens not only for diagnosis but also to maximize the availability of tissues for molecular studies. Hence, it is recommended that the histology technician follows the protocol for tissue preservation in the laboratory as well as that of reporting by the pathologist. The tumor fraction or purity of the specimen plays an important role in determining the success of diagnostic testing.[2] Areas of necrosis, hemorrhage, extracellular mucin, and marked fibrosis may result in low tumor content despite the presence of adequate tissue volume in the biopsy sample. A viable tumor fraction is a vital factor to consider as a low tumor fraction can result in unknown reliability of molecular diagnostics, leading to false-negative results.[2] Different types of diagnostic testing need different quantities of the specimen. A prototype example of a lung is illustrated in ►**Fig. 2**. For instance, 50 evaluable tumor nuclei per section are required for fluorescence in situ hybridization analysis,[45] whereas genomic sequencing and mutational analysis need at least 10 to 20% of tumor content.[2,20] The ideal tumor fraction for NGS assays varies from >10 to 20% (►**Box 7**).[2]

Postanalytical Variables—Tissue Storage Conditions

There is a requirement for the proper storage of the block after processing the specimen. Research has revealed a reduced recovery of nucleic acids from older tissue blocks (FFPE) compared with recent FFPE tissues.[19] The reduction rate is 5 to 50% for each decade of age.[19] However, the cause of this reduction is ambiguous. It is assumed that the decreased recovery can be due to embedding media, quality

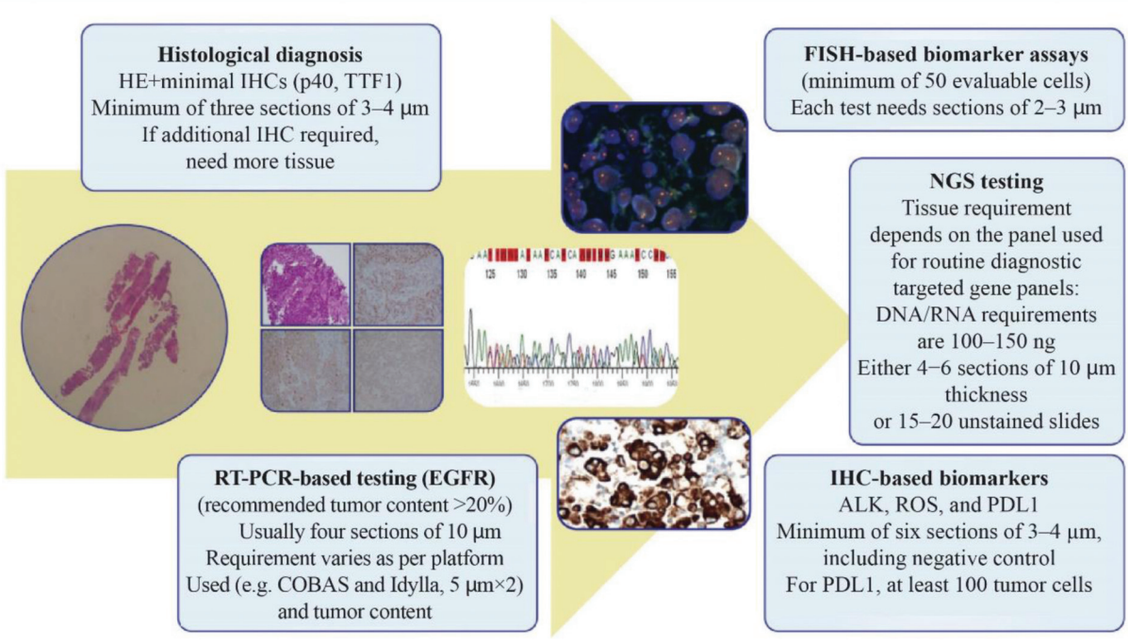

Fig. 2 Illustration of the minimum tissue requirements for various molecular testing procedures using lung cancer as an example.

Box 7 Expert opinion on biospecimen requirements for molecular testing

- Only a trained technician should handle the small biopsies.
- It is recommended not to club all the tissue cores into one paraffin block; at least two separate blocks should be made (one can be used for routine histopathological diagnosis, including IHC, and the other one for molecular workup (►**Fig. 3**).
- It is recommended that highly purified paraffin wax (which melts at 58–60°C) is used for tissue embedding.
- Review all available pathology material together so that unnecessary repetition of the same test is not done.
- IHC should be performed only when deemed necessary; it should always be performed judiciously.
- Reflex testing is preferred over sequential testing, and blocks should be cut a minimal number of times.
- Tumor fraction should be maintained at more than 10% for DNA extraction.
- Microdissection and macrodissection can be performed to enrich the tumor content.
- Low cellularity tumors require more unstained sections for DNA extraction.

Abbreviation: IHC, immunohistochemistry.

of tissue processing, or characteristics of reagents used.[19] The long-term storage conditions determine the long-term stability of tissue-based biomarkers.[46] The biospecimens are stored for a longer duration in two ways: FFPE tissues at ambient temperatures and frozen tissue at ultra-low temperatures (from −80 to −190°C).[33,47] At ultra-low temperatures, nucleic acids with higher molecular weights and enzymatically active proteins in tissues can be preserved for several years. Still, RNA may be degraded.[33] The embedding of the tissue specimen with paraffin increases its shelf life. Freezing the tissues at ultra-low temperatures is more expensive than FFPE blocks due to high maintenance, more space requirements, and increased laboratory costs.[33] Usually, the FFPE blocks are widely stored by the pathology departments compared with frozen tissues. This storage of tissues for a longer duration facilitates the formation of an extensive repository of tissue material and clinical details, thus, helping in translational clinical research (►**Box 8**).[33]

Discussion

Molecular analysis of the biospecimen is the keystone for diagnostic and therapeutic decisions in clinical practice. However, high-quality specimens are a prerequisite for accurate diagnosis. The procedures followed in the preanalytical phase of the biospecimen processing journey directly determine tissue quality.[1] The preanalytical phase includes collecting, processing, and storing the biospecimen until further molecular analysis.[9] The relevance of these preanalytical tissue factors is largely ignored in India.[48] This results in the wastage of resources,[49] particularly the expensive analytic components of molecular testing, yielding

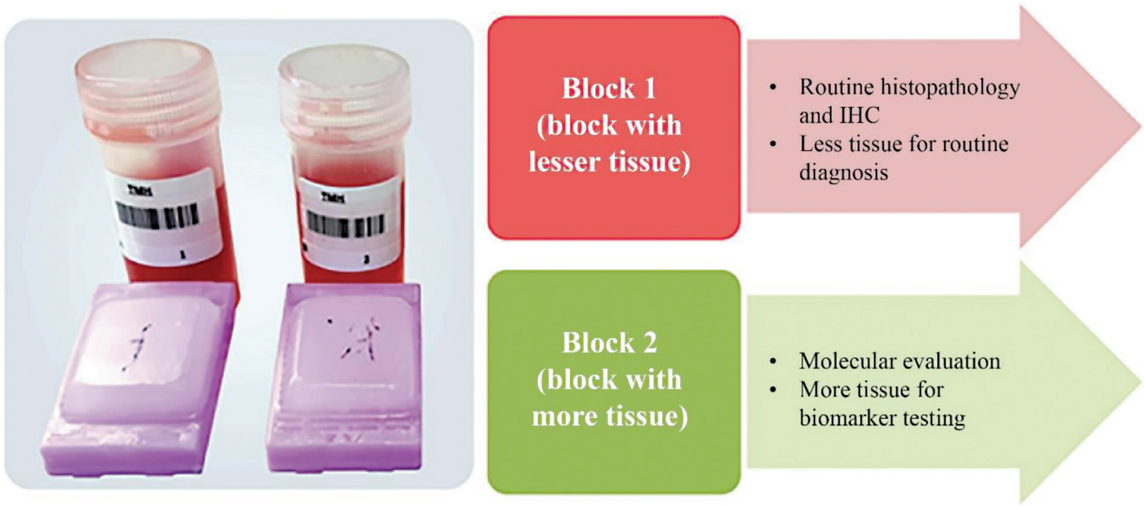

Fig. 3 Illustration of preparation of blocks for molecular testing (routinely employed in lung biopsies).

Box 8 Expert opinion on postanalytical variables—long-term tissue storage conditions

- Storage conditions: Dry, pest-free conditions at room temperature (defined as 18–25°C).
- Paraffin blocks should be stored in a temperature-controlled environment, protected from excessive humidity, dryness, and light.
- Establishment of a tissue repository for the fresh tissues that can be stored for several years for research purposes.
- Follow the College of American Pathologists guidelines for preanalytical precision medicine and tissue repository establishment.
- The date of preparation of tissue block and slide, conditions of block storage, temperature, and humidity of storage area should be recorded.
- Block retrieval and back filing should have some defined protocol so that this block becomes accessible whenever required.

suboptimal quality of nucleic acids, and thus, affecting the downstream processing and results. The expert panel provided recommendations for the collection, processing, fixation, and block preparation of the tissue to ensure the high quality of biospecimens. However, an audit of practices and improvements is suggested.

According to the American Society of Clinical Oncology and College of American Pathologists, for cold ischemia time, the interval between the collection and fixation of the biospecimen should be 1 hour or less.[1,50]As per the latest research, cold ischemia time of less than 1 hour for breast cancer specimens facilitates the assessment of structural and functional parameters for prognosis and treatment.[1,41,51] The expert panel proposed that cold ischemia time should be 1 hour or less based on literature evidence. As per the experts, the date, time, and place of collection of the specimen should be mentioned in the requisition form and submitted to the pathology department along with the specimen. This record would also serve the purpose of auditing these processes and enabling improvement in case of inadequacies.

Clinicians, researchers, and pathologists should carefully plan and efficiently coordinate if a patient/specimen is considered for molecular profiling. This is done to ensure that tissues are handled optimally and carefully to preserve the integrity of DNA, RNA, and proteins.[2] Initial handling includes transporting the specimen from the operating room to the pathology department and cutting the tissue into sufficiently small sections. Degradation of biomolecules can occur during this period, specifically proteins and RNA.[2,29] The method of transportation of surgical specimens may differ in hospitals according to the physical location of surgical rooms and pathology laboratories. Ideally, the biospecimen should be immediately fixed in the procedure room or transported as early as possible to the pathology department. The experts highlighted the importance of educating and training nurses, new trainees, and technologists on the proper fixation of tissues and keeping the cold ischemia time below 1 hour.

Fixation is the most critical step in tissue handling because this process is irreversible, and if fixation is poorly performed, it is impossible to recover the tissue. Generally, immunohistochemical staining is optimal when tissue specimens are fixed in 10 to 15% NBF.[52] Moreover, tissues should be fixed for 6 to 24 hours at ambient temperature to ensure optimal immunostaining, as per reports. Studies also suggest that fixation for more than 72 hours is counterproductive.[53,54] Under-fixation can cause nucleic acids and protein degradation or might change gene expression within tissue regions that have not been permeated by the fixative solution. Over-fixation can lead

to fragmentation of the DNA and extensive cross-linking, which challenges the extraction of usable nucleic acids and proteins.[2]

As per the experts, many laboratories in India presently use Bouin's fixative. The choice of fixative is critical. The experts approved the use of 10% NBF phosphate-buffered formalin at a pH of 7.0 as a fixative. They emphasized that the fixation time should not be less than 6 hours and not more than 24 to 36 hours.

The experts suggested that the formalin used for fixation should be freshly prepared and should be used within 5 to 7 days. The experts also recommended that while preparing formalin in the laboratory, standard procedures should be followed to ascertain the accurate concentration and pH of the solution. The pH of the commercially prepared formalin should be checked regularly, and it should be mentioned on the containers. Freshly prepared formalin should be available in operating room and endoscopy and radiology units. The stock solutions of formalin should be stored in sealed containers to prevent the conversion of formalin to formic acid. The volume of tissue to fixative ratio is recommended to be 1:10.

Regarding tissue storage and processing, experts agreed that FFPE is the most preferred method for tissue storage as it increases the shelf life of the tissues to several years. During tissue processing, the biospecimen is dehydrated and cleared. The experts recommended optimum dehydration time for core biopsies to be 3 hours and 8 to 10 hours for large tissues. The experts approved isopropyl alcohol as the dehydrating agent. The details such as time, temperature, presence of vacuum, equipment, and reagent used should be documented. The quality of the reagent should be monitored regularly. Studies comparing the conditions of processing the specimens and alternative reagents used in the tissue processing techniques are warranted.

The experts also highlighted the significance of the post-analytical phase of tissue processing and preservation. For tissue block preparation, the experts recommended the maintenance of paraffin blocks in dry, pest-free conditions at room temperature (25°C). Temperature and humidity should be monitored daily. The experts also suggested that housekeeping measures should be followed, and the storage area should be dust and pest free. Based on previous literature,[55] the acceptable thresholds for preanalytical factors for specific analytes were recommended by the experts (►**Supplementary Table S1**, available in the online version). In some instances, no relevant studies were available to provide evidence-based conclusions ("evidence not available"). However, for a few other factors, limited studies were available that were insufficient to draw definitive conclusions. The available evidence for those factors was constrained in terms of quality or relevance, which hindered a comprehensive examination of the investigated aspect ("evidence was insufficient") (►**Supplementary Table S1**, available in the online version).

The experts highlighted the significance of biorepositories in pathology. It serves as a reserve of high-quality tissues for biomarkers and provides information to the investigators about the content and characterization of the biospecimens along with the patient information.[56] The experts suggested that a tissue repository must be established where tissues can be stored for several years and used for research purposes later. They emphasized that these repositories facilitate a better understanding of the disease and patients because they collectively provide genetic, clinical, and lifestyle-related information. Moreover, they concluded that the appropriate identification and validation of biomarkers could help in the advancement of personalized medicine through novel drug development and pharmacogenomic studies.

Conclusion

The preanalytical handling of biospecimens is conducted in several steps, from surgical removal to paraffin embedding and storage of tissues. Each step is crucial and facilitates the preservation of morphological characteristics, antigens, and nucleic acids for molecular analysis. There are differences in specimen preparation practices that impact molecular quality and composition. The experts' recommendations for preanalytical quality control would ensure high-quality biospecimens for molecular analysis and precision medicine. These recommendations can enhance investigators' knowledge in clinics and pathology laboratories on optimal handling, collection, and storage of tissues for appropriate patient management and clinical trials.

Patient Consent

Patient consent is not required.

Authors' Contributions

All authors have contributed equally toward the conception, design, manuscript preparation, manuscript editing, review, and finalization of the manuscript.

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Conflict of Interest

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HER2 Low Status and Intratumoral Heterogeneity in Epithelial Malignancies and Their Therapeutic Implications

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Abstract

Human epidermal growth factor receptor 2 (HER2) continues to serve as a critical biomarker in breast cancer, but the introduction of evolving classifications such as HER2-low and HER2-ultra-low presents both opportunities and challenges in precision oncology. Targeted therapies like trastuzumab deruxtecan have broadened treatment possibilities, yet these classifications highlight critical challenges related to standardization, diagnostic precision, and equal access to care. The heterogeneity of HER2 expression adds further complexity, often limiting therapeutic effectiveness. Additionally, the exploration of HER2 as a target in nonbreast cancers underscores the urgent need for rigorous clinical validation in diverse malignancies. To advance HER2-targeted therapies, there is a critical need for comprehensive research, improved diagnostic protocols, and strategies to ensure equitable access to innovative treatments.

Keywords
- HER2-low
- heterogeneity
- treatment strategies
- breast cancer
- trastuzumab deruxtecan

Introduction

Over the past two decades, there has been remarkable progress toward understanding human epidermal growth factor receptor 2 (HER2) as a significant prognostic marker in breast cancer (BC) along with deeper insight on its presence across different epithelial malignancies.[1,2] It is a tyrosine kinase receptor, encoded by a proto-oncogene ERBB2, which expresses itself by homo- or heterodimerization resulting in signal transduction mediated by the activation of PI3K/AKT and Ras/Raf/MEK/MAPK pathways that ultimately affects cell proliferation, survival, motility, and adhesion.[3] HER2 overexpression or amplification is associated with higher histologic grade and stage, increased metastatic potential, decreased overall survival, resistance to endocrine therapy, and poor response to selected chemotherapy.[4] Genetic and pharmacological studies have established that HER2 is essential and sufficient for tumor development and maintenance in models of HER2-amplified BC. Since HER2 amplification drives the transformed characteristics of neoplasms, direct pharmacological targeting of HER2 has been suggested.[5]

Current Clinical Practices for HER2 Assessment and Treatment in Breast Cancer

As a prognostic and predictive biomarker, HER2 status is routinely assessed by immunohistochemistry (IHC) and/or in situ hybridization (ISH) in BC. As per the 2018 American Society of Clinical Oncology (ASCO) guidelines,[6] BCs are classified as either HER2-positive (IHC3+ or 2+ with gene amplification by ISH) or HER2-negative (IHC 0+ or 1+ or 2+ without ISH amplification). Patients with HER2 positive disease typically have a worse prognosis with characteristics of aggressive tumor progress and shorter patient survival. The current HER2 targeting drugs include antibodies, tyrosine kinase inhibitors (TKIs) and antibody-drug conjugates (ADCs). Antibody-mediated therapy has been a highly effective strategy for treating

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epithelial malignancies over the past 30 years. With the introduction of trastuzumab, a recombinant monoclonal antibody, HER2-positive BC treatment was revolutionized. Currently, the Food and Drug Administration (FDA)-approved HER2 monoclonal antibodies for BC treatment include trastuzumab (Herceptin) and pertuzumab (Perjeta) that inhibit HER2 overamplification via downregulation of HER2-induced signaling or preventing its dimerization itself, respectively. However, resistance to HER2-targeted therapies, including trastuzumab, poses a significant challenge. TKI drugs block the phosphorylation of tyrosine kinase residues in the PI3K/AKT and MAPK pathways, which regulate tumor cell proliferation, migration, angiogenesis, drug resistance, and apoptosis. Lapatinib, pyrotinib, tucatinib, and neratinib are FDA-approved TKIs that reduce HER2 overexpression. ADCs provide a novel approach by selectively delivering cytotoxic drugs to HER2-expressing tumor cells. Combining HER2-directed agents with cytotoxic drugs has shown potential to overcome resistance and improve outcomes. Trastuzumab emtansine (T-DM1) and trastuzumab deruxtecan (T-DXd) are antibody conjugates that received FDA approval for HER2 targeting.[7,8]

Emerging Insights into HER2 Clinico-Pathology

HER2-Low Status

The phase III DESTINY-Breast04 trial (NCT03734029) demonstrated the clinical actionability of HER2-low status, defined as HER2 expression of 1+ or 2+ by IHC without gene amplification, leading to the approval of T-DXd as the first HER2-targeted therapy for HER2-low BC. This has challenged the binary HER2 classification, paving the way for a ternary system: HER2-negative, HER2-low, and HER2-positive (►**Fig. 1**). HER2-low accounts for approximately 45 to 55% of all BC cases, with a higher prevalence in hormone receptor-positive (HR+) BC (55–65%) compared to triple-negative BC (TNBC, 35–40%). Additionally, the concept of HER2 ultra-low (IHC 0 with faint staining in $\leq$ 10% of tumor cells) has gained interest. HER2-low expression is emerging as a targetable biomarker, with significant therapeutic implications for HR+ BC and TNBC. However, questions remain regarding accurate assessment of HER2-low status, patient stratification, and its prognostic and biological significance. Further retrospective and prospective studies are required to refine the clinical and pathological understanding of HER2-low BC.[9]

HER2 Heterogeneity

HER2 intratumoral heterogeneity (ITH) is a well-known phenomenon in BC. The ASCO guidelines define HER2 heterogeneity as presence of a second population of tumor cells, where at least 10% have a different HER2 copy number and/or HER2/CEP17 ratio. A separate count of at least 20 nonoverlapping cells within this population must be performed and reported. The 2018 guidelines also recognized that unusual patterns of HER2 expression can occur, including strong and complete staining in fewer than 10% of tumor cells. Heterogeneous patterns of HER2 overexpression and amplification can be categorized into three types: the clustered type, where distinct tumor clones exhibit either HER2 amplification or normal HER2 status; the mosaic type, characterized by diffuse intermingling of cells with varying HER2 statuses; and the scattered type, where isolated HER2-amplified cells exist within a HER2-negative population. HER2 ITH contributes to variations in protein expression or gene amplification across different tumor regions, impacting prognosis and therapy outcomes. Studies have shown that HER2 ITH correlates with reduced disease-free survival in HER2-positive invasive BC and diminished trastuzumab efficacy in metastatic cases. While HER2 ITH is more common in HER2 IHC 2+/equivocal cases, recent findings highlight its notable presence in HER2-low tumors, emphasizing the need for further research.[10] HER2 ITH, characterized by the presence

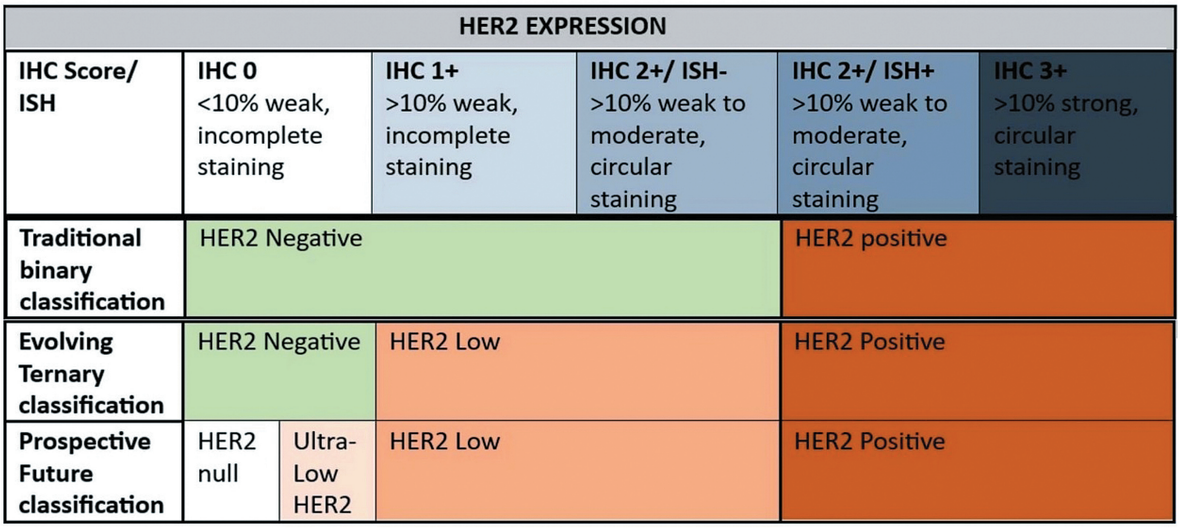

Fig. 1 Human epidermal growth factor receptor 2 (HER2) classification and current categories.

of at least two distinct cell clones with varying HER2 statuses within the same tumor, also poses significant challenges in accurately evaluating HER2 status in BC. HER2 heterogeneity, including both de novo and acquired resistance to anti-HER2 therapies like trastuzumab, presents significant hurdles in treating HER2-positive metastatic BC. It contributes to resistance by potentially causing inaccurate HER2 status assessment and inefficient drug targeting. Studies, such as the MARIANNE trial, show poorer performance of T-DM1 in patients with HER2 ITH compared to those with homogeneous HER2 expression. Patients with HER2 heterogeneity may require additional chemotherapy alongside anti-HER2 therapies, especially when ITH is significant.[11]

HER2 testing on small biopsies with ITH may not fully reflect tumor characteristics. Analyzing multiple slides or the entire slide, with separate ISH analysis for regions with differing HER2 IHC results, is recommended. ITH can cause discordance between IHC and ISH, impacting outcomes, especially in HER2-low patients. Advanced methods like the HER2 gene-protein assay, which combines IHC and ISH, could help detect HER2 microheterogeneity, which may drive resistance to targeted therapies. Hence, more efficient methods are needed to improve HER2 evaluations and therapy selection. Standardized criteria for HER2 discrepancies and ITH also need further investigation[12,13] (►**Fig. 2**).

Nonbreast Epithelial Malignancies

HER2 protein expression at a 3+ level, as identified through IHC, has been observed in a subset of nearly all carcinomas originating from epithelial tissues. HER2 positivity rates were reported as 64% in bladder carcinomas, 55% in gallbladder cancers, 22% in extrahepatic cholangiocarcinomas, 17% in cervical cancers, and around 21.3% in uterine cancers, comparable to the 30% HER2 overexpression rate seen in BC.[14–17] This highlights the potential of anti-HER2 therapies in nonbreast HER2-positive malignancies, having a meaningful impact on treatment strategies.[18]

In the global study of T-DXd for HER2-expressing solid tumors, it demonstrated promising objective response rate (ORR), particularly in IHC 3+ patients, along with durable clinical benefits and manageable side effects. Interim results suggest T-DXd as a potential treatment for HER2-expressing tumors. ORRs for various cancers were 57.5% (endometrial), 50% (cervical), 45% (ovarian), 39% (urothelial), 22% (biliary), and 4% (pancreatic).[19]

While HER2 is a proven predictive marker, its role as a prognostic factor in gastric cancer (GC) remains debated, with recent studies suggesting a negative impact on prognosis. HER2 overexpression in GC is associated with poor clinical outcome. Hence, inhibiting the HER family signal transduction is likely to contribute to improved survival of patients suffering from GC. The phase III ToGA trial demonstrated improved outcomes when trastuzumab was added to first-line fluoropyrimidine/platinum therapy in HER2-positive GC, establishing this combination as the standard of care.[20] HER2-targeted therapies, like trastuzumab, pembrolizumab, and T-DM1, have shown improved outcomes in HER2-positive cases. Emerging treatments, including margetuximab, zanidatamab, and KN026, demonstrate promise in clinical trials. Trastuzumab deruxtecan (T-DXd) and novel ADCs like ARX788 show significant efficacy in advanced settings, marking progress in HER2-positive GC treatment.[8]

HER2 overexpression in ovarian cancer varies widely (8–66%) and shows frequent ITH. While early anti-HER2 therapies like trastuzumab showed limited efficacy, newer drugs such as T-DXd have demonstrated promising outcomes, particularly in tumors with HER2 3+ scores. Preclinical and clinical studies have explored trastuzumab (Herceptin) and pertuzumab (Perjeta) in ovarian cancer, particularly HER2-amplified mucinous subtypes.[21] The DESTINY-PanTumor02 trial demonstrated significant efficacy of trastuzumab deruxtecan in HER2-expressing gynecological cancers, even in heavily pretreated patients, suggesting its potential as a tumor-agnostic therapy.[19,22] Phase II trials with trastuzumab and lapatinib showed limited responses in ovarian cancer, though trastuzumab emtansine achieved stable disease in some cases.[23] TKIs like gefitinib, erlotinib, and pan-HER inhibitors (lapatinib, neratinib) have been studied, with multitargeted TKIs (vandetanib, leflunomide) also showing promise by targeting HER and other pathways (e.g., platelet-derived growth factor receptor, vascular endothelial growth factor receptor).[24] Further phase III trials are needed to confirm these findings.

HER2-targeting antibodies like trastuzumab and pertuzumab show limited efficacy in HER2-mutated nonsmall cell lung cancer (NSCLC). Selective TKIs such as poziotinib and pyrotinib exhibit promising results, especially for HER2 exon 20 mutations, despite side effects.[25] T-DXd, an FDA-approved ADC, has shown significant antitumor activity in HER2-mutated NSCLC, with reduced adverse effects at lower doses. However, T-DM1 has limited efficacy in NSCLC patients, with only a few studies showing mild antitumor activity. Other ADCs, like RC48 and SHR-A1811, are under clinical trials for HER2-abnormal NSCLC. Further research is needed to improve outcomes.

In bladder cancer, HER2-targeting antibodies like trastuzumab, though not FDA-approved for bladder cancer, showed improved outcomes in combination with chemotherapy and radiotherapy but caused significant toxicity.[26] TKIs such as lapatinib, afatinib, and neratinib have shown promise, with afatinib improving progression-free survival in HER2/HER3-mutated cases.[27] ADCs like RC48, FDA-designated as "Breakthrough Therapy," have shown high ORR and survival benefits, especially in HER2-positive cases. T-DM1 and T-DXd also exhibit potential, though T-DXd combined with nivolumab has notable adverse effects. Further studies are needed to refine these treatments and manage toxicities.[28]

No HER2-targeted drugs are approved for biliary tract cancer (BTC), but trastuzumab showed a 66.6% ORR in HER2-amplified gallbladder cancer, and trastuzumab + pertuzumab achieved a 23% ORR in advanced BTC per the MyPathway trial.[29] Zanidatamab (ZW25) showed a 40% ORR, with further studies ongoing. Lapatinib lacked efficacy, while neratinib showed modest results.[30] HER2-targeting ADCs like RC48 and SYD985 showed promising outcomes, with ORRs of 36.4 and 25%, respectively.[31]

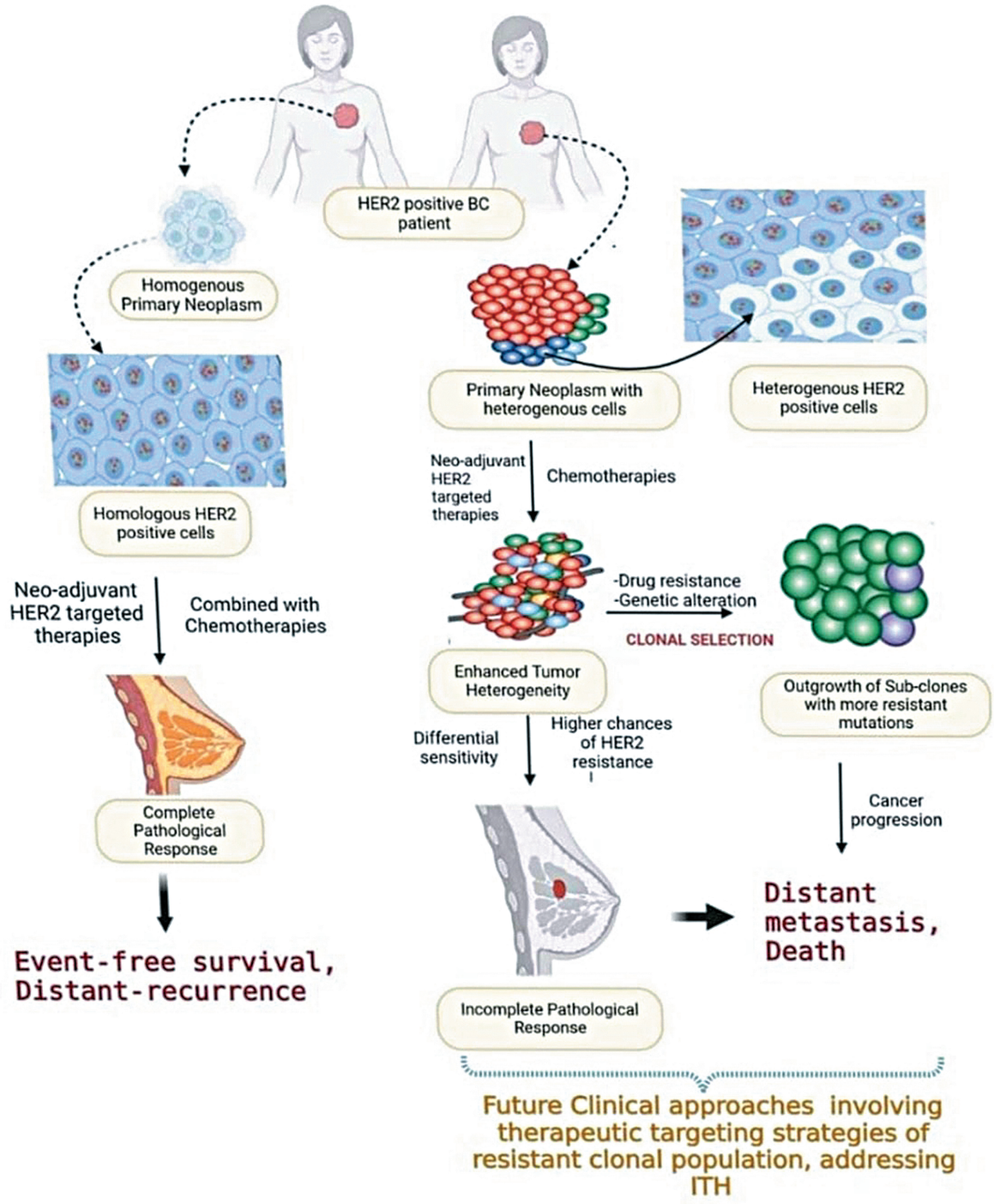

Fig. 2 Human epidermal growth factor receptor 2 (HER2) heterogeneity in breast cancer and its impact on therapy and disease progression.

HER2 monoclonal antibodies alone are ineffective in treating colorectal cancer, but combining them with TKIs improves outcomes. Trastuzumab and pertuzumab, combined with lapatinib, showed an ORR of 32% in metastatic colorectal cancer (mCRC).[32] Tucatinib and trastuzumab had an ORR of 55%, and pyrotinib and trastuzumab demonstrated promising results in ongoing trials. ADCs like T-DM1 and T-DXd also show efficacy. T-DM1 with pertuzumab offers a high disease control rate, and T-DXd monotherapy is recommended for HER2-amplified mCRC, but interstitial lung disease risk must be monitored.[33]

HER2 ITH, though rare in BC, is reported in significant percentages of other cancers, including gastric, gastro-esophageal junction, bladder, colorectal, lung, and

endometrial serous carcinoma. In GCs, HER2 ITH is observed in 14 to 79% by IHC and 23 to 54% by fluorescence in situ hybridization, higher than in BC. Endometrial serous carcinoma shows HER2 ITH in 31 to 53% of cases. However, no standard guidelines exist for evaluating HER2 heterogeneity in most nonbreast epithelial cancers, including GC, and its clinical significance remains unclear. Ongoing research focuses on novel and combination therapies to address HER2 variability, with ADCs showing promise so far.[34]

As the advantages of HER2-targeted therapies continue to expand, precise evaluation of HER2 status becomes increasingly critical, especially considering the variability in HER2 overexpression across different tumor types and within individual tumors. Alongside biological heterogeneity, technical issues such as the need for standardized and validated IHC and ISH protocols across histologies, the lack of specific guidelines for interpreting HER2 IHC in cancers beyond breast and gastric, and longer turnaround times due to growing workloads for technicians and pathologists present additional challenges. These factors emphasize the importance of further exploring HER2 expression in a broader range of cancers. Moreover, the demonstrated efficacy of ADCs in patients not traditionally considered HER2 "positive" highlights the necessity of gaining a deeper understanding of HER2 expression across all malignancies.[35] However, HER2-targeting drugs have shown promising antitumor effects in HER2-overexpressing non-BCs, but runing several well-designed clinical trials are warranted to prove potential positive efects of these drug in affected patients.[14,18,36]

Conclusion

HER2-targeted therapies have transformed cancer care, especially in more aggressive and advanced solid malignancies, offering hope for personalized treatment. However, challenges persist in refining diagnostic methods, ensuring equitable access, and balancing innovation with affordability. Well-designed clinical trials are essential to confirm these findings and optimize treatment regimens. While progress is ongoing, further data is needed to establish HER2-targeted therapies as a standard for nonbreast HER2-positive malignancies. Addressing these gaps is crucial to making precision medicine a reality for all.

Patient Consent

Patient consent is not required.

Conflict of Interest

None declared.

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Molecular Targets in Metastatic Colorectal Cancer: A Review

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Abstract

In recent years, the molecular and genetic features of colorectal cancer (CRC) have been used to categorize the disease, which has made it possible to develop therapeutic approaches based on predictive biomarkers. Valuable drivers for individualized treatment plans are biomarkers including *NTRK* fusions, *RAS* and *BRAF* mutations, HER2 amplification, and microsatellite instability (MSI). Furthermore, the regular use of molecular predictive diagnostics, including liquid biopsies and the reintroduction of anti-epidermal growth factor receptor (EGFR) monoclonal antibodies, presents new opportunities for the therapeutic management of patients with CRC. With an emphasis on recent developments in EGFR blockade and novel biomarkers (MSI, HER2, and NTRK), we have provided an overview of the state of targeted therapy for patients with metastatic CRC in this review.

Keywords
- colon
- neoplasm
- Ras
- Braf
- ctDNA

Introduction

Colorectal cancer (CRC) is the second cause of death globally and the third most common type of neoplasm.[1] When molecular targeted therapy and chemotherapy are combined, the median overall survival (OS) for patients with metastatic disease is between 25 and 30 months.[2]

Surgery and chemotherapy are the backbones of treatment for localized CRC. The development of biomarkers for targeted therapies, such as immune checkpoint inhibitors (ICIs): epidermal growth factor receptor (EGFR) inhibitors, BRAF inhibitors, HER2 inhibitors, or NTRK inhibitors, have improved therapeutic strategies in metastatic setting. *RAS* and *BRAF* mutations, microsatellite instability (MSI), and mismatch repair deficiency (dMMR), *HER2* amplifications, and *NTRK* fusions are now predictive indicators for patients with metastatic disease.

In this review, we examine the latest predictive biomarkers for patients with metastatic CRC (mCRC) and the new targeted therapy that include new developments for cancers with BRAFV600E mutation, anti-HER2 therapies, NTRK inhibitors, and emerging issues for anti-EGFR agents, such as primary tumor sidedness (PTS) and longitudinal follow-up using circulating tumor deoxyribonucleic acid (ctDNA).

Materials and Methods

We have searched PubMed (www.ncbi.nlm.nih.gov/pubmed) for full-text articles published from 2017 to January 31, 2025, using the keywords "colon," "neoplasm," "RAS," "BRAF," and "ctDNA." The full-text articles found were carefully examined. In addition, all abstracts presented at international conferences between January 2020 and January 2025 were reviewed.

Anti-EGFR Therapy and RAS/RAF Wild-Type mCRC

Predictive Drivers of Anti-EGFR Agent Effectiveness

Anti-EGFR resistance in CRC patients is caused by activating mutations of *KRAS* and *NRAS*.[3] Thus, 40 to 50% of patients with CRCs have a *KRAS* mutation, while 4 to 8% have an *NRAS*

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mutation.[4] *KRAS* exons 2, 3, and 4 (codons 12, 13, 59, 61, 117, and 146) and *NRAS* exons 2, 3, and 4 (codons 12, 13, 59, 61, and 117) are recommended for *RAS* mutation testing before starting any treatment in metastatic setting.[5,6] Anti-EGFR-targeting therapies are available for patients with KRAS/NRAS wild-type (WT).

There exists additional mechanism of resistance, like the mutations of the EGFR ectodomain that may implicate ineffectiveness of anti-EGFR.[7] In addition, although the BRAFV600E mutation was not officially shown to be a cause of resistance to anti-EGFR (see below), it may also be connected to the overactivation of a protein downstream from the EGFR in the mitogen-activated protein kinase (MAPK) pathway.[8] Monoclonal antibody (mAb) resistance may be a result of constitutional activation of the PI3K/Akt/mTOR pathway by *PIK3CA* exon 20 mutation or *PTEN* deletion.[9,10] Also, resistance to anti-EGFR therapy appears to be linked to amplifications of HER2, HER3, or MET and HER2-activating mutations.[11] Finally, the predictive significance of the microRNA miR-31-3p was recently revealed. The RAS signaling pathway is largely activated by Mir-31, and elevated expression of miR-31-3p may be an indication of the tumor's EGFR independence and, hence, its resistance to anti-EGFR. Numerous post hoc analyses of randomized trials demonstrated that miR-31-3p expression is a reliable indicator of anti-EGFR effectiveness.[12–14]

Management of Anti-EGFR Therapy

In adjuvant setting, resected stage III colon cancer, anti-EGFR mAbs do not improve outcomes.[15] The NEW EPOC study raises concerns about the use of anti-EGFR mAbs in the perioperative setting for patients with resectable liver metastasis in mCRC. According to this study, cetuximab is detrimental to OS and disease-free survival when combined with chemotherapy.[16] Anti-EGFR mAbs may be useful as a converting therapy to reduce resectable metastatic disease; however, they should not be used as a perioperative treatment for patients with resectable mCRC.[17]

Cetuximab and panitumumab, two anti-EGFR mAbs largely used in clinical practice, have been linked to better response rates, OS, and progression-free survival (PFS) in first-line mCRC, in combination with regimens based on oxaliplatin or irinotecan, as well as in second or later lines alone or in combination with chemotherapy.[18–29] Recent data from the phase III study TAILOR reveal that cetuximab can be safely added to FOLFOX for RAS WT mCRC patients,[30] even though NORDIC VII and COIN studies did not demonstrate a meaningful effect of cetuximab in combination with an oxaliplatin-based regimen.[31,32] Except for chemoresistant disease, where the ASPECCT study demonstrated the noninferiority of panitumumab compared to cetuximab in patients with chemotherapy-refractory KRAS WT (exon 2) mCRC, there is no direct comparative study between cetuximab and panitumumab.[30,33]

The Role of the Sidedness

Anti-EGFR activity appears to be determined by PTS. There is mounting evidence that PTS predicts responsiveness to anti-EGFR mAbs and it is a prognostic factor in RAS WT population.[34] A retrospective study of six randomized trials (CRYSTAL, FIRE-3, CALGB 80405, PRIME, PEAK, and 20050181) revealed that right-sided colon cancer had worse outcomes (OS, PFS, and response rates) than left-sided tumors. In patients with left-side mCRC, this meta-analysis demonstrated a predictive role of PTS. Indeed, chemotherapy plus anti-EGFR mAbs had a better outcome than chemotherapy with bevacizumab in left side mCRC.[35] The predictive role of PTS was limited to the KRAS WT population, according to a recent retrospective analysis of the ARCAD database. This analysis also validated the predictive role of PTS for cetuximab efficacy, with better results for patients with left-sided mCRC.[36] Conversely, anti-EGFR therapies appear to have a worse effect on patients with RAS WT right side mCRC.

Due to their retrospective nature, these results should be interpreted carefully, but they indicate that anti-EGFR mAbs plus chemotherapy should only be used as first line for patients with left-sided tumors KRAS/NRAS WT and that patients with right-sided mCRC may benefit more from chemotherapy plus an antiangiogenic agent.[37]

Rechallenge and Liquid Biopsy

Tumor clones with an intrinsic mutation of resistance are selected during treatment with anti-EGFR, causing acquired resistance to this drug. The tumor can recover sensitivity when the anti-EGFR mAb is discontinued, since this removes the positive pression selection on the sensitive clones. Tumor resistance can be overcome by a variety of methods, including reintroduction, dose intensification, sequential therapy, and rechallenge; in the case of anti-EGFR mAbs, rechallenge, this strategy appears to be the most promising.[38] For a tumor that first showed sensitivity to anti-EGFR therapy, retreatment following a progression could be referred to as a challenge of anti-EGFR therapy.[39]

For rechallenge strategy, longitudinal follow-up of mutant clones is interesting. According to studies using longitudinal ctDNA monitoring, RAS mutant clones developed in blood during anti-EGFR therapy have a half-life of 4 to 5 months before declining rapidly after end treatment.[40] The first prospective trial that demonstrated that a rechallenge strategy using cetuximab and irinotecan might be effective in RAS/BRAF WT mCRC patients with acquired resistance to cetuximab was the CRICKET phase II study. Blood samples from patients who reported partial response did not show any RAS mutation.[41,42] The utility of liquid biopsy in the context of anti-EGFR rechallenge was assessed in several clinical trials (i.e., CHRONOS, RASINTRO) that demonstrated the same results.[41]

Braf Mutation in mCRC

About 8 to 10% of mCRC exhibit *BRAFV600E* mutation, which causes a *RAS*- independent constitutional activation of the MAPK pathway promoting cell survival and proliferation and being linked to a poor prognosis.[43] While 22% of all *BRAF* mutations in CRC occur outside of the V600E hotspot, these mutations do not have the same biochemical, clinical, and therapeutic effects as the V600E mutation.[44] Although some

may be responsive to EGFR, these BRAF non-V600E mutant tumors are more likely to be left-sided, have a lower grade of differentiation, and have a better prognosis. They are also resistant to BRAF inhibitors.[45,46] These genetic changes appear to not provide resistance to anti-EGFR therapy and are linked to malignancies on the right side.[47,48]

Patients with BRAFV600E CRC are more likely to be older, female, and have right-sided tumors with a mucinous component. Furthermore, these patients are also most prone to have distant lymph node and peritoneal metastases, but fewer pulmonary metastases.[49] Significantly, the MSI phenotype, which is indicative of the effectiveness of ICIs regardless of the BRAF mutational status, is present in around 22% of BRAFV600E mCRC.[50]

Compared to BRAF WT, BRAFV600E-mutated mCRC are less likely to get second- line therapies. Intensification therapies appear to work well for these patients.[51–53] Compared to FOLFIRI (folinic acid, fluorouracil, and irinotecan) plus bevacizumab, first-line FOLFOXIRI (folinic acid, fluorouracil, oxaliplatin, and irinotecan) plus bevacizumab was linked to a nonsignificant improvement in OS for BRAFV600E mutants in the TRIBE study.[54] For patients with BRAFV600E mCRC chemotherapy-naive, FOLFOXIRI-bevacizumab is regarded as a viable treatment choice, notwithstanding the limited population sample included in this subgroup analysis. Crucially, a subgroup analysis on 33 patients BRAF Mut V600E in the TRIBE2 phase III trial, which compared mFOLFOX6 plus bevacizumab followed at progression from FOLFIRI plus bevacizumab like TML strategy, with FOLFOXIRI plus bevacizumab stop and go did not reveal any survival benefit for BRAFV600E patients.[55] The Fire 4.5 study (AIO-KRK-0116) phase II trial evaluated the triplet chemotherapy regimen with either cetuximab or bevacizumab (NCT04034459; see ►**Table 1**). The primary endpoint objective response rate (ORR) was on experimental arm of 51% and in the control arm of 61%.

Braf V600E Mutations and Antiangiogenic Drugs

To date, there are no studies that have demonstrated predictive markers for antiangiogenic drugs, and their efficacy in BRAFV600E mCRC patients has not been demonstrated. Adding bevacizumab to first-line IFL (bolus irinotecan, fluorouracil, and folinic acid) or capecitabine did not increase survival, according to the AVF2107 and AGITG MAX36 studies.[56,57] Although the limited size of the patients did not allow the evaluation of statistical significance, the VELOUR trial (FOLFIRI ± aflibercept) and the RAISE study (FOLFIRI plus ramucirumab) demonstrated that patients with BRAF V600E mutations tended to benefit from the antiangiogenic drugs in second line.[58,59] All things considered, this retrospective analyses imply that antiangiogenics in first line may be helpful for patients with BRAFV600E mCRC.[60]

Anti-EGFR and BRAFV600E Mutations

It is unclear if anti-EGFR treatments, either alone or with chemotherapy, are effective for BRAFV600E patients. There were two meta-analyses conducted. According to a meta-analysis by Pietrantonio et al, patients with BRAFV600E do not respond well to anti-EGFR drugs.[61] However, no discernible difference in the impact of anti-EGFR drugs between the BRAFV600E and BRAF WT populations was seen in another meta-analysis conducted by Rowland et al.[62] Furthermore, the FIRE-3 study (first-line FOLFIRI plus cetuximab vs. FOLFIRI plus bevacizumab in KRAS WT mCRC patients) revealed a greater response rate in the cetuximab arm, according to a retrospective analysis of the BRAFV600E subgroup.[63] Also, the subset of BRAFV600E patients showed a significant increase in objective response (71% vs. 22%, $n = 14$) in a recent study (VOLFI AIO KRK0109) evaluating the effectiveness of first-line FOLFOXIRI with or without panitumumab.[18] However, despite the conflicting data, the European Society for Medical Oncology and National Comprehensive Cancer Network guidelines do not recommend the first-line use of anti-EGFR in patients with Braf V600E mutated mCRC.

Inhibitors of BRAF

Unlike melanoma, BRAF inhibitors in mCRC alone were linked to unsatisfactory outcomes. One theory is that BRAF inhibition may encourage MAPK constitutive signaling by triggering feedback EGFR activation. One factor contributing to these cancers' innate resistance to BRAF inhibitor monotherapy is the EGFR-mediated reactivation of downstream signaling cascades.[64,65] Several combinations of BRAF inhibitors, anti-EGFR, PI3K inhibitors, or MEK inhibitors were explored with thisproblem in mind, and the findings were

Table 1 Ongoing clinical trials for patients with *BRAF*V600E metastatic colorectal cancer

Therapy	Phase	Condition	Primary endpoint	NCT identifier
Encorafenib[1] + cetuximab[2] + nivolumab[4]	1/2	2nd or 3rd line	ORR, DLT	NCT04017650
Encorafenib[1] + binimetinib[3] + nivolumab[4]	1/2	> 1st line	ORR, DLT	NCT04044430
Dabrafenib[1] + trametinib[3] + PDR 001[4]	2	Any line	ORR, DLT	NCT03668431
FOLFOXIRI + cetuximab[2] or bevacizumab[5]	2	1st line	ORR	NCT04034459
FOLFIRI + cetuximab[2] + vemurafenib[1]	2	–	ORR	NCT03727763
Irinotecan + AZD 1775[6]	1	> 1st line	DLT	NCT02906059
Panitumumab[2] + trametinib[3]	2	> 2nd line	ORR	NCT03087071

Abbreviations: DLT, dose-limiting toxicities; EGFR, epidermal growth factor receptor; NCT, National Clinical Trial; ORR: objective response rate; VEGF, vascular endothelial growth factor.
Note: [1]RAF inhibitor; [2]EGFR inhibitor; [3]MEK inhibitor; [4]anti-PD(L)-1; [5]anti-VEGF; [6]Wee-1 inhibitor.

intriguing.[66–70] These studies provided support for the design of the phase III BEACON, which compared chemotherapy (investigator choice regimen of cetuximab plus irinotecan or FOLFIRI) with encorafenib and cetuximab ± binimetinib. Randomization was performed on 665 BRAFV600E mCRC patients whose disease had progressed after one or two prior lines of chemotherapy. In the triplet and doublet experimental arms, the median OS was 9.3 months, while in the control arm, it was 5.9 months (hazard ratio [HR] = 0.60, 95% confidence interval [CI] 0.47–0.75 and HR = 0.61, 95% CI 0.48–0.77, respectively).[64,71] A statistical improvement was observed in the ORR, which was 2% in the control group and 20 and 26% in the doublet and triplet arms, respectively. The experimental groups experienced cutaneous and gastrointestinal side effects, but the toxicity was tolerable, with grade 3 or higher toxicities being similar across the three arms. Both the doublet and triplet groups had a lower chance of quality-of-life decline by over 40%, according to a supplemental quality-of-life analysis.

Recently was presented at ASCO GI 2025 the abstract of Breakwater study, a phase III that compares first-line Braf Mut V600E mCRC, encorafenib plus cetuximab and FOLFOX versus SOC. The primary endpoint, ORR, was met with a ORR of 60.9% for the experimental arm and 40.0% ($p = 0.0008$) for the control arm.[72]

Targeted Therapies in Patients with Ras Mutations

KRAS/NRAS mutations are present in more than 50% of patients with mCRC. As shown above, they are inherently resistant to anti-EGFR mAbs. Although there are no predictive biomarkers for the effectiveness of antiangiogenics (bevacizumab, aflibercept, and ramucirumab), these drugs appear to be beneficial in this population.[59,73,74]

One of the mutations for which a drug target is being studied is G12C (glycine 12 to aspartic acid). For this population, a novel class of KRAS inhibitors may prove revolutionary.[75] In the phase III Codebreak 300 study, AMG 510 (sotorasib) was administered in later lines to patients with G12C mutation mCRC. The study included three arms. The first enrolled patients with sotorasib 960 mg with panitumumab, the second arm sotorasib 240 mg with panitumumab. In the third arm, patients were started on treatment with TAS 102 or regorafenib at the investigator's choice. The primary endpoint was PFS.

After a median follow-up of 7.8 months, PFS was 5.6, 3.9, and 2 months, respectively. The statistical comparison between the first arm and the third arm was statistically significant in favor of the experimental arm (95% CI, 0.30–0.78; $p = 0.005$).[76]

Immune Checkpoint Inhibitors and Microsatellite Instability

Microsatellite Instability, Mismatch Repair Deficiency, and Colorectal Cancers

From 10 to 15% of CRCs originate from the MSI pathway, the majority grow through the chromosomal instability pathway (aneuploidy and loss of genetic material). A germline mutation in the MMR genes (*MLH1*, *PMS2*, *MSH2*, *MSH6*) that predispose to Lynch syndrome or an epigenetic inactivation of MLH1 (i.e., sporadic malignancies) results in a deficiency of the DNA dMMR pathway, so-called MSI. The BRAFV600E mutation is commonly linked to these isolated occurrences.[77] About 10 to 15% of localized CRC and 4 to 5% of mCRC at the fourth stage, have MSI/dMMR.[43,78] The right colon is the primary site of origin for MSI/dMMR CRCs, which exhibit distinct characteristics such as low differentiation, a high number of tumor-infiltrating lymphocytes, and characteristic metastatic patterns, including frequent distant lymph node metastases and peritoneal involvement.[49] MSI/dMMR is linked to a good prognosis in localized CRC.[79,80] In metastatic disease, data are more controversial. However, the existing trials indicates that, in comparison to microsatellite stable/MMR-proficient (MSS/pMMR) cancers, MSI/dMMR mCRC are less susceptible to traditional treatment.[81–83]

High tumor mutational burden (hypermutated phenotype) and highly immunogenic neoantigens resulting from frameshift mutations that cause high infiltration through activated cytotoxic T CD8+ cells are characteristics of MSI/dMMR CRCs.[84–86] Nevertheless, immunological checkpoints are upregulated in MSI/dMMR cancers, shielding MSI cancer cells from their tough immune environment.[87,88]

Immune System as a Target of Therapy

For patients with mCRC, MSI/dMMR has become a considerable prognostic biomarker for the effectiveness of ICIs. MSI/dMMR cancers were linked to significant sensitivity to immunotherapy (i.e., hot tumors), whereas MSS/pMMR CRCs are mostly resistant to ICIs (i.e., cold tumors). Several phase II trials have shown that ICIs are effective for patients with chemoresistant MSI/dMMR mCRC, with ORRs ranging from 33 to 58% and 12-month PFS rates between 31 and 71%.[50,89–94] Anti-PD1 and anti-CTLA4 mAb combinations may be more effective than anti-PD1 or anti-PDL1 alone, according to the findings of the nonrandomized CheckMate-142 trial. Indeed, in a third cohort of the CheckMate-142 study, 45 patients received nivolumab + ipilimumab in first-line chemotherapy-naive MSI/dMMR mCRC, demonstrating the effectiveness of ICIs as front-line treatment. The 1-year PFS estimate was 77%, and the ORR was 77%.[95] Another trial, the phase III KEYNOTE 177, demonstrated in fist line that pembrolizumab monotherapy had better PFS in MSI/dMMR mCRC patients compared to standard-of-care (investigator's choice of FOLFOX or FOLFIRI, with or without bevacizumab or cetuximab). The primary endpoint, median PFS, were 16.5 and 8.2 months (HR = 0.60, 95% CI 0.45–0.80). With pembrolizumab, the 12- and 24-month PFS rates were 55 and 48%, respectively, while with chemotherapy, they were 37 and 19%. For patients with newly diagnosed MSI/dMMR mCRC, pembrolizumab has become the standard of therapy.[96]

For patients with localized MSI/dMMR colon cancer, ICIs are presently being assessed. Their development in this context was made possible by the NICHE phase II trial, which may also improve treatment approaches for MSI/dMMR CRC in its early stages.[97] All 21 dMMR CRC patients experienced a

pathological response in this trial evaluating nivolumab with ipilimumab as a neoadjuvant treatment; 12 full pathological responses were among the 95% of major responses. These remarkable outcomes demonstrate that neoadjuvant immunotherapy is a viable approach that merits more investigation. In the ATOMIC trial (NCT02912559; FOLFOX ± atezolizumab) and the POLEM trial (NCT03827044; 24 weeks of single agent fluoropyrimidine chemotherapy or 12 weeks of oxaliplatin-based chemotherapy ± avelumab), ICIs are also assessed in conjunction with adjuvant chemotherapy for patients with stage III MSI/dMMR colon cancer.[28]

Predictive Biomarkers in Immunotherapy

MSI/pMMR patients respond to ICIs for a short period and then develop resistance to them. No other biomarkers are known to predict response to immunotherapy in this cohort of patients. Interestingly, a considerable number of cases with primary resistance to ICIs are caused by misinterpretation of MSI/dMMR status.[98,99]

The patients with tumors MSI/dMMR BRAF WT appear to be highly sensitive to ICI as the patients with MSI/dMMR, BRAFV600E mutated.[50] The resistance to ICI was not linked to major histocompatibility complex class I expression, beta-2-microglobulin mutations, or PD-1 expression.[100] ICI resistance in MSI/dMMR mCRC may be caused by loss-of-function mutations in Janus kinases JAK1/2.[101] Remarkably, in two small cohort trials (less than 33 patients), the tumor mutational burden was found to predict the effectiveness of ICI.[102,103] Interesting data, but not yet translatable to clinical practice, are available on the immune infiltrate. The degree of T cell infiltration was associated with improved response, PFS, and OS in a recent study by Loupakis et al.[99] Larger prospective studies should corroborate all of these findings.

HER2 and Anti-HER2

HER2 gene amplification is present between 1 and 8% of patients with CRC.[104–107] *KRAS* WT status and HER2 overexpression are linked and are more present in left mCRC, with a frequency of 4.3 to 5.4%.[108,109] To date, we know the role of HER2 as a negative prognostic factor for resistance to anti-EGFR.[110,111]

The Heracles diagnostic criteria established a standard procedure for HER2 testing in CRC, which included before immunohistochemistry (IHC) analysis and, if necessary, fluorescence in situ hybridization (FISH). An IHC 3+ score or an IHC 2+ score linked to FISH positivity is used to define positivity.[112]

The effectiveness of anti-HER2 drugs for patients with HER2-positive mCRC is verified. Phase II studies evaluated trastuzumab with lapatinib, trastuzumab plus pertuzumab, and trastuzumab plus tucatinib (Heracles-A, MyPathway, and Mountaneer, respectively). The median PFS was 4.7, 2.9, and 6.2 months, respectively, and response rates were 30, 32, and 55%.[113,114] The Mountaneer and Heracles-A studies did not include patients with HER2-positive and KRAS-mutated mCRC; nevertheless, it is noteworthy that one patient with HER2-positive and KRAS-mutated mCRC had an objective response in the MyPathway study.[113,114] The Heracles-B study, which involved the combination of pertuzumab and trastuzumab emtansine, did not achieve its primary endpoint (ORR) but had a median PFS of 4.7 months.[115] According to a recent study from the DESTINY-CRC01 phase II trial, trastuzumab–deruxtecan may change the future. This antibody drug conjugated, which consists of a topoisomerase I inhibitor and an anti-HER2 antibody, was used to treat 50 patients with chemoresistant HER2-positive mCRC. A confirmed ORR of 45% was obtained. With an ORR of 43.8%, this treatment was beneficial even for individuals who had previously used anti-HER2 drugs. Two patients succumbed to interstitial lung disease due to the drugs.

Although randomized trial data are insufficient for a thorough assessment of the additional value of anti-HER2, these drugs are generally very appealing treatments for the HER2-positive population. In patients with HER2-positive RAS/RAF WT mCRC, the only randomized study currently in progress is a phase II trial that compares trastuzumab and pertuzumab to cetuximab and irinotecan (SWOG S 1613 NCT03365882).

TRK Inhibitors and NTRK Gene Fusions

Recently, NTRK gene fusions have become a very appealing therapeutic target for cancer patients. Regardless of the histology type, TRK inhibitors (entrectinib, larotrectinib) showed remarkable therapeutic activity in various types of cancers. In single-arm trials, entrectinib had an ORR of 57% with a time of response greater than 6 months in 68% of patients, and larotrectinib demonstrated an ORR of 75% with a time of response greater than 6 months in 73% of cases.[116,117] Due to these findings, the Food and Drug Administration has arranged a fast-track approval for the use of the NTRK gene fusion to treat refractory solid tumors, regardless of the kind of tumor.

Depending on the likelihood of NTRK fusion, screening methods for this mutation rely on next-generation sequencing, reverse transcription polymerase chain reaction, and immunohistochemical FISH.[118,119] With an incidence of 0.23 to 0.97%, NTRK fusions are uncommon in CRCs.[120–123] Females, right-sided initial tumor site, RAS/RAF WT status, and MSI phenotype are characteristics of individuals with CRC that have NTRK fusion.[121] Interestingly, NTRK fusions were consistently linked to the MSI phenotype. More specifically, hypermethylation of the MLH1 gene promoter appeared to be associated with these genetic changes in BRAF WT tumors.[124,125] In this molecularly chosen sample, the estimated incidence of NTRK fusions was 42%.[48] The effectiveness of ICIs and NTRK inhibitors in this particular biological entity is not yet known.

Conclusion

Over the past 10 years, notable progress has been achieved in tailoring treatment plans for patients with mCRC. An expanded panel of biomarkers can be used to specifically

Table 2 Molecular subtypes of colorectal cancer and targeted treatment options

Molecular subtypes	Targeted therapies
MSI, whatever the *RAS*/*RAF* mutational status	Immune checkpoint inhibitor(s)
RAS/*RAF* wild-type	Anti-EGRF mAbs
*BRAF*V600E mutated	Encorafenib + cetuximab ± binimetinib
RAS mutated	No current targeted therapy, ongoing trials with new-generation KRAS inhibitors
HER2 amplified/mutated	Anti-HER2 mAbs/inhibitors (trastuzumab, pertuzumab, lapatinib), anti-HER2 antibody-drug conjugate (trastuzumab deruxtecan)
NTRK fusion-positive	TRK inhibitor (larotrectinib, entrectinib)

Abbreviations: mAb, monoclonal antibody; EGFR, epidermal growth factor receptor; MSI, microsatellite instability; TRK, tropomycin receptor kinase.

identify responders to anti-EGFR therapy, and ctDNA longitudinal follow-up can be used to optimize therapeutic approaches. Previously untreated patients with BRAFV600E mCRC now have access to efficient treatment alternatives. Beyond extremely attractive but extremely uncommon targets like NTRK fusions and HER2 amplification, ICIs—a breakthrough for patients with MSI/dMMR tumors—have brought about the most notable change in targeted therapy for patients with CRC. Because of the significant improvement in patient outcomes, researchers and clinicians were forced to consider CRC as at least two different diseases: the MSI/dMMR tumors and the rest (►**Table 2**). Crucially, methodological problems with the pseudoprogression phenomena and long-term survivals are linked to the creation of ICIs. This finding emphasizes the need to create novel study designs and to account for these problems in statistical analyses that are planned in the future.

Patient Consent
Patient consent is not required.

Conflict of Interest
None declared.

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An Observational Study of AR Expression in Indian Women with TNBC and Their Treatment Response and Overall Survival

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Abstract

Introduction Triple-negative breast cancer (TNBC) is a heterogeneous subtype of breast cancer with the worst outcome, is not amenable for known target therapies, and has a poor response to chemotherapy. Androgen receptor (AR) was evaluated as a predictive, prognostic, and therapeutic factor in TNBC, but with contradicting results and the cutoff used for positive was also varied among studies. Thus, we studied 104 Indian women with TNBC for proportion showing AR expression and responses and survival outcomes compared over a period of 60 months with standard of care.

Objectives Primary: To observe the proportion of AR expression in TNBC. Secondary: To compare (1) pathological response to neoadjuvant chemotherapy (NACT) and (2) overall survival (OS) of both groups.

Materials and Methods This is a prospective descriptive study of 104 female patients with TNBC who visited the medical oncology department at a tertiary hospital in South India over a period of 2 years (June 2018–June 2020). They were diagnosed with TNBC by Immunohistochemistry (IHC); hence, they tested negative for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) receptors. Patients with HER2 2+ IHC were confirmed negative by fluorescence in situ hybridization testing. They were analyzed with IHC for AR expression using EP140 rabbit monoclonal primary antibody interpreted by a single breast pathologist, and proportion of TNBC expressing AR were identified with a cutoff $>10\%$ nuclear expression. They were managed as per the standard of care necessary for a particular stage. Results were analyzed comparing the baseline characteristic, treatment response, recurrence rate, and survival outcomes over a follow-up period of 60 months.

Results Percentage of AR expression in TNBC in this study was 35%. Twenty-five percent patients (28/104) were treated with NACT and complete pathological response was seen in 1/13 (7.69%) versus 7/22 (31.8%) in AR-positive compared with AR negative group (p 0.003). The AR-positive group showed significant survival advantage compared with the AR-negative group. Median OS of AR-negative group was reached at 29 months whereas for the AR-positive group it was 49 months ($p=0.58$). The AR-positive group showed late recurrences after 24 months in follow-up.

Keywords
- TNBC
- AR
- 5-year-follow-up
- IHC
- prognosis
- response
- pCR

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Conclusion This study showed that the proportion of TNBCs showing AR expression was much higher. Assessment of AR status in patients with TNBC provides additional information on prognosis and also predicts response to chemotherapy. AR-positive TNBC represents a breast cancer subtype with unique features with potential targeted therapies.

Introduction

Breast cancer is the most frequently occurring cancer in women and the second leading cause of cancer deaths worldwide. Breast cancer incidence increases as socioeconomic status increases.[1] Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the lack of estrogen (ER), progesterone (PR), and human epidermal growth factor receptor 2 (HER2) receptors. This designation masks the heterogeneity of this patient population and the challenge of stratifying them for optimal treatment selection.[2]

Due to the paucity of treatment targets, cytotoxic chemotherapy is still the standard of care for TNBC. There is a need to develop new and more effective targeted treatments for these patients. Approximately 20% patients with TNBC are cured by standard therapy (tumor resection, radiation, and cytotoxic chemotherapy), but the remaining 80% patients progress to the metastatic stage of the disease.

One of the several therapeutic targets currently under study for the management of TNBC is the androgen receptor (AR).[3] It is a nuclear steroid hormone receptor that is expressed in 10 to 43% of TNBCs.[4,5] In the absence of ERα, AR drives "luminal-like" gene expression patterns. One of the TNBC molecular subtypes consistently identified via gene expression profiling is the luminal AR subtype.[3]

Studies have explored the prognostic role of AR in TNBC to better understand androgen action in TNBC, identify actionable factors that drive outcomes, and determine if testing for AR status should be included in routine clinical practice for diagnosing TNBC. The prevalence of AR positivity in female patients with TNBC is highly varying across the world (range: 11–56%) but data on the Indian population is lacking. The prevalence of TNBC worldwide is 11 to 15%.[6–14]

However, there are conflicting reports about the value of AR in treating TNBC.[13,15] AR-positive cells can be targeted with antiandrogen therapy.[1–5] There is no standard cutoff for AR expression in TNBC and various studies used different cutoffs.[6–14]

In this study, the AR expression was evaluated in 104 female patients with TNBC attending to the medical oncology department at a tertiary hospital in South India. All of the tumor samples were processed identically. Any differences in treatment protocols were noted to observe the innate differences between AR-positive and AR-negative subgroups of TNBC to standard treatment and survival outcome. These protocols were performed to solve our hypothesis on whether tailored management based on AR expression would be needed to treat TNBC.

In this study, our principal objective was to observe the proportion of AR expression in Indian women with TNBC and its implication on their response and survival outcomes. The primary objective was to identify the percentage of female patients with TNBC showing AR expression. The secondary objectives were to compare the pathological response and overall survival (OS) rate to neoadjuvant chemotherapy (NACT) between AR-positive and AR-negative groups.

Material and Methods

Study Design

A prospective descriptive study of 104 adult female patients diagnosed with TNBC (both nonmetastatic and metastatic) who presented to the medical oncology department and met the inclusion criteria.

They were evaluated for AR expression by immunohistochemistry (IHC) in the same specimen used for testing ER, PR, and HER2 receptors. The period of study was 2 years (June 2018–June 2020) and 5 years of follow-up period (June 2018–June 2024).

Sample Size

One hundred and four female patients diagnosed with TNBC (both nonmetastatic and metastatic) were included in the study.

Inclusion Criteria

(1) Women with breast cancer aged $\geq$ 18 years
(2) Patients with microscopic evidence of breast cancer
(3) Patients negative for ER, PR expression (by IHC), and HER2 amplification (by IHC; if equivocal (2 +) they are confirmed to be negative by a fluorescence in situ hybridization [FISH] test)
(4) All patients who received standard treatment as per stage

Exclusion Criteria

(1) Patients who are $\leq$ 18 years old
(2) Male patients with breast cancer
(3) Patients without microscopic confirmation of cancer
(4) Patients who were not treated at our hospital

Intervention

The same tissue sample used for ER, PR, and HER2 testing were used to evaluate AR status.

Inpatient and outpatient female patients with TNBC attending the department of medical oncology were thoroughly assessed for staging and pathological variants. Patient recruitment to study was completed in 2 years.

Specimens analyzed for the study were surgical samples collected from patients treated with primary surgery, patients with stage IV disease at presentation who had a diagnostic core biopsy, and patients treated with NACT followed by surgery. They were evaluated for AR expression by IHC by EP120 rabbit monoclonal antibody on the same specimen used for ER, PR, and HER2 testing (by IHC, if HER2neu was equivocal 2+ confirmed to be negative by FISH test). All slides were interpreted by a single breast oncopathologist. As majority of the prior studies have used a cutoff of $>10\%$, positive AR expression was defined as $>10\%$ nuclear staining.

All patients were treated with combined modality treatment according to the stage. All patients received standard chemotherapy with anthracycline and taxane (for two ineligible patients, alternative regimens like Cyclophosphamide, Methotrexate, Flurouracil Regimen (CMF) were provided).

Breast conservation surgery (BCS) was performed in 11 female patients with TNBC who presented at an early stage and all of them were given radiation treatment at the breast region subsequently. Modified radical mastectomy (MRM) with axillary nodal dissection was performed in 87 female patients with TNBC. Upfront surgery followed by adjuvant chemotherapy was performed in 70 female patients who were found to be operable at presentation. Adequate nodal yield and resection margins were achieved as per pathology report in all operated cases. MRM patients underwent radiation as per indication.

Complete NACT was provided presurgery to 35 patients who presented with locally advanced TNBC or had inoperable tumors. MRM was performed irrespective of response. Surgery was performed immediately if there was progression on NACT. During this study, the standard of treatment did not include adjuvant capecitabine, if complete pathological response (pCR) was not achieved after total NACT.

In summary, the patients were treated and followed-up through the study period on standard of care by various modalities as indicated. Additionally, they were followed-up postcompletion of treatment and assessed regularly. Patient follow-up period was for a median of 5 years (60 months).

Outcome was noted in the form of response to chemotherapy in neoadjuvant setting as pCR, partial response, stable disease, or progression on NACT. OS outcome for all was assessed in the follow-up period of 60 months/5 years after initiation of treatment.

Outcome

Patients were grouped into two groups based on their AR expression as group A, AR-positive TNBC, and group B, AR-negative TNBC.

Statistical Analysis

Patient data was collected in the study format (►**Supplementary material**) Available in online version, and entered in Microsoft Excel sheet for statistical analysis. Descriptive statistics were performed for patient demographics and clinical characteristics. For continuous variables, median and quartiles were computed. The chi-square test or the Mann–Whitney nonparametric test was used to study association between variables, according to their nature (categorical or continuous).

OS was defined as the time from initiation of treatment to death from any cause. The Kaplan–Meier method was used to estimate survival curves, and the log-rank test was used to test difference between groups. All reported p-values are two-sided, and a p-value of <0.05 is considered to be statistically significant. All analyses were done using SPSS (software version 27.0, IBM).

Ethical Approval

This study was approved by Krishna Institute of Medical Sciences (KIMS) Ethics Committee for Thesis (KIMS/EC/2018/23–13) on July 18, 2018. Written informed consent was obtained prior to study, and all procedures performed in studies involving human patients were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration, and its later amendments or comparable ethical standards.

Results

A total of 158 patients were diagnosed with TNBC from June 2018 to June 2020. One hundred and four of them met the inclusion and exclusion criteria and were analyzed irrespective of stage for AR expression by IHC.

Descriptive Characteristics

The median age at presentation was 53 years and 25% of patients were of premenopausal age (18–45 years). Twenty-five percent patients had radiological tumor size >5 cm, 65% patients had stage 3 disease, 92% patients had grade 3 tumors, and 50% patients had high K_i-67 ($>50\%$). Ten percent patients had rare histological subtypes like apocrine, metaplastic, medullary, papillary, lobular, and sebaceous of TNBC similar to previous studies.[12–15]

Percentage of AR Expression in TNBC

Among the 104 patients analyzed, 36 were found to express AR by IHC at a cutoff $>10\%$. Thus, the percentage of AR expression in TNBC in this study was 35%.

Comparison of Patient Characteristics between Two Groups

Based on AR presence, two subgroups were defined as "AR positive" and "AR negative" and were compared.

Median age, radiological tumor size, nodal status, and K_i-67 were comparable in both groups. However, the AR-negative group (57%) had higher proportion of patients with

grade 3 tumors than the AR-positive group (36%) (p 0.25). All apocrine subtypes were deemed AR positive, whereas lobular and sebaceous subtypes were deemed AR negative. Proportion of patients receiving NACT and adjuvant treatment was similar in both groups, 22/68 (32%) in the AR-negative group and 13/36 (36%) in the AR-positive group.

Surgical and Multimodality Treatment Outcomes

All patients had uneventfully completed the multimodality treatments like surgery and radiation on this study without any major adverse effects.

Patients were followed after the completion of treatment and were regularly assessed for any recurrence. Patients who were lost to follow-up were censored. Among the patients who received NACT ($n = 35$), their response was assessed in MRM specimens acquired postsurgery and was categorized based on response to chemotherapy into four groups.

Three patients had local tumor progression while on NACT (1/22), 4.5% in the AR-negative group, and 2/13 (15.4%) in the AR-positive group (p 0.03). All three patients had only local radiological tumor progression and immediately underwent MRM and remaining taxane chemotherapy was administered as adjuvant chemotherapy. One in each group had stable disease and partial responses, 13/22 (59%) in the AR-negative and 9/13 (69%) in AR-positive group. pCR was noted in 7/22 (31.81%) patients in the AR-negative group and 1/13 (7.69%) patients in the AR-positive group (p 0.03) (►**Table 1**) (►**Fig. 1**).

Survival Outcome Analysis

All the analyzed patients (104) after completion of standard of care treatment as per stage were on follow-up over the next 60 months. The following consort diagram shows the numerical flow of the study at intervals (►**Fig. 2**). An unplanned interim analysis was done at 24 months as the study suffered severe follow-up loss due to pandemic and lockdown restrictions. After confirming adequacy of sample size in both groups, the final OS analysis was done at 50 months without any modifications in the study, once median OS was reached in both the groups.

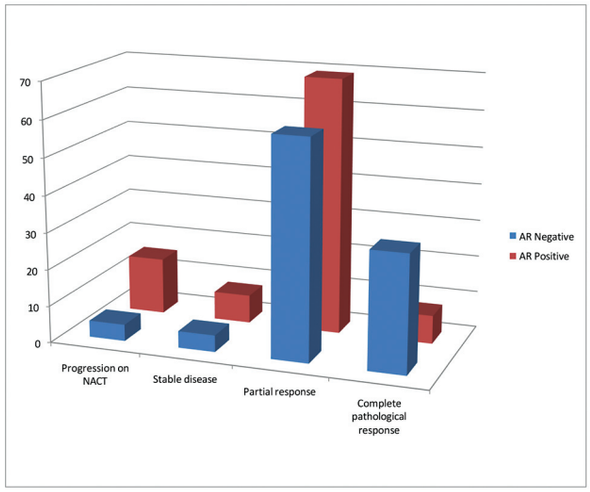

Fig. 1 Three-dimensional (3D) bar chart showing response to neoadjuvant chemotherapy (NACT) in each group.

Survival outcomes were assessed among both groups: AR positive and AR negative. OS was calculated as the period between initiation of treatment and death due to any cause (►**Fig. 2**). Median OS of the AR-negative group was calculated as 29 months whereas for the AR-positive group it was evaluated as 49 months. However, these calculations were not statistically significant ($p = 0.58$) (►**Fig. 3**).

Among upfront stage 4 patients who received palliative chemotherapy, the AR-positive group showed a median OS of 20 months, whereas in the AR-negative group it was 11 months, but not statistically significant ($p = 0.377$).

Discussion

TNBC is a heterogeneous disease. The identification of the subtypes is necessary for a better characterization and for

Table 1 Distribution and proportion of patients in both groups as per their response to NACT

Response to NACT, $n = 35$				
AR				
		Negative	Positive	Total
Progression on NACT	Count	1	2	3
	% within AR	**4.5%**	**15.4%**	8.57%
Stable disease	Count	1	1	2
	% within AR	4.54%	7.69%	5.71%
Partial response	Count	13	9	15
	% within AR	59.09%	69.23%	42.85%
Complete pathological response	Count	7	1	8
	% within AR	**31.81%**	**7.69%**	22.85%
Total	Count	22	13	35

Abbreviations: AR, androgen receptor; NACT, neoadjuvant chemotherapy.
Note: Table showing number and percentage of patients in either group in their respective response to NACT. The differences in proportions of progression on NACT and PCR in both the roups are highlighted.

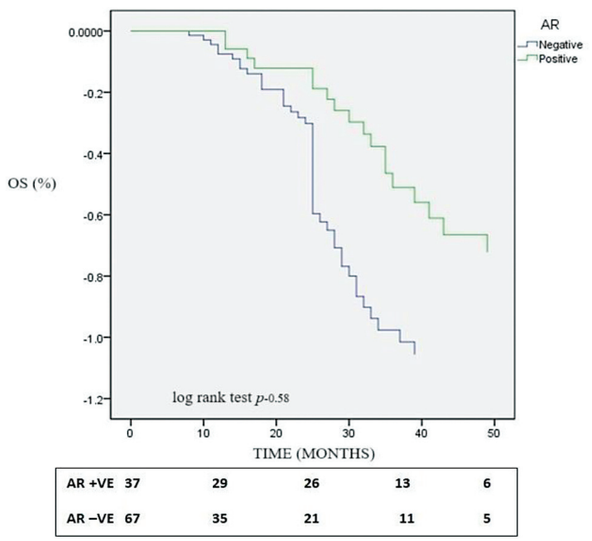

Fig. 2 Consort diagram of the study.

the construction of appropriate therapeutic strategies. AR expression varied widely as per countries' cohorts—8.3% in the Nigerian women with TNBC cohort, 55% women with TNBC in the United Kingdom cohort, etc.[8]

Baseline Characteristics

This study observed that the median age (53 years), tumor size (4.2 cm), and stage at presentation of Indian women with TNBC were similar to world data.[1]

Histologically, in majority of patients with TNBC, that is, 87.5% (91/104), invasive ductal carcinomas were diagnosed and other histological types consisted of $< 10\%$ of patients with TNBC. More than 90% patients had a high-grade tumor, whereas K_i-67 was $> 50\%$ in approximately 50% patients. All the clinical and pathological parameters were comparable with previous study data of TNBCs.[6,7,10,13]

Proportion of AR Expression

In this study, AR expression was observed in 35% patients at a cutoff of 10%. Compared with various studies worldwide and to the present Indian data (►**Table 2**), our study's value was found to be higher.[6–14] Thus, the role of AR expression on TNBC's tumor biology and clinical response in our population might be substantial.

Approximately 10% (11/104) patients with TNBC underwent BCS upfront. Approximately 7/104 (6.7%) patients with TNBC were diagnosed with stage 4 at presentation, 28/104 (25%) patients were treated with NACT, and the rest 70/104 (70%) patients were operated upfront.

Baseline characteristics of our study group (median age, menstrual status, grade, histological types, K_i-67, stage, and

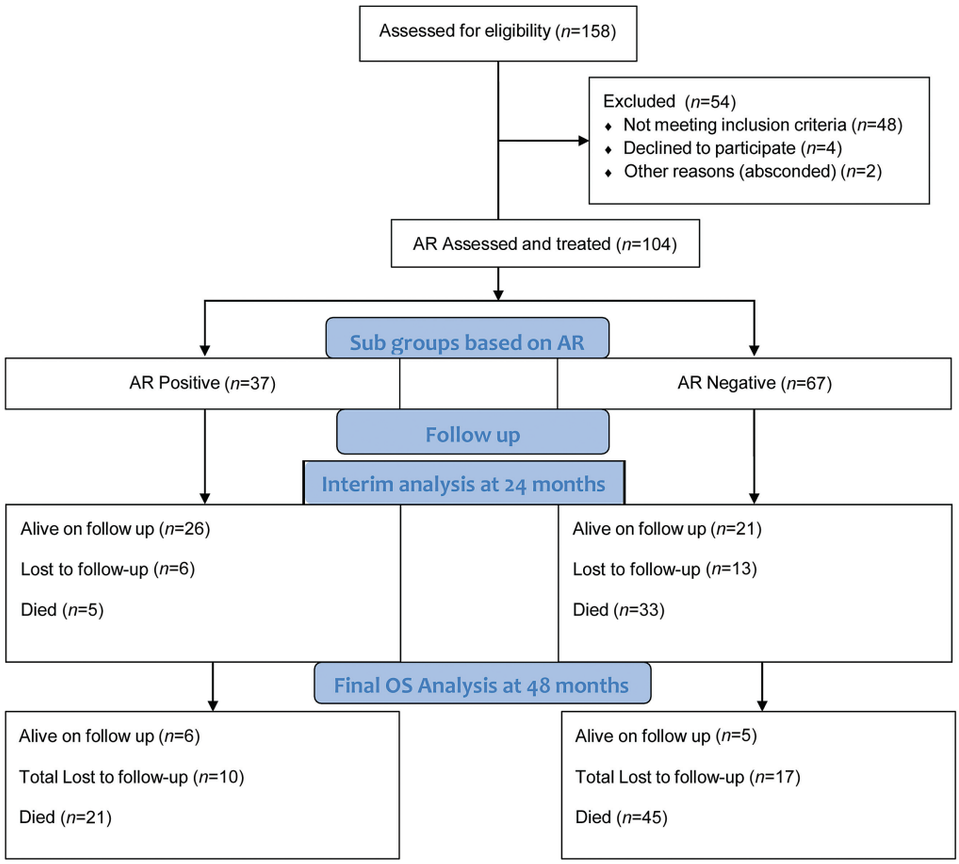

Fig. 3 Overall survival among both groups over the 5-year follow-up period.

Table 2 Comparison of AR cutoff values and percentage AR positives in various studies to this study

Author of the study (year of publication)	Cutoff percentage on IHC	Percentage of AR+
McGhan et al (2014)[7]	> 10	23
Ricciardi et al (2015)[9]	> 10	26.6
Choi et al (2015)[10]	> 10	17.7
Grogg et al (2015)[11]	≥ 1	11.4
Rampurwala et al (2016)[12]	> 10	15
Narayanan and Dalton (2016)[13]	> 10	15–70
Collignon et al (2016)[8]	≥ 1	12
Anand et al (2017)[15]	≥ 1	30
Patnayak et al (2018)[14]	> 10	20
Bhattarai et al (2019)[6]	≥ 1	22.7
This study	> **10**	**35**

Abbreviations: +, positive; AR, androgen receptor; IHC, immunohistochemistry.
Note: Comparison of our study AR cutoff and percentage to various Indian and other publications in tabular form shows higher AR expression even with higher cutoff. Study Result and AR Cutoff are highlighted.

nodal involvement at presentation) were comparable to previous studies.[6,12–15]

Comparison of Baseline Characteristics of Both Groups

Patients aged < 35 years were observed to be more in the AR-negative group (9/68, 13%) compared with the AR-positive group (1/36, 3%). The AR-negative group had more patients (43/68, 63%) aged < 55 years than the AR-positive group (18/36, 50%). But the mean age in both the groups were identical at 52 years in AR negative and 55 years in AR positive.

Similar proportion of pre- (26% vs. 22%) and postmenopausal patients (73% vs. 77%) were comparable between the AR-negative and AR-positive groups, respectively. Mean tumor size at presentation was smaller in the AR-positive group than the AR-negative group (4.2 vs. 5.2 cm). Proportion of patients with higher stage was more in the AR-negative group compared with the AR-positive group. The AR-positive group had significantly higher proportion of patients of stage 1 than the AR-negative group (11% vs. 3%) ($p = 0.077$). K_i-67 correlated with higher grade but was not significantly different between the two groups ($p = 0.79$).

Histological subtypes showed comparable proportion of Invasive ductal carcinoma (IDC) type, which was majority in both groups (88% vs. 87%). For the patients with apocrine type, all had AR expression of 100% (3/3), whereas among papillary, lobular, sebaceous, and signet cell type, none had AR expression. Medullary and metaplastic type occurrences were equal in both the groups. Both groups were comparable in the treatment pattern as there was no significant difference in rate of BCS (11% vs. 10%) or patients undergoing upfront surgery or NACT (27% vs. 26%).

Response to NACT

Only one patient in the AR-negative group had progressed, compared with two AR-positive patients on NACT. Thus, indicating the AR-positive group is chemoresistant than the AR-negative group. Even pCRs were significantly different in both groups—31.8% patients in the AR-negative group achieved pCR whereas only 7.69% patients in the AR-positive group achieved pCR ($p = 0.003$). This result was comparable to previous studies, which have suggested lower pCR rates in the AR-positive group than Quadraple negative breast cancer (QNBC).[13–15] Distant recurrence rate within 1 year of completion of treatment was higher in the AR-negative group (34%) compared with the AR-positive group (24%).

Survival Analysis

Mortality rate within 1 year was also higher in the AR-negative group than the AR-positive group (18/68, 26.5% vs. 7/36, 19.4%). Though the response to chemotherapy was more in the AR-negative group compared with the AR-positive group, the recurrence and mortality occurred earlier in the AR-negative group than in the AR-positive group.

Nonetheless, among stage 3 patients who were treated in an adjuvant setting, they showed significant survival advantage in the AR-negative group compared with the AR-positive group. At 18 months, 21/25 (84%) patients were alive in the AR-negative group and 8/11 (76%) patients in the AR-positive group ($p = 0.023$). Over the next 3 years, this advantage was lost as 63% of the AR-negative group versus only 27% in the AR-positive group who were on follow-up, showed recurrence and mortality ($p = 0.023$). Most of the recurrences were at metastatic sites and were treated with later lines of palliative chemotherapy and OS was noted at mortality.

In NACT setting, stage 3 patients showed significant survival advantage in the AR-positive group irrespective of the pathological response to chemotherapy (22 vs. 15 months) ($p = 0.003$). Thus, this occurrence suggested that the AR-positive group retains their survival advantage despite failing on chemotherapy. This also indicates that different biological drivers work in pathophysiology of both the groups and specific molecular targets need to be identified to treat either of them more effectively than usual.

Even in palliative setting for those with stage 4 disease at presentation, the AR-positive group showed survival advantage with a median OS difference of approximately 9 months (20 vs. 11 months) ($p = 0.3$).

Survival outcomes were assessed among both groups. The AR-positive group showed survival advantage irrespective of the pathological response to chemotherapy or in adjuvant setting compared with the AR-negative group (►**Fig. 3**).

Overall Survival

Median OS of the AR-negative group was reached at 29 months whereas for the AR-positive group it was 49 months, which is not statistically significant ($p = 0.58$).

In the AR-positive subgroup, most of those patients who crossed the 2-year follow-up period without recurrence had their follow-up period relaxed to a 6-month interval. After approximately 3 years, these individuals began to exhibit recurrence, reaching median OS at 4 years. Therefore, in this subgroup, a prolonged close follow-up period (beyond 24 months) and a long-term maintenance treatment, such as AR-targeted therapy, may be helpful.

Strengths

A well-executed, real-world, objective, prospective observational study with a sufficient sample size was performed in a single institution under the supervision of a skilled team of surgeons, pathologists, and mentors. All patients completed the course of therapy and there was more than 5 years of follow-up data.

Limitations

Patients on this study had a notable loss to follow-up during the pandemic period especially those who had lower risk of recurrence and had to be censored from final analysis. Majority of patients who had a recurrence had received subsequent lines of treatment, hence were on follow-up.

Generalizability

TNBC was managed as per standard of care during the study period. Though standard of care has changed to total NACT and addition of adjuvant capecitabine in later years, outcomes are still poor. Newer insights on the tumor behavior and subtyping especially with inexpensive and widely available tests like IHC is feasible and would have potential not only to predict but also to tailor the treatment based on AR expression.

Future Research and Directions

This study shows that the AR-positive subgroup of TNBC is innately more resistant to chemotherapy and behaves indolent like luminal A and shows delayed recurrences than the AR-negative subgroup. Hence, further studies are needed to compare with the addition of AR-targeted therapies for maintenance after standard treatment, which might benefit the AR-positive group in Indian women with TNBC as the proportion of AR expression is found to be higher than usual.

Conclusion

Percentage of AR expression in TNBC in this study was 35% at a cutoff of 10% for positivity, when compared with various studies worldwide and to Indian data this was much higher.

The AR-positive group had lower grade and lesser response rates to NACT. The AR-negative group despite showing better response to NACT had early recurrence and higher mortality reaching median OS within 3 years of completion of treatment.

The AR-positive group, despite having better survival compared with the AR-negative subgroup in the first 3 years, had significant late recurrence and mortality and even reached the median OS at approximately 4 years.

TNBC has poor prognosis and limited management options. Understanding subsets like the AR-positive subgroup and their natural course of disease will help tailoring the treatment strategy by avoiding unnecessary toxicity due to chemotherapy due to TNBC's_less chemosensitivity. It will also help in developing better follow-up strategies to detect late recurrence.

Further studies to target available treatment options like androgen blockers in the AR- positive subgroup for long-term maintenance might be beneficial for preventing the recurrence and mortality caused by TNBC.

Patient Consent

Informed patient consent was obtained for this study.

Conflict of Interest

None declared.

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Perspectives of Breast Cancer Survivors with Recurrence: A Qualitative Study from a Tertiary Cancer Center in Northern Kerala, India

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Abstract

Introduction Being diagnosed with breast cancer in itself is a trauma to a woman. Disease recurrence in a survivor is a separate entity with issues and challenges that differ from the initial diagnosis. Recurrence gives a message of incurability to the survivor.

Objective There is a dearth of qualitative studies from Kerala about the experiences of breast cancer survivors with recurrence. This study was undertaken to have a better understanding of the perspectives of these women.

Materials and Methods In-depth interviews were conducted among 10 survivors registered in the Hospital-Based Cancer Registry of 2016 in a Tertiary Cancer Center who had a recurrence in 2022, using an interview schedule. Interview transcripts were subjected to thematic analysis.

Results The Consolidated Criteria for Reporting Qualitative Research were used for the study reporting. The themes that emerged were: (1) diagnosis-related challenges, (2) work-related challenges, (3) financial challenges, and (4) treatment and cure-related perspectives.

Conclusion Survivors with disease recurrence had an array of multifaceted experiences that must be addressed.

Keywords
- breast neoplasm
- cancer survivors
- qualitative research
- cancer registry
- recurrence

Introduction

Presently, the most frequently diagnosed cancer among women globally is breast cancer. The state of Kerala in India has an age-adjusted rate of 35.6 per one lakh population.[1] Improved methods of diagnosis, better awareness, and advanced treatment have led to an increase in the number of breast cancer survivors.[2,3] Despite rising survival trends seen in India and the rest of the world,[2] one-fourth of the survivors are found to develop recurrence at later stages and die from disease dissemination.[4] Breast cancer has a wide window of recurrence spanning from months to decades from initial treatment,[5] and represents a separate entity, with challenges and issues different from the primary disease.[4,6] An individual is considered a cancer survivor from diagnosis to the rest of one's life.[7,8] Most studies focus on the quality of life of the survivor, and very few explore the specific issues and concerns from the perspective of those

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survivors with recurrence.[9,10] Research outputs on breast cancer itself are scarce in India. There are no studies on breast cancer survivors from Northern Kerala. This study aims to understand the issues and challenges faced by survivors with recurrence.

Materials and Methods

Study Design, Setting, and Participants

This qualitative study was conducted in a tertiary cancer center (TCC) in Northern Kerala, which provides comprehensive cancer care.

The number of patients with breast cancer registered in the TCC as per the Hospital-Based Cancer Registry (HBCR) in the year 2016 was 534. The detailed protocol is published elsewhere.[11] In this study, 10 female patients were found to have recurrence and progression to stage 4 as of 2022. A qualitative descriptive approach was used for this study.[12] Face-to-face in-depth interviews in the local language were conducted to understand their perspectives, using an interview schedule.

Objectives

The main objective of the current study was to have a deeper understanding of the perspectives of breast cancer survivors with recurrence after 6 years of treatment.

Inclusion criteria: Survivors diagnosed in 2016 as per the HBCR and undergoing treatment at the TCC for recurrence in 2022, were included in the study.

Exclusion criteria: Those who were unwilling or could not participate due to time constraints or health issues were excluded.

Participants were purposively selected. We asked them about their perceptions of disease recurrence, the financial burden of treatment for the second time, family support during the crisis, and the work-related challenges due to their ailments and treatments. Interviews were conducted during their treatment visits in the hospital, after obtaining consent and explaining the purpose and voluntary nature. Adequate privacy was ensured, allowing bystanders only if they wanted. Interviews were conducted by the first author, who was not their treating physician; hence, the participants could freely open up. Interviews were conducted only if the participants were comfortable; if not, it was postponed to the next visit. The interview lasted 45 to 50 minutes and the narratives were audio recorded and field notes taken down.

Primary outcome: The study will help to have a better understanding of the experiences of the survivors with recurrence and the challenges faced by them.

Secondary outcome: The findings can be used to improve patient care and policy-making based on the understanding.

Data Analysis

Data analysis was done manually due to the small numbers. Thematic analysis[13] was used for a rich and complex account of the data collected. All the interviews were transcribed and then translated verbatim into English, followed by reading and rereading to familiarize the data by authors. Codes were generated systematically, separately, by each author; constant comparison was made and similar ones were organized into categories. Discussion among authors helped reach a consensus. The ongoing exercise of refining the categories several times, organizing them into themes, and naming them led to the final results. For ensuring the trustworthiness of findings, the criteria of credibility, dependability, transferability, and confirmability were followed.[13] The first author, being a female trained in qualitative research, ensured credibility. The findings were checked with oncologists in the TCC to ensure the truth in the facts stated. All interviews were conducted by the first author, using an interview schedule for consistency in data collection. To ensure transferability, the characteristics of the sample, descriptions of study methods, data collection, and analysis are also detailed in the text.

Ethical Approval

All procedures performed in this study followed the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The approval

Table 1 Sociodemographic profile of study participants ($n = 10$)

Age	*n* (%)
≤ 50 y	3 (30)
> 50 y	7 (70)
Parity	
Yes	10 (100)
Marital status	
Married	9 (90)
Widow	1 (10)
Present stage	
Stage 4	10 (100)
Stage at diagnosis	
Stage 2	4 (40)
Stage 3	5 (50)
Stage 4	1 (10)
Education	
Middle	2 (20)
Secondary	7 (70)
College level	1 (10)
Year of diagnosis of recurrence/relapse	
2020	2 (20)
2021	6 (60)
2017	2 (20)
Job	
Manual laborer	2 (20)
Homemaker	8 (80)

Table 2 Major themes, subthemes, and codes

Major themes	Subthemes	Codes
Diagnosis-related challenges	Delay in initial diagnosis and delay in recognition of symptoms	Carelessness, ignored symptoms, fear, financial reasons, breastfeeding, not recognizing, feeling guilty, nature of the disease, not their fault, loss of trust in the treatment, decreased access to health facility
		Daughter's exam, daughter's delivery, family members taking it lightly, no one to accompany. Decreased awareness among spouses, spouse working abroad
	Health facility-related	Awareness regarding symptoms of recurrence, access
	Disease-related	Nature of disease
Work-related challenges	Symptom-related	Pain, breathlessness, inability to work, burden to family
	Financial-related	Repaying of loans, worry of depending on others
	Family support	Helping in work, doing all work, overprotective
Finance-related challenges	Government schemes	Treatment availed, out-of-pocket expenses, schemes exhausted, cancer pension, schemes not available, financial burden to family
Disease- and cure-related challenges	Facing treatment again	No courage, depression, crying, thinking of death, belief in a cure
	Hiding the reality	Not aware of the present condition
	coping	Optimistic, prayers, increased faith in God
	treatment-related worry	Worried about side effects of excessive medicine use
	Family-related expectations	Children have no time, children are employed, and loneliness

for the study was obtained from the institution where the author undertook her PhD study, and from the institution where the study was conducted (1617/IRB-IEC/13/MCC/26-05-2021/2 and SCT/IEC/1711/AUGUST/2021).

Results

The 10 survivors interviewed were aged between 50 and 68 years (mean age of 59.25). The sociodemographic profile of these survivors is given in ►**Table 1**. The themes, subthemes, and codes are given in ►**Table 2**. The following themes related to the perspectives of survivors emerged: (1) diagnosis-related, (2) work-related, (3) financial-related, and (4) treatment and cure-related challenges (►**Fig. 1**).

Theme 1: Diagnosis-Related Challenges

The survivors were asked for her perspective on why she got the disease a second time, though others who underwent treatment along with her were disease-free. The subthemes related to delayed initial diagnosis leading to recurrence were described under the following headings.

Delayed Initial Diagnosis

> *"I know that the disease recurred because of my carelessness. I ignored my symptoms initially."*

> *"It was my fault. I delayed the initial consultation due to fear and financial constraints."*

These were the words of two women: Survivor 1 (54-year-old) and survivor 2 (66-year-old widow), respectively. Looking back, they realized that the disease had recurred because they failed to get it diagnosed in the early stages, which now led to a feeling of guilt. They recalled that they either failed to recognize symptoms or to consult a health care worker on time.

Even in those who recognized that something was wrong, some reasons prevented them from undergoing a medical consultation immediately, such as family events, decreased awareness among family members, family situations, etc.

A 53-year-old, survivor 3, mother of three, recalls that "*I delayed initial consultation by almost three months as my daughter was having her degree examination*."

> *"When I noticed the lump, it was my daughter's delivery time. I knew that something was wrong as I was always actively involved in organizing cancer detection camps in our place, but still delayed consultation. Only if I had consulted earlier……."* The words of survivor 4 (66-year-old mother), who was diagnosed with stage 3 breast cancer and developed recurrence in 2021.

> *"Even though I told my husband, he said that the lump would go away on its own. There was nobody else to take me to a doctor. There was a delay of 3 months"* said a 50-year-old, survivor 5.

> *"My husband was abroad at that time. Though I disclosed it to my sister-in-law, she said it was normal. At that time, I was breastfeeding my child, too. It was late by the time my disease was diagnosed,"* said survivor 6, a 50-year-old with two children.

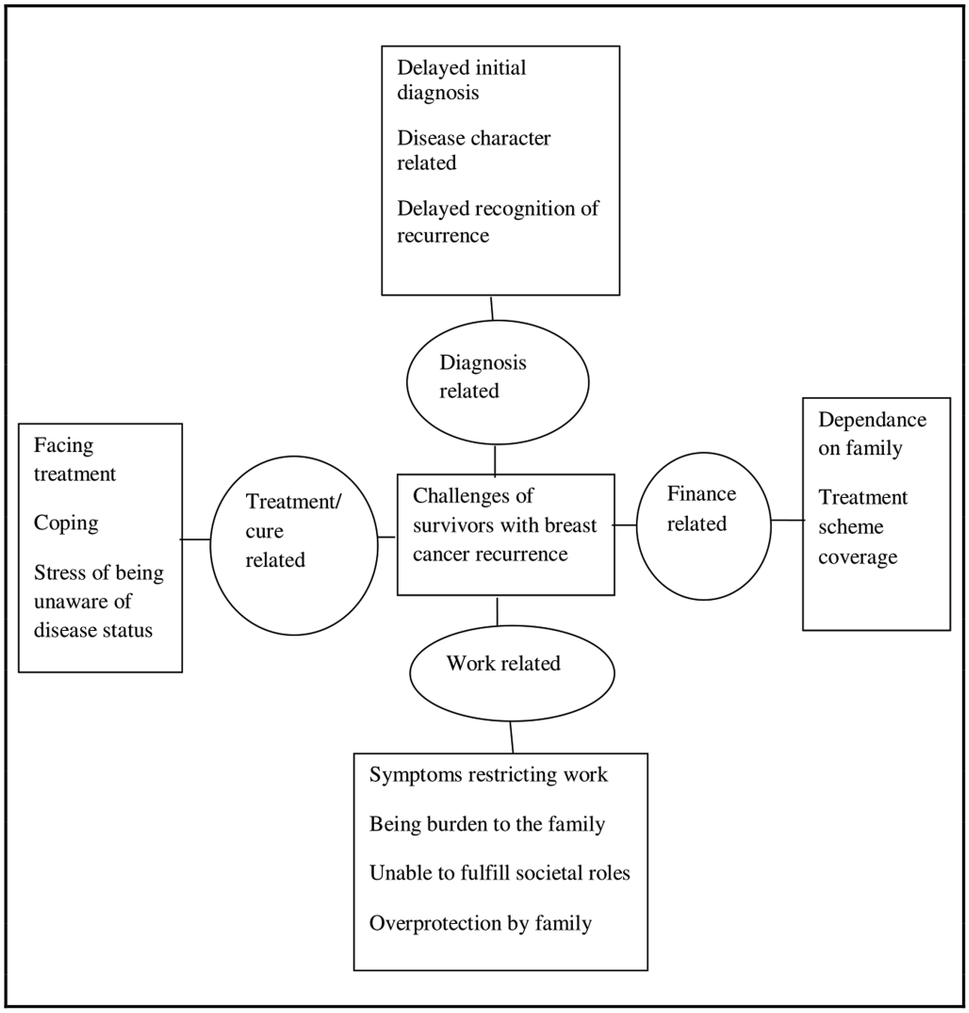

Fig. 1 Perspectives of survivors with recurrence of breast cancer.

Disease Characteristics Related

Two of the survivors, survivor 7 (63 years old) and survivor 4, stated that despite being diagnosed early, the disease came back. They believed that it was due to the nature of the disease called "cancer."

"I took all medications and did regular follow-up. I don't think that the disease came back because of my fault. The disease itself is so"

"I took all treatments and followed all instructions of my doctor, but still the disease recurred. I don't know why"

"I often feel that if my uterus was also removed during my initial treatment, it would not have recurred there," said survivor 8 (68-year-old mother of two).

A feeling of helplessness and loss of trust in the cure after treatment were reflected in their words.

Recognition of Recurrence

For some, the accessibility to a health facility enabled them to get treatment immediately. They did not have to wait for the decision from the family.[4]

"For me, when the disease came back, I recognized it and informed my doctor immediately, even though my family said that it may be just my feeling. I could do this because I was going to the hospital for regular follow-up."

"Though I felt something was wrong again, I could consult a doctor only after two months due to the COVID crisis. There should be some alternative," said survivor 5, diagnosed initially with stage 3 breast cancer.

Decreased self-awareness of the warning signs of recurrence and noncommunication from the health care providers were also described.

As stated by survivor 3, who developed recurrence in the lungs;

"I did not recognize. I thought the disease would come back only in the breast area. I had cough, but thought it was due to an allergy. There was painting work in the house in connection with my daughter's marriage. I consulted doctors only when the cough did not subside after 3 months…"

"I regularly checked my breasts. I did not know about any other warning signs to look for. Nobody told us," said survivor 8.

At the same time, most of the survivors were vigilant and more careful during the second time, as stated by survivor 7, who developed disease recurrence.

The words of survivor 7, a mother of four, also reflected the same sentiment. *"I regularly read health magazines. So, when I had severe back pain, I did not waste time consulting anywhere else, I came straight away to TCC."*

Theme 2: Work-Related Challenges

Women faced challenges related to their day-to-day activities as well as paid jobs due to the recurrence of the disease. These were related either to the symptoms of recurrence, or restrictions from family members.

Symptoms Restricting Work

"Now I cannot do any work due to cough and breathlessness. Cannot sleep at night"- this was stated by survivor 3.

Being a Burden to Family

Survivor 2 said, *"I cannot do any work now due to pain. I was a manual laborer. I wish I could continue my job."*

Overprotection by Family

Support from their family members made them happy, but overconcern from the family posed restrictions.

Survivor 7, now undergoing treatment, said, *"I am able to do my work, but my husband and children don't allow me due to concern for my health. Without their knowledge, I take pain medication and engage in gardening. It makes me happy.*"

Unable to Fulfill Societal Roles

"My daughter-in-law has to do all the household chores when I feel tired after treatment," said survivor 4.

Theme 3: Financial Challenges

The financial burden was a major concern as they were all undergoing treatment for the second time. The words of survivor 2 and survivor 3 state that apart from the symptoms, the inability to support the family financially and dependence on them for treatment expenses, worried them.

Dependence on Family

"I am a widow. My daughter's husband also died recently. I am worried about family matters now more than my disease. My daughter has to work and look after me. I had taken a loan previously. I thought I would continue my job and repay it, but now that cancer has recurred, it is difficult."

"My family has to spend money on my treatment. Nowadays, I cannot do any work due to breathlessness," said survivor 3, who is on chemotherapy now.

The medicines this time were expensive, my husband cannot work anymore, and the financial problem worries me," said survivor 5.

Coverage of Treatment Schemes

Though they were all beneficiaries of government treatment schemes, they had out-of-pocket expenses such as medicines, travel, etc. The words of survivor 5 and survivor 2 clearly state this.

"I am availing the benefit from the government scheme for my treatment. But still, the travel expenses and weekly blood tests all have to be borne by me," said survivor 2, who is on chemotherapy now.

"I got help from treatment schemes even for the second time, but all medicines were not covered".

For some, the amount available was already utilized during their first treatment. This is evident from the words of survivor 7.

"I availed 'Karunya' treatment scheme for the first treatment. Now for medicines, transport, tests, etc. I have to bear the expense. I get the Government pension for cancer patients, but it is very irregular."

Some could not claim the government schemes as they do not come under the criteria for beneficiaries.

"I am a taxpayer, hence did not get treatment schemes." said survivor 8, who is under treatment now.

Theme 4: Treatment and Cure-Related Concerns

We asked the survivors' thoughts about undergoing treatment for breast cancer recurrence and their idea of a cure. Both positive and negative perspectives were seen.

Facing the Treatment Again

Most of them found it difficult to go through the whole treatment and tests again. These were evident from the words of the survivors.

"First time I had no tension. But now it is not the same. I have no courage or strength to bear the treatment," as quoted by survivor 7.

"Though I fought the disease with courage the first time, I was completely depressed this time. I thought I was cured and that the disease will not come back after all these years," said survivor 8 who was diagnosed with stage 2 disease and is now undergoing treatment for recurrence.

Other concerns worried them equally.

"I have to take pain medicines now. I fear that my kidneys will be damaged due to this. The disease is already there, now if I lose my kidney too…" said a visibly anxious survivor 4.

The family was trying to support the survivor well, but sometimes could not come up to their expectations or fulfill their needs.

"I am only sad that my daughters are busy and cannot come and stay with me. I feel very happy when they are with me. I know that they have jobs and cannot come over frequently," said survivor 8.

Coping Strategies

Some were optimistic and courageously faced the disease even for the second time. They gained strength by engaging in faith-based practices like spiritual beliefs, prayers, and reading holy books, irrespective of age.

"I believe in prayers. I read the holy Bible. I am alive at least in this way, because of the prayers of my loved ones," in the words of survivor 5.

"I believe that I can still overcome. I spend my time in prayer, "said survivor 6.

"Don't know what will happen tomorrow. Whatever happens is for good," stated survivor 8.

Stress of Being Unaware of the Disease Status

This was expressed by two of the survivors:

"They did not tell me about my condition. I came to know about it only recently when my physician, who is treating me for diabetes, told me. I feel that family should not hide it from us," said survivor 9.

Survivor 10 (50-year-old) said, *"I don't know about the extent of my disease and why I am taking treatment even now.*"

"Only my daughter knows about my disease status. I asked her, but she did not tell me," said survivor 4, whose elder daughter was accompanying her for treatment.

Discussion

Delay either in the initial diagnosis or in recognizing the signs of recurrence and disease characteristics were described by the survivors. One-third of women presented in late stages during the initial diagnosis,[14] as the decision to seek care is often initiated by the women's perception and awareness regarding the "main" symptom.[14] Failure to recognize symptoms or issues related to self or family was described as the reason for delayed consultation. Awareness about cancer was found to be low among Indian rural women.[15] The daughter's delivery, marriage in the family, and children's examination were causes of delay, as in our study.[16] Most women disclose their symptoms first to their husbands,[14] which means awareness among spouses regarding breast cancer is an important factor that determines the wife's attitudes and practices.[17] The involvement of family members in medical-related decisions was reported as the cause of delay in other studies, as in ours.[14] All these can result in late stages at initial diagnosis and high chances of recurrence.[4] All our participants agreed that early diagnosis would have prevented a recurrence.

Our survivors also stated that knowledge about the symptoms of recurrence would have helped in early medical consultation. The overburdened health worker may not be able to give proper guidance in the regular hospital outpatient department.[18] Hence, tailored screening programs for those at higher risk of recurrence based on their clinicopathological and treatment parameters were suggested.[4] Alternate arrangements for consultation during crises like the coronavirus disease (COVID) pandemic are also needed as visits to a health care setting itself could be a source of infection, and most of the follow-up visits were either deferred or done through telemedicine at that time.[18,19]

Women were finding it difficult to do household chores due to their symptoms, like breathlessness and pain. Symptoms negatively affecting the fulfillment of social roles, day-to-day work, and impact on family were also reported in a review similar to our survivors.[10] Though family support was there, there was a feeling of helplessness, as those who were working after initial treatment also could not do so now due to health issues.[20] The overprotective nature of the family was also mentioned in other studies.[20] The change from a caregiver's role to someone receiving care was experienced by most of these women.[21]

Various government treatment schemes[22] were availed by these survivors even during the second round of treatment. However, not all medicines prescribed were covered by the schemes, as reported by them. Only 40% of patients with metastatic breast cancer in Asian countries receive second-line treatment through treatment schemes.[23] The expenses of the laboratory tests, travel, etc., have to be borne by the patients. Moreover, cancer care costs in the private sector are three times higher in India.[18]

Facing the disease again is more distressing to the woman than the primary diagnosis, as this points to its uncertain nature.[9,10] Though many had negative thoughts about cure,

positive coping strategies were exhibited by some. Religious beliefs and support structures were important coping strategies, as per literature, which was also found in our survivors.[24] The worry about complications following treatment, loneliness due to the lack of presence of near and dear ones, and stress due to the feeling of being a burden to the family were also expressed by the survivors. Adjusting to the new prognosis related to the disease, uncertainty about the future, and helplessness were looming in their words.[20] Though the family members thought that the patient would not be able to bear the reality of recurrence, and it was better to hide it from them, the patient's point of view was different. That information provision could lessen anxiety and improve understanding of the situation were also described in other qualitative studies.[20] As in our study, concerns of women regarding knowledge about their disease and receiving support from health workers and family was described in other studies too.[10,24] Though our study describes experiences and challenges of a limited number of survivors, we tried to include a heterogeneous group, and we believe that we could cover their perspectives in depth. This is a single-center study, which is a limitation. We tried to unravel a few perspectives of survivors with recurrence. More qualitative studies are needed for a deeper understanding of survivorship in India.

Conclusion

Recurrence, many a time, was the outcome of presenting late for the initial diagnosis, in addition to the clinicopathological characteristics of the disease. Improving awareness of cancer among spouses and family members in general is suggested. The findings also point to the need for health workers to provide awareness of signs of recurrence for early recognition and proper communication of disease status with the patient and help them cope with the reality. Financial assistance in treatment in the form of increasing the coverage of second-line drugs in government treatment schemes is needed. A system for regular disbursement of benefits to cancer patients, such as cancer-related pensions, should also be ensured. An overall health support system to deal with the challenges related to the fear of the unknown caused by the recurrence, and a strategy to deal with situations like COVID-19, is needed. More research is required to shed light in this direction.

Authors' Contributions

The manuscript has been read and approved by all the authors, and the requirements for authorship have been met and are provided in contributor's form. Each author believes that the manuscript represents honest work. Study conceptualization and Methodology, Data analysis, Review and editing, and Final approval of manuscript have been done by S.K. Study conceptualization and methodology, Data collection, Manuscript writing, Review and Editing and Final approval of manuscript have been done by N.A.P.

Conflict of Interest

None declared.

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Malnutrition among Pediatric Cancer Patients: A Study of Government Hospitals in Delhi

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Abstract

Introduction Research indicates a considerably higher incidence of malnutrition at the time of diagnosis among patients with pediatric cancer. Studies have also shown that malnutrition tends to worsen with anti-cancer therapies. However, there are limited studies conducted in the Indian context, and those available often involve small sample sizes.

Objectives This study aims to address this gap by analyzing data of patients with pediatric cancer treated at two government hospitals in Delhi.

Materials and Methods This retrospective study includes data from 1,042 patients with pediatric cancer, collected over 6 years from April 2018 to April 2024. The dataset includes age at diagnosis, cancer type, and anthropometric measurements recorded at the initial contact. The analysis focuses on the prevalence of malnutrition, stratified by gender, age group, and cancer type.

Results Among patients with pediatric cancer, more than 80% were diagnosed with hematological malignancies. This study identified an overall malnutrition prevalence of 39.7% (414 out of 1,042). Notably, the prevalence increases with age.

Conclusion Given the substantially higher levels of malnutrition among patients with pediatric cancer at baseline and the anticipated increase during anticancer therapy, there is a pressing need for close monitoring and the development of targeted, individualized nutritional interventions. Such measures are essential to mitigate the impact of malnutrition on treatment outcomes and quality of life.

Keywords
- malnutrition
- incidence
- pediatric cancer
- WHO norms
- acute lymphoblastic leukemia
- prevalence

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Introduction

Malnutrition is a critical concern among patients with pediatric cancer, with its impact varying across cancer types and treatment stages.[1] Several studies have explored malnutrition and undernutrition in patients with pediatric cancer. These studies underscore the critical role of nutritional status in influencing both the immediate treatment outcomes and the long-term prognosis in patients with pediatric cancer.

However, only three studies in the Indian context have been conducted in the past decade,[2–4] and these are limited by small sample sizes. Therefore, it is crucial to examine malnutrition among patients with pediatric cancer using a larger sample size, particularly with a focus on the North Indian population. This study focuses on patients with pediatric cancer receiving care at two major public sector hospitals in Delhi.

Materials and Methods

Study Design and Setting

This is a retrospective study analyzing data from patients with pediatric cancer who received treatment at two major hospitals in Delhi—Safdarjung Hospital and Kalawati Saran Children's Hospital. These patients were also supported through Cankids with other required supplementary cancer care services. The study covers data from the past 6 years, spanning from April 2018 to April 2024.

Inclusion Criteria

Children in the age group up to 18 years diagnosed for the first time with cancer, availing treatment from these hospitals, and supported through CanKids during the period under study were included.

Exclusion Criteria

Those patients with incomplete records were excluded.

The information collected for each patient are date of birth, date of diagnosis, and anthropometric measurements (weight, height, and body mass index [BMI]) at baseline (i.e., at the time of first contact). Anthropometric data were collected by professional dietitians using calibrated and standardized equipment. The data are maintained in Google spreadsheets with in-built auto-computation of BMI and nutritional status categorization. Age at diagnosis was calculated as the difference between the date of birth and the diagnosis date. The average height, weight, and BMI were calculated for each age separately for boys and girls. These have been compared with the Indian Academy of Pediatrics (IAP) and World Health Organization (WHO) median norms/standards. Importantly, WHO growth standards are used for children younger than 5 years[5], while IAP growth charts are applied for children aged 5 to 17 years. The nutritional status grading was done using the WHO classification of nutritional status of infants and children.[6,7] These are given in ►**Tables 1** and **2**.

Table 1 Nutritional status grading as per the WHO classification for 0 to 59 months

Grade	Nutritional status markers
Normal	Weight-for-length/height or BMI-for-age 0 (median) to −2 SD
Moderate acute malnutrition	Weight-for-length/height or BMI-for-age < -2 SD and ≥ -3 SD of the median
Severe acute malnutrition	Weight-for-length/height or BMI-for-age < -3 SD of the median

Table 2 Nutritional status grading as per the WHO classification for 5 to 18 years

Grade	Nutritional status markers
Normal	BMI-for-age 0 (median) to −2 SD
Thinness	BMI-for-age < -2 SD and ≥ -3 SD of the median
Severe thinness	BMI-for-age $<-$ 3 SD of the median

Statistical Analysis

An analysis of nutritional status was conducted based on gender, age group, and type of cancer. An appropriate test of significance (Chi-square test) was applied to assess differences in nutritional status between gender, age groups, and cancer types. A *p*-value of less than 0.05 was considered statistically significant. The analysis was conducted using SPSS version 24.

Ethical Approval

Since this is a retrospective study, ethical permission and consent from patients and their guardians were not needed.

Results

The sample consisted of 1,042 patients with pediatric cancer, of whom 707 (67.8%) were boys and 335 (32.2%) were girls. Regarding age distribution, 498 (47.8%) were younger than 5 years, 426 (40.8%) were pre-adolescents (ages 5–11), and 118 (11.3%) were adolescents (ages 12–17). A significantly large proportion of the sample, 872 (83.7%), were diagnosed with hematological malignancies (►**Table 3**).

Comparison of Anthropometric Parameters with WHO and IAP Norms

The average height, weight, and BMI of boys and girls were compared against the standard median norms of the WHO for children younger than 5 years and the norms of IAP for children 5 to 17 years to calculate growth achievement. This was assessed as the ratio of the observed mean values to the median norms for height, weight, and BMI, separately for boys and girls.

It was observed that the average height of patients with pediatric cancer was ∼94.2% of the expected values for boys

Table 3 Profile of study subjects according to gender, age groups, and cancer type

Category	Frequency	Percentage
Gender		
Male	707	67.8
Female	335	32.1
Age groups		
0–59 mo	429	41.1
5–11 y	488	46.8
12–17 y	125	11.9
Cancer type		
Hematological malignancies	872	83.7
Solid tumors (except CNS tumors)	78	7.5
CNS tumors	92	8.8

Abbreviation: CNS, central nervous system.

and 96.3% for girls (►**Table 4**). Similarly, the average weight was ~79.1% of the reference values for boys and 80.2% for girls (►**Table 5**). Furthermore, the average BMI was 89.6% of the corresponding benchmarks for boys and 86.6% for girls (►**Table 6**).

Nutritional Status

Nutritional status was graded using the WHO classification.

Measured in terms of sigma limits and categorized as normal, moderately malnourished, or severely malnourished, the following findings emerged (►**Table 7**):

1. Overall, 414 children (39.7%) were found to be malnourished, including a significant 202 children (19.3%) with weight-for-length/height or BMI-for-age ≤ -3 SD of the median (i.e., severely malnourished).
2. The prevalence of malnutrition was similar among boys (39.4%) and girls (40.3%), with the difference not being statistically significant ($p = 0.94$).
3. Malnutrition increased with age: 32.9% among children younger than 5 years, 41.9% among pre-adolescents, and 55.5% among adolescents. Among the severely malnourished, there were 69 (16.1%) children younger than 5 years, 92 (18.9%) pre-adolescents, and 42 (33.3%) adolescents. The differences were statistically significant ($p < 0.001$).
4. The prevalence of severe malnutrition was lower among patients with hematological malignancies compared with those with other cancers, with the differences being statistically significant ($p = 0.0005$).

Table 4 Comparison of average height with standard median norm by gender

Age (years)	Height (in cm)					
	Gender					
	Male			Female		
	Mean	Standard norms	Achievements of growth norms	Mean	Standard norms	Achievements of growth norms
1	77	75.7	101.7	78	74	105.4
2	84	87.1	96.4	87	85.7	101.5
3	89	96.1	92.6	89	95.1	93.6
4	95	103.3	92.0	94	102.7	91.5
5	104	108.9	95.5	105	107.5	97.7
6	110	114.8	95.8	102	113.5	89.9
7	114	120.7	94.4	118	119.4	98.8
8	123	126.4	97.3	124	125.4	98.9
9	122	131.8	92.6	127	131.4	96.7
10	132	137.2	96.2	129	137.4	93.9
11	137	142.7	96.0	139	143.3	97.0
12	139	148.4	93.7	136	148.4	91.6
13	140	154.3	90.7	146	152.2	95.9
14	136	159.9	85.1	149	154.7	96.3
15	152	164.5	92.4	146	156.1	93.5
16	160	168.1	95.2	–	–	
17	160	171.0	93.6	156	157.4	99.1
Average			94.2			96.3

Note: WHO growth standards are used for children younger than 5 years, while IAP growth charts are applied for children aged 5 to 17 years.

Table 5 Comparison of average weight with standard median norm by gender

Age (years)	Weight (in kg)					
	Gender					
	Male			Female		
	Mean	Standard norms	Achievements of growth norms	Mean	Standard norms	Achievements of growth norms
1	8.7	9.6	90.6	8.9	8.9	100.0
2	9.9	12.2	81.1	10	11.5	87.0
3	12.7	14.3	88.8	11.7	13.9	84.2
4	14.2	16.3	87.1	12.5	16.1	77.6
5	15.6	18.3	85.2	15	18.2	82.4
6	16.7	19.3	86.5	15.5	18.7	82.9
7	18	21.9	82.2	19	21.2	89.6
8	20.7	24.8	83.5	20.2	24.0	84.2
9	22.9	27.9	82.1	23	27.2	84.6
10	25.8	31.1	83.0	23.9	31.0	77.1
11	26.5	34.7	76.4	27	35.4	76.3
12	27.4	39.0	70.3	25.1	39.8	63.1
13	28.7	43.3	66.3	33.8	43.6	77.5
14	34.3	48.2	71.2	32.3	46.4	69.6
15	36.3	53.1	68.4	29	48.4	59.9
16	43	56.8	75.7	–	–	
17	40	59.5	67.2	44.1	50.9	86.6
Average			79.1			80.2

Note: WHO growth standards are used for children younger than 5 years, while IAP growth charts are applied for children aged 5 to 17 years.

Discussion

The study represents the longest cohort in India specifically covering childhood cancer and nutrition, highlighting the prevalence of malnutrition among children with cancer. Overall, 39.7% of the children were malnourished, with 20.3% moderately malnourished and 19.3% severely malnourished. The prevalence of malnutrition varied by cancer type, with hematological malignancies showing 37% malnutrition (21.9% MAM, 15.02% SAM), solid tumors (except CNS tumors) having the highest burden at 52.56% malnutrition (21.79% MAM, 30.77% SAM), and CNS tumors at 50.00% malnutrition (18.48% MAM, 26.09% SAM). A statistical review by Ward et al[8] provides a detailed breakdown of childhood cancer incidence rates, with acute lymphoblastic leukemia consistently showing the highest prevalence among leukemias and solid tumors, which aligns with our findings that hematological malignancies constituted the largest subgroup in our cohort.

Furthermore, a review study by Diakatou and Vassilakou[9] found that malnutrition is common at diagnosis and is linked to poor health-related quality of life and nutritional issues in survivors, reinforcing the need for early nutritional assessment and interventions to mitigate long-term complications in childhood cancer survivors.

The 39.7% prevalence of malnutrition observed in this study is comparable to the 56.8% reported by Jain et al using weight-for-age criteria.[2] In their study, they also assessed nutritional status using hematological and biochemical markers, with malnutrition reflected through low hemoglobin (82%), low total proteins (25%, i.e., <5.7 g/dL), low serum albumin (20.5%, i.e., <3.2 g/dL), low serum transferrin (27.3%, i.e., <210 mg/dL), and low serum iron (16.3%, i.e., <60 µg/dL). However, this is much higher than the level of 37.2% as reported by Sakthikumar et al in another Indian study.[3] This study suggested that early nutritional intervention should be an essential part of the multidisciplinary treatment protocol.[3]

In another Indian study by Radhakrishnan et al, undernutrition was seen in 44% of patients at diagnosis. He also reported that active nutritional intervention and education were able to significantly reduce the prevalence of undernutrition in patients by the end of treatment.[4]

Maia-Lemos et al evaluated 1,154 children and adolescents with cancer using various measures like weight, height, BMI, and arm measurements. They found that 10.85 to 27.32% of patients were malnourished at diagnosis, highlighting the need for early nutritional monitoring in pediatric cancer care.[10] A study in the Netherlands by Brinksma et al reported that 40 to 50% of patients with pediatric cancer experienced malnutrition during treatment. It emphasized the adverse effects of malnutrition on treatment outcomes and suggested the need for routine nutritional assessments and interventions in oncology care.[11]

Table 7 Nutritional status according to gender, age group, and cancer type

Nutritional status grade						
Category	Normal		Weight-for-length/-height or BMI-for-age < -2 SD and ≥ -3 SD of the median		Weight-for-length/-height or BMI-for-age < -3 SD of the median	
	Number	%	Number	%	Number	%
Overall						
	628	60.3	212	20.30	202	19.30
Gender						
Male	428	60.5	144	20.3	136	19.2
Female	200	59.7	68	20.3	67	20.0
$\chi^2 = 0.09$; $p = 0.94$						
Age group						
0–59 mo	288	67.1	72	16.8	69	16.1
5–11 y	284	58.2	112	23.0	92	18.9
12–17 y	56	44.4	28	22.2	42	33.3
$\chi^2 = 28.54$; $p < 0.001$						
Cancer type						
Hematological malignancies	546	62.61	191	21.90	131	15.02
Solid tumors (except CNS tumors)	37	47.44	17	21.79	24	30.77
CNS tumors	46	50.00	17	18.48	24	26.09
$\chi^2 = 19.96$; $p = 0.0005$						

Abbreviations: CNS, central nervous system.

Table 6 Comparison of average BMI for age with standard median norm by gender

Age (years)	BMI					
	Gender					
	Male			Female		
	Mean	Standard norms	Achievements of growth norms	Mean	Standard norms	Achievements of growth norms
1	14.7	16.8	87.5	14.6	16.4	89.0
2	14.0	16.0	87.5	13.2	15.7	84.1
3	16.0	15.6	102.6	14.8	15.4	96.1
4	15.7	15.3	102.6	14.1	15.3	92.2
5	14.4	14.7	98.0	13.6	14.3	95.1
6	13.8	14.9	92.6	14.9	14.5	102.8
7	13.9	15.1	92.1	13.6	14.9	91.3
8	13.7	15.5	88.4	13.1	15.3	85.6
9	15.4	15.9	96.9	14.3	15.8	90.5
10	14.8	16.4	90.2	14.4	16.5	87.3
11	14.1	17.0	82.9	14.0	17.2	81.4
12	14.2	17.7	80.2	13.6	18.0	75.6
13	14.6	18.2	80.2	15.9	18.8	84.6
14	18.5	18.7	98.9	14.5	19.4	74.7
15	15.7	19.3	81.3	13.6	19.9	68.3
16	16.8	19.9	84.4	–	–	
17	15.6	20.5	76.1	18.1	20.6	87.9
Average			89.6			86.6

Note: WHO growth standards are used for children younger than 5 years, while IAP growth charts are applied for children aged 5 to 17 years.

Another study by Lemos et al concluded that the prevalence of malnutrition was higher in malignancies.[12]

In our study, the prevalence of malnutrition increased with age, which aligns with the study by Huibers et al, where it was reported that malnutrition was more common in children aged ≥5 years (70.0%) compared with children aged <5 years.[13]

The study by Zimmermann et al, though reporting a low prevalence of malnutrition at diagnosis, showed a steady increase in malnutrition during anticancer therapy.[14] A review study by Barr mentioned that the prevalence and severity of malnutrition in children with cancer in LMICs demand attention.[15] Opportunities exist to conduct studies in India to examine the effects of nutritional interventions, including on the overall well-being of survivors.[15]

The findings of this study align with prior research emphasizing the critical impact of malnutrition on pediatric cancer outcomes. Zimmermann et al demonstrated that while the prevalence of malnutrition at diagnosis was relatively low, it worsened during therapy due to treatment-induced side effects such as reduced appetite and gastrointestinal complications. Similarly, a study by Brinksma et al identified that malnutrition during cancer therapy adversely affected treatment tolerance and recovery rates, underscoring the necessity for routine nutritional assessment.[11–14] Peccatori et al mentioned that nutritional support considerably improved 1-year event-free survival (EFS) by ∼13% compared with a historical cohort in their study.[16] Schoeman, Pedretti et al, and Bauer et al found that proactive nutritional management significantly improves treatment tolerance, reduces complications, and enhances overall outcomes for children undergoing cancer treatment.[17–19] Another study by Fabozzi et al provided practice recommendations for systematic nutritional management in pediatric oncology, reinforcing the importance of structured nutritional interventions to improve treatment outcomes and quality of life.[20]

While survival and toxicity data were not the focus of the current study, previous evidence strongly links poor nutritional status to both increased treatment toxicity and reduced survival. These insights highlight the importance of integrating tailored nutritional support into treatment protocols to mitigate therapy-associated nutritional deterioration and improve overall outcomes.

Strengths

This is one of the largest Indian studies on pediatric patients with cancer and malnutrition, analyzing data from 1,042 patients over 6 years. It draws from two major public hospitals, ensuring real-world relevance. Standardized anthropometric assessments and comparisons with WHO/IAP norms enhance data reliability. Stratified analysis by age, gender, and cancer type offers actionable insights for targeted nutritional interventions. The study fills a critical gap in Indian literature and supports the integration of nutrition into pediatric oncology care.

Limitations

Malnutrition can be assessed using various well-established indicators, such as mid-upper arm circumference (MUAC), height-for-age, weight-for-age, weight-for-height, BMI-for-age, and triceps skinfold thickness (TSF). In this study, malnutrition was measured using weight-for-height and BMI-for-age. However, incorporating additional measures, such as MUAC and TSF, could enhance the comprehensiveness and accuracy of the assessment, providing a more nuanced understanding of the nutritional status of pediatric patients.

Future Prospects and Gray Areas for Research

The study focuses primarily on two government hospitals, highlighting the need for data on additional measures of malnutrition to provide a more comprehensive understanding.

Generalizability of Study

To ensure proper generalization, it would be beneficial to include data from private hospitals and healthcare facilities in other regions of the country.

Conclusion

The considerably high prevalence of malnutrition among patients with pediatric cancer observed in this study underscores the urgent need for routine nutritional assessment and timely intervention as part of standard oncology care. Our findings highlight that nearly 40% of children were either moderately or severely malnourished at the time of diagnosis, with variation by cancer type and age group. This emphasizes the necessity for proactive nutritional planning and individualized care strategies to identify and support at-risk patients early. While this study did not directly assess clinical outcomes, therapy tolerability, or quality of life, the findings reinforce the importance of integrating structured nutritional support into multidisciplinary pediatric oncology care. Future research should aim to explore how early nutritional interventions may influence treatment outcomes, therapy adherence, and the overall well-being of patients with pediatric cancer.

Authors' Contributions

A.S.—Concept design, definition of intellectual content, clinical studies, data acquisition, manuscript preparation, manuscript editing, and manuscript review.

P.M.—Concept design, definition of intellectual content, manuscript preparation, manuscript editing, and manuscript review.

P.B.—Concept design, definition of intellectual content, manuscript preparation, manuscript editing, and manuscript review.

N.F.—Concept design, definition of intellectual content, literature search, data acquisition, manuscript preparation, manuscript editing, and manuscript review.

K.S.—Concept design, definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition, data analysis, manuscript preparation, manuscript editing, and manuscript review.
H.G.—Concept design, definition of intellectual content, manuscript preparation, manuscript editing, and manuscript review.
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A.K.—Concept, design, definition of intellectual content, literature search, manuscript preparation, manuscript editing, and manuscript review.
The manuscript has been read and approved by all the authors that the requirements for authorship have been met and that each author believes that the manuscript represents honest work.

Patient Consent
Patient consent is not required due to the retrospective nature of the study.

Conflict of Interest
None declared.

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Anemia at Diagnosis in Pediatric Solid Tumors: Prevalence, Severity, and Hematologic Patterns: A Single-center Retrospective Study

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Abstract

Introduction Anemia is a frequent clinical finding at the time of diagnosis in children with solid tumors and may reflect tumor biology, nutritional status, or bone marrow involvement. However, the pattern and severity of anemia across different solid tumor types in children remain underreported.

Objective The aim of this study was to evaluate the prevalence and characteristics of anemia at presentation among pediatric patients with various solid tumors.

Materials and Methods This retrospective observational study included 149 children with newly diagnosed solid tumors, aged 0 to 18 years. Anemia was classified based on the World Health Organization age-specific hemoglobin thresholds and further categorized into mild, moderate, and severe grades. Tumors were classified into bone tumors, central nervous system (CNS) tumors, abdominal tumors, soft tissue sarcomas, germ cell tumors, and others. Associations between anemia and tumor type were analyzed using descriptive statistics and chi-square tests.

Results Anemia was present in 67 (45%) patients at diagnosis. Bone tumors detected in 52 patients (34.9%) and CNS tumors detected in 34 patients (22.8%) were the most common malignancies. Among those with anemia, 36.4% had mild, 45.5% moderate, and 18.2% severe anemia. Statistical analysis revealed a significant association between red cell indices (mean corpuscular volume, mean corpuscular hemoglobin [MCH], red cell distribution width [RDW], mean corpuscular hemoglobin concentration) and anemia status ($p < 0.001$), with low MCH and high RDW suggesting the anemia was predominantly microcytic and hypochromic, with substantial anisocytosis.

Conclusion Anemia is a common presenting feature in pediatric solid tumors. Detailed investigations to delineate the etiology of anemia are necessary to guide targeted management of the tumor as well as to correct the anemia.

Keywords
- anemia
- prevalence
- red cell indices
- pediatric

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Introduction

Anemia is a common comorbidity in patients with malignancies, with an incidence as high as 90% in adults and may serve as a surrogate marker for disease burden and reduced quality of life.[1] While anemia is well documented in pediatric hematological malignancies, there are limited data on its prevalence, patterns, and severity in pediatric solid tumors at presentation, with reported rates between 20 and 74%. The reason for anemia at presentation in children with solid tumors can result from a multitude of factors, including chronic inflammation, bone marrow infiltration, blood loss, and nutritional deficiencies.[2,3] However, most studies focus on anemia during the course of therapy rather than diagnosis. The current study aims to assess the prevalence, severity, and hematological characteristics of anemia at the time of diagnosis in children with solid tumors.

Materials and Methods

Study Design and Setting

This retrospective cross-sectional study was conducted in the department of pediatric oncology at a tertiary care center in South India. All pediatric patients diagnosed with solid tumors between January 2020 and December 2024 were included. The sample size was determined by the total number of eligible patients diagnosed during the study period, and no prior sample size calculation was performed, as this was a retrospective analysis.

Inclusion Criteria

- Children aged 0 to 18 years.
- Histologically or radiologically confirmed diagnosis of a solid tumor.
- Availability of complete blood count at initial presentation before the initiation of therapy.

Exclusion Criteria

- Patients with hematological malignancies.
- Patients with incomplete hematologic records at presentation.
- Patients who had received any blood transfusion prior to initial presentation and blood sample collection (i.e., before inclusion in the study).

Objectives

- To determine the prevalence and severity of anemia at diagnosis among pediatric patients with solid tumors.
- To analyze the association between anemia and tumor type, age group, and gender.
- To assess the red cell indices mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW), and characterize the hematological patterns of anemia.
- To evaluate the prevalence and characteristics of anemia in children with advanced-stage/metastatic solid tumors.

Outcomes

Primary Outcome

- Prevalence of anemia at diagnosis in pediatric solid tumors, as defined by the World Health Organization (WHO) age-specific hemoglobin cutoffs.

Secondary Outcomes

- Distribution of anemia severity (mild, moderate, severe) by tumor type, age, and gender.
- Characterization of hematologic indices (MCV, MCH, MCHC, RDW) associated with anemia.
- Prevalence and severity of anemia in children with advanced-stage or metastatic solid tumors.

Data Collection

Demographic profile (age, gender, tumor type, stage/risk, presence or absence of metastasis) and hematological parameters (hemoglobin, red cell indices [MCV, MCH, MCHC, RDW], and peripheral smear findings) were retrieved from electronic medical records and laboratory information system. Anemia was diagnosed and classified into mild, moderate, and severe based on WHO criteria for age-appropriate hemoglobin cutoffs.[4]

Statistical Analysis

Data were analyzed using Jamovi v2.6.44 (The Jamovi Project, Sydney, Australia). Descriptive statistics were used to summarize demographic and clinical variables. The prevalence of anemia was expressed in proportions. Associations between anemia and hematologic parameters were tested using chi-square tests for categorical variables and Mann–Whitney's *U*-tests for continuous variables. A p-value of <0.05 was considered statistically significant.

Ethical Approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (1960). Ethical approval was obtained from the Institutional Ethics Committee of Kasturba Medical College, Manipal (IEC No.: 693/2023). As this was a retrospective study using anonymized data, the requirement for informed consent was waived.

Results

Prevalence of Anemia

Out of 181 pediatric patients with solid tumors initially screened, 149 met the inclusion criteria and were analyzed, while 32 were excluded due to incomplete hemogram data, prior transfusion, or relapse. The median age at diagnosis was 8 years, with a slight male predominance. Bone tumors and central nervous system (CNS) tumors were the most common diagnoses, together constituting more than half of the cohort. This pattern is consistent with the tumor distribution typically observed in pediatric oncology at tertiary care centers in India (►**Table 1**).

Table 1 Demographic profile

Variable	Category	*N* (%)
Age group	6 mo to <2 y	22 (14.8)
	2–5 y	38 (25.5)
	6–11 y	40 (26.8)
	12–14 y	23 (15.4)
	>14 y	26 (17.4)
Sex	Female	68 (45.6)
	Male	81 (54.4)
Diagnosis type	Bone tumors	52 (34.9)
	CNS tumors	34 (22.8)
	Abdominal tumors	23 (15.4)
	Soft tissue sarcomas	16 (10.7)
	GCT	13 (8.7)
	Other tumors	11 (7.4)
Anemia status	Yes	67 (45)
	No	82 (55)

Abbreviations: CNS, central nervous system; GCT, germ cell tumor.

Nearly half of the children are presented with anemia at diagnosis, with moderate anemia being the predominant pattern. Younger children (<5 years) and females were more frequently affected, suggesting possible age- and sex-related susceptibility (►**Table 2**).

Moderate anemia emerged as the most frequent category across tumor groups, while severe anemia was relatively uncommon. Abdominal and bone tumors showed the greatest burden of moderate-to-severe anemia, in contrast to CNS tumors, where most children had only mild anemia. These patterns highlight the tumor-type-specific variation in anemia severity (►**Fig. 1**).

Hematologic Indices and Anemia

Significant differences were observed in red blood cell indices between anemic and nonanemic patients ($p < 0.01$). Of 67 anemic individuals, 37 (55.2%) have low MCV, low MCH, and high RDW altogether, suggesting the anemia was predominantly microcytic and hypochromic, with significant anisocytosis in affected patients (►**Table 3**).

Table 2 Anemia characteristics and prevalence

Parameter	Category/subgroup	*N* (%)
Age group	6 mo to <2 y	16/67 (23.9)
	2–5 y	21/67 (31.3)
	6–11 y	11/67 (16.4)
	12–14 y	11/67 (16.4)
	>14 y	8/67 (11.9)
Sex	Female	42/67 (62.7)
	Male	25/67 (37.3)
Anemia severity	Mild	22/67 (32.8)
	Moderate	37/67 (55.2)
	Severe	8/67 (11.9)

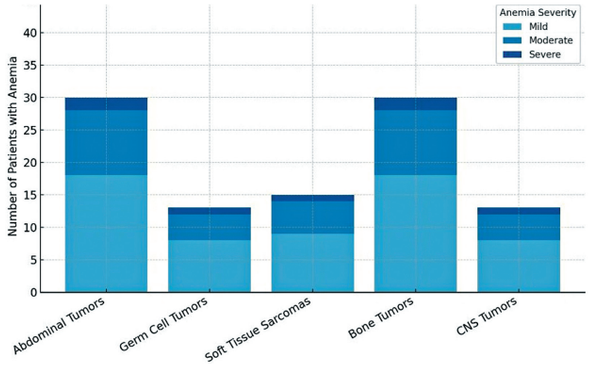

Fig. 1 Prevalence and severity of anemia disease-wise. CNS, central nervous system.

Table 3 Comparison of RBC indices—anemic versus nonanemic patients

RBC index	Anemic (mean ± SD)	Nonanemic (mean ± SD)
MCV (fL)	72.4 ± 6.1	82.6 ± 5.9
MCH (pg)	22.1 ± 2.5	27.8 ± 2.3
MCHC (g/dL)	30.5 ± 1.8	32.5 ± 1.5
RDW (%)	17.8 ± 2.1	13.2 ± 1.7

Abbreviations: MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red cell distribution width; SD, standard deviation.

Anemia in Advanced Disease

In a subgroup of 39 pediatric patients with Stage 3, Stage 4, or metastatic solid tumors (excluding neuroblastoma and rhabdomyosarcoma, which are known to involve bone marrow), 23 (59%) were anemic. Anemia was more common in the advanced-stage cohort compared with the overall cohort (59 vs. 45%). Bone tumors accounted for 35.9% ($n = 14$) of this group, with eight patients presenting with anemia. Among the anemic cases in this cohort, 8 (34.8%) had mild anemia, 13 (56.5%) had moderate anemia, and 2 (8.7%) had severe anemia. Disease-wise anemia prevalence in advanced solid tumors is detailed in ►**Table 4**.

Discussion

Anemia at presentation was observed in nearly half of pediatric patients with solid tumors in this study. This aligns with prior reports that estimate anemia prevalence between 51 and 74% in pediatric oncology patients at diagnosis.[2,5] Contributing factors may include chronic inflammation,

Table 4 Prevalence of anemia in advanced cancer

Diagnosis	Prevalence of anemia, *N* (%)
Abdominal tumors	6/6 (100)
Bone tumors	8/14 (57)
CNS tumors	0/6 (0)
GCT	3/4 (75)
Soft tissue sarcomas	6/8 (75)
Other tumors	0/1 (0)

Abbreviations: CNS, central nervous system; GCT, germ cell tumor.

nutritional deficiencies, bone marrow suppression, and tumor-related blood loss. Notably, this prevalence is lower than that observed in the general pediatric population. According to the National Family Health Survey (NFHS-5, 2019–21), the prevalence of anemia among children aged 6 to 59 months in India is 67.1%, with moderate-to-severe anemia comprising a significant portion of the burden.[6]

The observed anemia was primarily microcytic and hypochromic, as indicated by significantly lower MCV and MCH values. The markedly elevated RDW in anemic patients suggests anisocytosis due to ineffective erythropoiesis or iron-restricted conditions possibly reflecting anemia of chronic disease or iron deficiency anemia.[5,7,8] This phenotype contrasts with normocytic anemia typically seen in acute or hemolytic conditions.

Moderate anemia was the most prevalent, particularly in children with abdominal tumors (19.4%), bone tumors (11.9%), and germ cell tumors (GCTs) (9.0%). While only two cases of tumor rupture were documented, the high prevalence of moderate anemia in abdominal tumors may suggest subclinical blood loss or chronic inflammation. However, direct evidence of gastrointestinal or intratumoral bleeding was not consistently documented, and this hypothesis warrants further prospective evaluation.

Bone tumors also had the highest number of severe anemia cases (6.0%), suggesting a greater systemic impact or possible marrow involvement. In contrast, localized GCT and soft tissue sarcomas were predominantly associated with mild-to-moderate anemia, possibly due to lower marrow suppression or systemic inflammatory load.

This tumor-type-specific distribution emphasizes the need for tailored supportive care strategies, including timely nutritional assessment and correction of iron or micronutrient deficiencies, intravenous iron therapy in selected cases, use of erythropoiesis-stimulating agents where appropriate, and proactive monitoring in high-risk groups, such as those with abdominal or advanced-stage tumors.

Anemia is highly prevalent (59%) in children with advanced-stage and metastatic solid tumors (excluding those known to involve the bone marrow), particularly in bone tumors, abdominal tumors, and metastatic soft tissue sarcomas. Most cases were moderate in severity, suggesting chronic disease-related anemia, blood loss (tumor rupture). The absence of anemia in CNS tumors highlights the variation in anemia risk based on tumor type and biology. These findings underscore the need for early anemia screening and supportive care in high-risk groups within the advanced disease population.

Strengths

One of the few Indian studies assessing anemia at diagnosis in pediatric solid tumors, with a relatively large cohort and use of the WHO criteria for consistency.

Generalizability

Findings reflect patterns seen in similar tertiary care settings in India and are broadly comparable to international data, making them relevant to other low- and middle-income countries.

Gray Areas

Lack of iron studies, inflammatory markers, and nutritional markers limited the ability to identify specific anemia subtypes.

Future Research

Prospective multicenter studies with detailed etiologic work-up and evaluation of treatment outcomes are needed to strengthen evidence and guide supportive care.

Conclusion

Anemia was present in nearly half of pediatric solid tumor cases at diagnosis, with higher prevalence in younger children, females, and those with abdominal or advanced-stage tumors. The hematologic profile, predominantly microcytic and hypochromic anemia suggests iron-restricted erythropoiesis. While this cross-sectional study cannot assess causality or clinical outcomes, these findings highlight the need for anemia screening and context-specific supportive care at diagnosis. Prospective studies incorporating iron studies and long-term follow-up are warranted to better define the etiologic and prognostic implications of anemia in this population.

Authors' Contributions

V.B.K. conceptualized and designed the study and contributed to manuscript preparation and editing. S.P.M. contributed to the literature search, data acquisition, data analysis, manuscript preparation, and editing. A.M. was involved in data acquisition and analysis. N.S. contributed to data analysis and statistical analysis. A.M.V., E.A.R., S.B., and S.L.K. provided intellectual input and reviewed the manuscript. All authors have contributed to the manuscript in significant ways and have reviewed and agreed upon the manuscript content.

Patient Consent

Consent waiver was obtained from IEC as this was a retrospective study.

Conflict of Interest
None declared.

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"A Lot Happens After Best Supportive Care"—Unbottling the Countertransference of Health-Related Suffering in a Community Cancer Palliative Care Setting: A Qualitative Case Study

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Abstract

Introduction The Integrated Hospital-based Continuity of Care project at a government tertiary cancer hospital in the department of palliative medicine aimed to relieve serious health-related suffering and facilitate care along the continuum through home visits by a multidisciplinary team to patients on best supportive care. These patients transitioning through palliative care engender reciprocal feelings of suffering among the team members, impacting their well-being.

Countertransference includes the conscious and unconscious feelings experienced by the health care provider toward the patient. Accepted as appropriate and unavoidable, it is important to understand, recognize, and address the issues related to countertransference of health-related suffering. Following a debriefing session, the feelings documented by a downcast nurse, as a doodle, depicting the abandonment of a patient from her own home, formed the background for this study.

Objectives This study aimed to explore the experiences of the palliative care team caring for patients with cervical cancer in the home care setting.

Materials and Methods This qualitative case study method included the multidisciplinary team in the department of palliative medicine as participants. There were multiple sources of data like four sketches with captions depicting patients with cervical cancer at home drawn by the doctor and its interpretation by the team, reflective journaling notes, and transcripts from the focus group discussion. Following data familiarization and analysis, themes were derived.

Results The first theme described the dejection felt by the participants as they witnessed patients with disfigurement, stigma, and neglect. These memories lingered

Keywords
- countertransference
- home care services
- palliative care
- continuity of patient care
- grief

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and the second theme dealt with their deliberations as they navigated through self-doubt. The realization that home care is an invaluable experience was the third theme. The reflection that "every struggle is unique" and how art could help in training, learning, and catharsis was the fourth theme.

Conclusion The results of our study resonate with the dual process model of grief; moving from the loss-oriented response as they witnessed suffering in patient's homes toward the restoration-oriented response where they felt gratitude and acknowledged the value of caring for the person at home. Art was the ice breaker in enabling this reflection.

Introduction

Serious health-related suffering associated with death from cancer is estimated to double over the next four decades. By 2030, 70% of global cancer cases will be in low- and middle-income countries where late presentation and fewer resources lead to poor cure rates compared to high-income countries. More than half of low-income countries do not have palliative care programs. Thus, there is an overwhelming need to expand cancer programs that integrate palliative care.[1]

In addition to symptom control, integrating palliative care early in the trajectory of the disease enables cycling conversations over time and deepens prognostic awareness, thus supporting patients to develop adaptive coping strategies.[2] Timely palliative care delivery in the home care setting allows for structured and systematic follow-up, facilitates anticipatory care planning, and focuses on information sharing and psychosocial elements of care.[3]

With this in mind, an integrated hospital-based continuity of care project to supplement the services within the department of palliative medicine at a government tertiary cancer hospital was initiated with a multidisciplinary team of doctors, nurses, administrative staff, physiotherapist, and clinical psychologist in December 2021 and continues till date. The team provides palliative care services within the hospital outpatient and inpatient departments, through telephonic calls and in the community through home care provision. Home care is provided to patients on "best supportive care"[4,5] where no further disease-directed therapy is being continued and who live within a 100-km radius from the hospital.

Being a hospital-based community program, patients on home care have transitioned through early and/or concurrent palliative care and interacted with the palliative care team during the course of treatment. Clinical relationships built on the feelings and associations generated by the patient toward the team members along the course of illness, transference, can develop.

Countertransference applies to the reciprocal feelings, intuition, and inferences generated by the team members about patients and is important clinical information.[6] The team members recognize suffering and healing as core concerns in patients but it is unclear how patient suffering impacts the team member's well-being.[7,8]

Following a home care visit, a downcast nurse and a doodle depicting the abandonment of a patient with cervical cancer, from her own home, set the background for this case study. This qualitative case study aimed to explore experiences of the hospital palliative care team caring for patients with cervical cancer in the home care setting.

Materials and Methods

This descriptive qualitative study exploring the experiences of the hospital palliative care team members was reported according to the Consolidated Criteria for Reporting Qualitative Research[9] (►**Supplementary File S1**).

Study Participants

The study participants included all the multidisciplinary team members working in the palliative medicine department, narrating the experience. Hence, no formal sample size estimation was considered. The sample was adequate to narrate the complex and multifaceted phenomenon of patients with cervical cancer in the home care setting. There were six female and three male participants aged between 24 and 33 years. There were three doctors (D1, D2, D3), three nurses (N1, N2, N3), one physiotherapist (P1), one clinical psychologist (C1), and one administrative assistant (A1). Each of them had 6 months to 2 years of working experience in palliative medicine. This team supplemented the hospital palliative care outpatient and inpatient services. They followed up through telephonic calls and provided home care to the patients. These were planned home visits, triaged based on symptoms and psychosocial needs. The visits are usually done by two team members; nurse along with doctor/physiotherapist/clinical psychologist. The administrative staff were trained through the volunteer training program in palliative care and visited patient homes as part of their training protocol. Regular debriefing following the home visits was held.

Study Design and Setting

Qualitative case study method, where the system and people are part of the study, was used as the strategy of inquiry with multiple sources of data for in-depth exploration.[10]

The philosophical framework underpinning the research was the pragmatic model which allowed for the plurality of

methods to be part of the research plan. It offered a methodological framework where the situation was first encountered and recognized as a research problem. Then, the researcher reflected on the nature of the problem and reformulated the research question. Then, the choice of methods to best address the problem was decided, thus connecting the process of designing the research to the core research question and the design concerns to the methods.[11]

Data Collection

The palette of methods for data collection included:

(1) Four sketches drawn by the team doctor depicting patients with cervical cancer at home with captions (►**Fig. 1**) and its interpretation by the team. As the doodle was the trigger for this research study, following the debriefing session, four sketches of patients with cervical cancer seen in the home setting were drawn by one of the doctors, who is an amateur artist. This was then captioned and circulated within the participants for their interpretation.

(2) Individual reflective journaling notes (J) of the multidisciplinary palliative care team.
These included their notes relating to the sketches and also from their home care experiences of patients with cervical cancer.

(3) Focus group discussion was conducted, undisturbed, with all the participants in a meeting room in the hospital. It was around a table so that all the participants and the researcher were facing each other. Focus group was advantageous here as the participants were familiar with each other and the interaction could yield the best results. After participant consent, the discussion was video recorded for a total period of 1 hour. Care was taken to ensure that all participants could express their thoughts and share what they felt, saw, and heard. Those who dominated the conversation were monitored. The questions were broad and open-ended and focused on the experiences while visiting patients with cervical cancer in the home care setting and the reactions to the art.
The primary researcher was aware of her multiple roles as a complete participant engaging with the team, as an observer and also the person the team reported to. Descriptive and reflective field notes were made by her. She refrained from sharing personal experiences, which could have limited participant information and thus ensured bracketing.[10]

Qualitative Data Analysis

The focus group discussion was recorded and transcribed verbatim within 24 hours to ensure quality and reliability. The discussion was in English with some words in the local language, which were translated and transcribed. The transcript of the focus group discussion (T) and the journaling notes (J) from the individual participants were read and reread for familiarization of the data. The recording was also heard along with the transcript. This enabled the researcher to recreate the setting and engage in both the verbal and nonverbal data. The participants also reviewed the transcripts and provided feedback.

Validity

The validity of the study was determined using Yardley's criteria by demonstrating contextual sensitivity, commitment and rigor, transparency, coherence, and impact.[12]

The recording was heard and the transcript and journaling notes were examined by two colleagues (coauthors 3 and 13) of whom one was proficient in the local language to ensure trustworthiness of the data (coauthor 13).

After data familiarization and saturation, the process of coding was done by categorical aggregation. This was then collapsed to derive the subthemes and themes. The data

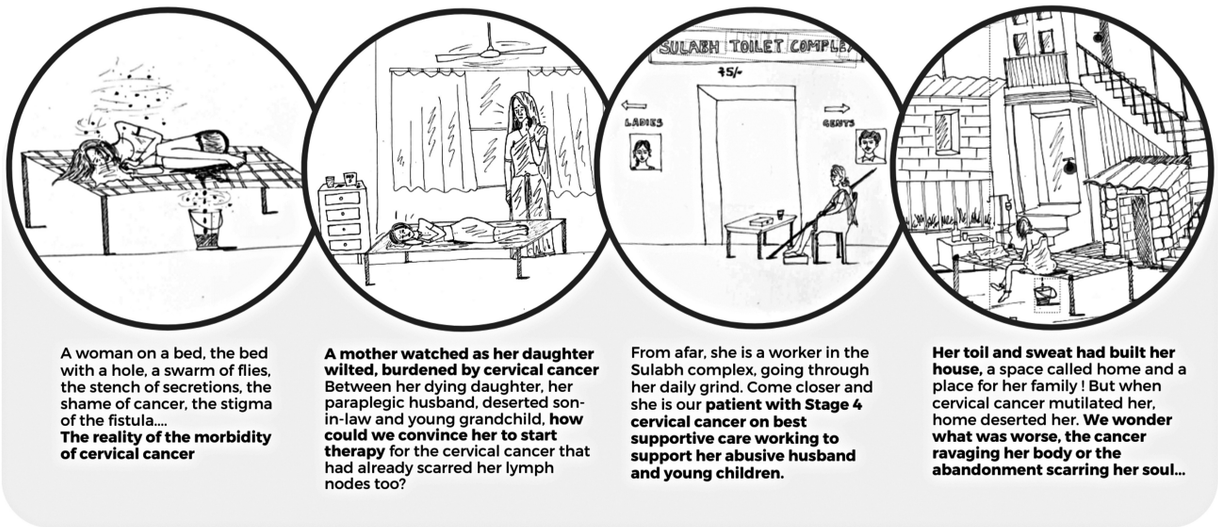

Fig. 1 Four sketches with captions depicting patients with cervical cancer at home. Original artwork created by coauthor 2.

analysis and interpretation were also examined by the coauthors 3 and 13.

Ethical Approval

The study protocol was submitted to the Institutional Ethics Committee and granted exemption from review IEC/0224/12000065/001.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Results

There were nine study participants including three doctors, three nurses, and one physiotherapist, clinical psychologist, and administrative assistant each. Ten subthemes and four themes were generated as described (►**Tables 1**–**4**).

Dejection

The team expressed their disappointment, sadness, and helplessness when they witnessed patients in the community; neglected, living in hiding with distorted body images, and living with shame and stigma. It is the bad memories that are haunting, they voiced. As professionals trained to relieve suffering and having decreased the symptom burden in the outpatient department, they were concerned if they were doing enough and wondered what more they could do. They brought forth the irony that those who needed looking after were being neglected. They also dwelled upon the inadequacies and inequity in health care provision especially when patients were only on best supportive care. This led to an agitated discussion on why newer modalities and interventions to bring down symptom burden and ease caregiver burden was not a priority (►**Table 1**).

Deliberations

As the team navigated through self-doubt and deliberated on the innovations needed, they also expressed regard for the courage of these women patients, who strived and worked with disease to support their homes. They admired the patients' willpower to stay alive in the midst of suffering and abandonment. This reminded them of why they worked and how they needed to keep "*knocking on doors*" (C1J) without losing hope.

The team spoke about some caregivers neglecting patients and others struggling to manage their responsibilities and caregiving. They recognized how important it was to be nonjudgmental as they had limited insight about the families' past and relationship dynamics. Acknowledging and supporting the caregiver was important, they agreed. They were concerned about whether it was imposing on the caregiver when they had to continue their activity alongside caregiving. Recognizing compassion fatigue, the team broached on the challenges of dealing with the concerns and fielding questions from different caregivers especially when they faced them at home. They spoke about societal norms, which contributed to caregiver conundrums and how fear, uncertainty, and stress added to caregiver distress. In

Table 1 Dejection

Quotes	Subthemes
"*I have seen patients come and whisper in my ear that they have white discharge because they are shy … because of society. They don't show if they have a huge ulcer, they don't tell unless it is infected, foul smell maggots. I have seen, opened it and been told the family was not willing to show because of stigma. How can I show this to my sons? How can I explain this to the others? (D3T)*	Women in hiding
"*So when we talk about cervical cancer per se, all patients will have similar symptoms – vaginal discharge, smell, fistula, stool p/v but the way they are treated in terms of hygiene and symptom burden that stays in our mind*" "We *must have visited more than 100 patients with cervical cancer in a period of 2 years. But the way they are treated is different from patient to patient. What stays in our mind are the patients who are being neglected, something similar to the pictures, patients kept outside, that stayed in our mind (P1T)*	Haunting memories
"*Am excited to see her on a home visit. On entering home, we get to know she is not taking medicines she is not seen by caregiver properly, stigma, and she has so many psychological concerns that she cannot open up in front of the caregiver. So being a professional, I am grateful that I did this service but also feel very helpless" (D2T)*	Helplessness
"Felt very bad 2 houses but she is outside the house"(N1T)	
"When palliative intent is starting, more research should come because as humans we are very responsible that fellow humans should not suffer. They should have better life, there will be end, suffering decreased or minimalised as much as possible." So, more modalities and innovations for the person with the disease and those taking care." (D1T)	
"Is the research and studies enough for us to answer this ladies distress, who was lying on the cot with the most terrifying environment (flies around her) leaves us speechless" (P1J)	
"Being a health care provider, we need to find some other way …"(N3J),	

Note: D1, D2, D3 are doctors 1, 2, and 3; N1 and N3 are nurses 1 and 3; P denotes physiotherapist; T means transcript quotes; J means journaling notes.

Table 2 Deliberation

Quotes	Subthemes
"*I observed in the picture that in the position also, she is giving a message to us – she is so brave, she is fighting with disease, even though she don't have that much love and affection and care from others but she is still fighting with the disease. (A1T)*	Resilience
"*And also when we see patients with disease working in toilets, (*this patient worked in a public toilet*) it encourages us to do more and support them …strong bold women*" *(C1T*)	
"You should go for work, you should earn money, you should take care …adds to the burden."(D1T).	Caregiver conundrums
"What becomes cumbersome is changing the diapers, changing the under sheets daily. If we see a patient, or even if it is our own father or mother, at one point; compassion fatigue" (P1T).	
"*The kind of questions they ask changes, at the Out-Patient Department, will the pain reduce? I want this to come down. But when we go for home visit, how long will the patient live?" (C1T).*	
"Most important, when patient is in hospital and visiting OPD, they have set the trust on us that something they will do to decrease the pain or decrease the symptom burden. When they are with the caregiver at home, they always have the distress that if some bigger symptom like shortness of breath or something happens, can they manage it alone or what and because of that fear, what they want …I always believe that the question how long the patient will live arises from this distress only that we can't manage, the fear of managing the patient is something happens suddenly, what we have to do?"(D1T)	
"We should not be judgmental to caregivers also…, because I feel that no one wants to lose their loved one so as I mentioned; some caregivers are taking care very nicely and some; neglect. The reason why they don't want them to suffer question arises How long? (N3T)	
"If we keep at home, they will repeatedly ask, why are you not getting admitted in hospital …. neighbors will question.". (D1T.)"	
"*Even caregivers have sleepless nights along with patients." (D3T)*	

Abbreviation: OPD, outpatient department.
Note: D1 and D3 are doctors 1 and 3; N3 is nurse 3; C1 is clinical psychologist; P1 is physiotherapist; A1 is administrative assistant; T means transcript quotes.

Table 3 Realization

Quotes	Subthemes
"How the patient is actually being treated; so the onion peeling we call in palliative care, I think home visit is the way of finding out more" (P1T)	Value of home care
"the real time situation, and the level of suffering our patients are going through" (D3T,D3J)	
"*but during home visits symptoms can deteriorate or alleviate or decrease. So the plan will be when we saw the patient last versus what we see real time". (P1T)*	
"*When we go to home visit, we realize what they are suffering. Sitting in the Outpatient Department, we think it is routine" (D3T)*	Challenges with routinization of symptoms
"When we go for Home Visit, main thing in our head is symptom control, plan in the mind – This patient has a wound …When we go and see, symptom stuff we are able to manage, but there is a lot beyond that we see. We start thinking, we are helping this patient, what more can we do? (C1T)	
"Cervical cancer, house (hesitatingly); daughter ladies help even without stigma. But if they are male, you find it difficult to counsel" (N2T).	

Note: D3 is doctor 3; N2 is nurse 2; P1 is physiotherapist; C1 is clinical psychologist; T means transcript quotes; J means journaling notes.

spite of the challenges they witnessed and faced, the team unanimously expressed that it was the home care visits that enabled them to realize the illness experience (►**Table 2**).

Realization

The team remarked that though comprehensive care plans are made when patients left the outpatient department, they witnessed the real situation only in the home care setting.

Symptoms which were considered routine in the outpatient setting were challenging to manage at home. Though they were comfortable with physical symptom management, it was the unforeseen societal and psychological distress that was visible during home care visits.

Female team members spoke about patients who whispered in their ears during home visits regarding discharge, ulceration, and maggots and were shy to reveal it to the males

Table 4 Reflection

Quotes	Subthemes
"*We did our best what and when we did; appreciate ourselves" .More self- growth for me .....self-learning as well(C1T)*	Introspection leading to growth
We have to fight with our problems, whatever we are facing with our life." *(A1T)*	
"*Grateful for a proper meal, grateful to enjoy the taste of food. At one point everything will end but till then, appreciate the sensations for myself. I realised that living a normal life is a blessing" (D1T).*	
"It doesn't take any time for the tables to turn we can be in this position, can you say that? One of us can be in this situation. This applies to everyone including health care provider and the caregiver" (P1T)	
"Every tear has a story, every struggle is unique but one thing in common is the resilience and the strength to cope" (C1J)	Every tear has a story
"*Depicts the true picture" (N3T)"And it connects and connects very easily*	
and even it is non-verbal and the person is not saying anything it will still connect. There is no language barrier" (C1T)	
"*We as Health Care Professionals can educate through these pictures and .... tell you what you don't have to do. You don't have to put the patient outside. Don't have stigma. Treat her like a normal human being What not to do." (D2T)*	Art as an enabler
"When we read, the diagrams stay with us. When it is a labelled diagram, it stays longer – picture of a memory. Experience we are trying to portray through art and take it forward for learning – experience learning and pictorial learning. So based on that, it is the best way of learning and can be incomparable and with words(captions)*-makes even more sense." "Actions speak louder than words but here it was the pictures speaking more than the memories because it was his memory and her memory but all of us could replicate or feel what was going on there" (P1T)*	
"It is the strength we all have...The strength of the team is in each individual and the strength of the individual is the team" (C1T)	

Note: D1 and D2 are doctors 1 and 2; C1 is clinical psychologist; P1 is physiotherapist; A1 is administrative assistant; T means transcript quotes; J means journaling notes.

in the family. Counseling was difficult too when there were only male caregivers. They realized how holistic care provision was facilitated by home care (►**Table 3**).

Reflection

Even with a similar disease, they contemplated how the illness experience was distinctive. The focus group discussion also brought forth the importance of family support being even more than wealth. They introspected and felt gratitude for what they had.

They surmised that art was the enabler which drew from the experiential and enabled them to connect and converse. They were confident that they could educate through art. For the artist, he drew from the memories; "*What it made me feel, I didn't think while drawing*" (D2T).The focus group discussion concluded with identifying the strength as individuals and as a team (►**Table 4**).

Reflexivity

The primary researcher, a female postgraduate, who conducted the study and the focus group discussion leads the palliative care department and has over a decade's experience in palliative care. The study was conducted keeping in mind the morbidity of cervical cancer witnessed by the researcher in her practice in palliative medicine for over a decade. The researcher was also conscious that the participants reported to her. This reflexive approach allowed for the researcher's subjectivity as a resource during data analysis.[10] It enabled the researcher to use her experience while exploring the phenomenon and maintaining an active role in the knowledge creation process. Thus, themes are meaning-based patterns, conceptualized and analyzed by the researcher, and not merely a superficial summary of the data. It involves significant critical engagement of the researcher with the data set, where the researcher is actively interpreting the data through the lens of her scholarly knowledge, sociocultural view, ideology, and theoretical suppositions.

To facilitate the focus group discussion, the researcher sat with the participants around a table to enable eye contact and ease conversations with each other. She ensured bracketing and could relate closely with the sketches, the focus group discussions, and the feelings, from angst to hope, which the participants went through. She could also relate to the gender dynamics when female participants expressed their difficulty in counseling male caregivers. She, through her field notes,[13] documented the silences when they related about the suffering witnessed. She noted the animated discussions regarding the need for more research in palliative care. She also observed how through deliberations the participants reflected on gratitude and their strength as a team.

Validity

Contextual Sensitivity

The six female and three male study participants were in the age group of 24 to 33 years and had an experience ranging from 6 months to over 24 months in palliative medicine. Home care was a core area of their work. The morbidity and mortality of cervical cancer in India is significant and the debriefing revealed that there was exploration needed to understand the countertransference of suffering experienced by the team. Hence, this study was designed with pragmatism as the framework with multiple sources of data collection.

Commitment and Rigor

The investigator was committed to executing every part of the study meticulously and carefully. Care was taken to respectfully engage the participants, conduct the focus group discussion, analyze the journaling notes and transcripts, and extract the essence of the study. The data was handled responsibly and diligently.

Transparency and Coherence

A detailed description of the process and methods of research has been made to ensure transparency. A rational association of the research question, the methodology, and the philosophical framework and data analysis has been made to achieve coherence. The documentation and maintained records have been examined by colleague researchers and analyzed.

Impact

The research process and outcomes will contribute to the impact the research has made. A good audit trail has been maintained. Adding to the quality of the research was also how the data shaped the conclusions. The study, though not generalizable, may be transferable.[14]

Discussion

Critical to the success of a therapeutic relationship, is the space between the patient and the clinician with the interplay of verbal and nonverbal interactions.[15] Transference and countertransference apply to the feelings and associations felt by the patient toward the clinician and the reciprocal ones generated by the clinician toward the patient. Countertransference is the inevitable emotional response, conscious and unconscious, of a health care professional toward the patient. When utilized correctly, it can help the physician to understand how patients relate to others and experience the world around them.[16,17] It is ubiquitous in a clinical encounter especially during exploration of psychological concerns and information gathering.[6,7] "How we experience countertransference varies; that we experience it does not."[15]

The basis of palliative care is a successful interpersonal and empathetic relationship that is built along the disease trajectory and transitions in care.[6] This is enabled in our hospital setting; as home care provision is integrated into the services and follows early/concurrent palliative care. It works as a continuum, thus enabling the team which interacts with the patient and caregivers in the outpatient unit to also follow them up at home. For those beyond the hospital home care radius, provision of care continues through collaboration and timely exchange of information and decisions.[18]

All the participant health care workers in the study were in the age group of 24 to 33 years with about 6 months to 24 months experience in palliative care. They were being trained to help those who suffer and also learning about their own responses to the suffering they witnessed. "*The expectation that we can be immersed in suffering and loss daily and not be touched by it is as unrealistic as expecting to be able to walk through water without getting wet!*"[19] The team members were young and yet to metamorphose[20] in their palliative care journey. The daily exposure to suffering and death, working as a unit with patients and families, and interacting with other health care professionals meant coping and finding a balance between the cost of care and the satisfaction of caring.[20]

In a study by Rowe,[21] some of the threats that lead to suffering of the healer are dealing with the vulnerable patient population, the high cost of empathy, and silence. Our home care visits involve caring for the most vulnerable and caring for many patients with different needs simultaneously.[21] It involves entering patients' spaces and conveying an understanding of their emotional response. The demands are significant and understanding responses to suffering is one way to ensure that team members are able to continue in the profession.

The phases[21] described in response to suffering from being mute to lamenting and then finding solidarity and support requires assistance. The need is to recognize, acknowledge, and discuss these feelings, in supervision or consultation, if necessary.[7,16,17]

It needs a place built into the work setting where they can talk to others who can empathize.

A healthy work environment[22] and debriefing sessions play a key role in providing intellectual and emotional support and helps maintain team efficiency.[21] Our study too, took root after a debriefing session following home care. The themes drawn from the study resonated with the dual process model of grief.[23] Dejection and deliberation dwelled on the loss-oriented response which was the sadness, angst, and self-doubt the team felt as they witnessed suffering in patient's homes. This then moved toward realization and reflection—the restoration-oriented response. Here, they felt gratitude and acknowledged the value of caring for the person at home. They reflected on how home-based palliative care is a direct look into the reality, on how it plays a unique and crucial role in providing a more personalized and holistic approach to managing serious health-related suffering in the patient's own environment. Though it could be challenging, it is also essential to mitigate suffering and offer home care to patients who are in need. Though spirituality was not explicitly discussed in our study, there were implicit references by participants who experienced a transformative

process, felt useful, reaffirmed their love for life, and developed flexibility and resilience.[20] One team member expressed how her own adaptive capacity had improved and others vocalized feeling grounded, grateful, and more courageous in their own lives.

Our participants also acknowledged that the support of the team members contributed to their work and each member drew strength from the team. Systemic countertransference[24] extends beyond the person into the shared space incorporating the team and culture of the organization. A dedicated means of processing the emotional experiences without marginalizing it, even if it takes time, can build team capacity and cohesiveness.[25] Thus, organizational culture should expect and acknowledge countertransference and encourage self-reflection, self-analysis, supervision, and psychotherapy.[7,15,20] Supervision and group support enlivens efficacy, well-being, and commitment to work. Along with working with whole patient care, the future of hospital-based care lies within the hospital system, its people, and the interactions between them.[25]

There is a need for ongoing reflective assessment, informal and formal personnel support, and pursuit of opportunities for healing.[7] This study was one such opportunity, and for our participants, art was the ice breaker.

The strength of arts-based research, using artistic process as a way of inquiry,[26] is its holistic and transdisciplinary approach.[27] This was also echoed by our participants. The sketches, drawn from memories, were impactful and able to capture the ineffable. Described as a metacognitive experience,[28] the art evoked empathy, deepened reflexivity, and triggered transformative understanding. The esthetic force can garner community engagement in academia and lead to wider dissemination of findings.[27] Individuals do vary in graphic aptitude, it could make some uncomfortable and can become ineffective when inquiries lose focus of the purpose. Our art focused on women living with cervical cancer in their homes seen during home care visits. It was sketched by the team doctor who is an amateur artist and the sketches were open to interpretation by all the participants.[29] The combination of the visual and the verbal allowed our participants a multifaceted understanding of women living with cervical cancers in their homes and resulted in an engaging, valuable, and cathartic interaction.

Art-based educational approaches have been applied to improve communication skills among oncology fellows.[30] Key competencies in oncology practice include interprofessional collaboration, lived experiences of people with cancer, person-centered care, understanding one's own limits, and self-care practices.[31]

Limitations of the Study

This study was conducted in a rural setting with constrained economic resources. It is context-specific to patients in the community with cervical cancer on best supportive care; a cancer predominantly seen in the lower socioeconomic strata in India. Our study team had young participants with experience in palliative care ranging from 6 months to 2 years. Thus, the results of the study though reliable, may not be generalizable.

Strengths of the Study

Our oncologists commented on how this could be an educational tool. In the "chain of education" proposed for oncology professionals, the important final key is "how" to educate, optimize, and enhance teaching and knowledge-sharing skills for impactful learning.[32]

We hope that this arts-based approach study would help oncologists introspect regarding countertransference, reflect on their patients who are now unable to come to the hospital, and create pathways to meaningfully integrate palliative care and facilitate home care services at their centers.

This study reprises the importance of debriefing in multidisciplinary teams and demonstrates the use of art as an enabler in unbottling the countertransference of suffering among the health care providers. The themes from the study have been interpreted with a theoretical lens; the dual process model of grief moving from the loss-oriented response to the restoration-oriented response as they introspected and realized the value of the home care service they were providing and the privilege of palliative care.

Conclusion

Timely palliative care in the home care setting can facilitate holistic care. For the health care providers addressing the needs of a vulnerable population, countertransference of serious health-related suffering is ubiquitous and unavoidable. This study reiterates the value of team debriefing and using artistic process as a way of inquiry. Art can be an engaging and an impactful tool for self-reflection and team building in addition to being a powerful aid in providing education and training.

Authors' Contributions

V.V. designed the study, conducted the research, analyzed the data, and wrote the manuscript. R.V.P., K.S., A.K., P.T., S.C.R., A.K., G.B., S.S., and D.S.K. participated in the study and reviewed and approved the data. D.F. and R.M. examined the data and assisted with the interpretation. D.F. and N.A. refined the final narrative and made critical contributions to the manuscript. All authors approved the final version. V.V. is the guarantor and corresponding author for this study. This manuscript is honest work which has been read and approved by all the authors.

Patient Consent

Patient consent is not required.

Conflict of Interest

None declared.

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A Patient with Adenocarcinoma Stomach on FLOT (5-Fluorouracil/Leucovorin, Oxaliplatin, and Docetaxel) Chemotherapy Presents with Tooth Discoloration: Spot the Diagnosis

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Description

A male in his 70s, with no known comorbidities or history of substance abuse, presented with complaints of abdominal discomfort and dyspepsia. Despite being prescribed proton pump inhibitors, his symptoms persisted. An upper gastrointestinal endoscopy revealed a gastric ulcer. Histopathological examination of the biopsy confirmed a diagnosis of moderately differentiated adenocarcinoma stomach. A positron emission tomography PET scan showed hypermetabolic, asymmetrical, circumferential wall nodular thickening involving the medial wall of the antropyloric region of the stomach, along with hypermetabolic enlarged perigastric lymph nodes. The patient was started on perioperative chemotherapy as per the FLOT (5-fluorouracil/leucovorin, oxaliplatin, and docetaxel) protocol. After completion of four cycles of chemotherapy, he underwent surgery. He was then started on postoperative adjuvant chemotherapy.

Following six cycles of chemotherapy, discoloration of the patient's teeth was observed. Specifically, yellow-black discoloration was noted on the lower teeth, and yellowish discoloration on the upper incisors (►**Fig. 1**) of the patient. The patient was not taking any additional medications and denied any history of tobacco use. What can be the differential diagnosis?

After completion of a total of eight cycles of chemotherapy as planned, he was then advised to have 3 monthly follow-up. At his 3-month review, the discoloration had partially resolved, implying chemotherapy to be the causative agent. (►**Fig. 2**) While chemotherapy-induced tooth discoloration has been previously reported, such occurrences remain relatively rare.[1–3] Discoloration of teeth and enamel hypoplasia may result from chemotherapeutic agents like vincristine, vinblastine, and cyclophosphamide, which can interfere with ameloblast activity, particularly by disrupting their microtubule-

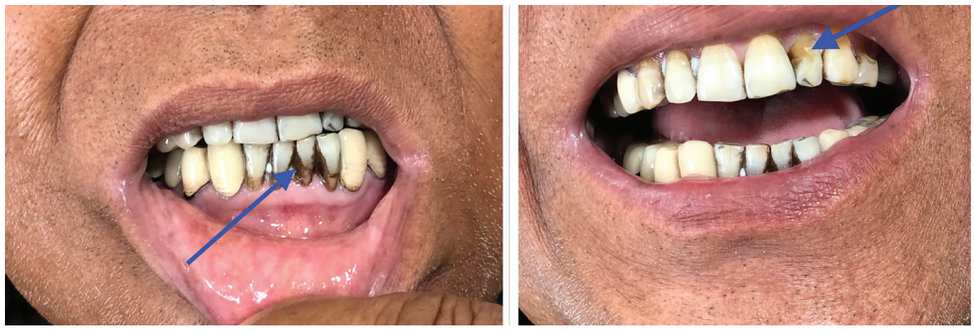

Fig. 1 Left: presence of yellow-black discoloration in the lower teeth (arrowhead). Right: yellowish discoloration in the upper incisors (arrowhead).

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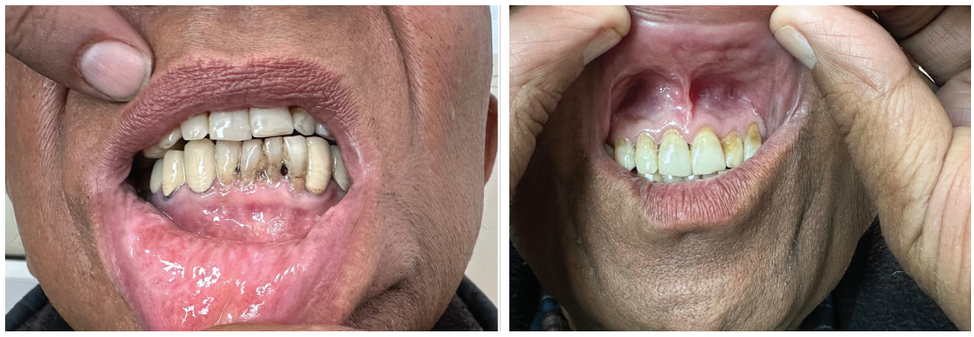

Fig. 2 Left: showing resolution of discoloration in the lower teeth 3 months post last chemotherapy. Right: showing resolution of yellowish discoloration in the upper incisors 3 months post last chemotherapy.

dependent calcium transport systems.[4] This is a rare case of FLOT chemotherapy-induced tooth discoloration. Clinicians must remain vigilant for this adverse effect while administering this chemotherapy regimen to patients.

Patient Consent

Patient consent has been taken for this article.

Acknowledgment

The manuscript has been read and approved by all the authors, and the requirements for authorship as stated earlier in this document have been met, and each author believes that the manuscript represents honest work.

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Data-Driven Realism: Why Every Oncologist Must Analyze and Publish Their Clinical Outcomes

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Introduction

Oncologists are at the front lines of cancer care. They navigate a complex landscape of rapidly changing treatments, technologies, and patient expectations. In this dynamic environment, it is essential for oncologists to carefully examine and share their clinical data. This practice is not just an academic task; it is vital for fostering a realistic understanding of cancer outcomes. It helps prevent undue influence from market-driven innovations and ensures optimal patient-centered care. Such care focuses on prevention and early intervention instead of resorting to last-minute technological fixes that can often be misleading.

Validation for Real-World Outcomes

The primary reason for oncologists to conduct thorough data analysis and publication is to build a grounded and realistic perspective on cancer outcomes. This perspective should remain clear of theories and marketing hype from the pharmaceutical and medical device industries. An oncologist's real-world data (RWD) provides a clear view of treatment effectiveness within their specific patient population.[1]

The pharmaceutical and medical device industries are powerful innovators, but they also respond to market forces. New drugs and technologies often launch with great fanfare and impressive efficacy rates from highly controlled clinical trials. While these trials are crucial for regulatory approval, they frequently operate under strict criteria that might not apply to the diverse patient populations encountered in everyday practice. Without solid internal data, oncologists risk being influenced by market narratives, which could lead to an overly optimistic and unrealistic view of treatment success for their patients. For example, a new targeted therapy might show excellent response rates in a clinical trial. However, an oncologist who analyzes its own patient group—made up of individuals with various health challenges, genetic differences, or different levels of access to care—could discover that the actual outcomes are less impressive.

While randomized controlled trials (RCTs) are considered the gold standard for evaluating drug efficacy, real-world evidence (RWE) analyses are increasingly challenging their findings, as seen in recent literature. For example, in clinical trials, sorafenib was shown to substantially improve the overall survival of patients with advanced hepatocellular carcinoma, extending it by 2 to 3 months compared to a placebo.[2,3] A later Surveillance, Epidemiology, and End Results (SEER)-Medicare database analysis of patients receiving sorafenib in clinical practice, a less selective group, found that their survival was much shorter.[4] Similarly, patients with castration-resistant prostate cancer who received docetaxel plus prednisone in a clinical trial had considerably better outcomes, including improved survival and less toxicity, than those who received the same treatment outside of a trial.[5,6] Again, when cetuximab combined with radiotherapy was shown an alternate standard of treatment for locally advanced head and neck squamous cell carcinoma with lesser toxicity since the Bonner study (IMCL 9815).[7] But subsequent clinical practice showed inferior outcome with increased toxicities.[8,9] This was confirmed in recent trials not supporting the routine use of cetuximab in a curative setting.[10] This finding supports the idea that the positive results from RCTs for new cancer treatments may not be fully replicated in routine clinical practice, where patients are less selected and can experience worse outcomes and more side effects.

This does not overlook the value of new therapies; it aims to provide a realistic view of their effectiveness in real life. By publishing these real-world outcomes, oncologists enrich

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the understanding of a drug's performance, highlighting potential gaps between trial results and everyday practice. This openness encourages better conversations with patients about their prognosis and treatment expectations, building trust and enabling shared decision-making based on a complete, honest picture. Their data acts as a reality check, helping oncologists stay grounded in their expectations for their unique patient population instead of being swayed by theoretical maximums.

Prioritizing Prevention Over Futile Technological Interventions

The second important reason for oncologists to audit and share data is to improve patient care. This approach helps prevent unnecessary toxicity and challenges the dangerous misconception that technology can merely "fix anything" when problems arise. The true error lies not just in the technological design but in the serious mistake of depending on a safety system to make up for ignoring established protocols. The blind trust in technology or advanced interventions without fully understanding their utility and potential may risk patients in real-time treatment.[11]

In oncology, the urge to use every available technological advancement or cutting-edge drug, especially as a patient's condition worsens, can be overwhelming. Oncology today features modern imaging, complex molecular diagnostics, advanced radiation systems, and strong systemic therapies. While these advances are transformative, they can also pose risks and lead to toxicities. Without carefully analyzing their clinical data, oncologists may overly rely on these tools, mistakenly assuming that more technology guarantees better outcomes, especially in critical situations. Importantly, we also have strong supportive care options like intensive care units (ICUs), powerful antibiotics, and advanced life support. These tools are vital and they can help within their established limits.

However, problems occur when oncologists treat these supportive measures and advanced technologies as an ultimate safety net, thinking they can rescue any situation without considering the patient's vulnerabilities. Medical professionals sometimes push patients to their physical limits. This may involve ignoring a patient's age or health issues, missing early warning signs, and relying on rescue measures instead of prevention.

A systematic review showed underreporting of toxic deaths in clinical oncology trials possibly due to low autopsy rates.[12] These might overestimate the effects of newer intervention while underreporting toxic deaths. In a SEER database analysis of 7,366,229 patients, 241,575 noncancer deaths (15.9%) were recorded in the first year following a cancer diagnosis. Patients have a 2.34-fold higher risk of dying from noncancer causes, such as cardiovascular and infectious diseases, compared to the general population. This risk is highest in the first month following a cancer diagnosis.[13] These may suggest probable deaths related to cancer-directed therapies. The side effects of cancer treatments should be prevented or detected early with monitoring, not just addressed after they become severe. An oncologist who carefully tracks and evaluates their patients' experiences with treatment side effects might notice trends that enable earlier interventions or even proactive measures. Their data could show, for example, that certain patient profiles face higher risks for specific adverse events, leading to closer monitoring or different treatment plans from the beginning. For example, by employing sepsis surveillance and the prompt use of antibiotics and Granulocyte colony-stimulating factor (G-CSF), along with early hospitalization, when necessary, reduced the occurrence of sepsis-related early deaths in patients with head-and-neck undergoing chemoradiation.[14] This forward-thinking approach, driven by RWD, is far superior and kinder than depending on ICU admission as a last resort. Another study examined the benefit of the audit in decreasing 30-day mortality by considering factors that may be associated with an increased risk of chemotherapy-related death.[15]

By sharing these real-world insights, especially about managing side effects, early warning signs, and the appropriate boundaries of supportive care, the broader oncology community gains greatly. It fosters sharing practical knowledge that reveals what truly works and what can be an ineffective or even harmful technological illusion when pushed too far.[14,15] Feliu et al developed and validated a highly accurate tool which can help physicians making decisions in elderly patients with cancer planned for chemotherapy using simple parameters like stage, Eastern Cooperative Oncology Group Performance Status, activities of daily living, serum albumin, body mass index, and hemoglobin.[16] This shared understanding can help develop more effective, evidence-based guidelines for preventing or managing crises, leading to safer, timely patient care focused on true benefits instead of last-minute, misleading "fixes" born from overreliance on an imagined safety net.

Ultimately, oncologists' commitment to examining and sharing their clinical data is not just an academic task; it is a deep commitment to truth, realism, and patient safety. By grounding themselves in their own data, they gain a realistic view of what treatments can genuinely achieve. By recognizing limitations and potential for harm, they avoid the illusion of technological perfection, focusing on prevention and early intervention. This dedication to insights based on data empowers oncologists to provide more transparent and effective patient-centered care, ultimately changing what it means to practice optimally in the complex world of oncology. In this direction, the U.S. Food and Drug Administration (FDA) had issued a document named "Framework for FDA's Real-World Evidence Program" to evaluate and use RWE to support regulatory decisions for drugs and biological products.[17] Also, to evaluate the potential use of RWE to help support the approval of new indications for already-approved drugs or to satisfy postapproval study requirements.

Patient Consent

Patient consent is not required.

Conflict of Interest

None declared.

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Beyond First-Degree Relatives: Unlocking the Genetic Insights from Extended Family History

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Abstract

In oncology, a thorough family history is a cornerstone of genetic risk assessment, yet it is often limited to first-degree relatives—parents, siblings, and children—thereby missing crucial hereditary patterns. This article highlights the importance of including extended family members, such as second- and third-degree relatives, in risk assessment to uncover hereditary cancer syndromes that might otherwise go undetected. This case exemplifies how extended family history can transform patient care by enabling accurate diagnoses, personalized treatment, and preventive strategies. Despite time constraints in clinical settings, tools such as targeted questioning, standardized questionnaires, and digital pedigree platforms can streamline the collection of a three-generation pedigree. Current guidelines from the American College of Medical Genetics and Genomics and National Comprehensive Cancer Network recommend such comprehensive histories, underscoring their clinical value. Incorporating extended family history should become standard practice in oncology to align with the principles of precision medicine and improve outcomes for patients and their families.

Keywords

- genetic screening
- extended family history
- oncology
- precision medicine
- hereditary cancer syndromes
- three-generation pedigree

Introduction

In oncology, a comprehensive family history is a cornerstone of genetic risk assessment, yet its full potential often remains underutilized. Traditionally, clinicians focus on first-degree relatives (parents, siblings, children) when evaluating hereditary cancer risk. While immediate family history is critical, a narrow focus can miss significant inheritance patterns that only emerge when second- and third-degree relatives are considered. For example, up to 30% of pathogenic mutations linked to breast cancer occur in women without a strong family history. This means many at-risk individuals might be overlooked if we ignore the broader family tree. Extended family history—including grandparents, aunts, uncles, nieces/nephews, and cousins—can reveal clusters of cancers or early-onset cases that first-degree history alone might not capture.[1,2] Identifying a hereditary cancer syndrome early can prompt life-saving enhanced screening or preventive measures for the patient and their relatives.

However, collecting a detailed three-generation pedigree in a busy clinic is challenging. Time constraints (studies show physicians spend on average < 3 minutes gathering family history in routine visits) and lack of standardized tools are major barriers. As a result, critical information about the patient's extended family is often not recorded. A U.S. survey found only about 31% of adults felt they knew their family's cancer history "very well," highlighting how often family history can be incomplete or inaccurate. This article addresses these gaps by exploring the clinical impact of extended family history in oncology, illustrating its value with a case study, reviewing current guidelines, and

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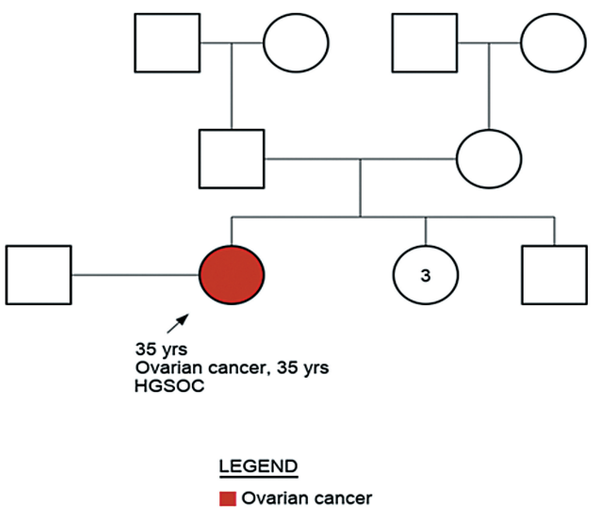

Fig. 1 Example of a pedigree with only first-degree relatives. Standard pedigree symbols are used (squares = males, circles = females, colored symbols indicate individuals affected by a certain condition "A").

describing practical tools (including digital pedigree platforms) to efficiently integrate extended family history into practice.

Case Example

Consider a 35-year-old woman diagnosed with high-grade serous ovarian carcinoma with no history of malignancy in first-degree relatives. Genetic testing revealed no BRCA1/2 mutations. Based on first-degree history alone, she does not meet the criteria for further testing (►**Fig. 1**).

However, a more detailed inquiry changes the picture. The patient recalls an extended family history: a maternal aunt was diagnosed with ovarian cancer at age 45, maternal uncle had colon cancer at 38, another paternal uncle had colon cancer at age 65, and paternal grandmother had endometrial cancer at age 50. These additional clues—ovarian, colon, and endometrial cancer on both the side of the family—are red flags for Lynch syndrome (hereditary nonpolyposis colorectal cancer). Lynch syndrome often involves colon, endometrial, ovarian, and other cancers across generations. Notably, having two or more relatives in the family with Lynch-associated cancers (e.g., one with endometrial, another with colorectal cancer, and another with ovarian cancer) greatly increases suspicion for this syndrome. The patient's first-degree relatives were cancer-free, but her second- and third-degree relatives suggested a pattern (►**Fig. 2**).

With this information, the care team pursued a broader genetic panel. A pathogenic MSH2 mutation was identified—confirming Lynch syndrome, which was initially missed when only first-degree relatives were considered. This diagnosis had profound implications: it explained the patient's ovarian cancer and indicated a high risk for other malignancies (like colon cancer) in her future and immunotherapy if required.[3] It also enabled cascade testing for her relatives. Several family members who would not have qualified for testing under narrow criteria were found to carry the same MSH2 mutation. They have since entered high-risk screening programs (e.g., colonoscopy at earlier ages and shorter intervals), a intervention which is proven to improve outcomes in Lynch syndrome by catching malignancies early.

Discussion

This case underscores the untapped value of extended family history. If we had adhered strictly to first-degree history, a heritable cancer syndrome would have gone undetected.

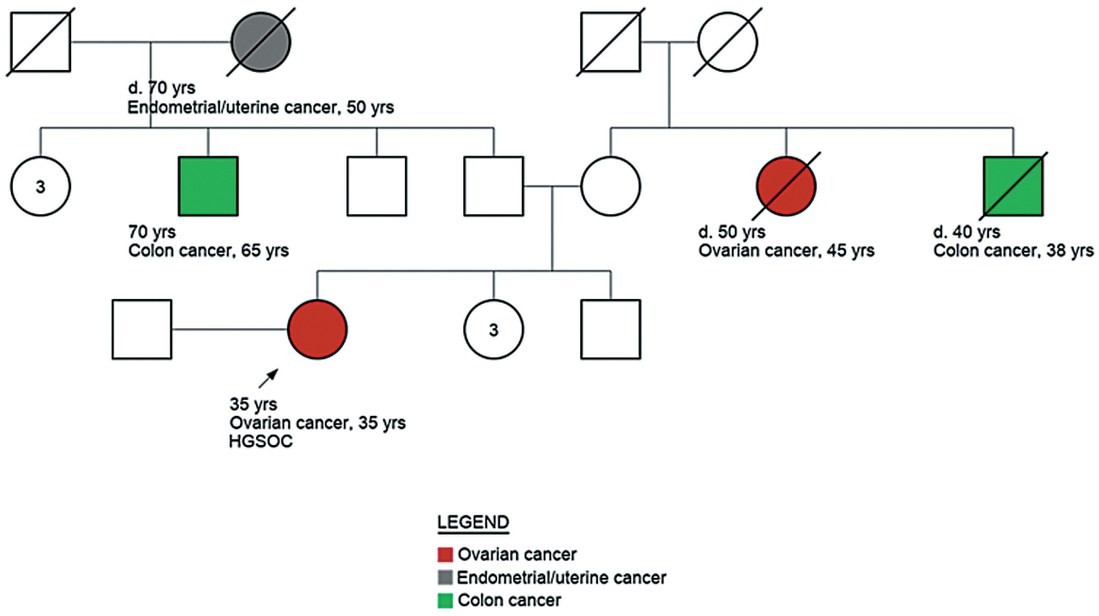

Fig. 2 Example of a pedigree with three generations.

Unfortunately, such scenarios are not rare. Many hereditary cancer cases fail to meet traditional testing criteria based on limited family data. For instance, criteria for BRCA1/2 testing heavily weigh early breast or ovarian cancer in close relatives—yet a significant proportion of BRCA mutation carriers lack an immediate family history of cancer (often because the mutation came paternally or through small families). Extended family history with at least three-generation pedigree thus directly impacted clinical care: enabling precision treatment (e.g., considering immunotherapy or pembrolizumab for MSH2-associated tumors) and appropriate surveillance for the patient, and predictive testing for her family.[2]

Professional guidelines in oncology strongly emphasize the collection of a three-generation family history for risk assessment. Both the American College of Medical Genetics and Genomics (ACMG) and the National Comprehensive Cancer Network (NCCN) recommend going beyond parents and siblings to include second- and third-degree relatives in the pedigree.[4] The ACMG/National Society of Genetic Counselors referral guidelines (2015) enumerate various "red flags" for inherited cancer syndromes—many of which involve patterns in the extended family (e.g., "two or more relatives with the same or related cancers, one of whom was diagnosed under age 50").[5] The NCCN guidelines for genetic/familial high-risk assessment (updated 2024) similarly advise documenting cancers in grandparents, aunts, uncles, nieces/nephews, and even great-grandparents or cousins if pertinent, as part of routine evaluation.[6]

Common hereditary cancer syndromes identified through such comprehensive histories include hereditary breast and ovarian cancer syndrome, most often caused by pathogenic variants in BRCA1 and BRCA2, which predispose to breast, ovarian, prostate, and pancreatic cancers; Lynch syndrome, associated with pathogenic variants in mismatch repair genes (MLH1, MSH2, MSH6, PMS2, and EPCAM), which increases the risk of colorectal, endometrial, gastric, and other gastrointestinal and genitourinary cancers; and Li–Fraumeni syndrome, caused by germline TP53 variants, which confer a high lifetime risk of sarcomas, breast cancer, brain tumors, adrenocortical carcinoma, and leukemia. Other well-recognized hereditary cancer syndromes include multiple endocrine neoplasia type 2 (MEN2) (RET mutations), associated with medullary thyroid carcinoma, pheochromocytoma, and parathyroid tumors; neurofibromatosis type 1 (NF1) and type 2 (NF2), predisposing to nerve sheath tumors, optic gliomas, meningiomas, and vestibular schwannomas; retinoblastoma (RB1 mutations), associated with early-onset eye tumors and increased risk for osteosarcoma and soft tissue sarcoma; Wilms tumor predisposition syndromes (e.g., WT1 mutations, Denys–Drash syndrome, Beckwith–Wiedemann syndrome); and polyposis syndromes such as familial adenomatous polyposis (FAP) (APC mutations) and MUTYH-associated polyposis (MAP) (MUTYH mutations), both increasing risk for colorectal and extracolonic cancers.

These syndromes can often be suspected through a detailed family history and subsequently confirmed by germline genetic testing—such as next-generation sequencing using hereditary cancer panels—to determine an individual's inherited risk. Depending on the clinical context, testing strategies may range from targeted multigene panels to more comprehensive approaches like whole-exome sequencing or whole-genome sequencing.

Collecting a detailed extended family history not only aids in identifying potential hereditary cancer syndromes or pathogenic genetic variants within a family but also guides subsequent management. When the proband is found to carry a pathogenic or likely pathogenic variant, this information enables cascade testing of at-risk relatives, facilitating timely risk stratification, implementation of targeted surveillance strategies, and initiation of preventive interventions. At every stage, genetic counseling plays a pivotal role in ensuring informed decision-making, addressing ethical considerations such as confidentiality and possible discrimination, and providing psychological support to alleviate anxiety and promote adaptive coping.

Tools and Best Practices for Collecting Extended Family History

Gathering extensive family history in a busy clinic can be daunting. However, several strategies and tools can streamline this process:

- Targeted questions ("Verbal Autopsy"): Rather than a generic "Any family history of cancer?," ask specific, pointed questions to jog patients' memory. For example: "Have any relatives (including grandparents, cousins) had cancer before age 50?" (Early-onset cancers in the family are red flags.) "Has anyone in your family had multiple cancers or bilateral cancers?" (E.g., someone with cancer in both breasts, or colon and endometrial cancer – suggestive of hereditary syndromes.) "Are there any histories of unusual cancers or tumors in your extended family, like male breast cancer or rare cancers?" (These can be clues to specific mutations.) "Any instances of colon polyps, young strokes (which might indicate MSH2-associated Muir–Torre syndrome), or other conditions in the family?"

Such focused questions function as a verbal checklist, ensuring the patient thinks beyond immediate relatives. Patients may not volunteer that "Grandpa had colon cancer at 45" unless specifically prompted about grandparents or early ages.[7]

- Use of family history questionnaires (FHQs): Previsit or in waiting rooms, patients can fill out a family history form. Standardized FHQs capture relatives' ages, health issues, and ages at diagnosis. These forms can be paper or electronic. Studies show that structured questionnaires substantially improve the quantity and quality of family history data recorded, compared to unprompted clinician interviews.
- Digital pedigree tools: Several digital platforms allow patients and providers to collaboratively build a pedigree.

For example, the Invitae Family History Tool and platforms like Progeny or FamGenix enable patients to enter their family data through a secure online interface, which then generates a pedigree chart and risk assessment analysis.[8]

When possible, drawing even a rough three-generation family tree during the consultation is incredibly valuable. As the saying goes, "a picture is worth a thousand words"—visually mapping out relationships and cancers often reveals patterns one might miss in text. The key is to incorporate the extended family routinely, not just stop at parents and siblings.

In the current era of artificial intelligence (AI), technology offers new possibilities for enhancing family history collection and utilization in oncology. AI-driven tools can automate patient history intake through digital questionnaires, detect missing or inconsistent information, and integrate these data with genomic and clinical databases to generate personalized risk assessments. Incorporating such capabilities into electronic medical records allows for interactive pedigree charts that can be updated in real time, shared across multidisciplinary teams, and linked to laboratory and imaging results. This integration will not only streamline clinical workflows but will also ensure that family history remains a dynamic and actionable component of precision cancer care.

To integrate extended family history into genetic risk assessment in oncology practice, consider the following structured approach (►**Fig. 3**):

Also, encourage communication of genetic findings to extended family, so that relatives who may also be at risk can undergo testing and prevention. This process is cyclical revisit of the family history periodically as the family evolves and update recommendations accordingly.

By following these steps, the care team ensures that an extended family history truly informs patient care at every juncture, from risk stratification to intervention. It transforms a pedigree from a static record into a living tool that guides dynamic decision-making in oncology.

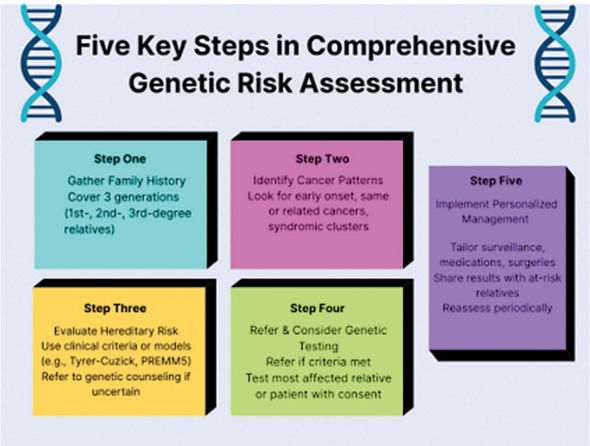

Fig. 3 Five key steps in comprehensive genetic risk assessment.

Conclusion

Limiting genetic risk assessment to first-degree relatives is outdated and risks missing hereditary cancer syndromes. Extended family history offers valuable insights that can uncover hidden risks and guide more precise care. As shown in our case, deeper pedigree analysis enabled appropriate testing and intervention. Today's tools and team-based approaches make comprehensive family history easier to implement, even in busy clinics. Embracing this broader view empowers not just individual patients but entire families, aligning with the goals of precision medicine. It is time to make extended family history a standard part of cancer risk assessment.

Call to Action

Start today. In your next patient encounter, go beyond the basics—ask about grandparents, aunts, uncles, and cousins. Consider developing a simple worksheet or adopting an electronic family history tool in your practice. If you already gather family history, make it a habit to update and delve deeper whenever possible. By doing so, you may uncover critical insights that alter the patient's preventive or therapeutic plan for the better. As the adage in genetics goes, "the family history is still the cheapest genetic test." Let us use it to its fullest extent in the fight against cancer.

Authors' Contributions

Study conception and design: A.R. and R.S. Manuscript writing: A.R. and A.K. Critical review of manuscript: A.K. and R.S. Approval of final article: All authors. Accountability for all aspects of the work: All authors.

Patient Consent

Patient consent is not applicable as no patient data, clinical details, or identifiable information are included in this report.

Conflict of Interest

None declared.

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Oral Biopsy Score: A Quantitative Approach to Clinical Decision Making for Biopsies in Suspicious Oral Lesions

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Abstract

Oral potentially malignant lesions are often underdiagnosed, leading to malignant transformation, progression, and spread of disease. It is also responsible for poor survival outcomes. To save these life years, early detection is a must. Unfortunately, it requires specialist access in many clinical settings. For faster, uniform screening, a quantitative approach, the oral biopsy score (OBS), has been formulated for risk stratification and sooner decision making. The OBS consists of risk factors such as tobacco/alcohol/areca nut use, size of the lesion, morphology, duration, location, and induration of the lesion. Each of these categories has an upper and lower score assigned. Depending on the added score, the inference will guide us in performing the biopsy or keeping it under surveillance. We advocate for validation of the OBS through multicentric prospective studies to assess its diagnostic performance. Incorporation into artificial intelligence-assisted image analysis will enhance the accuracy of the diagnosis. Ultimately, we believe the OBS can play a pivotal role in early detection of oral cancer, leading to reduction in morbidity and improvement in survival.

Keywords
- biopsy
- oral lesions
- oral cancer
- leukoplakia
- erythroplakia
- oral potentially malignant disorder
- oral biopsy score

Introduction

Oral potentially malignant disorders (OPMDs) and early oral cancers pose significant diagnostic and management challenges in clinical practice.[1] Despite increasing awareness about the importance of early detection, a substantial number of oral cancers are diagnosed at advanced stages, largely due to delays in detection, referral, and biopsy of suspicious lesions.[2] Presence of factors like tobacco/alcohol/areca nut use, size, duration, location, and characteristics of lesions pose a higher risk of malignant transformation in oral cavity cancer, especially in the Indian population.[3] For this critical need, we propose a structured and practical scoring system, the oral biopsy score (OBS), which aims to assist in clinical decisions regarding when to biopsy oral lesions. OBS is designed to be a user-friendly, practical tool to help general practitioners, dentists, and oral medicine specialists quickly recognize which oral lesions need urgent biopsy and histopathological testing. It is designed taking into consideration the known clinical signs that suggest a higher risk of malignant changes, combining with important patient risk factors with morphology of the lesion. Based on the malignant transformation rates, values have been given to the following risk factors.

Framework of the Oral Biopsy Score

The OBS assigns scores based on the following parameters, categorized into three domains, that is, patient habit, lesion

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morphology, and duration. Each parameter is scored as an "upper score" or "lower score," reflecting the presence or absence of high-risk factors ►**Table 1**.

1. Tobacco/alcohol/areca nut use (ever user)
   Upper: 1 (If the patient has history or is current user of above product)
   Lower: 0 (If the patient has no history of any of the above habits)
   These substances are International Agency for Research on Cancer (IARC) group 1 carcinogens, and their chronic use significantly elevates the risk of malignant transformation.[4] A systematic review by Asthana et al showed that smokeless tobacco products had a significant risk of oral cancer (4.44, 95% confidence interval [CI] = 3.51–5.61).[5] Another meta-analysis by Gandini et al concluded that tobacco smoking also has a high risk of causing oral cancer (relative risk [RR] = 3.43; 95% CI: 2.37–4.94).[6] Alcohol consumption significantly increases cancer risk in India, with a pooled odds ratio (OR) of 2.32 (95% CI: 1.50–3.47) in case–control studies and nearly doubles the risk of oral cavity cancer (OR: 1.92, 95% CI: 1.54–3.96).[7] Also, data from the IARC show that areca nut chewing also has a significantly high risk of causing oral cancer, independently (pooled adjusted RR, 7.9; 95% CI, 7.1–8.7).[8] According to Global adult tobacco survey 2 (GATS 2),more than 30% of all adult Indians consume tobacco. Tobacco is IARC approved Group 1 carcinogen. ACC Hence, tobacco, alcohol, and areca nut usage have been noted and given a score of 1.
2. Size of the lesion
   Upper: 1 ($>$ 2 cm)
   Lower: 0 ($<$ 2 cm)
   Larger lesions, particularly those exceeding 2 cm in diameter, are more likely to harbor dysplastic or malignant changes. A systematic review by Pimenta-Barros et al found that larger leukoplakic patches showed higher risk of malignant transformation (RR = 2.08, 1.45–2.96, $p < 0.001$).[9] Lesions of size more than 2 cm are more likely to have been there for a while, making malignant transformation probable. Therefore, the upper score of 1 has been allotted to larger lesions.
3. Duration of the lesion
   Upper: 1 ($>$ 5 years)
   Lower: 0 ($<$ 5 years)
   Lesions persisting for over 5 years are more likely to have undergone dysplastic changes without intervention, warranting an upper score of 1. Chronicity is a well-known predictor of malignant transformation.[9]
4. Site of the lesion
   Upper: 1 (Located on the tongue or floor of the mouth for all patients and located on the bucco-alveolar complex for patients with history of any habit)
   Lower: 0 (Located on the bucco-alveolar complex for patients with no history of habit and any other location for all patients)
   High-risk anatomical sites include the lateral tongue, floor of the mouth, and buccal mucosa-buccal alveolar complex (especially in chronic tobacco/areca nut abusers).[9]
5. Lesion morphology: homogeneity
   Upper: 2 (Heterogeneous, includes speckled, nodular, verrucous varieties)
   Lower: 0 (Homogeneous)
   Nonhomogeneous oral leukoplakia has a higher transformation rate than homogeneous types. A study from Southern Iran indicated a higher risk of malignant transformation in nonhomogeneous lesions (OR = 6.26).[10] Moreover, the meta-analysis by Pimenta-Barros et al also showed that heterogeneous leukoplakia had a higher risk of malignant transformation (RR = 4.23, 95% CI = 3.31–5.39, $p < 0.001$; nonhomogeneous: RR = 21.88, 95% CI = 16.44–27.81).[9]
6. Erythroplakia/proliferative verrucous leukoplakia
   Upper: 3 (Erythroplakia/proliferative verrucous leukoplakia)
   Lower: 0 (Other)
   These lesions are considered high-risk for malignant transformation (40–50%). A study by Wadde et al showed that approximately 40 and 9% cases of oral erythroplakia exhibit mild and moderate dysplasia, respectively, on the first biopsy.[11]
7. Ulcer with induration/irregular margins
   Upper: 3 (Ulcer with induration or irregular margins)
   Lower: 0 (Other)
   Features such as induration and irregular margins are clinical indicators of malignancy.
8. Nonhealing ulcers
   Upper: 3 (Nonhealing ulcer for $>$ 3 weeks)
   Lower: 0 (Resolves within 2–3 weeks)
   Persistence without resolution is a clinical red flag, as observed by the Pimenta-Barros et al review.[9]

Scoring and inference

The total score guides clinical decision-making:

Score $>$ 3: Immediate biopsy is recommended. Lesions in this category are considered high-risk.

Score = 3: A period of two-weekly surveillance is advised after removal of causative agents. If the lesion does not regress, biopsy is indicated.

Score $<$ 3: Two-monthly surveillance is recommended, with reassessment upon symptom escalation.

This approach allows for clinical flexibility with a structure based on risk stratification.

Implications for Practice

The OBS is not intended to replace clinical judgment but to complement it. It serves as an adjunctive tool for early detection, helping clinicians in decision-making and promote standardization, thereby reducing variability between clinicians. Moreover, it improves record-keeping, communication, and follow-up processes, particularly valuable in primary care settings where access to specialists may be limited. The strength of the OBS lies in its simplicity. With appropriate training, it can be widely generalized to support frontline health care providers. The scoring system is limited by validation and need real-world data and it also involves interobserver variability but it makes the diagnosis objective and data-friendly. OBS scoring system is designed for treatment-naive oral lesion, thus oral submucous

Table 1 Oral biopsy score assessment

	Upper limit	Lower limit
Tobacco/alcohol/areca nut use	1	0
Size > 2 cm (largest diameter)	1	0
Duration of lesion (> 5 years)	1	0
Located on: 1. Tongue and floor of the mouth (all) 2. Buccal mucosa and bucco-alveolar complex (for abuser)	1	0
Heterogeneous/nonhomogeneous (includes speckled, nodular, verrucous)	2	0
Erythroplakia/proliferative verrucous leukoplakia	3	0
Ulcer with induration/irregular margins	3	0
Nonhealing ulcer for more than 3 weeks	3	0
Inference		
Score	Decision	
> 3	Biopsy	
3	Two-weekly surveillance (after removal of cause, if any. And if there is no improvement in 2 weeks, then biopsy)	
< 3	Two-monthly surveillance (on follow up, action as per score. Reassess sooner if symptoms escalate)	

fibrosis and any prior history of oral cavity cancers should be excluded.

Conclusion

The OBS is a novel, practical tool created to assist clinicians in diagnosing OPMD or malignancy through timely biopsy. By combining well-known risk factors into a simple scoring system, the OBS makes it easier to detect oral cancer early. It is strongly recommended to validate the OBS through multicentric prospective studies and real-world database.

Patient Consent
Patient consent is not required.

Conflict of Interest
None declared.

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Beneath the Surface: Unmasking Carcinoma Erysipeloides in Metastatic Breast Cancer

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Dear Editor,

Carcinoma erysipeloides represents an uncommon variant of cutaneous metastasis wherein malignant cells infiltrate superficial dermal lymphatics, resulting in distinctive skin eruptions resembling cellulitis or erysipelas.[1] While predominantly associated with breast cancer, it has been infrequently reported in patients with lung, ovary, stomach, prostate, and thyroid cancers.[2] Given its rarity, it may be the sole indicator of underlying malignancy or an initial sign of disease progression during treatment. We report a case of carcinoma erysipeloides in a patient with metastatic breast cancer to highlight the diagnostic challenges and therapeutic considerations associated with this condition.

A 62-year-old postmenopausal woman, without any comorbidities, presented with hormone receptor-negative, human epidermal growth factor receptor-2 (HER2) positive metastatic breast cancer involving multiple bones and non-regional lymph nodes. Initial treatment comprised paclitaxel and trastuzumab combination, subsequently switched to lapatinib with capecitabine following disease progression after 9 months. Three months later, she developed painless, nonpruritic, erythematous, papular, and plaque-like lesions over her chest. Differential diagnoses included carcinoma erysipeloides, telangiectatic carcinoma, paraneoplastic eruptions, and tinea corporis. Biopsy revealed metastatic adenocarcinoma in cutaneous lymphatics with no epidermal involvement, confirming carcinoma erysipeloides. Immunohistochemistry findings were consistent with the primary tumor. Positron emission tomography/computed tomography scan indicated progressive disease with new skeletal lesions and lymph nodes, with skin lesions as the sole evidence of disease progression. Lapatinib-capecitabine was discontinued, and gemcitabine, carboplatin, and trastuzumab combination therapy was initiated. While initial cycles showed temporary improvement in skin lesions, subsequent cycles witnessed progressive expansion and redness, prompting vinorelbine chemotherapy as the fourth line.

Cutaneous metastasis occurs in approximately 5% of cancer cases, with breast cancer being the primary malignancy most frequently metastasizing to the skin, notably the chest.[3] Despite treatment advancements, carcinoma erysipeloides is associated with a poor prognosis,[4] underscoring the importance of vigilant monitoring and multidisciplinary management. We conclude that clinicians should maintain a high index of suspicion for cutaneous metastasis, particularly in patients presenting with acute-onset, firm, papulonodular lesions on the chest, unresponsive to antibiotics, and lacking systemic inflammatory markers. Early recognition and prompt intervention are crucial in optimizing patient outcomes.

Patient Consent

Informed patient consent was obtained for this study.

Conflict of Interest

None declared.

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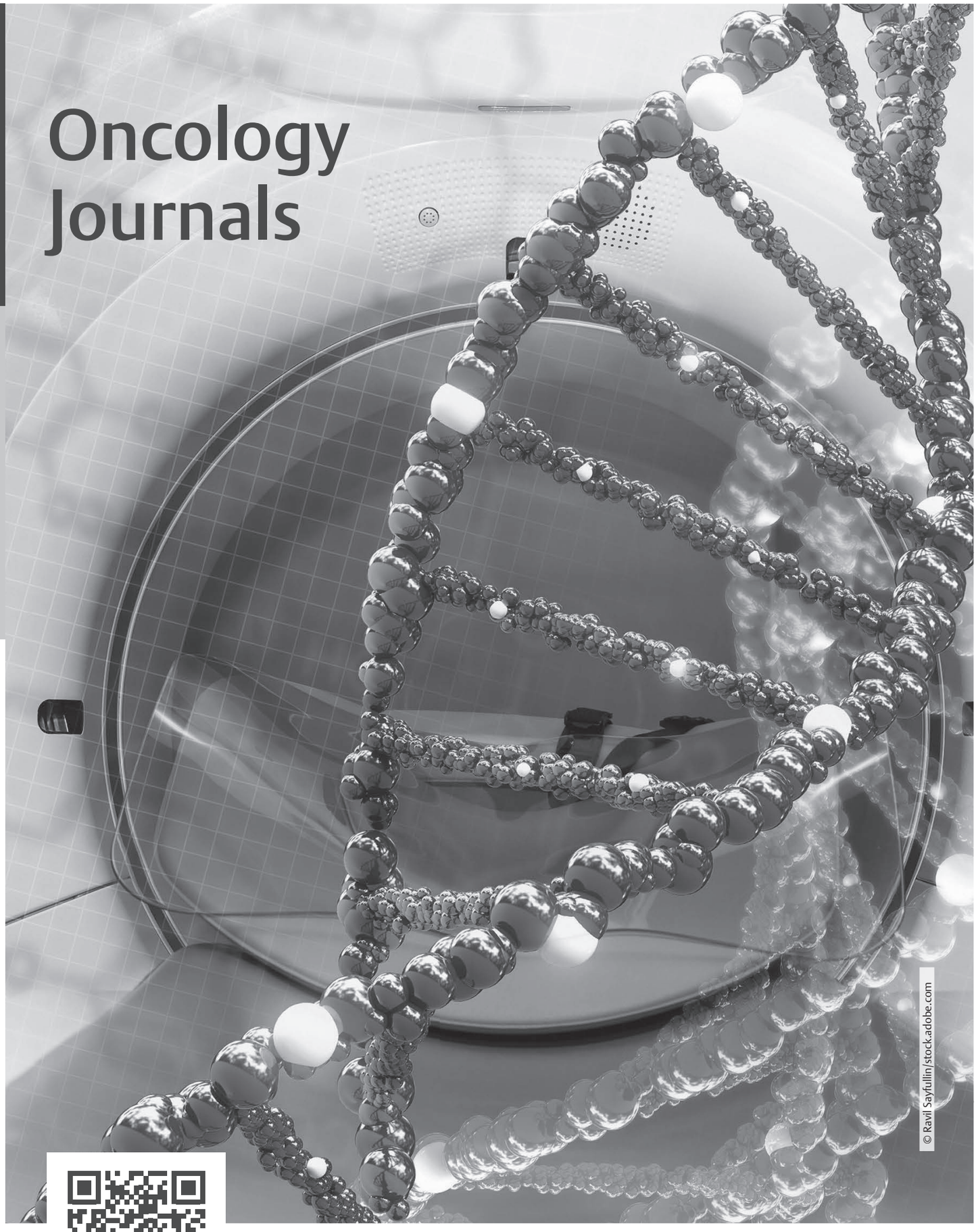

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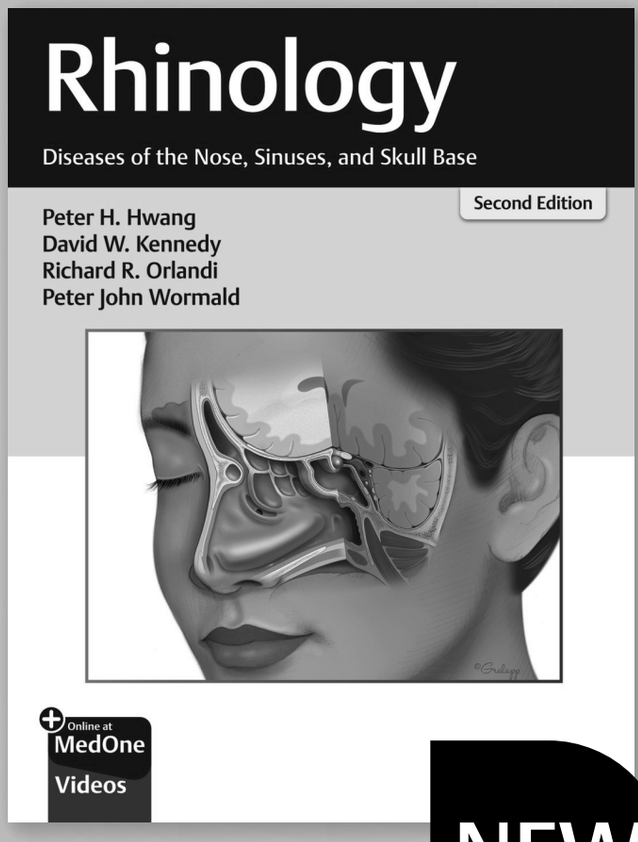

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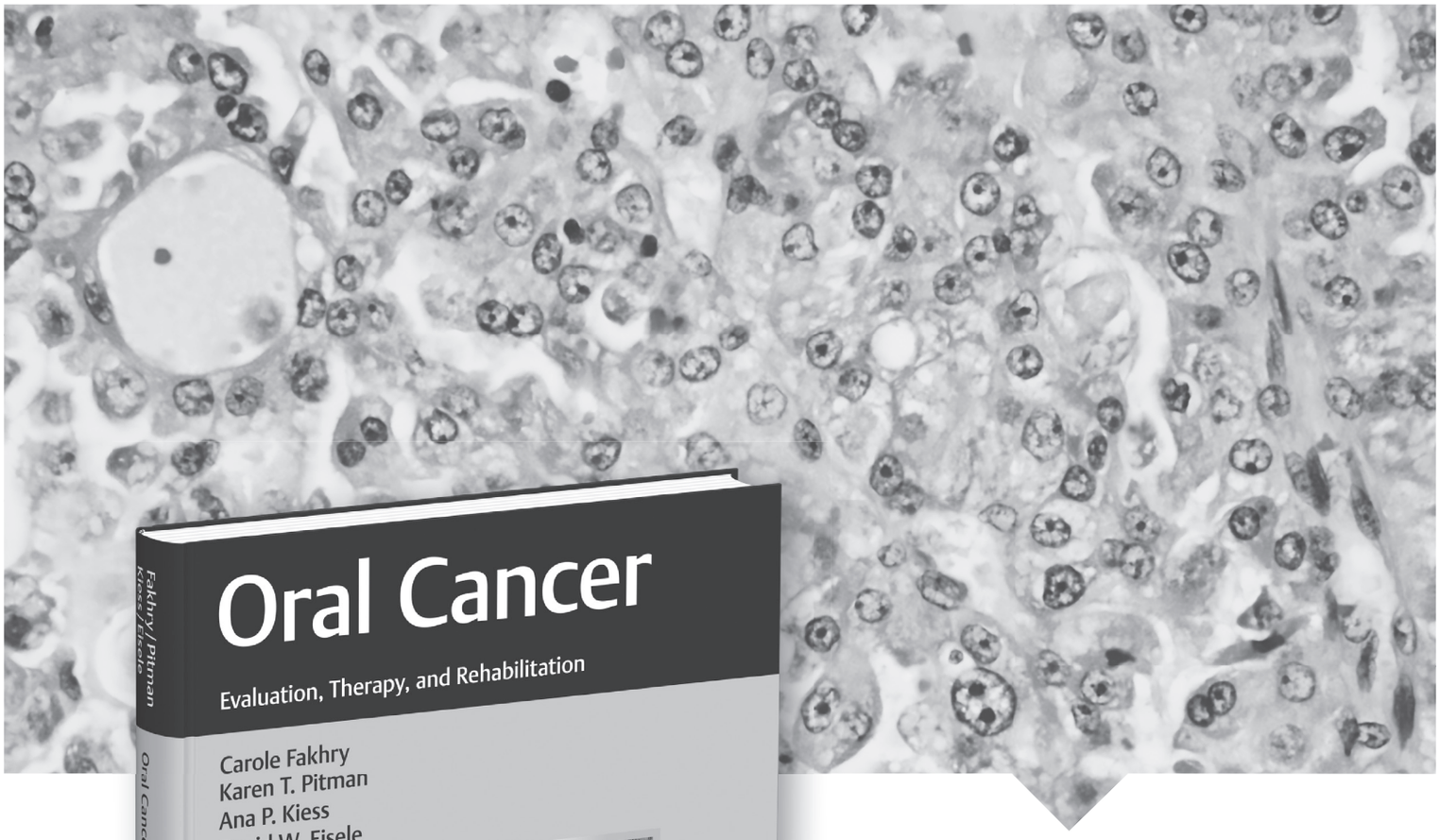

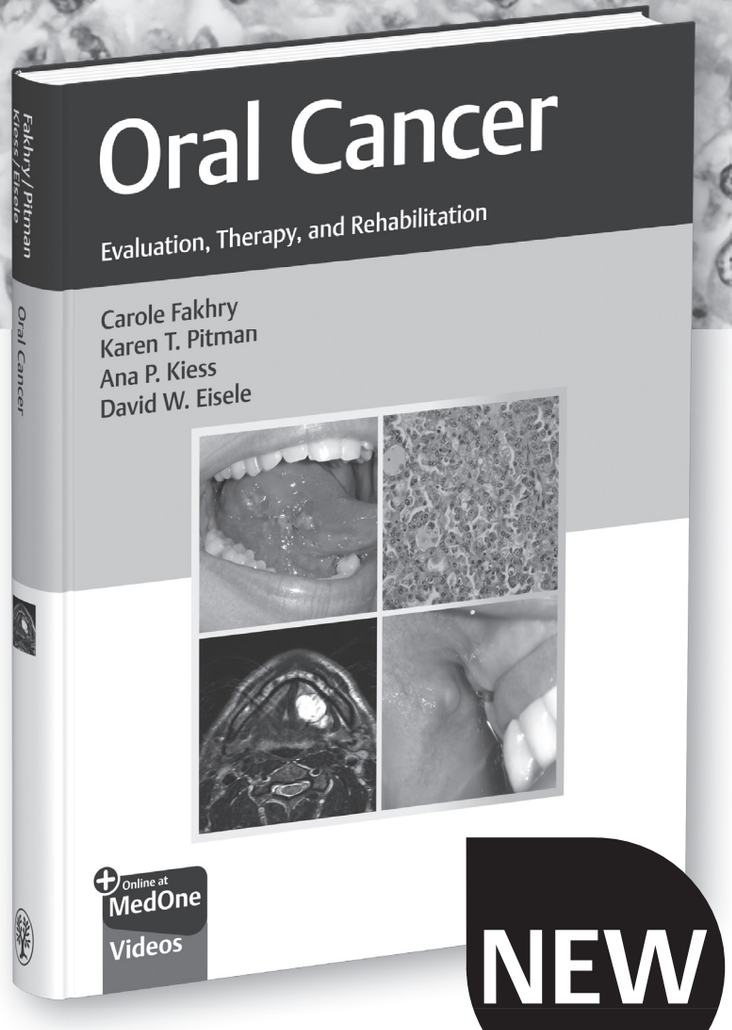

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