Cost-effectiveness of adjuvant alectinib versus platinum-based chemotherapy in resected stage IB-IIIA ALK-positive NSCLC: a French health economic evaluation

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R. SUPIOT[a], A. GHERARDI[b], L. du MANOIR de JUAYE[b], O. DOGHRI[a], M. SIVIGNON[a], M. DURUISSEAUX[c,d,e], C. CHOUAID[f,g]

[a]Putnam Associates, HTA operations, Paris, France. [b]Roche S.A.S, Health economics unit, Boulogne-Billancourt, France. [c]Respiratory Department and Early Phase (EPSILYON), Hôpital Louis Pradel, Hospices Civils de Lyon, Bron, France. [d]Centre de Recherche en Cancérologie de Lyon (CRCL), UMR INSERM 1052 CNRS 5286, Lyon, France. [e]Université Claude Bernard Lyon 1, Villeurbanne, France. [f]Centre Hospitalier Intercommunal de Créteil (CHIC), Service de Pneumologie, Créteil, France. [g]Université Paris-Est Créteil (UPEC), Créteil, France

BACKGROUND & OBJECTIVE

- Lung cancer remains the leading cause of cancer-related mortality in France, with more than 50,000 new cases annually[1]. Beyond its clinical impact, lung cancer also represents a major economic burden for the French healthcare system, with costs exceeding €3 billion in 2021 and increasing faster than patient incidence[2]. Within the ALK-positive subgroup, targeted therapies have reshaped treatment strategies.
- The phase III ALINA trial demonstrated that adjuvant alectinib significantly improved disease-free survival compared with platinum-based chemotherapy in completely resected stage IB–IIIA non-small cell lung cancer (NSCLC)[3].
- The objective of this study was to evaluate the cost-effectiveness of adjuvant alectinib versus platinum-based chemotherapy in patients with completely resected stage IB–IIIA (TNM7) ALK-positive NSCLC, given its recommendation in France for stage II–IIIB (TNM8)[4].

METHODS

Model structure

- A cohort-level semi-Markov model was implemented in Microsoft Excel®, with eight health states: disease-free survival (DFS); non-metastatic recurrence (treated/untreated); metastatic recurrence (first-line treated/untreated); metastatic recurrence (second-line treated/untreated); and death. Transitions were defined by time-dependent, treatment-specific probabilities with a monthly cycle length.

Population and clinical data

- The simulated population was the intention-to-treat cohort (IB–IIIA) of ALINA[3].
- DFS was estimated using ALINA Kaplan-Meier data (28 months of median follow-up), extrapolated with an exponential parametric function validated by French clinical experts.
- Post-recurrence progression and survival were informed by external sources reconstructed from digitized Kaplan-Meier curves when individual patient data were not available[5-10].
- Treatment patterns after recurrence (rechallenge with alectinib, brigatinib, lorlatinib, chemotherapy) were informed by expert elicitation and literature.
- A cure assumption was applied, considering patients disease-free for at least 5 years as cured, with a residual recurrence risk of less than 5% beyond year 5.

Economic perspective and costs

- The analysis was performed from the French collective perspective, following HAS guidelines[11], with a 40-year time horizon.
- All costs were expressed in 2024 euros and discounted at 2.5% per year up to 30 years, then gradually decreasing until reaching 1.5%.
- Treatment acquisition costs were derived from the French national drug database, using the formulation with the lowest cost per mg. Platinum-based chemotherapy acquisition was considered fully covered within DRG tariffs.
- Treatment administration costs (including medical transport) were applied only to intravenous chemotherapy regimens and were valued using ENC data and DRG tariffs. Oral TKIs such as alectinib, brigatinib, and lorlatinib were assumed to induce no administration costs.
- Disease management costs included ALK testing, tumour biopsies, and follow-up imaging procedures (CT scans, MRI), based on French oncology expert validation and CCAM unit costs.
- Adverse event costs (including medical transport) were estimated for grade ≥3 events observed in ALINA[3] for DFS stage only, mapped to ICD-10 codes, and valued using ENC or DRG tariffs.
- End-of-life care costs were derived from DRG tariffs for palliative care, with an additional one-way medical transport cost.
- Medical transport was estimated as a weighted average across ambulance, taxi, and light medical vehicles[12].

Table 1. Cost inputs

Inputs	Value	Inputs	Value
Treatment acquisition – per package		**Adverse events (continued) – per event**	
Alectinib	€3,834	Diarrhoea	€4,063
Brigatinib	€3,737	Embolism	€3,592
Lorlatinib	€3,810	Epigastric discomfort	€791
Treatment administration – per event		Fatigue	€1,309
Chemotherapy	€556	Febrile neutropenia	€3,664
Testing and diagnostic		Hyperbilirubinemia	€3,047
ALK testing, at model inclusion	€111	Hypertriglyceridemia	€3,064
Tumour tissue biopsy, per recurrence event	€77	Leukopenia	€3,664
Follow-up – per month		Liver function test increased	€951
Disease-free survival	€17	Lymphoedema	€1,868
Non-metastatic recurrence	€56	Myalgia	€1,097
Metastatic recurrence: first-line treatment	€144	Nausea	€1,063
Metastatic recurrence: second-line treatment		Neutropenia	€3,664
Adverse events – per event		Neutrophil count decreased	€3,664
Abdominal pain	€764	Pneumonitis	€4,319
Alanine aminotransferase increased	€951	Pulmonary embolism	€3,592
Anaemia	€2,005	Rash	€1,268
Appendicitis	€2,620	Rash maculo-papular	€1,268
Aspartate aminotransferase increased	€951	Regurgitation	€1,063
Asthenia	€1,309	Stomatitis	€4,863
Blood bilirubin increased	€951	Type 2 diabetes mellitus	€2,340
Blood creatine increased	€1,462	Urinary tract infection	€3,221
Blood creatine phosphokinase increased	€951	Vomiting	€1,063
Constipation	€1,077	White blood cell count decreased	€3,664
Cough	€901	**End-of-life – per event**	
Decreased appetite	€3,691	Palliative care	€5,609

Quality of life

- Health-related quality of life was assessed using the EQ-5D-5L questionnaire collected in the ALINA trial[3] for patients in the disease-free state. French-specific value sets were applied[13], and utilities were capped so as not to exceed general population norms[14].
- For post-recurrence health states, where ALINA did not collect data, utility values were informed by published literature in advanced NSCLC populations[15].

RESULTS

Clinical outcomes

- Over a 40-year horizon, alectinib was associated with gains of 5.2 life-years and 5.0 QALYs versus chemotherapy. Most of the benefit was driven by extended time in the disease-free state which translated in the model into extended overall survival when extrapolated.

Cost outcomes

- Despite higher upfront acquisition costs, total costs were lower with alectinib (€180,561 vs €237,011), generating an average saving of €56,449 per patient. Cost reductions were mainly driven by decreased treatment and management costs in the metastatic recurrence states (Table 2).

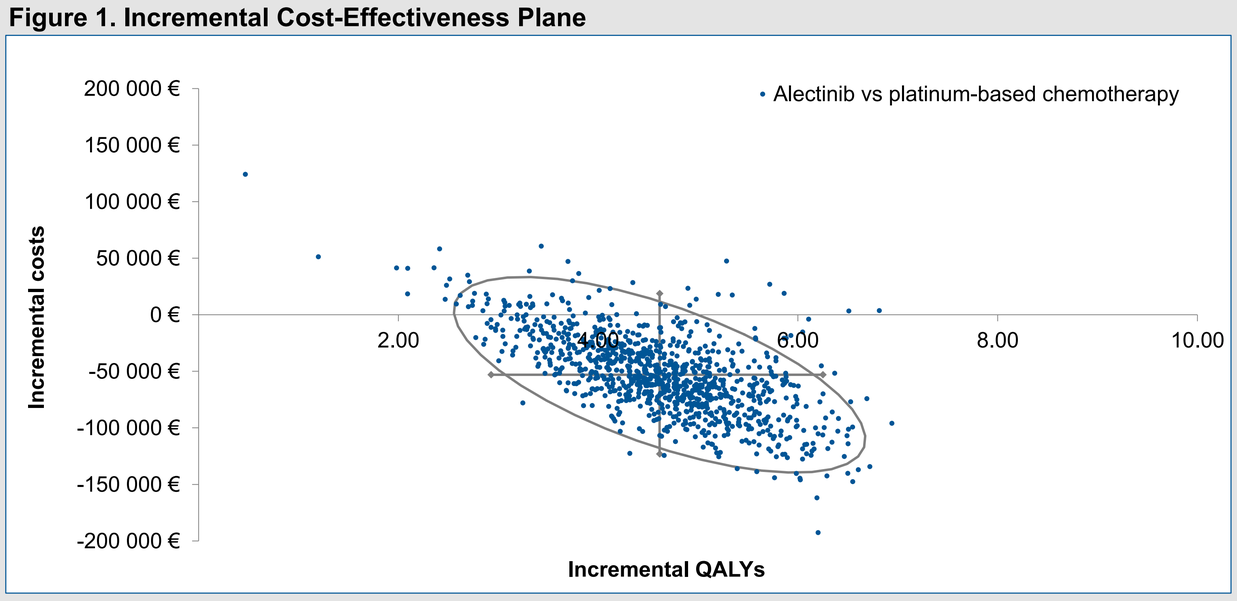
Table 2. Cost outcomes

Outcomes	Alectinib	Platinum-based chemotherapy	Increment
Disease-free survival			
Treatment (acquisition and administration)	€88,281	€2,182	€86,098
Treatment-emergent adverse events management	€236	€104	€132
Disease management	€892	€662	€230
Non-metastatic recurrence			
Treatment (acquisition and administration)	€1,793	€3,599	€-1,806
Disease management	€211	€423	€-212
Metastatic recurrence (first-line treatment)			
Treatment (acquisition and administration)	€59,830	€144,519	€-84,689
Disease management	€1,344	€3,761	€-2,417
Metastatic recurrence (second-line treatment)			
Treatment (acquisition and administration)	€25,034	€76,544	€-51,510
Disease management	€461	€1,410	€-949
End of life	€2,481	€3,807	€-1,326
Total	**€180,561**	**€237,011**	**€-56,449**

Base case and sensitivity analyses

- Alectinib is dominant over chemotherapy (more effective and less costly).
- The deterministic sensitivity analysis confirmed the robustness of the results, with alectinib remaining dominant across all parameter variations.
- The probabilistic sensitivity analysis showed that 93.5% of simulations fell in the southeast quadrant of the cost-effectiveness plane (Figure 1). The probability of alectinib being cost-effective reached 100% at a threshold of €15,500/QALY.
- The scenario analyses (different time horizons, cure assumptions, parametric distribution for DFS extrapolation) consistently supported the dominance of alectinib.

Figure 1. Incremental Cost-Effectiveness Plane



CONCLUSION

Adjuvant alectinib improves survival and quality of life in resected ALK-positive NSCLC patients while reducing overall costs by lowering recurrence-related expenditures. **It was consistently shown to be a dominant and cost-effective option over platinum-based chemotherapy in French clinical practice.**

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