Expert Consensus Recommendations on Biomarker Testing in Metastatic and Nonmetastatic NSCLC in Asia

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ABSTRACT

Introduction: Most published guidelines for genomic biomarker testing in NSCLC reflect the disease epidemiology and treatments readily available in Europe and North America. Nevertheless, 60% of annual global NSCLC cases occur in Asia, where patient characteristics, tumor molecular profiles, and treatments vary greatly from the Western world. For example, mutations in the EGFR occur at a higher prevalence in Asia than in other world regions. Although medical associations such as the International Association for the Study of Lung Cancer, European Society for Medical Oncology, and American Society of Clinical Oncology have described principles for tumor genomic biomarker testing in NSCLC, there is a need for recommendations specific for Asia.

Methods: This report provides consensus recommendations for NSCLC biomarker testing from Asian lung cancer experts for clinicians working in Asia to improve patient care. Biomarker testing approaches for actionable genetic alterations in EGFR, ALK, ROS1, and others are discussed.

Results: These recommendations are divided into nonmetastatic and metastatic forms of adenocarcinoma and squamous cell carcinoma. Owing to the higher prevalence of EGFR mutations in Asia, the experts emphasized the need for EGFR testing to include not just common mutations (exon 19 deletions and L858R substitutions) but also other uncommon EGFR mutations. In addition to the assessment of biomarkers in the tumor tissue, the role of assessing tumor biomarkers by liquid biopsy is discussed.

Conclusion: This consensus provides practical recommendations for biomarker testing in nonmetastatic and metastatic Asian NSCLC patients.

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Keywords: Non–small cell lung cancer; ctDNA; Biomarkers; Adenocarcinoma; Squamous carcinoma; Liquid biopsy

Introduction

Asia contributes 60% to the world’s 2 million annual lung cancer cases.1–3 Although lung cancer mortality has been steady or decreasing in Western countries, it has been increasing in Asia for the past two decades.4 This may be attributed to several factors, including the epidemiology and molecular characteristics of lung cancer and treatment inaccessibility in Asia.

Although smoking is the leading cause of lung cancer in both Western and Asian countries, among nonsmokers, the cause of lung cancer is still largely unknown. Risk factors such as indoor coal burning, cooking fumes, outdoor air pollution, infections, and family history of cancer may play an important role in the development of lung cancer in Asia.4–6 There is a noticeable difference in the smoking rate in patients with lung cancer by sex and by country within Asia. In a study by Mitsudomi7 in a cohort of Japanese patients with lung cancer, as many as 83% of female patients were never smokers, compared with only 10% of male patients. In contrast, data from the Western world reveal that most people with lung cancer are smokers irrespective of the sex of the patients.7

The molecular characteristics of lung cancer in Asia, particularly lung adenocarcinoma, are also considerably different from Western populations. Mutations in EGFR can be detected in 10% to 15% of lung adenocarcinoma in Caucasian patients, but they can be found in up to 60% to 70% of lung adenocarcinomas diagnosed in Asian never smokers.4,8,9 In contrast, KRAS mutations, the most common oncogenic driver in lung adenocarcinoma in Caucasian patients (26%), occur in less than 10% of Asian lung adenocarcinomas.10 The prevalence of other well-characterized genomic drivers seems to be similar in Asian and non-Asian lung adenocarcinomas. A pooled analysis of 2126 nonsmoking Asian patients with lung adenocarcinoma identified EGFR mutations in 74%, ALK rearrangements in 6%, ROS1 rearrangements in 0.8%,...
ERBB2 (HER2) mutations in 4%, and RET rearrangements and MET exon 14 skipping in 1% each of the studied subjects. In recent years, there has been a major shift in the management of NSCLC, from nonspecific treatments such as chemotherapy to targeted therapies. In tumors with driver alterations, targeted therapy markedly improves patient outcomes and quality of life. Therefore, screening NSCLC for a range of recommended predictive and prognostic biomarkers has become a necessary step.

Although tumor tissue including cytologic specimens is the traditional standard for the detection of mutations, adequate material may not be available for testing after initial histologic or cytologic diagnosis. In such cases, rebiopsy may be necessary, which may not be feasible for all patients. Liquid biopsy is gaining acceptance owing to its relative noninvasiveness and potential to overcome the limitations of tumor heterogeneity. Liquid biopsy assays are dependent on tumor DNA shedding into the bloodstream, which may be less common for patients with lower tumor burden or tumors limited to sanctuary sites such as the central nervous system. Furthermore, as with all DNA-dependent assays, sensitivity for the detection of complex genomic alterations such as rearrangements and large introns may be lower than with protein-based or RNA-based technologies. Despite the concern that circulating tumor (ct)DNA-based technologies may falsely attribute alterations from clonal hematopoiesis of indeterminate potential as having tumor origin, common clonal hematopoiesis of indeterminate potential–associated alterations and actionable NSCLC genomic alterations are largely mutually exclusive. Nevertheless, overall detection rates of clinically informative genomic biomarkers are similar for ctDNA panel testing and standard tissue testing.

Table 1 captures the most often used testing methods in NSCLC.

With the growing number of genomic alterations that can inform the choice of targeted therapies, international guidelines for biomarker testing in NSCLC have been established by the American Society of Clinical Oncology, College of American Pathologists/International Association for the Study of Lung Cancer (IASLC)/Association for Molecular Pathology, National Comprehensive Cancer Network, and European Society for Medical Oncology. For the most part, the recommendations are largely aligned; however, they were created predominantly in the context of non-Asian countries. One of the few guidelines that focused on Asian patients with lung cancer was issued by European Society for Medical Oncology in collaboration with the Chinese Society of Clinical Oncology; the Japan Lung Cancer Society also has a guideline on biomarker assessment. These described testing guidelines for EGFR, BRAF, ALK, ROS1, and programmed death-ligand 1 (PD-L1), but emerging diagnostic techniques and therapeutics were not the focus.

Countries in the vast Asia-Pacific region present high variations in access to diagnostic tests and targeted medicines (Supplementary Table 1); treatment decisions are strongly influenced by the availability of technology and resources to cover their costs. In Japan, chest radiograph with sputum cytology is recommended as a lung cancer screening for smokers, but there is no policy for lung cancer screening in countries such as Singapore, India, and Vietnam. Regarding the availability of emerging targeted therapies, health authority approval and reimbursement are

<table>
<thead>
<tr>
<th>Gene</th>
<th>Predictive Alteration</th>
<th>Examples of Mutations</th>
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<tr>
<td><strong>PD-L1</strong>&lt;sup&gt;41&lt;/sup&gt;</td>
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<td>NA</td>
<td>IHC</td>
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<td>Point mutation</td>
<td>L858R, T790M, G719X, S768I, L861Q, and others</td>
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<tr>
<td></td>
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</tr>
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<tr>
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<tr>
<td><strong>KRAS</strong>&lt;sup&gt;49&lt;/sup&gt;</td>
<td>Point mutation</td>
<td>G12C and others</td>
<td>PCR, NGS</td>
</tr>
</tbody>
</table>

Note: This is a dynamic list, please refer to the available test in your region.

FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NGS, next-generation sequencing; PCR, polymerase chain reaction; PD-L1, programmed death-ligand 1.
different from country to country but generally lag behind Europe and the United States (Supplementary Table 1).

Therefore, the application of current Western guidelines in this context, although potentially desirable, is not consistently practical for most Asian patients with lung cancer. In the IASLC survey on molecular testing in lung cancer, 64% of respondents from Asia expressed that less than half of their patients with lung cancer undergo molecular testing. Although the barriers to testing are diverse, the lack of recommendations that consider the unique epidemiology of lung cancer and accessibility to technology may be one of the contributing factors. Therefore, a pragmatic approach to lung cancer biomarker testing in Asia is warranted.

This consensus on biomarker testing for NSCLC in Asia is the result of extensive discussions among experts from several Asian countries. The experts discussed the needs and perceptions around biomarker testing in metastatic and nonmetastatic NSCLC, provided insights on the use of various testing platforms, and reached consensus during the six online meetings. We received editorial support from a company strictly under the direction of the authors. All the authors approved in writing, after multiple rounds of review, the content of this paper. The goal of this consensus is to help ensure that patients receive the newest available therapy and improve the quality of care so that the best possible outcomes for Asian patients with lung cancer can be achieved.

Recommendations for Biomarker Testing of Nonmetastatic NSCLC

The demographics of patients with lung cancer have changed in the past decade. With further implementation of lung cancer screening, we hope that a stage migration from metastatic to earlier stages of disease will also be observed.

The stage at presentation typically breaks down to the following: stage I at 10%, stage II at 20%, stage III at 30%, and stage IV at 40%. Most of the patients present with advanced stage or metastatic disease, which reduces the patient’s chances of survival with current therapies. Nevertheless, it is also true that there is a great heterogeneity in terms of stage at presentation even within Asia. For example, stage I accounts for 40% of newly diagnosed NSCLC cases in Japan.

On the basis of the presumption that detection of tumor molecular abnormalities as soon as possible after diagnosis will lead to a considerably longer survival, biomarker detection strategies have been tested for potential value in the early detection of lung cancer or prognostic and therapeutic guidance through the main methodologies implemented. These include detection of genomic changes by polymerase chain reaction (PCR) or next-generation sequencing (NGS) and detection of overexpressed proteins by immunohistochemistry (IHC).

In this section, we discuss the biomarkers used in clinical practice as predictive and prognostic biomarkers after diagnosis has been confirmed.

Recommendations

- Nonmetastatic resectable NSCLC
  - Adenocarcinoma
    - Stage IA: EGFR and PD-L1 testing as routine are not recommended at this time.
    - Above stage IA: Evaluate EGFR status by PCR at diagnosis. If the tumor is positive for either EGFR mutation or PD-L1 greater than 1%, follow the local treatment recommendations (Fig. 1).
  - Squamous cell carcinoma: EGFR testing as routine is not recommended at stages IA to IIIA, and PD-L1 testing is not recommended for stage IA.
- Nonmetastatic unresectable NSCLC
  - If the patient is fit for definitive chemoradiotherapy, then consider evaluating for PD-L1 status (regardless of histology of adeno or squamous cell carcinoma) and EGFR mutation (adenocarcinoma only) and follow local treatment recommendations (Fig. 2).
  - If the patient is unfit for definitive chemoradiotherapy, then follow testing recommendations for metastatic disease.
- In the case of unresected tumors, tissue biopsy used for diagnosis can be used for biomarker assessment.
- A turnaround time of approximately 3 weeks for test results from resected tumors is acceptable whereas less than or equal to 2-week turnaround time is preferred for unresectable cases owing to the urgency of treatment.

Recommendations for Biomarker Testing of Metastatic NSCLC

Test performance will vary owing to different sensitivities, specificities, and characteristics of the samples.
themselves (age, preservation conditions, tumor cellularity, etc.). Clinicians should be aware of test performance, and workflows for testing should be validated by external quality control programs.28

Tumor tissue is the preferred source of material for confirmation of the diagnosis of metastatic NSCLC and for initial biomarker testing; however, sometimes its availability can be a limiting factor. In such cases, tissue should be prioritized for biomarker assessment that can be performed only with tissue, such as PD-L1 testing. For patients who meet clinical requirements, rebiopsy can be considered to obtain additional tumor tissue before initial treatment. Nevertheless, such procedures are not feasible for all patients and could add to morbidity, costs, and delays in treatment. In this consensus, the term tissue biopsy also includes cytologic specimens.

Analysis of ctDNA has emerged as an effective and promising tool for genomic profiling in metastatic NSCLC. Evaluation of ctDNA can be particularly useful in situations where tissue biopsy is not safely obtainable owing to poor physical condition of the patient or inaccessible tumor biopsy location. Although specificity and positive predictive value are generally high, the sensitivity compared with tissue-based methods may be lower when small quantities of DNA are shed from the tumor into the bloodstream. Nevertheless, detection rates of actionable genomic biomarkers are similar between NGS-based ctDNA assays and tissue-based methods.14,15 In addition to identifying oncogenic driver mutations that can be treated with targetable therapy in the treatment-naive advanced NSCLC setting, ctDNA might prove useful in novel ways including monitoring during an advanced NSCLC patient’s treatment course (real-time monitoring) and determining mechanisms of resistance to therapy.29 A liquid biopsy may detect the presence of a genomic biomarker associated with NSCLC (e.g., EGFR mutation or ALK rearrangement) before a cellular-based diagnosis is obtained; however, the panel did not address whether targeted therapy should be initiated without supportive histology or cytologic results.

Biomarker Testing Before Initial Therapy

Adenocarcinoma. Initial Testing for Patients With Metastatic Adenocarcinoma. The selection of biomarkers for testing before initial therapy for advanced-stage lung adenocarcinoma depends on the known prevalence of specific genetic alterations, availability of targeted therapies, access to technology (single-gene or panel testing), and reimbursement of diagnostic procedures and therapies.

Along with PD-L1, clinicians should assess for driver alterations in EGFR, ALK, and ROS1 simultaneously. Depending on the resources and therapeutic products available, potentially informative or actionable alterations should also be assessed in other genes (BRAF V600E, RET, MET exon 14 skipping, KRAS, ERBB2, NTRK).

A variety of molecular testing approaches can be used, keeping in mind their advantages and limitations. Local laboratory testing of EGFR hotspot mutations can provide fast results and has the potential to identify most tumors with driver mutations in areas with a high probability of EGFR alterations. Nevertheless, hotspot testing, even with perfect sensitivity, can miss less common but actionable EGFR alterations and do not cover all possible pathogenic insertions and deletions. Because EGFR mutations are highly prevalent in lung adenocarcinoma in Asia, uncommon mutations in EGFR may occur more frequently than common alterations in other genes. Therefore, whenever...
feasible, EGFR assessment should include not only exon 19 deletions and L858R but also other activating point mutations and exon 20 insertions.

As the number of genes that need to be assessed for patients with NSCLC at diagnosis is continuously expanding owing to efficacious therapies, pressure to use the available tissue sample judiciously becomes imperative. Therefore, when assessing for alterations in multiple genes, simultaneous testing that incorporates NGS from a single sample is preferred, whenever feasible, so as not to exhaust available tumor specimens. Although tissue is the preferred material, the turnaround time for results may be 2 weeks (preferred) or longer. In cases where tissue may not be available, liquid biopsy-based, single-gene or NGS testing can be an option. Using plasma, single-gene testing can be completed in under 1 week; comprehensive testing can be completed in under 2 weeks.

For assessing gene rearrangements in ALK, ROS1, and other genes, test sensitivity is greater with protein-based or RNA-based technologies than with NGS of tumor-derived DNA. As tumor mutation burden is not yet an established marker for immune checkpoint inhibitors (ICIs) in NSCLC and microsatellite instability-high is a rare occurrence in NSCLC, both these biomarkers currently should not be routinely evaluated.

Recommendations (Fig. 3)

- All patients with lung adenocarcinoma should be tested simultaneously for PD-L1 and driver alterations in EGFR, ALK, and ROS1.
  - Consideration: Whenever possible, clinicians must wait for the results of driver biomarker testing before commencing first-line treatment. Treatment decisions should not be based solely on PD-L1 results.
  - When available, tumor tissue should be used for genomic testing. Nevertheless, if tissue is not available, or rebiopsy is not practical, ctDNA testing should be considered.
  - Recommended approaches for testing: PCR based for EGFR, IHC for ALK, and in situ hybridization or IHC for ROS1 rearrangements. Consider other methodologies such as NGS when it is necessary to cover a broad array of alterations.
  - EGFR testing should assess all common and uncommon driver mutations, including exon 20 insertions. PCR alone may miss some pathogenic alterations; therefore, NGS should be considered.
  - If targeted therapies are available, test for potential alterations in all relevant genes before initial treatment (in addition to EGFR mutations and ALK and ROS1 rearrangements, assess for BRAF V600E, MET exon 14 skipping, KRAS and ERBB2 mutations, and RET and NTRK rearrangements).
  - Consideration: If multiple genes will be tested, consider a panel test rather than sequential single testing for individual biomarkers.
  - The preferred turnaround time for obtaining test results is less than or equal to 2 weeks.
  - Routine testing for tumor mutational burden and microsatellite instability-high status is not recommended.

Steps If Initial Testing Does Not Provide an Informative Biomarker for Metastatic Adenocarcinoma. Genomic driver alterations are anticipated in more than 60% of lung adenocarcinoma cases in Asia; this can be as high as 90% in nonsmokers. As driver mutations are usually
mutually exclusive in treatment-naive NSCLC, the presence of any driver mutation suggests the absence of another driver, and testing can be considered complete. Given the high prevalence of driver mutations in Asian patients with lung adenocarcinoma, there remains a reasonable probability that an actionable genomic biomarker may still be present even if initial testing failed to detect one.

The success of biomarker testing depends on several technical factors and limitations in the type of test undertaken. The quantity and quality of the representative tissue samples and handling of the test material may all contribute to lack of detection of tumor DNA or a false-negative result. For biopsy specimens, a single sample may not represent a complete genomic profile of a potentially heterogeneous tumor. For plasma samples, ctDNA may not be detected when tumors are not shedding sufficient genetic material into the bloodstream or the tumor is limited only to sanctuary sites such as the brain. Hotspot tests are focused only on common loci of mutation and therefore may miss other uncommon but potentially actionable alterations, including insertions and deletions. For these reasons, the lack of detection of a driver mutation after initial testing does not rule out the presence of an actionable genetic alteration. Whenever practical, follow-on testing should be conducted before the initiation of first-line treatment when initial testing does not detect a clinically informative driver mutation. Panel testing, using tissue or plasma, is preferred to assess for multiple biomarkers simultaneously and to optimize turnaround time.

Recommendations (Fig. 3)

- In the absence of a driver mutation after initial testing (single-gene analysis of tissue or plasma), perform follow-on testing for genomic biomarkers.
  - Consideration: If an NGS-based panel (tissue or plasma) were used as initial testing, then follow-on testing is not routinely recommended.
  - Consideration: When follow-on testing is performed, an NGS-based panel (tissue or plasma) is preferred.
- For clinical situations that do not require immediate treatment, wait for results of follow-on testing before initiating therapy according to local treatment recommendations. Test turnaround time in this situation should be minimized (≤2 wk).
- For clinical situations that require immediate treatment, follow local treatment guidelines for genetic driver–negative metastatic NSCLC.

Metastatic Squamous Cell Carcinoma. The presence of genetic driver alterations in NSCLC with uniform squamous cell histology is uncommon. Driver mutations are more likely to be detected in tumors with mixed adenosquamous histology. In such cases, small tumor specimens from lung adenocarcinoma or mixed adenosquamous carcinoma may be misdiagnosed as pure squamous cell carcinoma. Therefore, a thorough pathologic evaluation of tumor specimens is required to confirm the diagnosis. If there is doubt regarding the histologic diagnosis, or clinical features more often associated with adenocarcinoma are present (nonsmoker, younger age, peripheral location), biomarker testing should be considered. Although uncommon, MET exon 14 skipping has a similar prevalence in both squamous carcinoma and adenocarcinoma.

Initial Testing for Patients With Metastatic Squamous Cell Carcinoma. Recommendations:

- Test all patients for PD-L1 in tumor tissue.
- Test for EGFR mutations in patients who are never or light smokers or based on clinical judgment. Consider testing for MET exon 14 skipping (highly recommended if sarcomatoid histology present).
- Testing for other biomarkers at this step is not recommended.
  - Consideration: If there is clinical suspicion of adenosquamous carcinoma or squamous carcinoma with an adenocarcinoma component as exemplified by squamous cell carcinomas in the peripheral lung or those occurring in nonsmokers, follow the recommended testing protocol for adenocarcinoma.
- EGFR testing, when performed, should assess all common and uncommon driver mutations, including exon 20 insertions.
- When available, tumor tissue should be used for genomic testing. Nevertheless, if tissue is not available or rebiopsy is not practical, ctDNA testing should be considered.
- The preferred turnaround time for obtaining test results is less than or equal to 2 weeks.

Steps If Initial Testing Does Not Provide an Informative Biomarker for Squamous Cell Carcinoma. Recommendations:

- Follow-on testing is not required if initial genomic testing of squamous cell carcinoma did not detect a driver alteration.

Biomarker Testing at Disease Progression

Nearly all patients with advanced-stage NSCLC who have been treated with systemic therapy will eventually develop tumor progression/progressive disease (PD),
After treatment with first- or second-generation EGFR tyrosine kinase inhibitors (TKIs), the most common cause (approximately 50%) of resistance is the acquisition of EGFR T790M. Alterations associated with acquired resistance to third-generation EGFR TKI include point mutations in EGFR (C797X and others), MET amplification, ERBB2 amplification, PIK3CA mutations, BRAF mutations, KRAS mutations, and small cell transformation. Similarly, disease progression and acquired resistance have been found in patients harboring ALK rearrangement–positive NSCLC, particularly those who have been treated with early generation ALK TKIs. Each ALK-targeting TKI has a unique profile that is resistant to or can overcome specific acquired point mutations in ALK.

The IASLC recommends biomarker testing in patients with EGFR-mutated lung cancer whose disease has progressed after initial TKI therapy. Given its convenience and relatively rapid turnaround time, the IASLC recommends ctDNA-based NGS testing as a first step; however, tissue biopsy is recommended if biomarker testing results are negative or if there is a strong suspicion of small cell transformation.

Recommendations (Fig. 4):

- PD after first-/second-generation EGFR TKI: Test for EGFR T790M in ctDNA or newly acquired tumor tissue, if feasible. If no actionable biomarker is detected in ctDNA, perform a biopsy and test tissue for EGFR T790M and assess histology.
- PD after third-generation EGFR TKI: Consider NGS panel test of ctDNA or newly acquired tumor tissue, if feasible. If no actionable biomarker is detected in ctDNA, perform a biopsy and assess histology.
- PD after other (non-ICI) targeted therapy: Newly acquired actionable alterations are less common in this setting. If resources are not a constraint, consider NGS panel testing of ctDNA or newly acquired tumor tissue, if feasible.

- For PD on ICI and/or chemotherapy (no history of targeted treatment):
  - If complete biomarker testing were performed in the past, with no finding of an actionable driver alteration: No additional biomarker testing recommended.
  - If biomarker testing were performed in the past, with an actionable driver alteration detected: No additional biomarker testing recommended.
  - If incomplete or no biomarker testing were performed in the past: Perform comprehensive NGS panel test of ctDNA or tumor tissue (archival or newly acquired).

- The preferred turnaround time for obtaining test results is less than or equal to 2 weeks.

**Figure 4.** Biomarker testing recommendations at disease progression. ctDNA, circulating tumor DNA; ICI, immune checkpoint inhibitor; NGS, next-generation sequencing; TKI, tyrosine kinase inhibitor.

Conclusions and Future Perspectives

Ongoing clinical trials are exploring the efficacy and safety of new therapies that target specific genomic alterations in NSCLC. As new targets are characterized and new treatments become available, the need to assess for the presence of genomic alterations and other biomarkers will increase so that physicians can apply precision medicine to patients who are most likely to benefit from it. This complexity requires effective diagnostic approaches. The testing platforms for genomic biomarkers have evolved over the years from standalone testing by reverse transcriptase-polymerase chain reaction, IHC, and fluorescence in situ hybridization to more comprehensive NGS panels which can assess several genes at once. Each of these testing platforms has its advantages and challenges. According to a global survey conducted by IASLC, less than half of the patient with lung cancer received any sort of molecular testing. The major barriers common to
all geographic regions were cost, quality, access, awareness, and turnaround time. Respondents also expressed their concerns regarding limitations of sample quality and interpretation of test results. Particularly in Asia, where the prevalence of genomic alterations in NSCLC is high but access to medicines and testing procedures is heterogeneous, a pragmatic, region-specific approach to testing must be implemented.

This expert group reached a consensus that relevant genomic alteration assessment is necessary at diagnosis and at disease progression, considering tumor histology and treatment history. At diagnosis, along with PD-L1, EGFR, ALK, and ROS1, other assessment for other driver alterations should be considered when relevant targeted therapies are available. At the time of disease progression on first-generation EGFR TKIs, assessment for the presence of EGFR T790M is essential. For progression on third-generation EGFR TKIs, more comprehensive testing may be considered. For progression on other targeted therapies, physicians should consider the probability of identifying a potentially actionable alteration before testing. In general, protocol for biomarker testing of advanced NSCLC depends on factors such as the clinical condition of the patient, prior treatment history, biomarker testing history, and access to relevant targeted therapies.

Tissue-based tests are preferred, but in cases of inadequate tissue samples or inconclusive results or when rebiopsy is not feasible, evaluation of plasma for ctDNA is a viable alternative. With an increasing number of genes to be assessed, comprehensive genomic profiling (using either tumor tissue or plasma) is becoming a more efficient method at the time of initial assessment, optimizing turnaround time for results and sparing tissue samples for other analyses.

The recommendations provided are intended to provide a practical approach to biomarker assessment for clinicians across Asia who treat patients with lung cancer. Nevertheless, health care providers are also advised to consider the particulars of each individual patient, including clinical history and comorbidities, accessibility to treatments, and testing procedures.

An obvious limitation of this consensus is the relevance of the recommendation in the face of a rapidly evolving landscape of actionable biomarkers, treatments, and diagnostic platforms. Therefore, it is advisable to track the developments and follow the most recent literature for the optimal diagnostic and treatment options.

This consensus aims to provide practical recommendations for genomic biomarker testing in early and advanced stage NSCLC for Asian patients with lung cancer. The timely diagnosis of the genomic alterations in NSCLC will help clinicians make more informed treatment decisions and ultimately improve patients’ outcomes.

**CRediT Authorship Contribution Statement**

The recommendations put forward are a result of extensive discussions among experts from several Asian countries, under the aegis of the Lung Ambition Alliance (LAA). The experts are the authors for this manuscript and have contributed equally to the manuscript.

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Supplementary Data
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