# Session 1. Timely diagnosis to enable personalized healthcare with clinical decision support tools

# Session 2: Navigating the lung cancer journey from early to advanced

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## Executive summary

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## Session 1: Timely diagnosis to enable personalized healthcare with clinical decision support tools

- Comprehensive genomic profiling (CGP) maximizes the ability to find clinically actionable alterations, **guiding treatment decisions** for individual patients across all cancer types.
- Molecular tumor board (MTB) serves as a critical platform for **optimizing next-generation sequencing (NGS) utilization and interpretation**, aiding in genetic information interpretation, treatment recommendations, and data generation. Adherence to MTB recommendations have led to **improved patient outcomes**, such as prolonged progression-free survival (PFS), overall survival (OS), and time to progression.[1-5]
    - In Taiwan, NGS will be reimbursed in Q3 of 2024; hence, **proper establishment of MTB is essential**. A Taiwan MTB consensus is currently under development and aims to provide guidance for implementation of a robust MTB system.
    - In Italy, NGS is reimbursed for tumors with European Society for Medical Oncology Scale for Clinical Actionability of Molecular Targets 1 or 2 molecular targets, which includes lung cancer, biliary tract cancer, and ovarian cancer. Select cases are discussed during weekly MTB sessions to **enhance the understanding of mutation biology** and **match the patient to the appropriate drug**.
- Clinicians and pathologists encounter a range of challenges in the implementation of precision medicine.
    - For clinicians, barriers to the implementation of precision medicine include lack of integration of data across multiple platforms, genomic and patient diversity across regions, absence of funding for precision medicine programs, and lack of access to treatments across diverse populations.
    - The challenges faced by pathologists mainly involve the **interpretation of sequenced data**, due to the wide range of genomic alterations available, and the accurate matching of gene alteration data with the appropriate treatment recommendation.
- The use of **digital solutions**, such as navify® Tumor Board and Oncology Hub, can support multidisciplinary discussions by integrating data from different systems and facilitating an efficient workflow.

## Session 2: Navigating the lung cancer journey from early to advanced

Anaplastic lymphoma kinase (ALK)-positive NSCLC

- ALK mutations occur in approximately 4–5% of patients with non-small cell lung cancer (NSCLC), and demonstrate **good prognosis** with a median OS of over 5 years when treated with an ALK tyrosine kinase inhibitor (TKI).
- 2nd generation ALK TKIs, such as alectinib and brigatinib, and 3rd generation ALK TKIs are the standard first-line (1L) treatment, as they result in **improved outcomes**, such as PFS and OS, compared with chemotherapy or 1st generation ALK TKIs.[6–8]
    - 2nd and 3rd generation ALK TKIs have also demonstrated **good intracranial activity**,[9,10] which is crucial in managing the elevated central nervous system (CNS) metastatic risk associated with ALK-positive disease.
    - The choice of treatment depends on the efficacy, safety, CNS activity, and cost of the treatment, the mutation profile of the tumor, and the clinician's preference.
- The **mechanism of resistance** after 1L treatment is heterogenous and affects subsequent treatment choices. Lorlatinib showed reasonable response after 1L treatment with a 2nd generation ALK TKI; however, use of lorlatinib in the later-line setting may lead to compound *ALK* mutations.

Epidermal growth factor receptor (EGFR)-positive NSCLC

- The prevalence of EGFR mutations in NSCLC is markedly higher in Asian populations (40–60%) compared with Western populations (10–15%).
- The 2023 European Society for Medical Oncology clinical practice guidelines for NSCLC recommend osimertinib as the **1L treatment option** for advanced EGFR-mutated NSCLC.[11] A range of other treatment options are under evaluation, including 1st/2nd generation EGFR TKIs alone, 1st generation TKIs combined with either chemotherapy or anti-angiogenic therapy, and osimertinib combined with either chemotherapy or mesenchymal epithelial transition-targeting therapy.
- A biopsy and mutation testing should be repeated after disease progression with 1L treatment. The **recommended second-line (2L) treatment option** is platinum-doublet chemotherapy if no resistance mechanism was identified.[11] Other 2L options include osimertinib (if a 1st/2nd generation EGFR TKI was used in 1L), the combination of atezolizumab, bevacizumab, and chemotherapy, and the combination of amivantamab, lazertinib, and chemotherapy.
- In clinical practice, the choice of treatment is influenced by drug-related factors (e.g. approval and reimbursement status, toxicity, and convenience), patient-related factors (e.g. age, comorbidities, performance status, preference, and quality of life), and disease-related factors (e.g. presence of CNS metastasis, mutation subtype, and disease burden).
- There is a **need for improved biomarkers**, such as circulating free deoxyribonucleic acid and p53 mutation, to improve patient stratification and selection of therapeutics.

Use of immunotherapy (IO) for treatment of early resectable NSCLC

- The positive data obtained from multiple Phase III clinical trials have led to the **integration of IO and targeted therapy** in the treatment of resectable NSCLC, representing a major advancement in standard therapeutic approaches.
- In early-stage NSCLC, results from multiple clinical trials indicate that neoadjuvant IO resulted in **similar or better outcomes** compared with adjuvant IO,[12–16] although such cross-trial comparison should be interpreted with caution.
    - Although the incidence of grade 3–4 treatment-related adverse events with neoadjuvant IO ranged from 27–44%, majority of the patients (74–94%) completed the planned dose of neoadjuvant IO. Moreover, neoadjuvant IO did not compromise the patient's eligibility for surgery, and may potentially improve the resectability of certain types of tumors.
- The decision to treat with adjuvant IO depends on the **pathological response** following neoadjuvant IO and surgery, with consideration for associated costs and toxicity of adjuvant IO.
- Patients with a **higher PD-L1 status** were associated with a better event-free survival and pathological complete response after treatment with IO, whereas patients who were never smokers or had stage II lung cancer had worse outcomes with perioperative IO.
    - Additional biomarkers, such as gene inflammatory signatures, aneuploidy, and co-mutations, should be explored as they can potentially guide IO treatment selection to optimize patient outcomes.

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