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THE EVOLVING TREATMENT LANDSCAPE IN *BRAF*^{V600E} MUTATED NSCLC

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DEVELOPED BY LUNG CONNECT

This programme is developed by LUNG CONNECT, an international group of experts in the field of thoracic oncology and brought to you alongside PRECISION ONCOLOGY CONNECT, an international group of experts in the field of detection and treatment of targetable genetic/genomic alterations in various cancers

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CLINICAL TAKEAWAYS

- *BRAF*^{V600E} is an actionable mutation for metastatic NSCLC with effective and well-tolerated treatment options available
- The *BRAF* mutation should be tested for at the time of first diagnosis for all patients with advanced NSCLC
- Only around half of patients with metastatic NSCLC receive a second-line treatment, so the most appropriate, efficacious treatments should be used in the first-line setting
- BRAF-targeted treatment combinations are approved for first-line treatment of NSCLC

NSCLC, non-small cell lung cancer

EDUCATIONAL OBJECTIVES

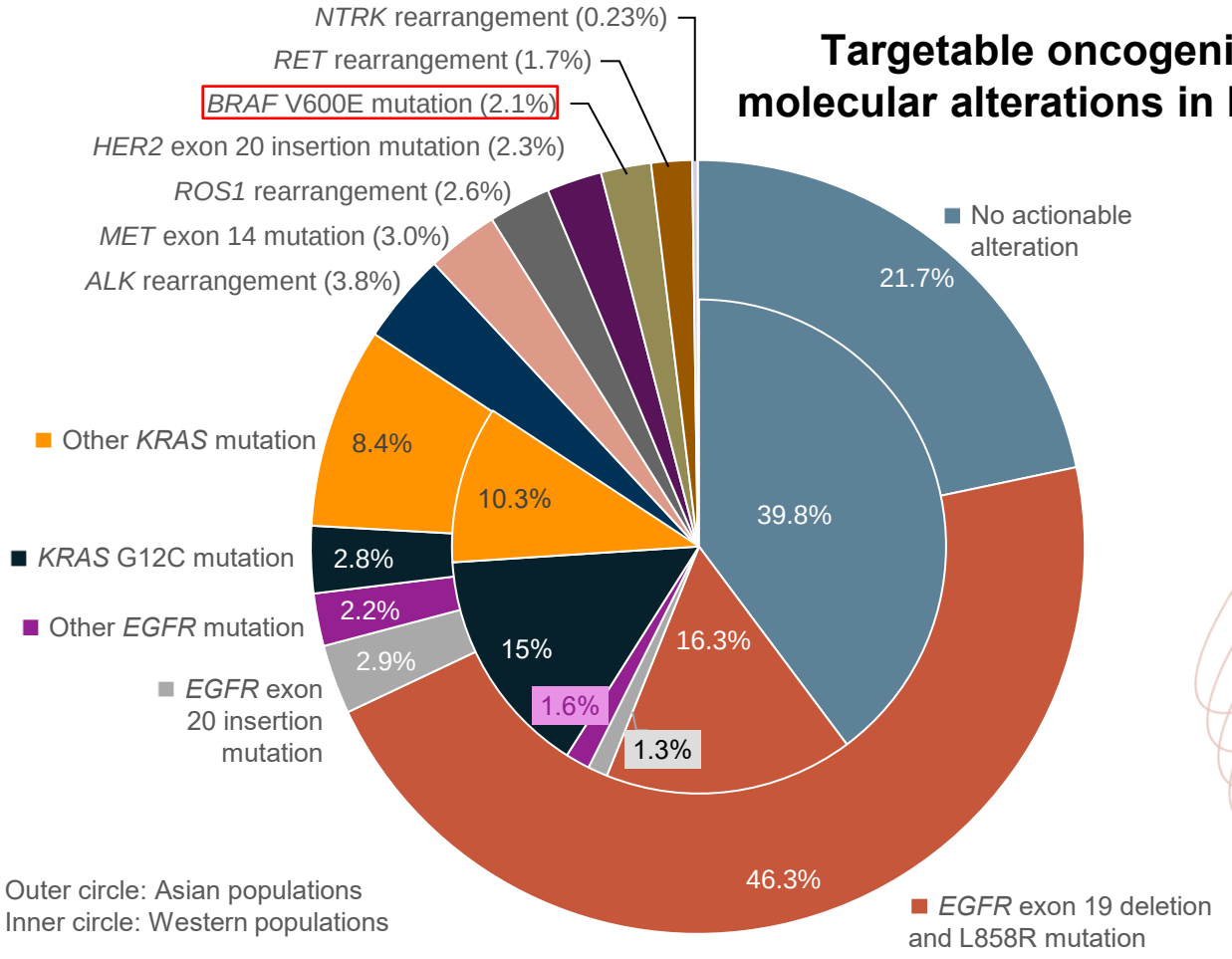
1. Understand the clinical trial data and emerging profile (efficacy and potential toxicities) of therapies for the treatment of *BRAF*^{V600E} mutated NSCLC

2. Recognise the appropriate placement of therapies for the treatment of *BRAF*^{V600E} mutated NSCLC across the patient journey

NSCLC, non-small cell lung cancer

DRIVER MUTATIONS IN NSCLC

- Non-small cell lung cancer (NSCLC), which constitutes >80% of all lung cancers, remains a leading cause of cancer-related deaths worldwide[1]
- Numerous oncogenic driver mutations that contribute to the molecular pathogenesis of lung cancers have been characterised, leading to the development of targeted therapies for NSCLC patients[2]



BRAF, B-Raf proto-oncogene; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; KRAS, Kirsten ras oncogene; MET, MET proto-oncogene; NTRK, neurotrophic tyrosine receptor kinase; RET, RET proto-oncogene; ROS1, ROS proto-oncogene 1 receptor tyrosine kinase

1. Zhen D, et al. Oncotarget. 2016;7:41691-41702; 2. Tan AC and Tan DSW. J Clin Oncol. 2022;40:611-25

OVERVIEW OF *BRAF* MUTATIONS

- Mutations in the **v-Raf murine sarcoma viral oncogene homolog B (*BRAF*) gene** are found in approximately 4–8% of all cancers, with the greatest number found in colorectal cancer, melanoma, and non-small cell lung cancer (NSCLC)[1]
- The most common *BRAF* mutation is a point mutation (T1799A) resulting in an amino acid substitution at codon 600 (V600E), which confers constitutive BRAF kinase activity[1]
- ***BRAF* V600E accounts for ~1–2% of NSCLCs**, making it an actionable therapeutic target[1]
- *BRAF* mutations are classified into three different classes based on their biological characteristics:
  - **Class 1: kinase activated, codon 600,** e.g. V600E, V600K, V600D[1-3]
  - **Class 2: kinase activated, non-codon 600**, e.g. K601E, L597V/Q/R, G469V/S/R/E/A, G464V[1-3]
  - **Class 3: kinase impaired,** e.g. G596R, D594Y/N/G/E, N581Y/S/I, G466V/L/E/ A, D287Y[1-3]
- Currently **approved BRAF inhibitors effectively inhibit only class 1** mutant proteins and show substantially less efficacy against BRAF-mutant dimers[1]

NSCLC, non-small cell lung cancer

1. Planchard D, et al. NPJ Precis Oncol. 2024;8:90; 2. Tabbò F, et al. Cancer Treat Rev. 2022;103:102335; 3. Guaitoli G, et al. Drugs Context. 2023;12: 2022-11-3

CLINICAL CHARACTERISTICS

- ***BRAF* mutations are predominantly found in adenocarcinomas (>85%).** However, there is no clear association of *BRAF* mutation status with other patient characteristics, such as age, ethnicity, and sex[1]
- The **majority of patients with *BRAF* mutated NSCLC are current or former smokers:**[2]
  - 20-30% of patients harbouring V600E mutations are never smokers
  - almost all patients with non-V600E alterations are heavy smokers
- **Metastatic spread to the central nervous system** appears to be frequent in patients with *BRAF* mutated NSCLC,[3] similar to other molecularly driven lung cancers[4]. The incidence of brain metastases at diagnosis is significantly lower for patients with class 1 alterations compared with class 2 and 3[5]

NSCLC, non-small cell lung cancer

1. Planchard D, et al. NPJ Precis Oncol. 2024;8:90; 2. Tabbò F, et al. Cancer Treat Rev. 2022;103:102335; 3. Guaitoli G, et al. Drugs Context. 2023;12: 2022-11-3; 4. Weller M, et al. Cancer Treat Rev. 2024;130102807; 5. Dagogo-Jack I, et al. Clin Cancer Res. 2019; 25: 158-65

COMBINATION OF BRAF INHIBITORS AND MEK INHIBITORS

- Despite effective anti-tumour activity of BRAF inhibitors **(vemurafenib, dabrafenib, encorafenib)** in mutated cancers, resistance eventually develops, mostly due to MAPK pathway reactivation, leading to subsequent disease progression[1]
- It was hypothesised that dual MAPK pathway inhibition with BRAF and MEK inhibitors in *BRAF*^{V600E}-mutant NSCLC might improve efficacy over BRAF inhibitor monotherapy based on observations in *BRAF*^{V600}-mutant melanoma and delay the onset of resistance[2]
- A number of BRAF inhibitor + MEK inhibitor combinations have shown efficacy in *BRAF*-mutant NSCLC[1,3]

BRAF inhibitor	MEK inhibitor
Dabrafenib	Trametinib
Encorafenib	Binimetinib

NSCLC, non-small cell lung cancer

1. Tabbò F, et al. Cancer Treat Rev. 2022;103:102335; 2. Planchard D, et al. Lancet Oncol. 2016;17:984-93; 3. Riely GJ, et al. J Clin Oncol. 2023;41:3700-11

TIMELINE OF TREATMENT ADVANCEMENTS FOR *BRAF* MUTATED NSCLC

- The identification of *BRAF* mutations, especially V600E, and their role in cancer led to the development of highly-selective BRAF inhibitors such as vemurafenib, dabrafenib, and encorafenib[1]
- Both vemurafenib and dabrafenib have confirmed activity against V600E, V600K, V600R, and V600D *BRAF* mutations[1]
- Encorafenib has confirmed activity against *BRAF*^{V600E} and *BRAF*^{V600K} mutants and *BRAF*^{WT} [1]

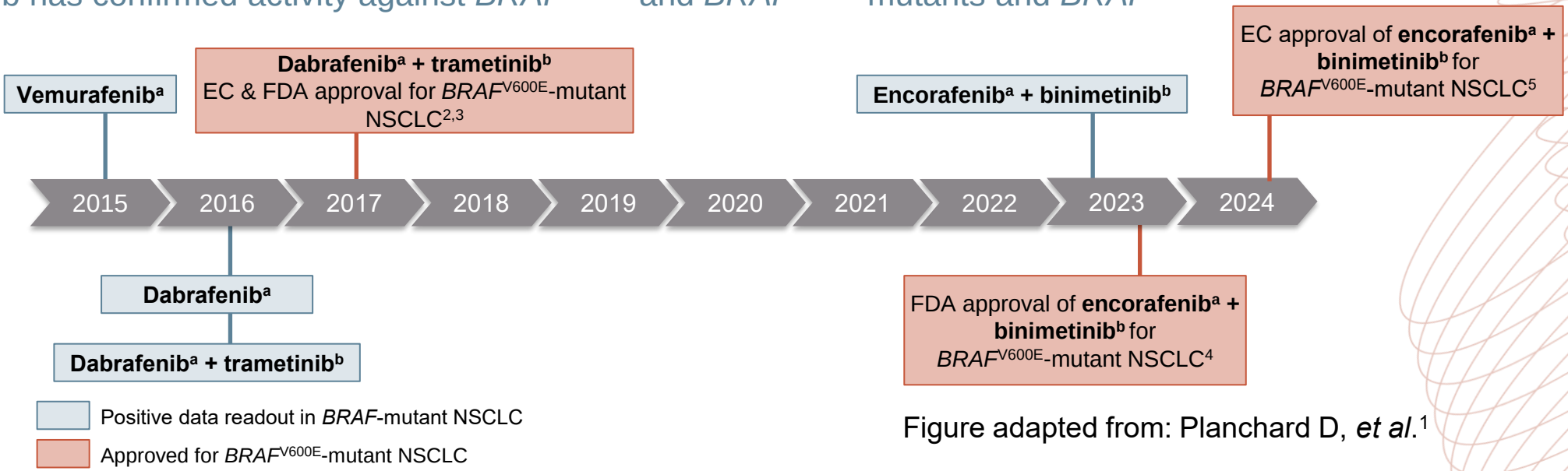


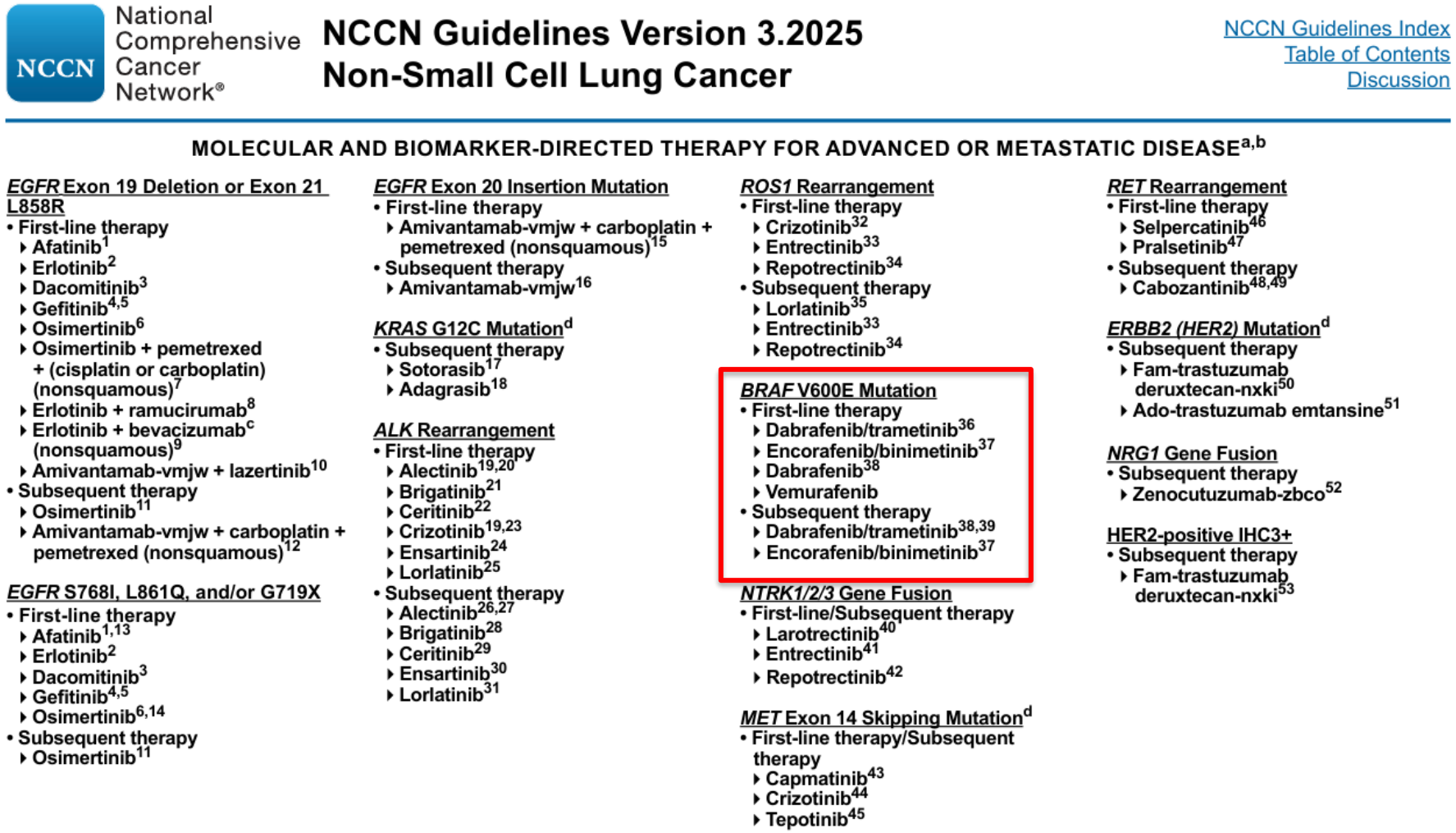
Figure adapted from: Planchard D, *et al*.[1]

[a] BRAF inhibitors. [b] MEK inhibitors.

EC, European Commission; FDA, Food and Drug Administration; NSCLC, non-small cell lung cancer; WT, wild-type

1. Planchard D, et al. NPJ Precis Oncol. 2024;8:90; 2. Novartis' lung cancer drug combination receives EU approval. Available here. 3. FDA grants regular approval to dabrafenib and trametinib combination for metastatic NSCLC with BRAF V600E mutation. Available here. 4. FDA approves encorafenib with binimetinib for metastatic non-small cell lung cancer with a BRAF V600E mutation. Available here. 5. EMA Recommends Extension of Therapeutic Indications for Encorafenib and Binimetinib. Available here. All accessed Feb 2025

NCCN: DRIVER MUTATIONS IN NSCLC AND TARGETED THERAPY OPTIONS



National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2025
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

MOLECULAR AND BIOMARKER-DIRECTED THERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b]

***EGFR* Exon 19 Deletion or Exon 21 L858R**
- First-line therapy
  - Afatinib[1]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6]
  - Osimertinib + pemetrexed + (cisplatin or carboplatin) (nonsquamous)[7]
  - Erlotinib + ramucirumab[8]
  - Erlotinib + bevacizumab[c] (nonsquamous)[9]
  - Amivantamab-vmjw + lazertinib[10]
- Subsequent therapy
  - Osimertinib[11]
  - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)[12]

***EGFR* S768I, L861Q, and/or G719X**
- First-line therapy
  - Afatinib[1,13]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6,14]
- Subsequent therapy
  - Osimertinib[11]

***EGFR* Exon 20 Insertion Mutation**
- First-line therapy
  - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)[15]
- Subsequent therapy
  - Amivantamab-vmjw[16]

***KRAS* G12C Mutation[d]**
- Subsequent therapy
  - Sotorasib[17]
  - Adagrasib[18]

***ALK* Rearrangement**
- First-line therapy
  - Alectinib[19,20]
  - Brigatinib[21]
  - Ceritinib[22]
  - Crizotinib[19,23]
  - Ensartinib[24]
  - Lorlatinib[25]
- Subsequent therapy
  - Alectinib[26,27]
  - Brigatinib[28]
  - Ceritinib[29]
  - Ensartinib[30]
  - Lorlatinib[31]

***ROS1* Rearrangement**
- First-line therapy
  - Crizotinib[32]
  - Entrectinib[33]
  - Repotrectinib[34]
- Subsequent therapy
  - Lorlatinib[35]
  - Entrectinib[33]
  - Repotrectinib[34]

***BRAF* V600E Mutation**
- First-line therapy
  - Dabrafenib/trametinib[36]
  - Encorafenib/binimetinib[37]
  - Dabrafenib[38]
  - Vemurafenib
- Subsequent therapy
  - Dabrafenib/trametinib[38,39]
  - Encorafenib/binimetinib[37]

***NTRK1/2/3* Gene Fusion**
- First-line/Subsequent therapy
  - Larotrectinib[40]
  - Entrectinib[41]
  - Repotrectinib[42]

***MET* Exon 14 Skipping Mutation[d]**
- First-line therapy/Subsequent therapy
  - Capmatinib[43]
  - Crizotinib[44]
  - Tepotinib[45]

***RET* Rearrangement**
- First-line therapy
  - Selpercatinib[46]
  - Pralsetinib[47]
- Subsequent therapy
  - Cabozantinib[48,49]

***ERBB2 (HER2)* Mutation[d]**
- Subsequent therapy
  - Fam-trastuzumab deruxtecan-nxki[50]
  - Ado-trastuzumab emtansine[51]

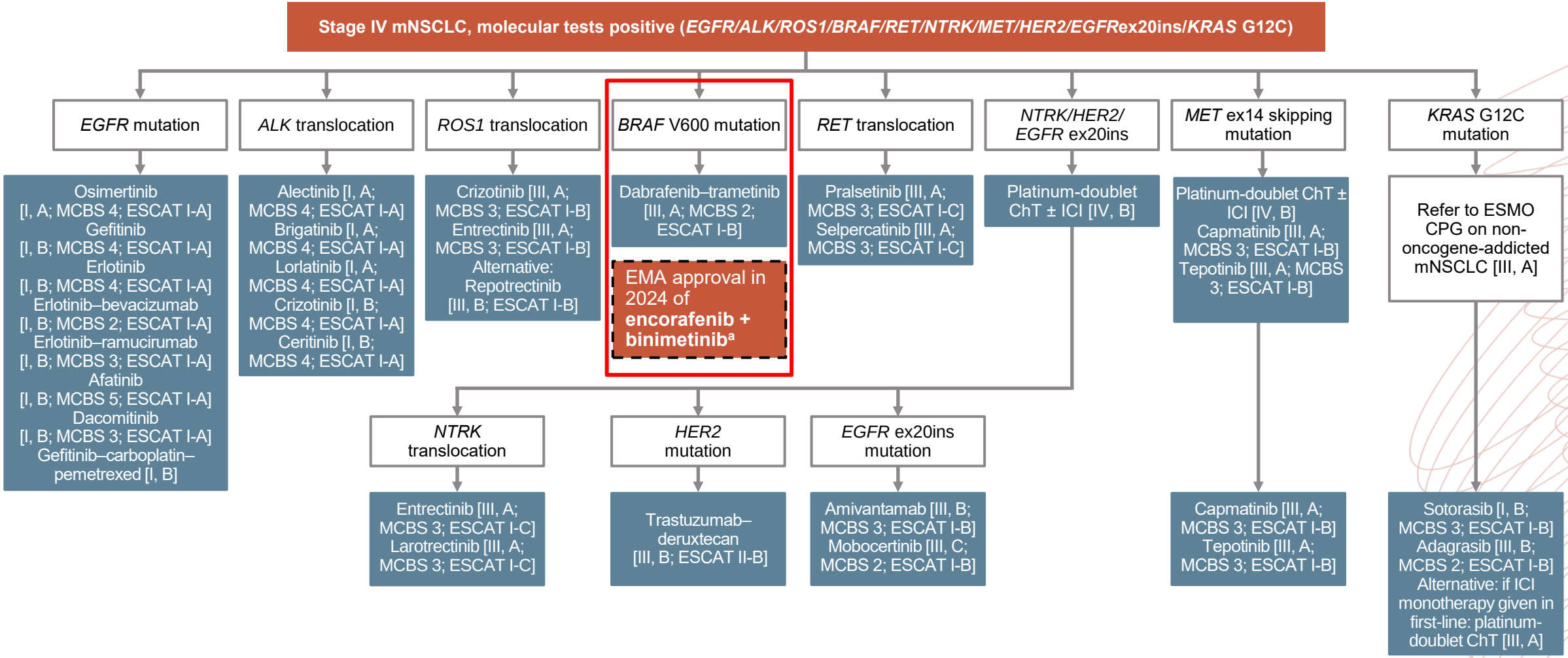
***NRG1* Gene Fusion**
- Subsequent therapy
  - Zenocutuzumab-zbco[52]

HER2-positive IHC3+
- Subsequent therapy
  - Fam-trastuzumab deruxtecan-nxki[53]

NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer

NCCN Guidelines Version 3.2025. Non-Small Cell Lung Cancer. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf (accessed Feb 2025)

ESMO: DRIVER MUTATIONS IN NSCLC AND TARGETED THERAPY OPTIONS[1]



[a] Encorafenib + binimetinib received EMA approval for the treatment of adult patients with advanced NSCLC with a *BRAF* V600E mutation in August 2024 – awaiting next update of ESMO guidelines[2]

ChT, chemotherapy, CPG, clinical practice guidelines; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; ESMO, European Medical Society for Oncology; ex20ins, exon 20 insertion; ICI, immune checkpoint inhibitor; MCBS, ESMO-Magnitude of Clinical Benefit Scale; (m)NSCLC, (metastatic) non-small cell lung cancer

1. Hendriks LE, et al. Ann Oncol. 2023;34:339-57; 2. EMA Recommends Extension of Therapeutic Indications for Encorafenib and Binimetinib. Available here (accessed Feb 2025)

DABRAFENIB PLUS TRAMETINIB: EFFICACY

IN PREVIOUSLY TREATED *BRAF*^{V600E}-MUTANT mNSCLC (COHORT B)

Anti-tumour activity[a]	Primary analysis (DCO Oct 7th 2015)[1] n=57	5-year analysis (DCO Feb 24th 2021)[2] n=57
Best response, n (%)		
CR	2 (4)	3 (5)
PR	34 (60)	36 (63)
SD	9 (16)	7 (12)
PD	7 (12)	7 (12)
NE	5 (9)	4 (7)
ORR (CR + PR), n (%); [95% CI]	36 (63.2); [49.3-75.6]	39 (68.4); [54.8-80.1]
DCR (CR + PR + SD), n (%); [95% CI]	45 (78.9); [66.1-88.6]	46 (80.7); [68.1-90.0]
Median PFS [95% CI], months	9.7 [6.9-19.6]	10.2 [6.9-16.7]
Median OS [95% CI], months	–	18.2 [14.3-28.6]
Median duration of response [95% CI], months	9.0 [6.9-18.3]	9.8 [6.9-18.3]

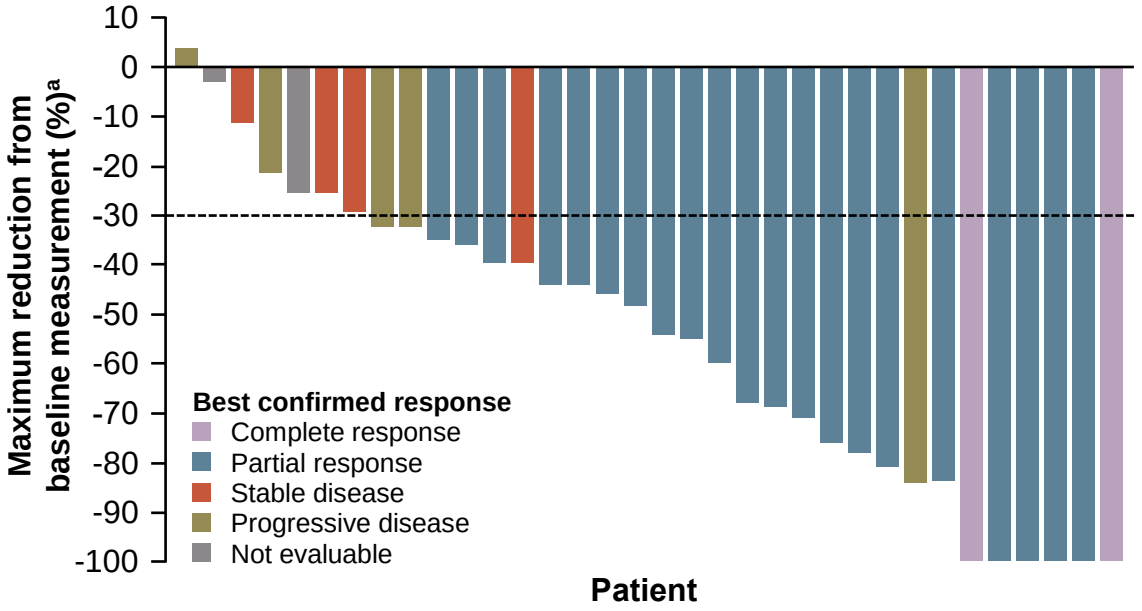
[a] Investigator assessed

CI, confidence interval; CR, complete response; DCO, data cutoff; DCR, disease control rate; mNSCLC, metastatic non-small cell lung cancer; NE, not evaluable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease

1. Planchard D, et al. Lancet Oncol. 2016;17:984-93; 2. Planchard D, et al. J Thorac Oncol. 2022;17:103-15

DABRAFENIB PLUS TRAMETINIB: TUMOUR RESPONSES

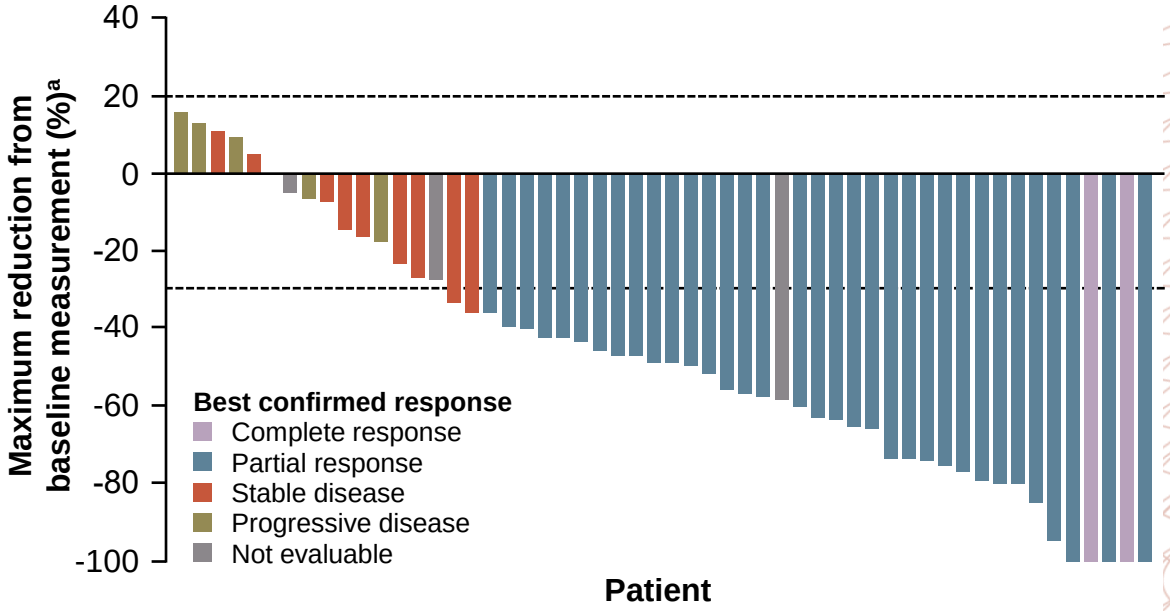
TREATMENT-NAÏVE PATIENTS[1]



Dashed line at −30% represents the threshold for partial response, according to RECIST version 1.1.

[a]By best confirmed response

PREVIOUSLY TREATED PATIENTS[2]



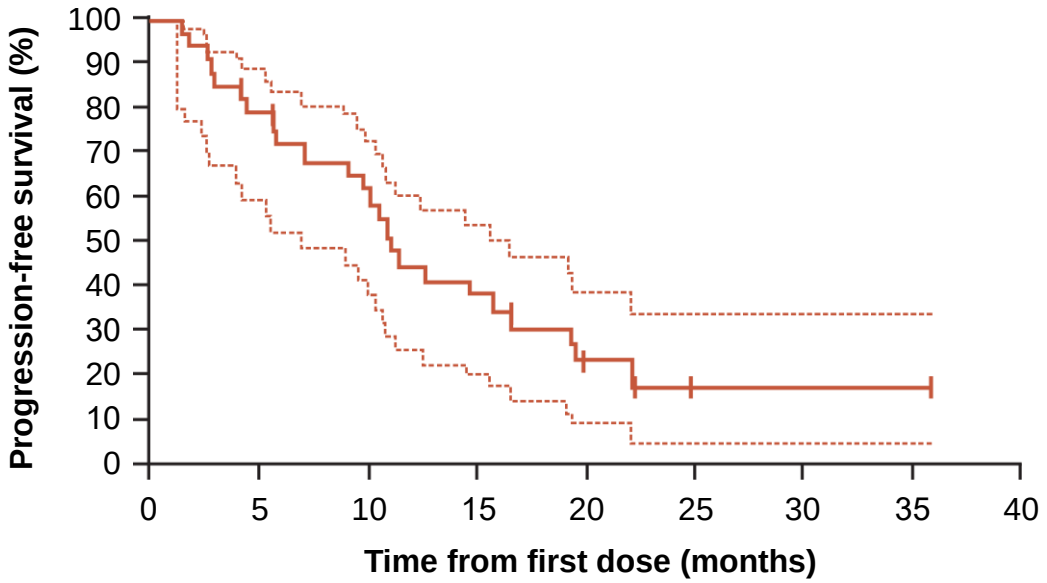
Dashed line at 20 represents the RECIST version 1.1 definition for progressive disease and the line at −30 represents the definition for partial response

RECIST, Response Evaluation Criteria In Solid Tumours

1. Planchard D, et al. Lancet Oncol. 2017;18:1307-16; 2. Planchard D, et al. Lancet Oncol. 2016;17:984-93

DABRAFENIB PLUS TRAMETINIB: PROGRESSION-FREE SURVIVAL

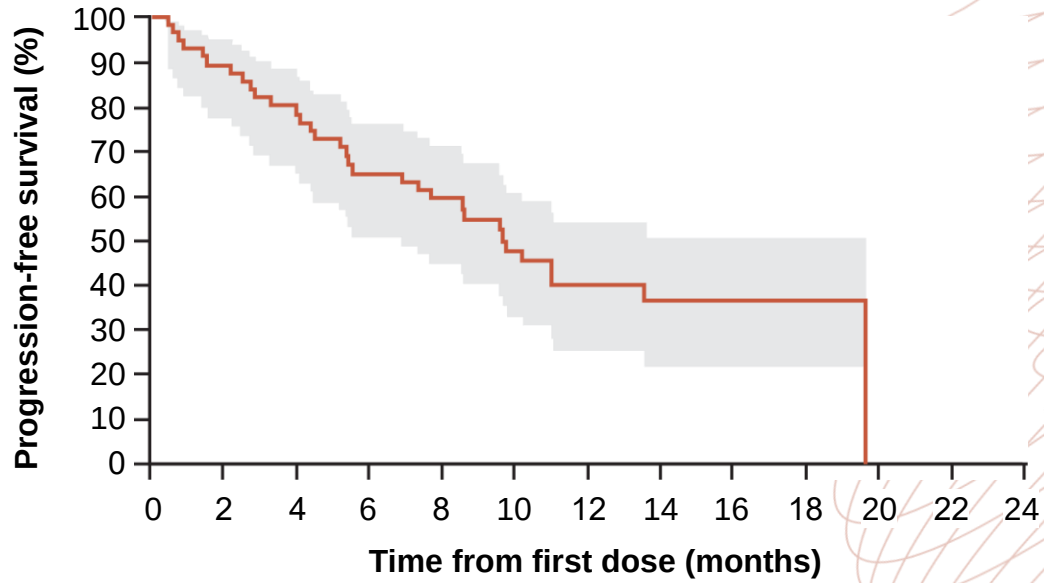
TREATMENT-NAÏVE PATIENTS[1]



No. at risk	36	25	18	11	4	1	1	1	0
No. censored	0	4	6	6	9	11	11	11	12

Tick marks represent censored patients. Dotted lines in Kaplan-Meier estimated curves represent 95% CIs.

PREVIOUSLY TREATED PATIENTS[2]



No. at risk	57	49	43	34	31	20	13	7	6	2	0	0	0
No. censored	0	2	3	4	4	10	14	19	20	24	25	25	25

Kaplan-Meier curve of investigator-assessed progression-free survival in patients receiving second-line or later treatment
Shaded area represents 95% CI. Number of patients censored represent cumulative totals

CI, confidence interval

1. Planchard D, et al. Lancet Oncol. 2017;18:1307-16; 2. Planchard D, et al. Lancet Oncol. 2016;17:984-93

TRAMETINIB PLUS DABRAFENIB: SAFETY

ADVERSE EVENTS (%) IN ≥10% OF PATIENTS[a]

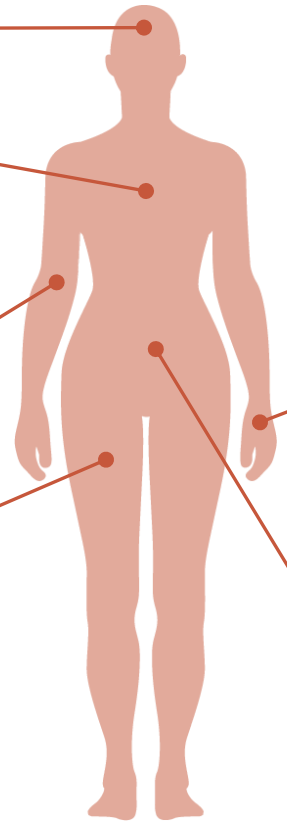
CNS	Grade 1/2	Grade ≥3
Dizziness	17	0
Headache	16	0

Respiratory	Grade 1/2	Grade ≥3
Dyspnoea	13	4
Cough	22	0
Chest pain[b]	11	0

Haematological	Grade 1/2	Grade ≥3
Anaemia	12	4
Neutropenia	6	6
ALP increased	10	0

Musculoskeletal	Grade 1/2	Grade ≥3
Arthralgia	16	1
Back pain	11	1
Myalgia	12	0

AEs led to dose modifications	
Dose reduction	37
Dose interruption	67
Permanent discontinuation	16



Systemic	Grade 1/2	Grade ≥3
Pyrexia	47	5
Chills	23	1
Fatigue	24	1
Asthenia	20	3
Hypotension	12	2
Hyponatremia	4	6
Peripheral oedema	28	0

Dermatological	Grade 1/2	Grade ≥3
Rash	19	2
Dry skin	28	1
Pruritus	12	2

Gastrointestinal	Grade 1/2	Grade ≥3
Nausea	46	0
Diarrhoea	32	2
Vomiting	31	3
Constipation	16	0
Decreased appetite	31	0
Decreased weight	14	1
Abdominal pain	12	1
Increased weight	8	2

[a] AEs shown for dabrafenib plus trametinib occurred in at least 10% of patients in combined data from interim analysis of treatment-naive and previously treated patients.
[b] Chest pain includes musculoskeletal chest pain

AE, adverse event; ALP alkaline phosphatase, CNS central nervous system

Adapted from Planchard D, et al. NPJ Precis Oncol. 2024;8:90

ENCORAFENIB PLUS BINIMETINIB: EFFICACY

IN TREATMENT-NAÏVE AND PREVIOUSLY TREATED *BRAF*^{V600E}-MUTANT mNSCLC

	Primary analysis (data cutoff: Sep 22, 2022)[1]		Current analysis (data cutoff: Apr 1, 2024)[2]	
	Treatment naïve n=59	Previously treated n=39	Treatment naïve N=59	Previously treated N=39
Objective response rate (95% CI), %[a]	75 (62, 85)	46 (30, 63)	75 (62, 85)	46 (30, 63)
Complete response, n (%)	9 (15)	4 (10)	9 (15)	4 (10)
Partial response, n (%)	35 (59)	14 (36)	35 (59)	14 (36)
Stable disease, n (%)	10 (17)	13 (33)	10 (17)	13 (33)
Progressive disease, n (%)	2 (3)	3 (8)	2 (3)	3 (8)
Disease control rate at 24 weeks (95% CI), %	64 (51, 76)	41 (26, 58)	64 (51, 76)	44 (28, 60)
Median time to response (range), months	1.9 (1.1-19.1)	1.7 (1.2-7.3)	1.9 (1.1-19.1)	1.7 (1.2-7.3)
Median duration of response (95% CI), months	NE (23.1, NE)	16.7 (7.4, NE)	40.0 (23.1, NE)	16.7 (7.4, NE)
Median PFS (95% CI), months	NE (15.7, NE)	9.3 (6.2, NE)	30.2 (15.7, NE)	9.3 (6.2, 24.8)
Median OS (95% CI), months	NE (26.7, NE)	NE (14.7, NE)	NE (31.3, NE)	22.7 (14.1, 32.2)

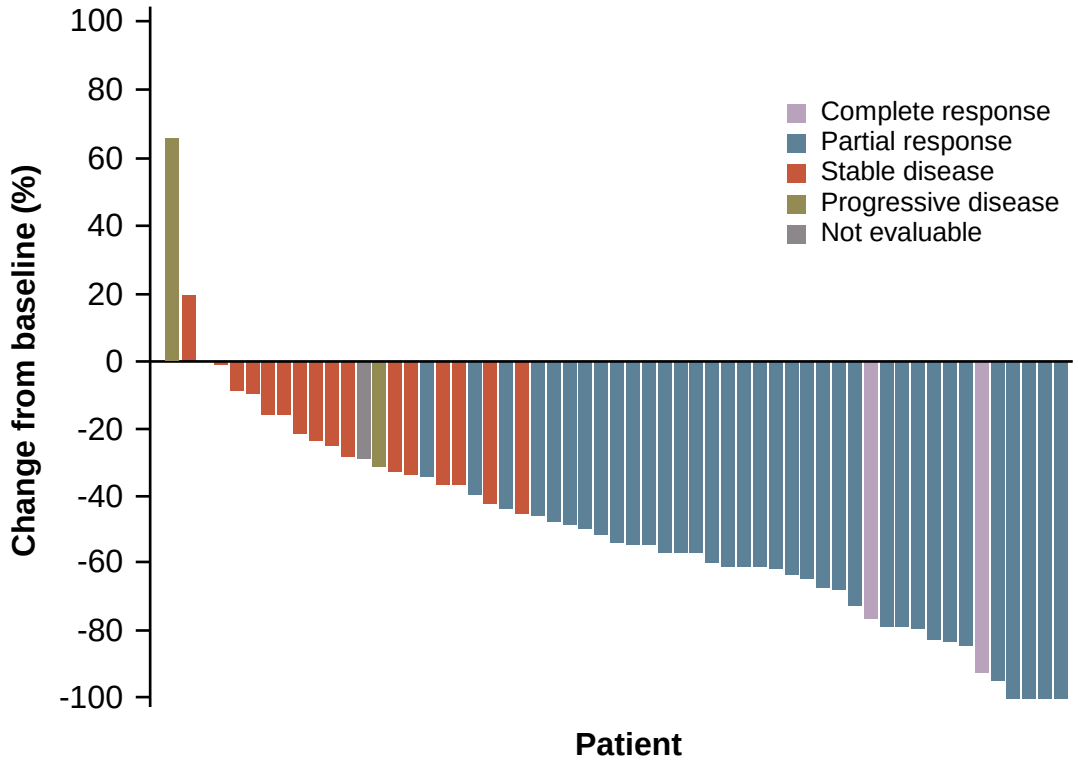
[a] Independent radiological review

CI, confidence interval; mNSCLC, metastatic non-small cell lung cancer; NE, not evaluable; OS, overall survival; PFS, progression-free survival

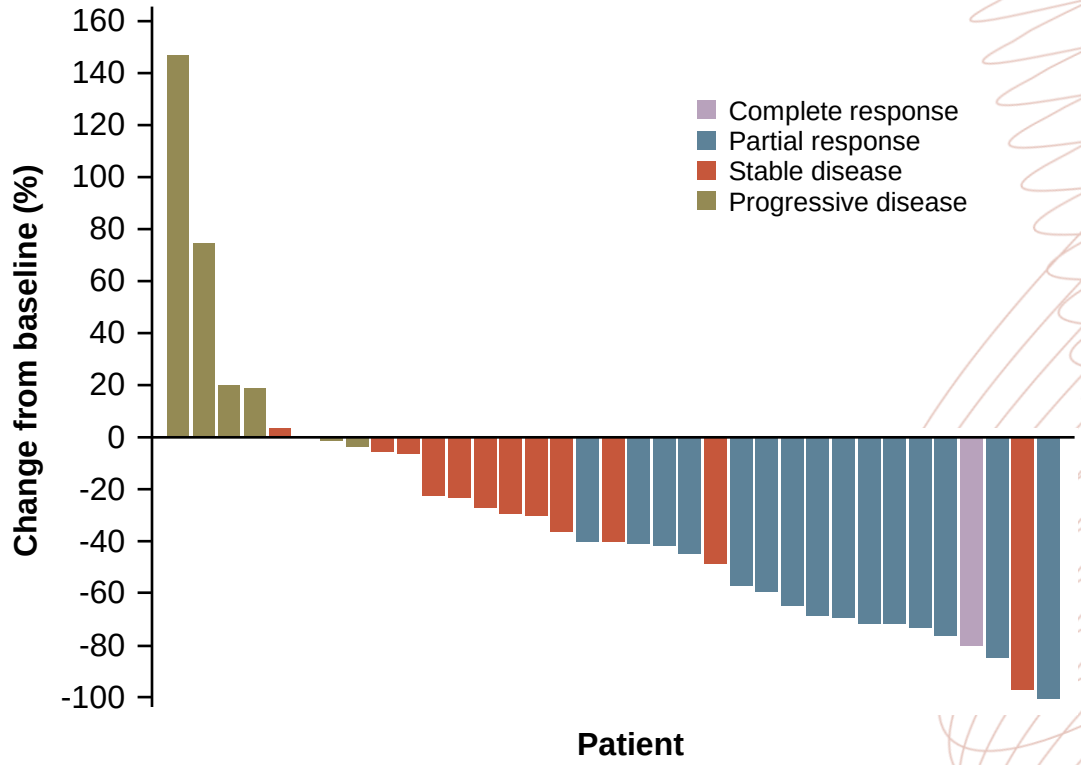
1. Riely GJ, et al. J Clin Oncol. 2023;41:3700-11; 2. Riely GJ, et al. Ann Oncol. 2024;35 (suppl 2):S1246-S1247 (ESMO 2024 oral presentation)

ENCORAFENIB PLUS BINIMETINIB: TUMOUR RESPONSES

TREATMENT-NAÏVE PATIENTS



PREVIOUSLY TREATED PATIENTS

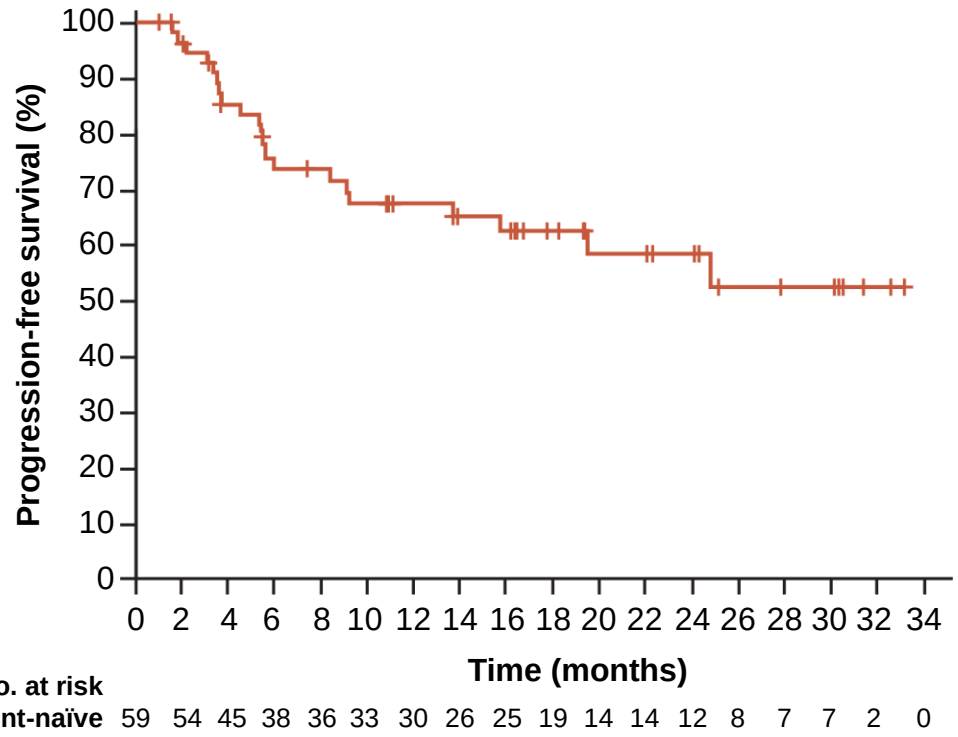


Patients for whom an assessment response was not evaluable at all tumour assessments were not included in this analysis

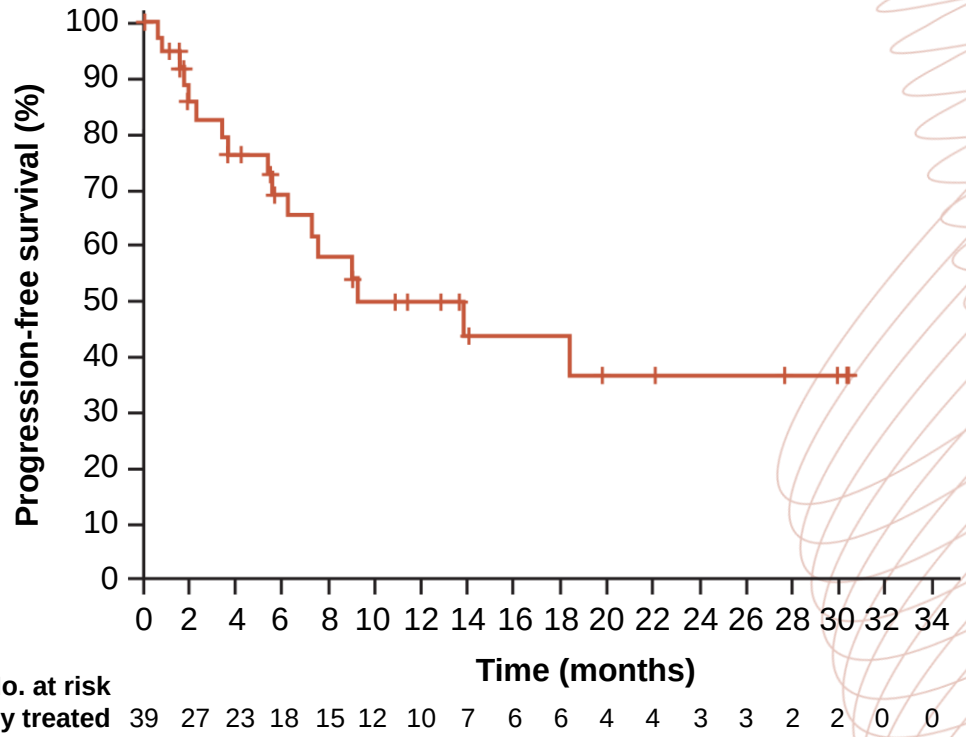
1. Riely GJ, et al. J Clin Oncol. 2023;41:3700-11

ENCORAFENIB PLUS BINIMETINIB: PROGRESSION-FREE SURVIVAL

TREATMENT-NAÏVE PATIENTS



PREVIOUSLY TREATED PATIENTS



PFS by independent radiology review

PFS, progression-free survival

1. Riely GJ, et al. J Clin Oncol. 2023;41:3700-11

ENCORAFENIB PLUS BINIMETINIB: SAFETY

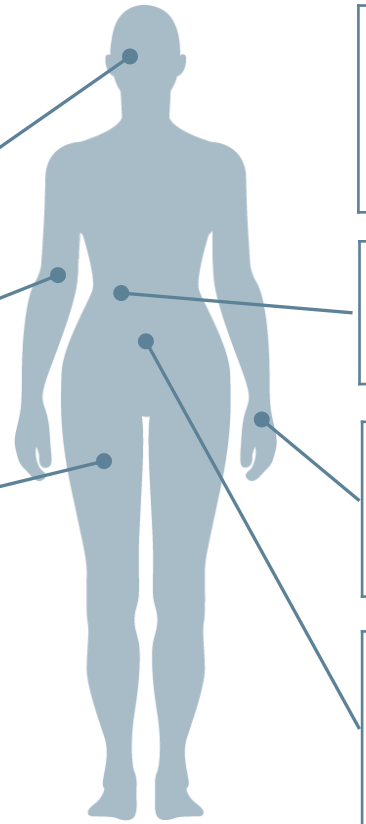
TREATMENT-RELATED AEs (%) IN ≥10% OF PATIENTS

Ocular	Grade 1/2	Grade ≥3
Blurred vision	16	1

Haematological	Grade 1/2	Grade ≥3
Anaemia	15	3

Musculoskeletal	Grade 1/2	Grade ≥3
Blood CPK increased	11	0

TRAEs led to dose modifications	
Dose reduction	24
Dose interruption	44
Permanent discontinuation	15



Systemic	Grade 1/2	Grade ≥3
Fatigue	30	2
Asthenia	7	3
Peripheral oedema	11	0

Hepatological	Grade 1/2	Grade ≥3
ALT increased	7	5
AST increased	5	7

Dermatological	Grade 1/2	Grade ≥3
Pruritus	12	0
Dry skin	10	0
Alopecia	10	0

Gastrointestinal	Grade 1/2	Grade ≥3
Nausea	47	3
Diarrhoea	39	4
Vomiting	28	1
Constipation	13	0
Abdominal pain	10	0

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; TRAE, treatment-related AE

Adapted from Planchard D, et al. NPJ Precis Oncol. 2024;8:90

BRAF-TARGETED TREATMENTS AVAILABLE – TEST NSCLC PATIENTS BEFORE TREATMENT!

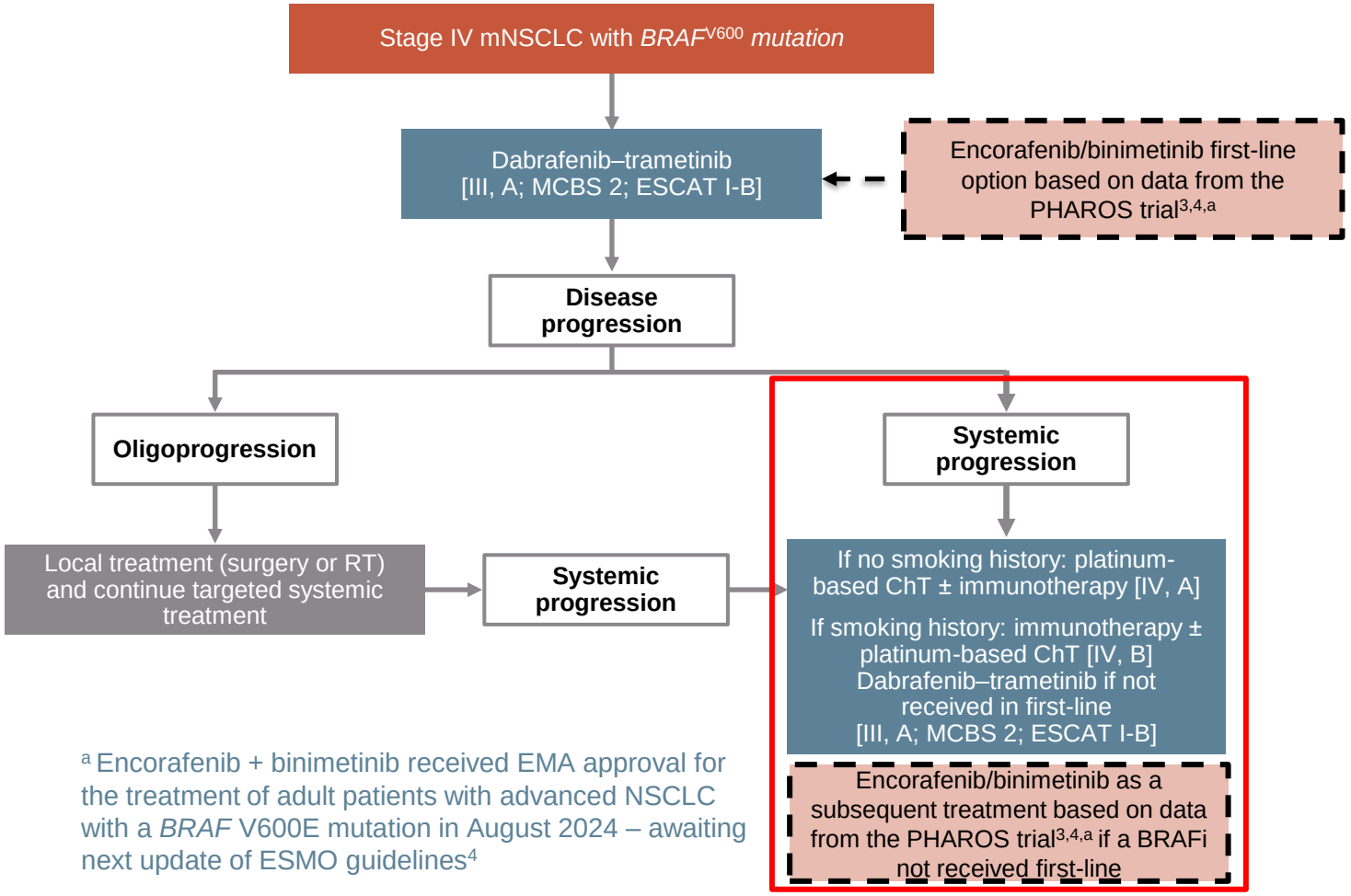
- **All patients with advanced NSCLC,** irrespective of smoking history, **should undergo comprehensive molecular testing** to identify molecular drivers— including but not limited to B*RAF*^{V600} mutations[1-3]
- **Tissue biopsy is the standard for molecular testing**.[2] **Liquid biopsy can be a complementary approach**,[2.3] but negative results should be confirmed by tissue testing.[2] Broad panel testing using NGS is preferable[2]
- **Real-time PCR and NGS using DNA sequencing** are the most used methodologies for examining *BRAF* mutation status[1,3]
- While an anti-BRAF p.V600E-specific monoclonal antibody is commercially available, and some studies have examined utilising this approach, it should only be deployed after extensive validation[3]

NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; PCR, polymerase chain reaction

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 3.2025. Non-Small Cell Lung Cancer. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf (accessed Feb 2025)

WHAT NEXT? PROGRESSION ON BRAF / MEK INHIBITION

ESMO GUIDELINES[1]



[a] Encorafenib + binimetinib received EMA approval for the treatment of adult patients with advanced NSCLC with a *BRAF* V600E mutation in August 2024 – awaiting next update of ESMO guidelines[4]

NCCN GUIDELINES[2]

BRAF^{V600E} mutation

- First-line therapy
  - Dabrafenib/trametinib
  - Encorafenib/binimetinib
  - Dabrafenib
  - Vemurafenib
- Subsequent therapy
  - Dabrafenib/trametinib
  - Encorafenib/binimetinib

At progression:[1]

- Consider mechanisms of resistance
- Local treatment for oligoprogression
- Re-biopsy if feasible

BRAFi, BRAF inhibitor; ChT, chemotherapy; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; ESMO, European Medical Society for Oncology; MCBS, ESMO-Magnitude of Clinical Benefit Scale; mNSCLC, metastatic non-small cell lung cancer; NCCN, National Comprehensive Cancer Network; RT, radiotherapy

1. Hendriks LE, et al. Ann Oncol. 2023;34:339-357; 2. NCCN Guidelines Version 3.2025. Non-Small Cell Lung Cancer. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf (accessed Feb 2025); 3. Riely GJ, et al. J Clin Oncol. 2023;41:3700-3711; 4. EMA Recommends Extension of Therapeutic Indications for Encorafenib and Binimetinib. Available here (accessed Feb 2025)

POTENTIAL LATER LINE TREATMENT OPTIONS FOR *BRAF*-MUTATED NSCLC

- Chemotherapy remains a second-line recommendation for patients with a BRAFV600 mutation
- Immunotherapy-based treatments are an option for patients with BRAFV600E-mutant advanced NSCLC

Treatment	Patients, n (*BRAF* mutation)	Treatment status	Median follow-up, mo	ORR, %	Median PFS, mo	Median OS, mo
Platinum-based doublet chemotherapy	7 (V600E)	Treatment-naïve	13.7	29	4.1	10.8
	7 (non-V600E)		13.7	71	8.9	15.2
Platinum-based doublet chemotherapy	23 (V600E and non-V600E)	Treatment-naïve	NA	NA	6.4	18.4
Immunotherapy	12 (V600E)	Treatment-naïve and previously treated	5.5	25	3.7	NE
	10 (non-V600E)			33	4.1	NE
Immunotherapy	17 (V600E)	Treatment-naïve and previously treated	16.1	24	1.8	8.2
	18 (non-V600E)				4.1	17.2
Immunotherapy	26 (V600)	Treatment-naïve and previously treated	9.2	26	5.3	22.5
	18 (non-V600)			35	4.9	12.0
Immunotherapy	8 (V600E)	Treatment-naïve	NA	38	10.5	NA
	7 (non-V600E)			43	10.8	NA
Immunotherapy as monotherapy or in combination	43 (V600E)	Treatment-naïve and previously treated	16.2	51.7	10.0	18.5
	16 (non-V600E)			31.1	8.0	16.0
Immunotherapy-combined chemotherapy	9 (V600E)	Treatment-naïve	NA	56	18.5	NA
	7 (V600E)	Previously treated	NA	29	1.9	NA

mo, months; NA, not available; NSCLC, non-small cell lung cancer; NE, not estimable; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival

Planchard D, et al. NPJ Precis Oncol. 2024;8:90

FUTURE TREATMENT OPTIONS?

- Possible **combinations of immune checkpoint inhibitors with BRAF-targeted therapies[1]**
  - Synergistic tumour effect but tolerability will be a consideration[1]
  - Triple combination therapies (BRAFi + MEKi + IO therapy) investigated in melanoma[2]

- **Next-generation BRAF inhibitors[2]**
  - First-generation BRAF inhibitors only effective in patients with class 1 *BRAF*^{V600E} mutations
  - Next-generation BRAF inhibitors designed to inhibit class 1-3

BRAFi, BRAF inhibitor; IO, immuno-oncology; MEKi, MEK inhibitor

1. Planchard D, et al. NPJ Precis Oncol. 2024;8:90; 2. Abdayem P and Planchard D. Clin Adv Hematol Oncol. 2022;20:662-72

SUMMARY

- *BRAF* mutated NSCLC occurs in smokers and non-smokers[1]
- **Treat patients with *BRAF*^{V600E} mutated NSCLC with BRAFi plus MEKi combination[2,3]**
  - Two combinations available, perhaps differing toxicity, similar efficacy
    - Trametinib plus dabrafenib
    - Encorafenib plus binimetinib
- Disease progression is inevitable and **only approximately 50% of mNSCLC patients receive second-line treatment[4]**
- **Test before commencing first-line treatment - use the most efficacious agents in the first-line setting** based on the patient's molecular profile[4]
- Reassess at progression, treat oligoprogression with local treatments, re-biopsy if feasible[5]
- Second-line treatment options include chemotherapy + IO therapy,[5] or BRAFi plus MEKi combination if not used for first-line[6]

BRAFi, BRAF inhibitor; IO, immuno-oncology; MEKi, MEK inhibitor; (m)NSCLC, (metastatic) non-small cell lung cancer

1. Zhen D, et al. Oncotarget. 2016;7:41691-702; 2. Tabbò F, et al. Cancer Treat Rev. 2022;103:102335; 3. Riely GJ, et al. J Clin Oncol. 2023;41:3700-11;
4. Planchard D, et al. NPJ Precis Oncol. 2024;8:90; 5. Hendriks LE, et al. Ann Oncol. 2023;34:339-57; 6. NCCN Guidelines Version 3.2025. Non-Small Cell Lung Cancer. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf (accessed Feb 2025)

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