



Prospective clinical validation of the InVisionFirst ctDNA assay for molecular profiling of patients with advanced NSCLC

Ramaswamy Govindan, Michael A. Pritchett, D. Ross Camidge, Manu Patel, Jamil Khatri, Steven Boniol, Elke K. Friedman, Abderrahim Khomani, Samir Dalia, Katherine Baker-Neblett, Vincent Plagnol, Karen Howarth, Nitzan Rosenfeld, Clive D. Morris; Alvin J Siteman Cancer Center at Washington University School of Medicine, St. Louis, MO; Pinehurst Medical Clinic & FirstHealth Moore Regional Hospital, Pinehurst, US; University of Colorado-Denver, Aurora, CO; Christiana Care Health Services, Newark, DE; Christus Cancer Treatment Center, Shreveport, LA; Virginia Cancer Institute, Richmond, VA; Gibbs Cancer Center & Research Institute, Spartanburg, SC; Mercy Clinic Joplin, Joplin, MO; Inivata Inc, Research Triangle Park, NC.



Dr. Ramaswamy Govindan

DISCLOSURE SLIDE

Relationships with commercial interests:

Honoraria: Inivata, Boehringer Ingelheim, Genentech, AbbVie

Advisory: Inivata, Merck Serono, GlaxoSmithKline, Boehringer Ingelheim, Genetech/Roche, Abbvie, Celgene, Novartis, AstraZeneca/MedImmune, Pfizer, Phillips Gilmore, Bristol Meyers-Squibb, Baxalta, ARAID, Astellas, Adamtimmune

Funding: Bayer, GlaxoSmithKline, MethylGene, Abbvie

Travel: Boehringer Ingelheim, Celgene, Merck, Amgen, Genentech, GlaxoSmithKline





InVisionFirst ctDNA assay for molecular profiling

- Non-small cell lung cancer (NSCLC) accounts for over 85% of lung cancer and the majority of patients present with advanced stage disease and are treated with systemic therapies.
- Targeted therapies require identification of specific molecular alterations in the cancer and guidelines recommend broad genomic profiling to assess for therapeutic targets
- Utilization of such comprehensive testing is still limited, often due to inadequate tumor tissue in many patients given the high tissue demands of comprehensive genomic profiling (CGP) testing.
- Guidelines advocate molecular profiling in the evaluation of advanced non-small cell lung cancer (NSCLC) and support the use of plasma circulating tumor DNA (ctDNA)-based profiling for patients with insufficient tissue
- Comprehensive validation of liquid biopsy assays is required to ensure confidence by the oncology community
- InVisionFirst has undergone robust analytical validation





InVisionFirst is a ctDNA NGS assay for detection of genomic alterations in 36 genes commonly mutated in NSCLC and other cancers.

AKT1	● ALK	BRAF	CCND1	● CDKN2A	CTNNB1
● EGFR	● ERBB2	ESR1	● FGFR1	FGFR2	FGFR3
GATA3	GNA11	GNAQ	GNAS	HRAS	IDH1
IDH2	KIT	KRAS	MAP2K1	● MET	MYC
NFE2L2	NRAS	NTRK1	NTRK3	PDGFRA	PIK3CA
PPP2R1A	● PTEN	● ROS1	● STK11	● TP53	U2AF1

SNVs + Indels - Hotspot Regions

● Fusions + SNVs + Indels

● CNVs + SNVs + Indels

● CNVs only

● SNVs + Indels - Exon Coverage 70% for PTEN, 88-100% for TP53, STK11 and CDKN2A





- 41 sites within North America participated in **2 prospective clinical validation studies**: (INI-001 [[NCT02906852](#)] & GRN-ALV [[NCT03116633](#)]). Samples from 10 patients also obtained from a biobank
- 264 patients recruited:
 - Male and female age ≥ 18 years
 - Stage IIIB/IV NSCLC
 - Treatment naïve
 - Plasma for ctDNA analysis taken within 12 weeks of tissue biopsy
- Cohort of patients with and without tissue for testing were recruited
- Tissue-based genotyping was undertaken when tissue was available (67% of patients)

Demographics	Patients without tissue for testing	Patients with tissue for testing	All patients
n	86	178	264
Age (mean (sd))	68.2 (10.9)	66.6 (11.1)	67.1 (11.0)
Smoking status (%)			
Current smoker	22.1	31.5	28.4
Former smoker	60.5	55.1	56.8
Never smoked	17.4	12.9	14.4
Missing	0.0	0.6	0.4
Race (%)			
American Indian or Alaska native	0.0	0.6	0.4
Asian	3.5	1.7	2.3
Black or African American	7.0	11.2	9.8
White	84.9	86.0	85.6
Other	4.7	0.6	1.9
Histology (%)			
Adenocarcinoma	94.2	96.1	95.5
Large cell carcinoma	1.2	0.0	0.4
Neuroendocrine carcinoma	0.0	0.6	0.4
Sarcomatoid	1.2	0.0	0.4
Missing	3.5	3.4	3.4
Sex = M (%)	51.2	47.2	48.5
Cancer stage (%)			
3B	10.5	16.9	14.8
4	88.4	79.2	82.2
Missing*	1.2	3.9	3.0

*All patients included were confirmed as eligible based on TNM staging



Overall Results

- Overall concordance for the full 36 genes in the InVisionFirst panel with matched tissue profiling was 97.8%.
- Considering the 8 genes of most clinical relevance the **PPV was 97.8%, 97.1% NPV with 73.9% sensitivity and 99.8% specificity.**

* ALK/ROS1 fusion detection is better characterized in a larger cohort of patients (presented separately at WCLC 2018)

	Tissue and liquid	Tissue only	Liquid only	No call	PPV	NPV	Sensitivity	Specificity
ALK/ROS1 fusions*	2	3	0	292	100.0	99.0	40.0	100.0
BRAF V600E	5	2	0	140	100.0	98.6	71.4	100.0
EGFR (exons 18-21)	13	5	0	146	100.0	96.7	72.2	100.0
ERBB2 exon 20 ins	2	0	0	137	100.0	100.0	100.0	100.0
KRAS	48	12	1	86	98.0	87.8	80.0	98.9
MET exon 14 splice	3	3	0	133	100.0	97.8	50.0	100.0
STK11	15	6	1	93	93.8	93.9	71.4	98.9
Key 8 genes*	88	31	2	1027	97.8	97.1	73.9	99.8
All Genes	156	65	32	4135	83.0	98.5	70.6	99.2

Note: all positive calls are based on exact variant observed within a gene.

*Includes SNV's, Insertions, deletions, Fusions





Our analysis supports the hypothesis that the assay will have clinical utility in over 50% of patients

	Liquid	Tissue
Patients with any results	264	178
Actionable	18.2%	14.4%
KRAS/STK11	35.6%	26.5%
Total	53.8%	40.9%

	Liquid	Tissue
Total with Results	264	178
EGFR (exons 18-21)	26	18
ALK-ROS1 fusions	5	5
BRAF V600E	6	7
MET (exon14 splice)	7	6
ERBB2 insertions	4	2
Total	48	38

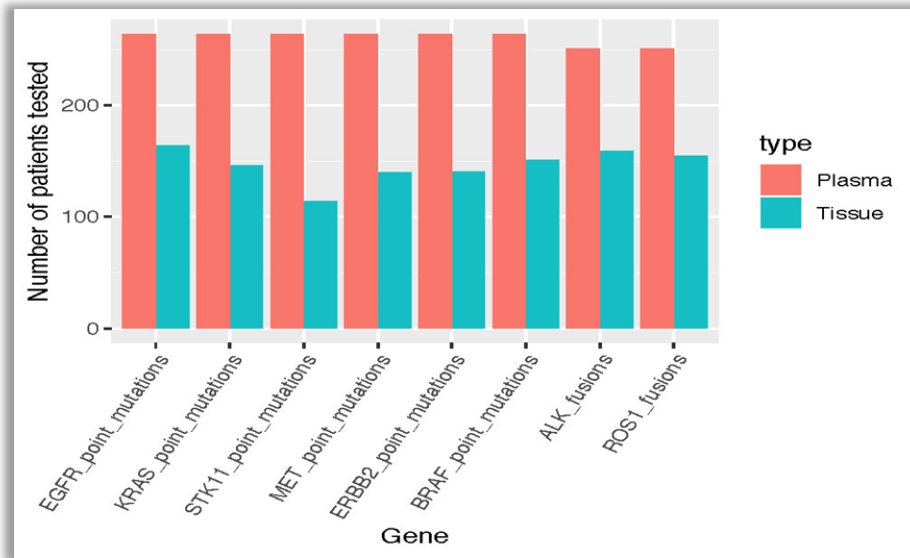
This Clinical Validation study supports the hypothesis that the *InVisionFirst* assay will have Clinical Utility in approximately 50% of patients in untreated advanced stage NSCLC

26% more actionable alterations found by InVision ctDNA than SOC tissue testing

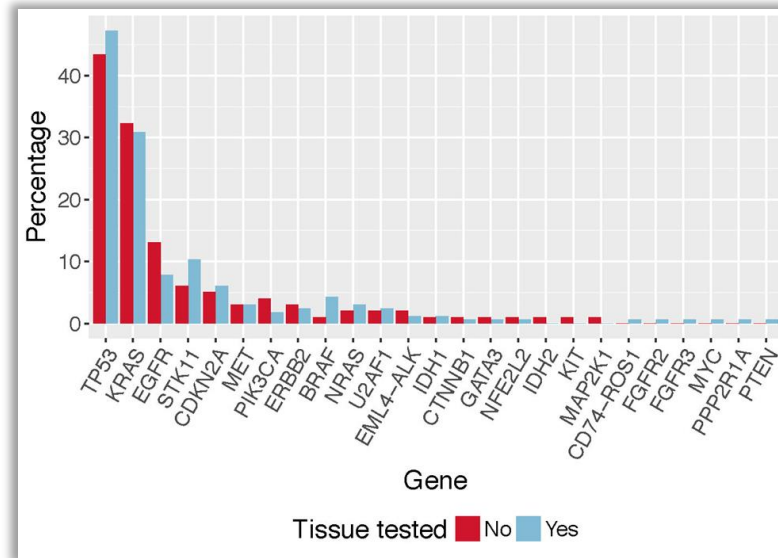




Plasma analysis enables comprehensive testing of patients who are inadequately profiled by tissue testing



The number of patients across the entire study successfully tested for key genomic alterations by InVisionFirst and tissue testing



Gene alteration frequencies detected in plasma defined by tissue testing status



Take home messages:

- InVisionFirst assay demonstrates excellent concordance with tissue profiling in this multi-centered prospective clinical validation study
- The performance of this assay in terms of overall sensitivity and specificity appears comparable if not higher than other established commercial ctDNA assays
- Utilization of InVisionFirst ctDNA testing led to the detection of 26% more actionable alterations than standard of care tissue testing
- This study supports the use of InVisionFirst for the molecular stratification of patients with advanced NSCLC





Acknowledgements and thanks:

We would like to thank the patients along with their families, friends and support groups.

Many thanks to all the investigators, nurses and research site teams along with the Inivata team.

- Holy Cross Hospital, Inc - Dr. David Drew
- Center for Biomedical Research (TN Cancer) - Dr. Russel Devore
- Jackson Oncology Associates, PLLC - Dr. Manu Patel
- North Shore Hematology Oncology Associates PC - Dr. David Chu
- Thomas Spann Clinic - Dr. Aftab Mahmood
- University of Colorado Denver - Dr. Ross Camidge
- Providence Health and Services – Washington d/b/a Providence Regional Medical Center Everett - Dr. Jason Lukas
- Christus Health Northern Louisiana d/b/a Christus Health Shreveport-Bossier d/b/a Christus Physician Group - Dr. Steven Boniol
- Feinstein Institute for Medical Research (on behalf of Northwell Health Inc) (Northern Westchester) - Dr. Jonathan Goldberg
- Edward H Kaplan MD & Associates - Dr. Edward Kaplan
- The West Clinic, P.C - Dr. Lee Schwartzberg
- Carolina Blood and Cancer Center - The Quality Cancer Care Alliance, LLC —Dr. Sashi Naidu
- Gettysburg Hematology - The Quality Cancer Care Alliance, LLC - Dr. Satish Shah
- North West Medical Specialties - The Quality Cancer Care Alliance, LLC —A Dr. Andrea (Rose) Veach
- Swedish Health Services—Dr. Howard West
- Washington University (St. Louis)—Dr. Ramaswamy Govindan
- Clinical Oncology Research Network (Mid-Florida)—Dr. Santosh Nair
- Trinity Health—Dr. Patanit Watanaboonyakhet
- W.A. Foote Memorial Hospital d/b/a Henry Ford Allegiance Health - Dr. Elias Hazzi
- Berkshire Medical Center, Inc—Dr. Trevor Bayliss
- Eastern Connecticut—The Quality Cancer Care Alliance, LLC Dr. Dennis Slater
- Pinehurst Medical Clinic & FirstHealth Moore Regional Hospital - Dr. Michael Pritchett
- Christiana Care Health Services, Inc—Dr. Michael Guarino
- The Charlotte-Mecklenburg Hospital Authority, d/b/a Carolinas HealthCare System (Levine Cancer Institute)—Dr. Kathryn Mileham
- Norton Hospitals, Inc d/b/a Norton Cancer Institute—Dr. Alfonso Cervera
- Tyler Hematology Oncology PA, d/b/a HOPE Cancer Center of East Texas—Dr. Arielle Lee
- East Carolina University—Dr. Paul Walker
- CH Allied Services, Inc d/b/a Boone Hospital Centera —Dr. Joseph Muscato
- Providence Health & Services – Oregon d/b/a Providence Portland Medical Center—Dr. Rachel Sanborn
- Cotton O’Neil Clinic d/b/a Cotton-O’Neil Clinical Research Center—Dr. Mehmood Hashmi
- Swedish Covenant—Dr. Gary Schreiber
- Virginia Cancer Institute—Dr. Elke Friedman
- Facey Medical Foundation, an affiliate of Providence Health System - Southern California —Dr. Albert Dekker
- Nebraska Methodist Hospital —Dr. Robert Langdon
- HealthPartners Institute (Park Nicolett)—Dr. Rachel Lerner
- Lehigh Valley Health Network – Dr. Brian Patson
- Mercy Hospital Cancer Center/Clinical Research at Ft Smith, AR – Dr. Tony A Flippin
- Mercy Cancer Center at Joplin, MO – Dr. Samir Dalia
- Mercy Clinic Oncology & Hematology at Oklahoma City, OK – Dr. Vikki A Canfield
- Mercy Clinic at Springfield, MO – Dr. Mohan Tummala
- Gibbs Cancer Center & Research Institute – Dr. Abderrahim Khomani
- Inivata team: Katherine Baker-Neblett, Vincent Plagnol, Karen Howarth, Nitzan Rosenfeld, Clive D. Morris, Tim Forshev, Emma Green, Shannon Blais, Greg Jones, Nathan Campbell, Karen Harrington, Cynthia Schandle, Anhthu Bui, John Calaway, Sarah Calaway, Catherine Leroy, Justin Lanier

