

ECONOMIC ANALYSIS OF ERLOTINIB, DOCETAXEL, PEMETREXED AND BEST SUPPORTIVE CARE AS 2ND LINE TREATMENT OF NON-SMALL CELL LUNG CANCER (NSCLC)

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INTRODUCTION

- More than half a million new cases of lung cancer are annually diagnosed worldwide¹;
- The estimated incidence of new cases of lung cancer/100,000 inhabitants in the latest years in Portugal is about 34 new cases (28 new cases/100,000 in men and 6 new cases/100,000 in women)² and mortality continues to increase³;
- NSCLC five year survival across all disease stages is about 12%¹;
- Surgery is the treatment of choice, but only about 20% of tumours are suitable for potentially curative resection¹;
- Docetaxel, pemetrexed or erlotinib are presently authorized for 2nd line treatment of NSCLC in advanced stage⁴;
- Erlotinib [an epidermal growth factor receptor/human epidermal growth factor receptor type 1 (EGFR also known as HER1) tyrosine kinase inhibitor] is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen⁵.

OBJECTIVES

To evaluate costs and clinical benefits of erlotinib as 2nd line treatment of locally advanced or metastatic NSCLC comparatively to docetaxel, pemetrexed or best supportive care performing a cost-utility analysis (incremental cost per Quality Adjusted Life Years – QALYs) and a cost-minimization analysis (incremental cost per Life Year Gained - LYG).

METHODS

Cost-utility analysis

A model with three health states (Figure 1) was used to estimate the cost-utility of erlotinib therapy *versus* other therapies (docetaxel, pemetrexed or best supportive care). All patients are in the "progression free survival" health state when simulation starts. Every monthly cycle, patients can stay in the "Progression Free Survival" state (A) or transit to the other health states (B or C); after progression, the patient can stay on the same state (D) or transit to dead (E).

The model does not operate in the traditional Markov Process way. There are no transition probabilities; Kaplan-Meier estimates concerning time spent in "progression free survival" health state and overall survival are directly used in the model.

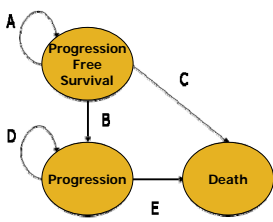


Figure 1 Structure of decision model

Cost-minimization analysis

Since there are no head-to-head clinical trials that directly compare the efficacy of erlotinib with docetaxel and/or pemetrexed, indirect comparisons between the three active therapies were performed, based on efficacy results from respective pivotal clinical trials. Given there is no evidence of differences in terms of survival, the cost-effectiveness results (that is, cost per Life Year Gained) were confined to a cost-minimization analysis.

Population

A hypothetical cohort of Portuguese patients with locally advanced or metastatic NSCLC with one previous chemotherapy regimen failure (2nd line) was considered. The model also allows results estimations regarding the following patient sub-populations: one or more previous chemotherapy regimens (2nd and 3rd lines); one or more previous chemotherapy regimens (2nd and 3rd lines) with ECOG PS 0 or 1 and two or more previous chemotherapy regimens (3rd line).

Model assumptions

- Three active therapies (erlotinib, docetaxel and pemetrexed) and best supportive care;
- When simulation starts all patients are in the "progression free survival" health state and the transition to other health states is performed in 1 month length cycles with an half cycle-correction;
- Time horizon is 24 months (2 years) (Figure 2), with the possibility of extrapolation up to 36 months (3 years) for ITT and 3rd line treatment populations, according to the Weibull and Log-logistic distribution;
- 5% annual discount rate for costs and consequences (QALYs, LYG)⁶;
- Portuguese National Health System (NHS) perspective (direct medical costs supported by NHS) was applied;
- Between the three active therapies progression free survival and overall survival are identical.

Table 1 Utility values used in the model

Health States	Utility	Standard Error (SE)
Progression free survival	0.451	0.170
Progression	0.217	0.011
Death	0	0
Adverse events		
Rash	0.403	0.166
Diarrhoea	0.325	0.148
Nausea	0.315	0.146
Stomatitis	0.321	0.136
Neutropenia	0.324	0.156
Febrile neutropenia	0.194	0.114
Neuropathy	0.306	0.163

Source: Utility study conducted in the UK (n=154)

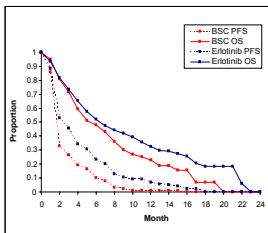


Figure 2. Kaplan Meier survival curves for 2 years (BSC – Best Supportive Care; PFS – Progression Free Survival; OS – Overall Survival)

- Utilities are taken from a utility study conducted among healthy people in the UK (n=154) using EQ-5D visual analogic scale.
- The utility scores associated with the "progression free survival" and "progression" health states were 0.451 (SE=0.170) and 0.217 (SE=0.011), respectively (Table 1).

Resource consumption and costs

- Resource consumption was estimated by a Portuguese expert panel (Delbecq panel) with 6 pneumologists and 1 oncologist;
- Medicinal product unit cost, speciality visits, hospitalizations, tests and procedures were estimated using official databases [namely, Homogeneous Diagnostics Groups table, hospital Analytical Account Reports and National Authority of Medicines and Health Products (INFARMED, I.P.)]. Costs were actualized to 2008 considering an annual inflation rate of approximately 3%;
- Costs of medicinal products exclusively used in hospitals were obtained using the *Administração Central do Sistema de Saúde (ACSS)* database (price without VAT);
- Treatment costs were calculated considering a body surface area of 1,7 m² and the recommended dose mentioned in the Summary of Product Characteristics of each medicinal product: 150 mg per day of erlotinib, 75 mg/m² of docetaxel (administered on day 1; cycles of 21 days) and 500 mg/m² of pemetrexed (administered on day 1; cycles of 21 days).

Table 2 Summary of costs used in the model		
Health states	Average total cost/patient/month	Resource consumption
Progression-free survival	€ 675.48	hospitalizations, visits, tests and procedures
Progression	€ 2,959.49	hospitalizations, visits, concomitant medication, tests and procedures
Adverse events		
Rash	€ 865.45	hospitalizations, visits and concomitant medication
Anorexia	€ 632.75	hospitalizations, visits and concomitant medication
Diarrhoea	€ 2,958.12	hospitalizations, visits and concomitant medication
Nausea	€ 893.71	hospitalizations, visits and concomitant medication
Infection	€ 1,908.65	Hospitalizations and visits
Stomatitis	€ 2,245.75	hospitalizations, visits, concomitant medication, tests and procedures
Neutropenia (grade 3)	€ 41.36	concomitant medication
Neutropenia (grade 4)	€ 602.24	hospitalizations, visits, concomitant medication, tests and procedures
Febrile neutropenia	€ 3,311.25	hospitalizations, visits and concomitant medication
Fatigue	€ 197.14	hospitalizations, visits and concomitant medication
Neuropathy	€ 108.85	hospitalizations, visits and concomitant medication
Unit cost		
Source		
Medicinal products		
Erlotinib (per 150 mg tablet)	€ 70.00	Roche Farmaceutica Quimica, Ltda
Docetaxel (per 1 vial of 20 mg and 80 mg, respectively)	€ 169.26 and € 666.74	ACSS database
Pemetrexed (per 1 vial of 500 mg)	€ 983.12	Average sale price (information obtained from two hospitals)

ACSS – Administração Central do Sistema de Saúde (database consulted between January and February 2008)

RESULTS

The base-case analysis results (2nd line treatment, 2 years) (Table 3) show that:

- QALYs per patient were higher with erlotinib (0.24) *versus* docetaxel (0.22), pemetrexed (0.23) or best supportive care (0.18);
- The treatment cost per patient with erlotinib (€ 26,428) was lower than with docetaxel (€ 29,160) or pemetrexed (€ 32,334) and higher than with best supportive care (€ 15,752);
- In the cost-utility analysis therapy with erlotinib is "dominant" (lower cost and higher efficacy) *versus* docetaxel and *versus* pemetrexed.

Table 3 Base-case analysis: 2nd line treatment with erlotinib vs. best supportive care, docetaxel or pemetrexed (per patients results)

2 year analysis	Erlotinib	Best supportive care	Docetaxel	Pemetrexed
Cost-minimization analysis				
Cost	€ 26,428	€ 15,752	€ 29,160	€ 32,334
Life Years Gained	0.76	0.60	0.74	0.76
Incremental cost per Life Year Gained	-	€ 67,215	Erlotinib is cost-saving	Erlotinib is cost-saving
Cost-utility analysis				
Cost	€ 26,428	€ 15,752	€ 29,160	€ 32,334
QALY	0.24	0.18	0.22	0.23
Incremental cost per QALY gained	-	€ 170,425	Erlotinib is dominant	Erlotinib is dominant
Type of resources				
Progression free	€ 2,781	€ 1,760	€ 2,781	€ 2,781
Post progression	€ 14,890	€ 13,726	€ 14,890	€ 14,890
Drug acquisition	€ 8,070	€ 0	€ 6,771	€ 11,335
Drug administration	€ 0	€ 0	€ 1,888	€ 1,888
Adverse Events	€ 686	€ 267	€ 2,830	€ 1,478
Total cost	€ 26,428	€ 15,752	€ 29,160	€ 32,334
Incremental cost vs. erlotinib	-	€ 10,676	€ 2,731	€ 5,906

- If 1,000 patients with locally advanced or metastatic NSCLC were treated with erlotinib, the annual savings for Portuguese NHS (substitution rates: 5%-65%) would range between € 133,911 - € 1,740,840 (docetaxel replacement) and € 280,937 - € 3,652,181 (pemetrexed replacement);
- The sensitivity analysis confirmed the robustness of the base-case analysis results. Considering other type of sub-populations (2nd line with ECOG 0-1; 3rd line treatment) and a time horizon of 3 years (Weibull or Log-logistic), erlotinib remained the therapy with lower cost per patient (*vs.* active therapies);
- Probabilistic sensitivity analysis (\pm 20% variation concerning resource consumption and cost); considering a € 30,000/QALYs threshold, erlotinib therapy is cost saving *versus* docetaxel (Figure 3) and *versus* pemetrexed (Figure 4), but there is no difference in terms of efficacy between erlotinib and each one of the comparators.

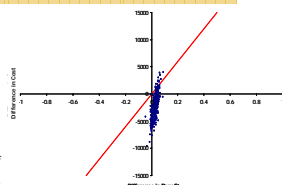


Figure 3 Scatterplot for erlotinib vs. docetaxel: 2 year analysis

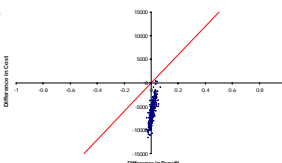


Figure 4 Scatterplot for erlotinib vs. pemetrexed: 2 year analysis

CONCLUSIONS

The use of erlotinib in the treatment of locally advanced or metastatic NSCLC patients instead of docetaxel or pemetrexed could result in savings for the Portuguese NHS, with a gain in terms of QALYs.

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