DANSKE KRÆFTFORSKNINGSDAGE 2025

ctDNA guidet immunterapi ved blærekræft (TOMBOLA)

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#DKD2025
#SamarbejdeOmKræft

Slido
#131525

Conflicts of interest

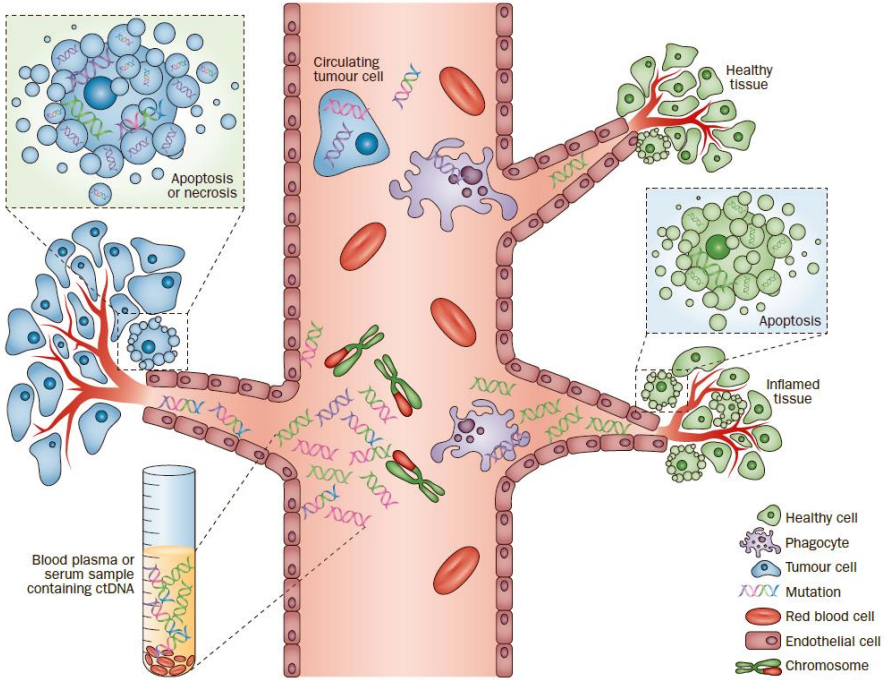
I have the following potential conflicts of interest to report:

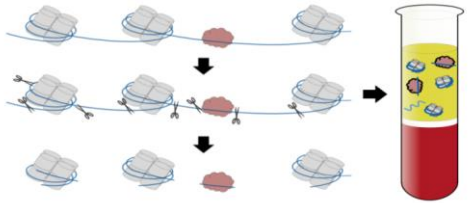
Grant/Research support from: Veracyte, C2i Genomics, Natera , AstraZeneca, Ferring, Photocure

Consultant for: Ferring, UroGen, CystoTech, MSD, AstraZeneca

Speaker honoraria from: Roche, Pfizer, MSD

ctDNA – tumor fragments in blood and urine





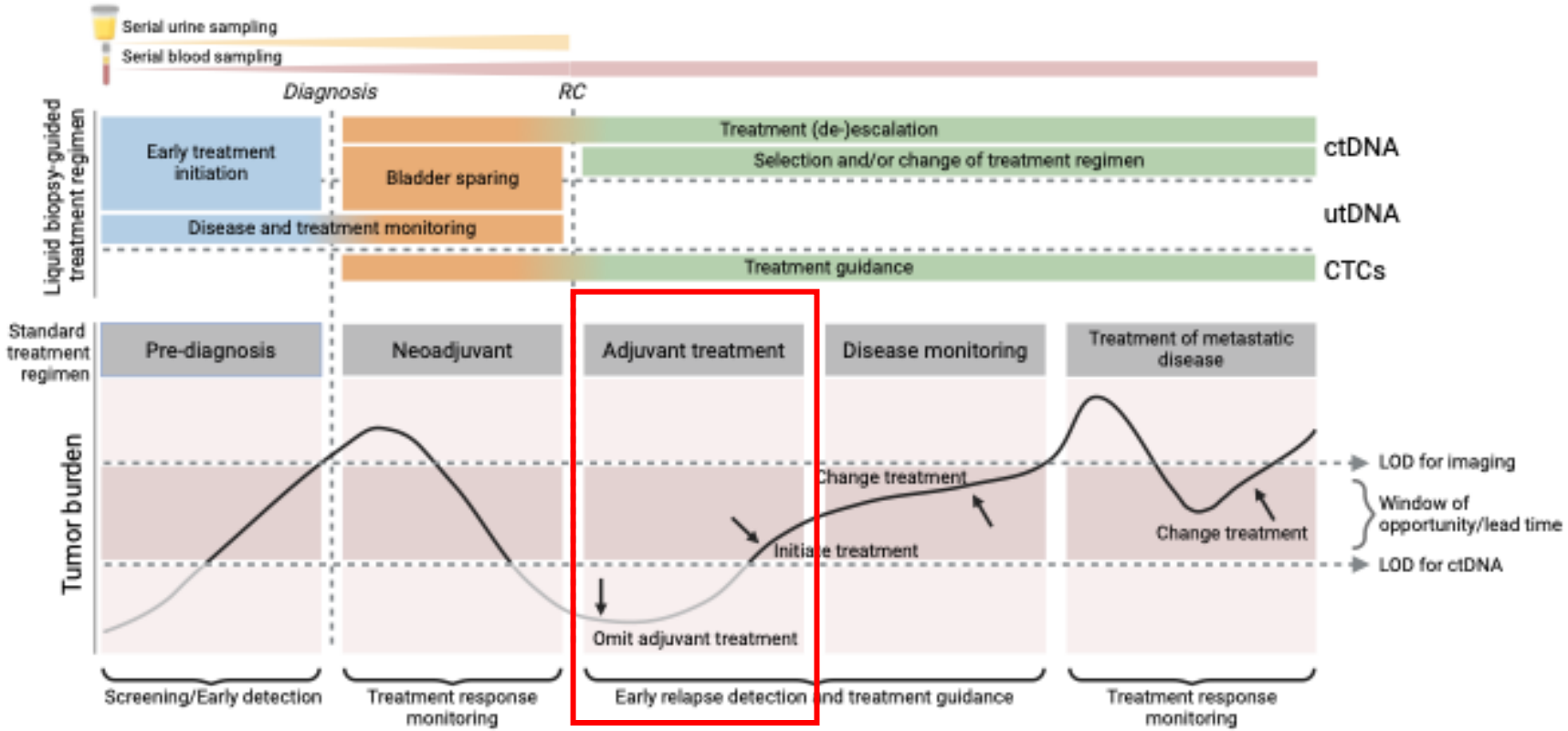
DNA fragments (<146bp)

Urine cfDNA
from renal clearence

cfDNA half-life <2 hours → enables real-time monitoring of tumor burden

Leary et al, Sci Transl Med, 2012
Crowley et al., Nature Reviews Clinical Oncology, 2013
Corcoran et al., New England Journal of Medicine, 2018

How ctDNA can guide treatment decisions in bladder cancer

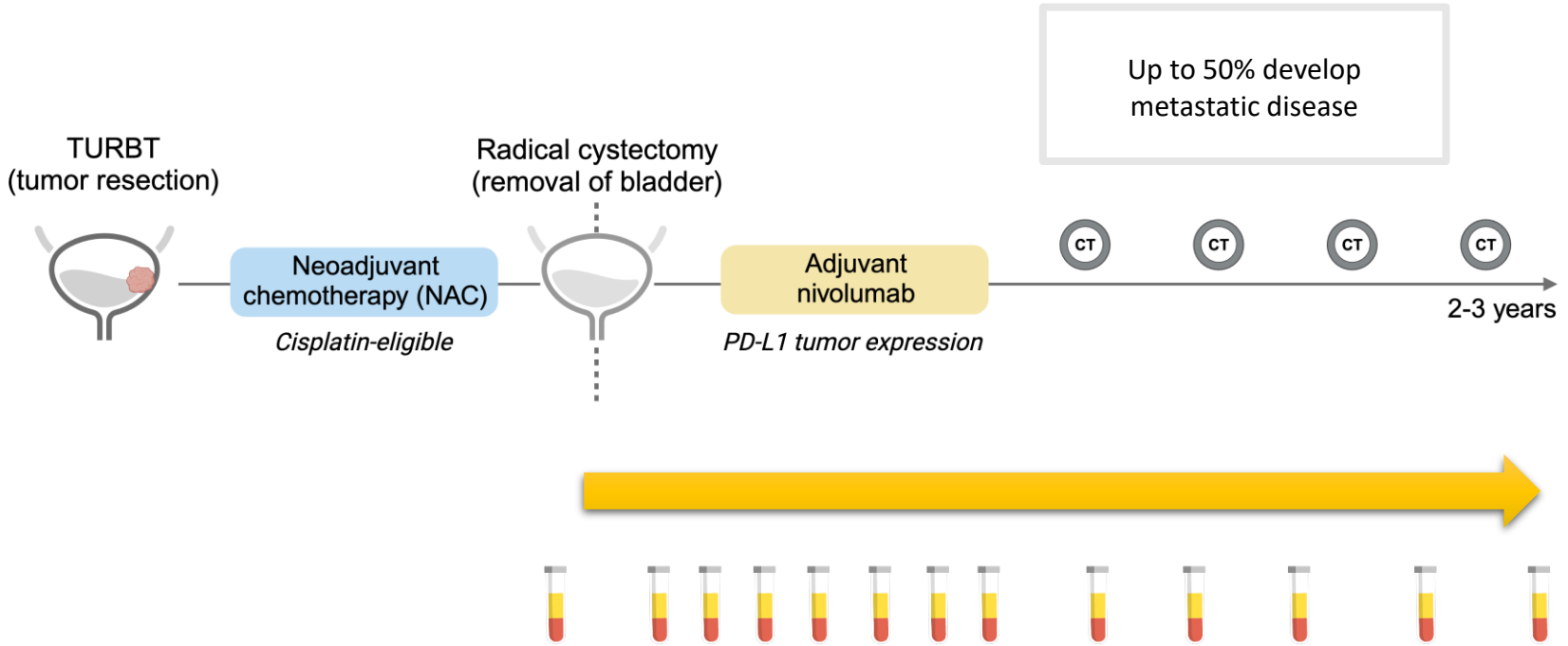


Treatment decisions for escalation and de-escalation

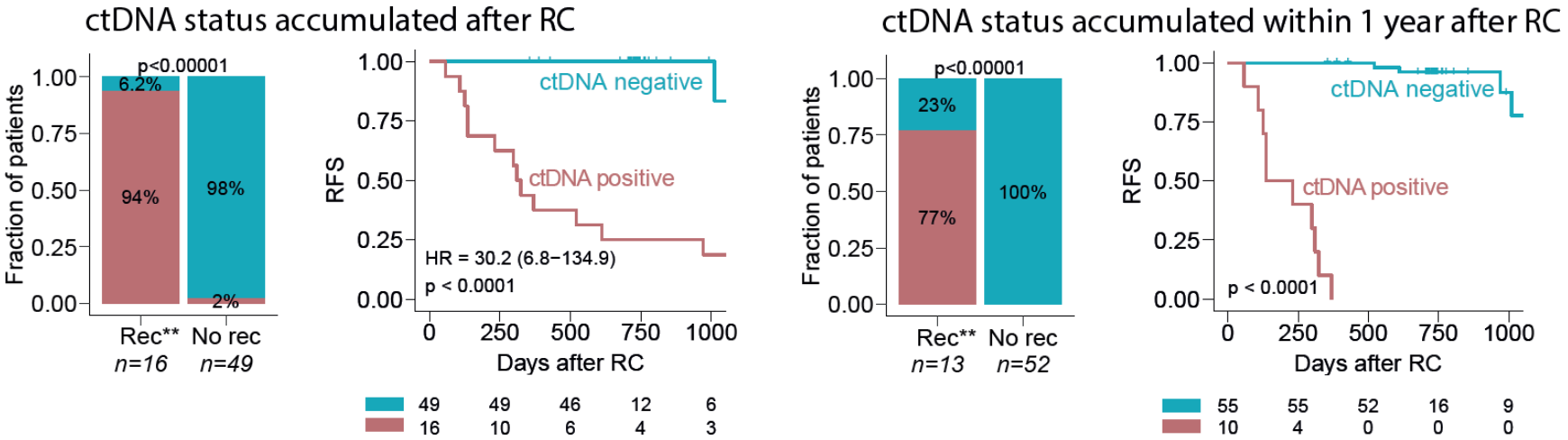
Sensitive and specific assays are required

Lindskrog et al., Nature Reviews Urology 2025

Clinical management of non-metastatic MIBC



ctDNA is prognostic in MIBC – also with long-term clinical follow-up



* Recurrence within 1 year after RC.

** Recurrence status within 2 years after the last plasma sample was analyzed.

Christensen et al., JCO, 2019

Lindskrog et al., CCR, 2023

ctDNA guided treatment - clir trial validation

TOMBOLA: ctDNA-guided treatment – a national phase IV trial

NCT04138628

Primary endpoint:

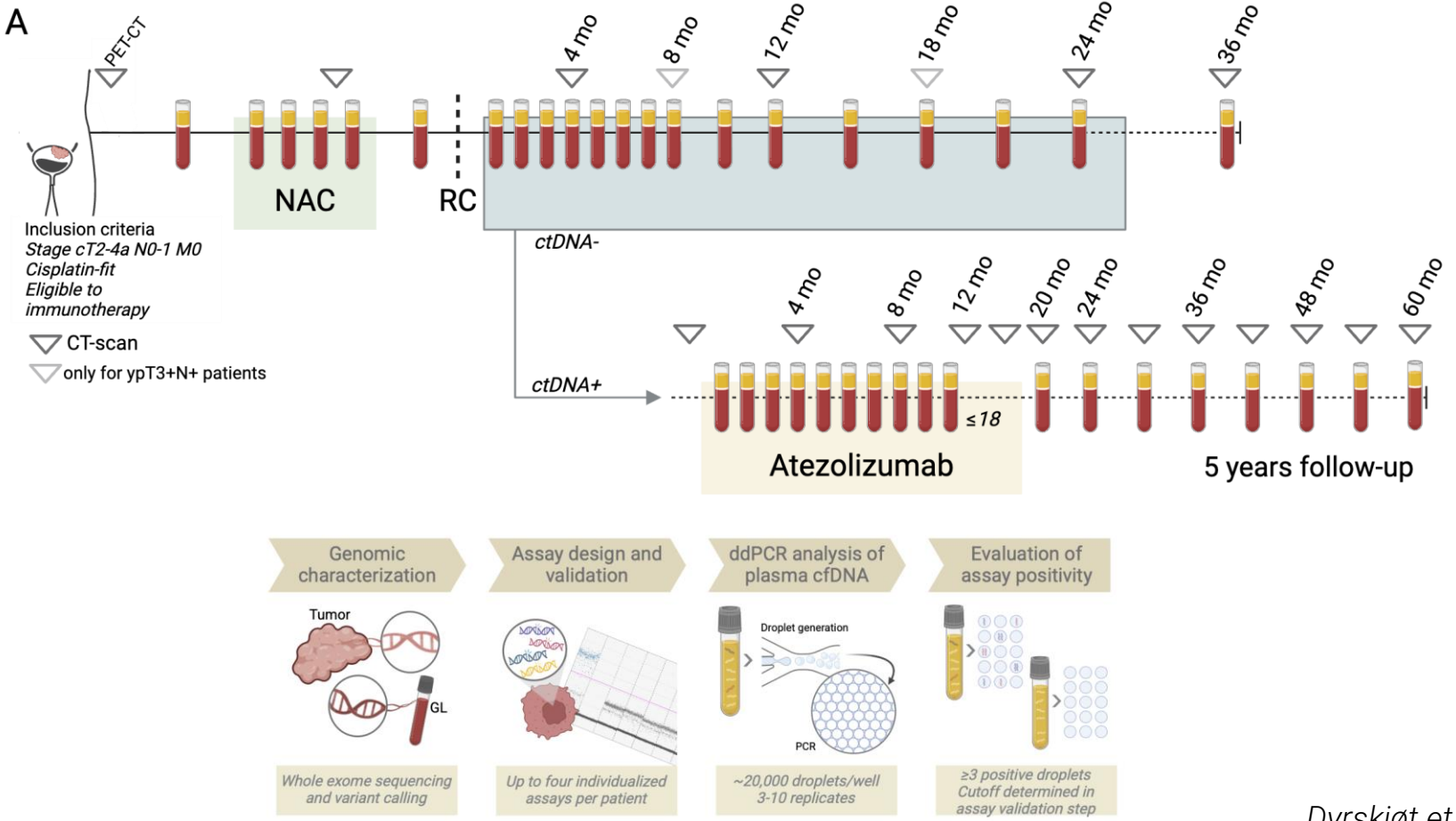
- Complete response (CR) after treatment with investigational agent initiated by ctDNA positive status after radical cystectomy.

  CR = NED (negative ctDNA and no visible metastasis on CT)

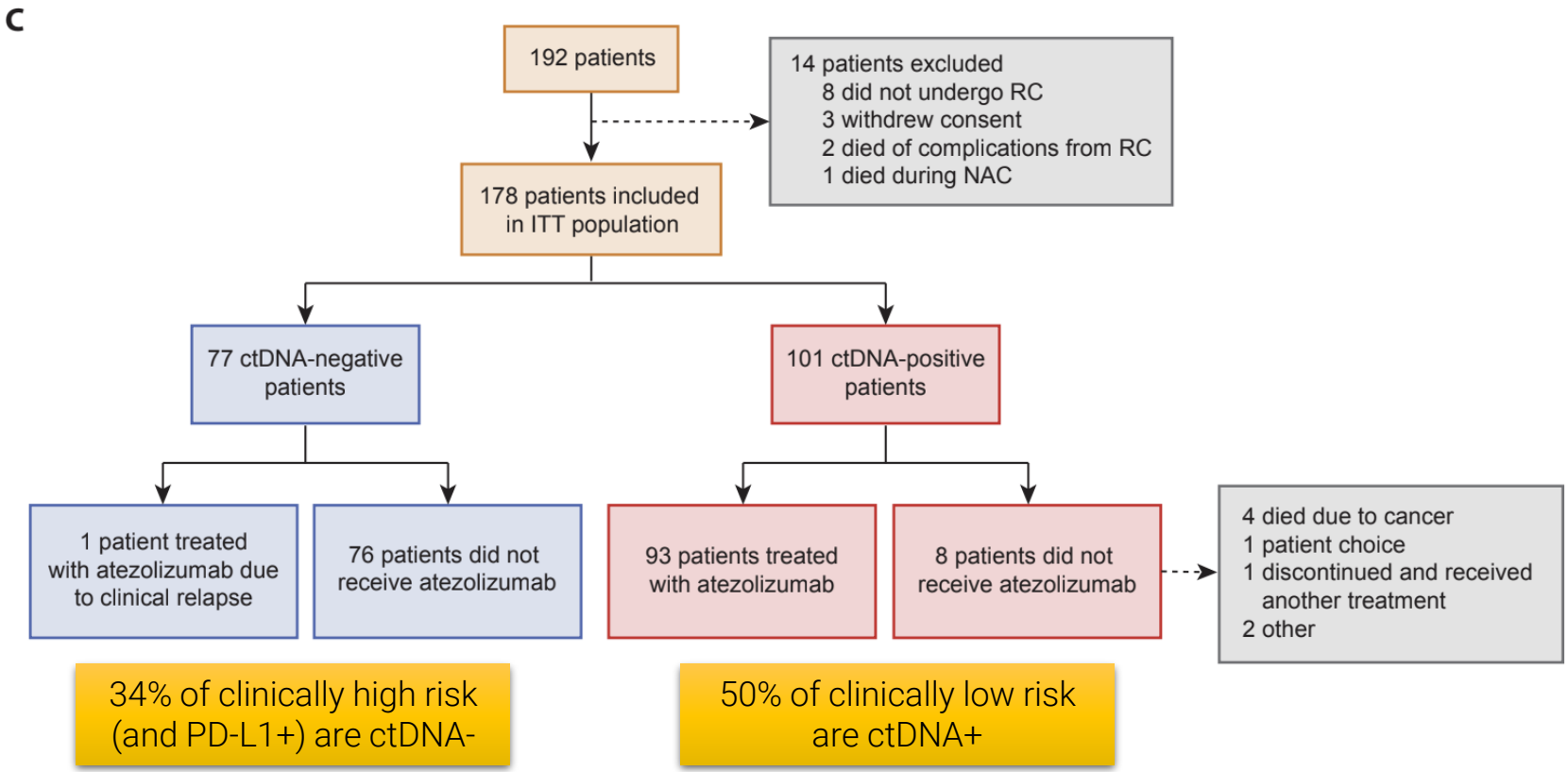
Secondary endpoints (selected):

- Overall survival after cystectomy in Study Subjects having biochemical relapse
- Cancer specific survival after cystectomy in Study Subjects having biochemical relapse
- Recurrence free survival after cystectomy in Study Subjects having biochemical relapse

TOMBOLA trial design and analysis strategy

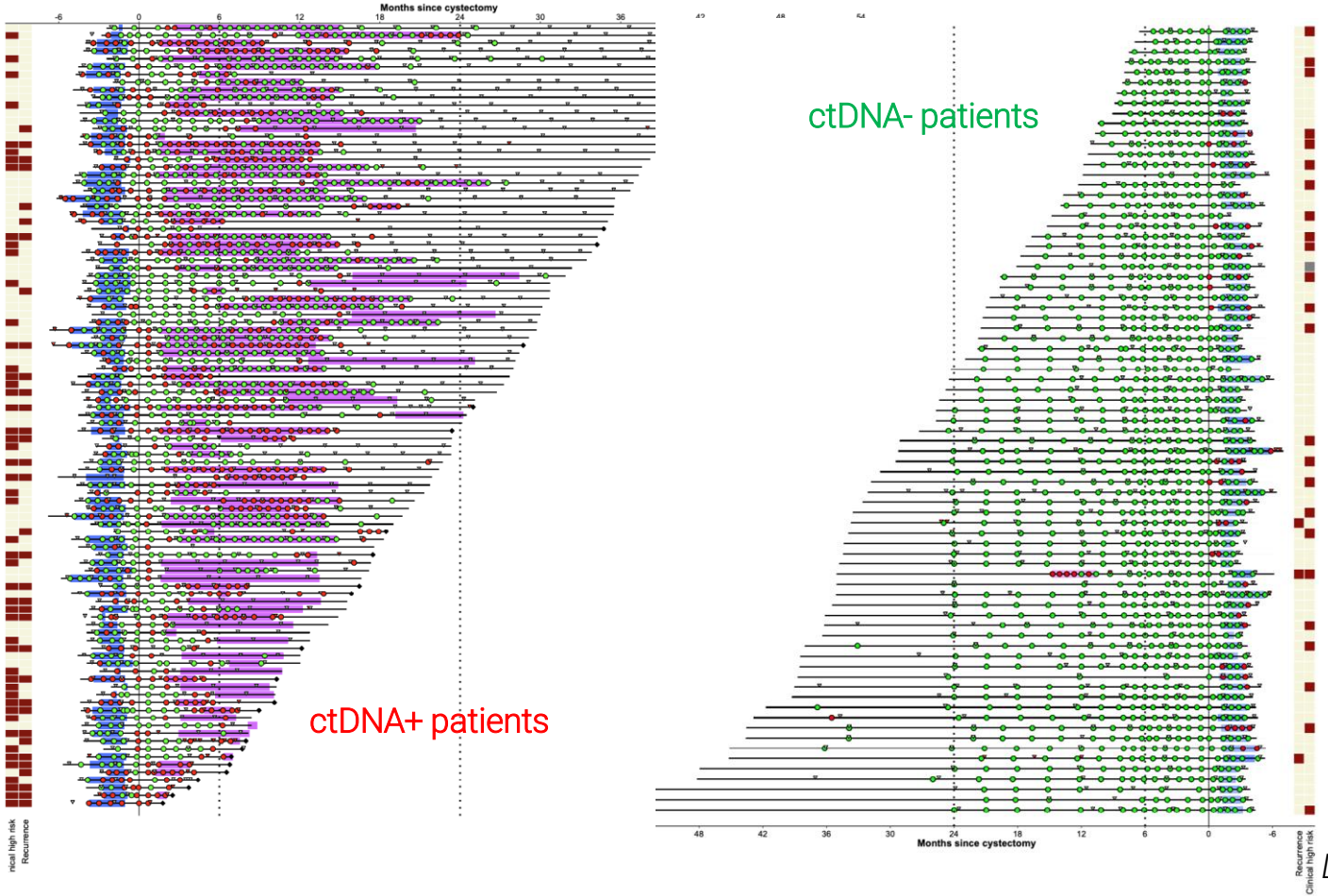


Dyrskjøt et al, EAU25



Dyrskjøt et al, EAU25

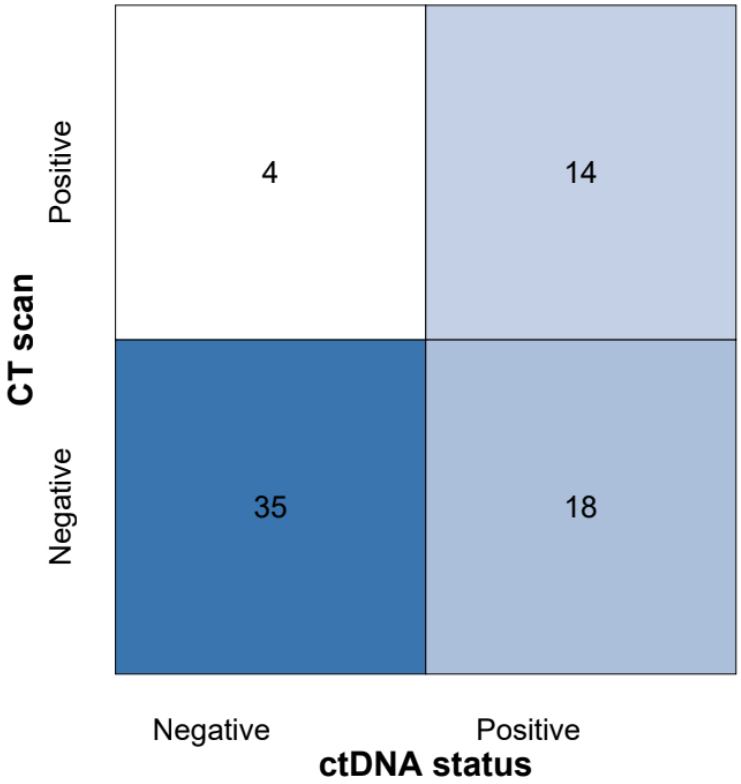
ctDNA refines treatment decisions beyond clinical risk

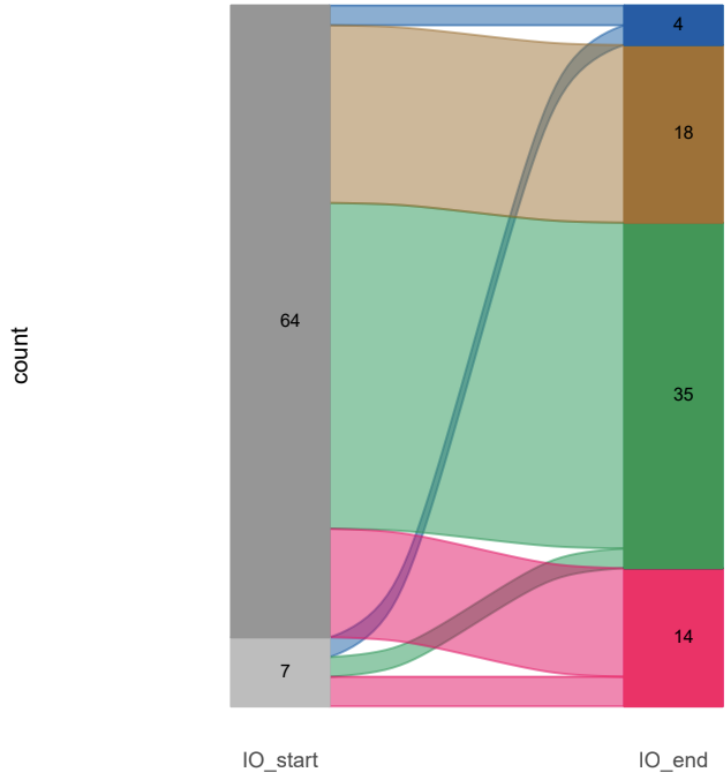


Dyrskjøt et al, EAU25

Primary endpoint

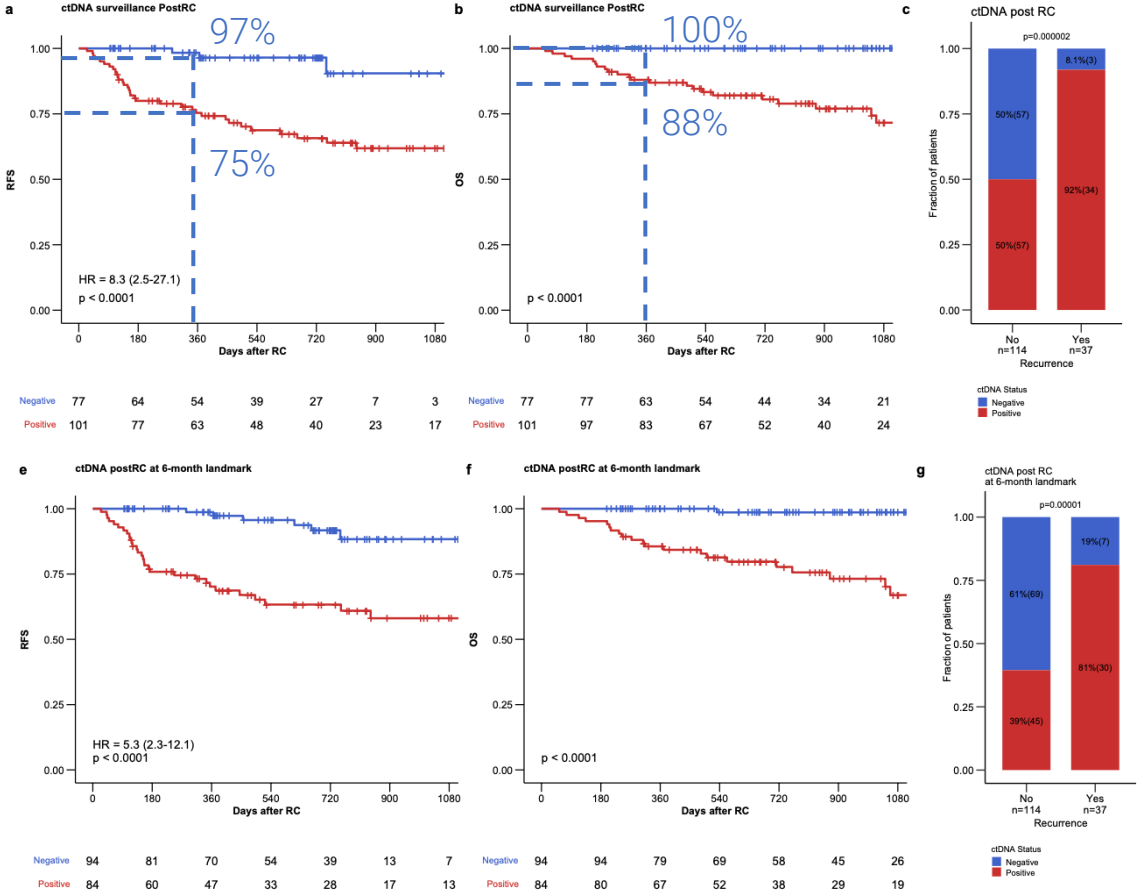
No evidence of disease (NED) following immunotherapy: 49%

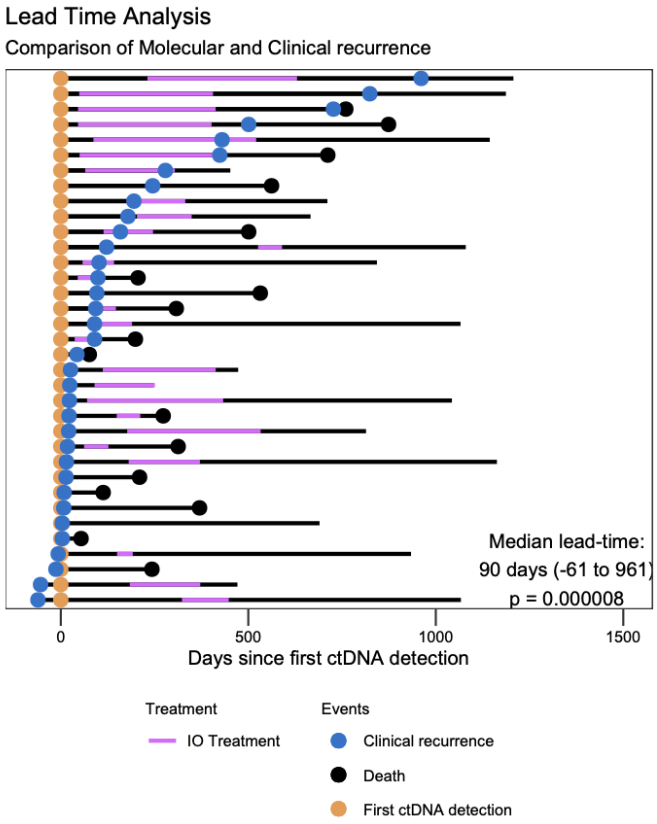




Dyrskjøt et al, EAU25

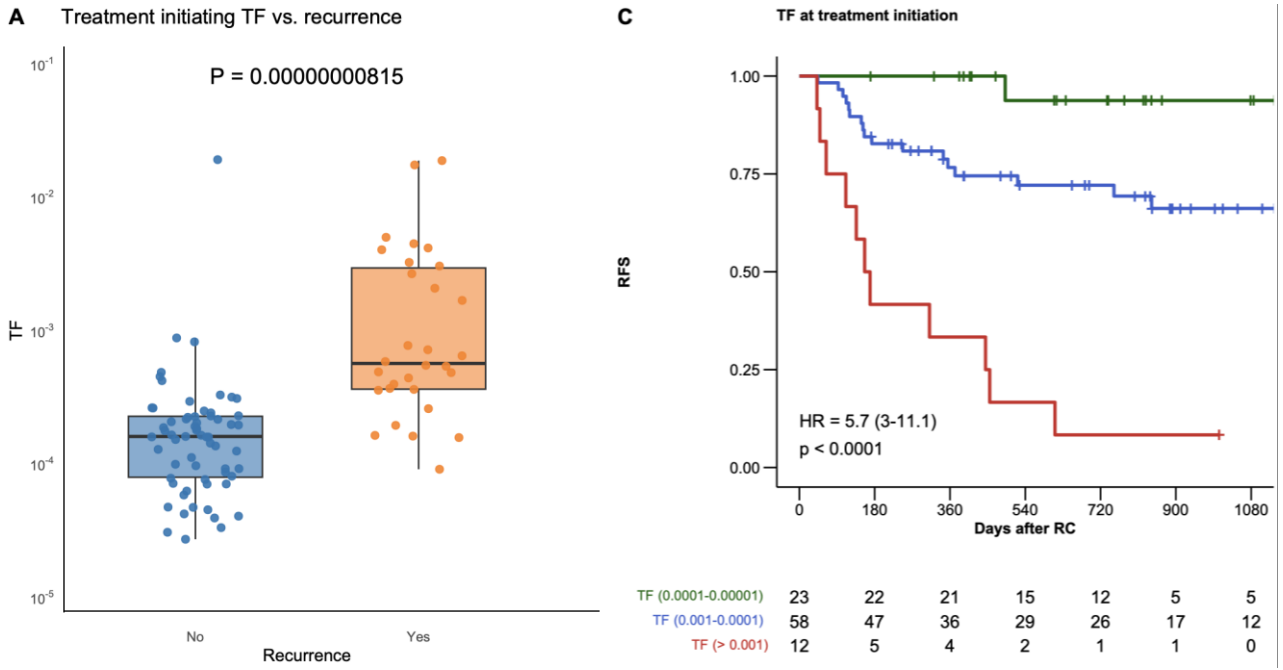
Secondary endpoints - survival





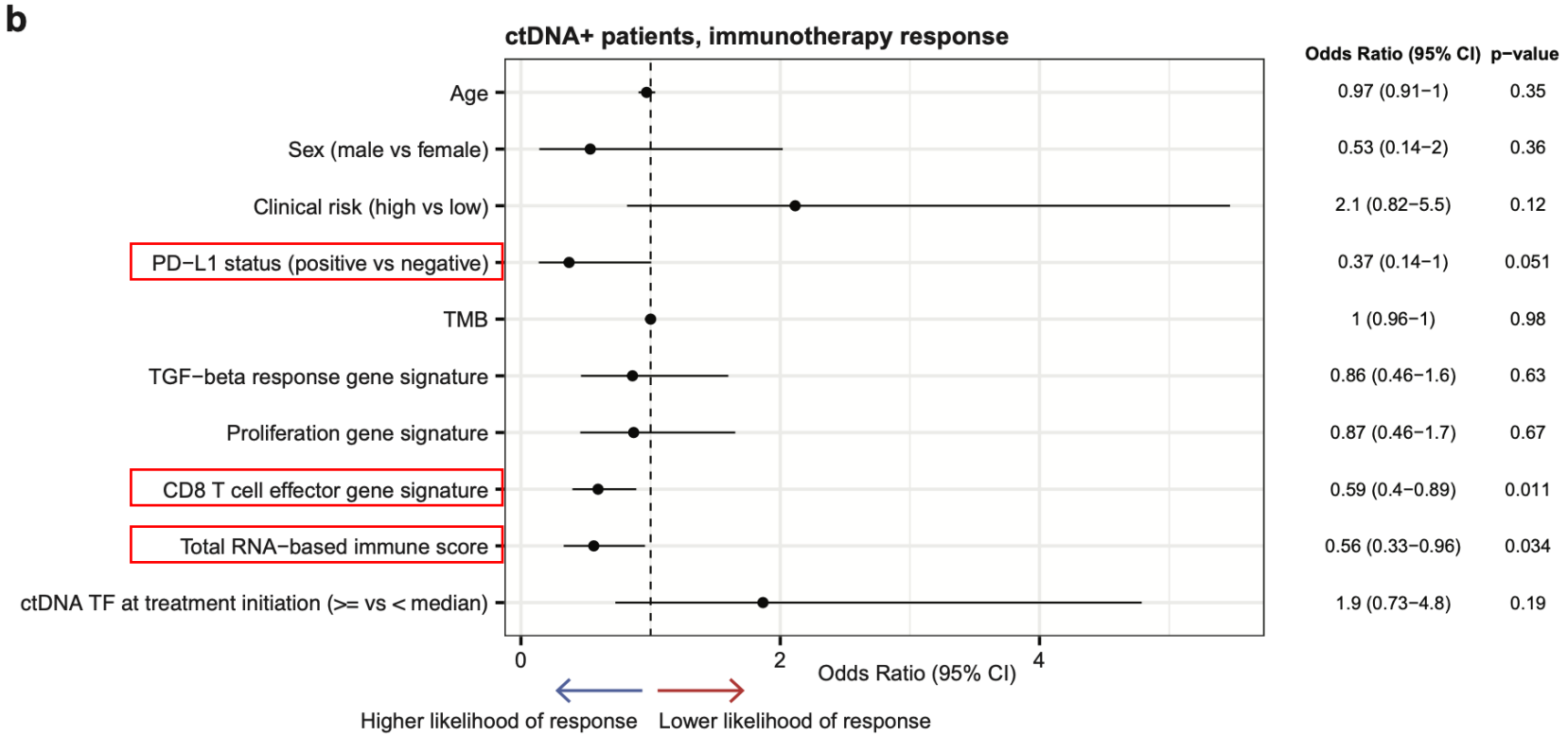
Dyrskjøt et al, EAU25

ctDNA levels correlate with recurrence



Dyrskjøt et al, EAU25

Additional biomarkers associated with response



Dyrskjøt et al, EAU25

ctDNA kan blive et centralt beslutningsværktøj i klinisk praksis i nær fremtid

- **Behandlings-deeskalering** kan være sikker for ctDNA-negative patienter
- ctDNA-status og clearance under immunterapi **informerer om respons**
- Randomiserede studier (IMvigor011, MODERN) er nødvendige for at bekræfte effekten
- ctDNA har potentiale til at **ændre klinisk praksis**

TOMBOLA trial study group

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Roche – Provided atezolizumab for study participants
Clinical staff – For their dedication and contributions to the trial
All patients – For their invaluable participation and commitment