NCCN Guidelines: Systemic Therapy for Patients with *BRAF* V600E Mutated Advanced NSCLC

First line

Targeted therapies	Other recommended systemic therapy (PS 0-1)	
Preferred • **Dabrafenib + trametinib** **Useful in certain circumstances** • **Vemurafenib** • **Dabrafenib** (Neither vemurafenib or dabrafenib are FDA approved for NSCLC as monotherapies)	Preferred: pembrolizumab + chemotherapy as appropriate for histology* Other: additional combination regimens • Atezolizumab†, • Nivolumab/ipilimumab, • Cemiplimab-rwlc, or • Tremelimumab-actl/durvalumab, as appropriate for histology*	Useful in certain circumstances Contraindications to PD-1/PD-L1 inhibitors • Chemotherapy as appropriate for histology* • Bevacizumab + chemotherapy for adenocarcinoma*

*Bevacizumab and pemetrexed not recommended for SCC
†Atezolizumab not recommended for first line treatment of SCC

Second line

Targeted therapies	Or other systemic therapy	
If not received previously: • **Dabrafenib + trametinib**	**If not received previously:** Preferred: pembrolizumab + chemotherapy as appropriate for histology*	Or other systemic therapy first line regimens as shown above (PS 0-1)

Subsequent lines

Preferred (no previous IO)
- Nivolumab
- Pembrolizumab
- Atezolizumab

Other (no previous or previous IO)
- Chemotherapy as appropriate for histology

See guidelines for full recommendations. PS, performance status; PD-1, programmed death protein 1; PD-L1, programmed death-ligand 1; SCC, squamous cell carcinoma; IO, immunotherapy. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 3.2023. Updated April 13, 2023. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1450.

Dabrafenib + Trametinib in *BRAF* V600E Mutated Advanced NSCLC

Efficacy Results

BRF113928

Phase 2, multicohort, multicenter, nonrandomized, open-label trial

- Metastatic NSCLC
- *BRAF* V600E mutated
- Cohort B: previously treated ≥1 platinum-based chemotherapy regimen, ≥3 systemic regimens
- Cohort C: no prior therapy

	Previously treated (n = 57)	Treatment-naïve (n = 36)
Objective response, n (%) (95% CI)	39 (68.4) (54.8–80.1)	23 (63.9) (46.2–79.2)
Disease control rate, n (%) (95% CI)	46 (80.7) (68.1–90.0)	27 (75.0) (57.8–87.9)
Median PFS, mo (95% CI)	10.2 (6.9–16.7)	10.8 (7.0–14.5)
Median OS, mo (95% CI)	18.2 (14.3–28.6)	17.3 (12.3–40.2)

Data cutoff date: Feb. 24, 2021. Median follow-up 16.6 mo for previously treated patients and 16.3 mo for treatment-naïve patients

FDA approved June 2017 for patients with metastatic NSCLC with *BRAF* V600E mutation
FDA approved June 2022 for adult and pediatric patients ≥6 years of age with unresectable or metastatic solid tumors with *BRAF* V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options

CI, confidence interval; PFS, progression-free survival; mo, months; OS, overall survival.

Planchard D et al. *J Thorac Oncol*. 2022;17:103-115; FDA Approved Drugs: Oncology (Cancer) / Hematologic Malignancies Approval Notifications /Oncology (Cancer) Approvals & Safety Notifications. Reviewed June 20, 2023. Accessed June 20, 2023. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm.

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Safety Results

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Safety population (n = 93)

	n (%)
Any adverse event (AE)	92 (99)
Grade ≥3	12 (12)

AEs in ≥30% of patients, n (%)		
	Any grade	Grade ≥3
Pyrexia	52 (56)	6 (6)
Nausea	47 (51)	0
Vomiting	38 (41)	3 (3)
Dry skin	36 (39)	1 (1)
Edema peripheral	35 (38)	0
Diarrhea	34 (37)	2 (2)
Decreased appetite	31 (33)	0
Cough	29 (31)	0

AE, adverse event.

Planchard D et al. *J Thorac Oncol*. 2022;17:103-115.