Article published online: 2024-06-25

Treatment Outcomes in Advanced Biliary Tract Cancers: Single Institution Retrospective Analysis

Nikhil Pathi[1] Senthil J. Rajappa[1] Santa Ayyagari[1] M V. T. Krishna Mohan[1] Pavan Kumar[1] Rakesh Pinninti[1] Pallavi Ladda[1] Sanath Kandem[1] Rohan Tewani[1] Kinjal Shah[1] Kripa Bajaj[1] Sree Rama Krishnaiah[1] Divya Gandrala[1]

[1] Department of Medical Oncology, Basavatarakam Indo-American Cancer Hospital & Research Institute, Hyderabad, Telangana, India

Ind J Med Paediatr Oncol 2025;46:370–376.

Address for correspondence Nikhil Pathi, MD, DrNB, Department of Medical Oncology, Basavatarakam Indo-American Cancer Hospital & Research Institute, Hyderabad 500034, Telangana, India (e-mail: nikhilpathi7@gmail.com).

Abstract

Purpose Biliary tract cancers (BTCs), particularly gallbladder cancers (GBCs), are prevalent in India. Yet there are limited data on treatment outcomes. To bridge this gap, we performed an analysis of advanced BTC treatment outcomes at our institute, seeking to offer insights into real-world scenario.

Materials and Methods This is a retrospective study comprising advanced BTC patients treated at our institute from January 2015 to March 2023. We assessed demographics, treatment approaches, progression-free survival (PFS), overall survival (OS), and associated toxicities.

Results Of the 411 patients analyzed, the majority were GBC (67.3%, $n = 277$), while the rest were cholangiocarcinoma (CCA) (32.6%, $n = 134$). The median age of study population was 56 years. Palliative chemotherapy was administered in 85% ($n = 349$) of all patients. Gemcitabine–cisplatin doublet was the most commonly used chemotherapy regimen (80.2%, $n = 280$). Platinum doublets yielded higher response rates compared with single-agent/nonplatinum chemotherapy (60 vs. 30%, $n = 133$). The median PFS was 4 months. The median OS was 8 months with platinum doublets and 5 months with single-agent/nonplatinum chemotherapy (hazard ratio [HR]: 0.60, 95% confidence interval: [CI] 0.43–0.84, $p = 0.0001$). OS was no different based on the type of platinum agent used. Patients receiving multiple lines of treatment lived longer compared with those who received single line only (14 vs. 6 months, respectively, HR: 0.36, 95% CI: 0.28–0.45, $p < 0.0001$). Significant prognostic factors for OS were treatment with chemotherapy, platinum doublets, platinum exposure in first line, and treatment beyond first line. Grade 3 or 4 adverse effects seen were anemia (13.9%, $n = 36$), vomiting (4.2%, $n = 11$), diarrhea (3.4%, $n = 9$), thrombocytopenia (3.4%, $n = 9$), and febrile neutropenia (3.1%, $n = 8$).

Conclusion This analysis confirms that chemotherapy is beneficial for advanced BTC. Platinum-based doublets are more effective than single agents. There is no significant difference between cisplatin and oxaliplatin. Patients who received multiple lines of treatment had better OS.

Keywords
- advanced biliary tract cancers
- first-line chemotherapy
- outcomes

article published online
June 25, 2024

DOI https://doi.org/10.1055/s-0044-1787750.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Biliary tract cancers (BTCs) are rare and vary in prevalence worldwide.[1] India contributes up to 10% of global BTC burden. Among BTC, gallbladder cancers (GBCs) are more prevalent in India (north vs. south India: 21.5 vs. 0.7/100,000 population).[2] Recent data from the Indian Council of Medical Research show GBC among the top 10 cancers in men in Assam and Jammu and Kashmir (2.6–6% of all cases) and women across northern and northeast regions. Cholangiocarcinomas (CCAs) are rare bile duct tumors, affecting less than 6 in 100,000 people. Their occurrence varies by geographic location, possibly due to different risk factors.[3] Clinical presentation of BTC is quite nonspecific during early stages in the majority. This leads to a delay in diagnosis, presentation in advanced stages making them ineligible for any curative treatments and thus overall poor outcomes.

Gemcitabine with cisplatin or oxaliplatin remains the initial chemotherapy regimen of choice in advanced BTC.[4,5] In a recent trial, there was no benefit to the addition of a third drug, paclitaxel to the standard doublet regimen.[6] Across Indian studies, the doublet combination has shown a median overall survival (OS) of 8.5 months.[7] Although two new randomized clinical trials have shown a modest survival benefit with the addition of an immune checkpoint inhibitor to the gemcitabine–platinum doublet, its applicability to a majority of our patients is questionable because of affordability issues.[8,9] Herein, we did a retrospective analysis of patients with advanced BTC treated at our institute to reflect real-world outcomes.

Materials and Methods

Database and Patient Population

This is a comprehensive analysis of treatment-naive patients with locally advanced/unresectable or metastatic adenocarcinoma of the biliary tract who presented to our institute from January 2015 to March 2023. Patient data were extracted from medical records and the hospital's electronic database. Patients deemed eligible were administered platinum-based doublet or single-agent chemotherapy at the discretion of the treating physician. Unfit patients were offered best supportive care (BSC) alone.

Outcome Variables

The parameters analyzed included demographics, treatment patterns, and outcomes. Data collected included specific regimens used (single agent vs. doublets, cisplatin/carboplatin vs. oxaliplatin), the number of lines of chemotherapy, objective response rates (ORR), progression-free survival (PFS), OS, and toxicity profile. Response evaluation to treatment was done after three or four cycles of chemotherapy or earlier at the discretion of treating physician. A clinical assessment followed by computed tomography (CT) scan, utilizing the Response Evaluation Criteria in Solid Tumors (RECIST version 1.1) was performed. Response rates and clinical benefit rates (CBRs) were reported as percentages. The primary outcome variables analyzed were ORR, PFS, and OS.

PFS was calculated from the date of starting therapy to progressive disease, follow-up loss, chemotherapy discontinuation due to adverse events of grade 3 or 4 severity, or death secondary to any cause. OS was determined from the date of diagnosis until the death of the patient or the last follow-up, as confirmed through hospital records or telephonic contact, whichever was feasible. Treatment toxicity was assessed as per National Cancer Institute—Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Statistical Analysis

Descriptive statistics (median values, frequencies, and percentages) were employed to characterize categorical variables such as age, gender distribution, treatment modalities, treatment response, and toxicities. Median PFS and OS were estimated using the Kaplan–Meier method. Hazard ratios (HR) for survival and 95% confidence intervals (CIs) were computed using the Mantel–Cox's test. Prognostic factors for PFS and OS were assessed using the log-rank test. Univariate analysis was performed using chi-square test and Fisher's exact test. Multivariate analysis by multiple logistic regression method was performed using SPSS 21.0 software (IBM, Armonk, New York, United States). A p-value less than 0.05 is considered significant.

Ethical Approval

This study received ethical approval from the Basavatarakam Indo-American Cancer Hospital & Research Institute, Institutional Ethics Committee Board (BIACH&RI IEC, Reg. no.: ECR/7/Inst/AP/2013/RR-20, protocol no.: IEC/2023/12, date: January 1, 2023). All procedures performed were by the ethical standards of the institution and/or national research committee. They were also in concordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards apart from Good Clinical Practice guidelines for the International Conference on Harmonization.

Results

Part I: Demographics and Patient Characteristics

A total of 411 patients with advanced BTC were analyzed. There were 277 cases (67.3%) of GBC and 134 cases (32.6%) of CCA. The median age of the study population was 56 years (range: 18–76 years). There was a slight preponderance of females (54.8%, $n = 152$) in the GBC and males (61.1%, $n = 82$) in the CCA subgroup. Liver (83.4%, $n = 343$) and nonregional nodes (83.2%, $n = 342$) were the most common sites of metastases, followed by the skeleton (4.8%, $n = 20$) and lungs (4.2%, $n = 18$). Among CCA, intrahepatic CCA was the most frequent subsite seen (88%, $n = 118$).

Part II: Treatment Data

In the entire cohort (►**Table 1**), 15.1% ($n = 62$) of all patients were ineligible for any chemotherapy due to poor performance status (PS). A platinum doublet combination was used in the treated majority (80.2%, $n = 280$). Gemcitabine–cisplatin was the most preferred regimen ($n = 269$, 96%). Among

Table 1 Demographic and treatment details

	Whole cohort	Gallbladder carcinoma	Cholangiocarcinoma
Total patients (*n*)	411	277 (67.3%)	134 (32.6%)
Median age (y)	56	56	56
Range (y)	18–76	23–80	18–76
Male	207 (50.3%)	125 (45.1%)	82 (61.1%)
Female	204 (49.7%)	152 (54.8%)	52 (38.8%)
ERCP + stent	46 (11.19%)	30 (10.8%)	16 (11.9%)
Histologic differentiation			
Well	38 (9.2%)	23 (8.3%)	15 (11.19%)
Moderate	265 (64.4%)	174 (62.8%)	91 (67.9%)
Poor	108 (26.2%)	80 (28.8%)	28 (20.8%)
Lines of treatment received			
0 (BSC)	62 (15.08%)	34 (12.2%)	28 (20.8%)
1	264 (64.23%)	184 (66.4%)	80 (59.7%)
2	61 (14.84%)	45 (16.2%)	16 (11.9%)
≥3	24 (5.83%)	14 (5.05%)	10 (7.4%)
Range	0–6	0–6	0–6
First-line chemotherapy received	349/411 (84.9%)	243/277 (87.7%)	106/134 (79.1%)
Platinum-based combination	280/349 (80.2%)	206/243 (84.7%)	74/106 (69.8%)
Gemcitabine–platinum	269 (96.04%)	197 (95.6%)	72 (97.2%)
5FU platinum	11 (3.9%)	9 (4.3%)	2 (2.7%)
Single-agent chemotherapy	69/349 (19.7%)	37/243 (15.2%)	32/106 (30.1%)
5FU	23 (33.3%)	12 (32.4%)	11 (34.3%)
Gemcitabine	46 (66.6%)	25 (67.5%)	21 (65.6%)

Abbreviations: BSC, best supportive care; ERCP, endoscopic retrograde cholangiopancreatography; 5FU, fluorouracil.

single agents, gemcitabine ($n = 46$, 66.6%) was used more frequently over capecitabine.

About 87.7% ($n = 243$) in the GBC and 79.1% ($n = 106$) in the CCA group received palliative chemotherapy. Platinum doublets were used in 84.7% ($n = 206$) of GBC and 69.8% ($n = 74$) of CCA patients. The preferred platinum partner was gemcitabine (GBC: 95.6%, $n = 197$ vs. CCA: 97%, $n = 72$). Single-agent chemotherapy was used less frequently (GBC: 15.2%, $n = 37$ vs. CCA: 30%, $n = 32$). Gemcitabine was the preferred single agent when used (GBC: 67.5% $n = 25$ vs. CCA: 65.6%, $n = 21$). Only 32.2% of all patients (entire cohort: $n = 85$, GBC: $n = 59$, CCA: $n = 26$) received treatment beyond first line. As second-line treatments, platinum doublets ($n = 35$, 41.1%), FOLFIRI ($n = 21$, 24.7%), irinotecan ($n = 13$, 15.2%), capecitabine ($n = 8$, 9.4%), and others were used.

Part III: Overall Survival

The median OS for the entire study group, GBC group, and CCA group was 6 months (►**Fig. 1**).

Patients treated with chemotherapy had better OS compared with BSC alone (entire cohort: 7 vs. 2 months, HR: 0.19, 95% CI: 0.11–0.33, $p < 0.0001$; GBC: 7 vs. 2 month, HR: 0.28, 95% CI: 0.19–0.41, $p = 0.0001$; and CCA: 8 vs. 3 months, HR: 0.22, 95% CI: 0.10–0.48, $p = 0.0001$).

Platinum doublets significantly improved OS compared with single/nonplatinum agents (entire cohort: 8 vs. 5 months, HR: 0.60, 95% CI: 0.43–0.84, $p = 0.0001$; GBC: 8 vs. 4 months, HR: 0.41, 95% CI: 0.26–0.63, $p < 0.0001$; and CCA: 9 vs. 5 months, HR: 0.50, 95% CI: 0.30–0.82, $p < 0.0006$).

The OS was better in patients who received multiple lines of chemotherapy compared with a single line (entire cohort: 14 vs. 6 months, HR: 0.36, 95% CI: 0.28–0.45, $p < 0.0001$, GBC: 13 vs. 6 months, HR: 0.34, 95% CI: 0.26–0.45, $p < 0.0001$; and CCA: 17 vs. 6 months, HR: 0.36, 95% CI: 0.24–0.54, $p < 0.0001$).

There was no difference in OS between cisplatin and oxaliplatin (entire cohort: 9 vs. 7 months, HR: 0.79, 95% CI: 0.59–1.06, $p =$ nonsignificant (NS); GBC: 9 vs. 6 months, HR: 0.72, 95% CI: 0.51–1.03, $p =$ NS, CCA: 10 vs. 8 months, HR: 0.88, 95% CI: 0.52 – 1.49, $p =$ NS).

Part IV: Progression-Free Survival

The median PFS was 4 months (range: 3–16 months), similar across the entire cohort and individual subgroups (►**Fig. 2**). Platinum doublets, in comparison to single-agent/nonplatinum chemotherapy, resulted in a better PFS in the entire

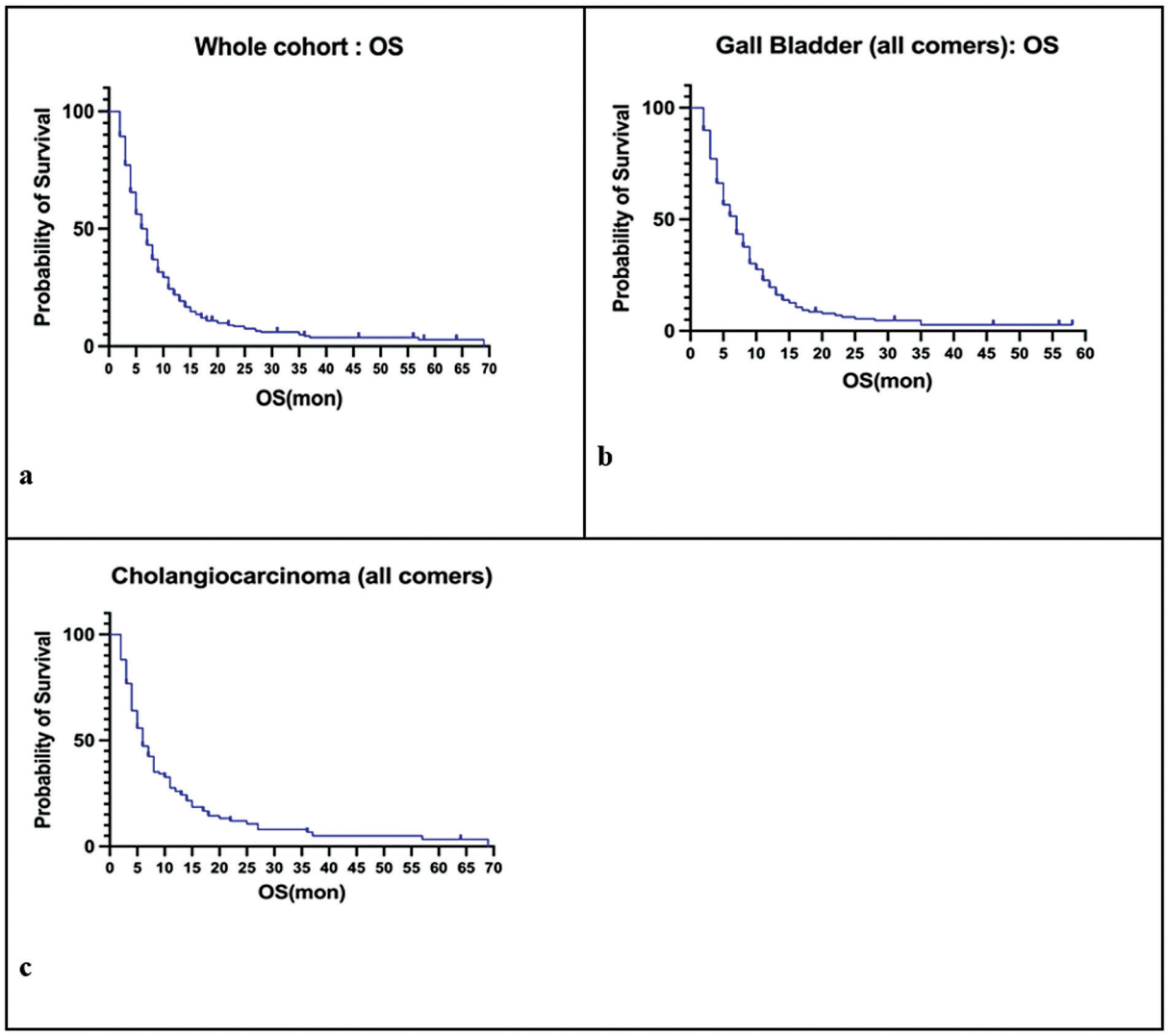

Fig. 1 Kaplan–Meier survival curves depicting overall survival (OS) for the whole cohort (a), gallbladder carcinoma (b), and cholangiocarcinoma (c).

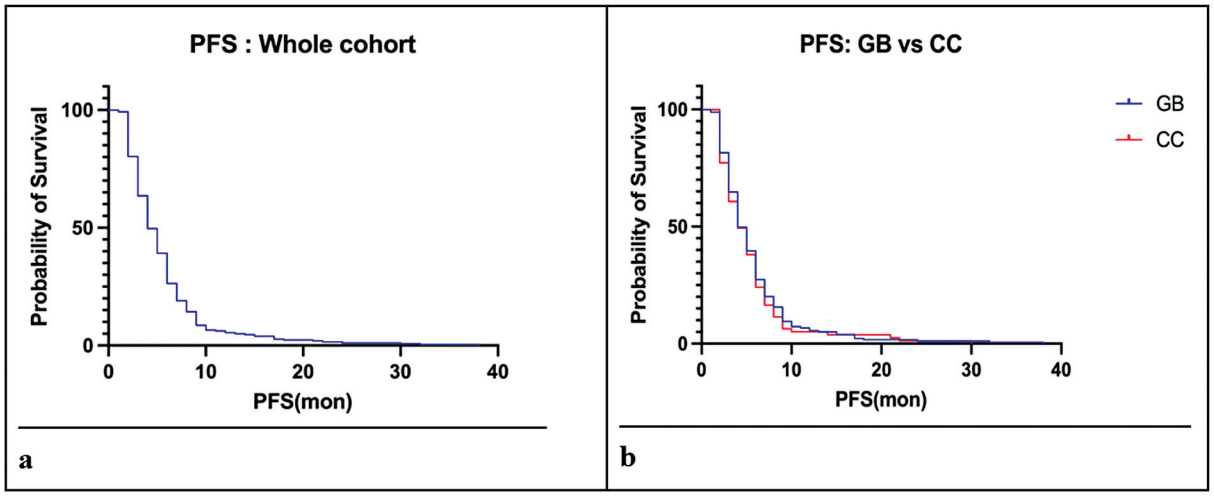

Fig. 2 Kaplan–Meier survival curves depicting progression-free survival (PFS) for the whole cohort (a), and gallbladder (GB) and cholangiocarcinoma (CC) (b).

cohort (5 vs. 3 months, HR: 0.61, 95% CI: 0.41–0.91, $p < 0.0001$) as well as in the CCA group (5 vs. 2 months, HR: 0.53, 95% CI: 0.29–0.98, $p = 0.004$). However, the same was not seen in the GBC group (5 vs. 3 months, HR: 0.69, 95% CI: 0.41–1.17, $p =$ NS). There was no difference in PFS between cisplatin and oxaliplatin.

Part V: Response Evaluation and Clinical Benefit Assessment

Response evaluation as per RECIST criteria was feasible in 258 patients (73.9%). Progression of disease (PD) was seen in 26.3% ($n = 68$), while 56.5% ($n = 146$) had a partial response (PR). Stable disease was observed in 16.6% ($n = 43$) of patients. Only one patient had a complete response. The CBR was 73.4% ($n = 191$).

Platinum doublets demonstrated higher responses in comparison to single/nonplatinum agent (PR: 61.2%, $n = 133$ vs. 31.7%, $n = 13$). Disease progression was also lower with doublets compared with single-agent/nonplatinum chemotherapy (PD: 22.1%, $n = 48$ vs. 48.7%, $n = 20$). The response rates did not differ significantly based on the type of platinum agent used.

Part VI: Toxicity Data (Only CTCAE Grade 3 or 4)

About 4.2% ($n = 11$) patients experienced chemotherapy-induced nausea/vomiting, while 3.4% ($n = 9$) had diarrhea. Anemia was seen in 13.9% ($n = 36$), more so when gemcitabine–platinum combination was used. Febrile neutropenia was noted in 3.1% ($n = 8$) and thrombocytopenia in 3.4% ($n = 9$) of cases. Biliary sepsis was documented in 3.8% ($n = 10$) patients. Transaminitis secondary to oxaliplatin was present in 4.2% ($n = 11$) cases. Change to oxaliplatin/carboplatin secondary to cisplatin-induced renal dysfunction was seen in four patients. Neuropathy was observed in 3.8% ($n = 10$) of cases.

Part VII: Prognostic Factors Affecting Overall Survival

In the multivariate analysis done by logistic regression stepwise forward conditional method (►**Table 2**), the prognostic factors for OS were: treatment group ($p < 0.001$), platinum doublet group ($p < 0.001$), platinum exposure in the first line ($p < 0.001$), and patients receiving multiple lines of chemotherapy ($p < 0.001$).

Discussion

The median age of our study population was almost a decade and a half earlier compared with the West (56 vs. 71.2 years).[10] This was similar to what has been reported in other Indian studies (Dutta et al: 58 years).[11] There was a slight preponderance of female in the GBC and male in the CCA group as was reported in other studies.[12] Hilar CCA was the dominant CCA subsite in our study, while some studies report the opposite.[13,14]

Across studies, CCA patients tend to live longer than GBC (OS range CCA vs. GBC: 11–16 vs. 7–11 months).[15,16] This could be due to differences in the tumor biology at these two sites. The CCA cohort of ours had a median OS of 9 months, which was inferior to that reported by Bhargava et al[23] (12 months), ABC-02 trial (11.7 months), and BT22 trial (11.2 months).

Based on the ABC-02 and BT22 studies, gemcitabine–cisplatin doublet became the standard-of-care regimen for advanced BTC. In GBC, the median OS reported with platinum doublet was 9 months by Amit et al and 9.5 months by Sharma et al.[17,18] Our study reports a median OS of 8 months, which is marginally inferior to the above. Possible explanation for this observation could be twofold. Primarily, one-third of our patients (34.8%) did not receive the above standard. The reason being poor PS prohibiting "any" chemotherapy in 15.08% ($n = 62$) and "doublet" chemotherapy in 19.7% ($n = 69$) of patients. Moreover, only a meager third of them (32.2%, $n = 85$) received treatment beyond first line. This was because, at disease progression, the majority had a rapid decline in PS precluding any further chemotherapy, while in a minority, it was deterioration in liver function. Literature also reports this happening with advanced BTC patients ranging from 30 to 45% across studies. Therefore, it is of utmost importance to use the most effective combination (platinum doublet) upfront to optimize survival outcomes.

André et al and Sharma et al demonstrated similar OS with gemcitabine–oxaliplatin regimen.[19] Ramaswamy et al reported no difference in outcomes between cisplatin and oxaliplatin (8 vs. 7.7 months, $p =$ NS). Findings in the present study also confirm the same.

Recent randomized trials have shown that there is a modest improvement in OS when gemcitabine–platinum agents are combined with either durvalumab (Topaz-1: 12.8 vs. 11.5 months) or pembrolizumab (KEYNOTE-966:

Table 2 Prognostic factors for OS

Dependent variable		Mean square	Partial eta squared	*p*-Value
Age	<50/>50	0.213	0.085	0.376
Sex	Male vs. female	0.222	0.071	0.665
Disease type	GBC vs. CCA	0.296	0.108	0.082
Biliary obstruction	Yes. vs. no	0.111	0.090	0.296
Treatment received	Chemotherapy vs. BSC alone	0.750	0.476	<0.001
	Platinum doublet vs. single/nonplatinum agent	2.875	0.423	<0.001
	Cisplatin/carboplatin vs. oxaliplatin	2.710	0.284	0.284
	Single line vs. multiple lines	2.390	0.351	<0.001

Abbreviation: BSC, best supportive care; CCA, cholangiocarcinoma; GBC, gallbladder cancer; OS, overall survival.

12.7 vs. 10.9 months). The clinical significance of such small incremental benefit in "our" patients is questionable due to prohibitive costs involved in treatment. Several phase 2 trials also suggest that Her2neu is an actionable target in advanced BTC.[20] Agents such as trastuzumab, pertuzumab, Trastuzumab emtansine (TDM1), and trastuzumab deruxtecan are currently being evaluated for Her2 amplified tumors.[21,22] Likewise for Her2 mutations, lapatinib and tucatinib are under trials. However, data from phase 3 randomized trials on optimal sequencing of various agents are still unknown.

In the present study, patients neither underwent molecular testing (Her2neu, MSI, NGS) nor received any of the novel therapies (anti-Her2neu, immunotherapy, TKI). This was because all patients in our study were treated under the state-sponsored schemes which do not support them. This also underscores the unmet need and areas for improvement in management of this disease.

The metastatic tumor burden at diagnosis, treatment group, continuation of maintenance chemotherapy, ability to receive second-line chemotherapy and beyond are some of the important prognostic factors affecting OS (Anadure et al).[24]

Drawbacks of the Study

The drawbacks of the study were as follows:

1. Retrospective study.
2. Heterogeneity of treatments.
3. Missing data regarding grade 1 or 2 toxicity.
4. Missing quality of life analysis.

Conclusion

This retrospective analysis confirms the benefit of chemotherapy in advanced BTC. Platinum-based doublets are more effective than single agents. There is no difference between cisplatin and oxaliplatin. Patients who received more than one line of treatment had better OS.

Authors' Contributions

N.P. contributed to conceptualization, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review. S.J.R. contributed to conceptualization, design, definition of intellectual content, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review. S., M.V.T.K. M., P.K., R.P., P.L., S.K., R.T, K.S., and S.R.K. contributed to data acquisition, manuscript preparation, and manuscript review. K.B. contributed to data acquisition and manuscript review. D.G. contributed to data analysis, statistical analysis, and manuscript review.

Patient Consent

Patient consent is not required due to the retrospective nature of the study.

Funding

None.

Conflict of Interest

None declared.

References

1 Randi G, Malvezzi M, Levi F, et al. Epidemiology of biliary tract cancers: an update. Ann Oncol 2009;20(01):146–159
2 Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: geographical distribution and risk factors. Int J Cancer 2006;118(07):1591–1602
3 Banales JM, Cardinale V, Carpino G, et al. Expert consensus document: Cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA). Nat Rev Gastroenterol Hepatol 2016;13(05):261–280
4 Ramaswamy A, Ostwal V, Pinninti R, et al. Gemcitabine-cisplatin versus gemcitabine-oxaliplatin doublet chemotherapy in advanced gallbladder cancers: a match pair analysis. J Hepatobiliary Pancreat Sci 2017;24(05):262–267
5 Patkar S, Ostwal V, Ramaswamy A, et al. Emerging role of multimodality treatment in gall bladder cancer: outcomes following 510 consecutive resections in a tertiary referral center. J Surg Oncol 2018;117(03):372–379
6 Shroff RT, Guthrie KA, Scott AJ, et al. SWOG 1815: a phase III randomized trial of gemcitabine, cisplatin, and nab-paclitaxel versus gemcitabine and cisplatin in newly diagnosed, advanced biliary tract cancers. J Clin Oncol 2023;41(04):A490
7 Sharma A, Kalyan Mohanti B, Pal Chaudhary S, et al. Modified gemcitabine and oxaliplatin or gemcitabine + cisplatin in unresectable gallbladder cancer: results of a phase III randomised controlled trial. Eur J Cancer 2019;123:162–170
8 Oh DY, He AR, Qin S, et al. A phase 3 randomized, double-blind, placebo-controlled study of durvalumab in combination with gemcitabine plus cisplatin (GemCis) in patients (pts) with advanced biliary tract cancer (BTC): TOPAZ-1. J Clin Oncol 2022;40 (4, suppl):378
9 Kelley RK, Ueno M, Yoo C, et al; KEYNOTE-966 Investigators. Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2023; 401(10391):1853–1865
10 Dutta U, Bush N, Kalsi D, Popli P, Kapoor VK. Epidemiology of gallbladder cancer in India. Chin Clin Oncol 2019;8(04):33
11 Dutta A, Mungle T, Chowdhury N, et al. Characteristics and outcomes of gallbladder cancer patients at the Tata Medical Center, Kolkata 2017-2019. Cancer Med 2023;12(08): 9293–9302
12 Mehrotra R, Tulsyan S, Hussain S, et al. Genetic landscape of gallbladder cancer: global overview. Mutat Res Rev Mutat Res 2018;778:61–71
13 Patkar S, Gupta V, Khobragade K, Goel M. The reality of cholangiocarcinoma in India- real world data from a tertiary referral centre. HPB (Oxford) 2022;24(09):1511–1518
14 Nair P, Rao H, Koshy AK, et al. Cholangiocarcinoma in South India: unprecedented, unanticipated and underreported. Int J Community Med Public Health 2021;8(08):3854–3863
15 Valle JW, Furuse J, Jitlal M, et al. Cisplatin and gemcitabine for advanced biliary tract cancer: a meta-analysis of two randomised trials. Ann Oncol 2014;25(02):391–398
16 Eckel F, Schmid RM. Chemotherapy and targeted therapy in advanced biliary tract carcinoma: a pooled analysis of clinical trials. Chemotherapy 2014;60(01):13–23
17 Amit RK, Anadure HP, Singh R, et al. A study on the clinical profile and treatment outcomes in gallbladder carcinoma from northern India. Oncology Journal of India 2020;4(03):128–132

18 Sharma A, Dwary AD, Mohanti BK, et al. Best supportive care compared with chemotherapy for unresectable gall bladder cancer: a randomized controlled study. J Clin Oncol 2010;28(30):4581–4586
19 André T, Tournigand C, Rosmorduc O, et al; GERCOR Group. Gemcitabine combined with oxaliplatin (GEMOX) in advanced biliary tract adenocarcinoma: a GERCOR study. Ann Oncol 2004; 15(09):1339–1343
20 Javle M, Borad MJ, Azad NS, et al. Pertuzumab and trastuzumab for HER2-positive, metastatic biliary tract cancer (MyPathway): a multicentre, open-label, phase 2a, multiple basket study. Lancet Oncol 2021;22(09):1290–1300
21 Lee CK, Chon HJ, Cheon J, et al. Trastuzumab plus FOLFOX for HER2-positive biliary tract cancer refractory to gemcitabine and cisplatin: a multi-institutional phase 2 trial of the Korean Cancer Study Group (KCSG-HB19-14). Lancet Gastroenterol Hepatol 2023;8(01):56–65
22 Ohba A, Morizane C, Kawamoto Y, et al. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing unresectable or recurrent biliary tract cancer (BTC): An investigator-initiated multicenter phase 2 study (HERB trial). Published online 2022:4006–4006
23 Bhargava PG, Kumar A, Simha V, et al. Presentation and outcomes with first-line chemotherapy in advanced cholangiocarcinomas-A relatively rare component of Biliary tract cancers in India. South Asian J Cancer 2020;9(04):209–212
24 Anadure R, Sreen A, Singh HP, et al. A study on the clinical profile and treatment outcomes in gallbladder carcinoma from Northern India. Oncol J India 2020;4(03):128–132