Cost-effectiveness analysis of durvalumab in adult patients with locally advanced unresectable non-small cell lung cancer after concurrent platinum-based chemoradiation in France

PCN145

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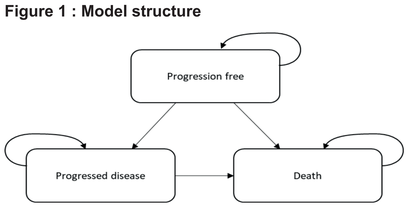
Background

- Non-small cell lung cancer (NSCLC) represents 85% of all lung cancers worldwide and has the highest mortality rate. In France, it is the 2nd and 3rd most common cancer among men and women respectively. The 5-year and 10-year survival rate is 14% and 9% respectively.
- Around 25% of NSCLC are diagnosed at a locally-advanced stage (stage III- according to the TNM classification) of which two thirds are diagnosed at an already inoperable stage. The current Standard of Care (SoC) for locally advanced unresectable NSCLC is a platinum-based doublet chemotherapy and radiotherapy (RT) administered concurrently with curative intent (cCRT). Following chemoradiotherapy treatment, the risk of relapse is about 60% in the following 12 months and the 5-year survival rate of patients remains low. SoC for these patients consisted only of a surveillance until progression and has remained unchanged for the last decade until the release of the PACIFIC trial results in 2017.
- In the EU, Durvalumab as monotherapy is indicated for the treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 on ≥ 1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy (*).

Objectives and Methods

- The objective of the study was to assess the cost-effectiveness of durvalumab compared to surveillance in the management of locally advanced, unresectable stage III NSCLC in patients with PD-L1≥1%, in France. All the assumptions below are aligned with those laid out by CEESP.
- A cost-effectiveness analysis was based on a 3 state-semi-Markov Model (Figure 1). The time horizon considered was 10 years and the mean age of patients was 63 years. Costs were estimated from a French payer's perspective (including patients, health insurance and communities). A discount rate of 4% was applied to both costs and benefits.
- Clinical inputs were derived from the PD-L1 ≥ 1% subgroup of the PACIFIC trial. Progression-free survival (PFS) of both treatment arms was extrapolated using the generalized gamma function assumed identical in both arms. PPS was extrapolated using an exponential distribution. All grade ≥3 adverse events (AEs) observed during the PACIFIC trial were included in the analysis.
- The model assumes a treatment waning effect at 36 months. After this timepoint, the probability of progression/death is equal and based on the routine surveillance arm.
- Utilities were derived using EQ-5D-5L data from the PACIFIC trial and converted to the French preferences. AE disutilities were taken from literature.
- The analysis included the following costs: Drug acquisition and administration, management of AEs, follow-up costs, transportation and palliative care. Costs were expressed in € 2018.
- Uncertainties were explored using deterministic and probabilistic analyses.

Figure 1 : Model structure



Results

Basecase analysis

- The results are presented in Table 1 and Table 2 below. Durvalumab is associated with a gain of 1.14 QALYs and 1.40 LYs for an additional cost of 60,723 € compared to surveillance. The ICER of the base case analysis is 53,332 €/QALY, with a 10-year time horizon.

Table 1 Results of the base case analysis in €/QALY

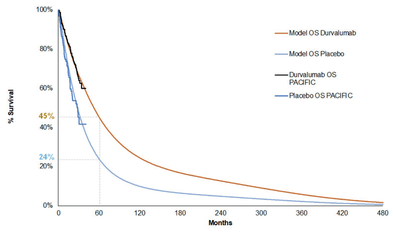
Strategy	Total costs	QALYs	ICER
Surveillance	27,287 €	2.43	-
Durvalumab	88,010 €	3.57	53,332

Table 2 Results of the base case analysis in €/LY

Strategy	Total costs	LYs	ICER
Surveillance	27,287 €	3.14	-
Durvalumab	88,010 €	4.54	53,332

- Extrapolated OS curves of durvalumab and placebo are presented in Figure 2. At 5 years, 45% of patients on durvalumab would still be alive compared to 24% in surveillance arm.

Figure 2 Overview of observed and estimated OS



Scenario analysis

- Several scenario analyses were conducted to assess variability according to the model assumptions (Table 3). With a life-time horizon of 30 years, the ICER would decrease by 36% to 33,991 €/QALY.

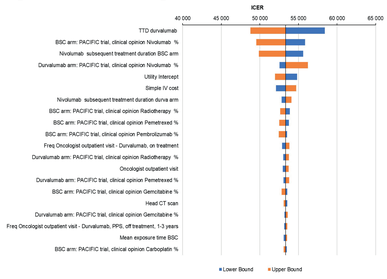
Table 3 Results of scenario analyses:

Scenario	Parameters	ICER (€/QALY)	Δ vs basecase (%)
Basecase	**-**	**53,332**	**-**
Time horizon	Lifetime (30 years)	33,961	-36%
Discount rate	0%	44,539	-16%
Individual extrapolation of PFS	Use of HR (HR = 0.46)	53,700	+1%
Extrapolation of PFS and of Time to progression (TTP)	Individual (without HR) : log normal	67,708	+27%
Extrapolation of PPS	Weibull	52,575	-1%
Treatment waning start of Durvalumab	No treatment waning	41,958	-21%
Disutilities associated to AEs	Not included	53,707	+1%
Vial sharing	Not included	58,602	+10%

Scenario Deterministic sensitivity analysis

- Deterministic sensitivity analysis consists of modulating the different settings of the model to determine the ones with the highest impact on the results of the analysis.
- Upper and lower values tested for the different settings correspond to the statistical indicators surrounding the value of the base case analysis (standard deviation, 95% confidence interval) or to an arbitrary variation of ±10% when statistical indicators are not available.
- Impact of the model setting's values was generally low. The ICER variation went from -8.5% (48,789 €/QALY) up to +9.6% (58,425 €/QALY), supporting the robustness of the results towards the values set.
- The model was most sensitive to treatment duration of durvalumab, distribution and costs of subsequent treatments (Figure 3).

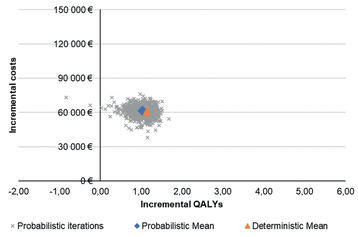
Figure 3 Tornado diagram



Probabilistic sensitivity analysis

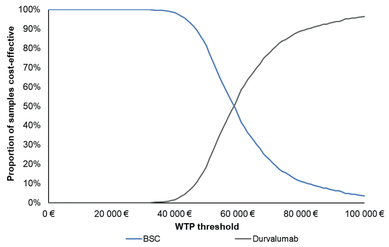
- The results of 1 000 simulations are located in the North-Eastern quadrant of the cost-effectiveness plane demonstrating that although durvalumab is more expensive, it is also more effective than surveillance.

Figure 4 : Scatter plot (1 000 simulations)



- At a willingness to pay of approximately 72,000 €/QALYs, the probability that durvalumab is the most cost-effective strategy is about 80%.

Figure 5 : Cost effectiveness acceptability curve



Conclusions

- In conclusion, durvalumab is considered by CEESP as a cost-effective use of healthcare resources when compared to surveillance. The robustness of the base case analysis is confirmed by the results of the sensitivity analysis performed.
- The PACIFIC study is the first and only study to have demonstrated positive results in unresectable Stage III NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy for 15 years, with a significant benefit on OS (the median has not been reached in the durvalumab arm) and 11.2-month gain in PFS.
- Durvalumab offers patients an opportunity for durable long-term response and the potential of a cure. After 36 months of follow-up, the median OS rate is still not reached (vs 28.7 months in the comparator arm). In addition, the analysis showed that durvalumab has the potential to improve the 5 year survival rate in France from 15-20% to 45%.

(*) At the request of EMA, AstraZeneca conducted an exploratory analysis not planned in the protocol (post-hoc) on the expression of PD-L1 according to a cut-off of 1% for OS and PFS

Supported by AstraZeneca

Presented at the 2019 ISPOR European Congress, Copenhagen, 2–6 November 2019