Tepotinib for the treatment of adult patients with metastatic non-small cell lung cancer harboring *MET*ex14 skipping alterations: A US cost-effectiveness analysis

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CONCLUSION

- **From the US Medicare perspective, tepotinib could be cost-effective relative to capmatinib in treating patients with mNSCLC harboring *MET*ex14 skipping**

INTRODUCTION

- In 2020, lung cancer was estimated as the third costliest tumor type ($23.8 billion)[1]
- Lung cancer is a leading cause of cancer-related death in the US, accounting for an estimated 21.4% of all cancer deaths in 2022;[2] NSCLC accounts for approximately 80–85% of cases[3,4]
- Approximately 3–4% of patients with NSCLC harbor *MET*ex14 skipping, which has been recognized as an oncogenic driver[5]
- Results from Phase II clinical studies indicate that the MET TKIs tepotinib (VISION; NCT02864992) and capmatinib (GEOMETRY mono-1; NCT02414139) may prolong survival in patients whose tumors harbor *MET*ex14 skipping;[6,7] both drugs have been approved by the US FDA, but their economic implications remain unclear

OBJECTIVE

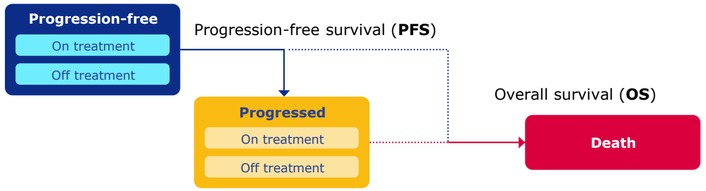
- To compare the cost-effectiveness of tepotinib and capmatinib, from the US Medicare perspective, for treatment-naïve (1L) and previously treated (2L+) adult patients with mNSCLC harboring *MET*ex14 skipping

METHODS

- A three-state (progression-free, progressed, and deceased) partitioned survival model was developed to evaluate the cost-effectiveness of tepotinib versus capmatinib from the perspective of US Medicare payers (**Figure 1**)
  - TTD curves stratified patients into those remaining on treatment and those no longer receiving therapy
  - Since FDA approvals for tepotinib and capmatinib do not specify line of therapy,[8,9] the model calculates the weighted average of outcomes for 1L and 2L+ using the observed baseline distribution of patients in VISION (i.e. 44.5% 1L, 55.5% 2L+)[7]

METHODS (cont.)

Figure 1. Model structure



- Standard parametric survival analysis techniques were applied to patient-level data from VISION (Feb 2021 data cut-off; Cohort A [n=152]; tissue biopsy only)[7,10] to extrapolate beyond the trial's follow-up duration
  - Exponential distributions were used to model OS, PFS, and TTD, as these demonstrated goodness of fit and were considered by clinical experts to exhibit clinical plausibility
  - OS and PFS for capmatinib were estimated by applying HRs derived from a MAIC study,[11] and TTD was based on the median duration of exposure reported in GEOMETRY mono-1[6] (**Table 1**)

Table 1. Inputs for the reference case

Input	Tepotinib 1L	Tepotinib 2L+	Capmatinib 1L	Capmatinib 2L+	Reference
Clinical efficacy					
OS HR vs tepotinib	NA	NA	1.19	1.32	VISION analysis;[12] MAIC with prognostic variables adjusted[11]
PFS HR vs tepotinib	NA	NA	1.18	1.67	
TTD, capmatinib (months [median])	NA	NA	11.1	5.1	VISION analysis;[12] Wolf 2020 (duration of exposure as proxy)[6]
Drug acquisition					
Drug acquisition cost (WAC)	$20,899		$9,469		IBM[13]
Unit size	225 mg		200 mg		
Unit per package	60		56		EMD Serono; FDA labels[8,9]
Drug dosing details	450 mg QD		400 mg BID		
Subsequent treatment costs					
One-off cost	$14,428		$14,335		VISION CSR;[14] KoL feedback
Disease management and treatment monitoring costs					
DM: Pre-progression (per cycle)	$874		$874		CMS.gov;[15] Dalal 2018;[16] Graham 2016;[17] KoL feedback
DM: Post-progression (per cycle)	$5,462		$5,462		
Disease progression (one-off)	$1,079		$1,079		Georgieva 2018[18]
Terminal care (one-off)	$4,063		$4,063		Chastek 2012[19]
Treatment monitoring (per cycle)	$25		$25		CMS.gov;[15] KoL feedback
Utility weights					
Progression-free	0.72				VISION trial[20]
Progressed disease	0.63				
AE management					
Total disutility due to Grade 3–4 AEs (one-off decrement; assumed to apply for a single model cycle)	−0.0010		−0.0015		Institute for Clinical and Economic Review 2016;[21] NICE TA578[22]
Total Grade 3–4 AE incidence and costs (one-off)	$2,492		$2,685		CMS.gov;[15] VISION CSR;[14] FDA labels;[8,9] Shimizu 2019;[23] Patel 2009[24]

- The model incorporated drug acquisition, AE and disease management, treatment monitoring, and subsequent treatment expenditures (inflated to 2021 USD; see **Table 1**)
- On discontinuation, patients accrued drug acquisition and administration expenses associated with post-tepotinib therapies. The composition and duration of treatment were derived from VISION (based on mean PFS for subsequent therapy [3.0 months])[14]
- HRQoL in the model reflected progression status and occurrence of AEs (**Table 1**)
  - Health state (pre- and post-progression) utilities were based on statistical analyses of VISION EQ-5D data[25]
- Other model settings included:
  - 20-year time horizon
  - Monthly model cycle, in alignment with dosing cycles
  - 3% annual discount rate for health and cost outcomes
- Results were interpreted with reference to the range of WTP thresholds recommended by the Institute for Clinical and Economic Review ($100,000–$150,000/QALY)

RESULTS

- Tepotinib was found to be cost-effective versus capmatinib in the base-case analysis (**Table 2**)
  - Tepotinib was associated with 0.41 incremental discounted LYs (2.10 and 1.69 for tepotinib and capmatinib, respectively) and 0.29 QALYs (1.43 and 1.15, respectively) over the model horizon
  - Tepotinib generated $30,205 in incremental discounted costs ($343,721 and $313,516 for tepotinib and capmatinib, respectively) over the cohort's lifetime
    - This was primarily due to differences in drug acquisition ($257,939 vs $235,813 for capmatinib) and disease management costs ($76,559 vs $67,429 for capmatinib)
  - The resultant base-case ICER ($105,173/QALY) was well within the range of WTP thresholds
- Cost-effectiveness vs capmatinib was preserved in nearly all scenarios considered (**Table 3**)

Table 2. Base-case analysis deterministic results

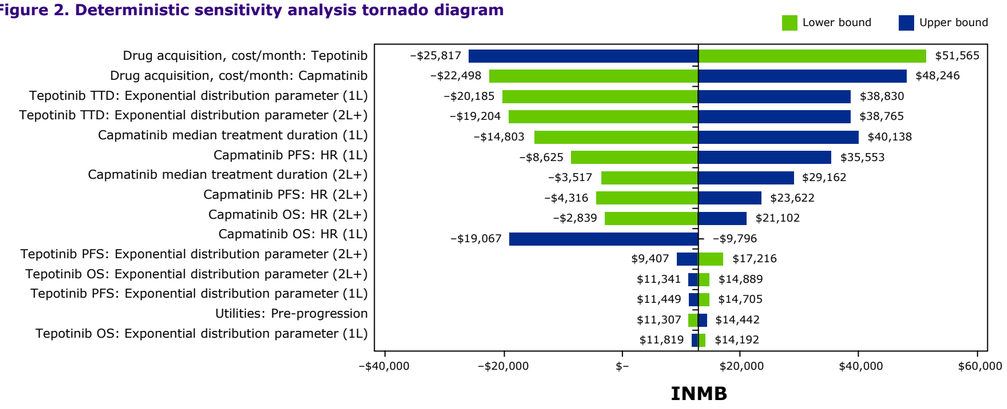
	Overall (line-agnostic)	
	Tepotinib	Capmatinib
Health outcomes		
Total QALYs	1.4334	1.1462
Progression-free LYs	1.1861	0.8687
Post-progression LYs	0.9109	0.8203
On-treatment LYs	0.9763	0.9168
Off-treatment LYs	1.1207	0.7722
Total LYs	2.0970	1.6890
Cost outcomes		
Drug acquisition	$257,939	$235,813
Administration	$0	$0
Treatment monitoring	$294	$276
AE management	$2,492	$2,685
Disease management	$76,559	$67,429
Subsequent treatment	$6,436	$7,313
Total costs	$343,721	$313,516
Incremental results		
Incremental costs	-	$30,205
Incremental LYs	-	0.4080
Incremental QALYs	-	0.2872
ICER ($/LY)	**-**	**$74,036**
ICER ($/QALY)	**-**	**$105,173**

Table 3. Scenario analyses

Scenario description	Incremental costs	Incremental QALYs	ICER/ QALY
Base-case analysis	**$30,205**	**0.2872**	**$105,173**
Assume treat until progression	$95,257	0.2872	$331,680
Include biomarker testing costs	$30,205	0.2872	$105,173
Include the vial sharing (IV therapies only)	$30,211	0.2872	$105,194
Employ alternative DM resource utilization	$27,801	0.2872	$96,802
Exclude subsequent treatment expenditures	$31,082	0.2872	$108,225
Double subsequent treatment frequencies	$29,328	0.2872	$102,120
1L patients only	-$47,188	0.2195	Dominant
2L+ patients only	$92,311	0.3415	$270,284
Literature-based PF and PD utility values	$30,205	0.2494	$121,126
Exclude AE disutilities	$30,205	0.2867	$105,355
5-year time horizon	$25,436	0.2214	$114,881
10-year time horizon	$29,447	0.2794	$105,383
5% cost and health outcomes discount rates	$29,081	0.2713	$107,202
0% cost and health outcomes discount rates	$32,188	0.3151	$102,157
Tepotinib log-normal PFS and OS	$34,505	0.4043	$85,342
Apply population weighting from Flatiron	$14,610	0.2736	$53,408
Apply $35 co-payment	$30,654	0.2872	$106,735
Apply 10% co-insurance	$28,079	0.2872	$97,768

- Deterministic sensitivity analysis results underscore the sensitivity of base-case results to uncertainty in the cost and comparative efficacy of tepotinib and capmatinib (**Figure 2**)
  - Estimated net monetary benefit was most sensitive to monthly drug acquisition costs for both tepotinib and capmatinib
- Probabilistic sensitivity analysis results aligned closely with the base-case, and suggest tepotinib may be cost-effective compared with capmatinib at conventional US cost-effectiveness thresholds
  - 61.9% of model iterations produced ICERs less than $150,000/QALY
  - Tepotinib was more effective than capmatinib in 94.3% of model runs

Figure 2. Deterministic sensitivity analysis tornado diagram



Abbreviations: 1L, first line; 2L+, second line or later; AE, adverse event; BID, twice daily; CMS, Centers for Medicare & Medicaid Services; CSR, clinical statistical report; DM, disease management; HR, hazard ratio; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; INMB, incremental net monetary benefit; IV, intravenous; KM, Kaplan–Meier; KoL, key opinion leader; LY, life year; MAIC, matching-adjusted indirect comparison; *MET*ex14, mesenchymal-epithelial transition factor gene exon 14; mNSCLC, metastatic non-small cell lung cancer; OS, overall survival; PD, progressive disease; PF, progression-free; PFS, progression-free survival; QALY, quality-adjusted life year; QD, once daily; TKI, tyrosine kinase inhibitor; TTD, time to discontinuation; WAC, wholesale acquisition cost; WTP, willingness to pay.

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Acknowledgements: The authors would like to thank patients, all investigators and co-investigators, and the study teams at all participating centers and at the healthcare business of Merck KGaA, Darmstadt, Germany. The trial was sponsored by the healthcare business of Merck KGaA, Darmstadt, Germany. Medical writing and editorial assistance was provided by Syneos Health, UK, and funded by the healthcare business of Merck KGaA, Darmstadt, Germany.

Disclosures: Mo Yang is an employee of EMD Serono. Helene Vioix and Boris Pfeiffer are employees of the healthcare business of Merck KGaA, Darmstadt, Germany. Rameet Sachdev, Matthew Stargardter and Jon Tosh are employees of Evidera. Paul K. Paik has an advisory role in AstraZeneca, Calithera, Lilly, Takeda, EMD Serono, Xencor, Bicara, Boehringer Ingelheim, CrownBio; and his research institution has received research expenses from EMD Serono, Boehringer Ingelheim, Bicara.

Presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Conference | May 15–18, 2022 | Washington, D.C., United States of America and virtual