NCCN Guidelines: Systemic Therapy for Patients with *MET* Exon 14 Skipping Mutation Positive Advanced NSCLC

First line

Targeted therapies	Other recommended systemic therapy (PS 0-1)	
Preferred • **Capmatinib** • **Tepotinib** **Useful in certain circumstances** • **Crizotinib** (Not an FDA approved therapy for *MET* exon 14 mutated NSCLC)	Preferred: pembrolizumab + chemotherapy as appropriate for histology* Other: additional combination regimens with • 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

Subsequent therapy

Targeted therapies	Or other systemic therapy
If not received previously: **Preferred** • **Capmatinib** • **Tepotinib** **Useful in certain circumstances** • **Crizotinib**	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.

Capmatinib in *MET* Exon 14 Skipping Mutation Positive Advanced NSCLC

Efficacy Results

Geometry mono-1

Phase 2 multicohort open label trial

- Stage IIIB/IV NSCLC (any histology)
- *MET* ex14 skipping mutation or *MET* amplification
- *EGFR* WT for L585R and delE19, *ALK* rearrangement negative
- Stable or asymptomatic brain metastases allowed
- *MET* amplification cohorts closed for futility
- Cohorts 6 and 7 = expansion cohorts

	Treatment-naive			Pretreated		
	Cohort 5b n = 28	Cohort 7 n = 32	All n = 60	Cohort 4 (2/3L) n = 69	Cohort 6 (2L) n = 31	All N = 100
Objective response, % (95% CI)	67.9 (47.6–84.1)	65.6 (46.8–81.4)	66.7 (53.3–78.3)	40.6 (28.9–53.1)	51.6 (33.1–69.8)	44.0 (34.1–54.3)
Disease control, % (95% CI)	96.4 (81.7–99.9)	100 (89.1–100)	98.3 (91.1–100)	78.3 (66.7–87.3)	90.3 (74.2–98.0)	82.0 (73.1–89.0)
Median duration of response, mo (95% CI)	12.6 (5.6–NE)	NE (5.5–NE)	12.6 (8.4–NE)	9.7 (5.6–13.0)	8.4 (4.2–NE)	9.7 (5.6–13.0)
Median PFS, mo (95% CI)	12.4 (8.2–23.4)	10.8 (6.9–NE)	12.3 (8.2–21.6)	5.4 (4.2–7.0)	6.9 (4.2–13.3)	5.5 (4.2–8.1)
Median OS, mo (95% CI)	20.8 (12.4–NE)	Not yet mature	-----	13.6 (8.6–22.2)	Not yet mature	-----

Data cutoff date: Sept. 18, 2020

FDA approved May 2020 for patients with metastatic NSCLC whose tumors have a mutation that leads to *MET* exon 14 skipping

WT, wild type; CI, confidence interval; PFS, progression-free survival; OS, overall survival.

Wolf J et al. *N Engl J Med*. 2020;383:944-957; Wolf J et al. Presented at ASCO 2021. Abstract 9020; 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.

Tepotinib in *MET* Exon 14 Skipping Mutation Positive Advanced NSCLC

Efficacy Results

VISION

Phase 2 multicohort open label trial

- Locally advanced or metastatic NSCLC
- *MET* exon 14 skipping mutation
- *EGFR* and *ALK* wild type
- ≤2 prior lines of therapy
- Stable or asymptomatic brain metastases allowed
- Cohort A reported here as primary analysis set

	Treatment-naïve (n = 69)	Previously treated (n = 83)	Overall (N = 152)
Objective response, % (95% CI)	44.9 (32.9–57.4	44.6 (33.7–55.9)	44.7 (36.7–53.0)
Disease control, % (95% CI)	68.1 (55.8–78.8)	72.3 (61.4–81.6)	70.4 (62.5–77.5)
Median duration of response, mo (95% CI)	10.8 (6.9–NE)	11.1 (9.5–18.5)	11.1 (8.4–18.5)
Median PFS, mo (95% CI)	8.5 (6.8–11.3)	10.9 (8.2–12.7)	8.9 (8.2–11.2)
Median OS, mo (95% CI)	----	----	17.6 (15.0–21.0)

Data cutoff date: July 1, 2021

FDA approved Feb. 2021 for patients with metastatic NSCLC harboring *MET* exon 14 skipping alterations

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

Paik PK et al. *N Engl J Med*. 2020;383:931-943; Le X et al. *Clin Cancer Res*. 2022;28:1117-1126. 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.