Matching-adjusted indirect comparison (MAIC) of safety outcomes with MET tyrosine kinase inhibitors (TKIs) in patients with *MET* exon 14 (*MET*ex14) skipping non-small cell lung cancer (NSCLC)

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CONCLUSION

- **These MAICs of safety outcomes with MET TKIs in patients with *MET*ex14 NSCLC can assist decision-makers in assessing targeted treatment options for this tumor type**
- **MAICs showed lower rates of TRAEs leading to treatment discontinuation with tepotinib versus capmatinib in both 1L and 2L+ treatment**
- **In MAICs across treatment lines, TRAE outcomes were generally comparable between tepotinib and crizotinib**
- **These data should be interpreted cautiously given potential differences in AE reporting and follow-up between the studies included**
- **These analyses further support tepotinib as a well-tolerated treatment in patients with *MET*ex14 skipping NSCLC**

INTRODUCTION

- Around 3–4% of NSCLC tumors exhibit *MET*ex14 skipping, which can be effectively targeted using selective MET TKIs[1–3]
- The selective MET TKIs tepotinib and capmatinib are approved in the EU to treat advanced *MET*ex14 skipping NSCLC after prior chemo- and/or immunotherapy[4,5]
- The non-selective MET TKI crizotinib is also sometimes used off-label in patients with advanced *MET*ex14 skipping NSCLC[6]
- Comparative safety is an important factor for payers and decision-makers, but head-to-head data are unavailable, and differences in study populations make side-by-side comparisons of individual studies unreliable
- MAIC is a pairwise indirect comparison method that provides a more accurate comparison of study data by adjusting for differences in baseline characteristics subject to possible unobserved, uncontrolled confounding factors[7]

OBJECTIVES

- To conduct MAICs of safety outcomes with tepotinib versus capmatinib or crizotinib in patients with *MET*ex14 skipping NSCLC based on data from published clinical trials

METHODS

- The MAICs utilized data from patients with advanced *MET*ex14 skipping NSCLC from global Phase II trials of tepotinib (VISION), capmatinib (GEOMETRY mono-1), and the Phase I trial of crizotinib (PROFILE 1001)[4–6] (**Table 1**)
- Patient-level data from VISION were reweighted to match the baseline characteristics of comparator trials based on median age, sex, ECOG PS 0, smoking history, adenocarcinoma histology, and treatment line (% 2L+)
- The following safety outcomes were compared: TRAE outcomes, including any grade, Grade ≥3 events, TRAEs leading to dose reductions, and TRAEs leading to treatment discontinuation
- Analyses were conducted either for the overall VISION population or stratified by treatment line (1L/2L+) depending on the comparator population
- Data are presented as unweighted and weighted medians and proportions

Table 1. Data sources used in the MAICs of tepotinib versus capmatinib and crizotinib

Trial		VISION[4]	GEOMETRY mono-1[5]	PROFILE 1001[6]
Treatment		Tepotinib 500 mg (450 mg active moiety) QD	Capmatinib 400 mg BID	Crizotinib 250 mg BID
Number of patients		Overall: N=313 1L: n=164 2L+: n=149	1L: n=28 (Cohort 5b) 2L+: n=69 (Cohort 4)	Overall: N=69 1L: n=26 2L+: n=43
Safety data sources	TRAEs	✓		✓
	Grade ≥3 TRAEs	✓		✓
	TRAEs leading to dose reduction	✓		✓
	TRAEs leading to treatment discontinuation	✓	✓	✓
	Data cut-off	Nov 20, 2022	January 6, 2020	January 31, 2018

RESULTS

VISION population weighting

- The patient population from VISION was successfully weighted to match the populations of GEOMETRY mono-1 and PROFILE 1001 (**Table 2**)
  - After reweighting, ESS for tepotinib were 112.3 in 1L and 145.3 in 2L+ for comparison with capmatinib, and 241.5 across treatment lines for comparison with crizotinib

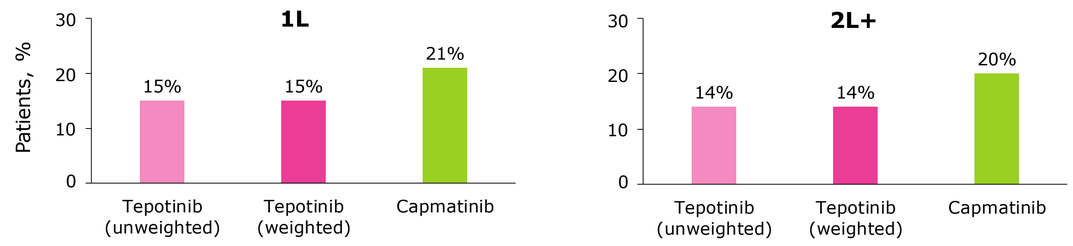
Table 2. Patient characteristics before and after weighting via MAIC for patients enrolled in VISION, GEOMETRY mono-1, and PROFILE 1001

	1L			2L+			Overall		
	Tepotinib unweighted	Tepotinib weighted	Capmatinib	Tepotinib unweighted	Tepotinib weighted	Capmatinib	Tepotinib unweighted	Tepotinib weighted	Crizotinib
n/ESS	164	112.3	28	149	145.3	69	313	241.5	69
Age (median), years	74	70.9	71	70.8	71	71	72	72	72
Male, %	50.6	35.7	35.7	47.7	42	42	49.2	42	42
ECOG PS 0, %	27.4	25	25	24.2	23.2	23.2	25.9	27.5	27.5
Smoking history, %	53.7	35.7	35.7	40.9	42	42	47.6	62.3	62.3
Adenocarcinoma, %	79.9	89.3	89.3	81.2	76.8	76.8	80.5	84.1	84.1
2L+, %	0	0	0	100	100	100	47.6	62.3	62.3

Comparison of safety outcomes with tepotinib versus capmatinib

- Unweighted and weighted rates for TRAEs leading to treatment discontinuation were lower for tepotinib versus capmatinib in 1L and 2L+ (**Figure 1**)
- Data for any grade and Grade ≥3 TRAEs, and TRAEs leading to dose reductions were unavailable for capmatinib

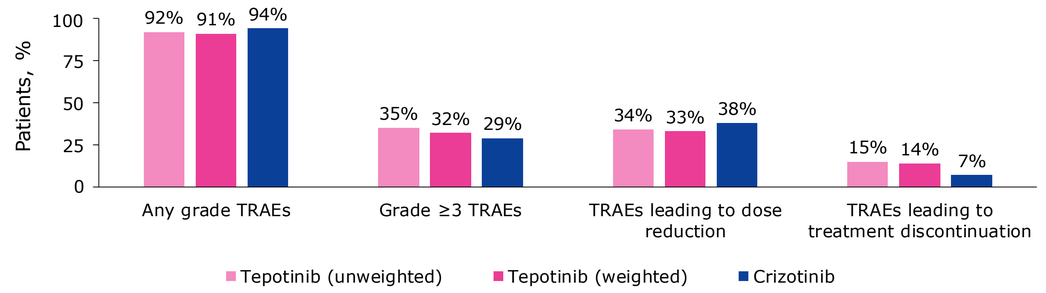
Figure 1. MAIC of TRAEs leading to treatment discontinuation with tepotinib versus capmatinib according to treatment line



Comparison of safety outcomes with tepotinib versus crizotinib

- Across treatment lines, MAICs generally showed comparable TRAE outcomes with tepotinib versus crizotinib (**Figure 2**)
- TRAEs leading to treatment discontinuation were lower for crizotinib versus tepotinib

Figure 2. MAIC of safety outcomes with tepotinib versus crizotinib



Abbreviations: 1L, treatment-naïve; 2L+, previously treated; AE, adverse event; BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; EU, European Union; MAIC, matching-adjusted indirect comparison; MET, mesenchymal–epithelial transition factor; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; QD, once daily; TKI, tyrosine kinase; TRAE, treatment-related adverse event.

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