New Platforms and Developments of Immunotherapy Biomarkers Beyond PD-L1 in Tissue

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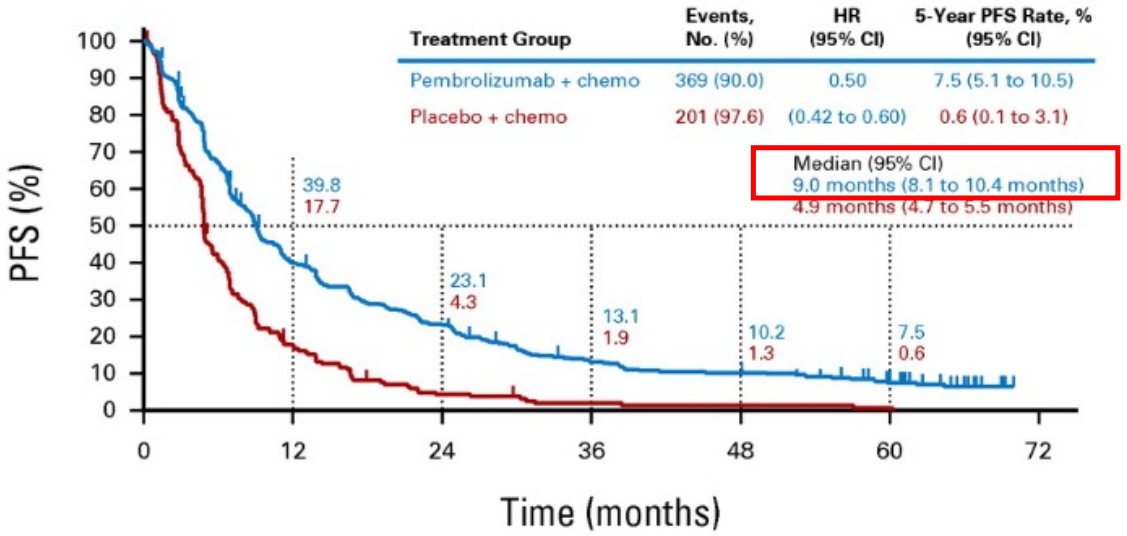
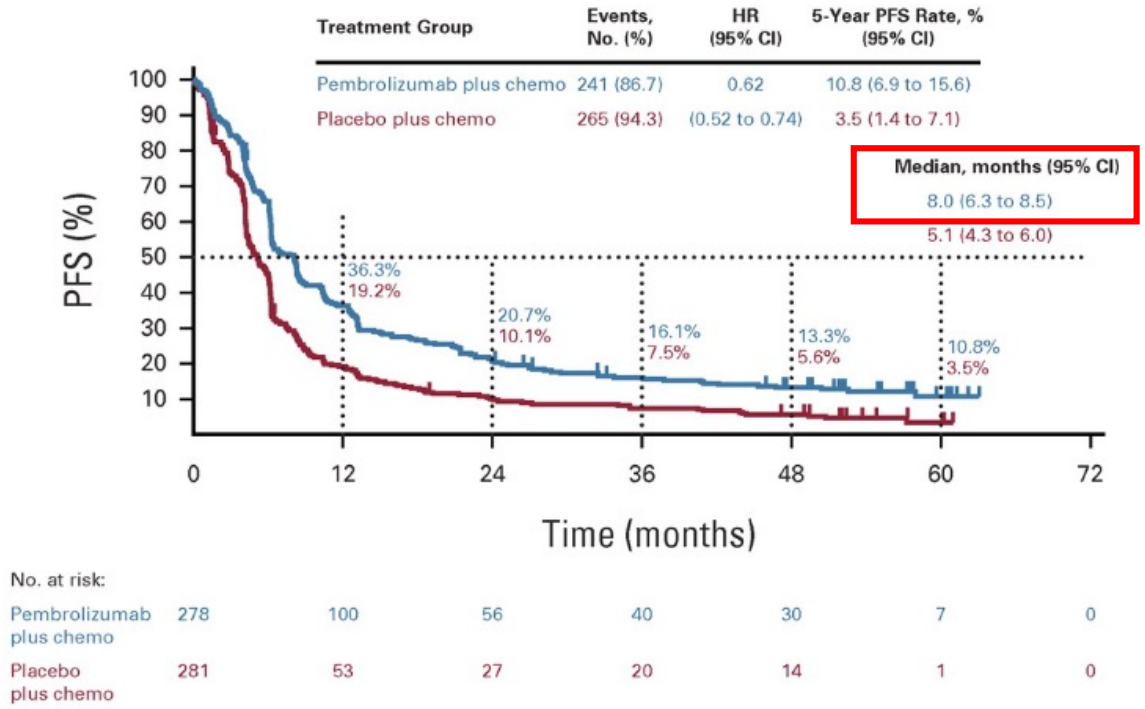
Approximately 50% of patients with advanced non-small cell lung cancer will develop disease progression within 8 to 9 months

KEYNOTE-189



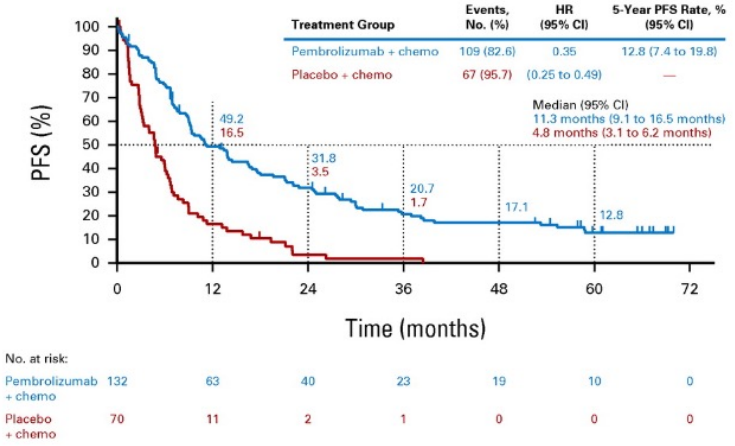
KEYNOTE-407



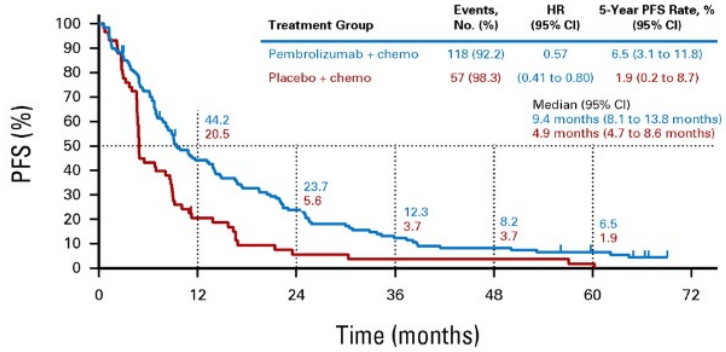
Garassino M. *J Clin Oncol*. 2023
Novello S. *J Clin Oncol*. 2023

How do we risk stratify these patients?

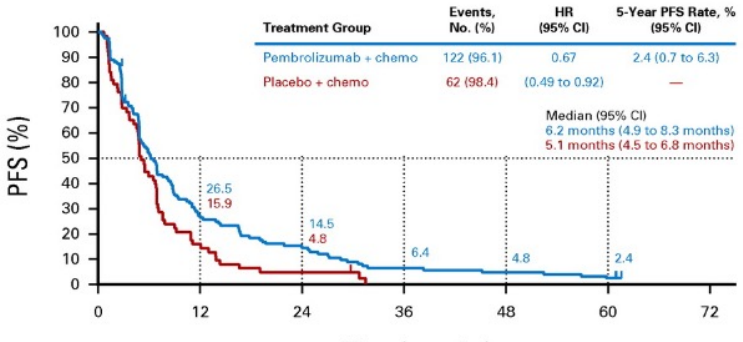
KEYNOTE-189



PD-L1 ≥ 50%
KN-189 mPFS= 11.3
KN-407 mPFS= 8.3

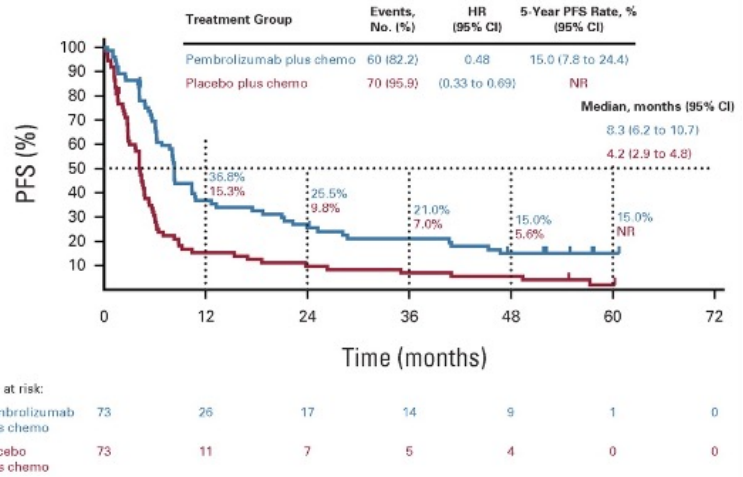


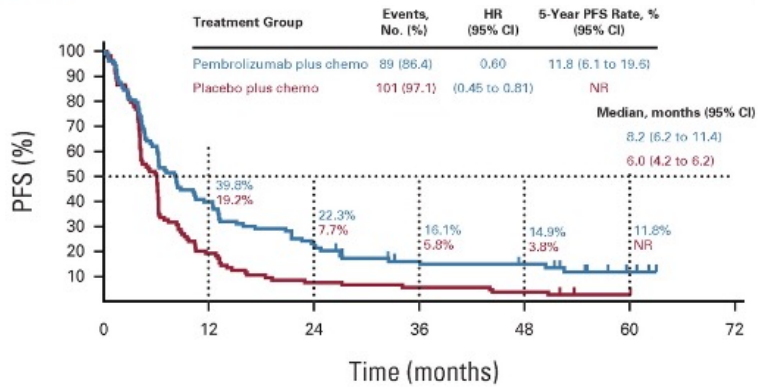
PD-L1 1-49%
KN-189 mPFS= 9.4
KN-407 mPFS= 8.2

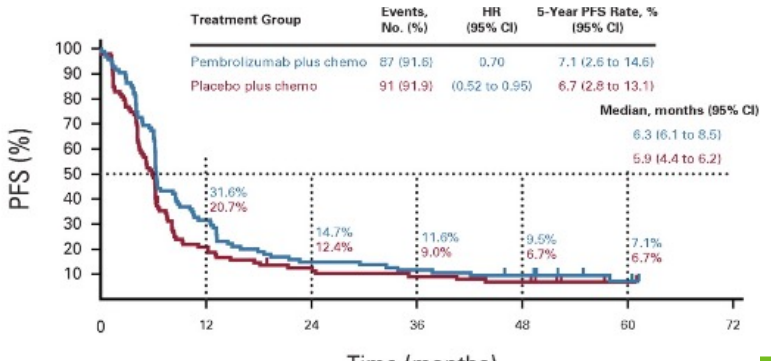


PD-L1< 1%
KN-189 mPFS= 6.2
KN-407 mPFS= 6.3

KEYNOTE-407



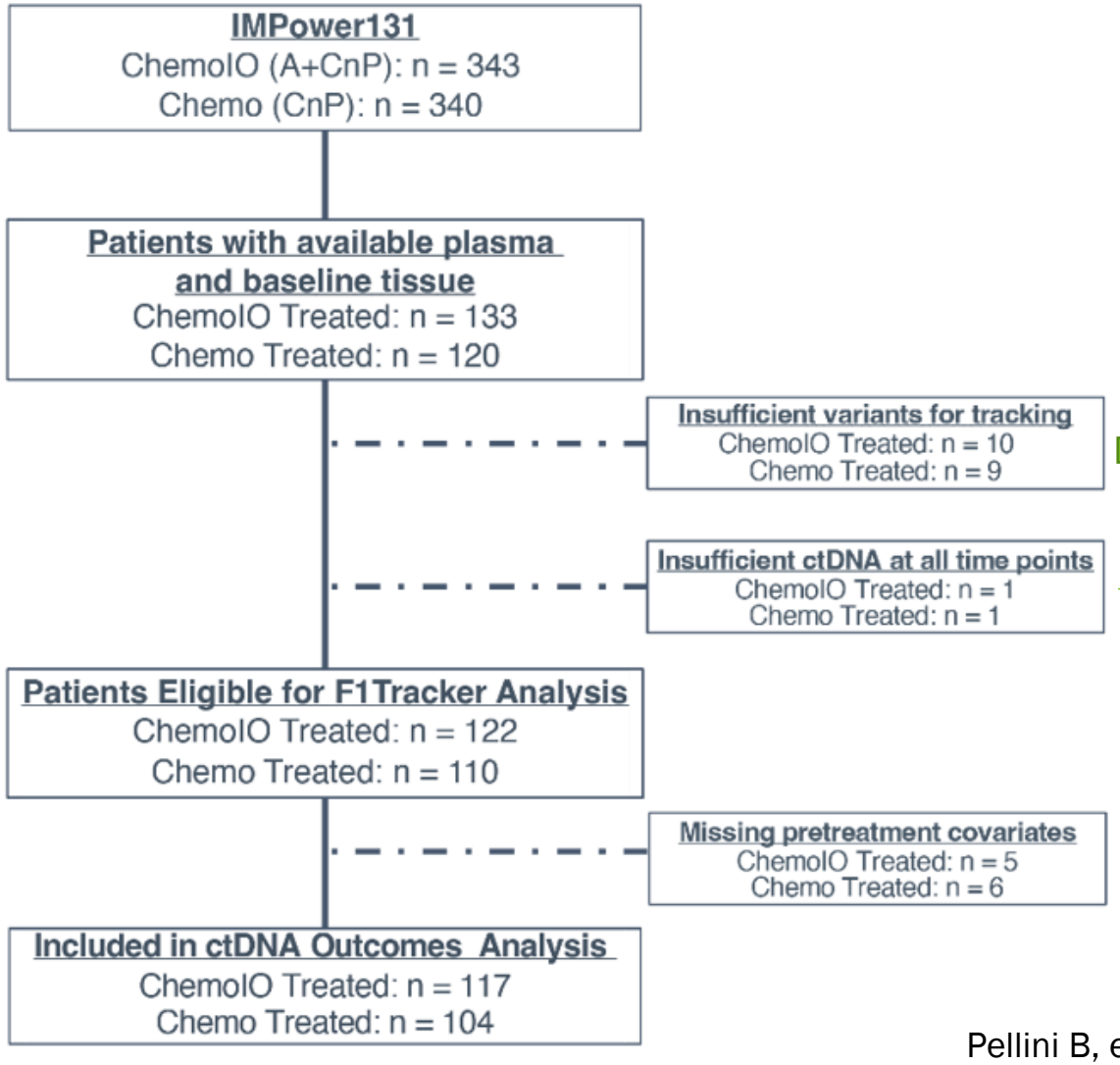




Garassino M. *J Clin Oncol*. 2023
Novello S. *J Clin Oncol*. 2023

Can ctDNA monitoring risk stratify advanced SCC prior to the start of maintenance atezolizumab in patients receiving carboplatin + nab-paclitaxel + atezolizumab (IMpower 131)?

Tumor-informed assay (FoundationOne Tracker)



Only 8% did not have enough variants for the development of their unique multiplex PCR

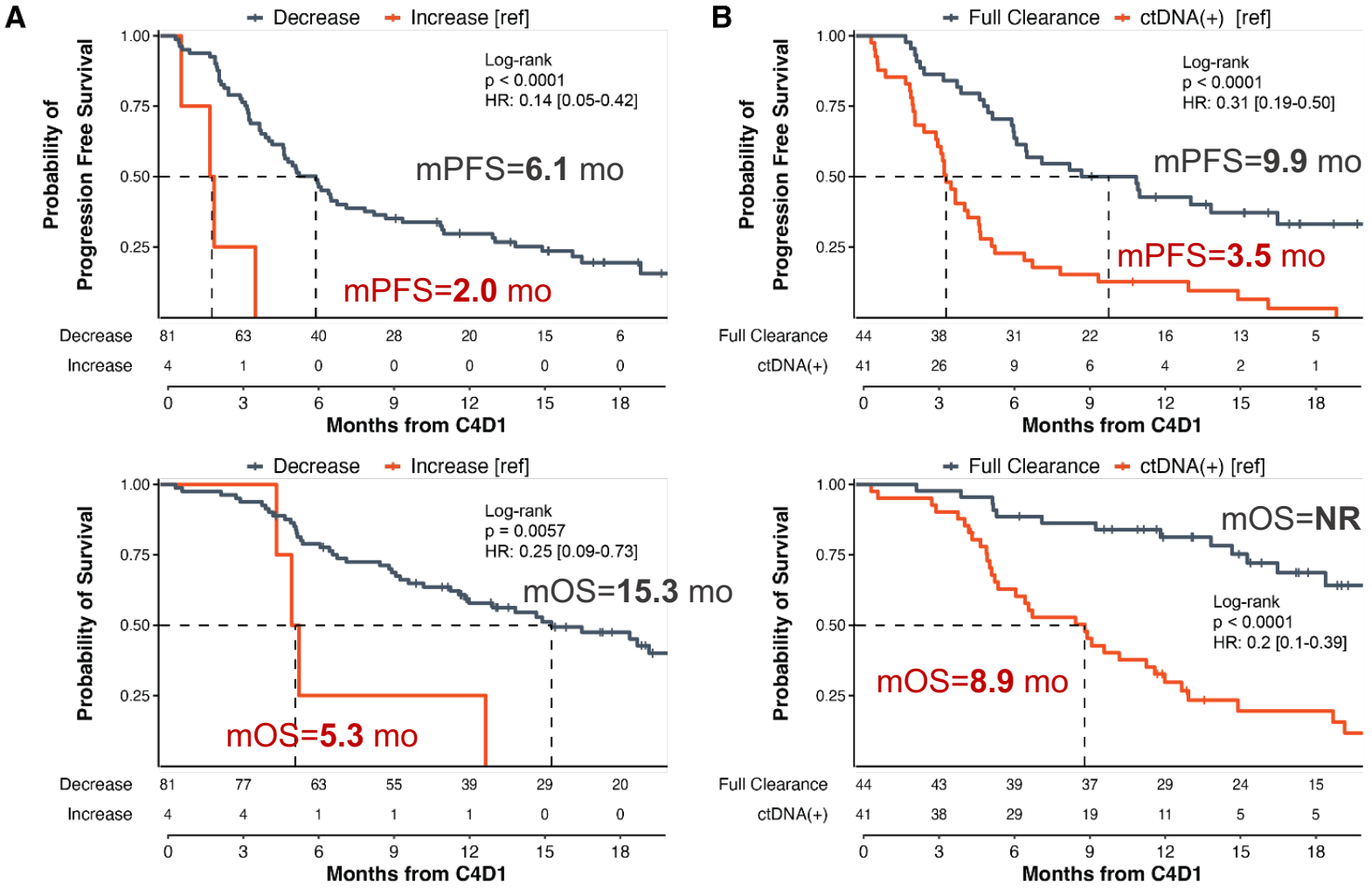
Only 1% did not have enough ctDNA for the analysis

Pellini B, et al. *Clin Cancer Res*.2023

ctDNA Monitoring on Atezolizumab + Carboplatin + Nab-Paclitaxel (A +CnP) identifies patients with SCC with higher risk for poorer outcomes

Analysis limited to the 85 patients with detectable ctDNA pre-treatment

Decrease is defined as *any* decrease



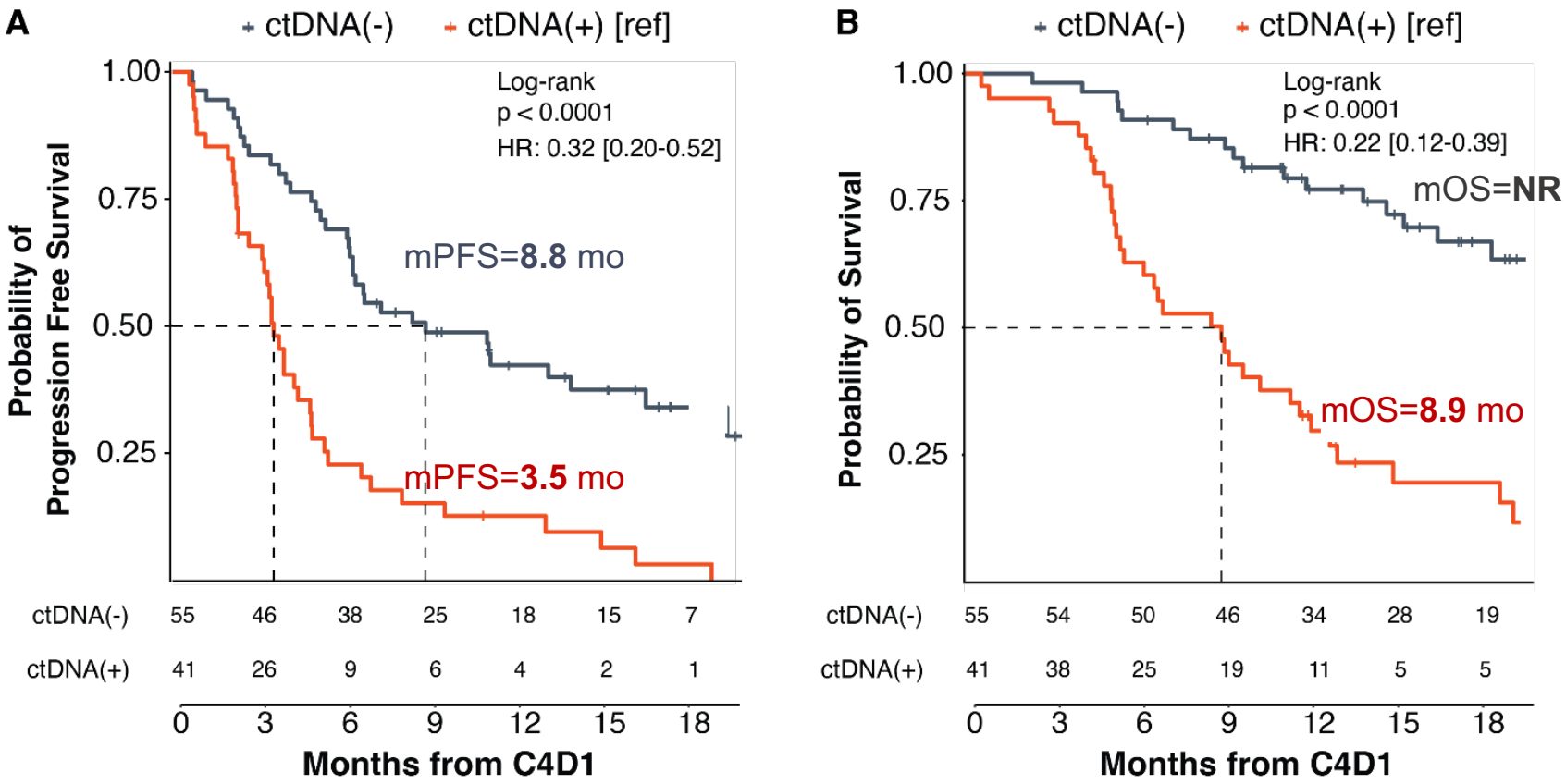
PFS and OS are landmarked from C4D1 (i.e., 9 weeks into induction therapy)

Pellini B, et al. *Clin Cancer Res*.2023

ctDNA detection at C4D1 on Atezolizumab + Carboplatin + Nab-Paclitaxel (A +CnP) can risk stratify patients with SCC before maintenance therapy start

PFS and OS are landmarked from C4D1 (i.e., 9 weeks into induction therapy)

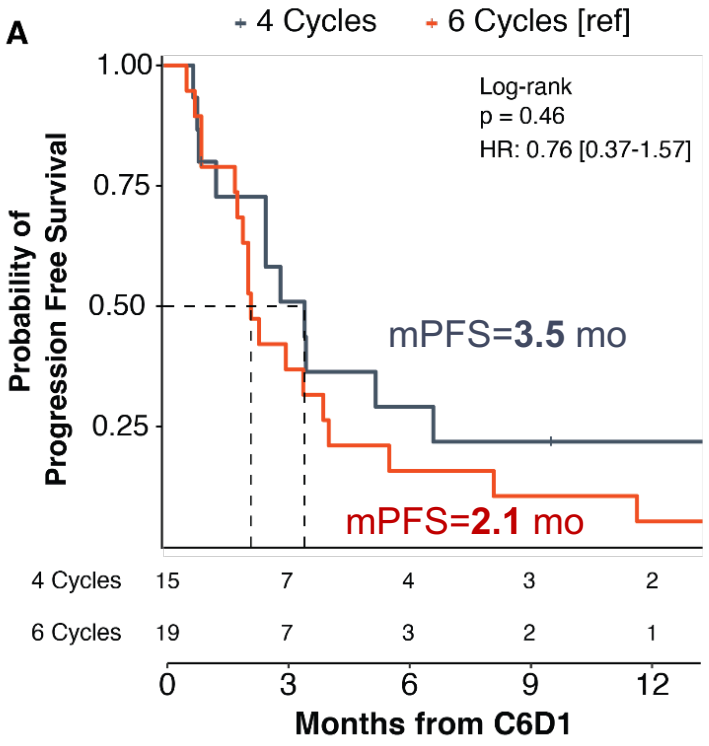
ctDNA + at C4D1

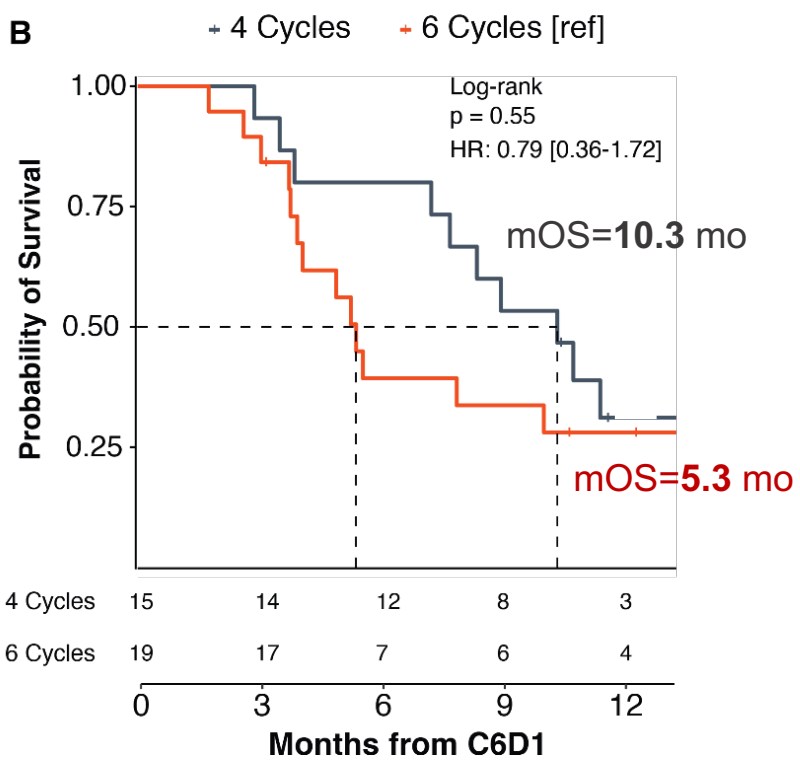


Analysis in 96 patients with available samples at C4D1 regardless of baseline sample availability

Pellini B, et al. *Clin Cancer Res*.2023

Additional cycles of induction Atezolizumab + Carboplatin + Nab-Paclitaxel (A +CnP) are not associated with improved outcomes in patients with ctDNA + at C4D1

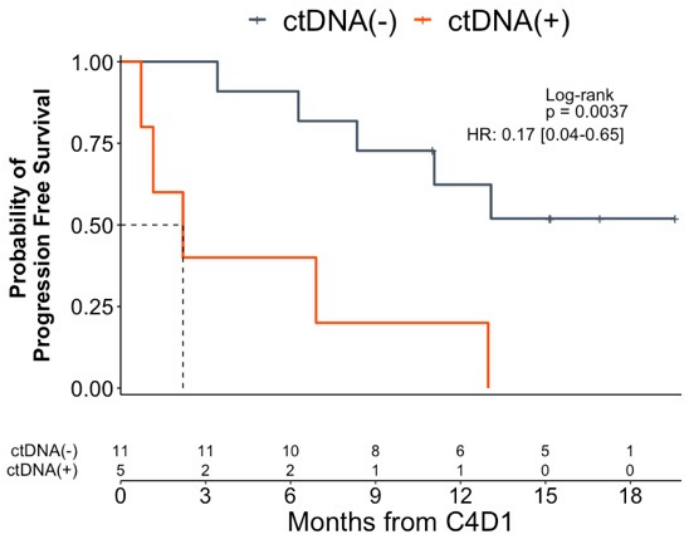




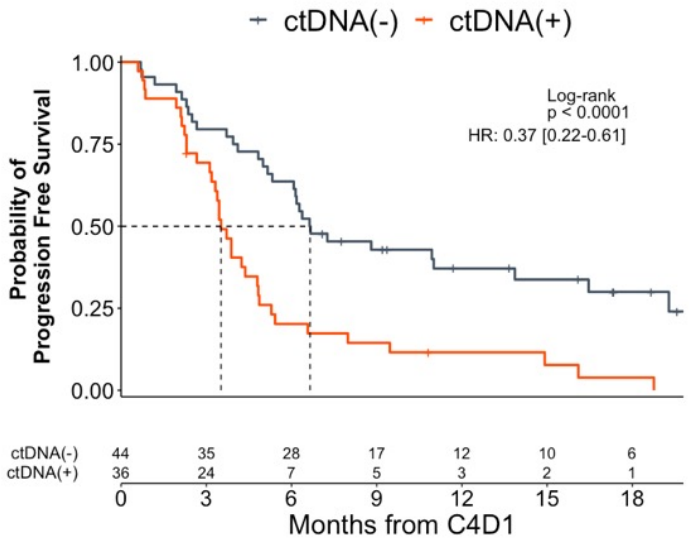
Pellini B, et al. *Clin Cancer Res*.2023

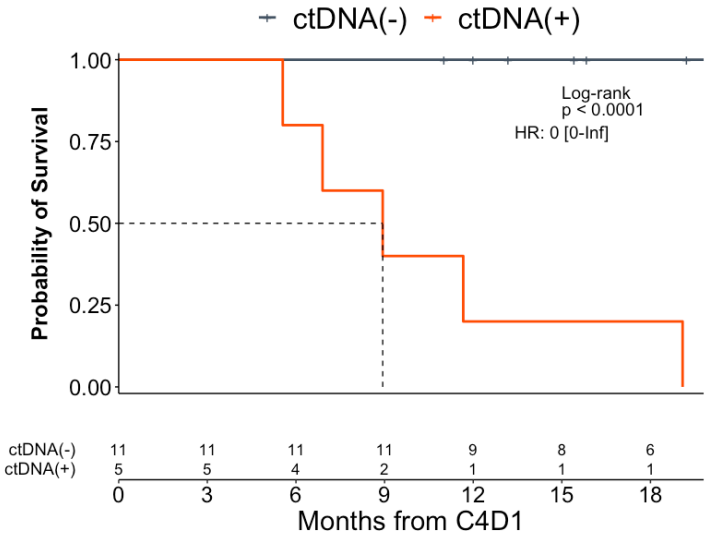
Full clearance of ctDNA at C4D1 on chemoIO identifies patients with poorer outcomes on IO maintenance, independent of PD-L1 status

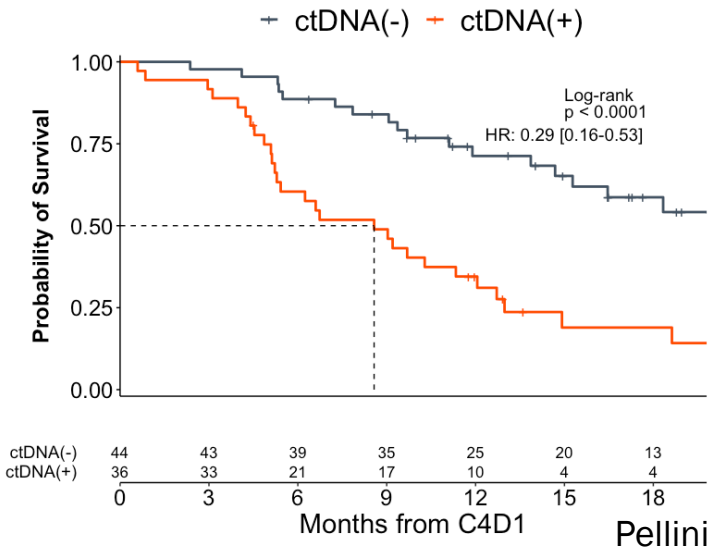
PD-L1 High



PD-L1 Low

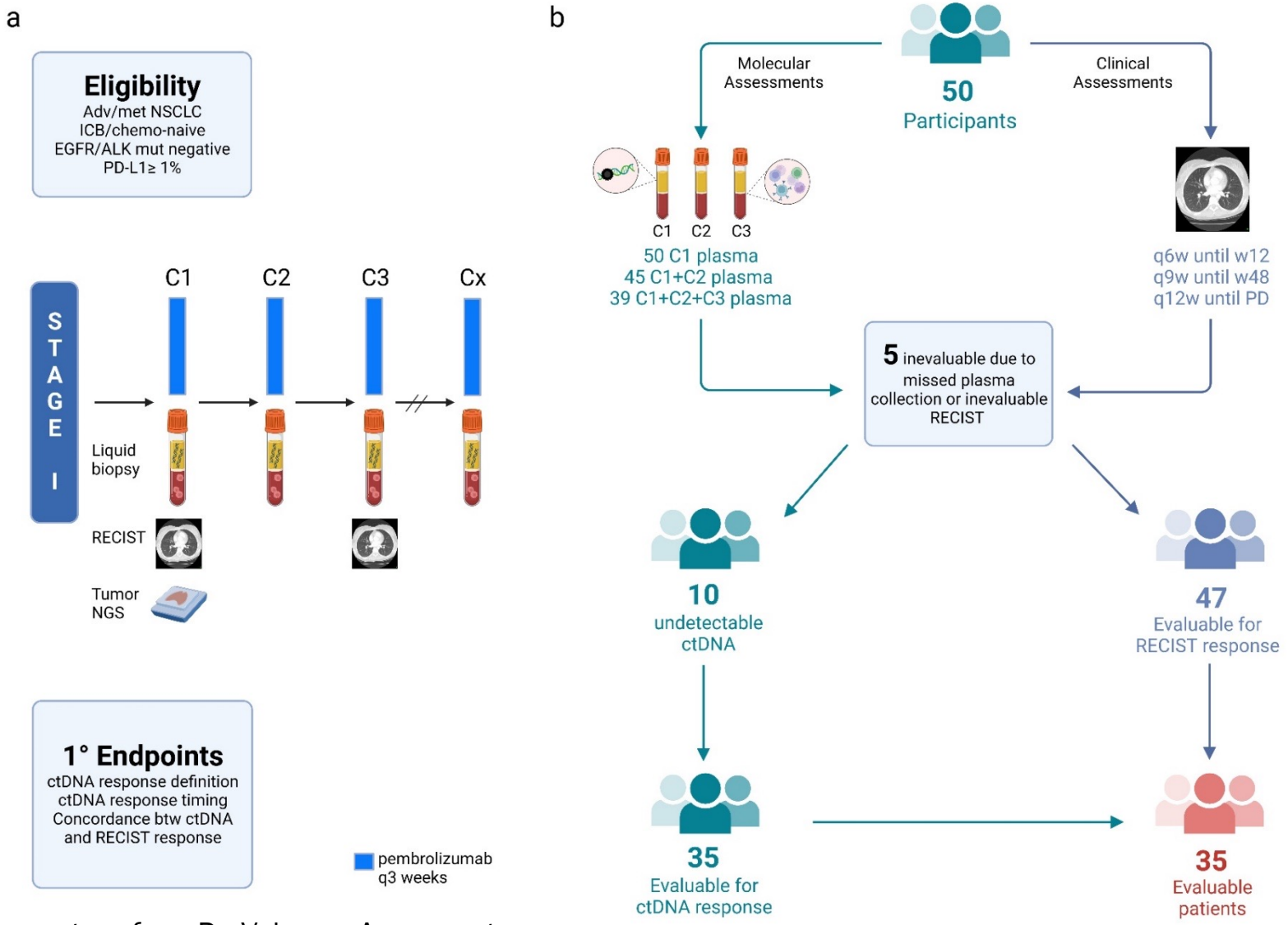






Pellini B, et al. *Clin Cancer Res*.2023

BR.36: A ctDNA-directed phase II study of molecular response adaptive immunotherapy in NSCLC



Tumor-uninformed assay (PGDx elio™ plasma resolve)

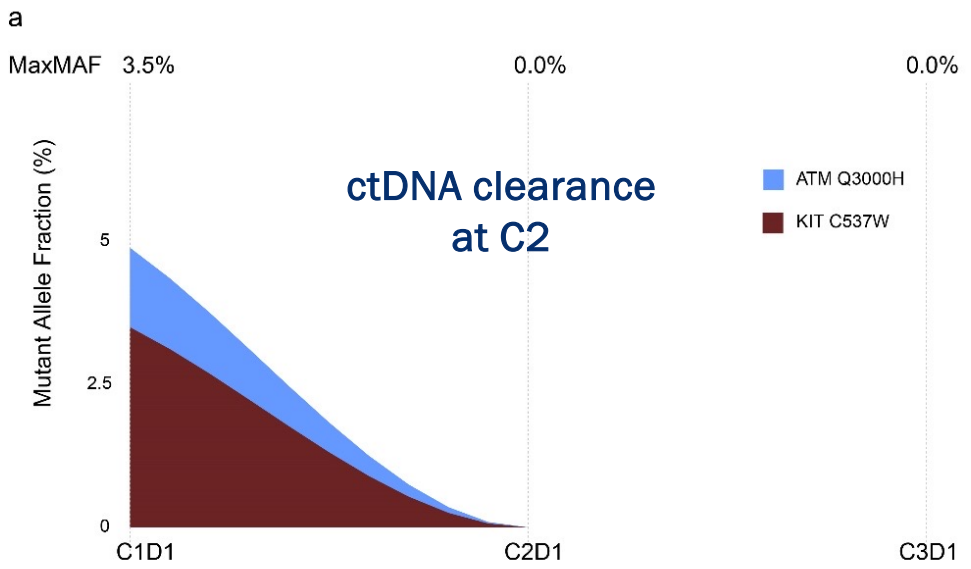
- NGS with 33-gene panel
- WBC-informed
- TAT 1 week

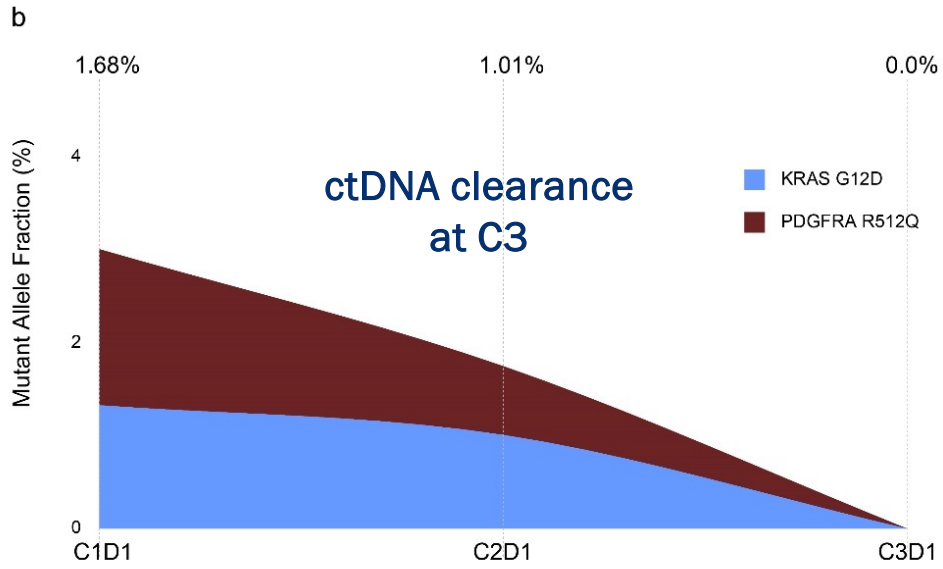
20% not evaluable for molecular response due to ctDNA (-) at baseline

Slide courtesy from Dr. Valsamo Anagnoustou

NCT04093167, Anagnostou et al., *Nat Med*, 2023

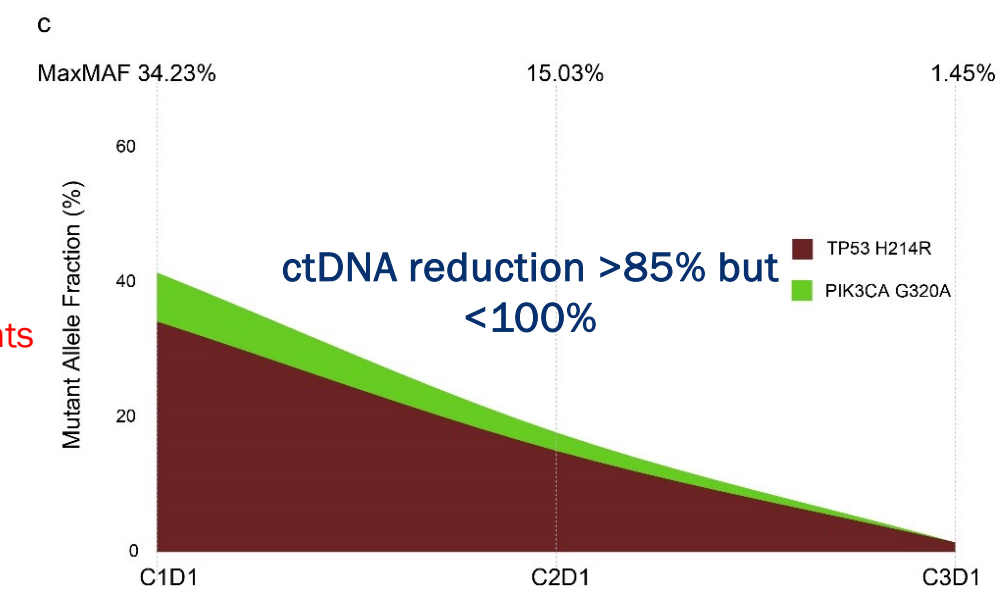
Patterns of ctDNA kinetics

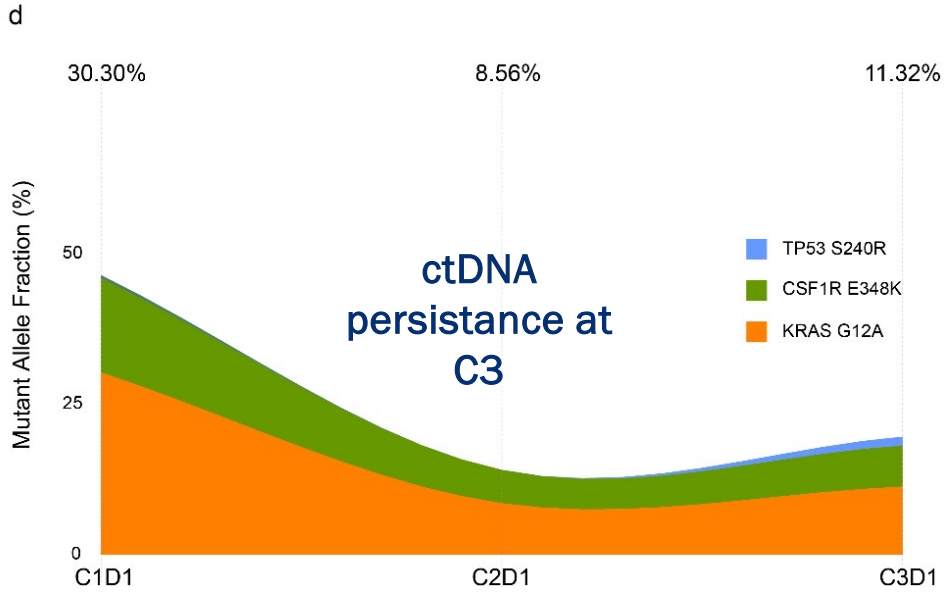




Only 2 patients

Only 2 patients





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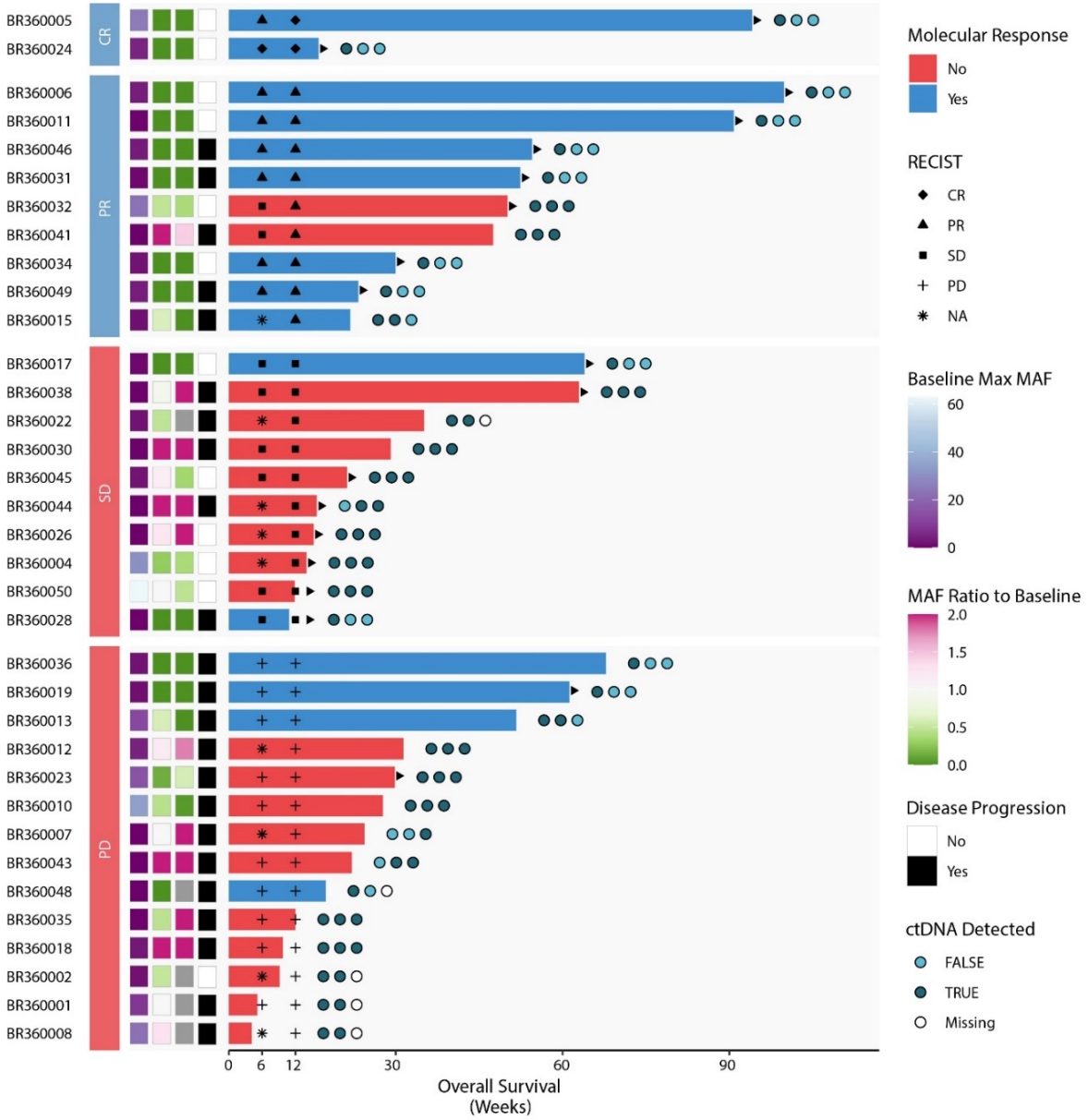
ctDNA-RECIST response concordance



BR.36 stage 1 met its primary endpoint.

The sensitivity of molecular response for RECIST best overall response was 82%, (90% CI: 52% - 97%), specificity was 75% (90% CI: 56.5% - 88.5%).

RECIST response (BOR)	Molecular response	
	mR	mPD
CR/PR	9 (82%)	2 (18%)
No RECIST response	6 (25%)	18 (75%)
iRECIST response		
iCR/iPR	10 (83%)	2 (17%)
No iRECIST response	5 (22%)	18 (78%)

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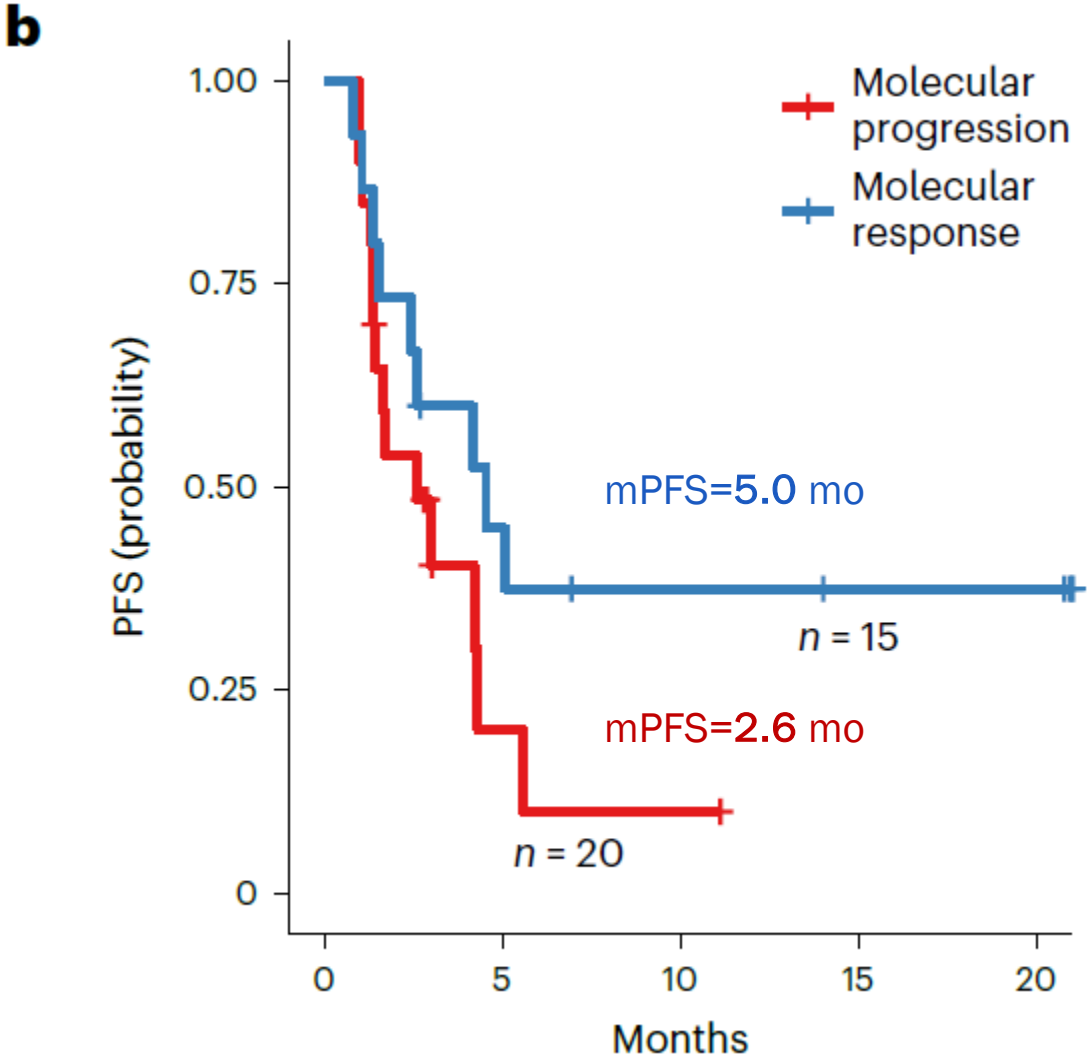
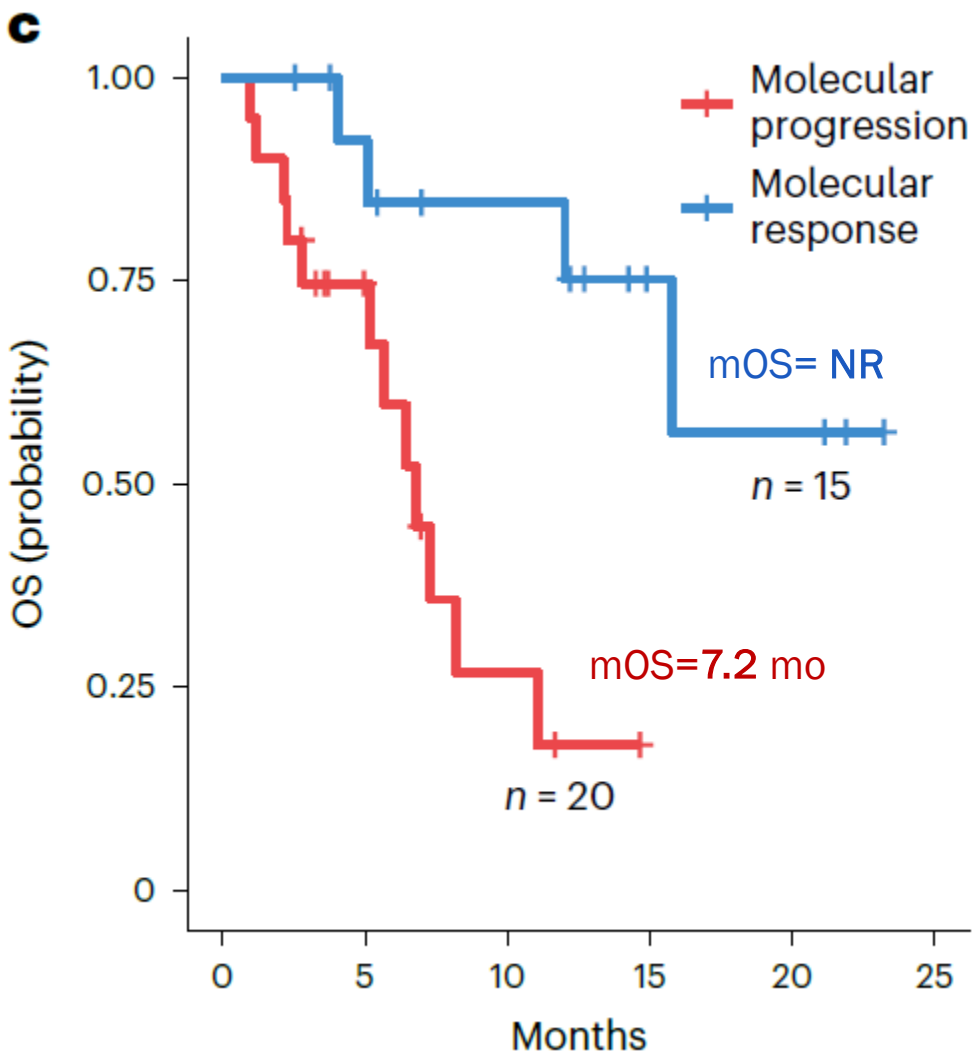
NCT04093167, Anagnostou et al., *Nat Med*, 2023

ctDNA molecular response risk stratifies patients with mNSCLC with PD-L1≥ 1%

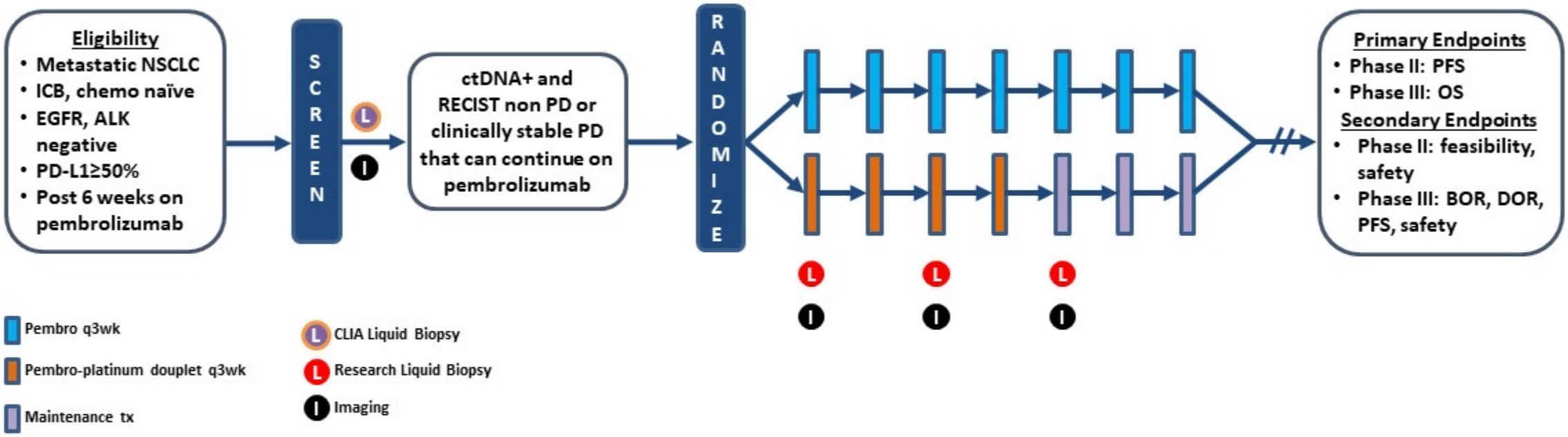




Median time to ctDNA response was 2.1 months

NCT04093167, Anagnostou et al., *Nat Med*, 2023

BR.36 stage 2-A Biomarker-Directed, Open Label, Multi-Center Phase II/III Study of Molecular Response Adaptive Immuno-Chemotherapy in Patients with NSCLC



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Conclusions

- CGP-informed ctDNA monitoring on chemoIO in advanced NSCLC can inform durability of treatment benefit
- ctDNA detection during induction chemoIO may offer an opportunity to identify patients at high-risk for disease progression and inform selection of novel personalized maintenance treatment strategies
- Tumor-uninformed (agnostic) ctDNA molecular response at 6-8 weeks into IO monotherapy in advanced PD-L1(+) NSCLC is can identify patients with improved clinical outcomes
- Treatment intensification with the addition of chemotherapy based on ctDNA MR for patients mNSCLC with PD-L1≥ 50% with is under investigation (NCT04093167)

Questions?

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