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Cost-effectiveness analysis of using FoundationOne Liquid CDx in patients with advanced non-small cell lung cancer (NSCLC) in whom tissue-based testing is not feasible

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BACKGROUND AND OBJECTIVES

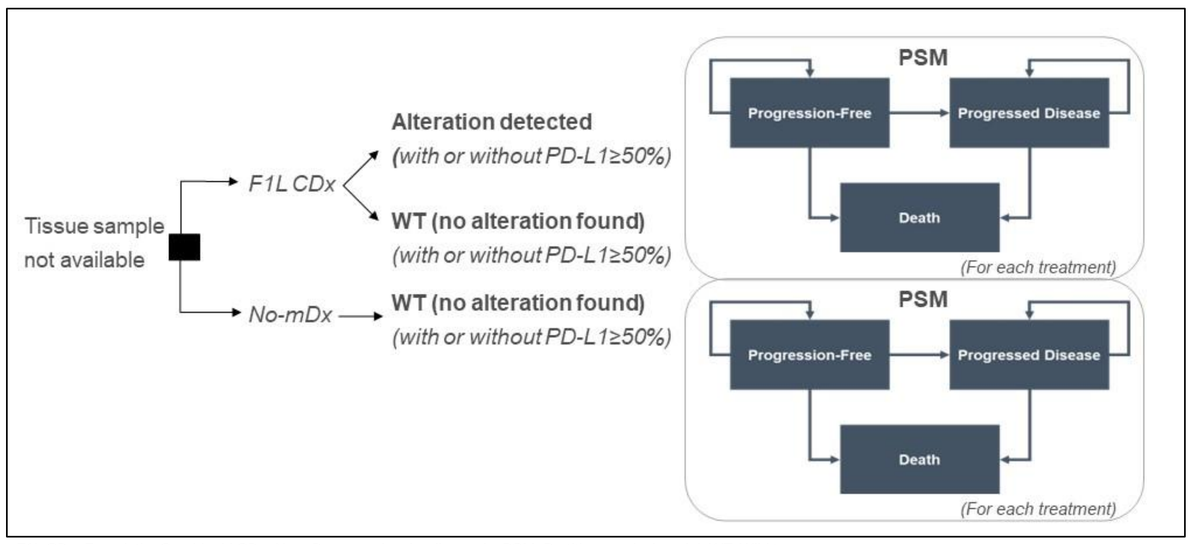
- In patients with advanced NSCLC, molecular characterization obtained from tissue biopsy is often not feasible due to insufficient amount, inadequate quality of tumor specimens or if re-biopsy cannot be performed safely[1-2].
- Liquid biopsy (LB) has emerged as a promising alternative method to detect genetic alterations, as it represents a less invasive tool that avoids tissue biopsy risks and specimen limitations[3].
- FoundationOne Liquid CDx (F1L CDx) is an NGS-based in vitro diagnostic device to identify alterations by LB, analyzing a panel of 324 genes using circulating cell-free DNA isolated from a blood sample[4].
- The aim of this preliminary analysis is to assess the cost-effectiveness of using F1L CDx in LB in advanced NSCLC patients in whom molecular diagnosis tissue sampling is not possible.

METHODS

Model structure

- A joint model combining a decision-tree and partitioned-survival models (Figure 1) was developed over a lifetime horizon, comparing costs and effects of performing a molecular diagnostic by LB using F1L CDx versus no-molecular diagnosis (no-mDx). 3% discount rate was applied for costs and health outcomes.
- The assumptions and inputs used in the model were validated by a panel of 11 oncologist from different Spanish centers.

Figure 1. Diagram Model



F1L CDx: FoundationOne Liquid CDx; No-mDx: no-molecular diagnosis; PSM: Partition-survival model; WT: Wild type.

Target Population

- Patients with a confirmed diagnosis of advanced NSCLC but in whom tissue biopsy samples are not adequate for molecular testing.

Parameters

- The analysis included level I and II biomarkers according to the ESCAT classification[5]: EGFR, ALK, ROS1, BRAF, NTRK, HER2, MET, RET and KRAS.
- **Diagnostic:** PD-L1 overexpression (TPS≥50%) is considered in parallel to F1L CDx and no-mDx. It was tested in 50% of the patients (0%-100% in sensitivity analysis).
- Table 1 shows biomarkers positivity rates using F1L CDx.

Table 1. Positivity rates F1L CDx

Biomarker analyzed	Positivity rates	
	Alteration only	*Alteration and PDL1≥50%*
EGFR	10.69%	2.11%
ALK	2.68%	0.53%
ROS1	1.25%	0.25%
BRAF^{V600E}	1.90%	0.37%
NTRK	0.35%	0.07%
HER2	1.92%	0.38%
MET $^{ex14\ skipping}$	1.58%	0.31%
RET	1.09%	0.22%
KRAS^{G12C}	11.27%	2.23%

- **Treatment allocation:** Defined by the expert panel, which established the distribution between starting 1L of treatment with targeted therapies, immunotherapies, chemo-immunotherapies, chemotherapy, enrollment in a randomized clinical trial, and no drug therapy.
- **Treatment efficacy:** Exponential models were fitted to the median PFS and OS obtained from the respective clinical trials[6-19].

Healthcare resources and costs

- The analysis was conducted from the perspective of the Spanish National Health System, so only direct medical costs were considered.
- Costs included: diagnostic costs (F1L CDx and PD-L1 testing), treatment-related costs (1L and 2L drugs cost, intravenous administration and adverse events costs), and healthcare costs associated with disease management. Unit costs were obtained from Spanish healthcare databases[20].

Sensitivity analysis

- Deterministic and probabilistic sensitivity analyses were also performed to assess the uncertainty of the variables used in the model and determine the robustness of the results.

RESULTS

- If F1LCDx is used in a hypothetical cohort of 1,000 patients, 392 alterations would be detected, 166 patients could be treated with targeted therapies and 53 patients could be enrolled in clinical trials. No alterations would be found if no-mDx is performed.
- In addition, using F1L CDx provides more quality-adjusted life-years (QALYs) and life years (LYs) than no-mDx, with an additional cost of €13,237,529.
- The incremental cost-effectiveness ratio (ICER) is around the cost-effectiveness threshold of €30,000/QALY commonly accepted in Spain[21].
- Table 2 shows our preliminary results for the base case.

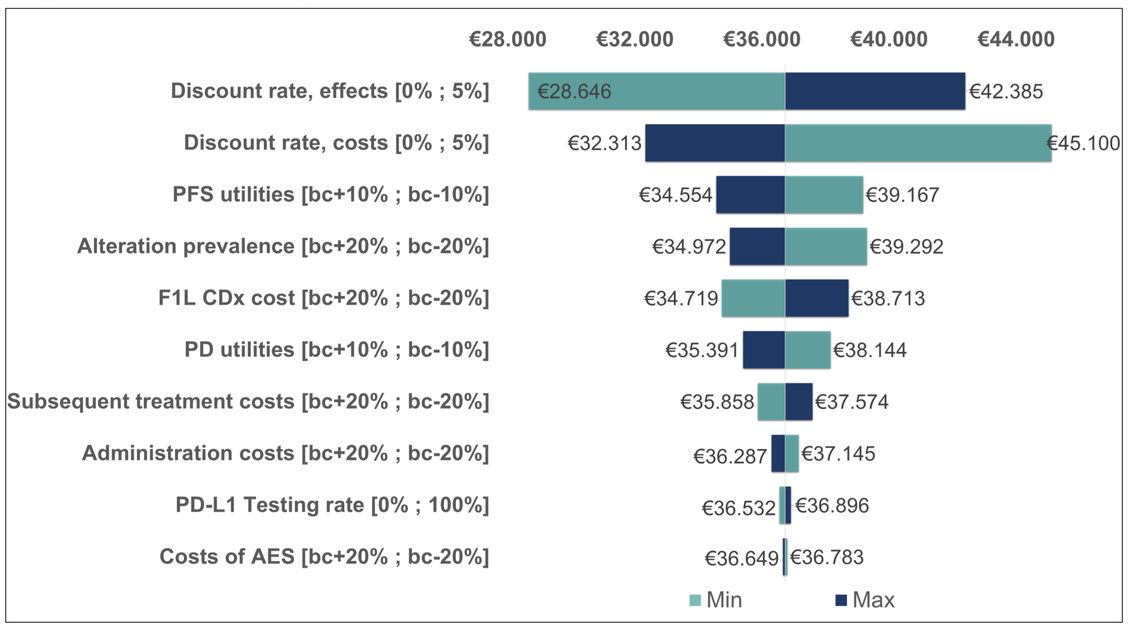
Table 2. Base case results

	F1L CDx	No-mDx	Increment
Total costs (€)	**135.567.857**	**122.330.328**	**13.237.529**
Diagnostic costs	*3,621,750*	*21,750*	*3,600,000*
Treatment & healthcare costs	*131,946,107*	*122,308,578*	*9,637,529*
QALYs	**2,248.49**	**1,887.95**	**€360.54**
LYs	**2,821.12**	**2,371.64**	**€449.48**
ICUR (€/ per QALY gained)	**€36,716/QALY**		
ICER (€ per LY gained)	**€29,451/LY**		

F1L CDx: FoundationOne Liquid CDx; No-mDx: no-molecular diagnosis; QALYs: quality-adjusted life years; LYs: life years; ICUR: incremental cost-utility ratio; ICER: incremental cost-effectiveness ratio

- Results of the one-way sensitivity analysis are represented by a tornado diagram (Figure 2), showing how individual changes in each variable modifies the base case ICER (€36,716/QALY).

Figure 2. Tornado diagram



BC: Base case: PD: Progressed disease; PFS: Progression-free; AEs; adverse events

- In a further publication, the results of this preliminary analysis will be updated using different parametric models instead of using exponential model fitted to median PFS and OS.

CONCLUSION

Our preliminary results shows that the use of F1L CDx in liquid biopsies might be a cost-effective strategy in Spain for those patients with advanced NSCLC in whom tumor biopsy samples are not adequate for molecular testing.

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