EE193

LORLATINIB AS A FIRST-LINE TREATMENT FOR ALK+ ADVANCED NON-SMALL CELL LUNG CANCER: A COST-EFFECTIVENESS ANALYSIS IN SPAIN

Presa M[1], Vicente D[2], Calles A[3], Salinas-Ortega L[1], Naik J[4], García LF[5], Soto J[5]

[1]Pharmacoeconomics & Outcomes Research Iberia (PORIB), Madrid, Spain; [2]Medical Oncology Department, Hospital Universitario Virgen de Macarena, Sevilla, Spain; [3]Medical Oncology Department, Hospital General Universitario Gregorio Marañon, Madrid, Spain; [4]BresMed Health Solutions Ltd, Sheffield, UK; [5]Pfizer, Madrid, Spain

BACKGROUND

- Non-small cell lung cancer (NSCLC) represents approximately 85% of all lung cancers[1], of which 65% will be diagnosed at advanced disease (IIIB-IV) and 12.2% will progress from early to advanced stage[2].
- The approval and adoption of tyrosine kinase inhibitor drugs targeting the anaplastic lymphoma tyrosine kinase receptor gene (ALK), which is present in approximately 3.4% of NSCLC patients[2], has contributed to a decrease in mortality rates[3]. However, disease recurrence, drug resistance and central nervous system (CNS) progression still constitute a major problem in the treatment of ALK+ advanced NSCLC[4,5,6].
- The efficacy and safety of lorlatinib (a third-generation ALK inhibitor), in the treatment of previously untreated ALK+ advanced NSCLC was evaluated in the CROWN clinical trial, a phase III study in which patients were randomized to receive lorlatinib monotherapy or crizotinib monotherapy. CROWN showed favorable results for lorlatinib in this new indication[7].

OBJECTIVE

The aim of this study was to assess the efficiency of lorlatinib versus alectinib and brigatinib for the first-line treatment of adult patients with ALK+ advanced NSCLC from the Spanish National Health System (NHS) perspective.

METHODS

- A partitioned survival model was used to estimate, over a lifetime horizon (30 years), the total accumulated costs and outcomes, in terms of life years gained (LYG) and quality-adjusted life years (QALYs).
- To capture the potential impact of CNS progression, the model included the following health states: pre-progression, non-CNS progression, CNS-progression, and death.
- Overall survival (OS) and progression-free survival (PFS) data were derived from the CROWN study for lorlatinib[7], and from a network meta-analysis of randomized controlled trials for alectinib and brigatinib.
- Subsequent treatments following progression of initial treatment were included and affected costs exclusively. Grade ≥3 adverse events (AEs) observed in ≥5% of patients treated with lorlatinib, alectinib or brigatinib were considered based on clinical trial data[7,8,9].
- Health-state utilities reflected EQ-5D-5L data obtained in the CROWN study for lorlatinib[7], in the ALEX study for alectinib[8] and in the ALTA-1L study for brigatinib[9]. To reflect the lower quality of life of patients with CNS-progression, a multiplier of 75.4%[10] was applied to the post-progression utility (Table 1).
- Healthcare resource consumption was defined by clinical experts in the oncology field.
- In accordance with the NHS perspective, the total costs (expressed in euros using a 2021 cost year) included drug acquisition, subsequent treatment, disease management, adverse event management, and end-of-life care (Table 1).
- Drug costs were estimated based on ex-factory prices[11] with national mandatory deduction applied[12].
- Unitary costs were derived from local databases[13] and the literature[14].
- A lifetime horizon was considered, and an annual discount rate of 3% was applied to costs and outcomes[15].
- One-way sensitivity analyses (OWSA) and probabilistic sensitivity analyses (PSA) were performed to confirm the robustness of the model.

Table 1. Utility values, drug costs and healthcare resource costs (€,2021)

	Lorlatinib	Alectinib	Brigatinib
Utility values[7,8,9]			
Pre-progression: • On treatment • Off treatment	0.85 0.77	0.81 0.81	0.79 0.79
Non-CNS progression: • On treatment • Off treatment	0.82 0.74	0.73 0.73	0.62 0.62
CNS progression: • On treatment • Off treatment	0.62 0.56	0.55 0.55	0.47 0.47
Costs (€, 2021)			
Drug acquisition cost*	€4,572	€5,319	€4,758
Subsequent treatment cost**	€10,373	€39,619	€42,035
Average AE management cost†	€812	€149	€541
Pre-progression management costs		€3,417	
Non-CNS progression management costs		€4,669	
CNS progression management costs		€5,321	
End-of-life care		€7,094	

*Drug cost estimated for 30-day model cycle considering the dosage, ex-factory price applying the Royal Decree-law 8/2010, and the relative dose intensity. ** Subsequent treatment cost estimated based on the proportion of patients treated after disease progression, drug and administration costs, and treatment durations. † AE management cost estimated based on the AE rates for each treatment and the unitary cost. AE, adverse events; CNS, central nervous system.

RESULTS

- Over a lifetime horizon, lorlatinib generated higher health outcomes than alectinib (+0.70 LYG/patient, +1.42 QALYs/patient) and brigatinib (+1.74 LYG/patient, +2.30 QALYs/patient) (Table 2).
- Lorlatinib was associated with a total cost of €268,827 per patient compared with €278,066 with alectinib and €232,200 with brigatinib (Table 2).
- Lorlatinib was a dominant option (more effective and less costly) relative to alectinib treatment. The incremental cost-utility ratio (ICUR) for lorlatinib versus brigatinib was €15,912/QALY gained (Table 2).

Table 2. Base case results

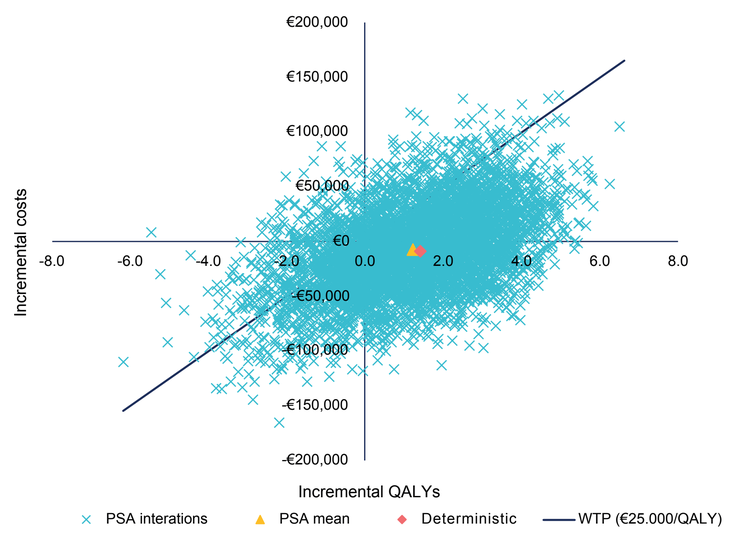
	Lorlatinib	Alectinib	Lorlatinib vs Alectinib	Brigatinib	Lorlatinib vs Brigatinib
Total LYG	**7.40**	**6.69**	**0.70**	**5.66**	**1.74**
LYG pre-progression	3.99	2.31	1.69	2.35	1.64
LYG post-progression	3.40	4.39	-0.98	3.30	0.10
Total QALY	**5.89**	**4.46**	**1.42**	**3.59**	**2.30**
QALY pre-progression	3.37	1.88	1.50	1.87	1.51
QALY post-progression	2.51	2.59	-0.07	1.72	0.79
Total Costs	**€268,827**	**€278,066**	**-€9,239**	**€232,200**	**€36,627**
Treatment costs	€222,545	€201,587	€20,958	€158,171	€64,374
Subsequent treatment costs*	€8,125	€32,561	-€24,436	€34,506	-€26,381
Health-state magament costs	€29,539	€37,831	-€8,292	€32,195	-€2,656
End-of-life costs	€5,400	€5,627	-€227	€5,870	-€470
AE costs	€3,218	€459	€2,758	€1,457	€1,760
ICER (€/LYG)			**Dominant**		**€21,040/LYG**
ICUR (€/QALY)			**Dominant**		**€15,912/QALY**

* Resulting subsequent treatment costs for lorlatinib, alectinib and brigatinib, were estimated base on the progression proportion and the discount rate applied through a lifetime horizon. AE, adverse events; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio; QALY, quality-adjusted life year; LYG, life-year gained

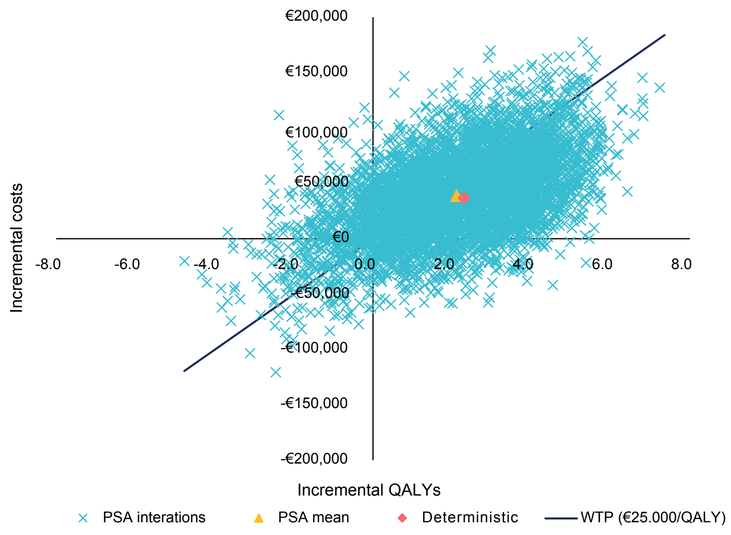
- Sensitivity analyses confirmed the model robustness. The OWSA showed that the primary drivers of the model results were the utility values, following by the acquisition drug costs and the time horizon. In the PSA, alectinib was extendedly dominated by lorlatinib (Figure 1A) and lorlatinib was associated with a mean ICUR of €18,508/QALY gained versus brigatinib (Figure 1B).

Figure 1. Cost-effectiveness plane: A (lorlatinib vs alectinib), B (lorlatinib vs brigatinib)

A



B



PSA; probabilistic sensitivity analysis; QALY, quality-adjusted life year; WTP, willingness-to-pay threshold

CONCLUSIONS

Lorlatinib dominated alectinib (more effective and less expensive) and was a cost-effective therapy compared to brigatinib, when considering the willingness-to-pay threshold of €25,000/QALY[16], for the treatment of previously untreated ALK+ advanced NSCLC in Spain.

REFERENCES

1. Majem M, et al. Clin Transl Oncol. 2019;21(1):3-17; 2. Salas C, et al. J Clin Pathol. 2022;75(3):193-200; 3. Majeed U, et al. J Hematol Oncol. 2021;14(1):108; 4. Bauer TM, et al. Target Oncol. 2020 Feb;15(1):55-65; 5. Gainor JF, et al. J Thorac Oncol. 2016 Feb;11(2):256-60; 6. Ali A, et al. Curr Oncol. 2013 Aug;20(4):e300-6; 7. Shaw AT, et al. N Engl J Med. 2020;383(21):2018-29; 8. Peters S, et al. N Engl J Med. 2017;377(9):829-38; 9. Camidge DR, et al. J Clin Oncol. 2020;38(31):592-3603; 10. Roughley A, et al. Value Health. 2014;17(7):A650; 11. Bot Plus 2.0. https://botplusweb.portalfarma.com/; 12. Royal Decree-Law 8/2010. http://www.boe.es/boe/dias/2010/05/24/pdfs/BOE-A-2010-8228.pdf; 13. eSalud. http://www.oblikue.com/bddcostes; 14. Llibre-Codina JM, et al. Enferm Infecc Microbiol Clin. 2007;25(2):98-107; 15. López-Bastida J, et al. Eur J Health Econ. 2010;11:513–20; 16. Vallejo-Torres L, et al. Health Econ. 2018;27(4):746-61

ISPOR Improving healthcare decisions

Presented at ISPOR Europe 2022 6-9 November

Designed by porib