Circulating tumor DNA (ctDNA) monitoring to inform maintenance outcomes in patients (pts) with advanced NSCLC treated with induction atezolizumab+carboplatin+nab-paclitaxel (A+CnP).

Background
Chemoinmunotherapy (ChemIO) is a prevalent first-line treatment for advanced NSCLC with driver mutations, with maintenance therapy recommended after induction. However, real-world data suggest variability in maintenance therapy’s timing, and duration. Motivated by evidence that ctDNA monitoring can predict outcomes in patients receiving IO for advanced cancers, we hypothesized ctDNA monitoring could inform outcomes in advanced NSCLC prior to the start of maintenance therapy.

Materials and Methods
• This retrospective study included 221 patients from a completed phase III trial of atezolizumab+carboplatin+paclitaxel (A+CnP) vs. carboplatin+paclitaxel (CP) in squamous NSCLC (MPower13, NCT02567974).
• ctDNA monitoring utilized FoundationOneCDx, involving: 1) Comprehensive genomic profiling (CGP) of pre-treatment tumor tissue 2) Variant selection using an algorithm to filter out non-tumor variants 3) Multiplex PCR of up to 100 variants of interest and quantity plasma mean tumor molecular per mL (MTM/mL).
• Progression-free survival (PFS) and overall survival (OS) were estimated with Kaplan-Meier analysis.
• Hazard ratios (HR) were calculated using multivariate Cox proportional hazard models adjusting for sex, age, smoking history, PD-L1 status, liver metastases, and ECOG performance status.
• PFS and OS analyses were landmarked from C4D1 unless otherwise stated; patients with progression/death before the landmark date were excluded.
• Baseline ctDNA levels considered high if MTM/mL was greater than or equal to the median MTM/mL from all pre-treatment plasma specimens.
• TC or IC ≥ PD-L1 expression on ≥50% of tumor cells (TC) or ≥20% of tumour-infiltrating immune cells (IC); TC/IC or IC/TC ≥ PD-L1 expression on ≥8% of TC or IC, and TC/IC ≥ PD-L1 expression on <1% of TC and IC.

Consort Diagram

Patient clinical and genomic characteristics

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<th>Table 1: Baseline clinical and genomic characteristics of eligible patients from the trial to detect prevalent from (MPower13)</th>
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<td>MTM/mL &amp; mtDNA Levels</td>
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<td>Baseline MTM/mL</td>
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<td>Baseline mtDNA</td>
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ctDNA monitoring on A+CnP identifies patients with poorer outcomes

![Graph showing ctDNA monitoring on A+CnP identifies patients with poorer outcomes](image)

ctDNA detection during A+CnP can inform outcomes of patients that will receive IO maintenance

![Graph showing ctDNA detection during A+CnP can inform outcomes of patients that will receive IO maintenance](image)

Conclusions
• CGP-informed ctDNA monitoring on chemotherapy in advanced NSCLC can inform durability of treatment benefit.
• For patients with ctDNA at C4D1, prolonged induction chemotherapy was not associated with improved outcomes.
• ctDNA detection during induction chemotherapy may offer an opportunity to identify patients at high risk for disease progression and inform selection of novel personalized maintenance treatment strategies.