Cost-effectiveness Of Tepotinib For Patients With Previously Treated Advanced Non-small Cell Lung Cancer Harboring *MET*ex14 Skipping Alterations In Spain

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CONCLUSION

In previously treated patients with aNSCLC *MET*ex14, tepotinib is expected to provide clinically meaningful life expectancy increase and is considered a cost-effective alternative in Spain

Patients receiving tepotinib are associated with a QALY gain of 0.34, 0.21 and 0.25 versus IO, CT and SoC, respectively

For all comparisons, the ICER remained below the WTP acceptable in Spain (50.000€/QALY for end-of life treatments and 30.000€/QALY in general). PSA confirmed a probability higher than 89% for tepotinib to be cost-effective from the Spanish NHS perspective at a WTP threshold of 50.000€/QALY.

INTRODUCTION

- Alterations resulting in the *MET* exon 14 (*MET*ex14) skipping mutation account for 3-4% of non-small cell lung cancer (NSCLC)[1] and are associated with a poor prognosis[2-5].
- In the VISION study - single arm, largest of a MET inhibitor in patients with METex14 skipping NSCLC – tepotinib demonstrated robust and durable efficacy[6].
- Tepotinib is an oral, once daily, highly selective inhibitor of MET TKI indicated as monotherapy for the treatment of adult patients with advanced NSCLC harboring alterations leading to *MET*ex14 skipping, who require systemic therapy following prior treatment with immunotherapy (IO) and/or platinum-based chemotherapy (CT), according to the European marketing authorization[7].

OBJECTIVES

This study evaluated the cost-effectiveness of tepotinib vs. alternatives considered to be the standard of care in Spain before the launch of the MET inhibitors in previously treated advanced NSCLC (aNSCLC) patients harboring METex14 skipping alterations from the Spanish National Health System perspective.

METHODS

Model structure

- A partitioned survival model was developed to represent the natural history of aNSCLC over a 30-year time horizon with a three-health state structure (Figure 1).
- The proportion of patients within each health state are based on overall survival (OS) and progression free survival (PFS) curves and calculated as follows:
  - Progression-free = PFS; Progressed = OS – PFS; Death = 1 - OS
- The adaptation to the Spanish context was done considering the following assumptions:
  - Three categories of comparators were set: immunotherapy (IO), chemotherapy (CT) (Table 1) and standard of care (SoC). SoC was defined as a distribution based on the contribution IO and CT alternatives and a targeted therapy for MET (crizotinib) available in Spain according to clinical experts (Table 2).

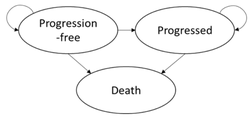


Figure 1. Partitioned survival model health state transitions

Table 2. SOC composition

SoC	Contribution (%)
IO	15%
CT	80%
Crizotinib	5%

Table 1. Categories composition

Categories	Contribution (%)
Immunotherapy	
Pembrolizumab	20,0%
Atezolizumab	40,0%
Nivolumab	40,0%
Chemotherapy	
Docetaxel/ platinum	0,0%
Gemcitabine/ platinum	1,0%
Paclitaxel/ platinum	10,0%
Vinorelbine/ platinum	0,0%
Pemetrexed/ platinum	28,0%
Docetaxel monotherapy	18,0%
Docetaxel/ nintedanib	40,0%
Docetaxel/ gemcitabine	0,0%
Gemcitabine monotherapy	1,0%
Vinorelbine monotherapy	1,0%
Bevacizumab/ carboplatin/ paclitaxel	1,0%

- For tepotinib, to estimate the projected proportion of patients in each health state (progression-free, progressed and death) PFS and OS data from VISION study were used. For the comparators, efficacy was estimated using a real-world cohort (comprising several data sets), propensity-score weighted to match the population in VISION.
  - Parametric modelling of curves was performed. Visual inspection and comparison of the Akaike information criterion (AIC) and Bayesian information criterion (BIC) were used to compare which distributions provided the best fit to the Kaplan-Meier data and has clinical plausibility of long-term projections.
- Utilities associated with each health-state were derived from VISION. Adverse events and age-associated disutilities were extracted from the literature[8-20].
- Adverse event incidence was extracted from VISION for tepotinib and, from the literature for the comparators.
- Use of resources were adjusted to Spanish clinical practice, according to clinical expert opinion.
- Annual discount rates for costs and QALY were set to 3.5%.

Costs

- Unitarian costs (inflated to €2022) were extracted from national Spanish tariffs databases when available and from literature.
- To better mirror the costs for the Spanish Health System due to the huge differences that exist between the notified and the financed drug acquisition costs[21], the financed cost were used based on expert opinion with the exception to those drugs[a] already included in the reference price list[22] (regularly published by the Spanish Ministry of Health).

Model results

- Model results were expressed in life-years (LY), quality-adjusted life-years (QALY) and incremental cost-effectiveness ratio (ICER).
- Willingness to pay (WTP) threshold was set to 50.000€/QALY, as tepotinib is considered an end-of-life targeted therapy according to the definition described in GENESIS guidelines[23]. Also in Spain, a more general WTP threshold is set at around 30.000€/QALY[24-25].

Sensitivity analysis

- A probabilistic sensitivity analysis (PSA) with 1000 iterations was conducted for IO and CT comparisons.

RESULTS

- Over a 30-year time horizon, model results revealed that:
  - Previously treated patients receiving tepotinib experienced an extended life expectancy of 0.65, 0.35 and 0.43 LY versus IO, CT and SoC (Table 3).
  - When adjusted by quality of life, total QALY gain was also higher for tepotinib compared to IO, CT and SoC (additional QALY: 0.34, 0.21 and 0.25, respectively) (Table 2).
- The ICER remained below 50.000€ in all pairwise comparisons (Figure 2).

Table 3. Results from the Base Case analysis.

Treatments	Total		Incremental	
	LYs	QALYs	LYs	QALYs
Tepotinib	2,75	1,62		
Immunotherapy	2,10	1,27	0,65	0,34
Chemotherapy	2,40	1,41	0,35	0,21
Standard of care	2,32	1,37	0,43	0,25

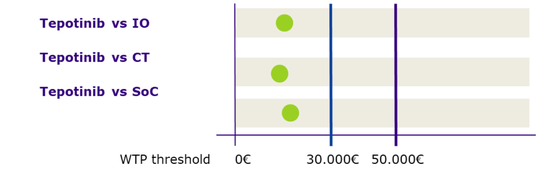
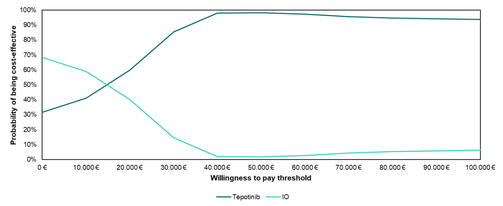


Figure 2. Results from the Base Case: Willingness to pay analysis. Pairwise results.

Probabilistic sensitivity analysis results

- PSA suggested a high probability of tepotinib to be cost-effective compared with IO and CT, respectively, for both WTP considered (Figure 3A and 3B).

A.

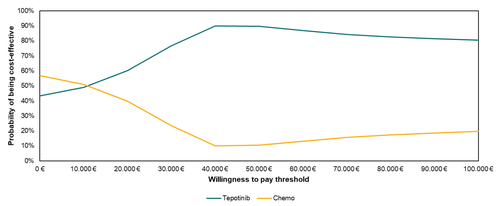


Probability of tepotinib to be cost-effective vs IO

85.4% at 30.000€ WTP threshold

98.2% at 50.000€ WTP threshold

B.



Probability of tepotinib to be cost-effective vs CT

76.6% at 30.000€ WTP threshold

89.6% at 50.000€ WTP threshold

Figure 3. Cost-effectiveness acceptability curves. A) tepotinib and IO, B) tepotinib and CT.

[a] Carboplatin, cisplatin, docetaxel, paclitaxel, vinorelbine, gemcitabine.

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