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Tepotinib Versus Chemotherapy in *MET* Exon 14 (*MET*ex14) Skipping Non-Small Cell Lung Cancer (NSCLC): Real-World Evidence (RWE) and Matching-Adjusted Indirect Comparison (MAIC) to Explore the Impact of Subsequent Therapy

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CONCLUSION

- **OS differences appear confounded by subsequent treatment use, though the evidence presented suggests an OS benefit for tepotinib versus chemotherapy**
- **Tepotinib provides longer PFS than chemotherapy based on indirect comparisons using TOGETHER real-world data and published studies**
- **Although cross-study comparisons can be complex, using a combination of individual and aggregate level data, hypotheses (such as the impact of subsequent therapies) can be tested, overcoming the limitations of a single data source**

INTRODUCTION

- Chemotherapy is widely used in previously-treated advanced/metastatic non-small cell lung cancer (NSCLC). However, limited chemotherapy efficacy evidence is available in specific, recently identified, biomarker-driven populations, such as *MET* exon 14 (*MET*ex14) skipping[1,2]
- By pooling seven real-world datasets of patients with *MET*ex14 skipping NSCLC (the TOGETHER study), it is possible to estimate the comparative effectiveness of chemotherapy versus tepotinib, a highly selective, oral monotherapy targeted for the treatment of adult patients with advanced NSCLC harboring *MET*ex14 skipping.[1] This analysis represents a comparison post-introduction of immunotherapy to the treatment pathway
- Additionally, a matched-adjusted indirect comparison (MAIC) of published data in non-oncogenic-driven NSCLC (predating the introduction of immunotherapies) was conducted, with the purpose of exploring the comparative efficacy of tepotinib against chemotherapy and to understand the impact of subsequent therapy on overall survival (OS)

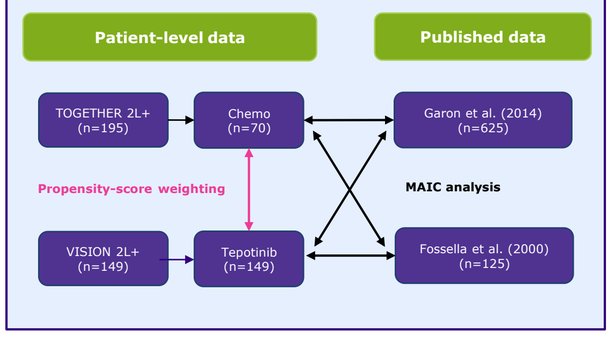
OBJECTIVES

To explore the impact of subsequent therapy on comparative efficacy, before and after the introduction of immunotherapy for NSCLC

METHODS

- The TOGETHER study is a common data model (CDM) comprising seven secondary data sources of patients with NSCLC harboring *METex*14 skipping
- The VISION inclusion/exclusion criteria were applied to the TOGETHER data, then propensity score weighting was implemented to compare patients treated with tepotinib and chemotherapy. In total, 70 previously-treated patients received chemotherapy at a second or later line (2L+), with data from 149 previously-treated patients available from the tepotinib VISION study (NCT02864992)[3,4]
- To explore the impact of subsequent therapy use, a comparison to published evidence on docetaxel[5,6] was undertaken by MAIC-adjusting both the TOGETHER CDM and VISION data **(Figure 1)**. The selected studies were chosen as they represent evidence predating the introduction of immunotherapies and MET inhibitors
- The time-to-event outcomes progression-free survival (PFS) and OS were compared both between treatments (chemotherapy and tepotinib) and across analyses (propensity-score weighting of TOGETHER and MAICs to published evidence)

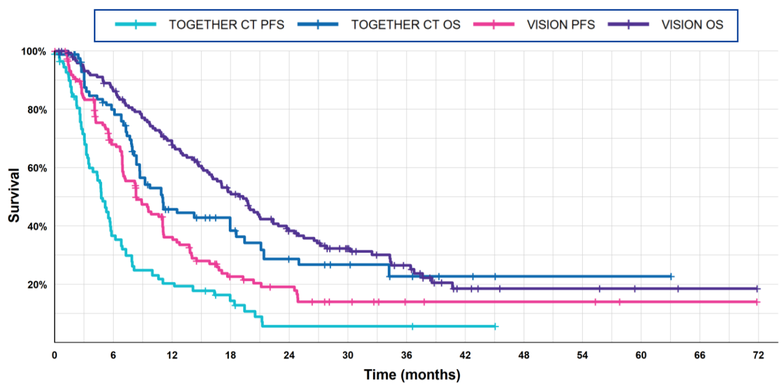
Figure 1. Analyses performed



RESULTS

- Tepotinib showed greater PFS than chemotherapy in the propensity score comparison versus TOGETHER (median 8.3 vs 4.8 months [**Table 1, Figure 2**])
- Tepotinib also showed greater OS than TOGETHER chemotherapy (24-month Restricted Median Survival Time [24m RMST] 16.6 vs 13.6 months). However, a convergence in OS curves is observed in the tail end of follow-up (**Table 1**, **Figure 2**)

Figure 2. PFS and OS KM – TOGETHER chemotherapy weighted to VISION



- Consistent with the propensity-score analysis, greater PFS for tepotinib was observed in the MAIC analysis against Garon et al. (11.0 vs 3.1 months), and Fossella et al. (8.2 vs 2.0 months). Similarly, an OS increase was also reflected, with 24m RMSTs of 17.2 vs 11.2 months in Garon et al., and 15.6 vs 9.5 months in Fossella et al. (**Table 1**, **Figures 3** and **4**)

Figure 3. PFS and OS KM – VISION and TOGETHER versus Garon et al. (2014) using MAIC

Figure 4. PFS and OS KM – VISION and TOGETHER versus Fossella et al. (2000) using MAIC

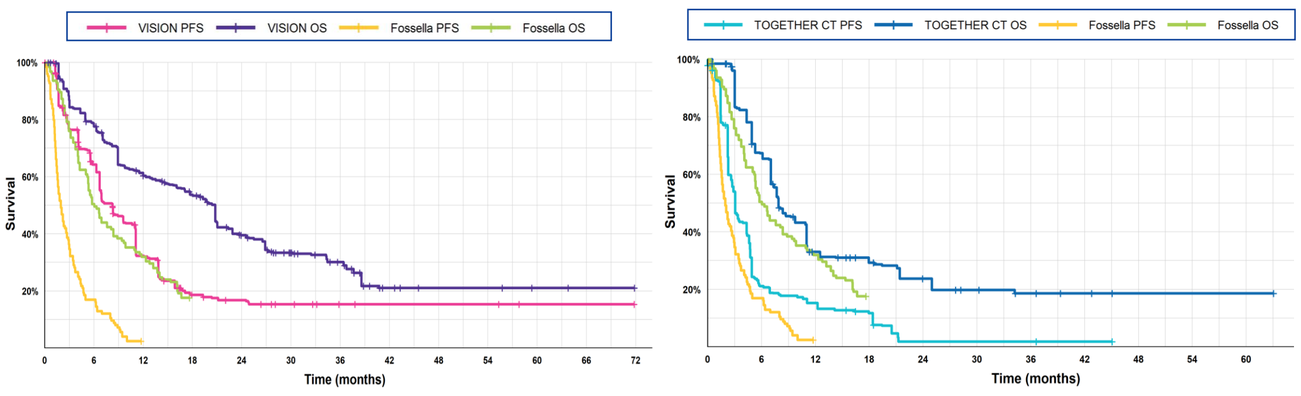


Table 1. Propensity-score weighted and MAIC median, and 24-month RMST by outcome and treatment

Analysis	Treatment	N (ESS)	PFS		OS	
			Median	24m RMST	Median	24m RMST
Propensity-score weighting	VISION	149	8.3	11.1	19.3	16.6
	TOGETHER	142.6 (64.8)	4.8	7.4	11.0	13.6
MAICs to Garon et al. (2014)	Garon	625	3.1	4.9	9.3	11.2
	VISION	58.9 (26.9)	11.0	12.5	26.8	17.2
	TOGETHER	47.0 (33.7)	4.3	6.9	9.7	13.0
MAICs to Fossella et al. (2000)	Fossella	125	2.0	3.4	6.0	9.5
	VISION	69.3 (33.8)	8.2	10.2	20.8	15.6
	TOGETHER	36.2 (23.1)	3.1	5.6	7.9	11.6

- MAIC-adjusting the TOGETHER chemotherapy data to match the published chemotherapy data, the observed PFS was similar (4.3 vs 3.1 months in Garon et al., and 3.1 vs 2.0 months in Fossella et al. [**Table 1**, **Figures 3** and **4**])
- Although the medians and 24m RMSTs are similar, MAIC-adjusted TOGETHER shows greater OS in the tails of the curves compared with the chemotherapy data from the published studies (**Figures 3** and **4**)
- The increased OS observed for TOGETHER chemotherapy may be explained by the introduction of immunotherapy to the treatment pathway. As such, the tail of the TOGETHER OS curve could be inflated by the subsequent use of immunotherapy after progression, rather than as an effect of the chemotherapy treatment itself

Abbreviations: 2L+, second or later line (i.e., previously-treated); CDM, common data model; Chemo, chemotherapy; ESS, effective sample size; KM, Kaplan–Meier; *MET*ex14, *MET* exon 14; m, months; MAIC, matching-adjusted indirect comparison; n, number; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; RMST, restricted-mean survival time; RWE, real-world evidence.

References: 1. Corrales L, et al. *Front Med (Lausanne).* 2017;4:13; 2. Bittoni M, et al. *Lung Cancer.* 2021;159:96–106; 3. Paik PK, et al. *N Engl J Med.* 2020;383(10):931–943; 4. Mazieres J, et al. JAMA Oncol. 2023 Sep 1;9(9):1260-1266; 5. Garon EB, et al. *Lancet*. 2014;384(9944):665–673; 6. Fossella FV, et al. *J Clin Oncol*. 2000;18(12):2354–2362.

Funding: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945).

Disclosures: HW, AH, and EH are employees of Delta Hat, who were contracted and funded by Merck to conduct the analyses. PC has received research funding from Amgen, AstraZeneca, Boehringer Ingelheim, Merck, Novartis, Roche, Takeda; advisory board/lecture fees: AstraZeneca, Boehringer Ingelheim, Chugai, Daiichi Sankyo, Gilead, Novartis, Pfizer, Roche, Takeda. SE receives an unrestricted grant from Boehringer Ingelheim for Investigator Initiated Study; non-renumerated Expert Meetings sponsored by MSD, BMS, Takeda, AstraZeneca, Amgen, Boehringer Ingelheim. FG honoraria: Amgen, AstraZeneca, BMS, Janssen, MSD, Roche, and Sanofi; research funding (for institution): Pfizer, Roche, and Takeda. HV is an employee of Merck.

Presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe 2023 | November 12–15, 2023 | Copenhagen, Denmark and virtual