CO168

A propensity score-based comparison of tepotinib versus immunotherapy with/without chemotherapy, using real-world data in previously untreated *MET* exon 14 (*MET*ex14) skipping non-small cell lung cancer (NSCLC)

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CONCLUSION

- **Consistent with published observational data, the analysis found time-to-event efficacy outcomes in patients with *MET*ex14 skipping NSCLC were poor for patients treated with IO**
- **Versus tepotinib, time-to-event efficacy outcomes were shorter for IO in 1L**
- **Despite limited patient numbers, the evidence presented suggests similar patterns for IO+CT**
- **PFS is estimated to be greater for tepotinib, while evidence on OS remains uncertain and confounded by subsequent treatment use. However, the evidence presented suggests a marginal OS benefit for tepotinib**

INTRODUCTION

- With the approval of immunotherapies (IOs) and IO combinations with chemotherapy (IO+CT), several IO-based treatment options are available for patients with non-oncogenic non-small cell lung cancer (NSCLC) and are primarily used in first line (1L). However, in specific mutations such as *MET* exon 14 (*MET*ex14) skipping, observational studies suggest IOs do not perform as well compared with non-oncogenic NSCLC, and no evidence exists for anti-PD-1 and anti-PD-L1 IO+CT in this population[1–3]
- *MET*ex14 skipping specifically have been identified as a biomarker with distinct characteristics, constituting 3–4% of the overall NSCLC population, and are associated with poor prognosis[4,5]
- The single-arm Phase II VISION study (NCT02864992) investigated the efficacy and safety of tepotinib in 1L and previously-treated (2L+) patients with advanced NSCLC harboring *MET*ex14 skipping
- By pooling seven real-world datasets of patients with *METex*14 skipping NSCLC (named the TOGETHER study), a comparison of IO-based treatments can be performed with tepotinib, a highly selective, targeted, oral MET inhibitor

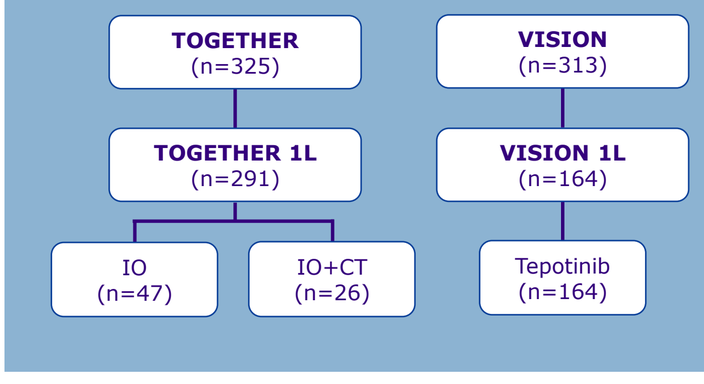
OBJECTIVES

This study explores the comparative efficacy of IO and IO+CT versus tepotinib in 1L patients with advanced NSCLC harboring *MET*ex14 skipping

METHODS

- TOGETHER is a common data model comprising seven secondary individual patient-level data sources of patients with advanced NSCLC harboring *MET*ex14 skipping. TOGETHER includes 291 previously-untreated patients, 47 of whom received IO, and 26 received IO+CT as their 1L treatment. The remaining 218 patients were treated with chemotherapy, MET inhibitor, and investigational therapies **(Figure 1)**
- The TOGETHER data were matched to the VISION inclusion/exclusion criteria, before propensity scoring (via logistic regression) was implemented to compare the patients treated with IO and IO+CT to the 164 previously-untreated patients from the VISION study.[5] Patients were weighted on: prior treatment experience, age, advanced/metastatic disease, sex, adenocarcinoma histology, and presence of smoking history
- Propensity score weighting was implemented to account for differences in patient characteristics, based on clinical input. The IO-based treatment data from TOGETHER were weighted to match VISION to ensure no omission of data, and to allow the tepotinib cohort to remain the same between the comparisons to IO and IO+CT
- Time-to-event outcomes (progression-free survival [PFS] and overall survival [OS]) are compared with the November 2022 data cut-off from VISION, using Kaplan–Meier (KM) plots and Cox hazard ratios (HRs)

Figure 1. Patient-level data available to inform comparisons



RESULTS

- Patients in TOGETHER receiving IO (n=47) and IO+CT (n=26) were weighted on their baseline characteristics to match the data of 1L patients receiving tepotinib in VISION
- The weighting resulted in 165.1 patients treated with IO (effective sample size [ESS] of 40.8) and 164 patients treated with IO+CT (ESS of 21.2), with whom to compare with the 164 tepotinib-treated patients from VISION
- After weighting, patient and disease characteristics were balanced across groups (**Table 1**), with no statistical differences observed

Table 1. Weighted patient characteristics

Patient characteristic		IO	IO+CT	Tepotinib
N (ESS)		165.1 (40.8)	164 (21.2)	164
Age (mean, years)		74.1	73.9	73.7
Advanced/ metastatic disease, n (%)	Advanced	10.7 (6.5)	12.1 (7.4)	11 (6.7)
	Metastatic	154.4 (93.5)	151.9 (92.6)	153 (93.3)
Sex, n (%)	Male	88.8 (53.8)	92.4 (56.3)	83 (50.6)
	Female	76.3 (46.2)	71.6 (43.7)	81 (49.4)
Histology, n (%)	Adenocarcinoma	118.2 (71.6)	140.3 (85.5)	131 (79.9)
	Other	46.9 (28.4)	23.7 (14.5)	32 (20.1)
Smoking history, n (%)	Yes	86 (52.1)	87.3 (53.2)	88 (53.7)
	No	79.1 (47.9)	76.7 (46.8)	76 (46.3)

- **Figure 2** presents the KM of PFS and OS for VISION and weighted IO. Patients who received tepotinib in 1L had longer PFS (median 8.7 months) than patients receiving 1L IO (median 3.6 months) with a Cox HR of 0.55 (95% confidence interval [CI]: 0.38, 0.80). OS marginally favored tepotinib (median 21.3 vs 19.0 months), with a Cox HR of 0.77 (95% CI: 0.52, 1.14)
- **Figure 3** presents the KM of PFS and OS for VISION and weighted IO+CT. Similar to the comparison with IO, tepotinib showed a PFS benefit over IO+CT (medians of 8.7 and 6.7 months), with a Cox HR of 0.72 (95% CI: 0.44, 1.19). A median OS benefit of 2 months was observed for tepotinib in 1L (21.3 vs 19.3 months), though the Cox HR 95% CI spanned 1 (HR: 0.85; 95% CI: 0.51, 1.42)

Figure 2. PFS and OS KM – IO (weighted to VISION) and tepotinib

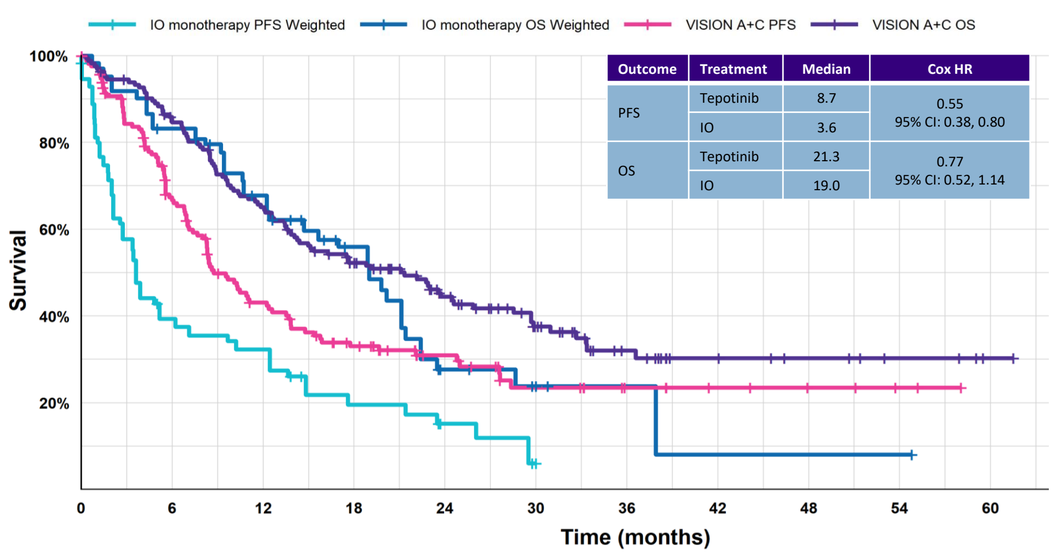
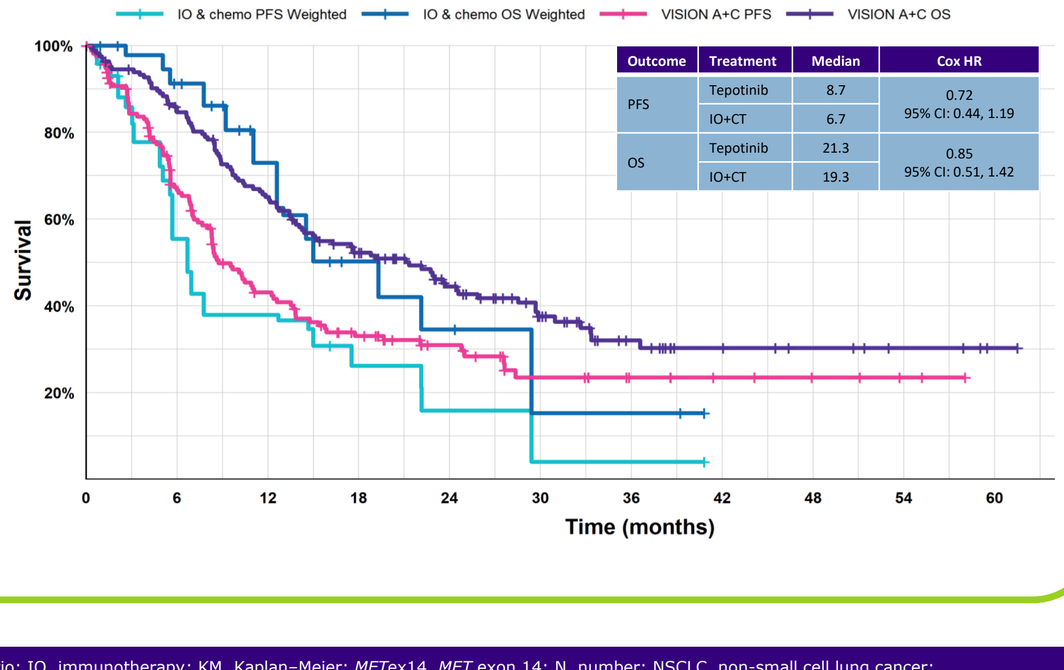


Figure 3. PFS and OS KM – IO+CT (weighted to VISION) and tepotinib



Abbreviations: 1L, first line; 2L+, second line or later (i.e. previously-treated), CI, confidence interval; CT, chemotherapy; ESS, effective sample size; HR, hazard ratio; IO, immunotherapy; KM, Kaplan–Meier; *MET*ex14, *MET* exon 14; N, number; NSCLC, non-small cell lung cancer; OS, overall survival; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

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