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INTERPRETING MOLECULAR ALTERATIONS FOR CLINICAL PRACTICE

Clinical outcomes in patients with advanced NSCLC treated with targeted therapies, with actionable mutations identified by InVisionFirst ctDNA assay

Jordi Remon[1], Sandra Ortiz-Cuaran[2], Laura Mezquita[1], Aurelie Swalduz[2], Karen Howarth[3], Cecile Jovelet[4], Ludovic Lacroix[4], Etienne Rouleau[1], Frank De Kievit[3], Katherine Baker-Neblett[3], Simon Roitt[3], Vincent Plagnol[3], Clive Morris[3], Emma Green[3], Maurice Perol[2], David Planchard[1], Pierre Saintigny[2], Benjamin Besse[1,7]

[1]Gustave Roussy, Department of Cancer Medicine, Villejuif, France; [2]Centre Leon Berard, Lyon, France, [3]Inivata, Granta Park, Cambridge, UK [4]Laboratoire de Recherche Translationnelle, Gustave Roussy, Villejuif, France; [5]Université Paris-Saclay, Orsay, France

INTRODUCTION

- Circulating tumor DNA (ctDNA) can be used for somatic mutation detection, such as *EGFR*, *BRAF* or *KRAS* mutations as well as fusions (ALK and ROS1), in NSCLC patients.
- ctDNA-based comprehensive genomic profiling (CGP) using multi-gene next-generation sequencing (NGS) panels is rapidly gaining traction in clinical practice
- However, prospective clinical outcomes of patients with genomic alterations in plasma ctDNA by NGS panels remain poorly described
- Here, we describe outcomes in advanced NSCLC patients with actionable alterations identified in plasma by InVisionFirst™-Lung

METHODS

- We performed a pooled-analysis across advanced NSCLC patients with actionable alterations detected by amplicon-based NGS (InVisionFirst-Lung)
- Patients treated with matched targeted therapies evaluable for disease control at 3 months were collated for clinical outcomes analysis, based on disease stage and class of therapy
- All patients provided written consent approved by the institutional ethics committee under which the studies were conducted

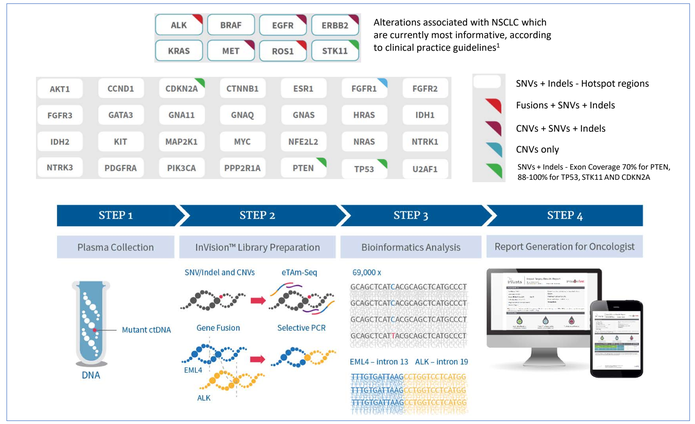

Figure 1. The InVisionFirst™-Lung assay identifies SNVs, indels, CNVs and gene fusions with whole gene and gene hotspots, using an amplicon-based technology to selectively amplify genomic breakpoints. The sequence of the junctions are then identified using NGS, allowing the genomic breakpoint in ctDNA to be mapped[4]

RESULTS

- 82 patients were evaluable for outcome analyses
- 71 patients (87%) had disease control at 3 months of therapy
- The response rate at 3 months was 61%

Prior therapy for advanced disease	Genomic alteration	N	Number still on targeted therapy at 3 months	% still on targeted therapy at 3 months
Untreated for advanced disease	**All**	9	7	78%
	EGFR mutation	6	5	83%
	Braf v600 mutation	2	1	50%
	ALK / ROS1 fusion	1	1	100%
Prior cytotoxic chemotherapy for advanced disease but no targeted therapy	**All**	18	16	89%
	EGFR mutation	9	8	89%
	Braf v600 mutation	2	1	50%
	ALK / ROS1 fusion	7	7	100%
Prior therapy with targeted therapy	**All**	55	48	87%
	EGFR mutation (49 with T790)	49	42	86%
	ALK / ROS1 fusion	6	6	100%
Overall		82	71	87%

Table 1. Summary of patients with actionable genomic alterations detected by InVision ctDNA testing in these studies. Patients included those with all the classes of alterations predicting response to current FDA approved drugs (EGFR activating mutations, EGFR T790M mutations, ALK gene Fusions, ROS1 gene fusions and BRAF mutations)

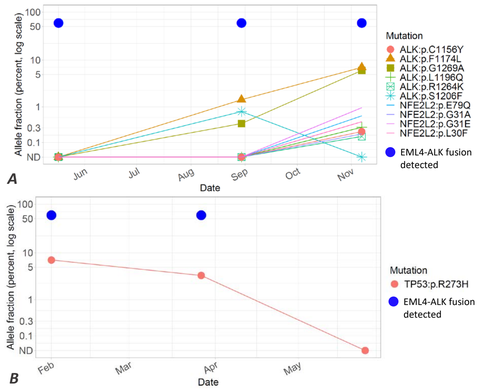

Figure 2A & B Case studies of 2 patients A) EML4-ALK fusion patient previously untreated with TKI, who clinically progressed on crizotinib at 11 months and B) EML4-ALK fusion patient previously untreated with targeted therapy, with durable clinical response to ceritinib at 6 months follow-up

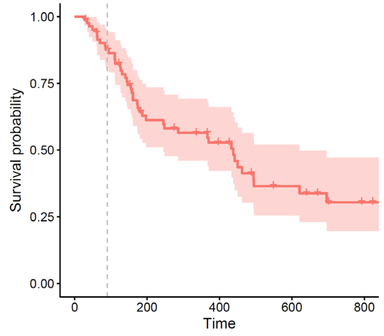

Figure 2: Kaplan-Meier curve of time to progression/termination of therapy (with 95% CI) of the combined analysis of the Untreated, Untreated with Targeted therapy, and the Recurrent patients

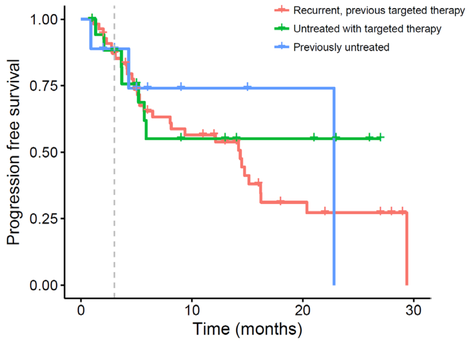

Figure 3: Kaplan-Meier curve with stratification of groups, demonstrating the progression-free survival (PFS) for patients on an appropriate targeted therapeutic agent as determined by the identification of an actionable mutation. There was no significant difference in PFS between these groups (p=0.616) as described previously[5,6]

CONCLUSION

- Clinical outcomes in patients who have been treated with targeted therapy based on actionable alterations detected by amplicon-based NGS ctDNA analysis by InVisionFirst are consistent with those reported based on tissue profiling
- ctDNA molecular profiling using InVisionFirst is an accurate and reliable tool for the detection of clinically relevant molecular alterations in advanced NSCLC patients

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