162 – Validation of recurrence prediction using circulating tumor DNA in patients with curatively treated early-stage non-small cell lung cancer

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Introduction

- Stage I-III NSCLC is treated curatively. However, with a 5-year survival rate of 58% the majority of patients are not cured, with minimal residual disease (MRD) persisting
- There is a clinical unmet need to identify patients at risk of relapse who may benefit from additional treatment
- Circulating tumor DNA (ctDNA) has the potential to identify MRD ahead of clinical recurrence

Study aim

Determine the clinical performance of a tissue-informed personalized ctDNA assay for **MRD detection** and **recurrence prediction**

Methods

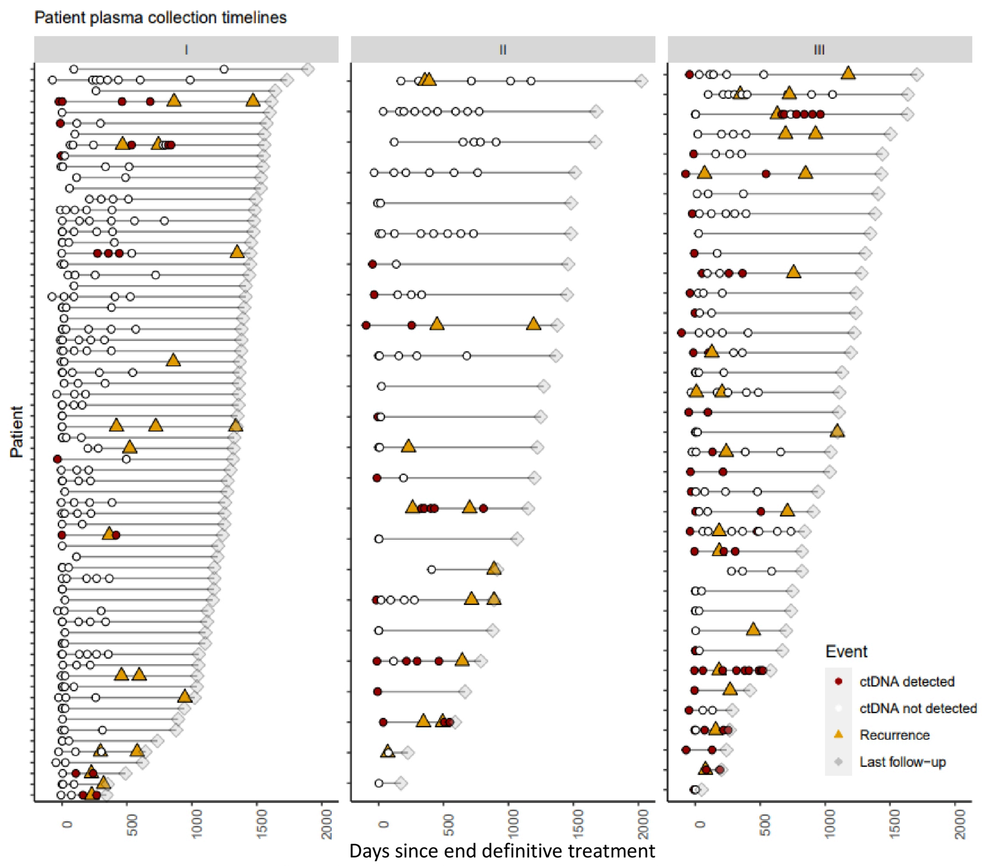
- 217 patients from two cohorts (LEMA, presented here and LUCID, previously published*) were included
- Exome sequencing of FFPE tissue identified patient specific variants. Up to 48 per patient were included in a personalized multiplex PCR assay (RaDaR^{TM})
- Germline and CHIP (Clonal Hematopoiesis of Indeterminate Potential) variants were identified during panel sequencing, and excluded from the analysis

	LEMA (n=129)	LUCID (n=88)	Total (n=217)
Stage, I/II/III (%)	53/19/29	49/28/23	51/23/26
Histology, n (%)			
Adenocarcinoma	89 (69%)	55 (62%)	144 (66%)
SCC*	29 (22%)	27 (31%)	56 (26%)
Other	11 (9%)	6 (7%)	17 (8%)
Treatment, n (%)			
Surgery	117 (92%)	69 (78%)	186 (86%)
Chemoradiotherapy	12 (8%)	19 (22%)	31 (14%)
Adjuvant treatment, n (%)	50 (39%)	9 (10%)	59 (27%)
Smoking status, n (%)			
Active smoker	38 (29%)	16 (18%)	54 (25%)
Ex- smoker	85 (66%)	64 (73%)	149 (68%)
Never smoker	6 (5%)	8 (9%)	14 (7%)
Plasma timepoints, n			
Baseline (pre-Trx)	87	78	165
Follow-up	358	285	643

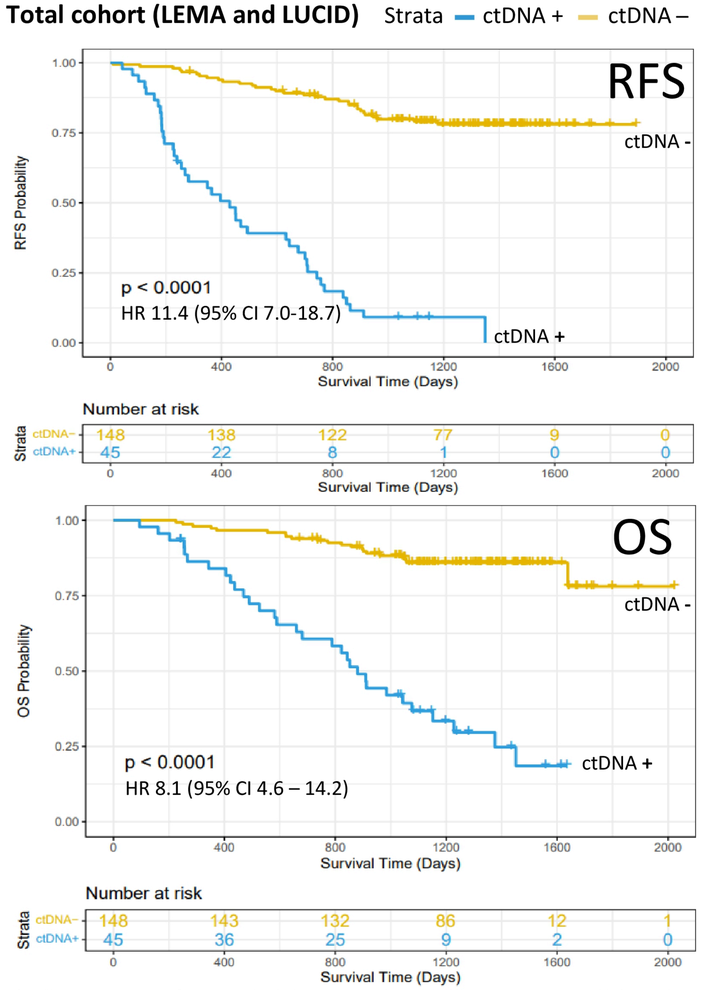
Results

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Total cohort (n=193)	63	97	91	84
Stage I (n= 102)	53	99	91	90
Stage II and III (n= 91)	67	93	91	74
• LEMA cohort (n=116)	62	97	92	85
Stage I (n= 62)	50	100	100	89
Stage II and III (n= 54)	68	93	89	77
• LUCID cohort* (n=77)	64	96	90	82
Stage I (n= 40)	57	97	80	91
Stage II and III (n= 37)	65	94	93	68

* A patient was regarded as ctDNA-positive if at least one sample ≥14 days after end of treatment was positive for ctDNA. PPV = Positive Predictive Value, NPV = Negative Predictive Value. LUCID; Gale et al. Annals Oncol 2022



* See Gale et al. for equivalent swimmer plot from the LUCID cohort



*RFS = recurrence free survival, OS = overal survival, patients are split based on ctDNA detection in samples collected ≥14 days after end of treatment

Conclusion

- ctDNA detection by RaDaR predicted recurrence in two independent cohorts
- In stage I patients:
  The high specificity of 99% and PPV of 91% may enable addition of treatment if ctDNA is detected
- In stage II-III patients:
  The NPV of 74% may support Tx de-escalation
- Our results confirm the potential of ctDNA as a decision support tool for guiding treatment

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