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Cost-effectiveness of sequential treatment containing crizotinib for non small cell lung cancer (ALK+) patients

Sabater Cabrera E[1], Puente J2, Oyagüez I[1], García-Campelo R[3], Reguart N[4], Rodríguez-Abreu D[5], Cobo M[6], Soto J[7], Moran M[7]

[1]Pharmacoeconomics & Outcomes Research Iberia (PORIB), Madrid, Spain, [2]Hospital Clinico San Carlos, Madrid, Spain, [3]Hospital Universitario A Coruña, A Coruña, Spain, [4]Hospital Clinic de Barcelona, Barcelona, Spain, [5]Complejo Hospitalario Universitario Insular- Materno Infantil, Las Palmas de Gran Canaria, Spain, [6]Hospital Regional de Malaga (Carlos Haya), Malaga, Spain, [7]Pfizer Spain, Alcobendas, Spain

INTRODUCTION

- Non-small-cell lung cancers (NSCLC) represent the 85%–90% of lung cancers[1]. It is estimated that the prevalence of ALK alterations in approximately the 3–7% of unselected NSCLC patients[2].
- Crizotinib is approved in first-line for NSCLC ALK positive patients.

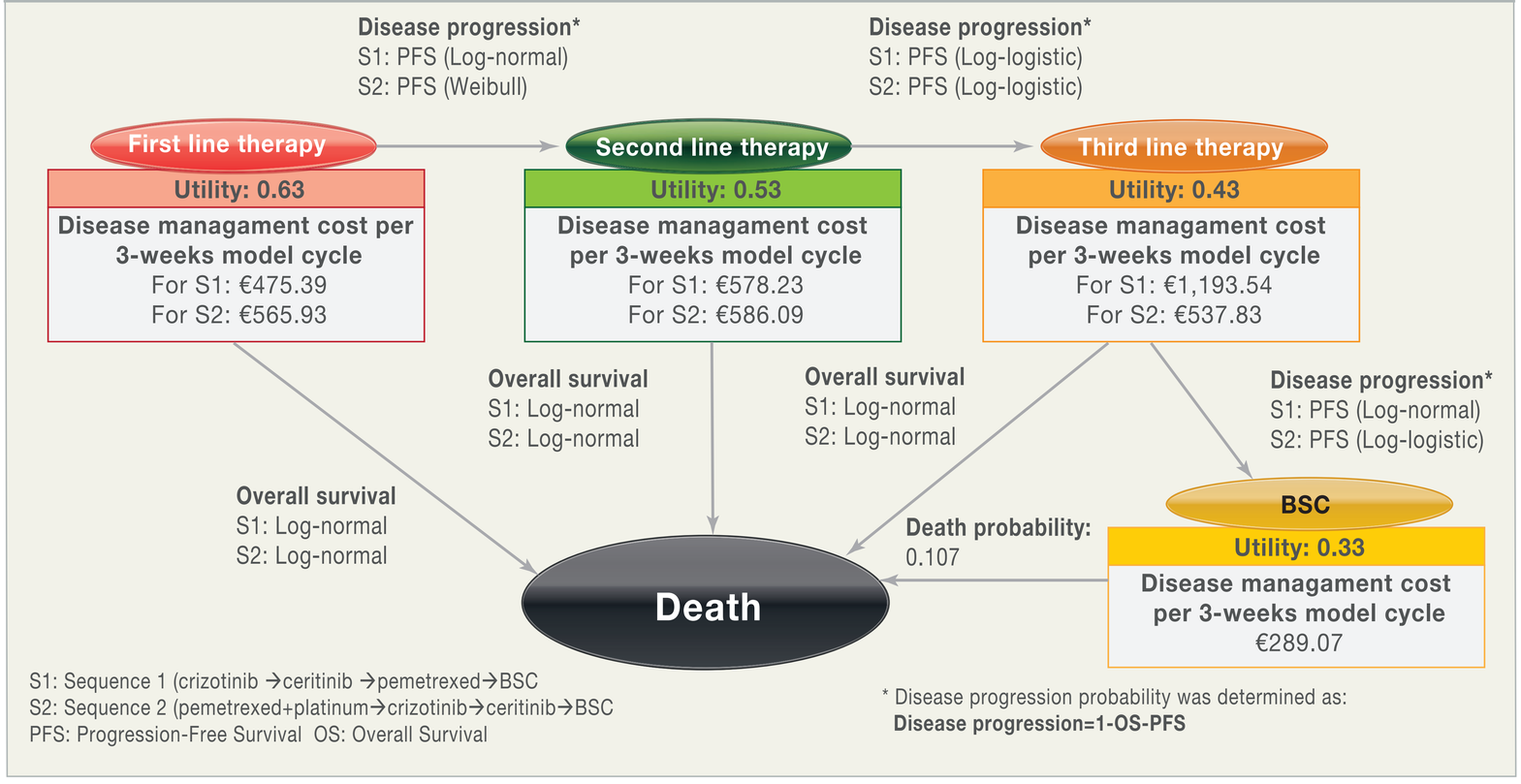
OBJECTIVE

This study aimed to assess the cost-effectiveness of two different containing Crizotinib sequential treatments, in Spain.

METHODS

- A Markov model was designed based on the potential treatment lines (Figure 1), in order to compare two treatment sequences in a cohort of NSCLC patients.
  - Sequence 1 with crizotinib as first-line: crizotinib → ceritinib →pemetrexed →Best Supportive Care [BSC]
  - Sequence 2 with crizotinib positioned in 2nd-line: pemetrexed+platinum →crizotinib →ceritinib →BSC.
- Outcomes (life year gained, LYG; quality adjusted life year, QALY) and total costs were estimated for a lifetime period.
- Transitions between treatment lines were driven by the disease progression, by means of the progression free survival (PFS) data observed in clinical trials[3-6].
- The Overall survival (OS) was used to reflect the probability of death[3,5,7]. Death probability in BSC health state was obtained from the literature[8].
- Parametric functions with best fit to PFS and OS Kaplan-Meier curves were selected to extrapolate the data available from trials beyond the observed period covering the simulation period. (Figure 1)
- Utility values were obtained from the literature[9].
- Considering the National Health System (NHS) perspective, the total cost estimation (€,2016) included drug acquisition, administration for intravenous chemotherapy (only pemetrexed, perfussion lasting; less than 30 min €126.45 and more than 2h €252.88), disease management, AE management and end-of-life costs (€26,027.00 one-off cost)[10].
- Adverse event considered were: anemia (€1,654,48 per event), diarrhea (€286.79 per event), fatigue (€0,00 per event), leukopenia (€1,404.62 per event), lipase increase (€577.51 per event), nauseas (€256.37 per event), neutropenia (€1,404.62 per event), transaminases increase (€627.29 per event), thrombocytopenia (€1,404.62 per event) and vomiting (€256.37 per event).
- Drug cost were estimated based on the authorized dosages, considering the ex-factory list prices and the official deduction for reimbursed drugs[11,12]. Conservatively, for ceritinib, price was set 0€ as, currently it is acquired free by the Spanish NHS. (Table 1)

Figure 1. Markov model diagram



- An oncologists' board validated and provided the health resource consumption data associated to BSC and disease and AE management.
- Unitary cost for health resources were obtained from a local database[13].
- Annual discount rate (3%) was applied to both health benefits and costs[14].
- Several sensitivity analysis (SA) were performed.

Table 1. Drug costs (€, 2016)

DRUGS	Dosages	Cost per model cycle (21 days)
Ceritinib	750 mg once daily. Oral route.	€0,00
Crizotinib	250 mg b.i.d. Oral route.	€3,386.55
Pemetrexed	500 mg/m^2 on day 1 of 3-weeks cycle in 10 min intravenous perfussion	€1,887.00
Pemetrexed plus platinum	500 mg/m^2 on day 1 of 3-weeks cycle in 10 min intravenous perfussion, followed by cisplatinum , 75 mg/m^2 in 2h intravenous perfussion	€1,915.43

RESULTS

- Sequence 1 resulted in a more effective option, yielding 0.88 LYG and 0.68 additional QALY than sequence 2.
- Total costs for sequence 1 resulted €194,460 compared to €149,415 for sequence 2.
- The incremental cost-effectiveness ratios were €51,078/LYG and €66,486/QALY gained with crizotinib first-line-sequence versus the sequence 2, crizotinib in second-line. (Table 2)
- SA results are shown Figure 2.

Figure 2. One-way sensitivity analysis results

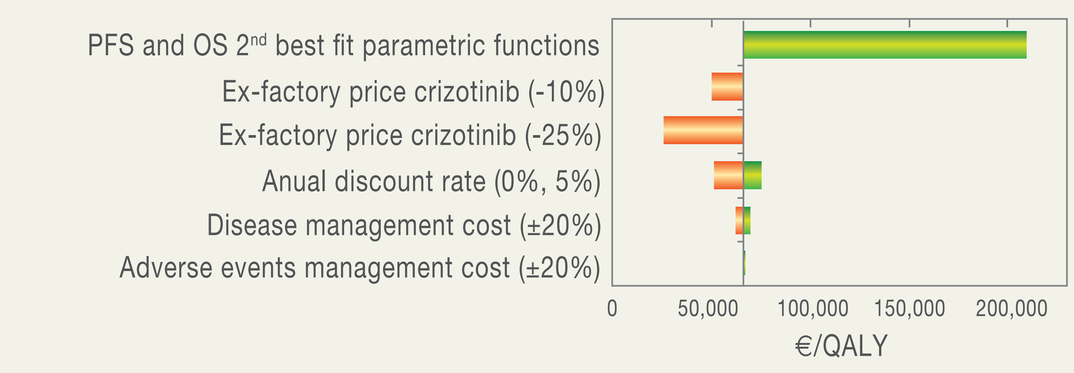


Table 2. Cost-effectiveness results

	Sequence 1 (S1)	Sequence 2 (S2)	Incremental (S1 vs S2)
Effectiveness			
LYG	**4.17**	**3.29**	**0.88**
QALY gained	**2.29**	**1.61**	**0.68**
Costs			
Drug acquisition	€126,236.22	€92,217.95	€34,018.26
Intravenous administration	€1,094.44	€1,326.33	€-231.89
AE management	€1,688.22	€1,356.79	€331.43
Disease management	€42,540.48	€30,817.02	€11,723.46
End-of-life	€22,900.94	€23,696.52	€-795.58
Total cost	**€194,460.30**	**€149,414.61**	**€45,045.69**
ICER (S1 versus S2)	**€51,078.33 per LYG**		
ICUR (S1 versus S2)	**€66,486.29 per QALY gained**		

CONCLUSIONS

A treatment sequence based on crizotinib in first-line resulted in a cost-effective option for NSCLC patients (ALK+) in Spain, compared to an alternative sequence with crizotinib in second-line.

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