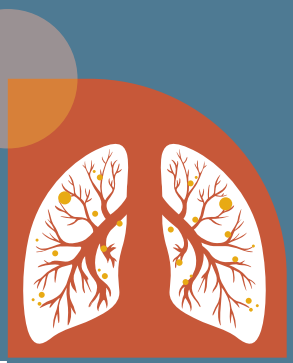
*BRAF*V600E mutations in NSCLC: Testing & treatment



1. Why it matters[1]

- *BRAF*V600E is a Tier 1 actionable mutation in NSCLC
- *BRAF*V600E targeted therapy improves outcomes in the 1st line setting as well as 2nd line
- Identify early to initiate the right therapy first

2. Optimal testing strategy[1–3]

WHEN

At diagnosis
of advanced/ metastatic NSCLC

Before
initiating systemic therapy

At disease progression
(rebiopsy when possible)

WHAT

Tissue biopsy preferred
(FFPE block)

Liquid biopsy
is an option if tissue is insufficient, or as a complementary approach

Cytology samples
acceptable with validation

HOW

Next-generation sequencing (NGS)
is preferred. Full panel testing including *BRAF* plus other relevant mutations/alterations (e.g., *ALK*, *EGFR*, *ERBB2* (*HER2*), *KRAS*, *MET*, *NTRK*, *RET*, *ROS1*)

Polymerase chain reaction (PCR)
acceptable for single gene testing strategies but quantity of tissue needs to be considered if using a step-by-step testing approach

3. Interpreting and reporting results

Report using a clinically relevant nomenclature, not only in a formal nomenclature. For example: *BRAF* p.V600E (c.1799T>A)

Include:

- Allele frequency
- Clinical significance (predictive of response to targeted therapy, ESCAT classification (where appropriate))[4]
- Recommended action (e.g., "Eligible for BRAF/MEK inhibitor therapy")

1. Planchard D, et al. NPJ Precis Oncol. 2024;8:90. **2.** Hendriks LE, et al. Ann Oncol. 2023;34:339-57 (including Supplementary appendix).
3. NCCN Guidelines Version 8. 2025: Non-Small Cell Lung Cancer. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf (Accessed Aug 2025).

COR2ED
THE HEART OF MEDICAL EDUCATION

4. Avoid delays and sub-optimal treatment[4]

- Don't start chemotherapy/chemo-immunotherapy without mutation status unless patient has rapidly progressing disease
- Targeted therapy can be more effective and less toxic than chemotherapy/chemo-immunotherapy
- Develop systems to:
  - Expedite testing
  - Coordinate sample handling
  - Communicate results quickly

5. Therapeutic implications for NSCLC patients with *BRAF*V600E mutations[5–9]

Ideally first-line treatment with targeted therapy (BRAF & MEK inhibitors):

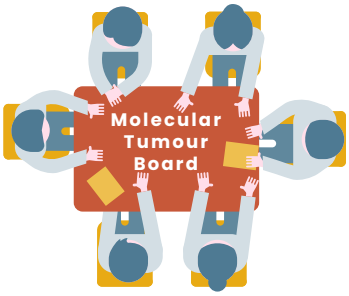
- **Dabrafenib + trametinib**
- **Encorafenib + binimetinib**
  - Approved in 1st and 2nd line settings
  - Durable responses in both previously treated and treatment-naive patients
  - Common adverse events: pyrexia and GI related AEs (nausea, diarrhea, vomiting, fatigue)

6. Multidisciplinary collaboration is critical

Pathologists + Oncologists + Pulmonologists + Radiologists

Molecular tumour boards accelerate:

- Interpretation of biomarker results and consideration of patient characteristics
- Prioritisation of co-mutations
- Therapy initiation
- Clinical decision-making



7. Reassure patients

- Reframe: "A mutation" = **an opportunity**
- Targeted therapy = personalised treatment, oral therapy, fewer side effects than chemotherapy
- Helps set expectations and improves trust in care plan

TEST EARLY INTERPRET ACCURATELY TREAT PRECISELY

For patients with *BRAF*V600E-mutated NSCLC, timing and teamwork make all the difference.

Abbreviations: AEs, adverse events; ESCAT, ESMO Scale for Clinical Actionability of molecular Targets; ESMO, European Society for Medical Oncology; FFPE, Formalin-Fixed Paraffin-Embedded; HCP, health care professionals; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; PCR, polymerase chain reaction; ROI, Republic of Ireland; UK, United Kingdom.

Supporter acknowledgement: Supported by an Independent Educational Grant from Pierre Fabre Laboratories. This content is intended for HCPs outside the UK & ROI only.

4. Mateo J, et al. Annals of Oncology 2018;29: 1895-902. **5.** Planchard D, et al. Lancet Oncol. 2016;17:984-93. **6.** Planchard D, et al. Lancet Oncol. 2017;18:1307-16. **7.** Planchard D, et al. J Thorac Oncol. 2022;17:103-15. **8.** Riely GJ, et al. J Clin Oncol. 2023;41:3700-11. **9.** Riely GJ, et al. Ann Oncol. 2024;35:S1246-S1247 (presented at ESMO 2024).

COR2ED
THE HEART OF MEDICAL EDUCATION