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BUDGET IMPACT OF SEQUENTIAL TREATMENT WITH AFATINIB FOLLOWED BY OSIMERTINIB VERSUS FIRST-LINE OSIMERTINIB IN NON-SMALL-CELL LUNG CANCER PATIENTS WITH COMMON EGFR MUTATIONS IN THE NETHERLANDS

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INTRODUCTION

- Lung cancer is the leading cause of cancer mortality worldwide, with 40% of patients having subtype adenocarcinoma in non-small-cell lung cancer (NSCLC).[1,2] At diagnosis the majority of patients have advanced or metastatic disease. Mutations in the epidermal growth factor receptor (EGFR) gene are common in NSCLC and the mutation status improves predictions of the behaviour and characterisation of tumours.[3]
- 10–20% Of Caucasian patients with non-resectable lung adenocarcinoma have EGFR mutations, leading to approximately 294 new patients annually in the Netherlands.[4]
- The therapeutic landscape for these patients has changed radically with EGFR-tyrosine kinase inhibitors (TKIs) becoming the new first-line standard treatment. Eventually the majority (50-70%) progress on first-line TKI treatment by developing secondary mutations such as the T790M point mutation.
- **A budget impact analysis was performed to assess the value of sequential treatment for NSCLC patients with common EGFR mutations with first-line afatinib versus first-line osimertinib, followed by subsequent treatments in the Netherlands.**

METHODS

- A decision analytic model was constructed in Microsoft Excel with a Dutch healthcare perspective over a time horizon of 5 years in accordance with the ISPOR's good practices for budget impact analysis.[5] See table 1 for an overview of model parameters.
- Comparison of 2 treatment strategies:
  - ★First-line afatinib, followed by second-line osimertinib (when T790 mutation+) or by chemotherapy (when T790 mutation-), followed by third-line chemotherapy.
  - ★First-line osimertinib, followed by second-line chemotherapy.
- Out of 9175 patients with NSCLC in 2017 in the Netherlands, approximately 294 patients have EGFR deletion 19 or L858R mutations initiating first-line treatment every year.[2,4] Leading to an assumed monthly mean of 24.5 new patients entering the model per month.
- A survival model with reconstructed individual patient time-to-event data and a Weibull distribution was fitted using digitized progression free survival (PFS) curves with data from: FLAURA, AURA3 and IMPRESS studies for osimertinib and chemotherapy.[6,7,8] Patient level data from the LUX-Lung 3 clinical trial were used to fit the PFS curves for afatinib.[9] A network meta-analysis (NMA) was performed and the modelled PFS values were used as proxy to estimate time on treatment.[10]
- Only direct medical costs were taken into account. The mean cost for having grade 3 adverse events was calculated per patient per treatment step.[21]
- Scenario analyses and one-way sensitivity analysis tested the model robustness.

Table 1: Overview of model parameters for the budget impact model for sequential treatment with afatinib versus first-line osimertinib in NSCLC patients with common EGFR mutations

		Mean	Afatinib	Osimertinib		Chemotherapy	BSC/ Death	Source & Assumptions
				First-line	Second-line			
Transition probabilities – Afatinib treatment arm								
T790M mutation-positive	First-line		63%			--	--	[11]
	Second-line	--		88%		--	12%	Assumption
	Third-line	--	--			41%	59%	[7]
	Fourth-line	--	--			--	100%	Assumption
T790M mutation-negative	First-line		37%			--	--	[11]
	Second-line	--	--			88%	12%	[7, 12]
	Third-line	--	--			--	100%	Assumption
Transition probabilities – Osimertinib treatment arm								
First-line		--	--	100%	--	--	--	
Second-line		--	--	--	--	58%	42%	[6]
Third-line		--	--			--	100%	Assumption
Health states								
First-line		0.710	0.688	0.707		0.672	--	[6-9,12-14]
Second-line		0.730	0.708	0.727		0.692	--	
Third-line		0.620	0.598	0.617		0.582	--	
Simulated mean PFS from survival model								
First-line		--	16.99	20.80		--	--	[6,7,9]
Second-line		--	--	15.23		6.71	--	
Third-line		--	--	--		6.71	--	[8]
Costs								
Treatment costs/month		--	€2 440.15	€6 181.33		€3 679.04	--	[15-17]
T790M mutation testing		€157.02	--	--		--	--	[18]
Total cost per treatment for adverse events		--	€371.11	€62.46	€60.54	€554.33	--	[17,19-22]

RESULTS

The total budget impact over five years was €110.4 million for the sequence starting with afatinib and €158.6 million for the sequence starting with osimertinib, leading to a total incremental cost of €48.15 million over 5 years. The incremental cost savings were €6.06M, €12.25M, €12.26M, €9.87M and €7.72M for years 1 to 5 respectively, see figure 1.

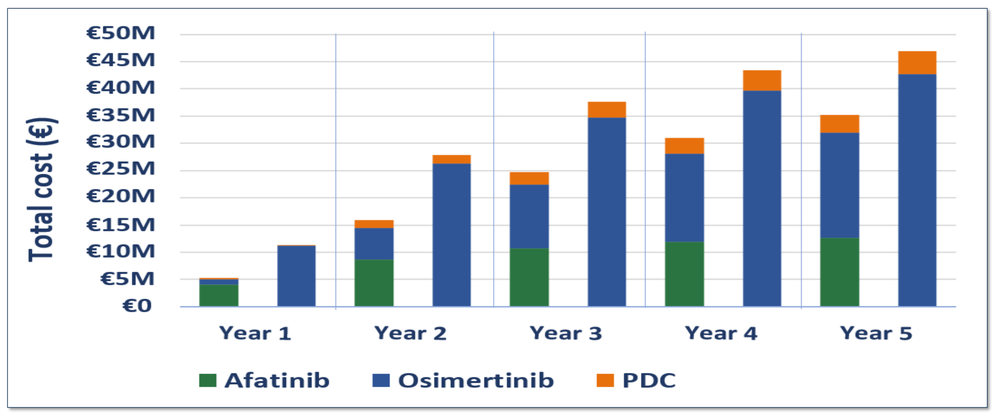

Figure 1: Total cost (€) per year for first-line treatment strategies afatinib versus osimertinib

Sequential treatment with first-line afatinib showed mean total time on treatment of 29.1 months, quality-adjusted life months (QALMs) of 20.2 with mean cost of €108,166 per patient versus first-line osimertinib with mean total time on treatment of 24.7 months, QALM of 17.4 and mean cost per patient of €143,251.

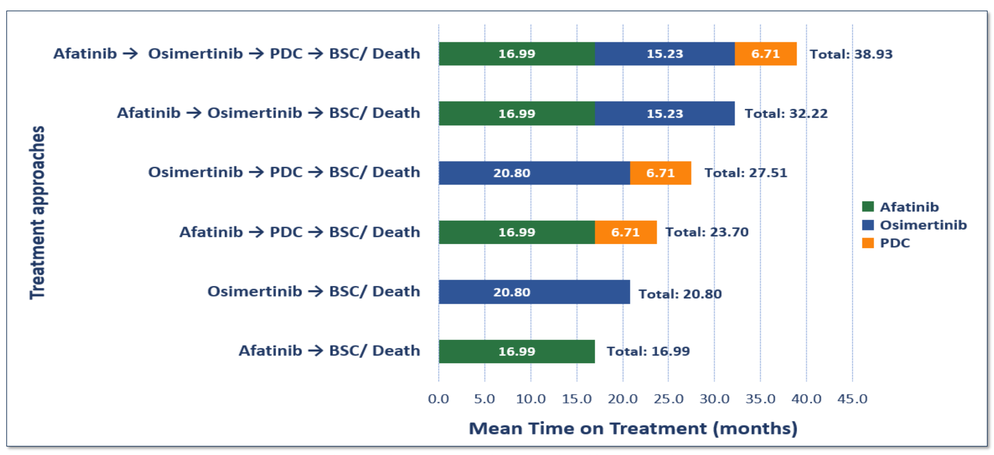

Figure 2: Outcomes survival analyses with Weibull-distribution in decision analytic model: total mean Time on Treatment for patients by treatment paradigms

Sensitivity analyses showed that the results were most sensitive to the price of osimertinib and afatinib, shown in figure 3. Results were also sensitive to the percentage of patients with T790M mutation+ disease receiving subsequent treatment, the percentage of patients testing positive for T790M mutations and the percentage of subsequent treatment after first-line therapy with osimertinib.

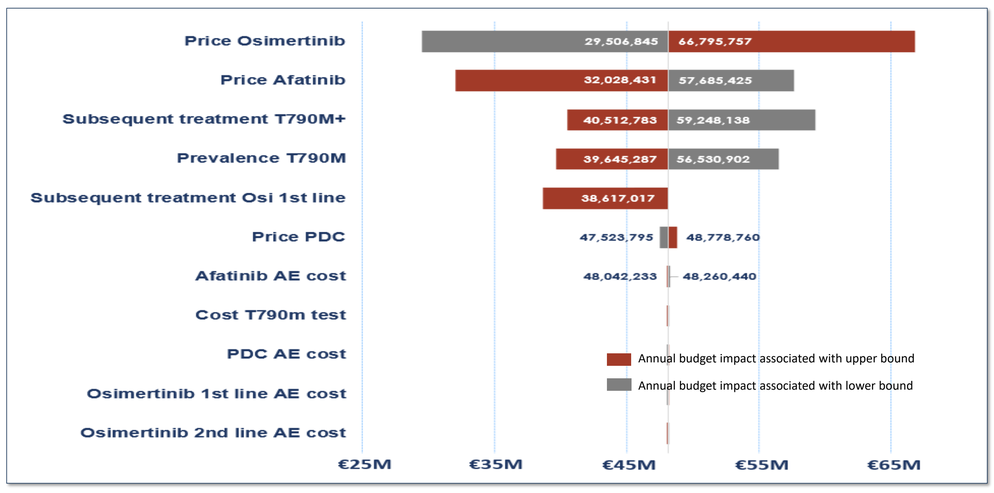

Figure 3: One-way sensitivity analysis: impact of changes of input parameters on the change in total annual budget in year 5

CONCLUSION

Over the last decade various treatment options showed improved PFS data in clinical trials and will support improvement of the burden of disease for lung cancer. The availability of these treatment options has an economic impact.

Sequential treatment with afatinib as a first-line treatment approach compared to a sequential treatment approach starting with osimertinib could be of high value since incremental cost savings were estimated at €48.15 million over 5 years, together with an incremental Time on Treatment of 4.5 months and an incremental QALM of 2.8 in patients with EGFR mutation positive NSCLC.

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