

20th ANNUAL

ATLANTA

LUNG CANCER SYMPOSIUM

MRD status should be used to guide adjuvant therapy –YES

Jennifer Carlisle, MD

November 7, 2026

Partners for Advancing Clinical Education

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Disclosure: This was the topic of a recent Emory debate...

9:00 – 9:20 AM	**DEBATE** Should We Perform MRD Testing in Patients With Resectable NSCLC in the Postoperative Setting?		
9:00 – 9:08 AM	• Yes	Conor E. Steuer, MD	PDF
9:08 – 9:16 AM	• No	Hirva Mamdani, MD	PDF
9:16 – 9:20 AM	• Rebuttals and Discussion		

Conor now gets to adapt these beautiful slides from Dr. Mamdani...

The Clinical Reality

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MRD -

- Early-stage disease
- Low shedding tumors
- Brain-only disease
- Patients with baseline negative ctDNA
- Assay sensitivity
- Timing

False negative

- Is one time point enough?
- What is the optimum frequency of testing?
- Sufficient to de-escalate therapy?

True negative

False reassurance

Is it real?

MRD +

- Now what?
  - More treatment?
  - Which treatment?
  - More frequent surveillance?
  - How frequent?

True positive

Psychologic cost

- CHIP mutations
- Now what?

False positive

And this is what I have to work with...

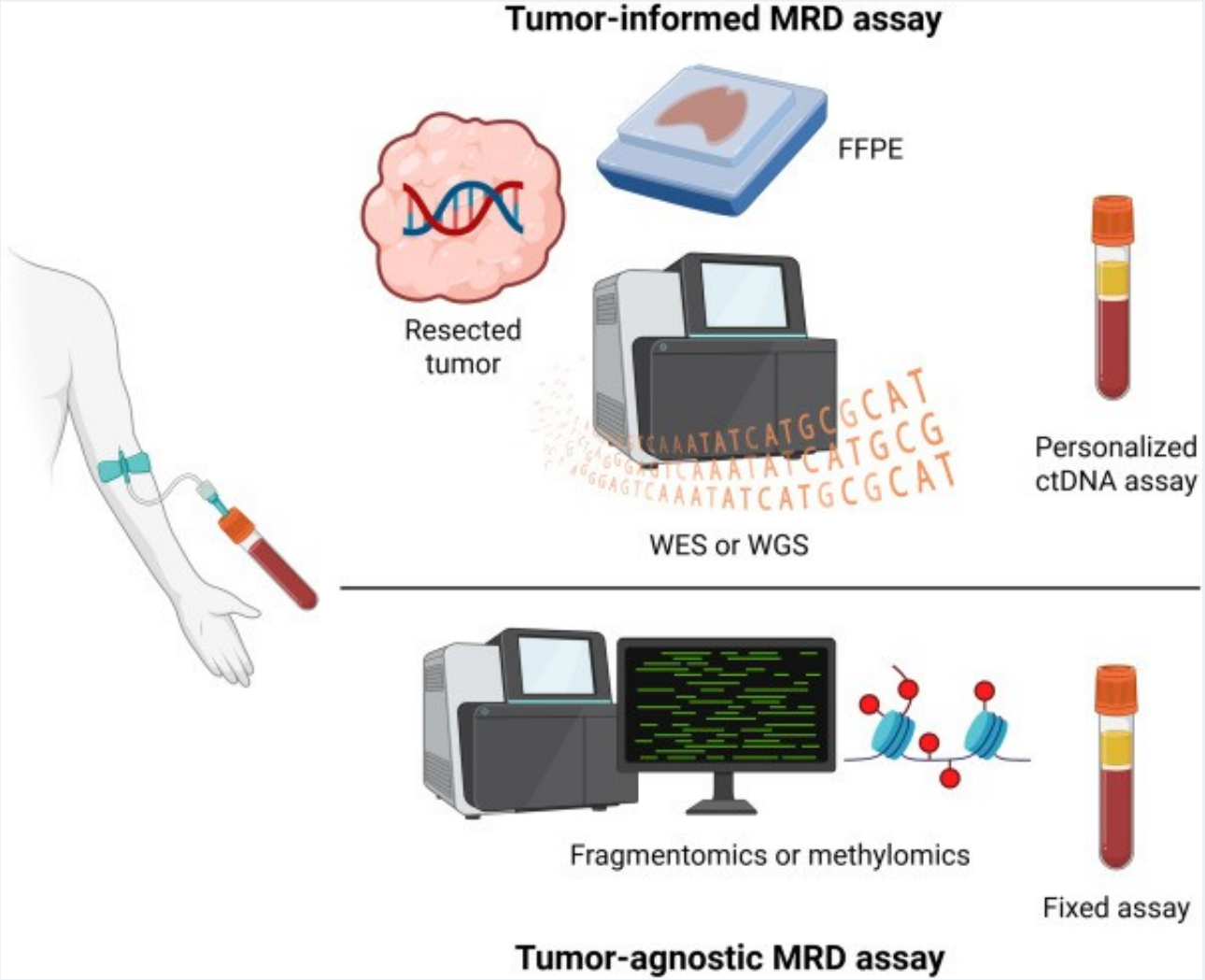
To demonstrate I have the correct side of the debate, will enlist Sci-Fi masterpiece Blade Runner to help emphasize my viewpoint



Dr. Steuer is a a fan of fantasy and science fiction



Tumor informed versus tumor agnostic MRD testing



Pro	Con
Higher sensitivity	Tissue requirement
Noise filtering (exclude CHIP)	Longer turn around time
Personalized	Miss clonal evolution

Pro	Con
No tissue required	Lower sensitivity
Rapid turn around time	False positive/Noise
Cost effective/universal	Less personalization

Tan et al. JTO 2026

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MRD status is prognostic!

MRD Testing in Resectable NSCLC

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Of course we are excited!!

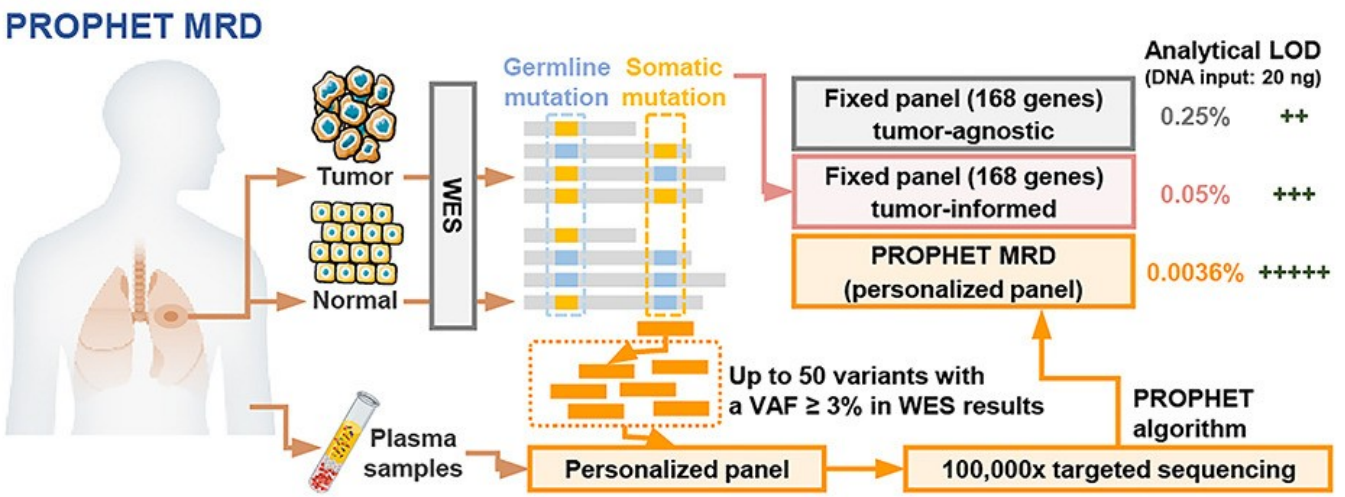


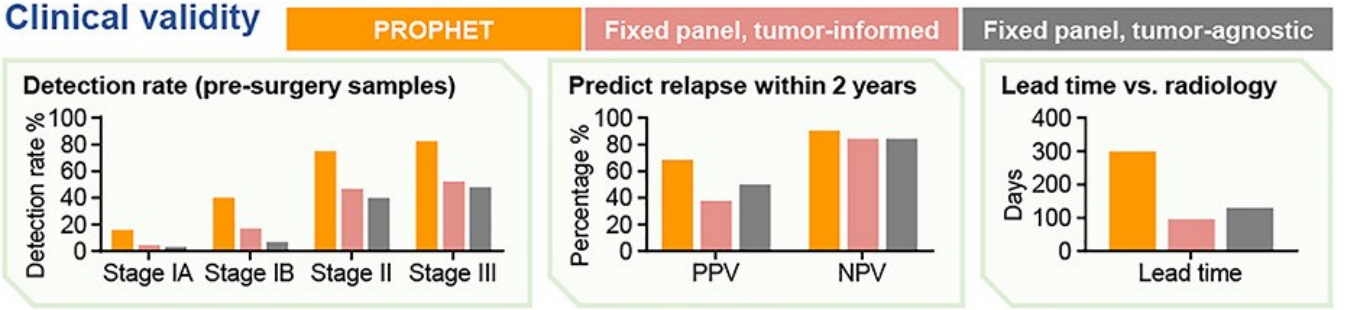
- ✓ Non-invasive tool!
- ✓ Elegant science!!
- ✓ Plethora of emerging data demonstrating its <u>prognostic</u> value:
  - Clearance of ctDNA -> prolonged survival[1,2]
  - Detectable ctDNA -> increased risk of recurrence and death[3,4]
  - Offers prognostic value beyond pCR in resectable NSCLC following neoadjuvant chemoimmunotherapy[5]

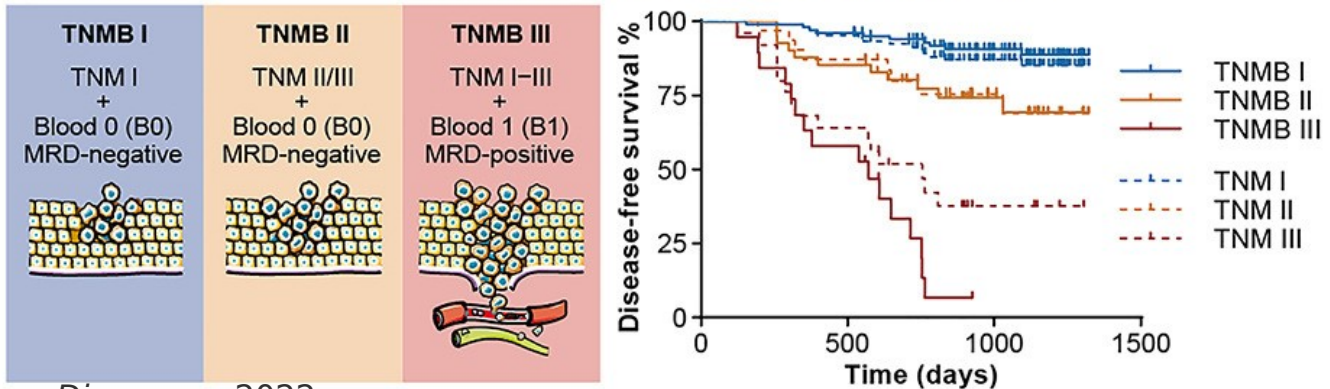
[1] Abbosh et al., Nature 2017; [2] Chaudhuri et al., Cancer Discov 2017; [3] Zhang et al., Cancer Discov 2022; [4] Verze et al., TLCR 2022; [5] Provencio et al., Clin Cancer Res 2026

Individualized tumor-infor ctDNA analysis for post-o monitoring of NSCLC

- integrating landmark ctDNA MRD and TNM, improves prognosis prediction
- illustrates a median lead time of 299 days to radiological recurrence







Zhang et al. in *Cancer Discovery* 2022

ctDNA based MRD detection in stage III NSCLC treated with chemoradiotherapy and durvalumab

Journal of Thoracic Oncology

Context

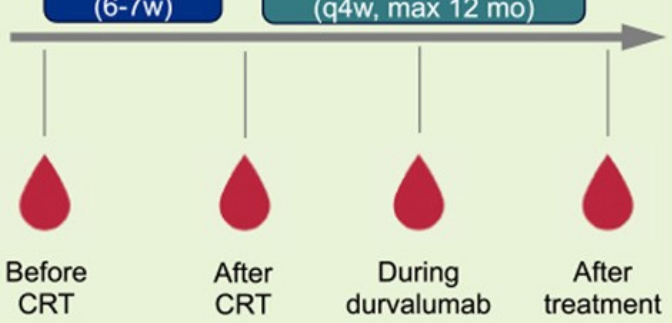
84 patients

Unresectable stage III NSCLC

CRT → durvalumab

Serial ctDNA monitoring

659 plasma samples



Key results

Detectable ctDNA during and after durvalumab identified patients at high risk of progression

- After CRT: not prognostic
- During durvalumab: **HR 2.45**
- 3 mo after treatment: **HR 5.37**

Time-dependent Cox model:
HR 2.95, $p < 0.001$

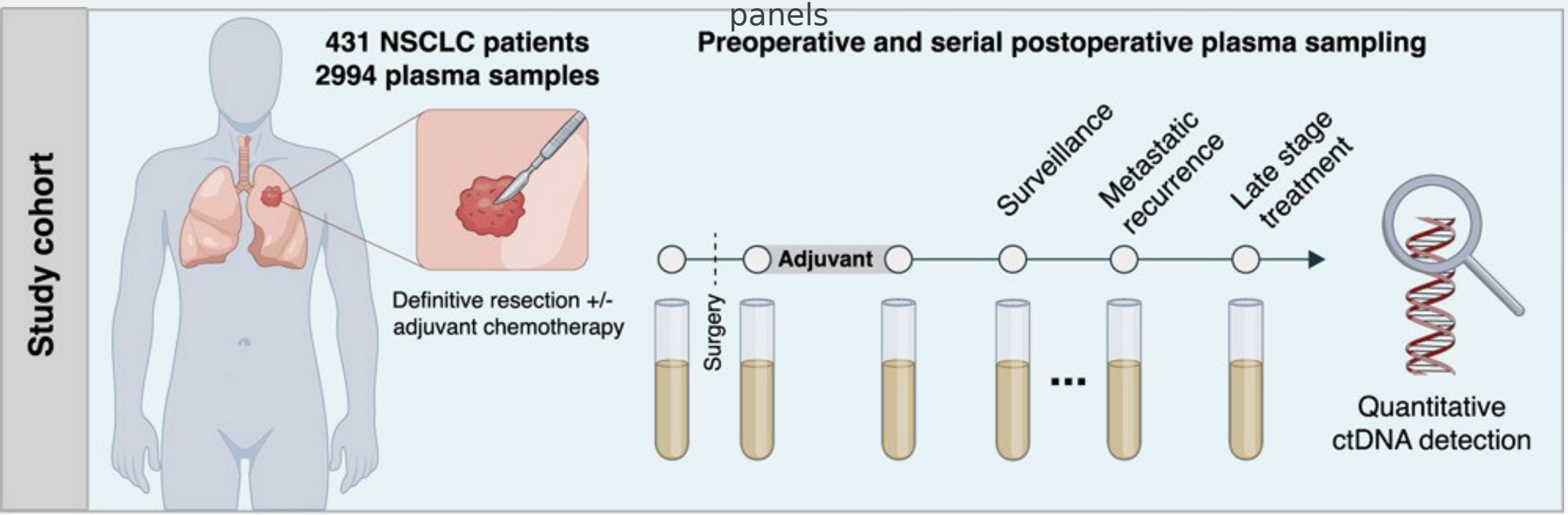
CONCLUSION: Detectable ctDNA during and after durvalumab was associated with markedly shorter PFS in unresectable stage III NSCLC

IASLC

Horndalsveen H, Haakensen VD, Madebo T, et al. *J Thorac Onc* (2026)

TRACERX Study

tumor-informed patient-specific liquid biopsy panels



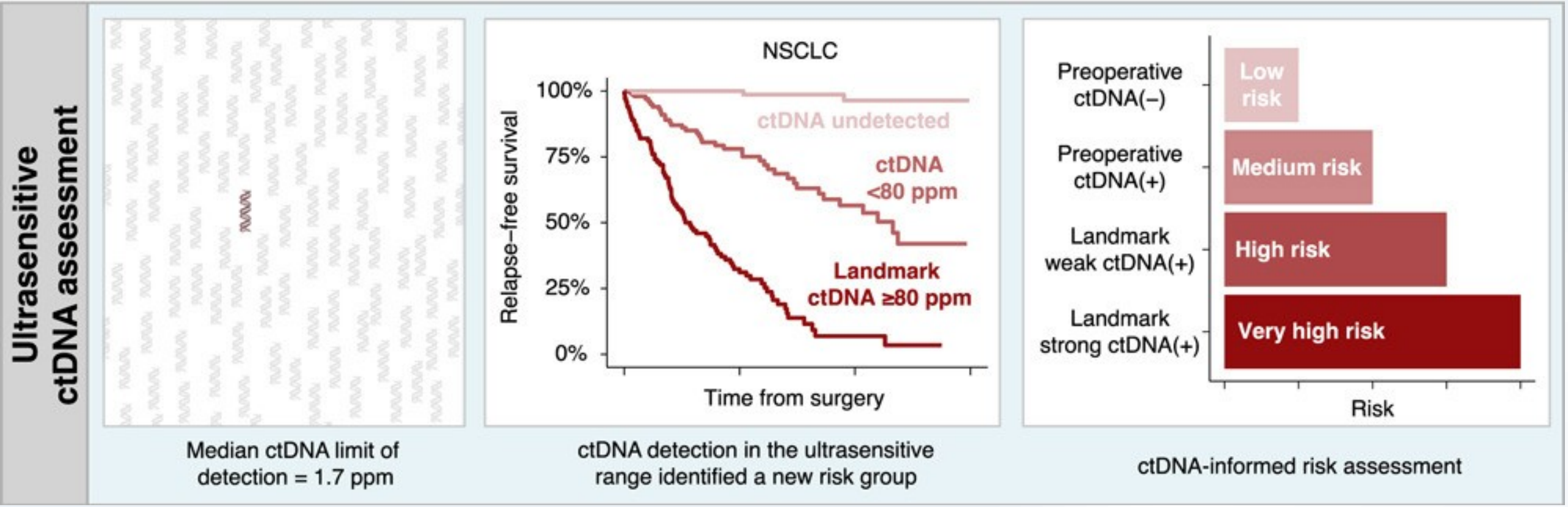
250 males and 181 females, between 2014 and 2021, median age of 69 years (range 34–92 years). 54.3% (*n* = 234) adenocarcinoma

Adjuvant platinum-based chemotherapy in 55.1% of patients (*n* = 162) with stage II/III disease, as well as a subset of those with stage IB disease (*n* = 6);

Defined landmark poing as any time point occurring between days 10 and 120 postoperatively, prior to the start of adjuvant therapy or disease recurrence

Black et al. Cell 2025

TRACERX Study:

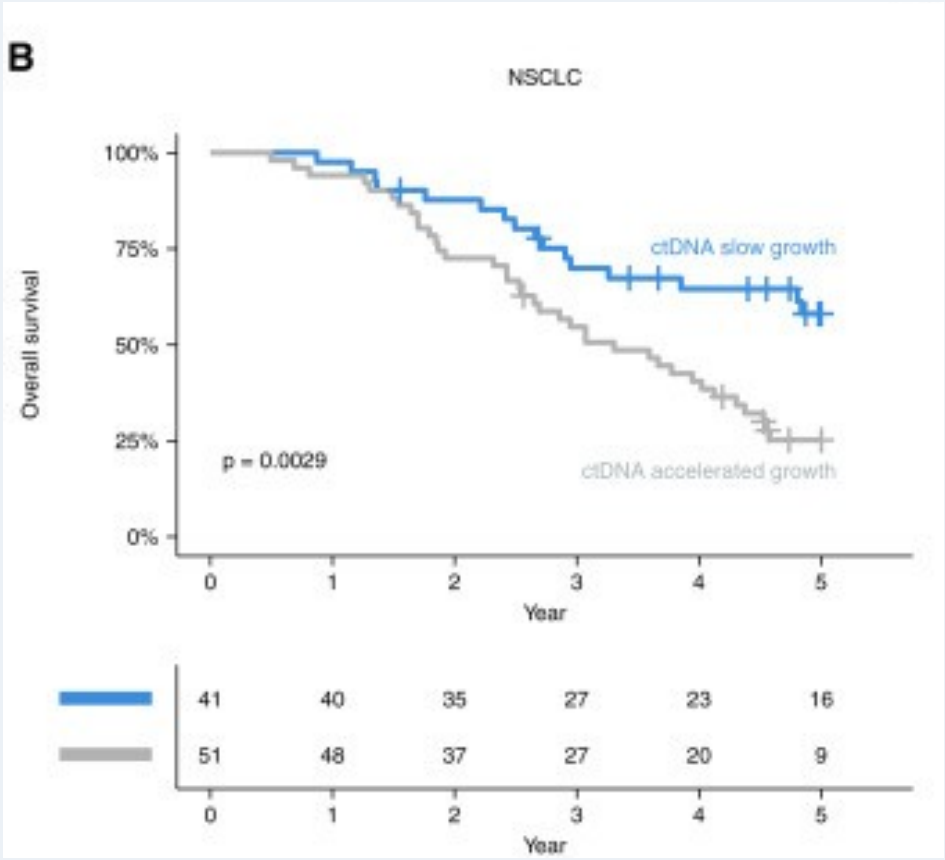


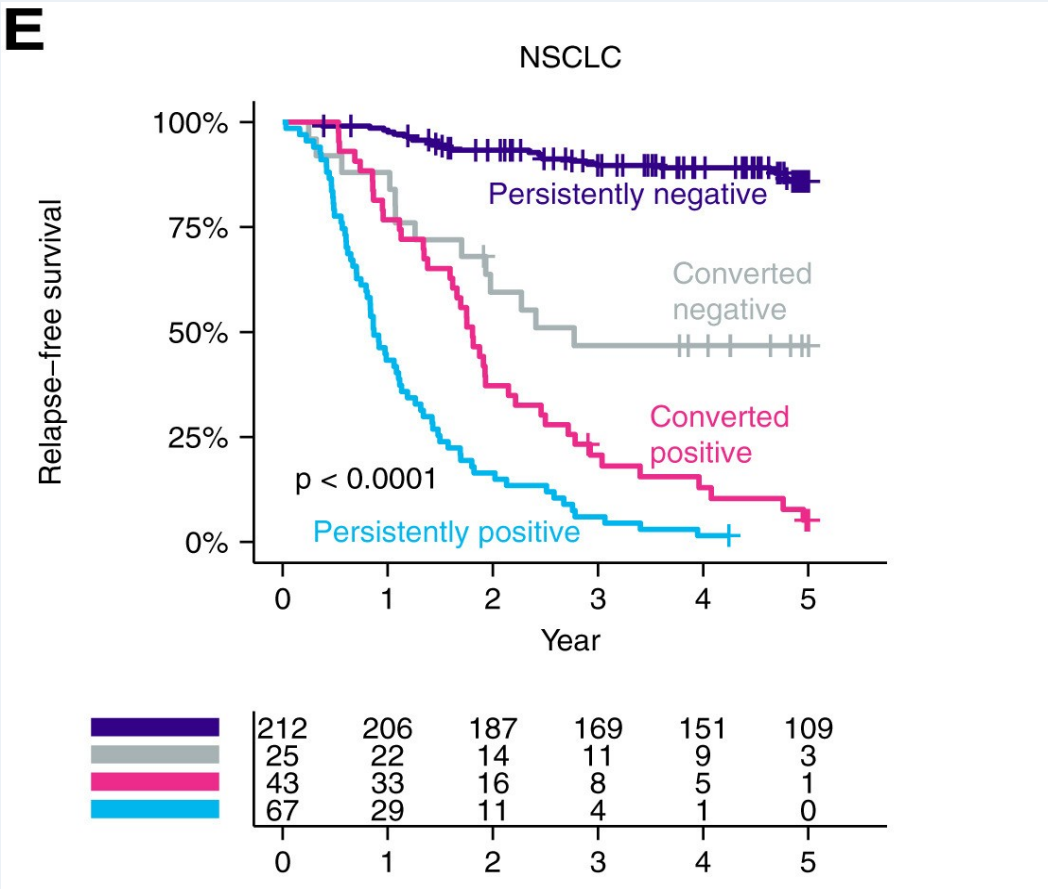
defined landmark as any time point occurring between days 10 and 120 postoperatively, prior to the start of adjuvant therapy or disease recurrence

Black et al. Cell 2025

Black et al. Cell 2025

TRACERX Study: ct DNA kinetics is also informative





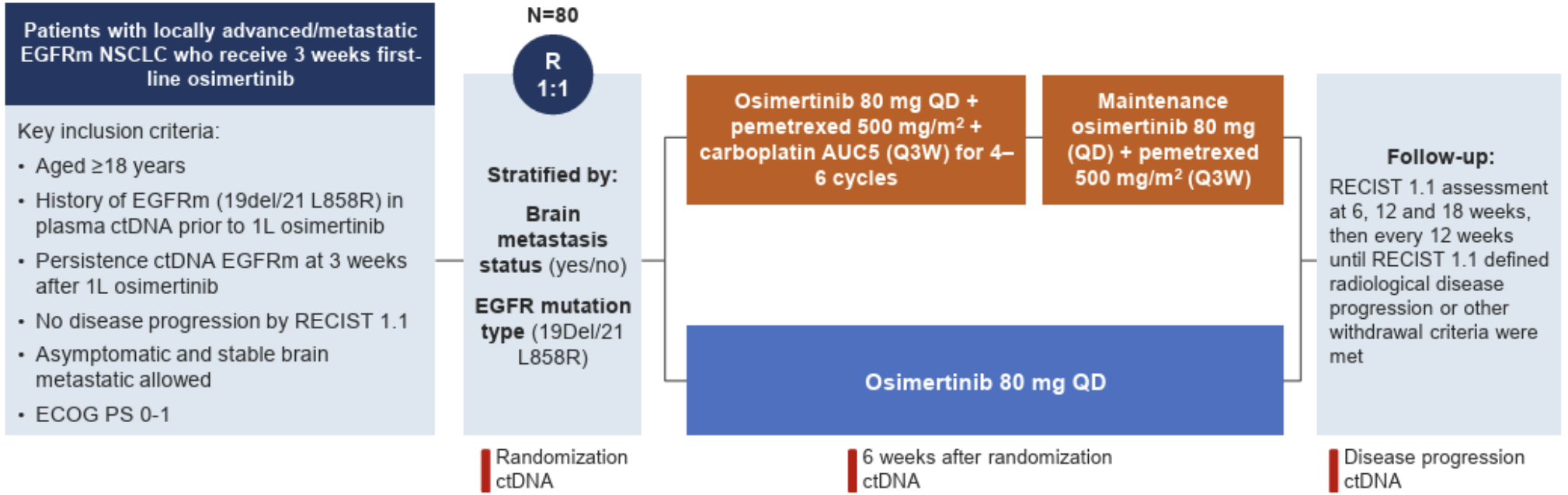
Black et al. Cell 2025

Black et al. Cell 2025


Show me the data.
MRD in NSCLC
Earlier detection
Risk stratification
MRD-guided therapy
100
50
0
MRD Positive (%)
MRD+
MRD-
Time on Treatment
Lung Cancer
Immunotherapy
Targeted Therapy
Clinical Trials
Better Outcomes
FANTASY SCI-FI LUNG CANCER

FLAME: Osimertinib ± Chemotherapy for Persistent ctDNA at Week 3

Study Design



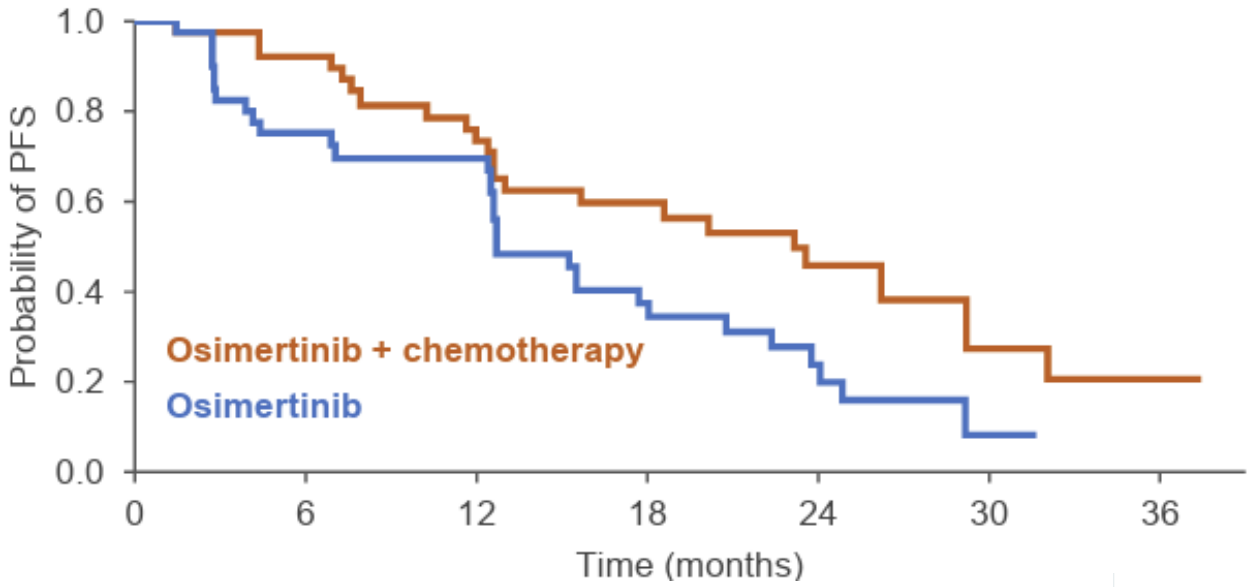
Design

- Multicenter randomized phase 2 (China), **80** patients with EGFR ex19del or L858R and persistent plasma EGFR ctDNA **3 weeks** after starting first-line osimertinib; randomized 1:1 to add carboplatin/pemetrexed (4–6 cycles, then pemetrexed maintenance) or continue osimertinib alone
- 135 of 448 screened (30%) had persistent ctDNA

Wang Z et al. ASCO 2026. Abstract LBA101 (presented by J. Zhong).
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FLAME: Osimertinib ± Chemotherapy for Persistent ctDNA at Week 3

Progression-Free Survival (Primary Endpoint)



Median PFS **23.1** vs **12.7** months; HR **0.54** (90% CI, 0.34–0.86); p=0.028. 18-month OS 76% vs 75% (immature)

Results

- ORR **50%** vs **35%**; grade ≥3 TEAEs **73%** vs **17%**; discontinuation for AE 16% vs 5%
- Persistent ctDNA at week 3 was associated with higher intratumor heterogeneity and more co-alterations

First prospective test of ctDNA-guided early intensification; proof of concept, 70% power, one-sided design; not practice-changing on its own. Baseline ctDNA detectability is prognostic in FLAURA2 and MARIPOSA (appendix).

Wang Z et al. ASCO 2026. Abstract LBA101 (presented by J. Zhong).

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Reminder we are debating if:
MRD status should be used to guide adjuvant therapy

Adjuvant trials count as adjuvant therapy!!

The guidelines agree:

Given its strong prognostic value, MRD is a valuable tool for patient stratification. Prospective clinical trials investigating both therapy escalation (in MRD-positive patients) and de-escalation (in MRD-negative patients) are recommended. 93%

Tan et al. Consensus Statement on ctDNA Minimal Residual Disease Testing in Early-Stage NSCLC; JTO 2026


Conor Steuer, MD
Wizard of
Lung Cancer
Lung Cancer
Immunotherapy
Targeted Therapy
Clinical Trials