Cost-Effectiveness of early liquid biopsy in patients with suspicious metastatic lung cancer alongside the LIBELULE randomized phase III trial

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Objective

Genomic profiling is a major component for first-line treatment decisions in patients with non-small cell lung cancer *(NSCLC)* and the timeliness of biomarker testing is essential to improve time to treatment initiation *(TTI)* or avoid inappropriate treatment. The aim of this study was to conduct a cost-effectiveness analysis *(CEA)* based on patient-level data from the LIBELULE *(LIquid Biopsy for the Early detection of LUng cancer Lesion)* multicenter, randomized, comparative, open-label phase III *(NCT03721120)*.

Methods

Study population

- The CEA was designed as part of the phase III trial conducted in 15 participating French centers *(four comprehensive cancer centers, two university hospitals, six general hospitals, and three other private not-for-profit hospitals) [1]*.
- Eligible patients with clinico-radiological suspicious presentations of lung cancer *(metastatic or locally advanced disease not amendable to loco-regional treatment)* were randomized *(1:1)*.
- In the liquid biopsy *(LB)* arm, a LB was performed at the first visit using the InVisionFirst-Lung® assay *(NeoGenomics Laboratories, Inc.)*, an amplicon based NGS panel covering 37 NSCLC-associated genes, including fusions and diagnostic procedures planned according to each center practice. In the control arm, diagnostic procedures were planned according to each center practice and local liquid biopsies were allowed.

Cost and incremental cost-effectiveness ratio (ICER)

- Individual consumptions were provided by the case report and local hospital discharge database.
- Costs were assessed from the French National Health perspective with an 12 months time horizon.
- The international Classification of Individual Consumption by Purpose *(COICOP 06.3.0.0 - Hospital services)* was used to expressed costs in 2023 euros *[2]*.
- LB using the InVisionFirst®: price was derived from Aziz Z *et al*. *[3]*.
- Incremental cost-effectiveness ratio *(ICER)* was expressed in cost per progression-free life year gained *(PF-LYG)*.

Statistical analysis

- The analyses were conducted in the intent-to-treat *(ITT)* population.
- Uncertainty was handled by bootstrapping *(1,000 replications)* and cost-effectiveness acceptability curves *(CEAC)* were generated.

Results

Patient characteristics

- A total of 319 patients were randomized from April 2019 to August 2022. Data of 298 patients *(151 for the liquid biopsy arm and 147 for control)* were available for the CEA.

Costs and ICER

- In the final analysis, total mean costs per patient were €28,268 *(SD: 30,624)* in the liquid biopsy group and €26,722 *(SD: 32,774)* in the control group.
- Mean progression free survivals were 0.555 *(SD: 0.383)* and 0.495 *(SD: 0.397)* year respectively.
- The corresponding ICER was €25,815 per PF-LYG.
- The probability of the ICER belonging to each quadrant of the cost-effectiveness plane was the highest for the North-East quadrant *(62.3%)*, where the liquid biopsy arm was both costlier and more effective than the control arm. Results were robust at 25% *(cf. Fig.1)*.
- The CEAC shows that at a willingness-to-pay *(WTP)* threshold of €50,000 per PF-LYG, the LB has a 36% probability of yielding the highest net benefit *(cf. Fig. 2)*.

Costs (€2023)	*Arm A: Liquid biopsy (N=151)* *Mean (SD)*	*Arm B: Cytological or histological sampling (N=147)* *Mean (SD)*	*P-value*
Hospitalization	15,200.94 (13,361.54)	16,233.39 (15,182.84)	0.534
Incl. diagnosis-related groups	*13,464.47 (11,851.20)*	*14,064.10 (13,496.77)*	0.684
Incl. transportation	*1,438.24 (1,712.46)*	*1,435.50 (1,741.40)*	0.989
InVisionFirst® test	869.92 (0.00)	0.00 (0.00)	-
Drugs*	11,715.66 (25,295.27)	10,012.69 (25,103.12)	0.56
Emergency room visit	8.13 (58.44)	4.73 (33.05)	0.536
Ambulatory medical consultation	221.67 (710.42)	183.97 (498.18)	0.596
Ambulatory medical Imaging	161.50 (193.16)	156.31 (209.23)	0.824
Outpatient consultation	89.90 (185.22)	131.28 (379.23)	0.235
Total cost	**28,267.72 (30,623.83)**	**26,722.37 (32773.76)**	0.675

*derived from the innovative and high-cost drugs list also called "liste-en-sus" (https://www.atih.sante.fr/unites-communes-de-dispensation-prises-en-charge-en-sus)

Table 1: Mean costs per patient (€ 2023)

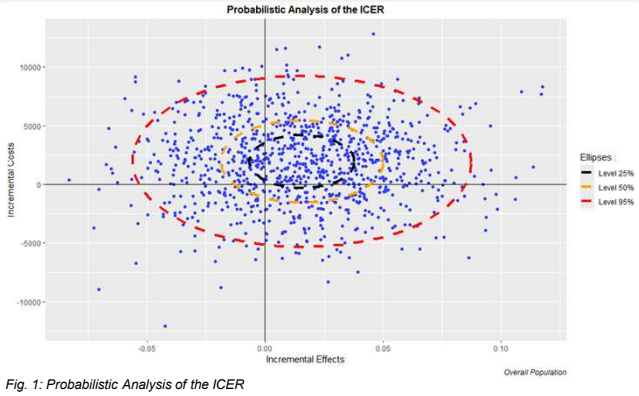

Fig. 1: Probabilistic Analysis of the ICER

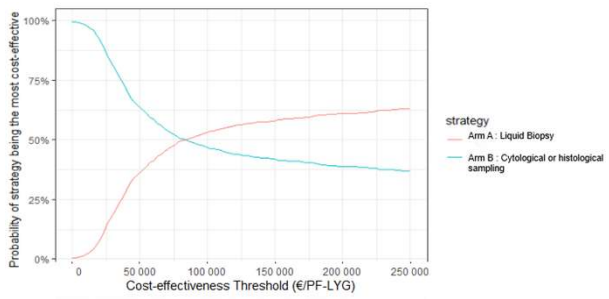

Fig.2: Acceptability curve (PF-LYG)

Conclusion

- The CEA is based on the first large prospective randomized trial to evaluate the impact of early LB. This trial did not meet its primary endpoint, i.e. the time from randomization to initiation of appropriate treatment *(TTI)* based on informative genomic *(on liquid or tissue biopsy)* and pathological results. Nevertheless, sensitivity analyses revealed a clinically relevant reduction in TTI in patients initiating systemic treatment *[1]*.
- The CEA indicated that LB is deemed to be more effective, albeit at a higher cost, compared to the control for PFS *(ICER = €25,815 per PF-LYG; probability of being in the North-East quadrant = 62.3%)*. However, results were robust only at 25% as Fig. 1 shows.

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[1] Swalduz A, Schiffler C, Curcio H et al. LIBELULE: A Randomized Phase III Study to Evaluate the Clinical Relevance of Early Liquid Biopsy in Patients With Suspicious Metastatic Lung Cancer. J Thorac Oncol. 2025 Apr;20(4):437-450. doi: 10.1016/j.jtho.2024.12.011. Epub 2024 Dec 16. PMID: 39694415.
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Ethics: The protocol *(NCT03721120)* was conducted in accordance with the Declaration of Helsinki principles, the current International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use guidelines for Good Clinical Practice, and in compliance with French and European laws and regulations in force, as well as any applicable guidelines *(ID-RCB number: 2018-A00810-55)*. All patients provided written informed consent before enrolment

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