

2026

DEBATES AND DIDACTICS
in **Hematology**
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Should We Perform MRD Testing in Patients With Resectable NSCLC in the Postoperative Setting? YES!

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



“Quite an experience to live in fear, isn't it?”



Why do we even need to consider MRD?

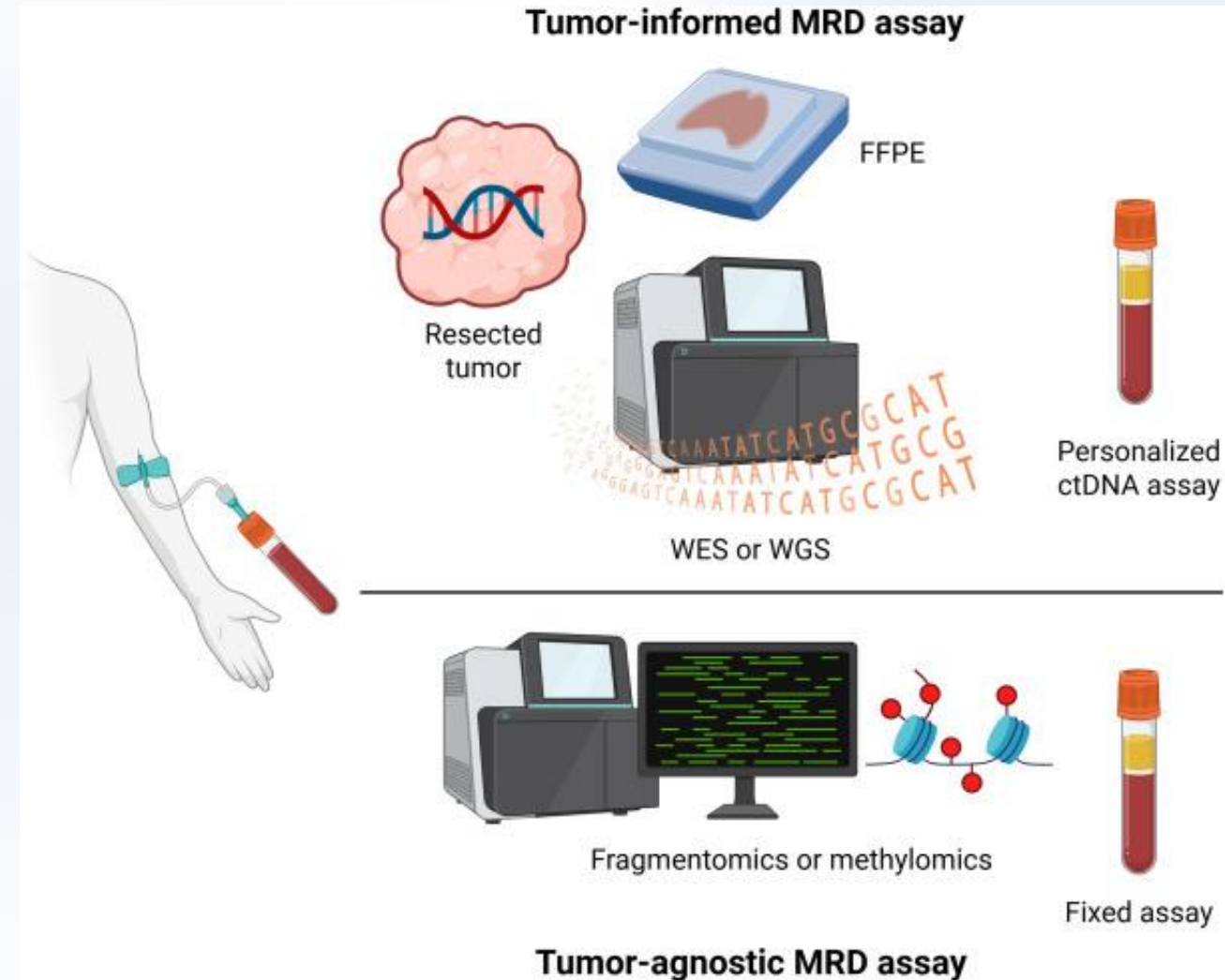
- Curative-intent surgical resection is the standard of care in early stage NSCLC, yet disease recurrence is common and survival outcomes remain poor.
- Depending on a variety of factors such as histology, stage, etc., cure rates can be 40-80%
- Also, some patients may be cured early on, and then go on to receive potentially unnecessary treatments.
- Scan anxiety is real, and easy to collect data informing patients and their physicians is a welcome addition
- Can lead the way to a more personalized approach to patient care

A sensitive test that can accurately depict risk

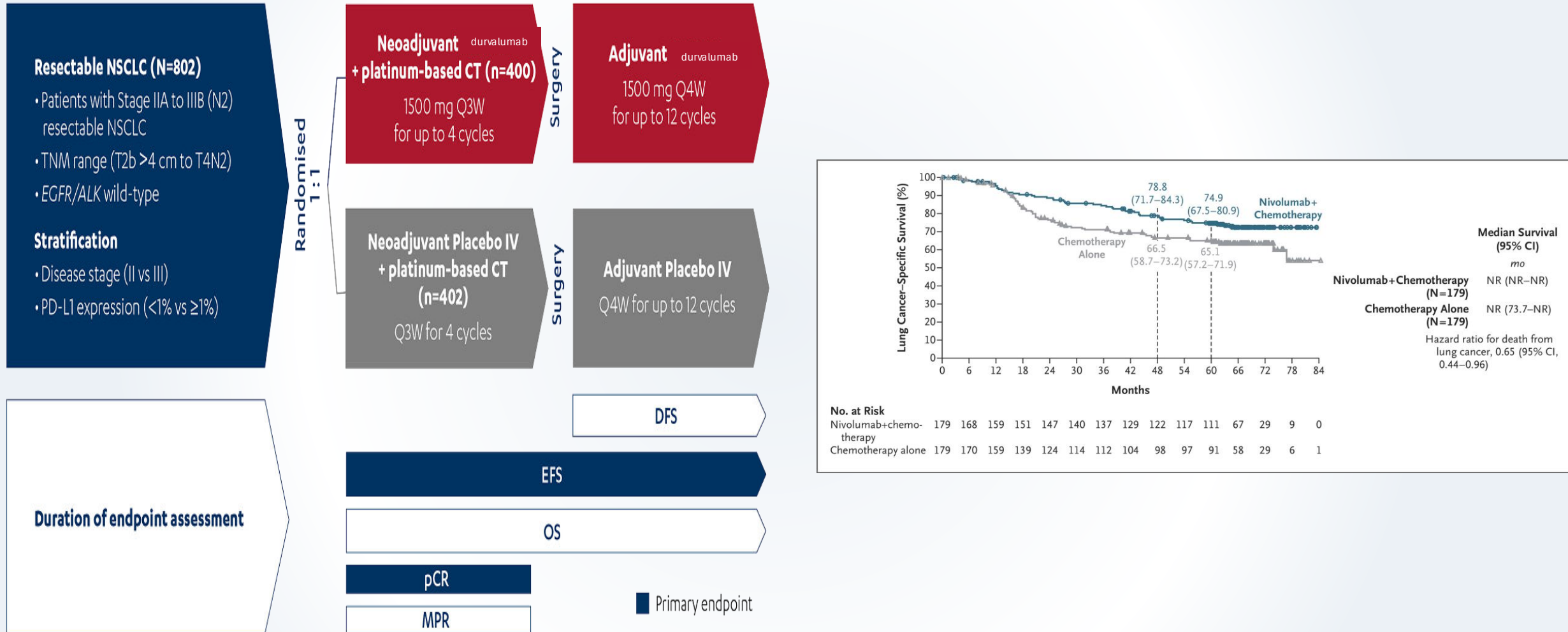


Broad MRD overview

- The technology is complicated, and beyond the scope of this short debate
- However, two main approaches exist. Tumor-informed approaches utilize patients' own tissue to guide the liquid-based assay MRD test. Highly specific but more cumbersome with its tissue requirement.
- Tissue agnostic MRD testing is more flexible but sacrifices some sensitivity.

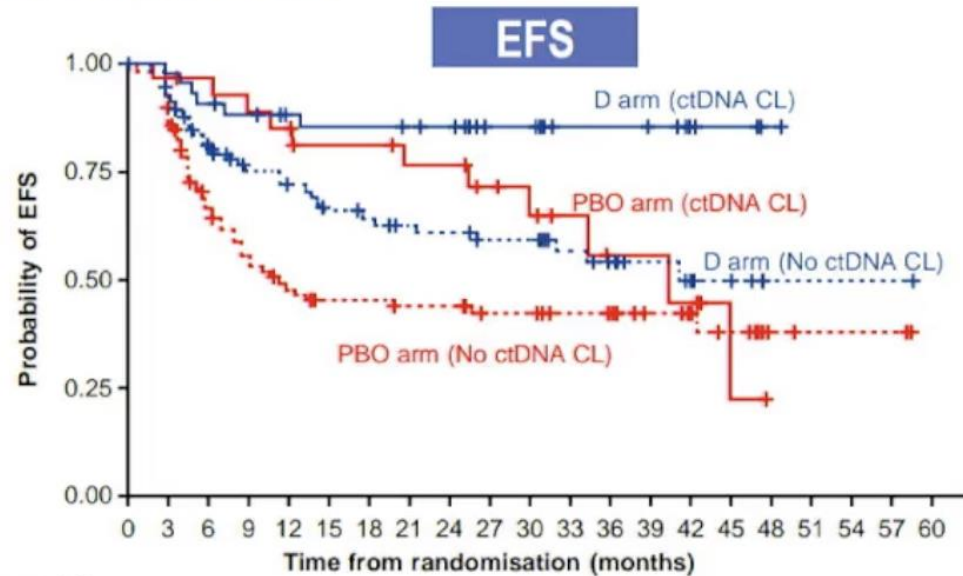


AEGEAN Study



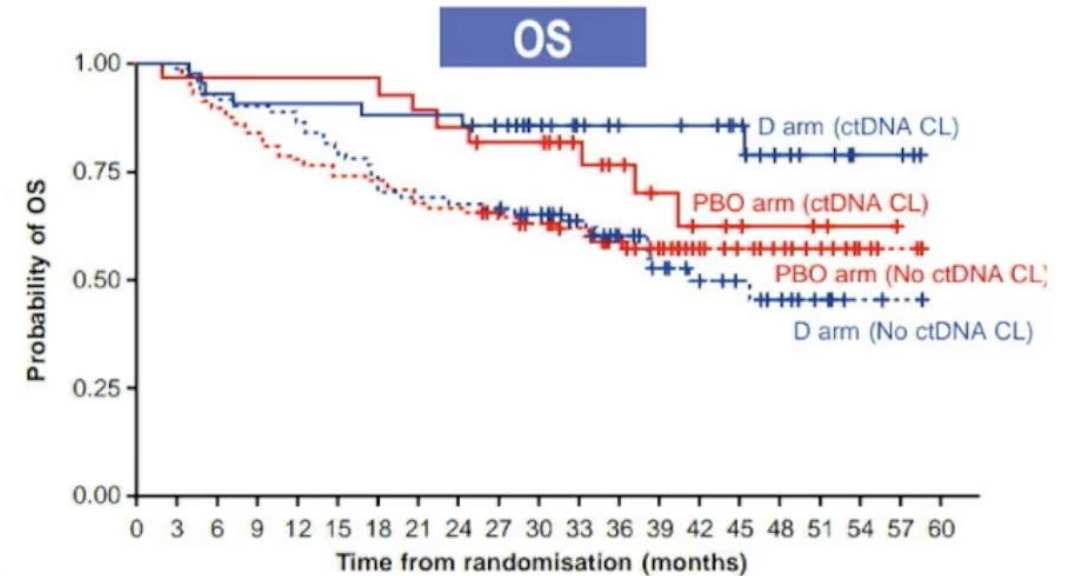
Associations of ctDNA Clearance at Neoadjuvant C2D1 with EFS and OS

- As early as neoadjuvant C2D1, patients in the D arm with ctDNA clearance had longer EFS and OS compared to patients without clearance, and versus the PBO arm*



No. at risk

D arm (ctDNA CL)	41	40	37	35	32	31	31	30	29	21	21	14	14	13	9	7	1	0	0	0	0
PBO arm (ctDNA CL)	27	26	25	23	22	19	19	17	17	12	11	7	5	5	4	1	0	0	0	0	0
D arm (No ctDNA CL)	80	73	61	51	47	42	40	37	36	33	33	22	19	13	10	8	1	1	1	1	0
PBO arm (No ctDNA CL)	92	85	57	45	39	34	34	32	31	25	25	21	20	13	11	8	3	2	2	2	0



No. at risk

D arm (ctDNA CL)	41	41	38	37	37	37	36	36	36	32	26	22	19	18	17	14	8	6	3	3	0
PBO arm (ctDNA CL)	27	26	26	26	26	26	24	23	21	21	16	13	9	7	6	4	2	1	0	0	0
D arm (No ctDNA CL)	80	79	73	72	69	63	58	55	54	52	47	38	29	20	14	12	9	5	2	1	0
PBO arm (No ctDNA CL)	92	92	82	77	71	68	67	63	60	58	50	46	36	29	21	18	14	11	4	2	0

	D arm	PBO arm
EFS HR for ctDNA CL vs No ctDNA CL	0.30 (95% CI: 0.12–0.71)	0.53 (95% CI: 0.27–1.02)
EFS HR for the D vs PBO arm (ctDNA CL)	0.31 (95% CI: 0.11–0.85)	–
EFS HR for the D vs PBO arm (No ctDNA CL)	0.62 (95% CI: 0.40–0.97)	–

	D arm	PBO arm
OS HR for ctDNA CL vs No ctDNA CL	0.32 (95% CI: 0.14–0.72)	0.61 (95% CI: 0.28–1.31)
OS HR for the D vs PBO arm (ctDNA CL)	0.55 (95% CI: 0.20–1.52)	–
OS HR for the D vs PBO arm (No ctDNA CL)	1.07 (95% CI: 0.68–1.69)	–

TRACERX Study

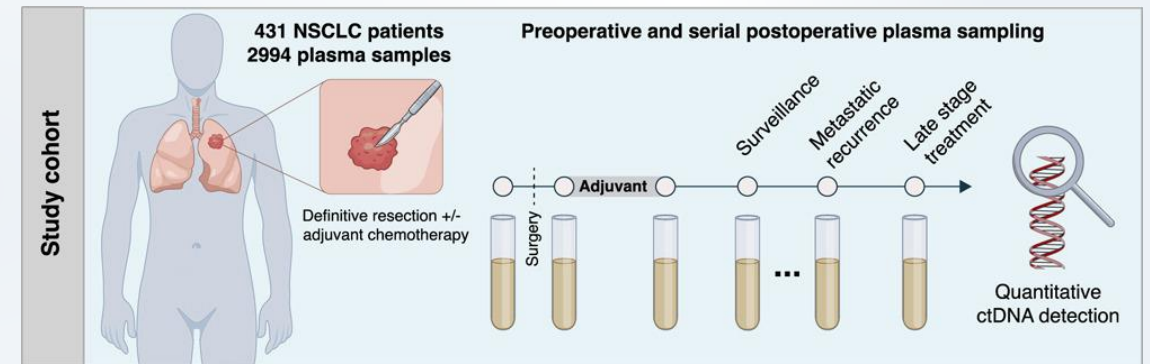
The **TRACERx** (TRAcking Cancer Evolution through therapy) study was a large, comprehensive, longitudinal effort to understand how NSCLC evolves over time.

Some main findings include:

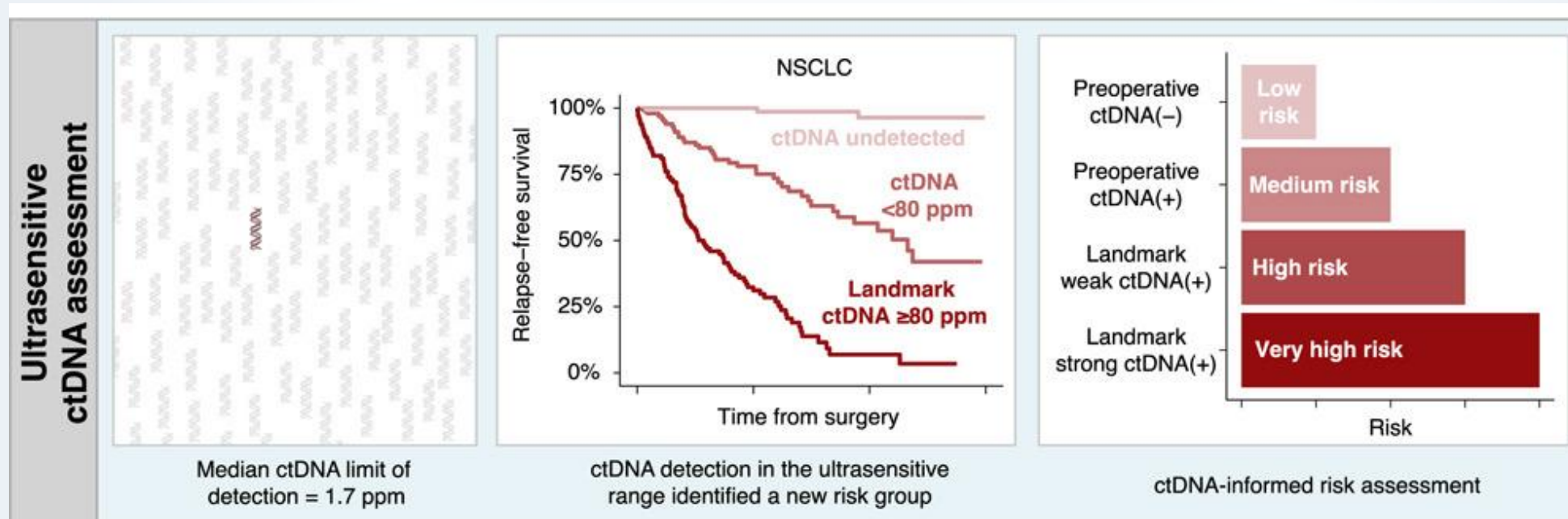
- Intratumor heterogeneity mediated through chromosome instability was associated with an increased risk of recurrence or death, a finding that supports the potential value of chromosome instability as a prognostic predictor
- Detailed description of tumor evolution during metastatic seeding and progression
- Describing the Utility of Ultra-Sensitive MRD Detection after surgical resection

TRACERX Study

- It was a whole-genome, tumor-informed circulating tumor DNA (ctDNA) detection approach to address this challenge, leveraging 1,800 variants across 2,994 plasma samples from 431 patients with non-small cell lung cancer (NSCLC) from the TRACERx study
- This comprised 250 males and 181 females, recruited between 2014 and 2021, with a median age of 69 years (range 34–92 years). 54.3% ($n = 234$) and 45.7% ($n = 197$) of the patients were diagnosed with tumors of LUAD or non-LUAD histology.
- Adjuvant platinum-based chemotherapy was given as standard of care for 55.1% of patients ($n = 162$) with stage II/III disease, as well as a subset of those with stage IB disease ($n = 6$); no neoadjuvant treatment was administered.
- Defined landmark point as any time point occurring between days 10 and 120 postoperatively, prior to the start of adjuvant therapy or disease recurrence



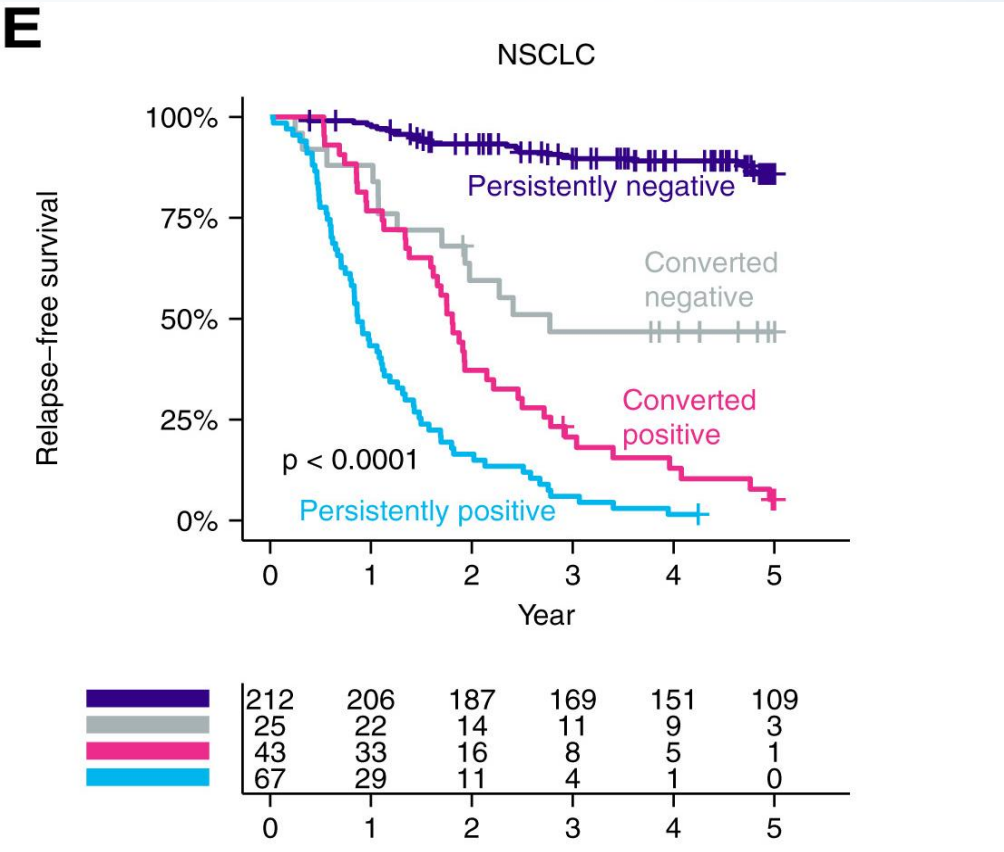
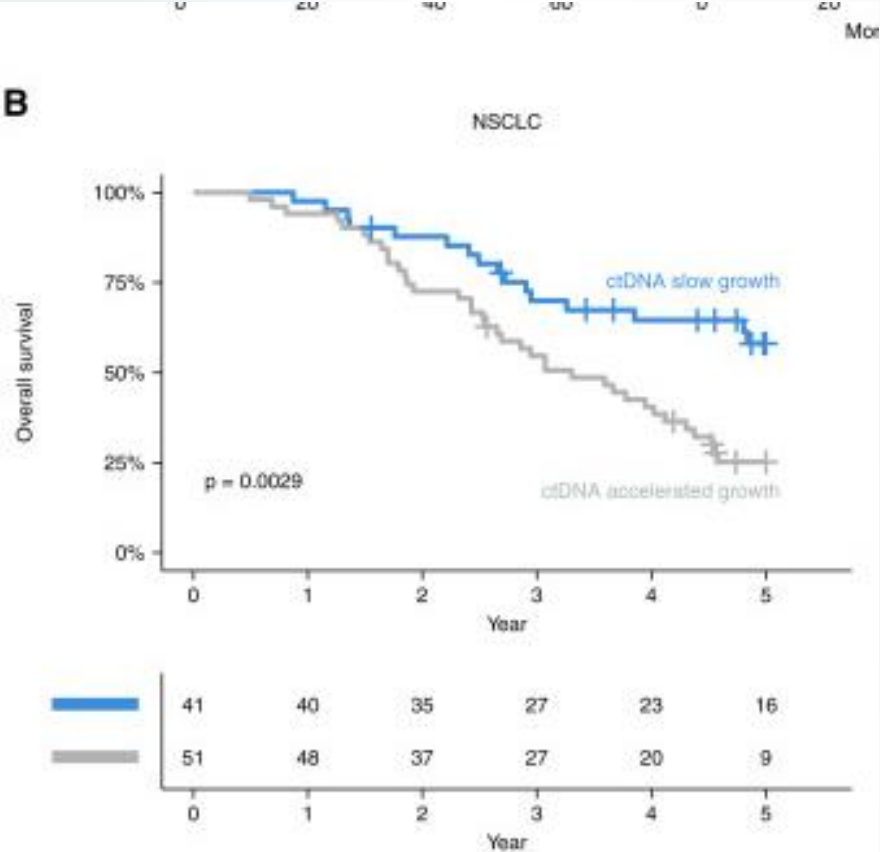
Landmark ctDNA highly prognostic of relapse



Landmark ctDNA negative: Do they even need adjuvant treatment?

High Landmark ctDNA: Stepping up of adjuvant therapy?

ctDNA kinetics is also informative



Early vs Late detection using MRD: Would you rather?

Identify recurrence ASAP?



Wait until it is obvious?

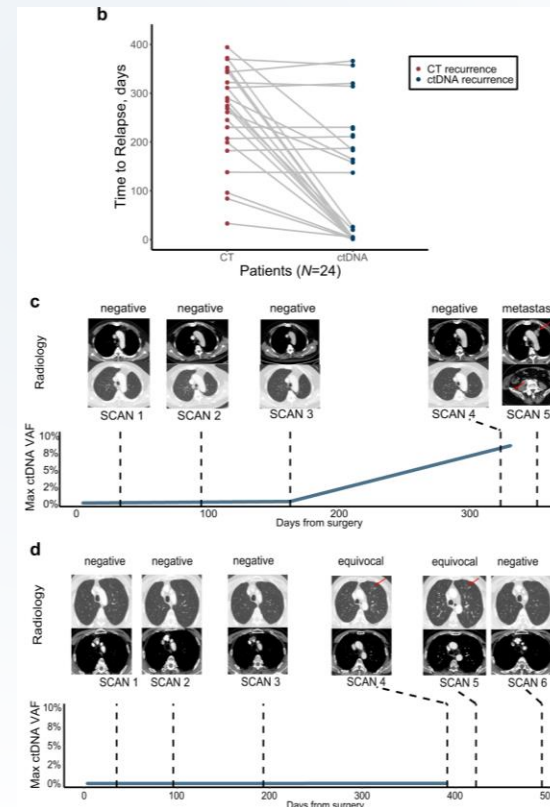


ctDNA predicts recurrence earlier than relapse

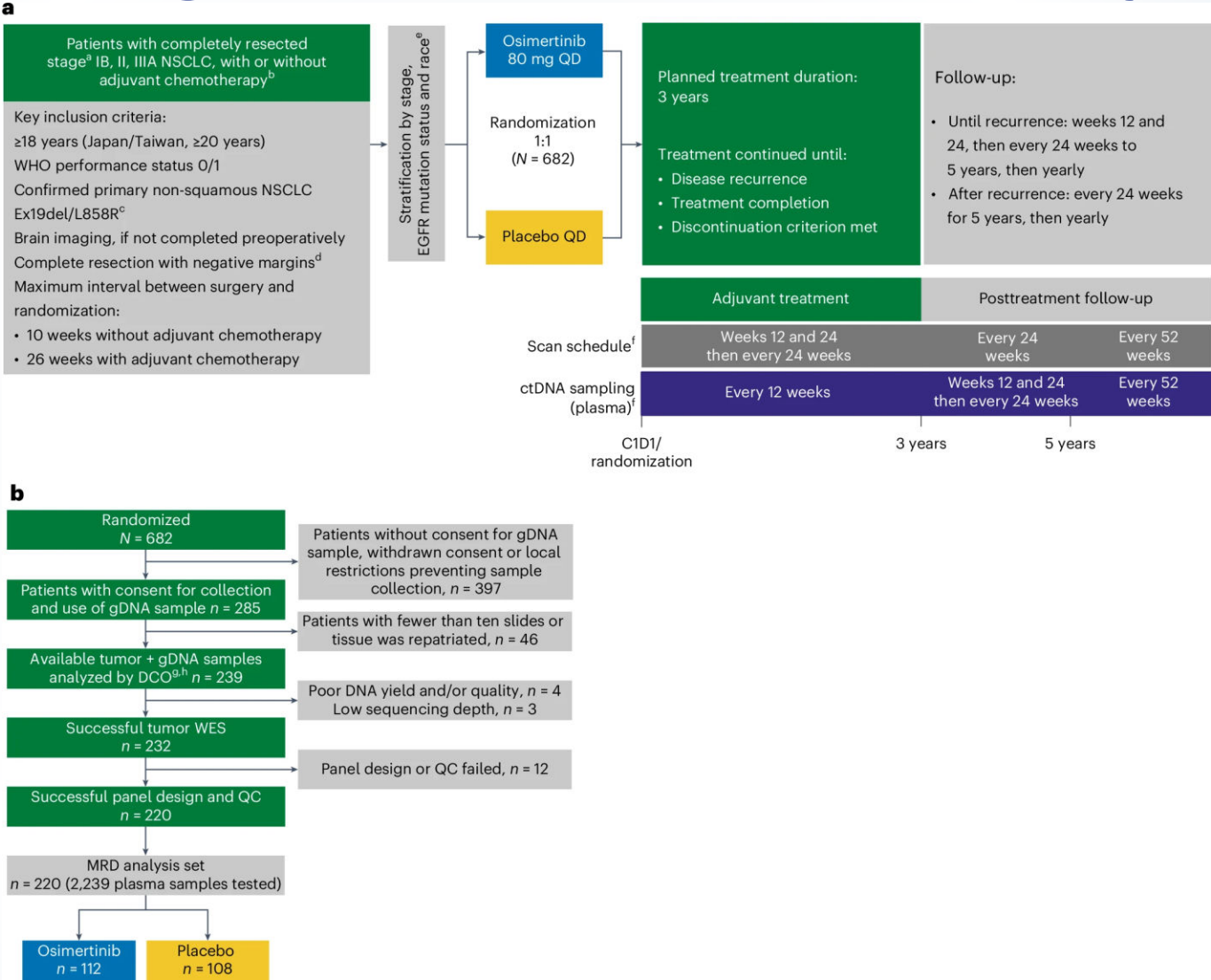
Under longitudinal surveillance, disease relapse was predicted with a sensitivity of 86%, and a PPV of 90%, while maintaining high specificity (91%) and NPV (88%)

The lead time between ctDNA detection and relapse ranged from 0 to 1,732 days (median 158 days).

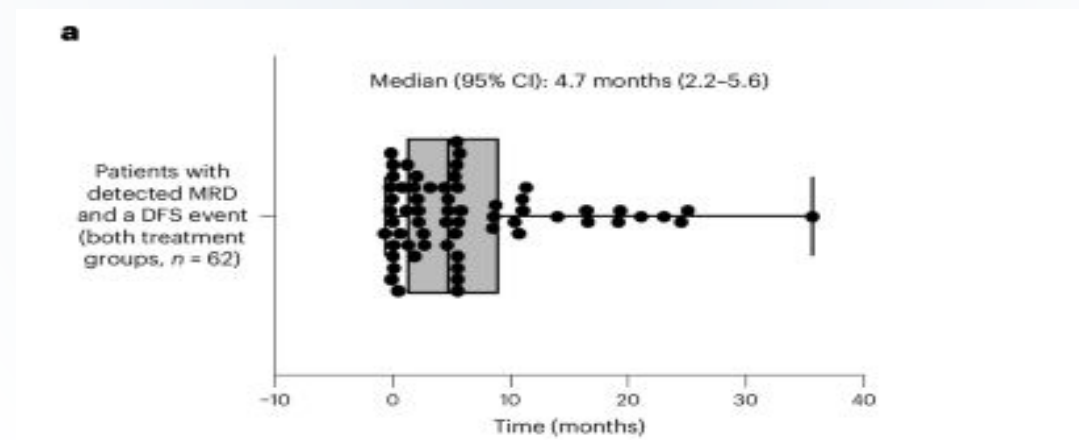
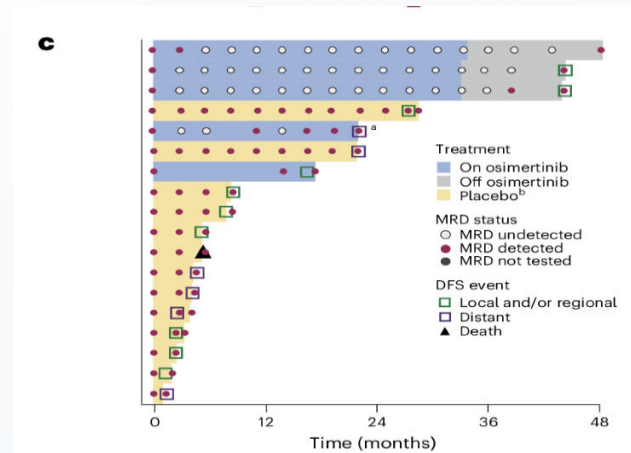
Qiu et al study



MRD for adjuvant targetable NSCLC: ADAURA study



MRD for adjuvant targetable NSCLC: ADAURA study



Conclusions to the benefits and potential of MRD in NSCLC

- ctDNA before, and after resection in landmark analysis is a highly prognostic indicator
- This can perhaps influence treatment decisions if on the fence (i.e., adding adjuvant immunotherapy to a patient that got neoadjuvant chemotherapy and IO)
- Can also, perhaps with more data, de-escalate adjuvant therapy as well
- Potentially can guide radiographic imaging
- Assess for resistance mutations, etc for driver mutated NSCLC
- Utilize ctDNA kinetics in adjuvant space

