

ECONOMIC ANALYSIS OF ERLOTINIB, DOCETAXEL, PEMETREXED AND BEST SUPPORTIVE CARE AS 2ND AND 3RD LINE TREATMENT OF NON-SMALL CELL LUNG CANCER

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BACKGROUND

- 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;
- Non-small cell lung cancer (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.

OBJECTIVE

To evaluate costs and benefits of erlotinib in 2nd or 3rd line treatment of advanced or metastatic NSCLC versus docetaxel, pemetrexed or best supportive care performing a cost-utility analysis (incremental cost per Quality Adjusted Life Years - QALY) 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 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 other health states (B or C). After "Progression", a patient can stay on the same state (D) or transit to "Death" (E).

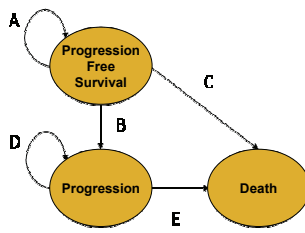


Figure 1 Structure of decision model

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.

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 LYG) were confined to a cost-minimization analysis.

Population

A hypothetical cohort of Portuguese patients with locally advanced or metastatic NSCLC who have failed one or more previous chemotherapy regimens (2nd and 3rd lines) was considered, according to the characteristics of patients included in 3 pivotal clinical trials used in the model.

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 a half cycle-correction;
- Time horizon is 24 months (2 years) for 2nd 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;
- Utilities are taken from a utility study conducted among healthy people in the UK (n=154) using EQ-5D visual analogue 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);
- QALY calculation per cycle was performed considering the proportion of patients with or without adverse events.

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 UK (n=154)

Resource consumption and costs

- Resource consumption was estimated by a Portuguese expert panel (Delbecq panel) with 6 pneumologists and 1 oncologist (Table 2);
- 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.) database]. Costs were actualized to 2008 considering an annual inflation rate of approximately 3% (Table 2);

- 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
	Unit cost	Source	
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
Medicinal products		Unit cost	Source
Erlotinib	€ 70.00 (per 150 mg tablet)		Roche Farmacéutica Química, Lda.
Docetaxel	€ 169.26 and € 666.74 (per 1 vial of 20 mg and 80 mg, respectively)		ACSS database
Pemetrexed	€ 983.12 (per 1 vial of 500 mg)		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 and 3rd line treatment, 2 years) (Table 3) show that:

- The total cost per patient was lower with erlotinib (€ 26,478) vs. docetaxel (€ 29,262) or pemetrexed (€ 32,762) and higher vs. best supportive care (€ 16,112);
- QALYs per patient were higher with erlotinib (0.250) vs. docetaxel (0.225), pemetrexed (0.241) or best supportive care (0.186);
- Erlotinib was "dominant" in the cost-utility analysis, with a lower cost and a higher efficacy vs. docetaxel and pemetrexed.

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

2 year analysis	Erlotinib	Best supportive care	Docetaxel	Pemetrexed
Cost-minimization analysis				
Cost	€ 26,478	€ 16,112	€ 29,262	€ 32,762
Life Years Gained	0.77	0.62	0.77	0.77
Incremental cost per Life Year Gained	-	€ 70,424	Erlotinib is cost-saving	Erlotinib is cost-saving
Cost-utility analysis				
Cost	€ 26,478	€ 16,112	€ 29,262	€ 32,762
QALY	0.250	0.186	0.225	0.241
Incremental cost per QALY gained	-	€ 161,742	Erlotinib is dominant	Erlotinib is dominant
Type of resources				
Progression free	€ 2,973	€ 1,817	€ 2,973	€ 2,973
Post progression	€ 14,192	€ 14,027	€ 14,192	€ 14,192
Drug acquisition	€ 8,625	€ 0	€ 7,236	€ 12,114
Drug administration	€ 0	€ 0	€ 2,017	€ 1,977
Adverse Events	€ 687	€ 268	€ 2,843	€ 1,506
Total cost	€ 26,478	€ 16,112	€ 29,262	€ 32,762
Incremental cost vs erlotinib	-	-€ 10,366	€ 2,784	€ 6,284

- Probabilistic sensitivity analysis results (± 20% variation concerning resource consumption and cost) are described in Table 4. These results confirmed the robustness of the base-case analysis results.

Table 4 Sensitivity analysis: 2nd and 3rd line treatment with erlotinib vs best supportive care, docetaxel or pemetrexed (per patient results)

2 year analysis	Erlotinib	Best supportive care	Docetaxel	Pemetrexed
Type of resources				
Progression free	€ 2,968	€ 1,814	€ 2,973	€ 2,985
Post progression	€ 13,957	€ 13,912	€ 13,933	€ 13,942
Drug acquisition	€ 8,627	€ 0	€ 7,254	€ 12,126
Drug administration	€ 0	€ 0	€ 2,022	€ 1,979
Adverse Events	€ 686	€ 267	€ 2,470	€ 1,494
Total cost	€ 26,237	€ 15,994	€ 28,653	€ 32,526
Incremental cost vs erlotinib	-	-€ 10,243	€ 2,416	€ 6,289

CONCLUSIONS

The use of erlotinib instead of docetaxel or pemetrexed could contribute with annual savings for the Portuguese NHS (substitution rates: 5% - 65%) that would range between € 135,046 - € 1,755,602 (docetaxel replacement) and € 291,801 - € 3,793,409 (pemetrexed replacement), with a gain in terms of QALYs.

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