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Residual ctDNA after treatment predicts early relapse in patients with early-stage NSCLC

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Residual ctDNA after treatment predicts early relapse in patients with early-stage NSCLC

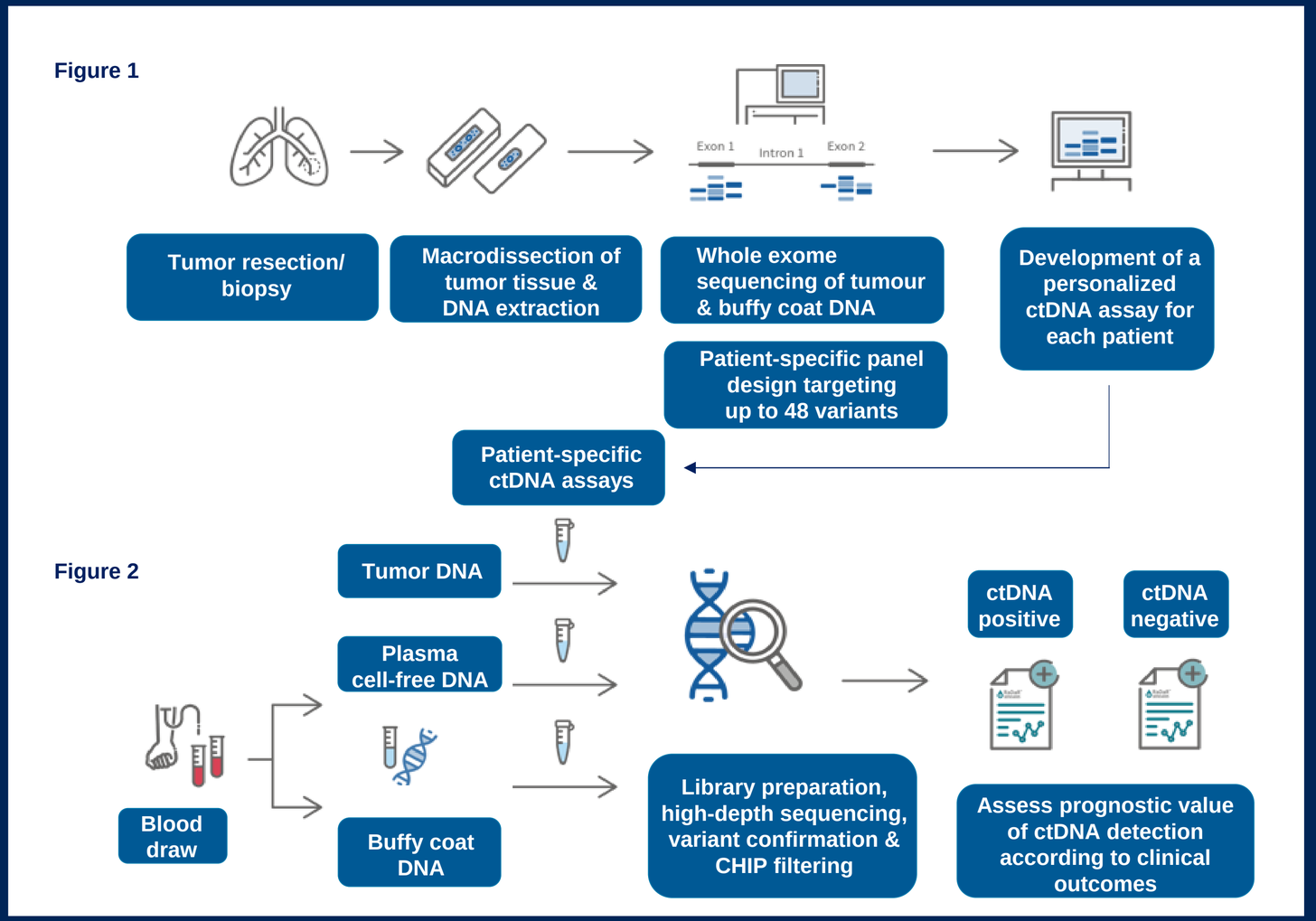
- Identification of MRD in patients with localized NSCLC following treatment with curative intent has potential for identifying patients who are at higher risk of relapse who may benefit from adjuvant therapy
- Circulating tumor DNA (ctDNA) is being investigated as a liquid biopsy for detection of residual disease and recurrence
- Objective of study to test the feasibility and prognostic value of detecting ctDNA at or before relapse in stage IA - IIIB NSCLC patients (n=88) on the LUCID (LUng cancer - CIrculating tumor DNA) study following treatment with curative intent, either surgery (n=69) or chemoradiotherapy (n=19)
- Plasma samples (n=363) were collected before and after treatment, and at 3, 6 and 9 months. For 17 patients, additional plasma was collected at disease relapse. Patients were followed for a median 3 years (9 months - 5 years)

Table 1: Patient demographics

Characteristics	Patients (n=88)
Age, Median (range)	
Stage I	73 (52-88)
Stage II	74 (57-83)
Stage III	67 (44-78)
Sex	
Male	45 (51.1%)
Female	43 (48.9%)
Smoking status	
Never	8 (9.1%)
Ex-smoker	63 (71.6%)
Smoker	16 (18.2%)
Cancer history	29 (33%)

Characteristics	Patients (n=88)
Histology	
Adenocarcinoma	55 (62.5%)
Squamous cell carcinoma	27 (30.7%)
Other	6 (6.8%)
Pathology	
Stage I	43 (48.9%)
Stage II	25 (28.4%)
Stage III	20 (22.7%)
Treatment	
Surgery	69 (78.4%)
ChemoRadiation	19 (21.6%)
Time points	
Baseline	78
Follow-up	285

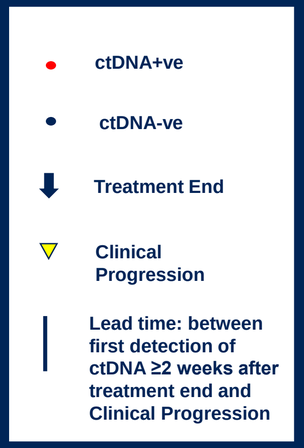
Overview of the development of patient-specific ctDNA assays & analysis of patient samples

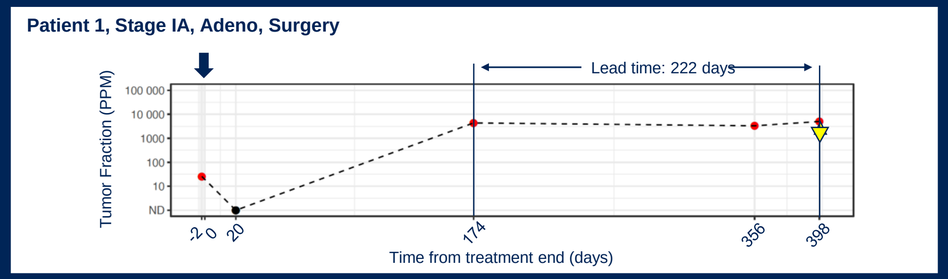


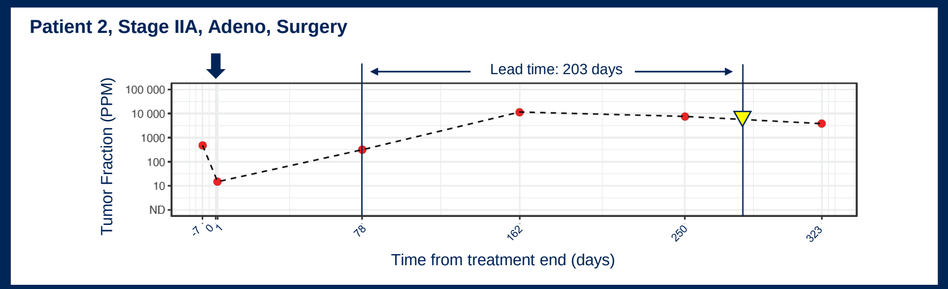
Detection of ctDNA using patient-specific ctDNA assays

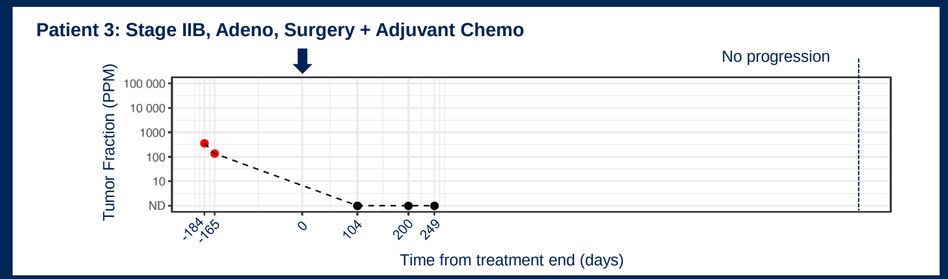
- ctDNA was detected prior to treatment in 24%, 77% and 87% of patients with stage I, II and III disease respectively
- Overall, ctDNA was detected in 26% of all samples collected at baseline and follow-up, at a median variant allele fraction (VAF) of 0.047% (range: 0.0007% to >2%)

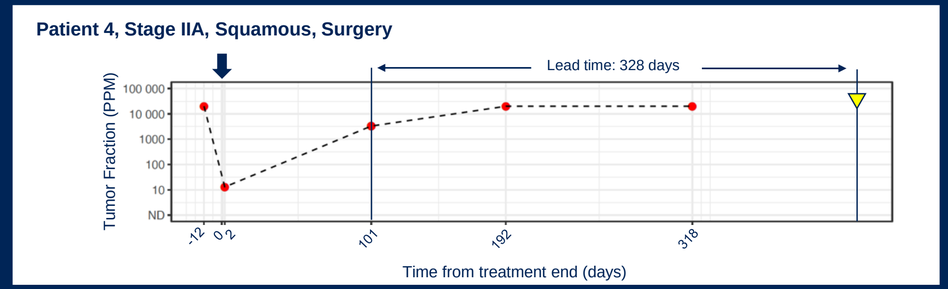
Figure 4: Longitudinal monitoring of ctDNA in four patients





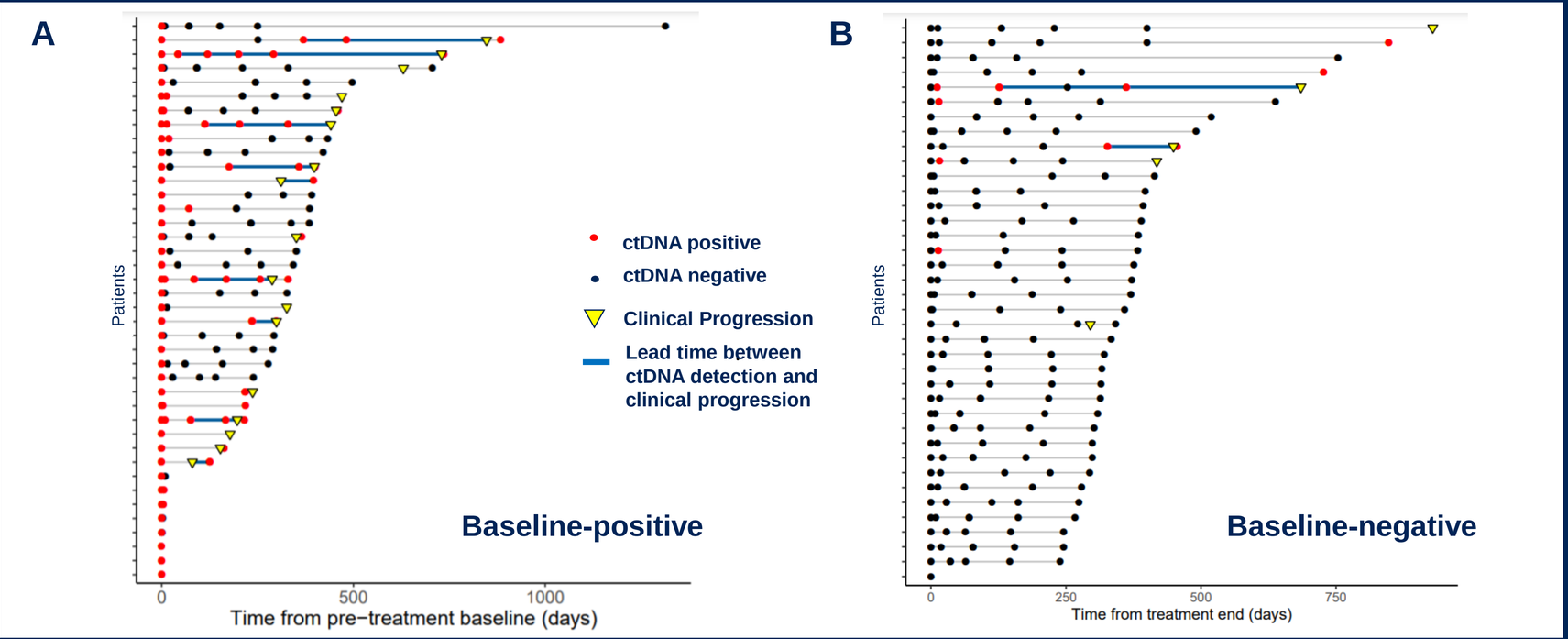






Longitudinal monitoring of plasma from patients with (A) ctDNA detected (n=40) and (B) ctDNA not detected prior to treatment (n=38), and identification of clinical progression

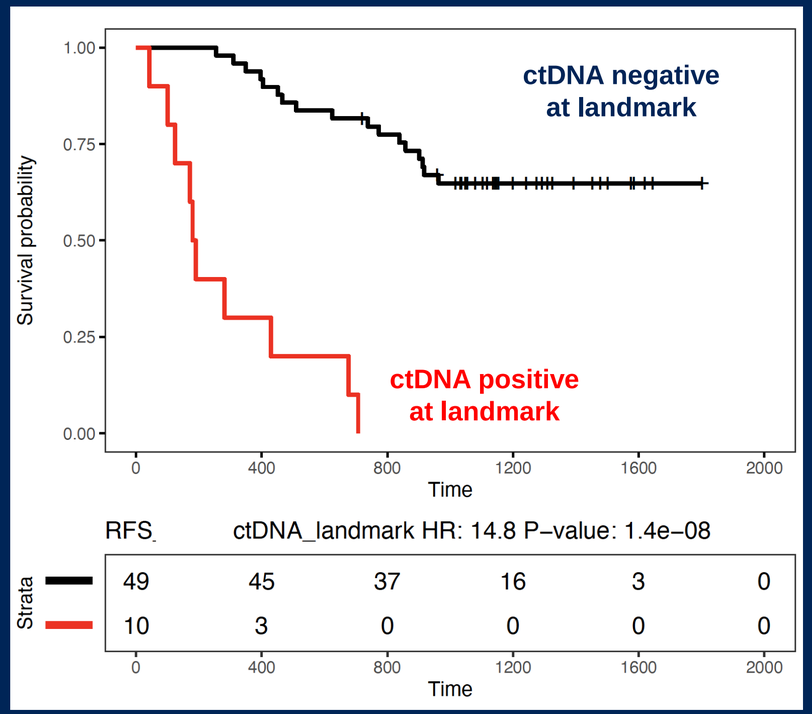
Figure 6

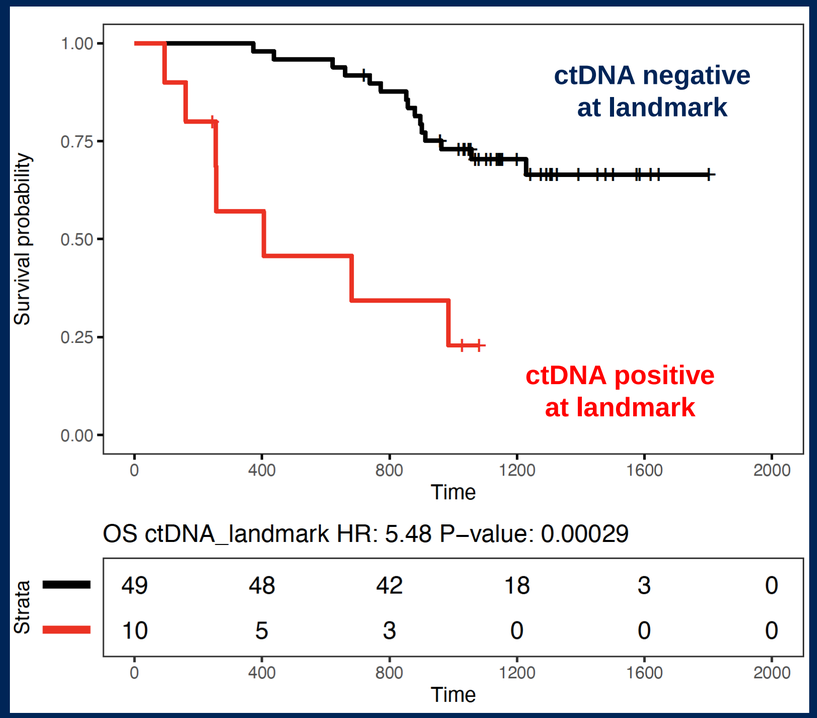


- In samples collected ≥2 weeks after the end of treatment, ctDNA was detected at any timepoint in 20 cases
- Of these, 17 had clinical progression (85%), 2 patients were diagnosed with a second primary cancer, 1 patient died of other causes, & 5 patients had no samples available in the 200 days prior to progression
- In the remaining 12 patients with available samples, ctDNA detection preceded clinical progression by a median of 212.5 days

ctDNA detection after treatment is associated with shorter relapse free survival

Figure 7





- **In survival analysis of 59 patients, plasma was available within a landmark timepoint between 2 weeks - 4 months after the end of treatment, and ctDNA detection was strongly predictive of clinical disease relapse (RFS Hazard Ratio: 14.8, p-value<10^{-5}; OS Hazard ratio: 5.48, p-value<0.0003)**
- **All 10 patients with ctDNA detected at landmark had clinical progression within the study period**
- **These results support emerging evidence that using a sensitive patient-specific assay, ctDNA can be used to reliably detect MRD in NSCLC patients treated with curative intent, many months before clinical progression, and offers an opportunity to identify ctDNA-positive patients who may benefit from adjuvant therapy**