

Capmatinib and Tepotinib Registrational Trials

Safety Results

Capmatinib: Geometry mono-1

All patients from *MET* exon 14 skipping mutation and *MET* amplification cohorts (N = 373)

AEs in >20% of patients, n (%)		
	Any grade	Grade 3/4
Any AE	367 (98.4)	256 (68.6)
Peripheral edema	202 (54.2)	36 (9.7)
Nausea	168 (45.0)	9 (2.4)
Vomiting	105 (28.2)	9 (2.4)
Increased blood creatinine	99 (26.5)	0
Dyspnea	87 (23.3)	25 (6.7)
Fatigue	83 (22.3)	16 (4.3)
Decreased appetite	79 (21.2)	4 (1.1)

Tepotinib: VISION

All patients enrolled in cohorts A and C as of July 1, 2020 (N = 255)

AEs in >10% of patients, n (%)		
	Any grade	Grade 3/4
Any AE	220 (86.3)	62 (24.3)
Peripheral edema	138 (54.1)	19 (7.5)
Nausea	51 (20.0)	1 (0.4)
Diarrhea	50 (19.6)	1 (0.4)
Increased blood creatinine	45 (17.6)	1 (0.4)
Hypoalbuminemia	37 (14.5)	6 (2.4)

Peripheral edema associated with (% of patients):

- Dose reductions 14.1%
- Dose interruptions 16.1%
- Permanent discontinuation 3.5%

AE, adverse event.

Wolf J et al. *N Engl J Med.* 2020;383:944-957; Wolf J et al. Presented at ASCO 2021. Abstract 9020; Paik PK et al. *N Engl J Med.* 2020;383:931-943; Le X et al. *Clin Cancer Res.* 2022;28:1117-1126.

Peripheral Edema and MET Targeted Agents

Peripheral edema is a common side effect of small molecule MET inhibitors

- Usually mild to moderate severity but high symptom burden that can affect daily activities and quality of life
- May require dose reductions or interruptions, rarely requires discontinuation

Incidence of peripheral edema in clinical trials of MET inhibitors

Capmatinib	21%-54%
Crizotinib	31%-50%
Savolitinib	21%-54%
Tepotinib	26%-63%

Diagnosis and evaluation

- Evaluate for pre-existing conditions that might cause edema and address
- Distinguish between generalized, systemic edema, and localized lymphedema caused by other cancer treatments
- Patient education: what to expect, how to manage, how to care for skin and feet to avoid secondary cellulitis



Management

- Diuretics
- Lower limb elevation
- Compression stockings
- Lymphatic massage
- Exercise and diet changes
- Dose reduction or interruption for persistent Grade ≥ 2