Expert Consensus on Diagnosis and Molecular Testing Strategies for Non-Small-Cell Lung Cancer in India

Bivas Biswas[1] Trupti Pai[2] Nirmal Raut[3] Vidya Manur Narasimhamurthy[4] Bijal Kulkarni[5] Ashish Singh[6] Sunil Pasricha[7] Jayesh Deshmukh[8] Sewanti Limaye[9]

[1] Department of Oncology, Apollo Multispecialty Hospital, Kolkata, West Bengal, India
[2] Department of Pathology, Tata Memorial Centre, Mumbai, Maharashtra, India
[3] Department of Oncology, Bhaktivedanta Hospital & Research Centre, Mira-Bhayandar, Maharashtra, India
[4] Department of Pathology, Manipal Hospitals, Bengaluru, Karnataka, India
[5] Department of Histopathology and Cytology, Cytogenetics - Laboratory Medicine, Kokilaben Dhirubhai Ambani Hospital, Andheri, Mumbai, Maharashtra, India
[6] Department of Oncology, Christian Medical College, Vellore, Tamil Nadu, India
[7] Department of Pathology, Rajiv Gandhi Cancer Institute & Research Centre, New Delhi, Delhi, India
[8] Department of Medical and Scientific Affairs, Roche Diagnostics India, Mumbai, Maharashtra, India
[9] Department of Oncology, Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India

Address for correspondence Sewanti Limaye, MS, Department of Oncology, Sir H. N. Reliance Foundation Hospital and Research Centre, Prarthana Samaj, Raja Ram Mohan Roy Road, Girgaon, Mumbai, Maharashtra 400004, India (e-mail: sewanti.limaye@gmail.com).

Ind J Med Paediatr Oncol 2026;47:85–93.

Abstract

This review aims to establish expert consensus on biomarker testing for non-small-cell lung cancer (NSCLC) in India, evaluating diagnostic practices, adherence to international guidelines, and test utility and comparing clinically validated assays with laboratory-developed tests. In round 1, experts voted on 41 statements covering various aspects of NSCLC diagnostics. Responses were graded using a 5-point Likert scale, categorizing agreement levels as high, moderate, or low based on expert consensus percentages. After thorough deliberations during round 2, consensus was reached on 32 statements underscoring the necessity for early diagnosis of NSCLC. Key issues include misdiagnosis with tuberculosis and low or delayed specialist referral rates. Although formal programs are limited by awareness, resources, and data gaps; low-dose computed tomography (LDCT) screening in community settings is advocated. Consensus was reached among experts that most lung cancers are diagnosed at advanced stages in India. The delay in diagnosis was mainly due to misdiagnosis with tuberculosis and delayed referrals to specialists for evaluation. The consensus acknowledged the need to enhance lung cancer awareness and utilization of LDCT in high-risk individuals as a screening methodology in the community.

Biomarker testing for both early-stage and advanced-stage NSCLC is recommended, with reflex testing at diagnosis, longitudinal testing at disease progression, and liquid biopsies when tissue is unavailable/inadequate. Biomarker testing for common driver mutations associated with available targeted therapies can be performed in resource-

Keywords

- non-small-cell lung cancer
- next-generation sequencing
- biomarkers
- companion diagnostic
- reflex testing
- targeted therapies
- low-dose computed tomography

article published online
June 19, 2025

DOI https://doi.org/10.1055/s-0045-1809375.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Private Limited, A-13A, Graphix Tower 1, 6th floor, Sector 62, Noida 201309, Uttar Pradesh, India

limited settings using sequential testing or hotspot panels. PD-L1 testing for all advanced-stage cases is recommended, especially when molecular driver mutations/fusions are negative. Despite longer turnaround times, next-generation sequencing (NGS) would be preferred for its comprehensive gene assessment. Multigene assays are recommended for advanced stages, and upfront broad-panel tests are ideal. Testing for *EGFR*, *ALK*, proto-oncogene ROS1, and PD-L1 is essential for NSCLC. We urge standardized histopathological and molecular practices and acknowledge challenges in NGS availability and the complexities of interpreting results. This consensus underscores the importance of streamlined approaches to enhance NSCLC diagnostics in resource-constrained settings in India.

Introduction

Lung cancer ranks as the most commonly diagnosed cancer worldwide, accounting for 2.48 million new cases in 2022, with an associated mortality of 1.8 million deaths annually.[1,2] In India, the crude incidence rate of lung cancer is 7.1 cases per 100,000 people, with projections indicating a likely increase in the coming years.[3] Non-small-cell lung cancer (NSCLC) constitutes approximately 85% of all lung cancer cases globally.[4] Among the subtypes of NSCLC, adenocarcinoma is the most prevalent, representing approximately 40% of all lung cancer cases.[5] Adenocarcinomas account for approximately 34.3% of lung cancers in males and 52.7% in females, while squamous cell carcinomas constitute 11.5% of all lung cancer cases in India.[6] Most NSCLC cases (>90%) are detected late, specifically in stage III or IV, limiting curative options. Only 31.7% of patients with stage I–IIIb NSCLC receive surgery or radical radiotherapy.[7–9] While stage IV is often managed with palliative care, stage III can be treated with curative intent. The 5-year survival rate of lung cancer stands at 63.7%. Most cases are diagnosed after metastasis, highlighting the need for early detection and treatment.[10]

The selection of treatment is influenced by the disease stage, the patient's overall health, and the presence of specific biomarkers.[4] To ensure the effectiveness of targeted therapies in patients with advanced-stage NSCLC, molecular analyses are standard for identifying genetic mutations or rearrangements, including *EGFR*, *ALK*, proto-oncogene ROS1, and others presented in ►**Supplementary Table S1** (available in the online version only).[11–13] Biomarker identification enables targeted therapies and immunotherapy to be directed to the most suitable patients, improving treatment outcomes.[14]

International guidelines from the National Comprehensive Cancer Network (NCCN), European Society for Medical Oncology (ESMO), and International Association for the Study of Lung Cancer (IASLC) emphasize the importance of comprehensive molecular testing for NSCLC. Although the guidelines highlight the importance of conventional methods for single-gene testing, such as polymerase chain reaction (PCR), immunohistochemistry (IHC), and fluorescence in situ hybridization (FISH), to assess specific biomarkers, next-generation sequencing (NGS) and comprehensive genomic profiling are advocated for providing a broader analysis.[15–18]

The evolving NSCLC diagnostic landscape requires continuous updates to integrate new biomarkers but is hindered by operational and logistical challenges.[19] The 2019 Indian consensus guidelines primarily emphasize early screening and detection of NSCLC and biomarker testing for advanced cases.[19] Since then, early- and advanced-stage NSCLC management advancements have necessitated revisions. While these guidelines are based on scientific evidence, practical factors—such as affordability and availability of tests and drugs, out-of-pocket costs, and insurance coverage—must also be considered.[11] Additionally, testing for emerging resistant mutations is essential for patients resistant to *EGFR* tyrosine kinase inhibitors (TKIs).

This modified Delphi consensus aimed to achieve the following objectives:

- To investigate the role of biomarkers in diagnosing early- and advanced-stage NCSLC.
- To assess the applicability of international guidelines (such as those from the NCCN, ESMO, and IASLC) for NSCLC diagnostics in the Indian context.
- To evaluate the utility and feasibility of various diagnostic tests, such as NGS, in managing NSCLC in resource-constrained settings in India.
- To determine the accuracy and reliability of various clinically validated assays compared with laboratory-developed tests in the Indian context.

Materials and Methods

Study Design

This study used the modified Delphi method to solicit input from a select panel of experts specializing in NSCLC diagnostics. This iterative and structured approach aims to synthesize the collective expertise of a diverse panel of experts to achieve consensus on complex or uncertain topics.[20]

Panel of Experts

The expert panel comprised four oncologists and four pathologists from various institutions, each recognized as a leader in medical oncology, precision oncology, oncopathology, histology, and cytology. The panel members brought experience from public and private health care sectors across different regions of India, ensuring a well-rounded perspective that

accounted for variations in clinical practices and health care infrastructure.

Delphi Questionnaire Development

The modified Delphi process entailed an initial round of expert voting on the 41 statements. Statements were graded based on available evidence from the literature,[21] with responses recorded on a 5-point Likert scale (strongly agree, agree, neither agree nor disagree, disagree, and strongly disagree). Consensus levels were categorized as "high" ($\geq$75% agreement), "moderate" (55–74% agreement), or "low" ($<$55% agreement). Open-ended responses were collated and summarized.

A total of 41 statements spanning the following thematic domains were voted upon and deliberated by the experts:

- Challenges in early diagnosis of NSCLC.
- Diagnosis and biomarker testing in NSCLC.
- NGS testing in NSCLC.
- Practical considerations in NSCLC management.

The experts were provided access to the consensus statements and questionnaire on a proprietary platform via an electronic link. They comprehensively examined the challenges, considerations, and recommendations pertinent to NSCLC management pathways in the Indian context.

Two-Round Modified Delphi Process

Subsequently, statements without consensus in round 1 were discussed in a face-to-face meeting during round 2. Here, statements were refined, added, or removed based on expert discussion. A final consensus was reached on statements with high agreement levels.

Results

In the first round of voting, 41 statements were evaluated: 24 statements achieved a high level of agreement, 15 showed a moderate level of agreement, and two statements presented as open-ended questions did not fall into either category. During the discussion, statements that required additional clarification were determined. These statements were revised and reworded in the second round. These modifications resulted in a more substantial consensus among the experts. By the conclusion of round two, 32 statements were finalized, each attaining a high level of consensus. Several statements were further reframed for clarity.

Discussion

The discussion synthesizes expert insights on critical themes in NSCLC care, including early diagnosis, biomarker and NGS testing, and practical management considerations, with a focus on real-world challenges and practices in India.

Challenges in the Early Diagnosis of NSCLC

Early diagnosis of NSCLC is critical for enabling prompt treatment, which can lead to improved outcomes, higher cure rates, and enhanced survival rates.[22] Five statements on the early diagnosis of NSCLC attained high consensus (►**Table 1**).[22–24]

A retrospective analysis (2008–2016) of 1,370 patients with NSCLC in India revealed that 95% were diagnosed at advanced stages, with considerable delays in obtaining a definitive diagnosis. Misdiagnosis is a major contributing factor to delayed NSCLC diagnoses due to its overlapping symptoms with endemic tuberculosis.[22] Additionally, insufficient awareness about the early signs and risk factors of lung cancer contributes to delayed detection.[25]

Low-dose computed tomography (LDCT) screening has proven reliable in the early identification of NSCLC in high-risk individuals. As per the NCCN guidelines, annual LDCT screening is advised for individuals at high risk for lung cancer.[26] The National Lung Screening Trial demonstrated a reduction in mortality among high-risk individuals who underwent LDCT compared with those who underwent standard chest X-ray screenings.[27,28] Barriers to adopting LDCT include a limited understanding of its effectiveness and advantages and inadequate infrastructure.[29] Despite the high

Table 1 Statements on screening for NSCLC

Statemen t No.	Statement	Level of evidence	Consensus achieved
1.	In India, most patients with lung cancer are diagnosed at an advanced stage, which emphasizes the need for early diagnosis.[22]	3b	75%
2.	Misdiagnosis plays a major role in the late diagnosis of NSCLC due to overlapping symptoms with endemic tuberculosis.[22]	3b	87%
3.	Low referral of patients to specialist centers could contribute to a delayed diagnosis of NSCLC.[22]	3b	87%
4.	LDCT screening for high-risk individuals, especially in resource-limited nations, may substantially help diagnose NSCLC early.[23]	2b	75%
5.	There is no formal screening program that includes LDCT for patients with lung cancer due to the unavailability of clinical data in the Indian population.[24]	5	100%

Abbreviations: LDCT, low-dose computed tomography; NSCLC, non-small-cell lung cancer.

incidence of lung cancer in India, there are no structured national screening programs in place.[30] Resource limitations, low awareness among health care providers, and inadequate infrastructure pose substantial challenges, hindering early lung cancer diagnosis. Key obstacles also include high false-positive rates (mainly due to the high prevalence of tuberculosis) and reluctance among high-risk individuals to undergo screening.[24,31]

A pilot retrospective study in India involving 350 smokers who underwent LDCT screening found lung nodules in 93% of individuals, with category two nodules being the most common (41%) and category four nodules found in 14%. Seven patients with category 4 nodules were diagnosed with lung cancer (six adenocarcinomas and one small cell lung cancer), resulting in an overall cancer incidence of 2%. This demonstrates that LDCT can effectively detect malignant lung nodules even in a tuberculosis-endemic country.[32] Experts recommend that LDCT should ideally be integrated into routine screening in India. Given existing limitations, its implementation should be phased, beginning with high-risk individuals.

Diagnosis and Biomarker Testing in NSCLC

All statements on the diagnosis and biomarker testing for NSCLC achieved high consensus (►**Table 2**).[11,19,33–47]

Histological assessment guides initial diagnosis and obtaining adequate biopsy samples is pertinent. Tissue

Table 2 Statements on diagnosis and biomarker testing in NSCLC

Statement No.	Statement	Level of evidence	Consensus achieved
6.	Reflex biomarker testing, where the pathologist initiates biomarker testing at the time of initial NSCLC diagnosis, should be strongly considered over testing after consultation with an oncologist or a multidisciplinary team.[33,34]	3b	87%
7.	Diagnostic utility and clinical validity play a major role in IHC testing.[35]	3b	100%
8.	Single biomarker testing is commonly adopted in resource-limited settings.[36]	5	100%
9.	Testing for *EGFR*, *ALK*, and PD-L1 is suggested for patients with early-stage NSCLC.[19]	5	100%
10.	Testing for *EGFR*, *ALK*, and *ROS1* is strongly advisable for all patients with advanced-stage NSCLC, irrespective of histologic subtype, for treatment decision-making.[19]	5	100%
11.	In a relatively asymptomatic patient, it may be advisable to wait for molecular testing results before choosing the optimal first-line treatment.[37]	5	100%
12.	EGFR testing is recommended for all stages of NSCLC, as it is the most common driver mutation in patients with lung cancer in India.[38]	2b	100%
13.	T790M testing should be performed after progression on first-line first- and second-generation TKIs.[11]	1a	100%
14.	For T790M testing, a liquid biopsy is preferable; however, if the results are negative, a tissue biopsy should be performed.[11,39]	3b	100%
15.	Liquid biopsy can be used as a complementary test to tissue biopsy.[40]	2b	100%
16.	In diagnosed cases of NSCLC, liquid biopsies that assess mutations in circulating DNA offer less-invasive alternative(s) for biomarker testing.[41]	3b	100%
17.	ALK IHC is a US FDA-approved companion diagnostic for various ALK inhibitors with high concordance with FISH and NGS.[42,43]	3b	100%
18.	ROS1 IHC is a valuable screening test, but positive cases need to be confirmed with FISH/NGS.[44]	2a	100%
19.	Longitudinal testing (re-biopsy at progression) is key to guiding treatment decisions by identifying tumor evolution, resistance pathways, and new molecular alterations.[45]	3b	100%
20.	PD-L1 testing is recommended for all NSCLC cases, irrespective of the stage.[11]	1a	100%
21.	For PD-L1 testing in NSCLC, the SP263 assay can be used as an alternative to the DAKO platform, given the strong concordance between the SP263 and 22C3 clones.[46]	1a	87%
22.	22C3 testing is preferable for treatment with pembrolizumab.[47]	2b	100%
23.	There is a need for homogenization of histopathological and molecular practices among pathologists regarding appropriate tissue triaging and reporting of various indicators (tissue adequacy, tumor microenvironment, necrosis, background cellular component, etc.) that influence downstream molecular testing and its interpretation.[19]	5	100%

Abbreviations: ALK, anaplastic lymphoma kinase; DNA, deoxyribonucleic acid; *EGFR*, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NGS, next-generation sequencing; NSCLC, non-small-cell lung cancer; PD-L1, programmed death-ligand 1; *ROS1*, proto-oncogene tyrosine-protein kinase; T790M, threonine-to-methionine substitution at amino acid position 790; TKI, tyrosine kinase inhibitor; US FDA, United States Food and Drug Administration.

biopsy remains the gold standard for NSCLC diagnosis, in classifying tumors and identifying actionable mutations. Optimal tissue samples should be obtained to ensure accurate histological diagnosis and molecular testing, enabling personalized treatment decisions.[18] Tissue samples should adequately represent the tumor's cellular and microenvironmental characteristics. Since tissue requirements vary by assay, prioritization is necessary to optimize its use.[48]

Molecular testing for "druggable" mutations is essential in enhancing diagnostic precision, guiding targeted therapies, and improving treatment outcomes.[19] The various diagnostic methods employed for single-gene testing include PCR, IHC, FISH, and NGS.[35] In resource-constrained health care systems, such as India, the reliance on sequential single-gene testing persists due to cost and accessibility limitations.[49] Reflex biomarker testing should be considered at diagnosis.[33,34]

While PCR is a widely used method for detecting *EGFR* mutations,[17] IHC is recommended for *ALK*, *ROS1*, and PD-L1 testing. IHC is a reliable tool for detecting *ALK* rearrangements and *ROS1* fusions in NSCLC.[43] Literature suggests that IHC is a robust, cheap, and widely available method and an essential diagnostic test for *ALK* rearrangements in NSCLC. Alternatively, FISH can be used for *ALK* rearrangement detection. Cases with equivocal staining can be further confirmed with FISH.[43] However, FISH requires greater technical expertise and is expensive.[43] The *ALK* (D5F3) IHC is a U.S. Food and Drug Administration-approved companion diagnostic assay and does not need further confirmation by FISH. Results from a concordance study comparing various IHC antibodies with FISH as the gold standard showed that IHC using D5F3 and 5A4 clones is rapid and cost-effective for detecting various *ALK* gene rearrangements.[50] IHC is an important screening method for *ROS1* fusions. However, positive cases must be confirmed with FISH or NGS.[17]

While tissue-based biopsy remains essential for diagnosis, it is expensive. Other disadvantages of tissue-based biopsies include the need for an invasive procedure, challenges with certain tumor locations, limited tissue availability, and difficulty in capturing tumor heterogeneity.[40] Additionally, single-gene testing may require sequential tests, which can be compromised by limited tissue availability. Multiple tests may also result in treatment delays.[51,52]

Liquid biopsy can be recommended where tissue is inadequate for molecular testing or re-biopsy is not feasible.[53] They can also be used in cases of progression after TKI treatment (*EGFR*, *ALK*) or when faster results are needed. Liquid and tissue biopsies complement each other by identifying more actionable genomic alterations when used together than individually.[40] Liquid biopsy can overcome intratumor or inter-tumoral heterogeneity for the detection of molecular alterations.[54] Liquid biopsies enable detection by analyzing circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs).[53] The analysis of CTCs in monitoring treatment response and prognosis is currently restricted to clinical trials.[55] Additionally, liquid biopsy may be utilized to monitor residual disease after surgery and assess early molecular response to targeted therapy through ctDNA clearance, although it remains experimental.[53,56,57] The ESMO guidelines recommend liquid biopsy in patients ineligible/unwilling for repeat biopsy or when tissue samples are insufficient.

Similarly, the NCCN guidelines advise performing a liquid biopsy to detect the threonine-to-methionine substitution at amino acid position 790 (T790M) mutation in cases with cancer progression.[54] Along with advantages such as minimal invasiveness, patient acceptability, high repeatability, and reduced costs, the sensitivity of liquid biopsies in detecting the T790M mutation is comparatively higher than that of tissue biopsies.[54] Moreover, liquid biopsies or re-biopsies play a valuable role in detecting new gene alterations during NSCLC progression and in detecting histological changes.[55,58]

In early-stage NSCLC, testing for *EGFR* mutations, *ALK* fusion, and PD-L1 expression is recommended, as these are common driver mutations and have targeted therapies and immunotherapies available.[38,59–61]

PD-L1 testing can be considered in all cases of NSCLC, regardless of stage. However, experts opined that in early-stage, resectable NSCLC, the role of PD-L1 testing is limited when using perioperative chemo-immunotherapy approaches.[62] Similarly, in stage III NSCLC, durvalumab is approved as maintenance therapy post-chemoradiotherapy (CTRT) in India, irrespective of PD-L1 status.[12] Higher PD-L1 expression in immune cells is associated with improved overall survival in patients.[63,64] PD-L1 testing is primarily conducted using IHC. The tumor cell expression score is highest when using the 22C3 antibodies compared with assays such as SP142. This makes 22C3 testing preferable as it reliably identifies patients eligible for pembrolizumab therapy.[47]

Experts reiterate that early diagnosis, followed by timely biomarker testing, can notably improve survival outcomes by enabling the selection of appropriate targeted therapies and immunotherapies.[38,59–61]

In India, approved treatments include erlotinib, dacomitinib, afatinib, gefitinib, and osimertinib for *EGFR* mutations; crizotinib, alectinib, ceritinib, and lorlatinib for *ALK*; and entrectinib for *ROS1*. ►**Supplementary Table S1** (available in the online version only) lists the different testing methods categorized as mandatory, preferable, and optional biomarkers with the approved drugs.

NGS Testing in NSCLC

NGS-based assays, which analyze multiple biomarkers simultaneously, have demonstrated good clinical utility in NSCLC diagnostics.[65] Evidence suggests that RNA-based NGS assays effectively detect gene rearrangements and fusions, and combining them with DNA-NGS enhances the identification of clinically relevant mutations.[66,67]

Broad-panel NGS is preferred over sequential single-gene testing to guide treatment decisions when feasible and affordable.[65,68]

Despite its longer turnaround time, NGS offers a faster, more comprehensive approach.[51,52] Although NGS has a higher initial cost, it can be more cost-effective over time by focusing on clinically relevant biomarkers[65] and minimizing the need for multiple tests.

In India, NGS remains underutilized due to cost constraints and limited availability.[69] However, experts highlighted that cost-effectiveness could be improved through strategic panel selection. Challenges persist, including a lack of clinical validation and standardization of NGS panels. Limited laboratory infrastructure and a shortage of trained personnel are other barriers. Generating clear NGS reports and adhering to best practice guidelines are crucial for ensuring accurate interpretation and high-quality outcomes.[65,70]

Experts noted variations in pathologists' practices due to the absence of guidelines in India, emphasizing the need for standardization. Reporting of indicators such as the quality and adequacy of tissue for testing, and its cellular components were of utmost importance in optimizing downstream molecular testing and its interpretation.

Consensus statements regarding NGS testing are listed in ►**Table 3**.[11,71–75]

Practical Considerations in NSCLC Management

Reflex testing initiated by pathologists can expedite biomarker testing, ensuring broader coverage.[35] Our expert consensus underscores the importance of tissue adequacy for reflex testing and prioritizing molecular diagnostic assays in managing NSCLC. We advocate for the wider adoption of reflex testing practices, particularly in India, to enhance diagnostic efficiency.

Furthermore, considering the affordability and accessibility of tests and drugs, we recommend incorporating a broad-panel NGS testing along with PD-L1 IHC, where feasible.

It is important to ensure an adequate tissue sample for testing and consider repeating biopsies as necessary. When tissue samples are insufficient for comprehensive molecular testing, alternative methods such as IHC and FISH can be employed to assess *ALK* and *ROS1*. These techniques require smaller tissue samples and can provide information on genetic alterations. Timely assessments by pathologists and accurate labeling for molecular testing are essential to maintain diagnostic precision. Traditionally, biomarker tests for lung cancer are ordered by the treating oncologist only after a confirmed pathological diagnosis, which can lead to delays in treatment. Finally, comprehensive technician training and the establishment of in-house genomic protocols to enhance the efficiency of molecular testing for NSCLC diagnosis are recommended. Standardizing practices among pathologists for tissue triaging and identifying tissue adequacy that impacts molecular testing is essential. Improved communication and multidisciplinary collaboration among radiologists, pulmonologists, pathologists, and oncologists to advance patient care in NSCLC management are urgently needed.

Table 3 Statements on NGS testing in NSCLC

Statement No.	Statement	Level of evidence	Consensus achieved
24.	In India, limited in-house availability and affordability limit the use of NGS technology, and there is a need for its clinical validation.[71]	3b	100%
25.	NGS testing is associated with the longest average turnaround time as compared with other methods, such as PCR, qPCR, IHC, and FISH.[36]	5	72%
26.	There is a high concordance between clinically validated multigene NGS panels and single-gene assay for detecting *EGFR* mutations and *ALK* fusions.[72]	3b	87%
27.	Compared with serial single-gene testing, NGS testing at CAP/CLIA/NABL-accredited laboratories to investigate multiple genes in a single run is preferable, timesaving, and cost- effective.[73]	3b	100%
28.	NGS assays enable the assessment of multiple genes simultaneously with high sensitivity while saving time and tissue compared with sequential single-gene testing. However, these assays are complex in design, performance, and interpretation.[74]	3b	87%
29.	Targeted hotspot panel testing is preferable over CGP in resource-constrained settings due to affordability and availability.[11]	1a	100%
30.	Multigene assays can be recommended upfront for advanced-stage NSCLC (stages IIIb–IV).[11]	5	100%
31.	Broad-panel tests should ideally be performed upfront, but if missed, they should be performed later.[75]	3b	100%
32.	RNA-based NGS panels are recommended for detecting fusions involving *ALK*, *ROS*, *RET*, *NTRK*, and *NRG1* genes, preferably from FFPE samples.[74]	3b	87%

Abbreviations: ALK, anaplastic lymphoma kinase; CAP, College of American Pathologists; CGP, comprehensive genomic profiling; CLIA, clinical laboratory improvement amendments; *EGFR*, epidermal growth receptor factor; FFPE, formalin-fixed paraffin-embedded; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NABL, National Accreditation Board for Testing and Calibration Laboratories; NGS, next-generation sequencing; *NRG1*, neuregulin-1; NSCLC, non-small-cell lung cancer; *NTRK*, neurotrophic receptor tyrosine kinase; PCR, polymerase chain reaction; qPCR, quantitative polymerase chain reaction; RET, rearranged during transfection; RNA, ribonucleic acid; *ROS1*, proto-oncogene tyrosine-protein kinase.

Table 4 Key recommendations on diagnosis of NSCLC in India

Early diagnosis is vital for patients with lung cancer in India, where most cases are advanced. LDCT screening in communities can aid early NSCLC detection while improving referrals to specialist centers, which is key to avoiding diagnosis delays.
For molecular testing, *EGFR*, *ALK*, and PD-L1 testing should be prioritized in both early-stage and advanced-stage NSCLC cases to guide treatment decisions. In addition, *ROS1* testing needs to be prioritized in advanced-stage NSCLC.
T790M testing is recommended after progression on first-line first- or second-generation *EGFR*-TKIs, starting with liquid biopsy, followed by tissue biopsy if liquid biopsy results are negative.
PD-L1 testing is essential for treatment decision-making in advanced-stage NSCLC and should be considered for early-stage cases as well. The PD-L1 SP263 assay can be used if the DAKO platform is unavailable for PD-L1 testing.
Reflex biomarker testing at initial diagnosis is recommended to expedite treatment initiation.
Multigene assays can be recommended upfront for advanced-stage NSCLC, as they offer greater efficiency and cost-effectiveness compared with serial single-gene testing.
Efforts should focus on improving the availability and affordability of NGS technology in India, as it is preferable for comprehensive gene analysis in advanced-stage NSCLC.

Abbreviations: ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; LDCT, low-dose computed tomography; NGS, next-generation sequencing; NSCLC, non-small-cell lung cancer; PD-L1, programmed death-ligand 1; ROS1, proto-oncogene tyrosine-protein kinase; TKI, tyrosine kinase inhibitor; T790M, threonine-to-methionine substitution at amino acid position 790.

The strengths of this review include the use of a structured modified Delphi method, involvement of a multidisciplinary expert panel, and their representation from diverse health care settings across India. However, as with any consensus-based review, the findings may not fully reflect evolving clinical practices or future developments. The recommendations are particularly applicable to health care settings with limited resources. Persistent gaps in evidence, particularly related to early diagnosis, biomarker testing workflows, and NGS implementation, warrant further research and validation in real-world settings.

The key recommendations from this consensus are provided in ►**Table 4**.

Conclusion

This review highlights the need for enhancing lung cancer awareness and introducing formal screening programs, specifically using LDCT for early diagnosis and improved survival. Biomarker testing is decisive in the precision-based management of lung cancer and enables personalized treatment to enhance survival and maintain quality of life. Biomarker analyses focusing on *EGFR*, *ALK*, *ROS1*, PD-L1, and, if feasible, a multigene assay are crucial for precision-based NSCLC management. While broad-panel NGS assays are recommended, challenges such as clinical validation, standardization, costs, and infrastructural requirements must be considered. This consensus provides practical recommendations to overcome barriers, optimize diagnostic strategies, and advance targeted care for improved patient outcomes.

Authors' Contributions

The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work. B.B.: concepts, design, literature search, manuscript preparation, manuscript editing, manuscript review; T.P.: concepts, design, literature search, manuscript preparation, manuscript editing, manuscript review; N.R.: literature search, manuscript editing, manuscript review; V.M.N.: literature search, manuscript editing, manuscript review; B.K.: literature search, manuscript editing, manuscript review; A.S.: literature search, manuscript editing, manuscript review; S.P.: literature search, manuscript editing, manuscript review; J.D.: concepts, design, literature search, manuscript preparation, manuscript editing, manuscript review; S.L.: concepts, design, literature search, manuscript preparation, manuscript editing, manuscript review.

Patient Consent

No patient data was used in this article. Hence patient consent is not applicable for this manuscript.

Conflict of Interest

B.B. received honorarium for lectures/presentations from AstraZeneca, Pfizer, BMS, Intas, DRL, and Alkem. T.P., N.R., V.M.N., B.K., A.S., S.P., J.D., and S.L. declare no conflict of interest.

Acknowledgments

The authors would like to thank BioQuest Solutions Pvt Ltd. for their editorial support.

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