Clinical validation and utility of InVision ctDNA in advanced non-small cell lung cancer (NSCLC) patients

Jordi Remon1 & Laura Mezquita1, David Planchard1, Cecile Jovelet2, Ludovic Lacroix2, Karin Howarth3, Vincent Plagnol3, Clive Morris3, Emma Green3, Cecile LePechoux4, Caroline Caramella5, Julien Adam6, Benjamin Bese7

1Gustave Roussy, Department of Cancer Medicine, Villejuif, France; 2Laboratoire de Recherche Translationnelle, AMMICA, INSERM U823/CNRS U53655, Gustave Roussy, Villejuif, France; 3Inivata, Grant Park, Cambridge, UK; 4Gustave Roussy, Department of Oncology Radiotherapy, Villejuif, France; 5Gustave Roussy, Department of Radiology, Villejuif, France; 6Gustave Roussy, Department of Pathology, Villejuif, France; 7Universite 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.

- Comprehensive molecular profiling using liquid biopsy ctDNA is rapidly gaining traction in routine clinical practice
- However, there has been variable degree of accuracy and performance published to date
- Also, there is a lack of prospective data on clinical outcomes for patients with actionable genomic alterations in liquid biopsy

Here, we describe the clinical validation and utility of the InVision platform (InvisionFirst™-Lung, InvisionSeq™-Lung) in a large prospective cohort of advanced NSCLC patients

METHODS

- We performed a prospective, single-centre, observational study enrolling advanced NSCLC patients including treatment-naïve, on TKI treatment or at progression to targeted therapy
- ctDNA molecular analysis was performed using amplicon-based NGS (InVision platform) and where available, in tissue by Sanger sequencing or a sensitive validated allele-specific technique
- Clinical validation was performed for core gene variants of EGFR Exons 18-21, BRAF V600, MET Exon 14, ERBB2 Ins 20, ALK & ROS1 fusions, KRAS and STK11, according to clinical practice guidelines1
- Patients treated with matched targeted therapies evaluable for disease control at 3 months, according to RECIST1.1 criteria by Investigator, were collated for outcome analyses

RESULTS

- 362 advanced NSCLC patients recruited
- 172 treatment-naïve
- 190 were pre-treated with known tissue molecular profile (EGFR, BRAF, ALK, ROS1, MET)

For clinically-relevant gene variants, concordance agreement was 94% where ctDNA and tumor tissue analysis was available, with 76% sensitivity and 97% specificity

Median progression free survival was 5.7 months

89% had disease control at 3 months of therapy

58 patients were evaluable for outcome analysis

- 89% had disease control at 3 months of therapy
- Response rate at 3 months was 61%
- Median progression free survival was 5.7 months

CONCLUSION

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

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References:

3NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer

Table 1 Statistical summary of clinical validation ( Concordance, Sensitivity and Specificity analyses) for Invision platform to clinically relevant core gene variants and overall panel, as compared to tissue molecular analysis

Table 2 Summary of Results: Breakdown of patients by disease setting and by genomic alteration along with their 3-month disease control rate.

Figure 2A & B: Invision liquid biopsy comprehensive genomic profiles of (A) treatment-naïve and (B) pre-treated patients

Figure 2. Concordance of amplicon-based assay for liquid biopsy compared to tissue biopsy analysis

Figure 1.

Figure 1. The InvisionFirst™-Lung assay (identifies SNVs, Indels, CNVs and gene fusions with whole gene and gene exons, 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)

Figure 2A & B: Invision liquid biopsy comprehensive genomic profiles of (A) treatment-naïve and (B) pre-treated patients

Figure 2. Concordance of amplicon-based assay for liquid biopsy compared to tissue biopsy analysis

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