

Longitudinal ctDNA Dynamics in Oligometastatic NSCLC Undergoing Radio-Immunotherapy

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Clinical trial in progress —
no efficacy or survival results are
available at the time of
presentation.

1) BACKGROUND

- Oligometastatic non-small cell lung cancer (NSCLC) is a distinct disease state in which locally consolidative therapies, especially radiotherapy, combined with immunotherapy may improve outcomes.
- Patient responses remain heterogeneous, and robust biomarkers for treatment monitoring and prognostication are still lacking.
- Circulating tumor DNA (ctDNA) is a promising non-invasive biomarker for minimal residual disease detection, treatment response assessment, and real-time disease monitoring.
- The role of longitudinal ctDNA monitoring in oligometastatic NSCLC receiving combined radiotherapy and immunotherapy has not been systematically characterized.

2) STUDY OBJECTIVE

- Primary objective:** evaluate the association between ctDNA dynamics and progression-free survival (PFS).
- Secondary objectives:** overall survival (OS), patterns of progression and correlation with radiographic response by RECIST v1.1.

3) WHY THIS STUDY MATTERS

- May identify early molecular response or resistance.
- May improve risk stratification during radio-immunotherapy.
- May support individualized surveillance and treatment adaptation.
- May detect molecular progression before radiographic progression becomes evident.
- May help define clinically meaningful ctDNA kinetic patterns for future biomarker-guided treatment strategies.

4) STUDY DESIGN

- Prospective, observational cohort study.
- Planned enrollment: approximately 60 patients.
- Population: histologically confirmed oligometastatic NSCLC, defined as ≤ 5 metastatic lesions in ≤ 3 involved organs.
- Treatment context: radiotherapy (stereotactic body radiotherapy or hypofractionated radiotherapy) combined with immune checkpoint inhibitors.

5) ELIGIBILITY

Inclusion - Histologically confirmed oligometastatic NSCLC - Planned treatment with radiotherapy plus immunotherapy	Key exclusion - Actionable driver mutations with available targeted therapy - Prior immunotherapy exposure
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6) STUDY SCHEMA

Enrollment

Baseline assessment and blood draw

Systemic immunotherapy /planned radiotherapy

Pre-radiotherapy blood draw

Radiotherapy

Post-radiotherapy blood draw

Follow-up

Analysis

- Prospective enrollment of patients with oligometastatic NSCLC undergoing combined radio-immunotherapy.
- Blood sampling at three predefined time points: pre-treatment, pre-radiotherapy, and post-radiotherapy.
- Radiotherapy delivered using SBRT or hypofractionated radiotherapy in combination with immune checkpoint inhibition.
- Longitudinal clinical and imaging follow-up with response assessment according to RECIST v1.1.
- ctDNA kinetics will be correlated with PFS, OS, radiographic response, and patterns of progression.

7) ctDNA SAMPLING AND ANALYSIS

- Peripheral blood will be collected at three predefined time points: pre-treatment, pre-radiotherapy, and post-radiotherapy.
- ctDNA will be analyzed using next-generation sequencing with a comprehensive panel of cancer-associated genes.
- ctDNA kinetic patterns of interest: clearance, persistence, and emergence.

ctDNA Blood Sampling Timeline

1

2

3

Pre-treatment

Pre-radiotherapy

Post-radiotherapy

8) STATISTICAL PLAN

- Survival analysis: Progression-free survival (PFS) and overall survival (OS) will be estimated using the Kaplan – Meier method.
- Association analysis: The associations between longitudinal ctDNA dynamics and clinical outcomes will be evaluated using Cox proportional hazards regression models.
- Response correlation: ctDNA kinetic patterns, including clearance, persistence, and emergence, will be correlated with radiographic response and patterns of disease progression.

9) TRIAL STATUS

- Registered prospective observational study.
- Target enrollment: approximately 60 patients.
- Patient recruitment and longitudinal biospecimen collection are ongoing.
- Clinical outcome data are not yet mature for efficacy analysis.

This study is currently in the active enrollment and follow-up phase. Serial ctDNA samples are being collected according to the predefined schedule, together with prospective clinical and radiographic outcome data. Final analyses will be performed after sufficient follow-up has been reached to evaluate the associations between longitudinal ctDNA dynamics, treatment response, progression patterns, and survival outcomes.