IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

wclc.iaslc.org #WCLC25

ISET® CTC-DNA shows higher sensitivity than ctDNA in early-stage lung cancer patients

F. Lococo*, M. Heidary#, Y. Liu#, I. Desitter#, J. Evangelista*, A. Campanella*, M. Giannakoulis#, K. Vasileiou#, K. Prevost#, A. Decina#, D. Brechot#, **P. Paterlini#**

*Policlinico Universitario A.Gemelli IRCCS, Rome, Italy

Rarecells, Faculté de Médecine Necker Paris, France.

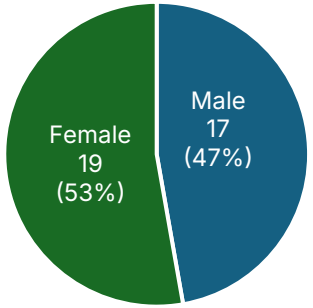
Introduction

- Circulating Tumor Cells (CTCs) are recognized as potentially highly informative, non-invasive liquid biopsy markers.
- Unlike circulating tumor DNA (ctDNA), however, CTC-DNA–based assays are not yet established in clinical practice, mainly due to challenges in sensitivity, scalability, and practicality.
- In this study, we applied the ISET® CTC-DNA workflow to blood samples from patients with early-stage lung cancer.
- The ISET® CTC-DNA protocol was designed to optimize:
  - Sensitivity (95% at LLOD: 1 CTC in 10 mL of stabilized blood)
  - Practicability (enabling analysis of both CTC-DNA and ctDNA from the same blood sample),
  - Scalability (using stabilized blood – Streck tubes).
- We present our preliminary data, in terms of sensitivity and tumor heterogeneity, obtained by comparing ISET® CTC-DNA and ctDNA in patients with early-stage lung cancer.

Patients and Methods

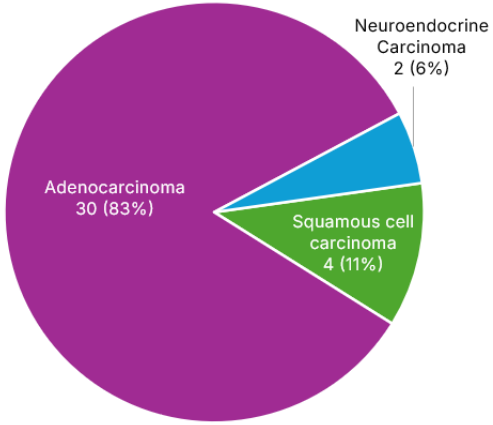
Patients

- 36 patients with early-stage Lung Cancer undergoing surgery
  - Stage I = 21 (20 LUAD)
  - Stage II = 12 (8 LUAD)
  - Stage III = 3 (3 LUAD)



Samples

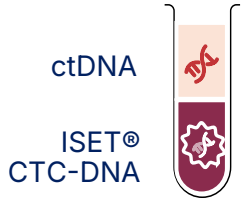
- 10 mL blood on Streck® before surgery
  - Plasma isolation>>>ctDNA
  - Cellular Part>>>ISET® CTC-DNA
  - White blood cells>>>WBC DNA
- Tumor Tissue collected as FFPE



ctDNA: plasma separation, DNA extraction

CTC-DNA: ISET® CTC isolation, cell lysis, DNA extraction. **WBC:** DNA extraction

FFPE: DNA extraction



from same Streck® tube

Next Generation Sequencing

Performed on all the DNA samples using a Lung Cancer specific panel (Agilent Technologies, Inc.) targeting 983 regions from 53 target genes.

Libraries prepared with the SureSelectXT technology (Agilent Technologies, Inc.) following the manufacturer's instructions.

Paired-end (2×150 bases) sequencing performed on a NovaSeq X Plus sequencer (Illumina, Inc.).

Bioinformatics workflow:

Map reads to hg38 with BWA. Remove duplicates using UMIs + Sambamba/fgbio

GATK HaplotypeCaller + Fisher's Exact Test. MuTect2 (+ Fisher's test, PON filtering)

Rescue variants with VarScan2. Annotate with VEP, gnomAD, 1000G, Kaviar, in-house DB

Pathogenicity prediction: DANN, FATHMM, MutationTaster, SIFT, PolyPhen

Clinical databases: ClinVar, COSMIC, OncoKB, RegulomeDB

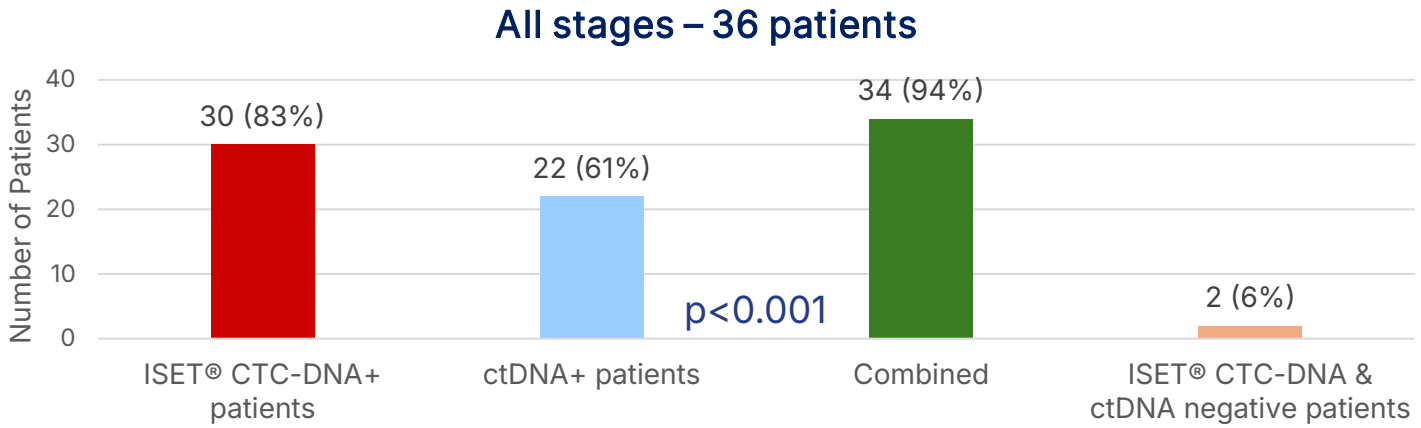
Variants found in Liquid Biopsy and Tumor Tissue

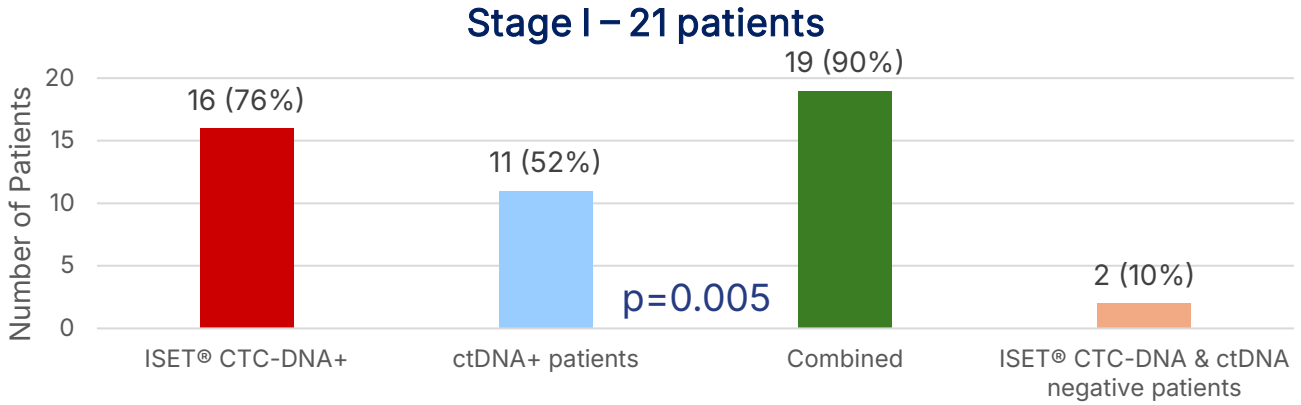
Positivity: ≥ 1 variants

ISET® CTC-DNA provides higher sensitivity than ctDNA

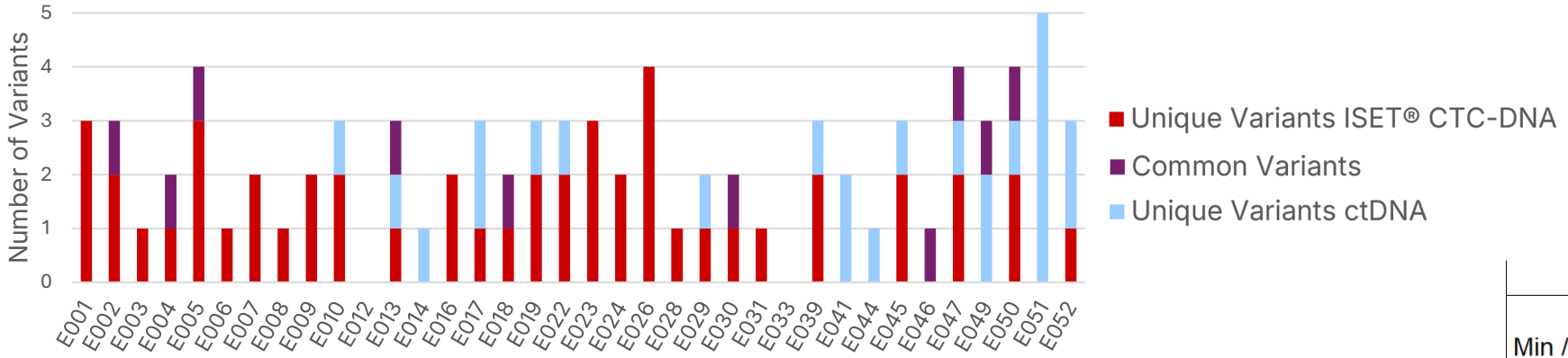
Positivity: ≥ 1 variant

Stage	Patients	CTC-DNA+	Patients ctDNA+	Combined
All stages	36	30 (83%)	22 (61%)	34 (94%)
Stage I	21	16 (76%)	11 (52%)	19 (90%)
Stage II	12	11 (92%)	9 (75%)	12 (100%)
Stage III	3	3 (100%)	2 (67%)	3 (100%)





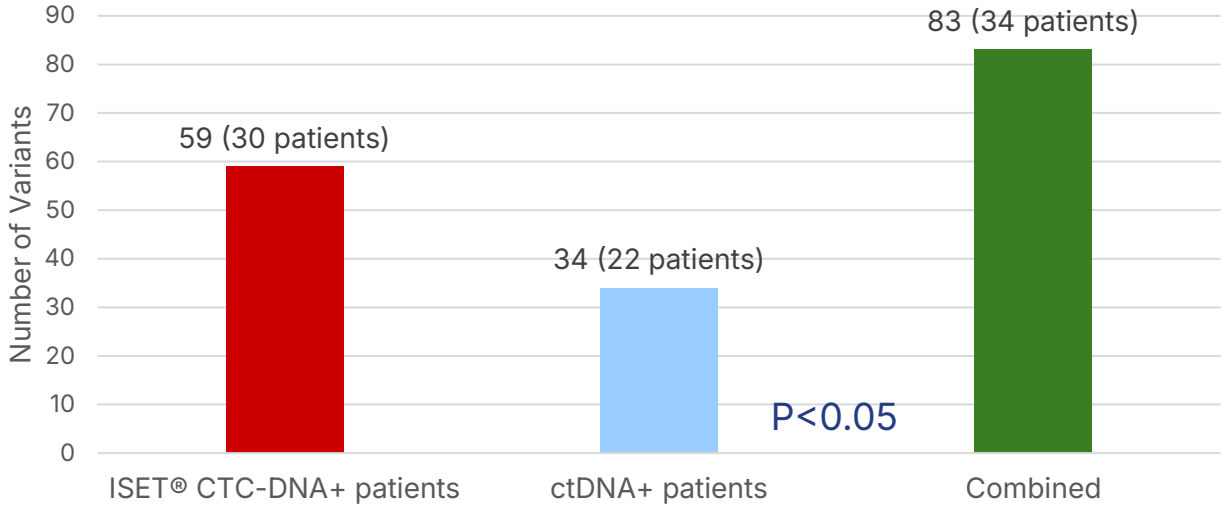
ISET® CTC-DNA detects higher tumor heterogeneity than ctDNA



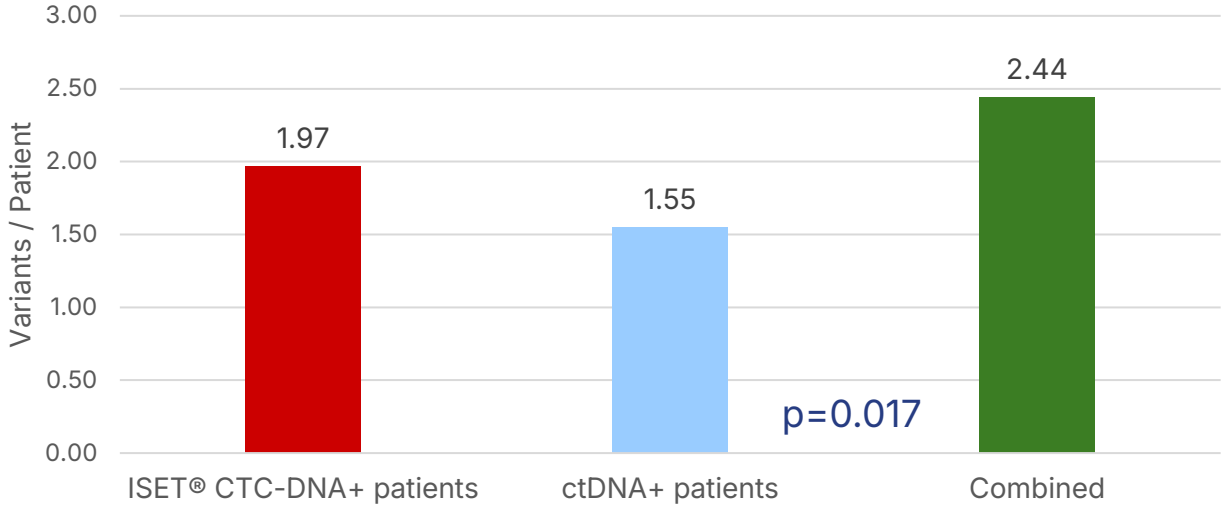
Stage	Patients	Variants CTC-DNA+	Variants ctDNA+
All stages	36	59	34
Stage I	21	35	14
Stage II	12	18	17
Stage III	3	6	3

	Variants CTC-DNA+	Variants ctDNA+	Combined
Total	59	34	83
Min / Max per patient	0 - 4	0 - 5	0 - 5
Average per patient	1.97	1.55	2.44

Oncogenic Variants Number



Average number of oncogenic variants per patient



Summary and Perspectives

- In this cohort of patients with early-stage lung cancer, oncogenic variants were identified more frequently and in higher numbers in ISET® CTC-DNA than in ctDNA.
- Combining ISET®CTC-DNA with ctDNA provided the most informative results, improving both sensitivity and tumor heterogeneity assessment.
- The technical advance allowing to obtain, with high sensitivity, both CTC-DNA and ctDNA from the same stabilized blood sample offers combined results with higher sensitivity and a more comprehensive appraisal of tumor heterogeneity.
- Work is ongoing in the same patients during follow-up to compare ISET®CTC-DNA and ctDNA in the MRD (Minimal Residual Disease) setting.
- Future work should include combining ISET® CTC-DNA with commercial ctDNA assays to further validate and extend these findings.

Thank You

patrizia.paterlini@rarecells.com

rarecells