EE372

Modelling the cost-effectiveness of tepotinib versus chemoimmunotherapy (CT+IO) in untreated patients with non-small cell lung cancer (NSCLC) harboring *MET* exon 14 (*MET*ex14) skipping

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CONCLUSIONS

- **Using different modelling approaches, tepotinib demonstrated a progression-free QALY and survival benefit versus CT+IO, thus providing evidence of clinical benefit; the greatest differences in the data are driven by post-progression survival**
- **One of the methods relies on data specifically in a *MET*ex14 skipping population; while other methods rely on the wider NSCLC population, which is a limitation of the analysis**

INTRODUCTION

- *MET*ex14 skipping has been identified as a biomarker with distinct characteristics, constituting 3–4% of the overall NSCLC population, and are associated with poor prognosis[1,2]
- Based on outcomes from clinical trials, clinical guidelines currently recommend chemoimmunotherapy (CT+IO) as first-line treatment in non-oncogenic NSCLC for untreated patients.[3] **There are, however, no published clinical trials available for CT+IO in *MET*ex14 skipping NSCLC**
- Tepotinib is a highly selective, targeted, orally administered MET inhibitor. In the single-arm Phase II VISION study of patients with NSCLC harboring *MET*ex14 skipping, tepotinib demonstrated robust and durable clinical activity, with a manageable safety profile[1,2]

OBJECTIVES

- This study explores different modelling approaches and sources to estimate the relative effectiveness of tepotinib versus CT+IO in an untreated adult population of patients with advanced NSCLC harboring *MET*ex14 skipping

METHODS

- A three-state partitioned survival model was developed to represent health states of patients with NSCLC over a 30-year time horizon (**Figure 1**)
- Within the model, three methods were implemented to compare the efficacy of tepotinib versus CT+IO, with the aim of showing survival outcomes and benefits (**Figure 2**)

Figure 1. Partitioned survival model diagram

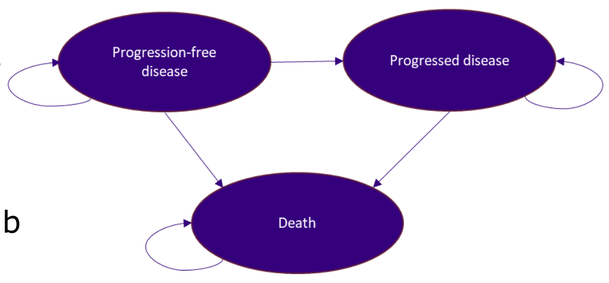


Figure 2. Efficacy methods

Method 1. Real-world data (RWD)

Tepotinib: Parametric survival models (PSMs) fit to the previously untreated patient cohort in VISION

CT+IO: PSMs fit to RWD, specifically in a population with *MET*ex14 skipping NSCLC, weighted to the untreated cohort in VISION

Method 2. Hazard ratio (HR)

Tepotinib: PSMs fit to the untreated cohort in VISION

CT+IO: Published HRs from a CT+IO versus chemotherapy trial (KEYNOTE-189)[18] in the wider NSCLC population, applied to PSMs fit to real-world chemotherapy data in *MET*ex14 skipping NSCLC population, weighted to the untreated cohort in VISION

Method 3. Match-adjusted indirect comparison (MAIC)

Tepotinib: PSMs fit to match-adjusted untreated VISION cohort matched to the CT+IO KEYNOTE-189 population

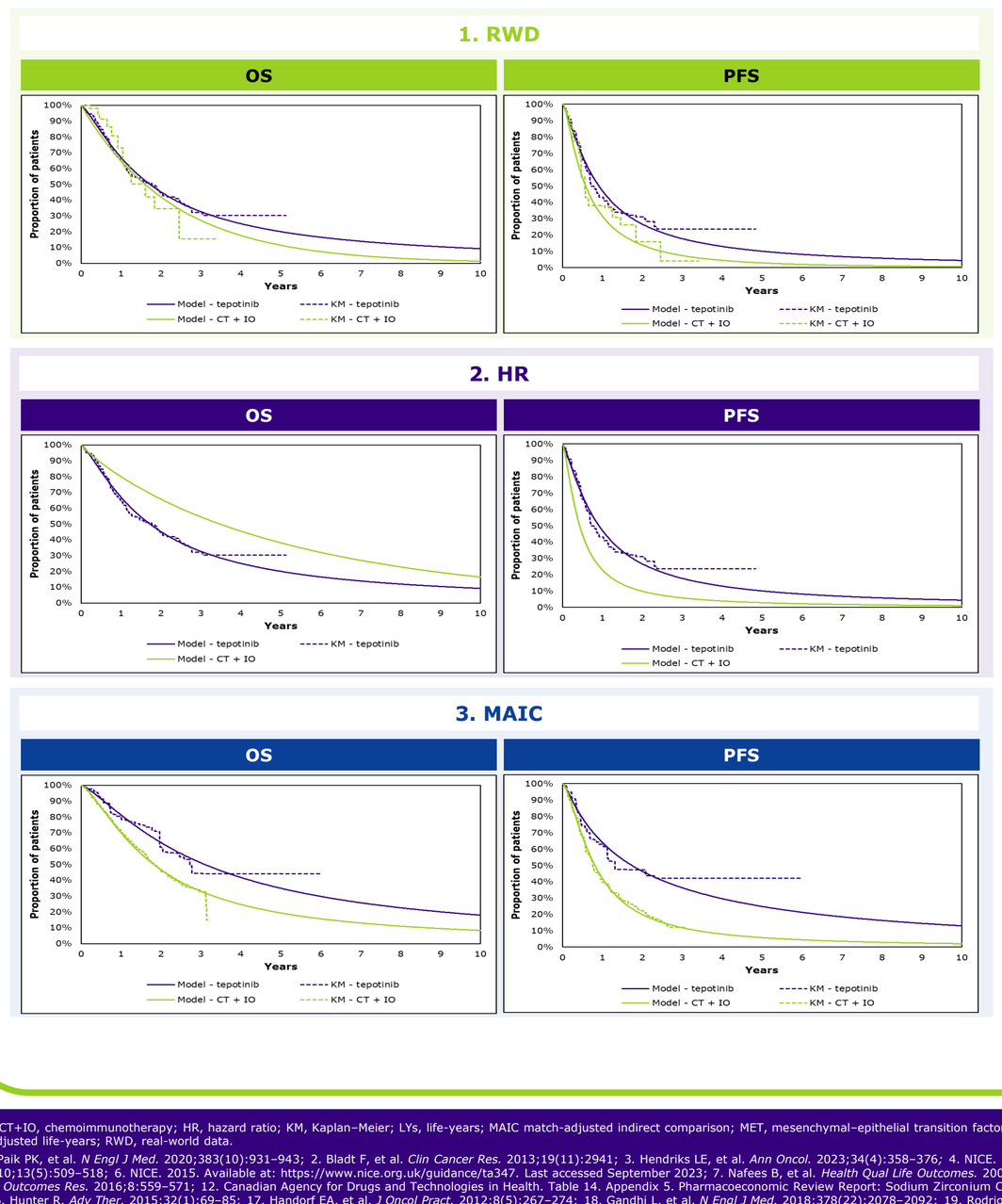
CT+IO: PSMs fit to pseudo patient-level data from digitized KEYNOTE-189 data[19]

- Annual discount rates for quality-adjusted life-years (QALYs) were set to 3.5%[3]
- Utilities for each health state were derived from the VISION study,[1] with adverse events and age-associated disutilities extracted from the literature[5–17]
- For each approach, visual inspection alongside statistical fits were used to compare which distribution(s) best fit the (un)adjusted Kaplan–Meier data, alongside predicting plausible long-term projections

1. **RWD:** Tepotinib OS: Log-logistic; PFS: Log-logistic. CT+IO OS: Exponential; PFS: Log-normal
2. **HR:** Tepotinib OS: Log-logistic; PFS: Log-logistic. CT+IO OS HR: 0.64; PFS HR: 0.75[18]
3. **MAIC:** Tepotinib OS: Log-logistic; PFS: Log-normal. CT+IO OS: Log-logistic; PFS: Log-logistic

RESULTS

Figure 3. OS and PFS PSMs for tepotinib vs CT+IO using each method



- **Figure 3** presents the base case survival curves for OS and PFS. In all approaches, tepotinib is projected to have higher PFS in the long term. With the exception of the HR approach (Method 2), tepotinib is projected to have longer OS
- **Table 1** presents the total life-years (LYs) and QALYs associated with each method
- The MAIC approach (Method 3) estimated the greatest survival benefit for tepotinib versus CT+IO at 2.28 years (5.94 vs 3.66), followed by the RWD approach (Method 1) with 1.25 years (3.56 vs 2.31)
- The HR approach (Method 2) showed a survival decrement of 1.75 years (3.56 vs 5.31)
  - This is due to the OS curves predicting higher outcomes for CT+IO. The CT+IO curves rely on the RWD of first-line chemotherapy, which is impacted by subsequent therapies (e.g. immunotherapy or MET-targeted treatments)
- When assessing the impact on PFS, the results of tepotinib versus CT+IO ranged from 0.52 to 2.85 LYs, whilst their QALY gain ranged from 0.33 to 1.46 QALYs. Total incremental QALYs ranged from −0.86 to 1.17

Table 1. Resulting base case QALYs and LYs for tepotinib vs CT+IO

Drug	Total						Incremental					
	LYs			QALYs			LYs			QALYs		
	PF	PD	Total	PF	PD	Total	PF	PD	Total	PF	PD	Total
1. RWD												
Tepotinib	2.22	1.34	3.56	1.33	0.69	2.02						
CT+IO	1.10	1.21	2.31	0.72	0.70	1.42	1.12	0.13	1.25	0.60	−0.01	0.60
2. HR												
Tepotinib	2.22	1.34	3.56	1.33	0.69	2.02						
CT+IO	1.70	3.62	5.31	1.01	1.87	2.88	0.52	2.28	−1.75	0.32	−1.18	−0.86
3. MAIC												
Tepotinib	4.51	1.43	5.94	2.49	0.71	3.20						
CT+IO	1.66	2.00	3.66	1.04	1.00	2.04	2.85	0.57	2.28	1.45	−0.29	1.17

Abbreviations: CT+IO, chemoimmunotherapy; HR, hazard ratio; KM, Kaplan–Meier; LYs, life-years; MAIC match-adjusted indirect comparison; MET, mesenchymal–epithelial transition factor; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressed disease; PF, progression-free; PFS, progression-free survival; PSM, parametric survival model; QALYs, quality-adjusted life-years; RWD, real-world data.

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