EPH148

Insights from a French Post-Marketing Authorization Early Access (MA EA) mechanism: Projecting Clinical and Economic Benefits of Neoadjuvant Nivolumab plus platinum-based chemotherapy (PDC) in Resectable Non-Small Cell Lung Cancer (NSCLC)

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Background

CheckMate-816 is an open-label, phase 3 trial in which patients with stage IB to IIIA resectable NSCLC (7th TNM classification) were randomly assigned to receive nivolumab plus platinum-based chemotherapy or chemotherapy alone, followed by resection.[1] Patients were stratified at inclusion according to their status of tumour programmed death ligand 1 (PD-L1) expression (<1 or ≥1%). The primary endpoints were event-free survival and pathological complete response (0% viable tumour in resected lung and lymph nodes [pCR]), both evaluated by blinded independent review. Overall survival was a key secondary endpoint. On June 26, 2023, nivolumab received marketing authorization in European Union in combination with PDC as neoadjuvant treatment of resectable NSCLC at high risk of recurrence in adult patients whose tumours have PD-L1 expression ≥ 1%.[2]

In France, there are different types of EA mechanisms authorized by the French National Health Authority (HAS): pre-MA EA and post-MA EA. An EA authorisation has been granted in September 2023 in France for nivolumab in combination with chemotherapy as neoadjuvant treatment of resectable NSCLC at high risk of recurrence in adult patients whose tumours have PD-L1 expression ≥ 1%, and without known Epithelial Growth Factor Receptor (EGFR) mutation or Anaplastic Lymphoma Kinase (ALK) translocation.[3] A total of 1,307 patients received neoadjuvant nivolumab plus chemotherapy for resectable NSCLC with tumour PD-L1≥1% through post-MA EA between September 2023 and February 2025. The Health Technology Assessment conducted by the HAS concluded that nivolumab plus chemotherapy was a dominant strategy in neoadjuvant NSLC, as it is associated with quality-adjusted life year (QALY) gain and cost savings over chemotherapy alone.[4]

Objectives

This study assesses the clinical and economic impacts of neoadjuvant nivolumab plus chemotherapy *versus* chemotherapy alone through its post-MA EA mechanism over 5 years from the French Health Insurance perspective.

Methods

A semi-Markov model with four health states (event-free [EF], locoregional-recurrence [LR], distant-recurrence [DR] and death) was used to simulate the clinical trajectories of 1,307 patients included in the post-MA EA in France. The model compared the real-world scenario in which patients were treated with neoadjuvant nivolumab plus chemotherapy through its post-MA EA mechanism and a scenario where patients received neoadjuvant chemotherapy alone.

Age (mean: 64.5 years), weight (mean: 73.2 kg) and body surface area (mean: 1.87 m^2) of patients were based on characteristics of patients included in the EA in France. Proportion of women was based on patient characteristics in CheckMate-816 (26.4%). The extrapolation of survival results was based on Akaike and Bayesian information criteria (AIC and BIC), visual inspection, and long-term plausibility, considering treatment-specific time to recurrence (TTR) in patients expressing PD-L1≥1% and clinical results in the ITT population for other transitions. Progressing patients were distributed into the LR or DR health states in accordance with the distributions observed in CheckMate-816 (61% of LR and 39% of DR). Adverse events with an incidence of ≥5% in CheckMate-816 were included in the analysis. Survival in each health-state was associated with utilities derived from the EQ-5D-3L answers to questionnaires delivered within CheckMate-816 in the ITT population, estimated by mixed model for repeated measures and valued according to the preferences of the French general population (0.878 in EF health-state ; 0.809 in LR health-state ; 0.695 in DR health-state). Disutilities related to grade ≥3 adverse events were estimated from the literature. Costs of neoadjuvant treatment acquisition and administration, lung resection and adjuvant treatment, disease monitoring, management of grade ≥3 adverse events, subsequent treatments post-recurrence, transportation, and end-of-life care were considered. Costs were informed by a published study from French hospital discharge database (BRONTES study) and French tariffs.[5] Subsequent treatment distribution for patients with LR and DR was based on CheckMate-816 in ITT population, distinguishing treatment arms and type of recurrence.

It was assumed that the neoadjuvant treatment had no impact on the subsequent strategy (surgery, radiotherapy and/or systemic treatment) which is driven by the nature of first recurrence (LR of DR) and decided by clinicians. However, among the systemic treatment options, and as observed in CheckMate-816, the neoadjuvant treatment with nivolumab leads to a reduction in the use of immunotherapies in case of recurrence in favor of the use of tyrosine kinase inhibitor (TKI) treatments or chemotherapy protocols (Table 1).

Table 1. Distribution of subsequent treatment post-recurrence in CheckMate-816

Subsequent treatment distribution	Nivolumab plus chemotherapy	Chemotherapy alone
Locoregional recurrence (LR)		
Radiotherapy	**26.3%**	**26.3%**
Surgery	**1.1%**	**1.1%**
Systemic treatment	**62.1%**	**62.1%**
Immunotherapy +/- chemotherapy	37.5%	51.4%
TKI	4.2%	25.7%
Chemotherapy alone	58.3%	22.9%
Distant recurrence (DR)		
Radiotherapy	**43.1%**	**43.1%**
Metastasis surgery	**15.5%**	**15.5%**
Systemic treatment	**58.6%**	**58.6%**
Immunotherapy +/- chemotherapy	25.0%	73.1%
TKI	37.5%	7.7%
Chemotherapy alone	37.5%	19.2%

Results

Over 5 years and a cohort of 1,307 patients, neoadjuvant treatment with nivolumab plus chemotherapy was estimated to prevent 223 recurrences and subsequent treatments (-17%) and 145 deaths (-11%) compared to chemotherapy alone, generating 394 additional life-years (LY) or 399 QALY (+9%). Moreover, neoadjuvant treatment with nivolumab plus chemotherapy was associated with 397 additional complete pathologic responses and 100 additional lung resections. Adjuvant therapies were avoided by 347 patients (Figure 1).

These results are explained by the improvement of the event-free survival and the overall survival demonstrated by nivolumab plus chemotherapy *versus* chemotherapy alone in CheckMate-816, illustrated by the patient flow of patients in different health states in the simulation over time (Figure 2).

Figure 1. Patient flow in the different health states

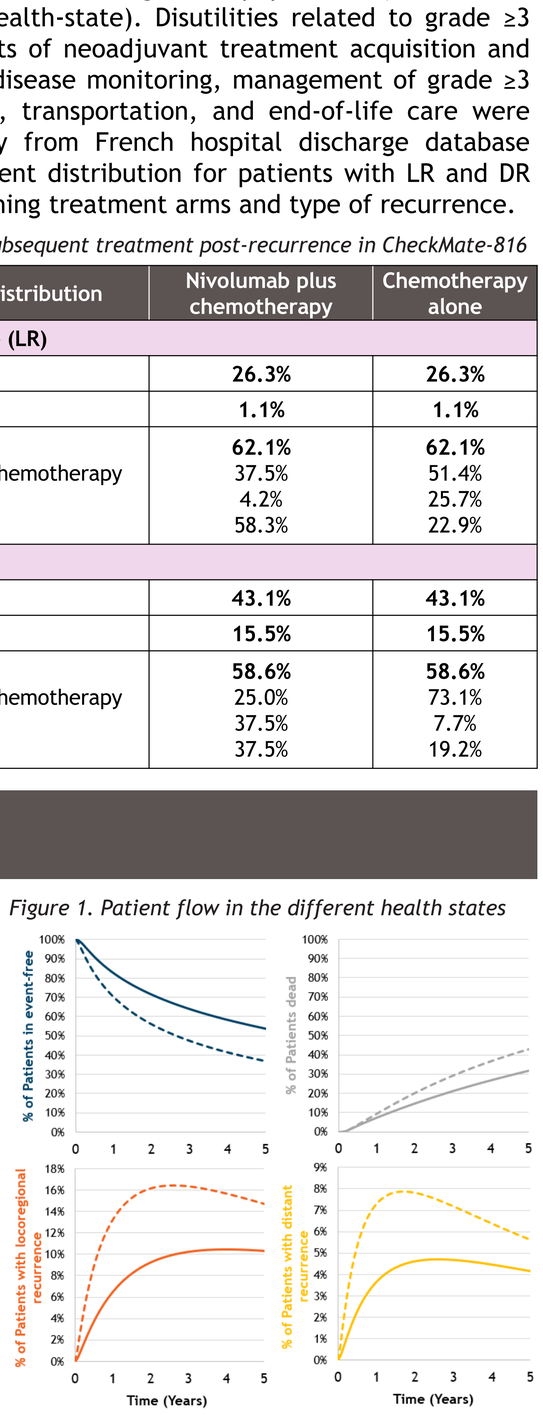
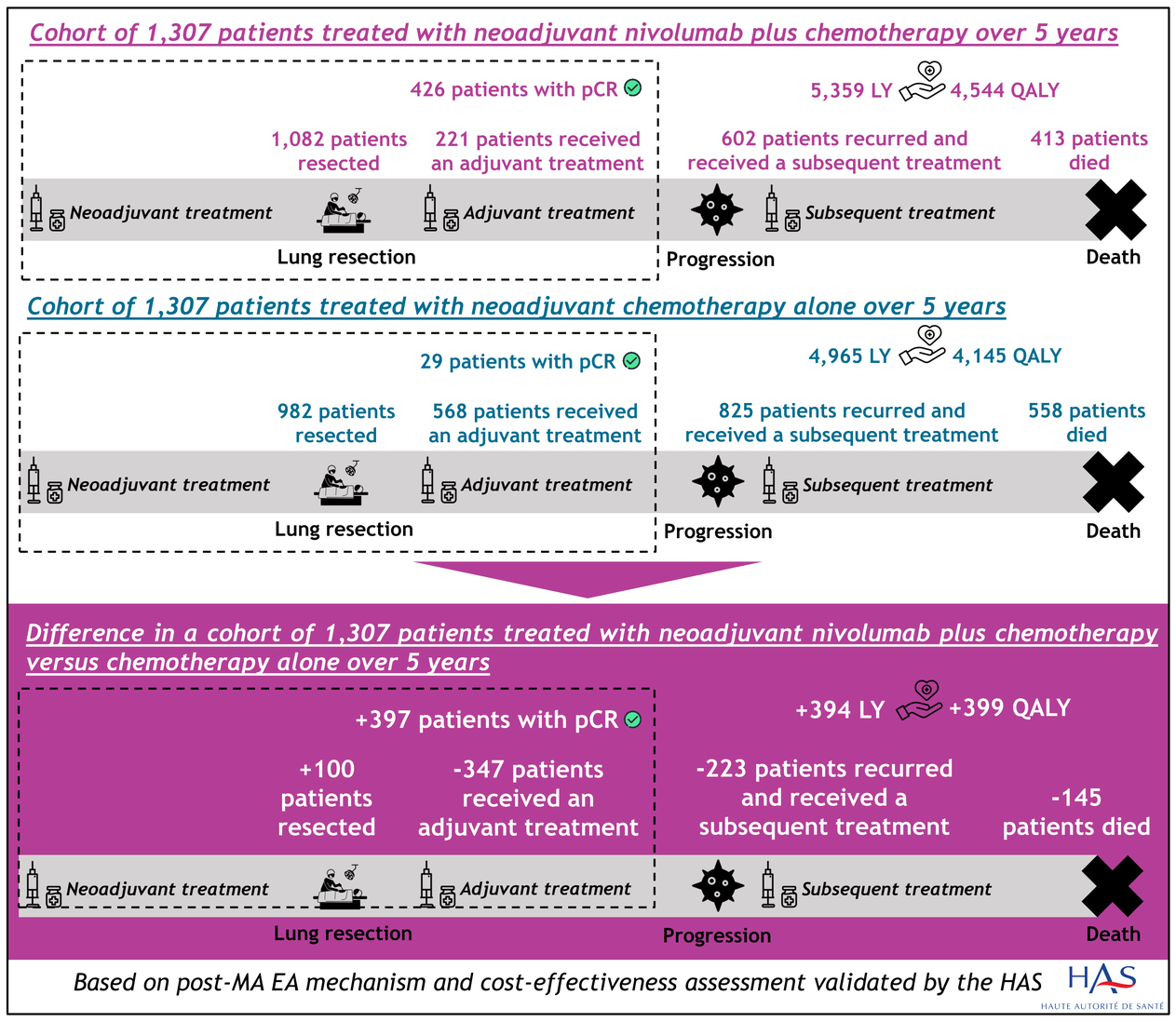


Figure 2. Illustration of the clinical benefits of neoadjuvant nivolumab plus chemotherapy versus chemotherapy alone over 5 years for 1,307 patients treated through post-MA EA mechanism in France



In total, treatment of patients with nivolumab plus chemotherapy through its post-MA EA mechanism resulted in €3.65 million in saving for French Health Insurance over 5 years. The savings generated on adjuvant therapy, subsequent treatments following locoregional or distant recurrence, monitoring and management of adverse events, and end-of-life costs (€19.3 million in total) more than offset the additional costs of treatment with nivolumab and surgery (€14.8 million in total) in patients treated with nivolumab plus chemotherapy *versus* patients treated with chemotherapy alone (Figure 3 and Table 2). This represents an average saving of €2,789 per patient over 5 years.

Figure 3. Budget impact over 5 years in 1,307 patients treated with nivolumab plus chemotherapy versus chemotherapy alone

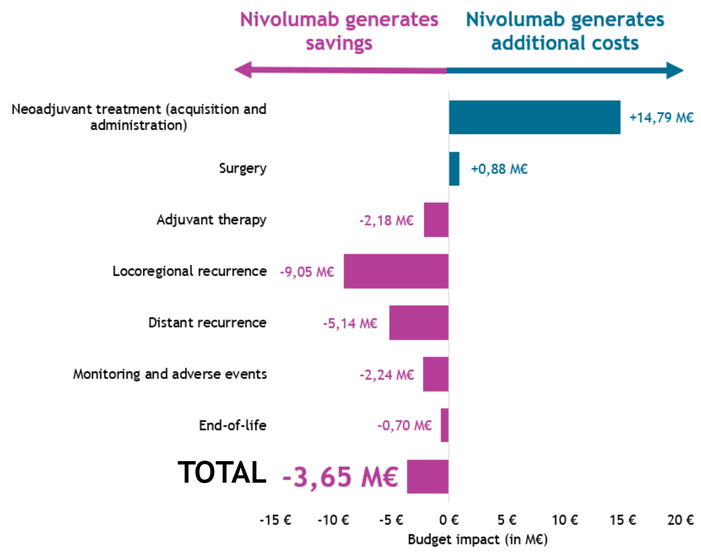


Table 2. Total costs over 5 years in 1,307 patients treated with nivolumab plus chemotherapy and chemotherapy alone

Total costs	Nivolumab plus chemotherapy	Chemotherapy alone
Neoadjuvant treatment (acquisition and administration)	18,34 M€	3,55 M€
Surgery	13,05 M€	12,17 M€
Adjuvant therapy	1,32 M€	3,51 M€
Locoregional recurrence	6,62 M€	15,68 M€
Distant recurrence	3,94 M€	9,08 M€
Monitoring and adverse events	8,88 M€	11,12 M€
End-of-life	2,01 M€	2,71 M€
Total	**54,17 M€**	**57,81 M€**

Conclusion

- **Neoadjuvant nivolumab in combination with chemotherapy delivers substantial clinical improvements — including higher pathological response rates and reduced recurrences associated with subsequent treatments — and economic benefits while simultaneously demonstrating superior cost-effectiveness outcome compared to chemotherapy alone.**
- **Expanding access to nivolumab in France beyond the post-MA EA has the potential to generate measurable benefits for individuals and the healthcare system, supporting more effective resource allocation and improved long-term outcomes.**

References

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