Ultra-sensitive detection of minimal residual disease (MRD) through whole genome sequencing (WGS) using an AI-based error suppression model in resected early-stage non-small cell lung cancer (NSCLC)

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Background

- Early detection of recurrence and monitoring of MRD post-surgery is critical for clinical decision-making to tailor adjuvant therapy[1]
- In early-stage NSCLC, circulating tumor DNA (ctDNA) detection is especially challenging, requiring highly sensitive and specific assays[2]
- C2inform[3] is a patient-specific WGS approach for ultra-sensitive ctDNA detection in NSCLC patients undergoing curative surgery
- The primary objective was to determine whether C2inform status (positive/negative) at the landmark timepoint (collected at first follow-up within 6 months after surgery) was associated with relapse

C2inform Assay

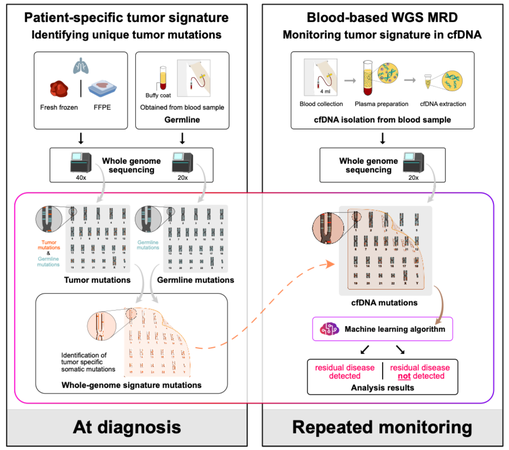

Figure 1. C2inform assay protocol

Study Design

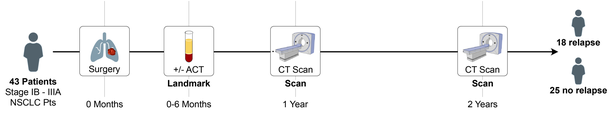

Figure 2. Study design

Patient Characteristics

	N (%)
Age (median, range)	62 (46-79)
Gender	
Female	13 (30)
Male	30 (70)
Smoking Status	
Non-smoker	20 (47)
Current or former	23 (53)
Histology	
Adenocarcinoma	34 (79)
Others	9 (21)

	N (%)
Stage	
IB	11 (26)
II	16 (37)
III	16 (37)
EGFR mutated	21 (49)
Chinese ethnicity	35 (81)
Received adjuvant therapy	26 (60)
Disease relapsed	18 (42)
Alive at data cut-off	10 (23)

Table 1. Patient characteristics (N=43)

Association of ctDNA Detection and Relapse

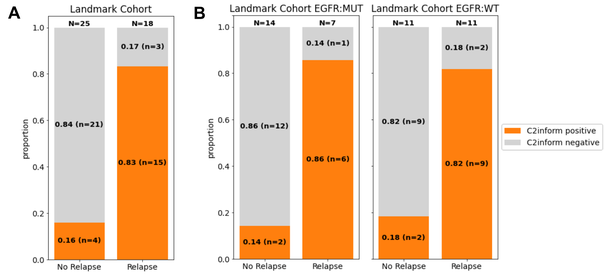

Figure 3. The association of relapse with presence of ctDNA in (A) the landmark cohort and (B) the *EGFR* mutated and wild type (WT) subgroups.

ctDNA was detected (C2inform positive) in 83% of patients that relapsed (sensitivity 83%), compared to 16% that did not relapse (specificity 84%)

Landmark Cohort Patient Level Overview

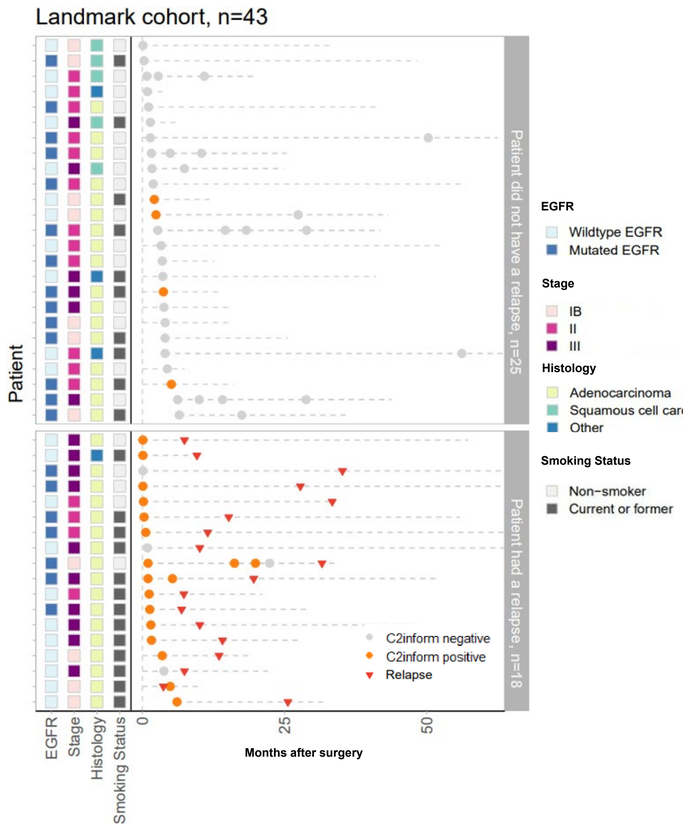

Figure 4. Plasma samples from 43 patients in the landmark cohort were collected post-surgery and analyzed for the presence of ctDNA (C2inform positive). All post-surgery plasma samples are shown.

Association of ctDNA Detection and Recurrence Free Survival (RFS)

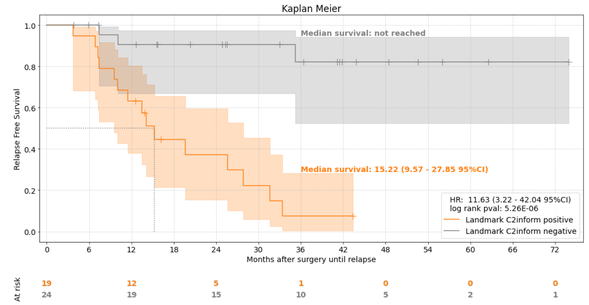

Figure 5. Association of C2inform status at landmark with relapse

Conclusions

- Using a robust patient-specific WGS implemented AI-based computational platform (C2inform), the study demonstrate high sensitivity and specificity detection of MRD at the landmark post-surgery timepoint in both *EGFR* mutated and wildtype NSCLC.
- With an increasing number of therapeutic options in the adjuvant setting for NSCLC,[4,5] an ultra-sensitive MRD assay has the potential to facilitate personalized clinical decision-making for tailoring both the need and choice of adjuvant therapies.

References

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