Ology Medical Education

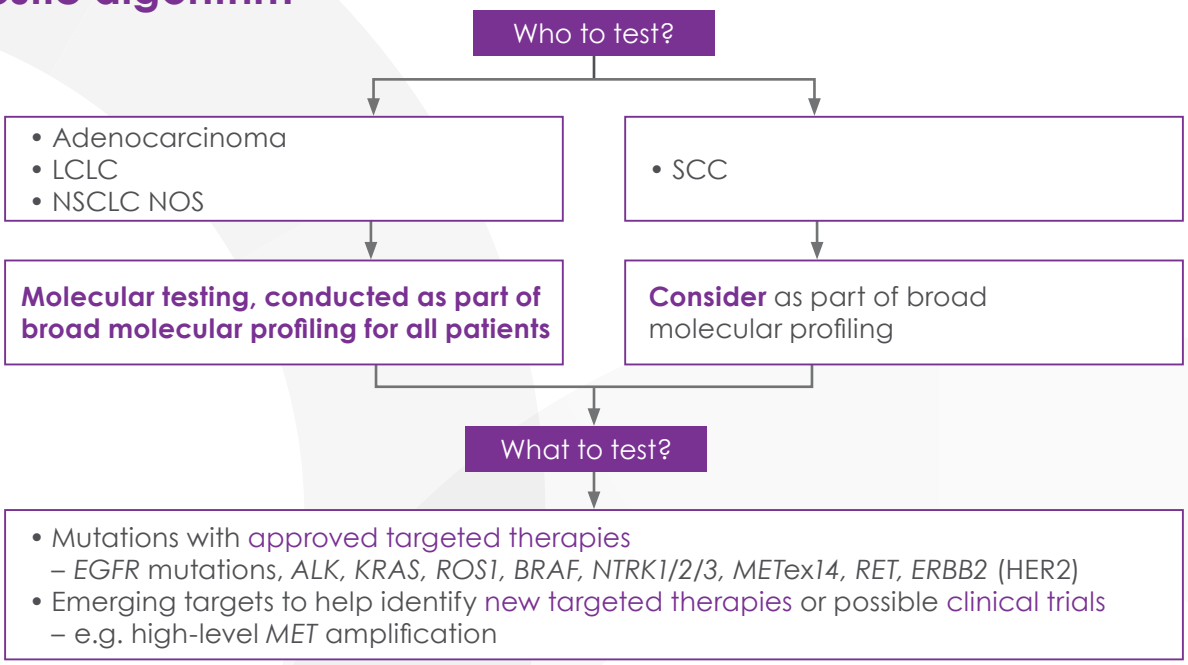
Practice guide

Biomarker landscape in advanced NSCLC care

Biomarkers and targeted therapies in NSCLC

- NSCLC is a diverse disease with multiple oncogenic drivers; individual patients display a wide variation in the drivers that are present
- The introduction of numerous treatments targeting specific oncogenic alterations has allowed for personalized, precision care in NSCLC
- Biomarker testing is necessary to choose the optimal initial therapy for advanced NSCLC and avoid therapies unlikely to provide clinical benefit
- Testing should also be considered after acquired resistance to targeted therapy

Diagnostic algorithm



What type of molecular testing should be performed?

The use of NGS, rather than single-gene testing, is preferred

- Conventional tests such as PCR and FISH may lack sensitivity for many important biomarkers

RNA-based NGS may improve diagnosis of some mutations (e.g. fusions and *MET*ex14)

- Consider for patients without identifiable driver oncogenes in broad panel DNA testing (especially in never smokers)

Tissue samples or "liquid biopsies" (blood-based; cfDNA testing) can be used for molecular testing

- Concurrent use of tissue and liquid biopsy has been shown to improve biomarker detection

Developed in collaboration with Stephen Liu, MD.

Current targeted therapies for biomarker-positive advanced NSCLC

Mutation	Recommended targeted therapies[a]
EGFR exon 19 deletion or L858R mutation positive	Osimertinib[a], afatinib, gefitinib, dacomitinib, erlotinib (± ramucirumab or bevacizumab)
EGRF S768I, L861Q, and/or G719X mutation positive	Afatinib[a], osimertinib[a], erlotinib, gefitinib, dacomitinib
*EGRF*ex20 insertion mutation positive	Amivantamab[b], mobocertinib[b]
ALK rearrangement positive	Alectinib[a], brigatinib[a], lorlatinib[a], ceritinib, crizotinib
KRAS G12C mutation positive	Sotorasib[c]
ROS1 rearrangement positive	Crizotinib[a], entrectinib[a], ceritinib
BRAF V600E rearrangement positive	Dabrafenib[a] + trametinib[a], vemurafenib, dabrafenib
*NTRK*1/2/3 gene fusion positive	Larotrectinib[a], entrectinib[a]
*MET*ex14 skipping mutation positive	Tepotinib[a], capmatinib[a], crizotinib
RET rearrangement positive	Selpercatinib[a], pralsetinib[a], cabozantinib
ERBB2 (HER2) mutation positive	Fam-trastuzumab deruxtecan-nxki[ac], ado-trastuzumab emtansine[c]

[a] NCCN preferred therapy. [b] For patients who have progressed on or after platinum-based chemotherapy.
[c] For patients who have received at least one prior systemic therapy.

Abbreviations

ALK, anaplastic lymphoma kinase; *BRAF*, B-rapidly accelerated fibrosarcoma; CME, continuing medical education; cfDNA, cell-free DNA; *EGFR*, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; HER, human epidermal growth factor receptor; *KRAS*, Kirsten rat sarcoma; LCLC, large-cell lung carcinoma; *MET*, mesenchymal epithelial transition; *MET*ex14, MET exon 14 skipping mutation; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; NOS, not otherwise specified; NSCLC, non-small-cell lung cancer; *NTRK*, neurotrophic tyrosine receptor kinase; PCR, polymerase chain reaction; *RET*, rearranged during transfection; *ROS*, reactive oxygen species; SCC, squamous cell carcinoma.

References

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Access the CME program "Expert insights on biomarker testing in advanced personalized NSCLC care" at **https://ologyeducation.org**

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