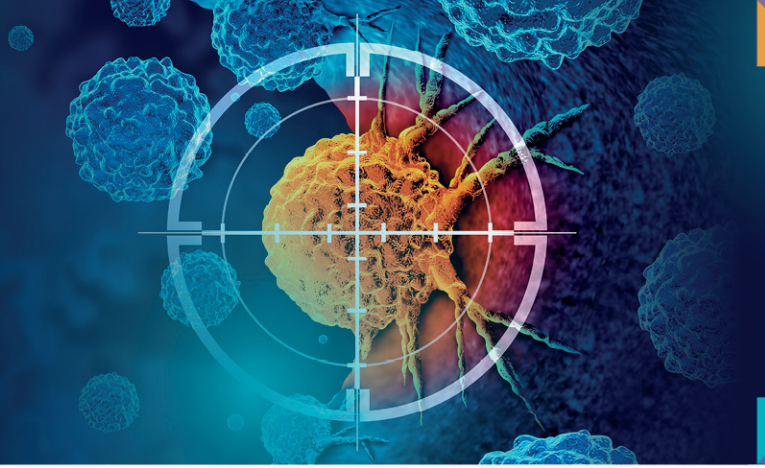
XVIII SIMPOSIUM

BASES BIOLÓGICAS DEL CÁNCER E INNOVACIÓN TERAPÉUTICA

MÁS DE 20 AÑOS A LA VANGUARDIA DE LA FORMACIÓN EN LA BIOLOGÍA Y TRATAMIENTO DEL CÁNCER

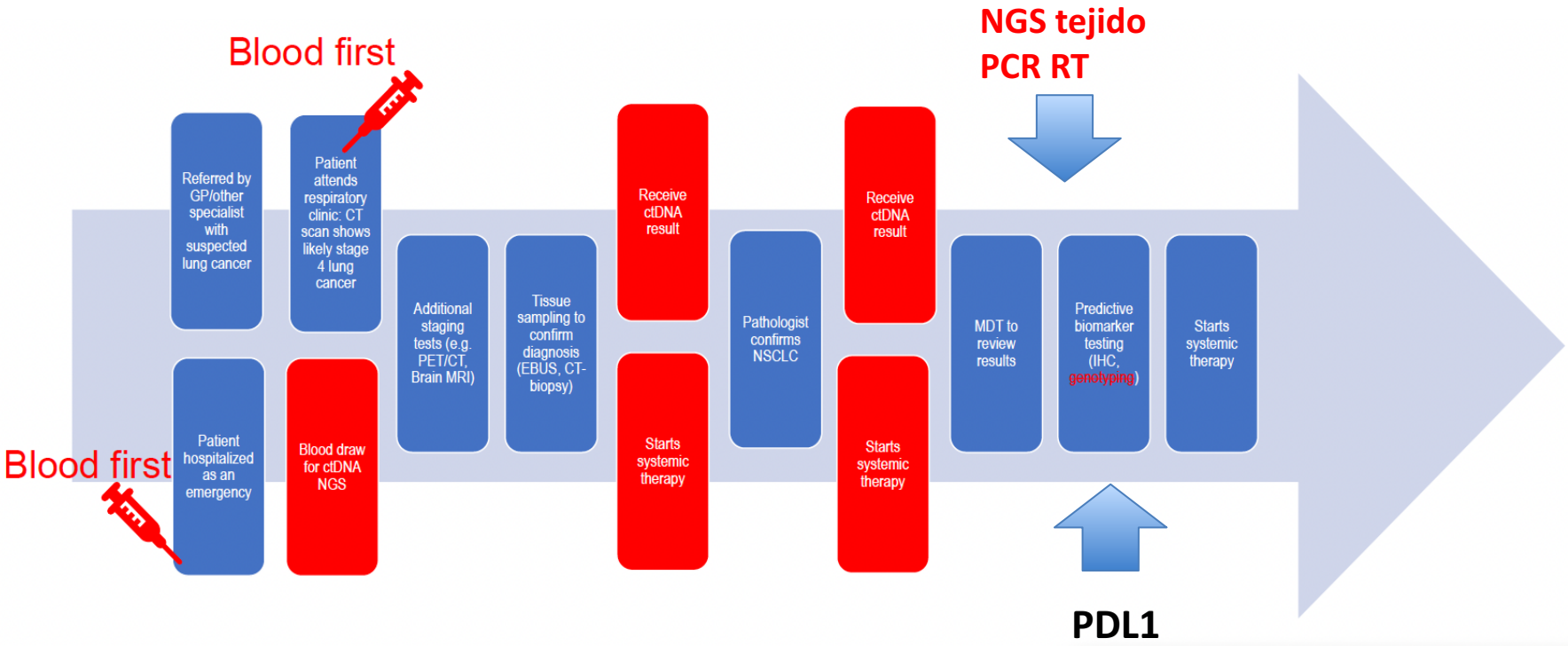


¿Quién se beneficia realmente de la inmunoterapia? De PD-L1 a la enfermedad residual molecular

Dra. Mónica Antoñanzas Basa

Oncología médica

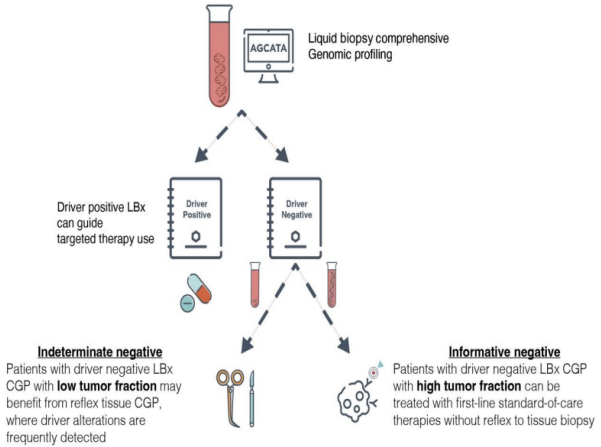
Descartar rápidamente quién NO se beneficia (Driver)

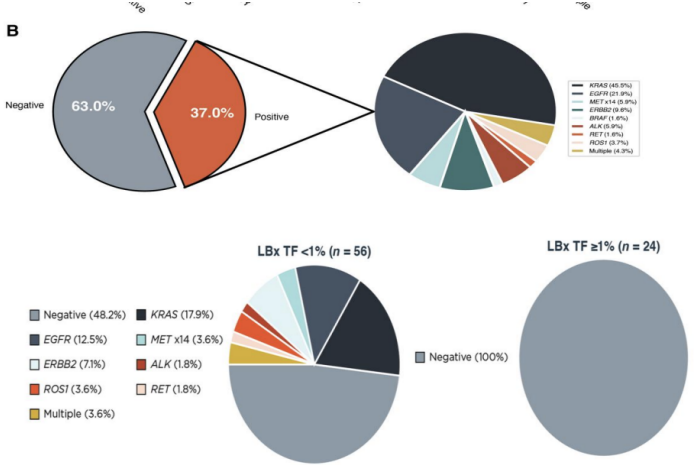


Modified Sanjay popat ELCC 2026

CAN A NEGATIVE LIQUID BIOPSY BE INFORMATIVE?

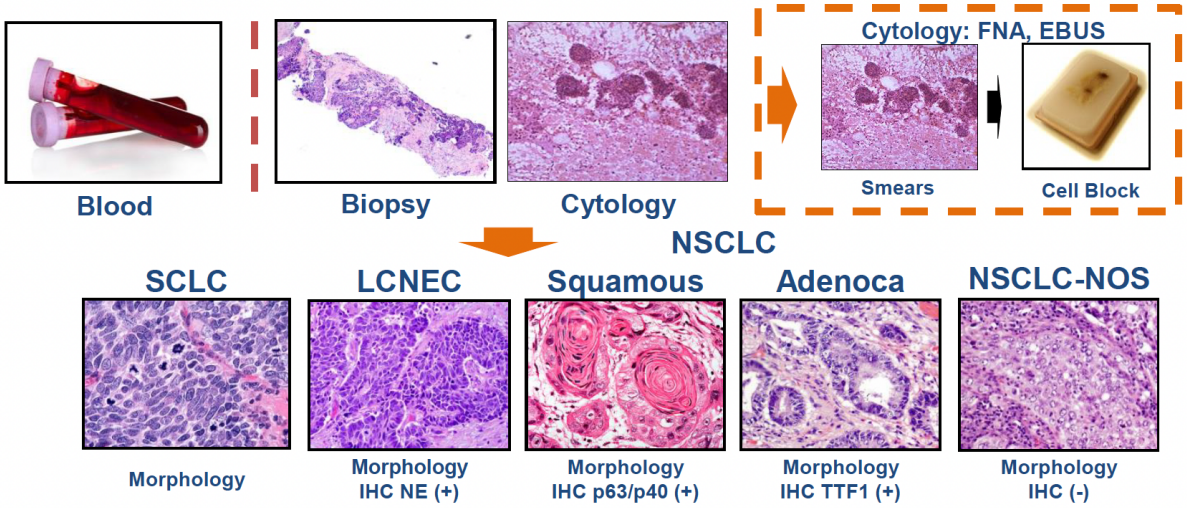
Tumor Fraction Identifies Informative Negative Liquid Biopsy Results





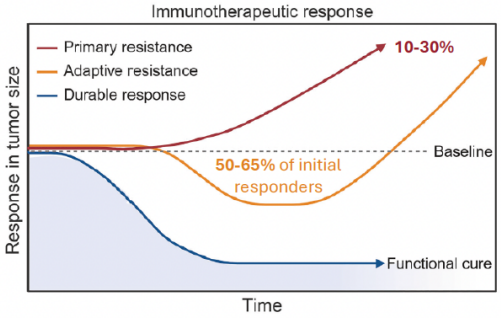
Patients with lung cancer with negative LBx and ctDNA TF ≥1% are unlikely to have a driver detected on confirmatory tissue testing; such informative negative results may benefit instead from prompt treatment initiation.

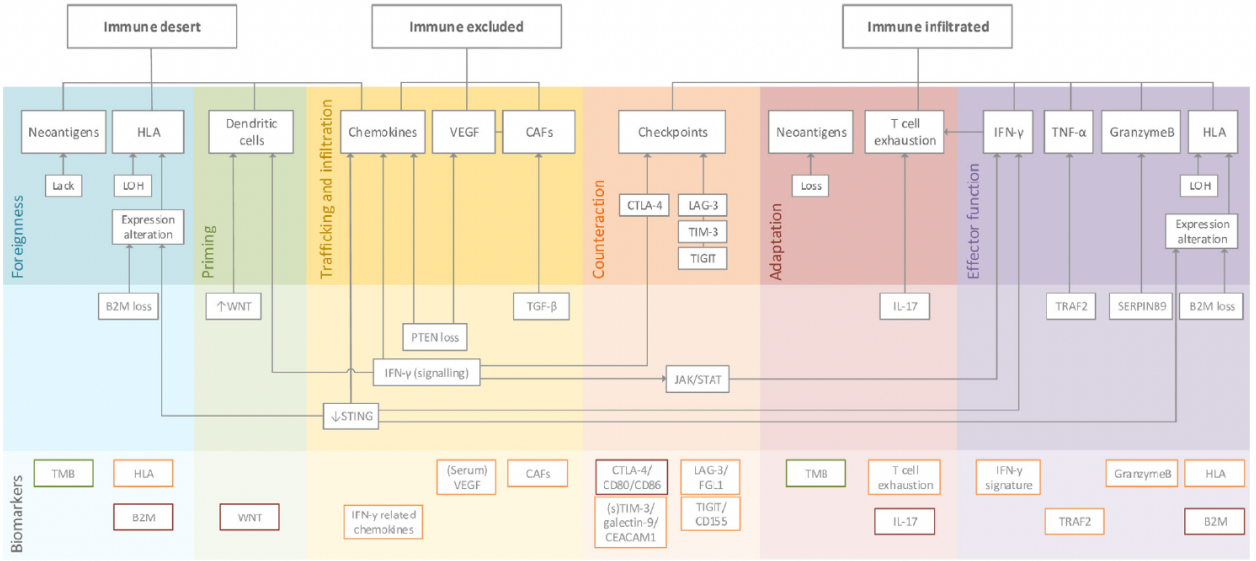
Algoritmo diagnostico Cancer de pulmón



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Factores del ambiente tumoral e inmunitario





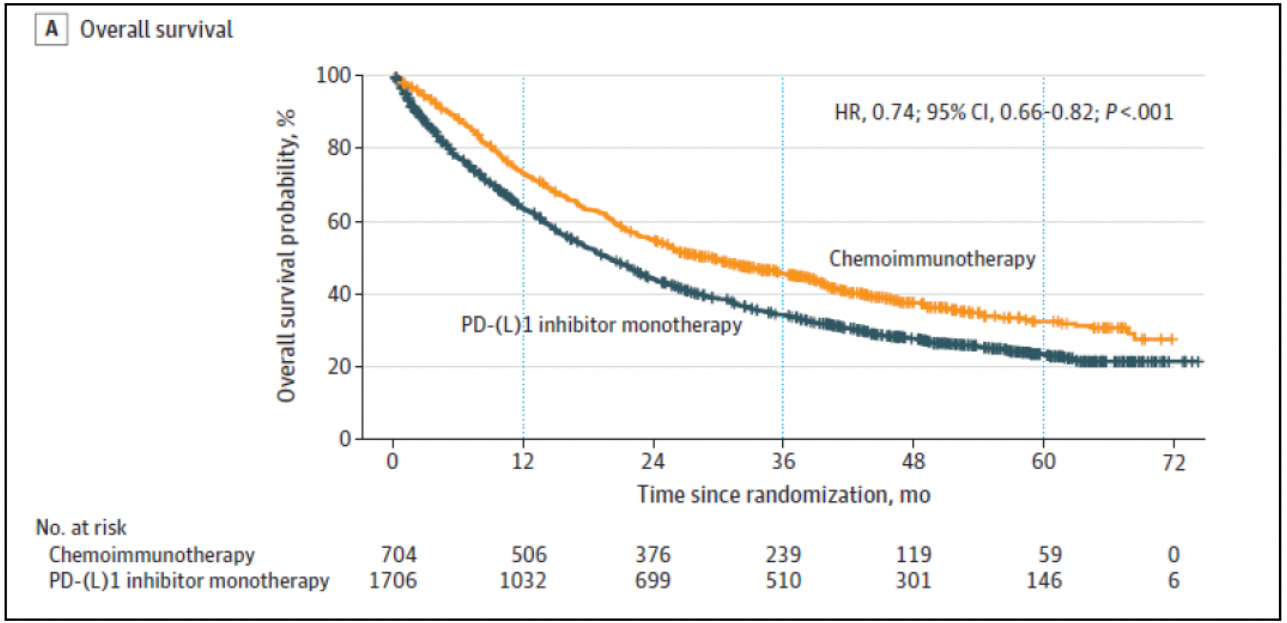
Yang K, et al. Cell Mol Immunol. 2026;

JAMA Oncology | Original Investigation

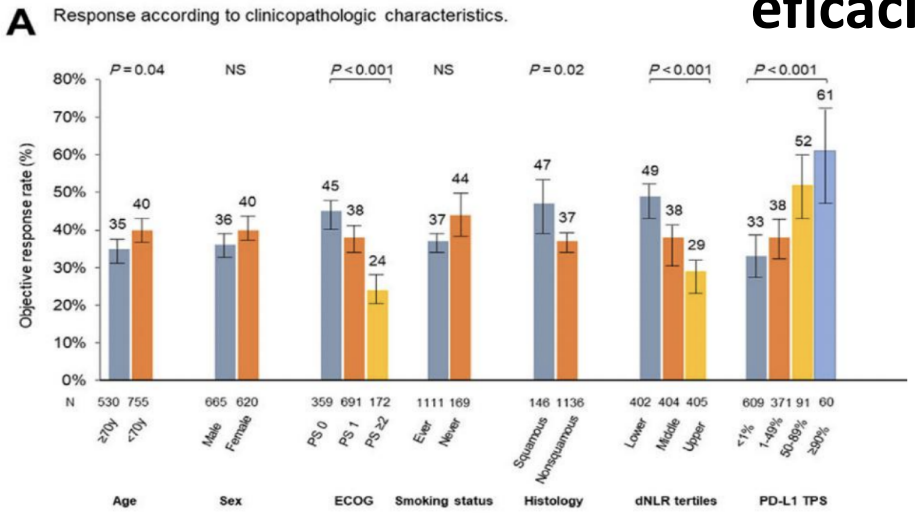
PD-(L)1 Inhibitor Monotherapy vs Chemoimmunotherapy for Advanced NSCLC With High PD-L1 Expression

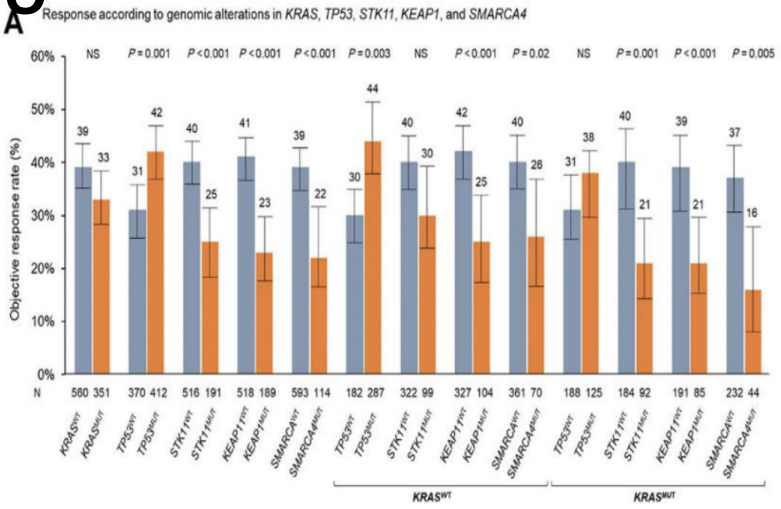
A Systematic Review and Meta-Analysis

Nuestro marcador PDL1 50%



Factores clínicos y genómicos que van a impactar en en la eficacia IO





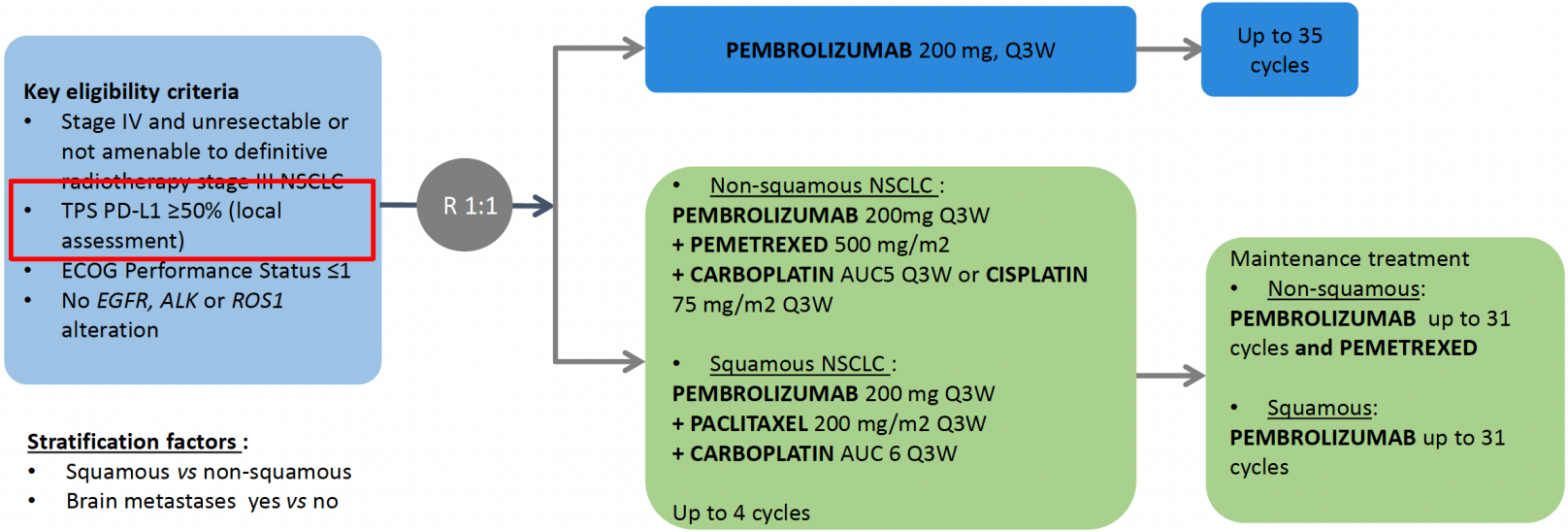
A mayor expresión de PD-L1

Mejor ECOG
¿Alta carga tumoral?
Low LIPI
TMB muy alto
STK11/KEAP1/SMARCA4

Alessi et al. J Thorac Oncol 2023

PERSEE Trial

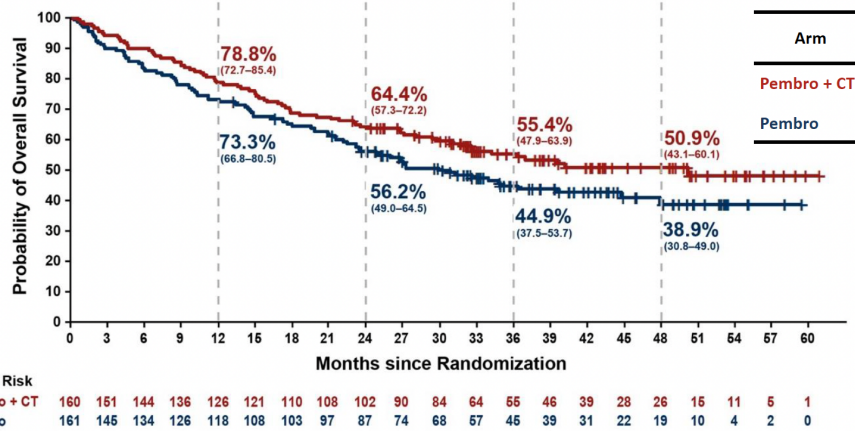
A phase III, multicenter, open-label, randomized trial



Primary endpoint: PFS by BCR per RECIST v1.1.
Key Secondary endpoints: PFS by investigators, OS, ORR, DoR, DCR, efficacy according to PD-L1 sub-groups expression, safety.
Key Exploratory endpoints: incidence of early progression, PFS2, QoL, translational analyses

PERSEE Trial

Secondary endpoint : Overall survival (ITT)



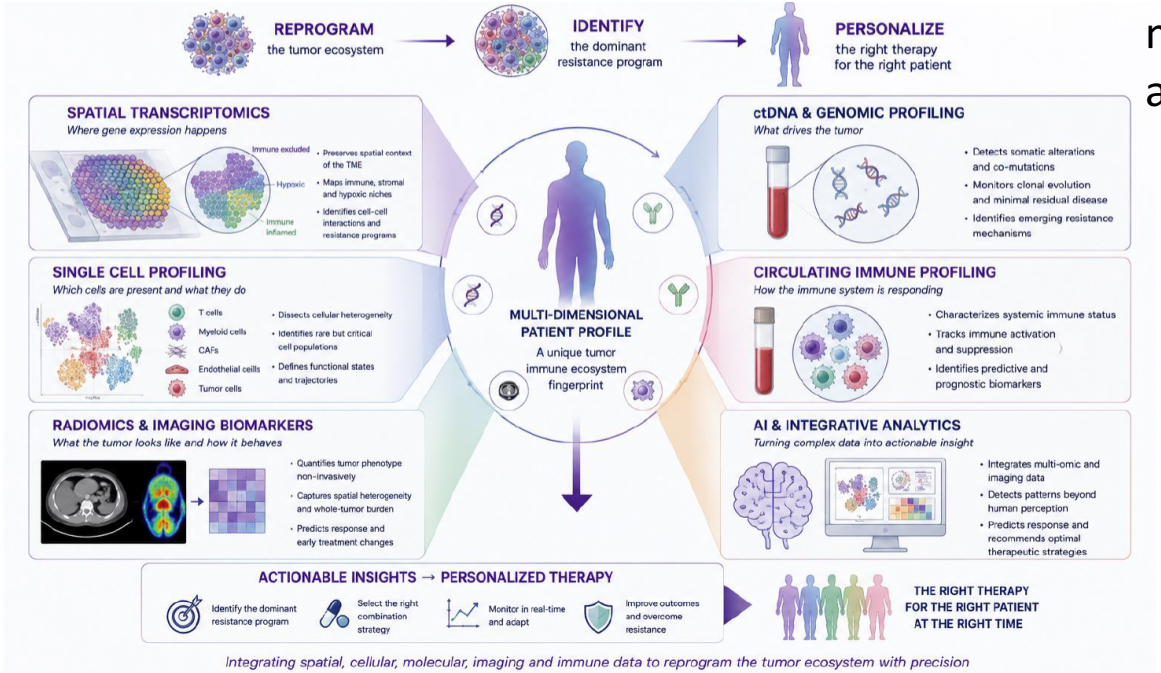
Arm	Events n (%)	Median OS (95% CI), months	HR (95% CI)
Pembro + CT	74 (46.3)	50.2 (32.6–NC)	0.77 (0.56–1.05)
Pembro	89 (55.3)	29.9 (23.4–47.9)	

A numerically longer median OS of 50.2 months in the pembro-CT group was observed compared with 29.9 months in the pembro group. The trial was not powered to demonstrate an overall survival difference.

66.7% and 64.7% of patients who progressed received a second line treatment in pembro-CT and pembro arm respectively.

¿CHEMO IO Todos?

Inmunoterapia de precisión



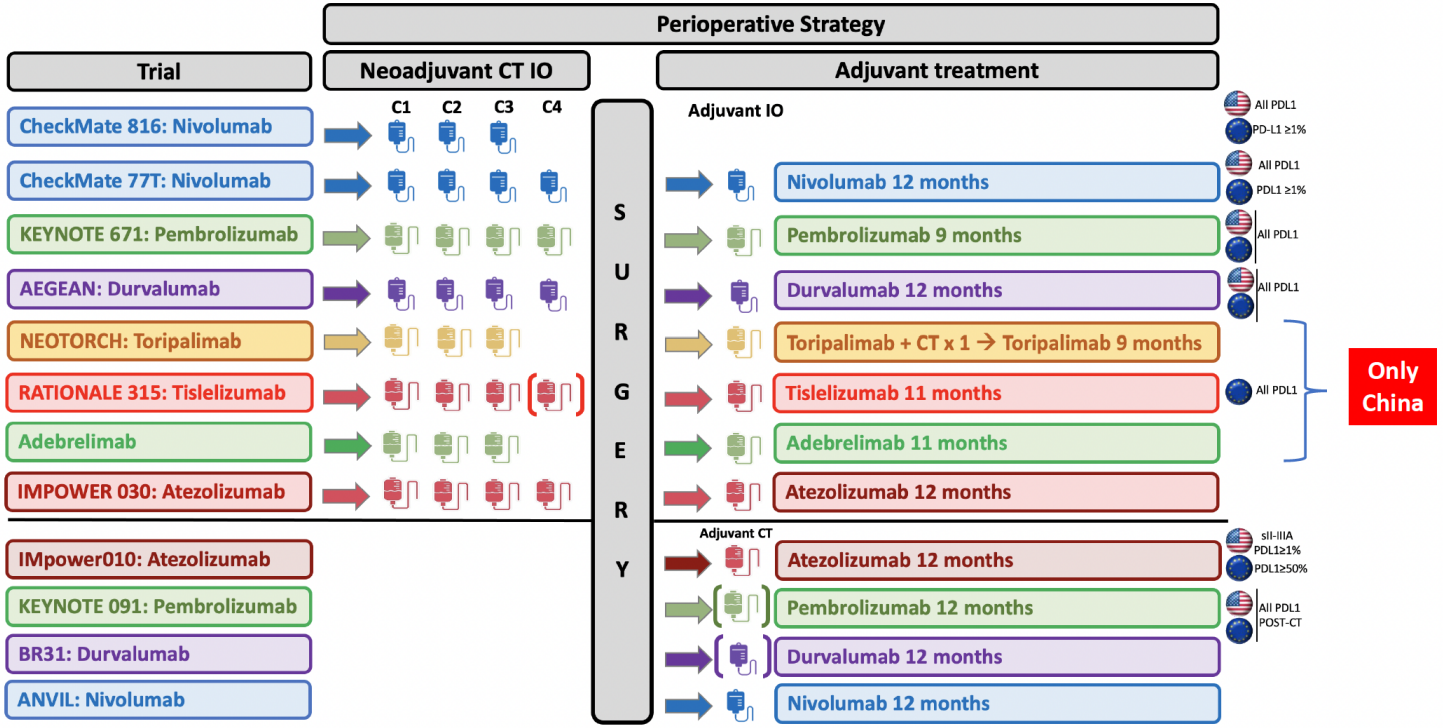
Immune resistance is multidimensional, spatial and dynamic.

PERSONALIZE IO: Integrar todos biomarcadores longitudinales para adaptacion

.

Mazzaschi G. IASLC 2026

Tratamiento Localizado



Remon ESMO 2026. ASCo educational book 2026

Strategy	Neoadjuvant	Perioperative						
Trial	CheckMate-816	KEYNOTE- 671	AEGEAN	CheckMate-77T	ADEBRELIMAB	RATIONALE-315	NEOTORCH	IMpower 030
Nº of patients	358	797	740	461	501	453	501	440
IO drug	Nivolumab	Pembrolizumab	Durvalumab*	Nivolumab	Adebrelimab*	Tislelizumab	Toripalimab	Atezolizumab*
Stage III	7th TNM 64%	8th TNM 70%	8th TNM 71%	8th TNM 64%	8th TNM 63%	8th TNM 58% (IIIA)	**8th TNM 81%**	8th TNM 59%
PDL1 negative	43%	33%	33%	40%	45%	39%	**26%**	33%
Non-Sq	49%	57%	51%	49%	21%	20%	22%	55%
Cisplatin	80%	100%	27%	21%	NR	54%	NR	NR
Surgery cancelled (IO arm)	17%	18%	19%	22%	11%	16%	16%	11%
Surgery cancelled (control arm)	21%	21%	20%	24%	17%	24%	25%	10%
Pneumonectomy (% in IO arm)	21%	12%	9%	9%	NR	8%	9%	9%
pCR CTIO vs CT	**24% *vs.* 2.2%**	**18% *vs.* 4.0%**	**17.2% *vs.* 4.3%**	**25.3% *vs.* 4.7%**	**31% *vs.* 7.6%**	**41% *vs.* 5.7%**	**25.6% *vs.* 1.2%**	**31% *vs.* 8.7%**

Remon ESMO 2026. ASCo educational book 2026

NEO / perioperative trials: benefit according PDL1

	CheckMate 816	AEGEAN	KEYNOTE671	Neotorch	NADIM II PDL1 neg *vs* pos	CheckMate 77T
PDL1 ≥50%	EFS HR 0.29 pCR* 40%	EFS HR 0.60 pCR* 27.5%	EFS HR 0.42	EFS HR 0.31	PFS HR 0.22 pCR* 53%	EFS HR 0.26 pCR* 51.1%
PDL1 1-49%	EFS HR 0.63 pCR* 23.5%	EFS HR 0.70 pCR* 16.3%	EFS HR 0.51	EFS HR 0.31		EFS HR 0.76 pCR* 26.5%
PDL1 negative	EFS HR 0.87 pCR* 14.1%	EFS HR 0.76 pCR* 9%	EFS HR 0.77	EFS HR 0.59	PFS HR 0.85 pCR* 15%	EFS HR 0.73 pCR* 12.9%

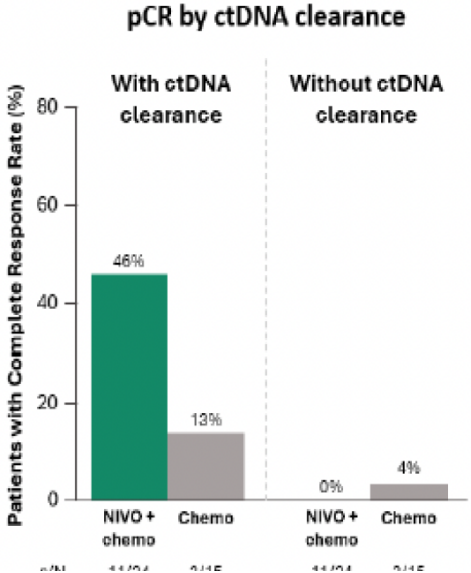
pCR*: pathologic complete response rate in the immunotherapy arm

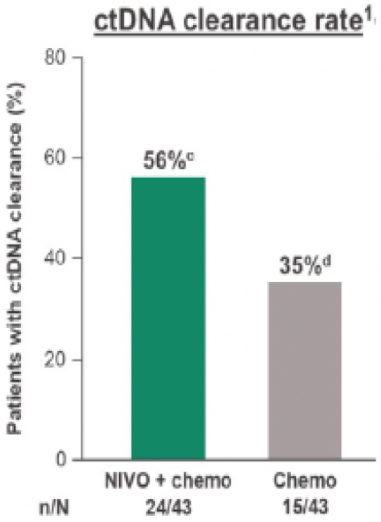
Spicer ASCO 2023, Heymach AACR 2023, Wakelee NEJM 2023, Shun Lu ASCO 2023, Provencio NEJM 2023, Cascone ESMO 2023

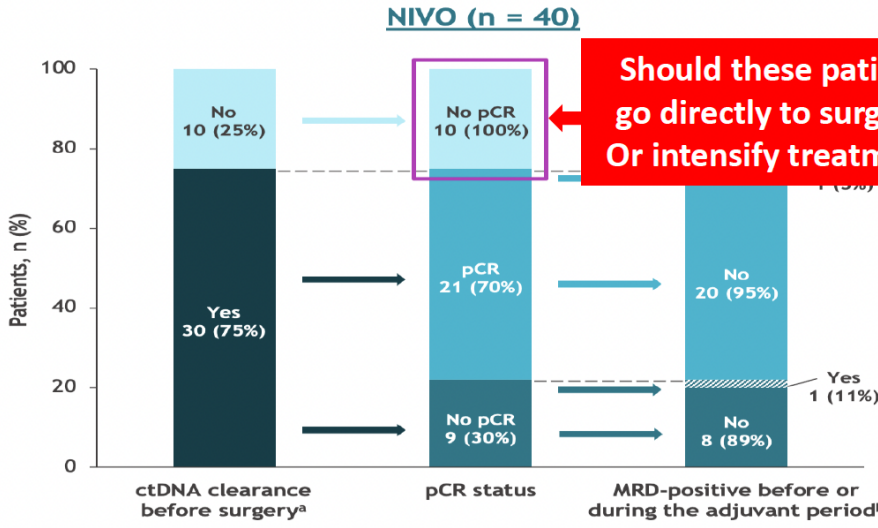
The benefit of neo/perioperative immunotherapy CT+ICI is higher in patients with PDL1+

Adapted Felip E. IASLC 2026

CheckMate 816: Nivolumab (hTMB not associated with pCR) **CheckMate 777: Nivolumab**



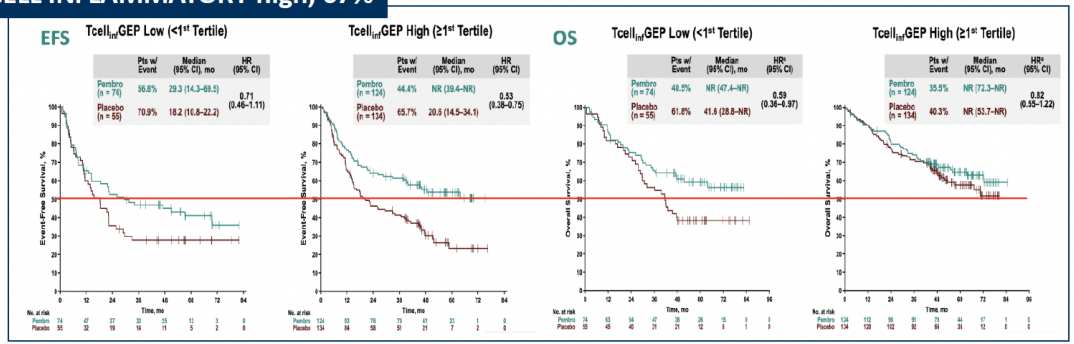




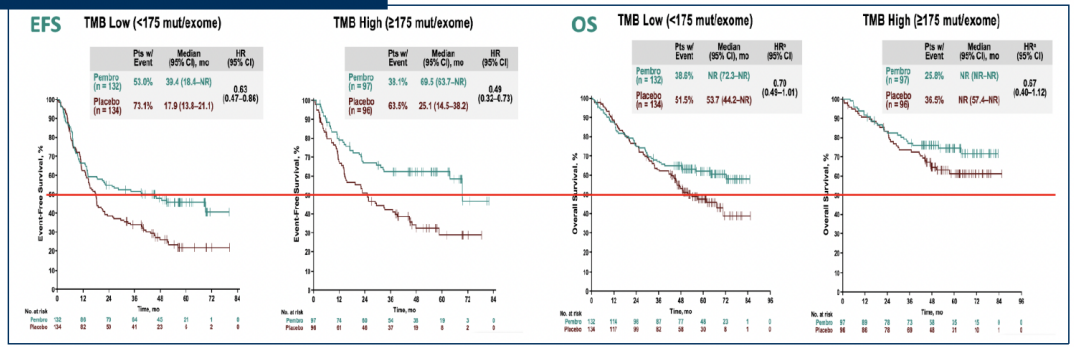
KEYNOTE 671

Biomarker analyses (primary tissue) in ~50% of patients: 1) T-cell inflam signature. 2)RNA seq for TMB / KRASm status

T-CELL INFLAMMATORY high, 67%



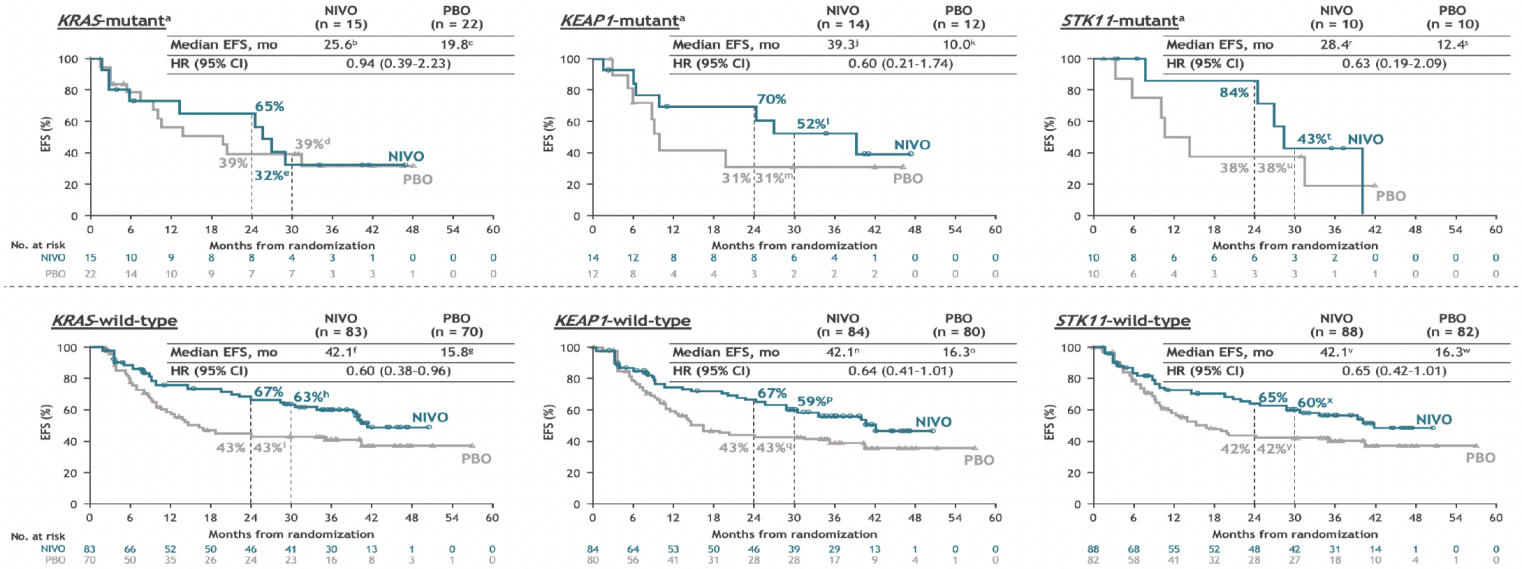
HIGH TMB, 42%

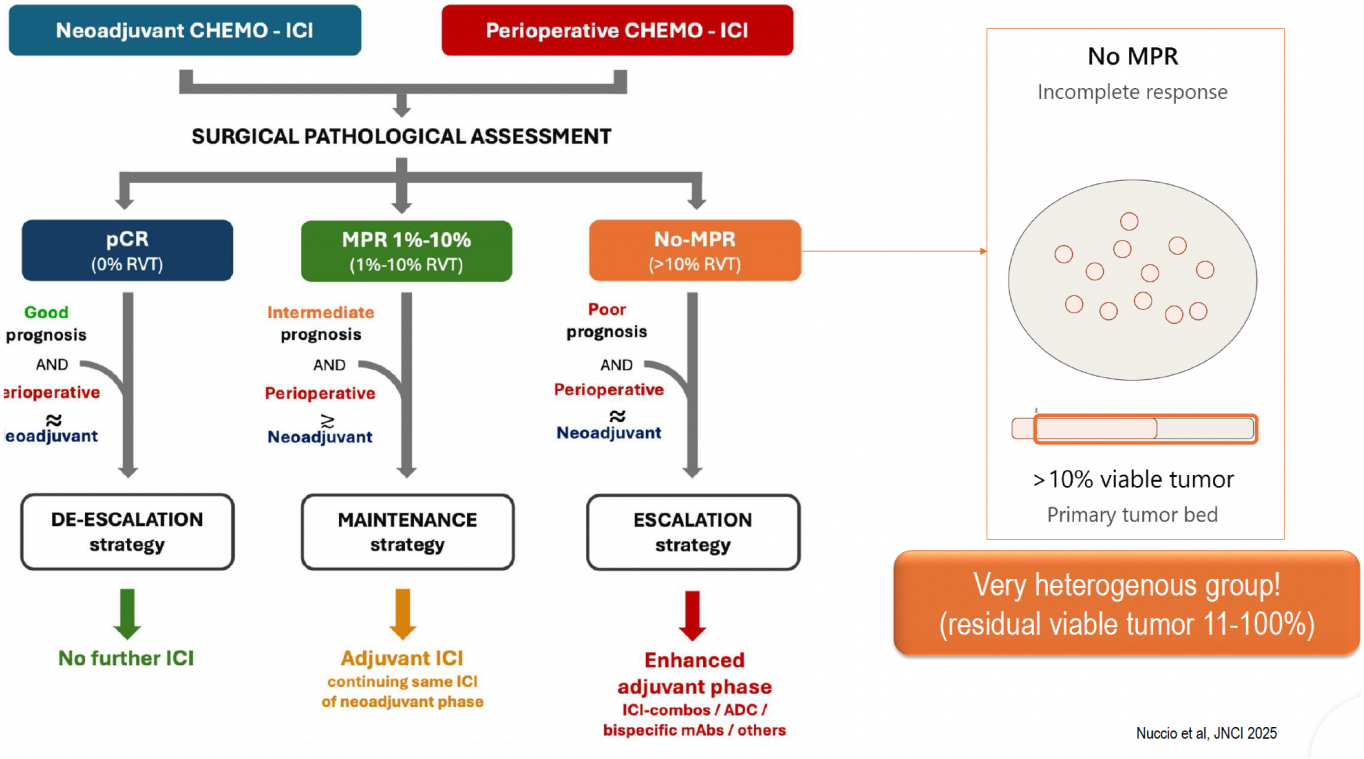


hTMB mas pronostico que predictivo?

EFS beneficio nivolumab en todos los subgrupor genómicos analizados

CheckMate 77T Biomarker evaluable population: 41% (190/461). ***KRAS*m 19%.** *KEAP1*m 14%. *STK11*m 11%

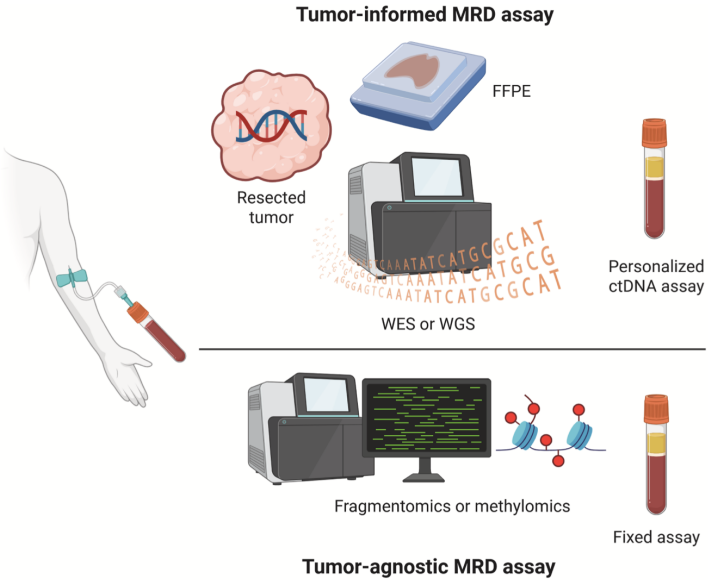




Nuccio et al, JNCI 2025

Early stage

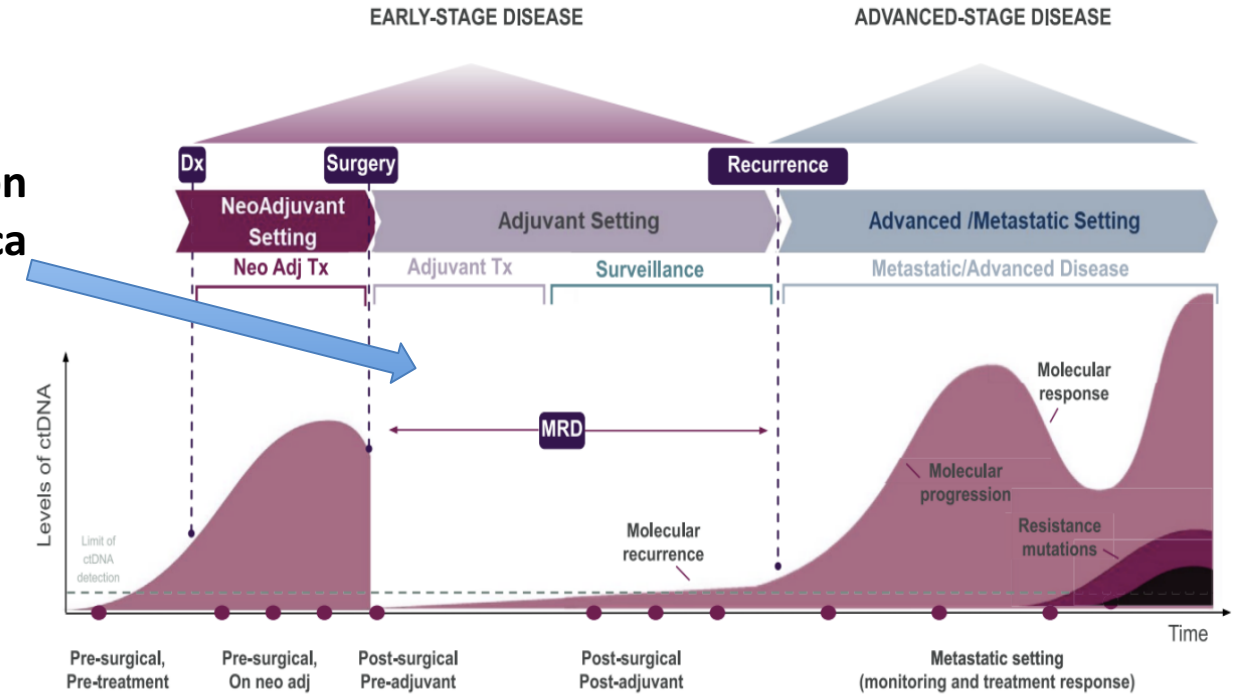
Molecular residual disease (MRD)	Minimal residual disease, measurable residual disease	The subclinical presence of a cancer-associated biomarker indicating a high risk of recurrence which cannot be detected by standard imaging techniques
Molecular residual disease (MRD) assay		A method for determining the presence of cancer-associated biomarkers from liquid biopsies that are associated with a remnant or recurrence of residual disease following curative intent



BLOODPAC Consortium Sci Rep 2025

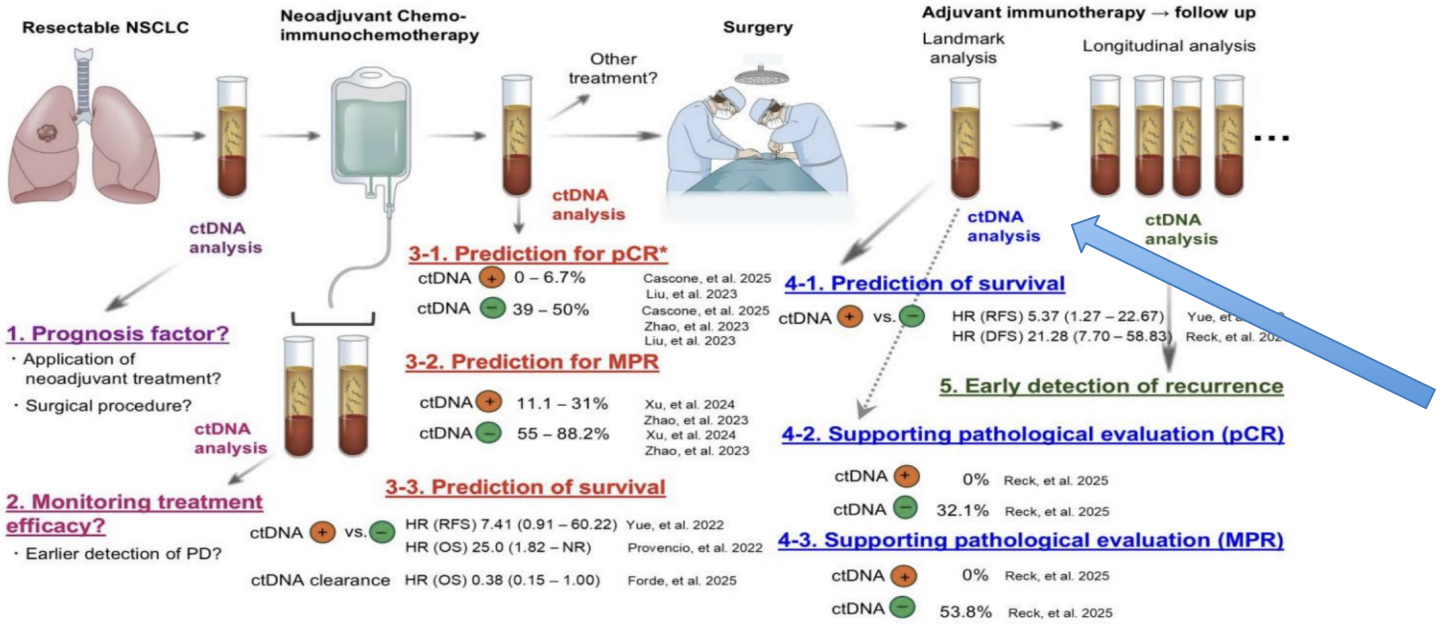
En que momento utilizar ctDNA

MRD: Adaptación terapéutica



Alix-Pnabieres et al, Cancer Cell 2025

En que momento utilizar ctDNA Early stage



MRD: Adaptación terapéutica

Ohara. Cell 2025
T an et al. JTO 2026

¿Cómo tiene que ser un test de Molecular RD?

MRD assay should have high sensivity and negative predictive value for supporting de-escalation of treatment

MRD assay should have high especificity and positive predictive value for supporting escalation of treatment

MRD 1º generación
Tienen un alto valor predictivo positivo
Pero una sensibilidad no tan alta

MRD es pronostico pero

Meta-analysis of the sensitivity of ctDNA detection in predicting relapse and in NSCLC patients who received definitive therapy

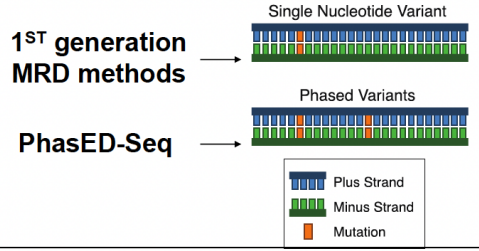
Subgroup analysis for surveillance liquid biopsy		Sensitivity	Specificity
Lung cancer type[b]	Lung cancer (stage I–III)	0.76 (0.70–0.82)	0.86 (0.83–0.89)
	NSCLC (stage I–III)	0.76 (0.70–0.82)	0.87 (0.84–0.90)
	SCLC[a]	0.82 (0.48–0.98)	0.67 (0.30–0.93)
Stage	Patients at stage I ≥ 50% (NSCLC)	0.75 (0.64–0.84)	0.89 (0.85–0.93)
	Patients at stage I < 50% (NSCLC)	0.77 (0.69–0.84)	0.84 (0.78–0.88)
	Patients at stage I < 50% (lung cancer)	0.77 (0.70–0.84)	0.83 (0.78–0.87)
Detection method	Amplicon NGS (NSCLC)	0.77 (0.64–0.87)	0.82 (0.72–0.89)
	Hybrid Capture NGS (NSCLC)	0.76 (0.68–0.82)	0.88 (0.84–0.91)
	Hybrid Capture NGS (lung cancer)	0.76 (0.69–0.82)	0.88 (0.84–0.90)
Detection strategy	Tumor-informed (NSCLC)	0.69 (0.61–0.77)	0.84 (0.79–0.88)
	Tumor-agnostic (NSCLC)	0.91 (0.75–0.98)	0.63 (0.49–0.76)
	Tumor-agnostic (lung cancer)	0.88 (0.75–0.96)	0.65 (0.51–0.76)

Methodological heterogeneity
makes it difficult to define thresholds for ctDNA detection
and relationship to MRD

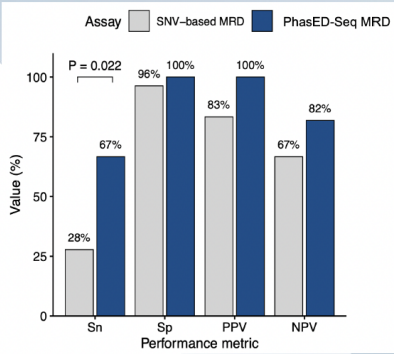
Lovely IASLC 2026

Next Steps: Ultrasensitive ctDNA MRD Detection with PhasED-Seq

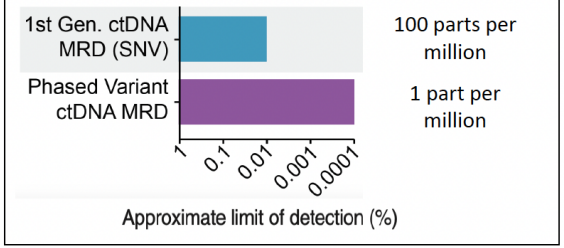
PhasED-Seq tracks a different class of mutations with lower error rates



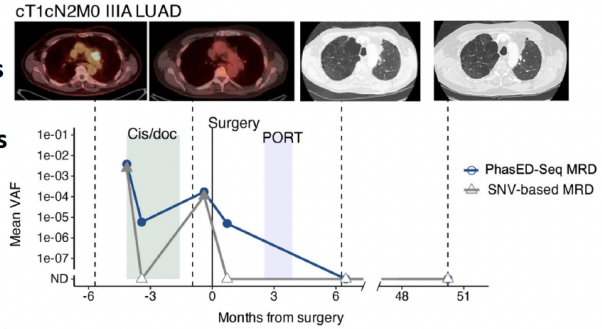
PhasED-Seq can detect >2x more MRD in early stage NSCLC patients with better specificity



PhasED-Seq is 100x more sensitive than 1st generation MRD methods



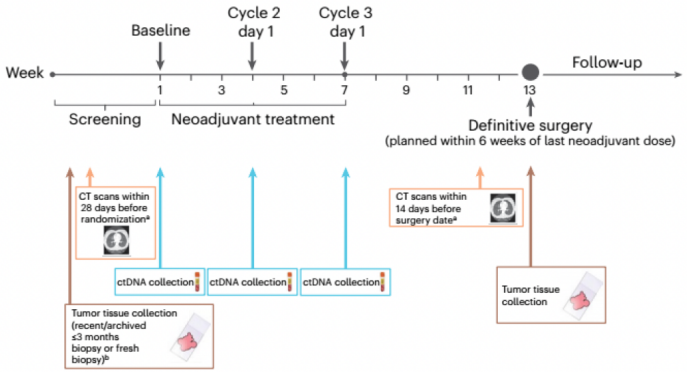
PhasED-Seq detects MRD when 1st generation methods report false negatives



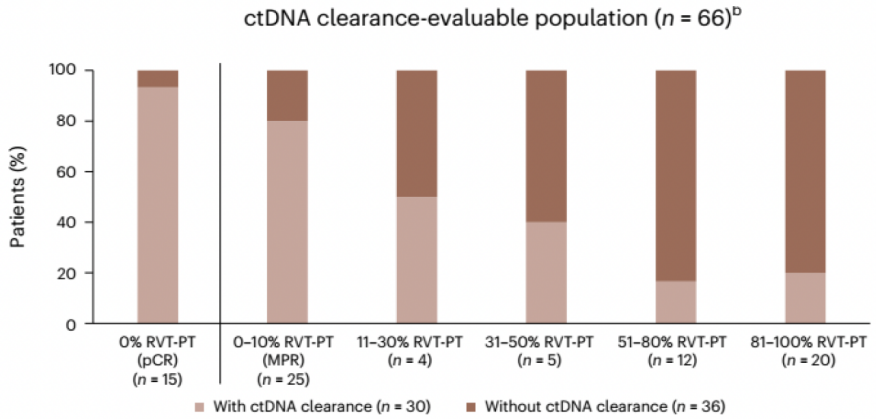
Dieh M. ELCC 2026

Checkmate 816 (preop)

Tumor informed assay: requires whole-exome sequencing of *pretreatment* tumor sample

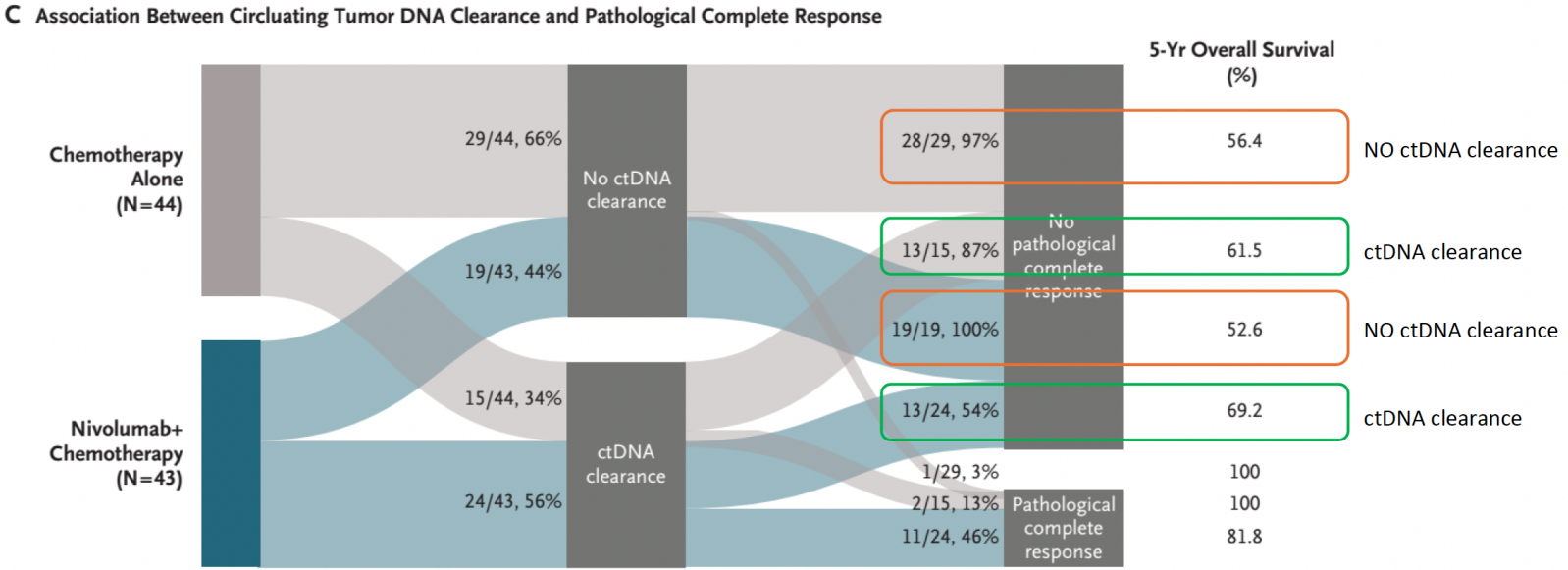


- Correlation between ctDNA clearance and pCR



Brandao ESMO 2026

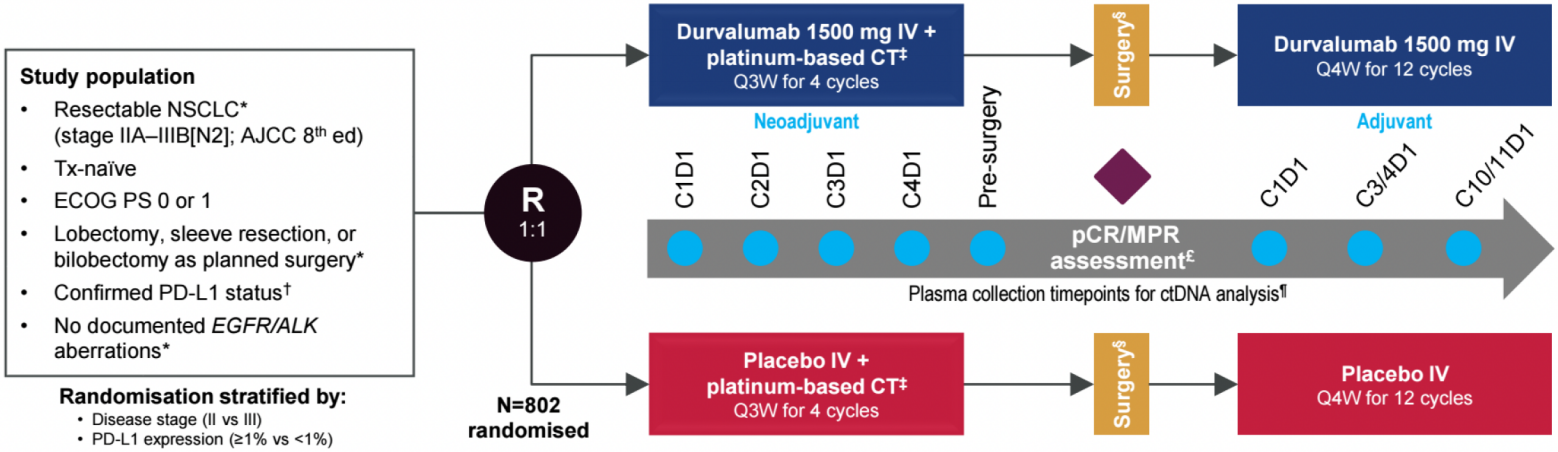
Checkmate 816 (preop)



Brandao ESMO 2026

MRD: AEGEAN

AEGEAN (peri-operative)

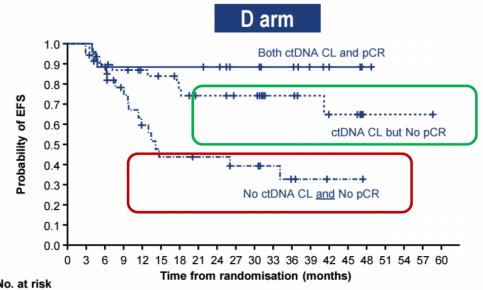


- Plasma samples were collected at protocol-specified timepoints, including prior to each neoadjuvant Tx cycle, surgery, and adjuvant Tx at select cycles
- ctDNA analysis was performed using Invitae Personalized Cancer Monitoring,™ a tumour-informed MRD assay,€[1] with the exploratory analyses reported here based on data from the second EFS interim analysis
  - Patient-specific tumour-informed panels were designed to include 16-50 variants, identified by whole exome sequencing of Tx-naïve diagnostic biopsies only (rather than on-study surgical resections) to avoid selection bias

Brandao M ESMO 2026

ctDNA clearance *before* surgery, pCR and EFS

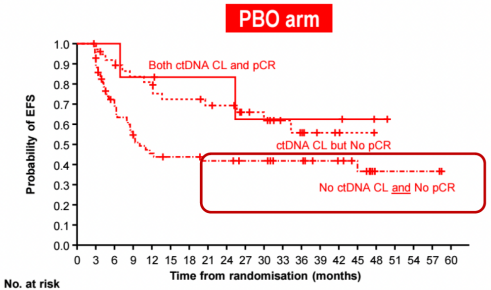
(peri-operative)



No. at risk

Both ctDNA CL and pCR	26	26	23	23	23	23	23	22	18	18	14	14	11	9	7	1	0	0	0	0
ctDNA CL but No pCR	39	39	34	32	29	27	24	21	21	17	17	10	10	8	5	5	1	1	1	0
No ctDNA CL and No pCR	35	33	29	21	15	11	11	10	10	8	8	6	4	3	1	1	0	0	0	0

	Both ctDNA CL and pCR	ctDNA CL but No pCR
HR vs No ctDNA CL and No pCR	0.14 (95% CI: 0.04–0.48)	0.35 (95% CI: 0.16–0.76)
HR vs ctDNA CL but No pCR	0.39 (95% CI: 0.11–1.41)	–



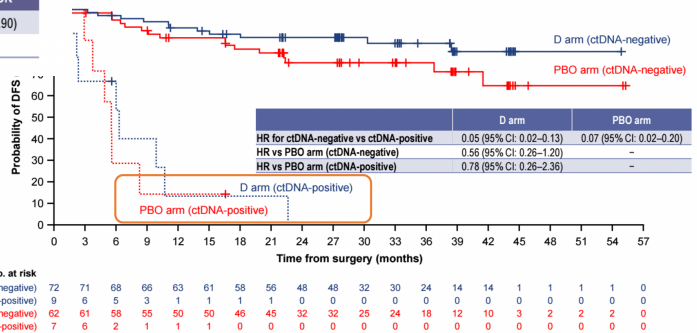
No. at risk

Both ctDNA CL and pCR	6	6	6	5	5	4	4	4	4	3	3	3	3	3	3	2	1	0	0	0	0
ctDNA CL but No pCR	39	38	34	30	29	25	25	23	22	17	16	10	7	3	2	1	0	0	0	0	0
No ctDNA CL and No pCR	63	60	41	31	25	23	23	21	21	17	17	14	14	11	10	7	2	2	2	2	0

	Both ctDNA CL and pCR	ctDNA CL but No pCR
HR vs No ctDNA CL and No pCR	0.40 (95% CI: 0.09–1.65)	0.48 (95% CI: 0.26–0.90)
HR vs ctDNA CL but No pCR	0.80 (95% CI: 0.18–3.55)	–

e *after* surgery and EFS

AEGEAN
(peri-operative)

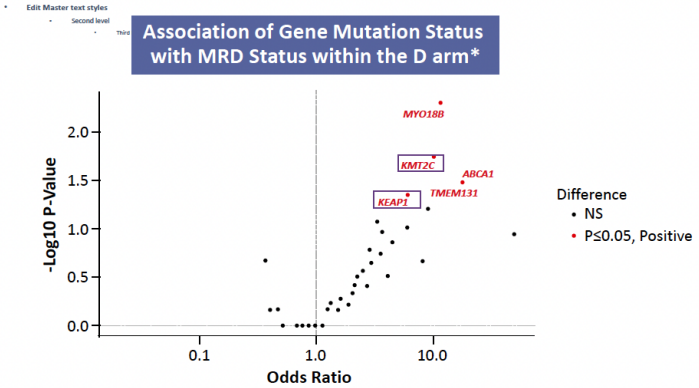


	D arm	PBO arm
HR for ctDNA-negative vs ctDNA-positive	0.05 (95% CI: 0.02–0.13)	0.07 (95% CI: 0.02–0.20)
HR vs PBO arm (ctDNA-negative)	0.56 (95% CI: 0.26–1.20)	–
HR vs PBO arm (ctDNA-positive)	0.78 (95% CI: 0.26–2.36)	–

No. at risk

D arm (ctDNA-negative)	72	71	68	66	63	61	58	56	48	48	32	30	24	14	14	1	1	1	1	0
D arm (ctDNA-positive)	9	6	5	3	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
PBO arm (ctDNA-negative)	62	61	58	55	50	50	46	45	32	32	25	24	18	12	10	3	2	2	2	0
PBO arm (ctDNA-positive)	7	6	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

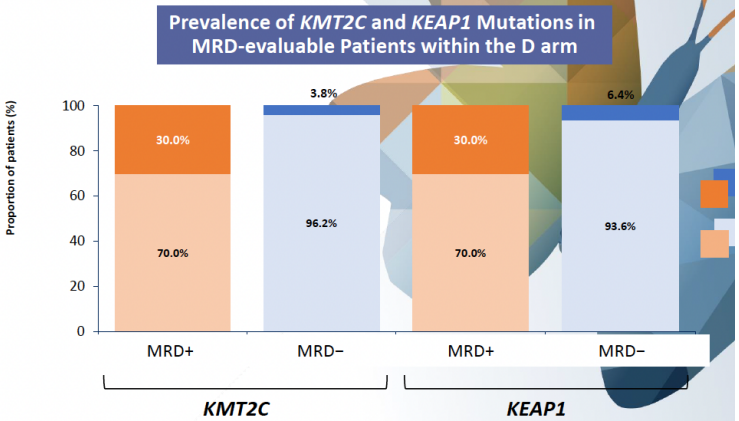
AEGEAN Exploratory Exomewide Analysis to Identifv Candidate Mutations Assoc w/MRD



	D arm		PBO arm		Regardless of Tx	
	OR	P	OR	P	OR	P
ABCA1	17.917	0.033	0	1	4.822	0.114
TMEM131	17.917	0.033	0	1	3.189	0.188
MYO18B	11.656	0.005	0	1	4.280	0.038
KMT2C	10.165	0.018	0	0.587	2.260	0.209
KEAP1	6.042	0.044	0	1	3.345	0.107

- Within the PBO arm, mutated genes associated with MRD+ status included *SLC4A4*, *F5*, and *GRM7*

- Within the D arm, a higher proportion of MRD+ vs MRD− patients had *KMT2C* (30.0% vs 3.8%) and *KEAP1* (30.0% vs 6.4%) mutations



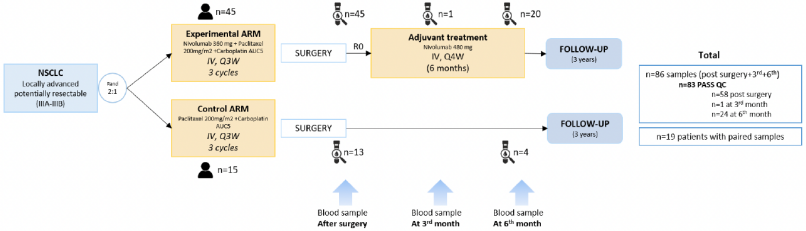
- 62.5% (15/24) and 47.6% (10/21) of patients with *KMT2C* and *KEAP1* mutations, respectively, had persistent ctDNA all evaluable neoadjuvant timepoints

MRD es pronostico independiente de PCR?

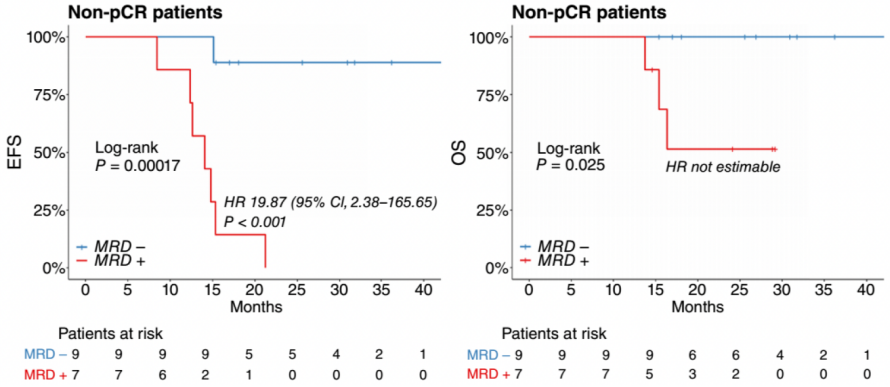
ctDNA clearance *after* surgery, pCR and EFS

NADIMII (peri-operative)

Provencio et al, Clin Cancer Res 2026



Guardant Reveal assay: tumor-agnostic, methylation-based MRD assay



Mariana Brandão, MD/PhD – I
Content of this presentation is c

NADIM II Periop

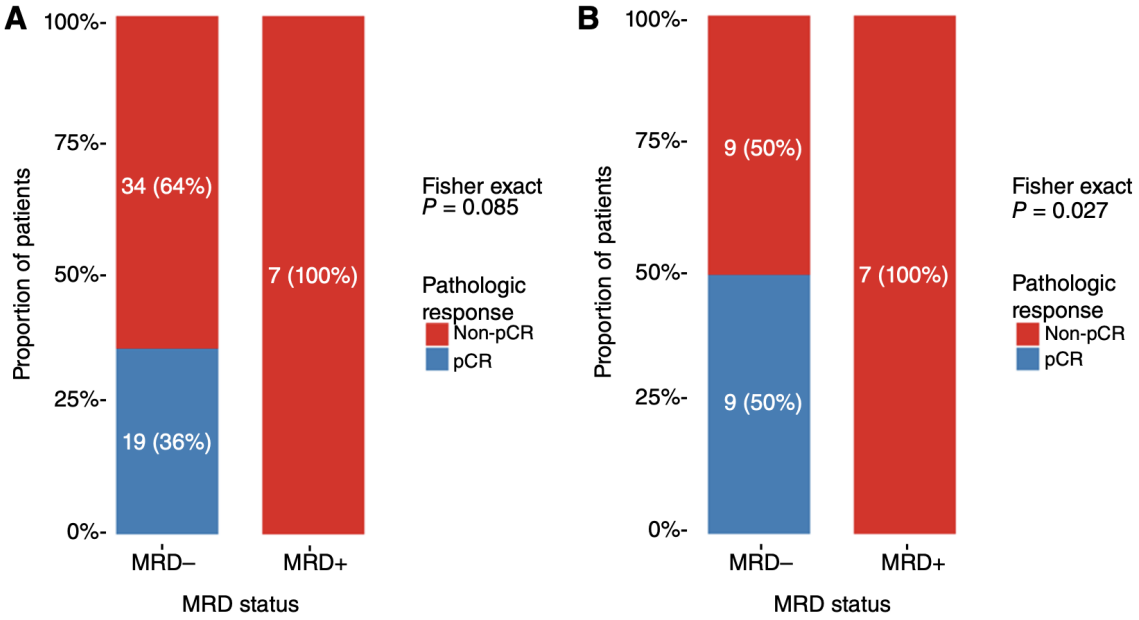
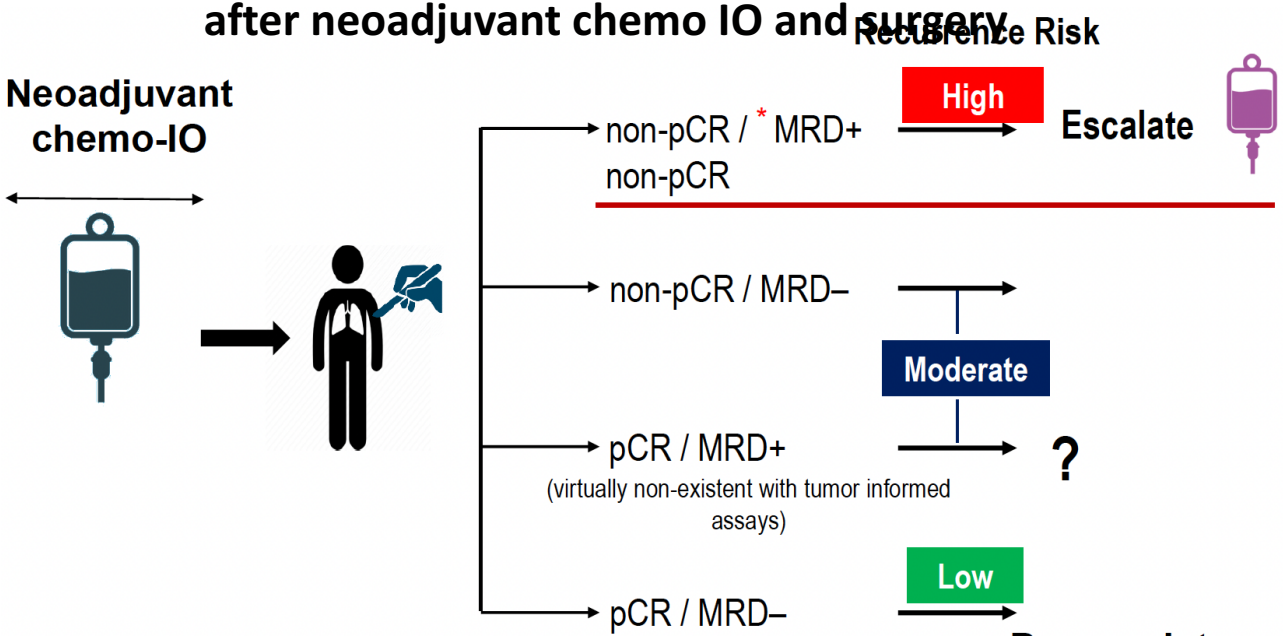


Figure 1.

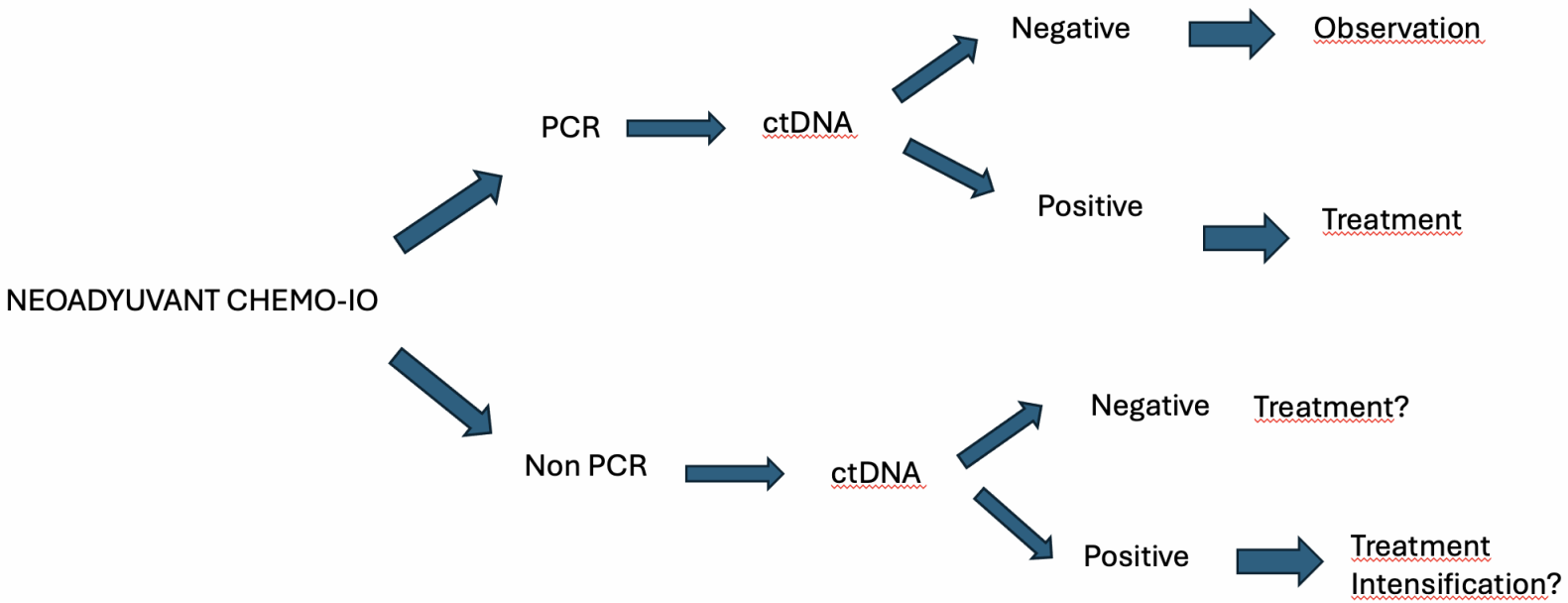
Association of pCR with MRD detection in the whole cohort (**A**) and in the subset including only cases in which MRD was called negative in at least two consecutive plasma samples (**B**).

Response-guided integrative approach to tailor adjuvant therapy in resectable NSLC after neoadjuvant chemo IO and surgery



Agelaki S. IASLC 2026

Estrategias basadas en MRD



Should we perform adjuvant treatment after induction CTIO?

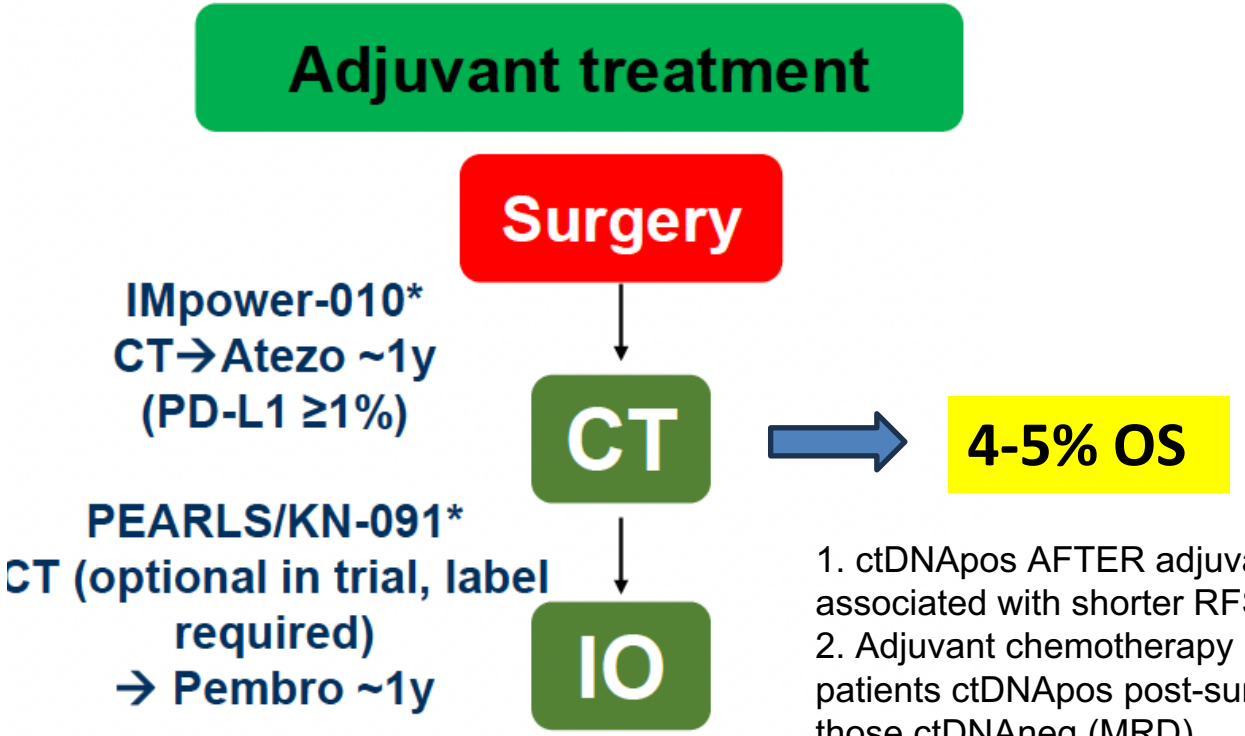
- ADOPT-Lung trial, NCT06284317
- INSIGHT Trial, NCT06498635, enrolling patients with only pCR

What is the optimal adjuvant treatment for patients whose tumors reach no-pCR after CTIO?

- Phase III TroFuse-019 trial (NCT06312137): ADC Anti-Trop2
- Phase III ARIAN trial (NCT06431633): ADC anti-TROP2
- Phase III INTerpath-009 (NCT06623422): mRNA vaccine

Remon ESMo 2026, T an et al. JTO 2026

Cirugía: Tratamiento advuvante (MRD?)

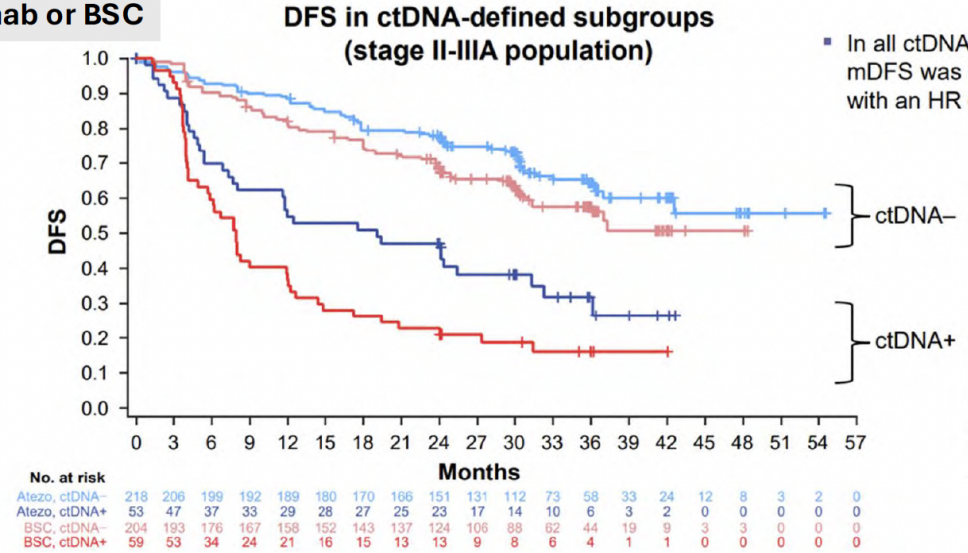


1. ctDNApos AFTER adjuvant chemotherapy associated with shorter RFS
2. Adjuvant chemotherapy beneficial in patients ctDNApos post-surgery; but not in those ctDNAneg (MRD)

Atezolizumab adyuvante. MRD (solo pronostico, no predictivo de respuesta)

Adjuvant chemo followed by Atezolizumab or BSC

Slide courtesy of Prof Solange Peters



- In all ctDNA-evaluable stage II-IIIA patients, mDFS was NR (atezo) vs 31.4 months (BSC), with an HR of 0.69 (95% CI: 0.53, 0.89)

ctDNA–	Atezo (n=218)	BSC (n=204)
mDFS, mo	NR	NR
HR (95% CI)	0.72 (0.52, 1.00)	

Benefit only In PD-L1 ≥50%

ctDNA+	Atezo (n=53)	BSC (n=59)
mDFS, mo	19.1	7.9
HR (95% CI)	0.61 (0.39, 0.94)	

Benefit regardless of PD-L1

Zhou C et al. Ann Oncol 2021
Felip E et al Ann Oncol 2022

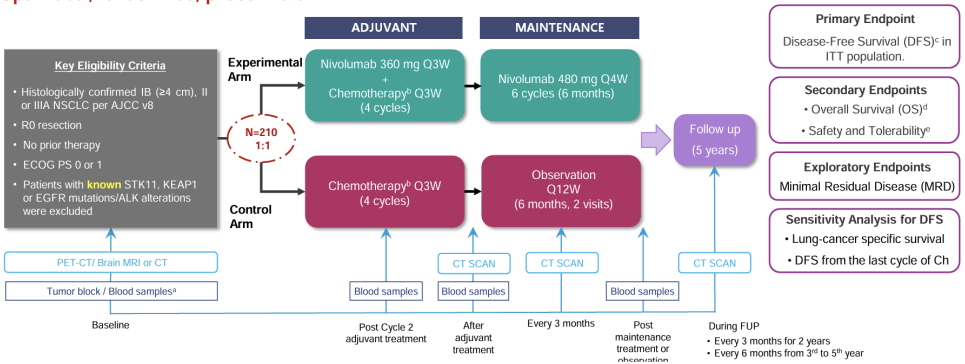
Signatera™ can detect VAF down to 0.01%. It is tumour-informed

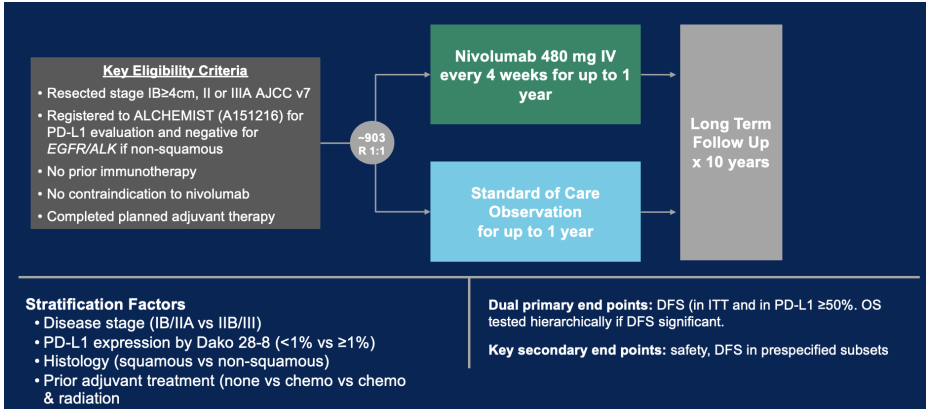
Tratamiento adyuvante con IO tras cirugía

- NADIM ADYUVANT and ALCHEMIST/ANVIL

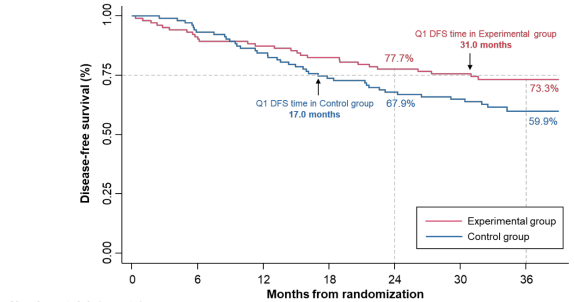
NADIM ADJUVANT STUDY DESIGN

Open-label, randomized, phase III trial





PRIMARY ENDPOINT: DISEASE-FREE SURVIVAL (DFS)



	Experimental (n=103)	Control (n=103)
Median DFS (95% CI), months	Not reached	Not reached
HR_{3years} (95% CI)	0.65 (0.40-1.07)	
P value	0.085[a]	

Median follow-up: 34.0 mo (IQR: 32.6-36.6)

Maturity data: 57%

Results

HR 0.97
DFS (ITT)
p = 0.78

HR 0.86
PD-L1 ≥ 50%
p = 0.43

25%
Grade 3-5 toxicity

Consenso GECP: Recibir Inmunoterapia adyuvante (independiente de MRD)

Table 4 Suggestions for postoperative evaluation of patients with resected NSCLC (updated*)

Statement	GoR/LoE
Adjuvant radiation therapy for patients with resected NSCLC indication should be individualized and discussed within an MTC. It is reasonable to administer this local treatment in case of R1 resection. In case of confirmed N2 nodal involvement, it is also reasonable in specific cases, including extracapsular nodal disease in the affected N2 station and R1 and R2 lymph node resection	IIIC
Patients with resected NSCLC, tumors ≥5 cm or with positive nodes and PD-L1 ≥50%, non-mutated *EGFR* and without *ALK* rearrangement should receive platinum-based chemotherapy followed by atezolizumab as adjuvant treatment*	IA
Patients with resected NSCLC, tumors ≥4 cm, or positive nodes, regardless of PD-L1 level, should receive platinum-based chemotherapy followed by pembrolizumab as adjuvant treatment*	IA

Ospina-Serrano et al. Early and locally advanced NSCLC: GECP expert consensus

Important Considerations for Evaluating ctDNA MRD Results in Early Stage NSCLC



A **positive** ctDNA MRD result implies an extremely high risk of recurrence

- >90-95% of patients will recur in absence of further treatment



A **negative** ctDNA MRD result does not mean cure

- Up to two-thirds of patients whose cancer will ultimately recur have initially false negative ctDNA MRD results
- Indicates higher sensitivity MRD assays are needed

Conclusiones

- No existen comparaciones directas entre los enfoques de quimioterapia e inmunoterapia (QT-ICI) neoadyuvantes y los perioperatorios en pacientes con CPCNP.

- La respuesta patológica completa (pCR) y la respuesta patológica mayor (MPR) se asocian firmemente con mejores resultados en diversos estudios

- , la expresión de PD-L1 y la eliminación del ADN tumoral circulante (ctDNA) se relacionan con tasas más elevadas de pCR y MPR.

- Los pacientes que presentan tumor viable residual tras la QT-ICI neoadyuvante, o que mantienen ctDNA detectable en plasma, muestran una peor supervivencia libre de eventos (EFS) y supervivencia global (OS) en los distintos estudios. ESCALAR

XVIII SIMPOSIUM

BASES BIOLÓGICAS DEL CÁNCER E INNOVACIÓN TERAPÉUTICA

arly and locally advanced NSCLC: ESMO Clinical Practice Guidelines Published online: 28 August 2025 - Annals of Oncology Zer A, Ahn MJ, Barlesi F, et al., on behalf of the ESMO Guidelines Committee

• There have been no direct comparisons between neoadjuvant and perioperative ChT–ICI approaches in patients with NSCLC.

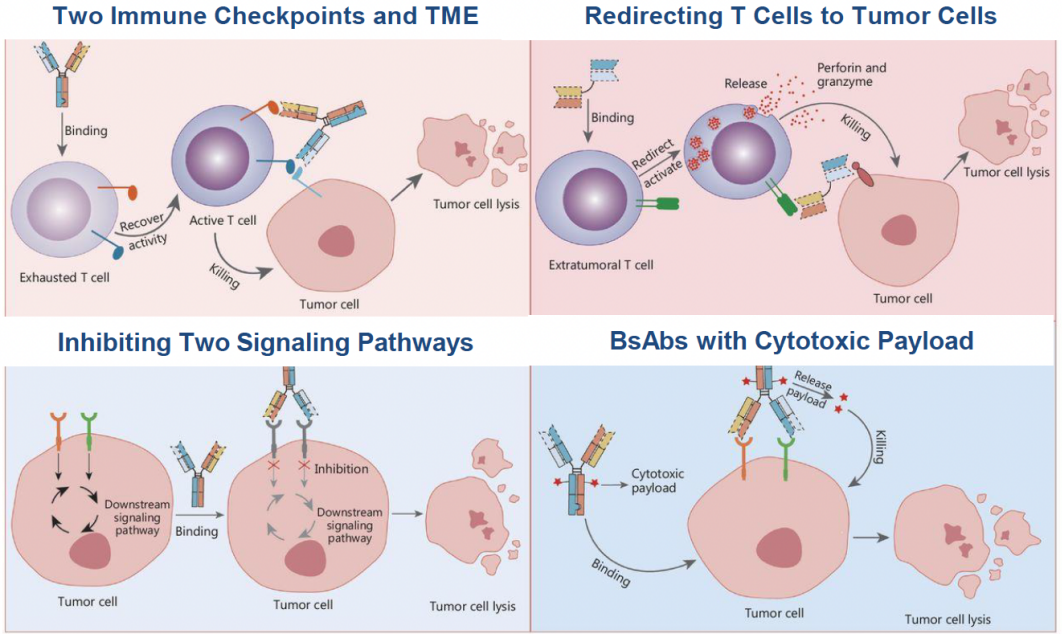
• pCR and MPR are strongly associated with better outcomes across studies, while PD-L1 expression and ctDNA clearance are associated with higher rates of pCR and MPR. Further studies are needed to define which patients require only neoadjuvant ChT–ICI versus continued ICI after resection; for example, in the setting of pCR after neoadjuvant ChT–ICI.

• Patients with residual viable tumor after neoadjuvant ChT–ICI or persistent ctDNA in plasma have poor EFS and OS across studies. Additional approaches to improve outcomes are needed.

• Discussion of these challenging scenarios at MDT is encouraged along with clinical trials addressing opportunities for treatment de-escalation and intensification

Bispecific Antibodies (BsAbs) Targets & Biomarkers

- PDL-1
- LAG-3
- TIGT
- VEGF/R
- TGFβ

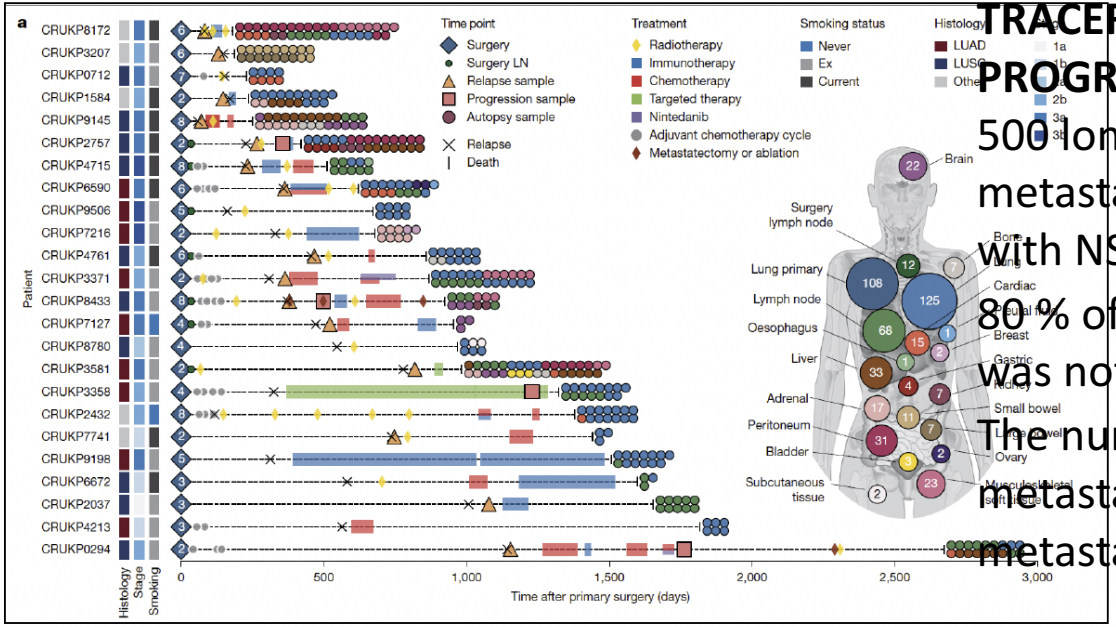


- EpCAM
- CEA
- DDL3 (SCLC)

- EGFR
- HER2
- C-Met
- HER3

- EGFR
- HER3
- FRα

Junxu Wen et al. Cancer Biology & Medicine, 202



TRACER-X LUNG STUDY AND PEACE AUTOPSY PROGRAM

500 longitudinally collected primary and metastatic tumor samples from 24 patients with NSCLC

80 % of metastases contained a subclone that was not detected in any other metastasis

The number of subclones detected per metastasis increased with the number of metastasis regions sampled

Hessey et al. Nature 2026

Tissue NGS: limitations and false negatives

The "gold standard" has significant real-world constraints

Tissue NGS: the gold standard with significant real-world limitations

Small biopsy samples (EBUS-TBNA, CT-guided biopsy) frequently yield insufficient tumour cellularity for NGS; tissue stewardship is critical

In US real-world studies, as few as 18% of patients with aNSCLC had sufficient tissue to screen all guideline-recommended biomarkers

UK NGS failure rates: <5% for DNA, 10–20% for RNA; 5–10% for PD-L1 IHC — confirmed by National Lung Cancer Audit data

DNA-only assays miss gene fusions (ALK, ROS1, RET, NTRK, NRG1) — RNA co-testing essential but poor uptake & high failures due to over fixation

Biological and pre-analytical sources of false negatives

Intra-tumour heterogeneity: biopsy may not capture spatially distinct subclonal drivers of resistance mutations8

Formalin fixation artefacts, decalcification damage, low tumour fraction following IHC use, and degraded FFPE nucleic acids all reduce sensitivity

Exhaustion of limited tissue before NGS due to excess IHCs and poor tissue cutting protocols

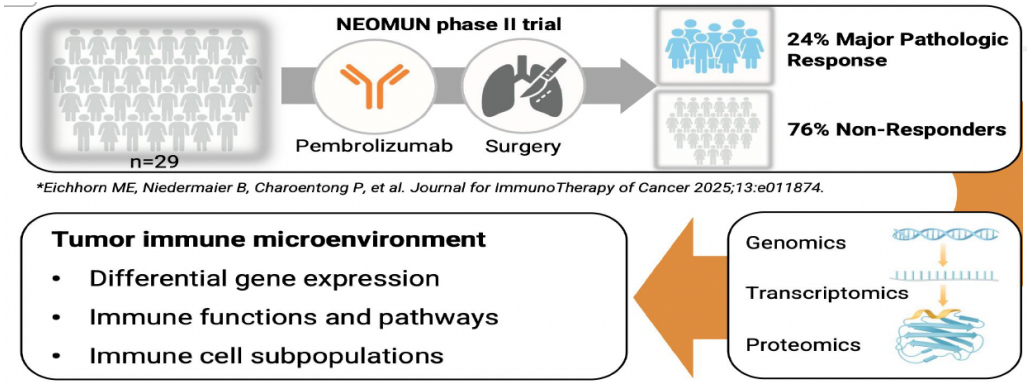
3 potential genomes under analysis:

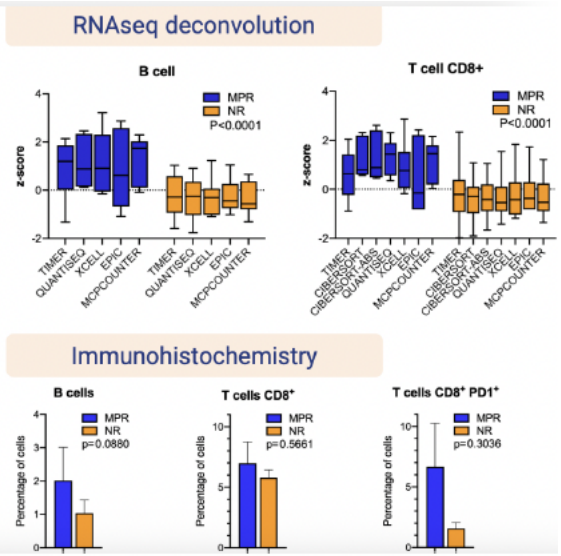
1. Somatic genome (the cancer under scrutiny)
2. Germline genome (the human being sampled)
3. Leucocyte genome (CHIP variants)
4. Another potential concurrent cancer (incidental cancer)

5.Variants from other benign tissues

PLUS escasos "SHEDDERS "

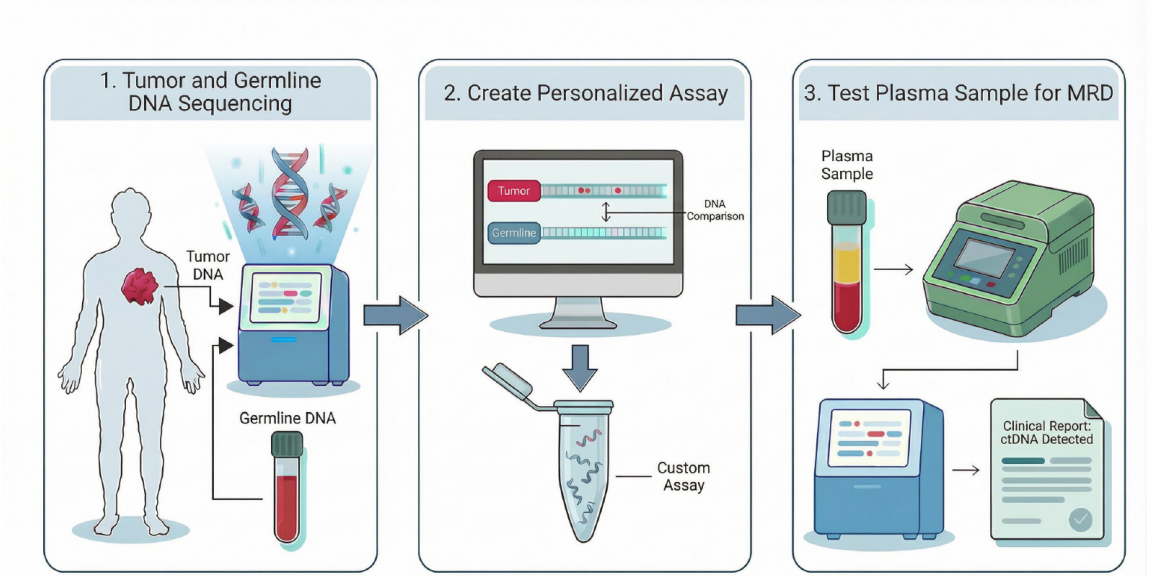
Multi-omics Analysis of Neo-Adj Pembro





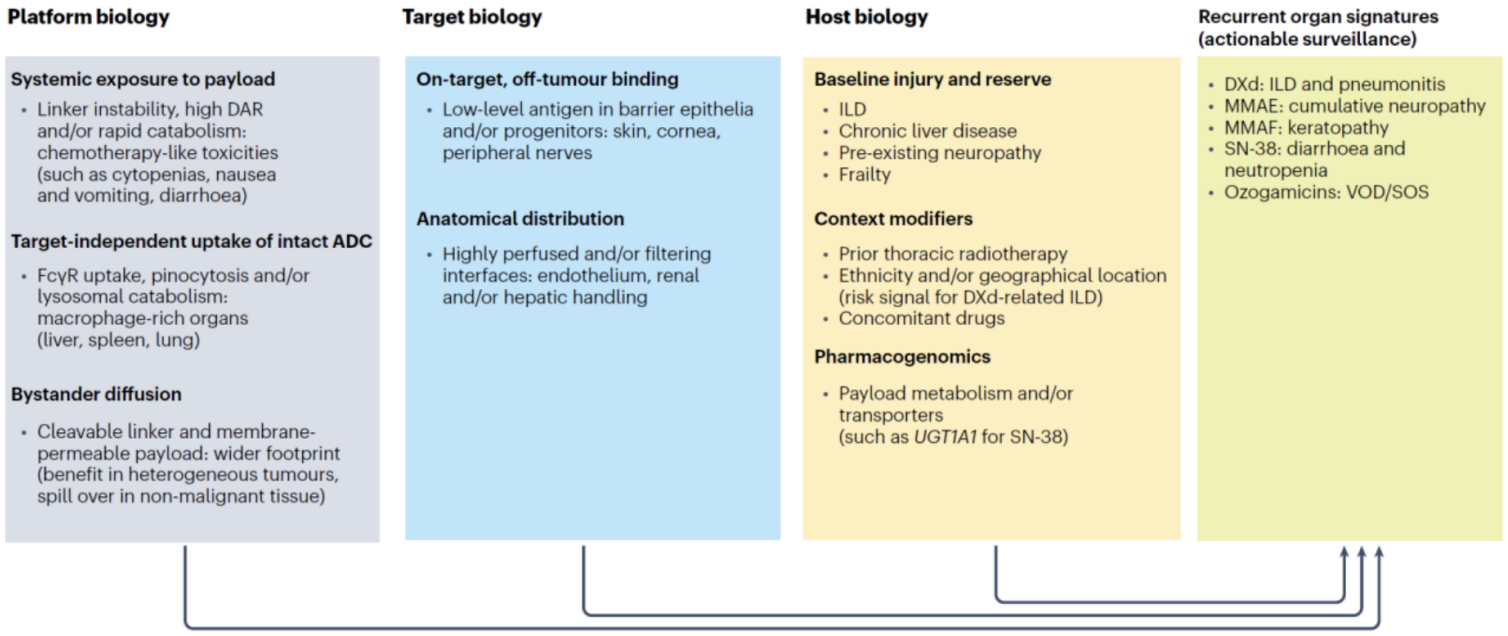
- The immune microenvironment in MPR-tumors differs from Non-Responders
- Confirms **T cell immunity** as key effector of Pembrolizumab
- Highlights the importance of **B cell immunity** in facilitating immunotherapy response

Tumor-Informed MRD Testing Workflow



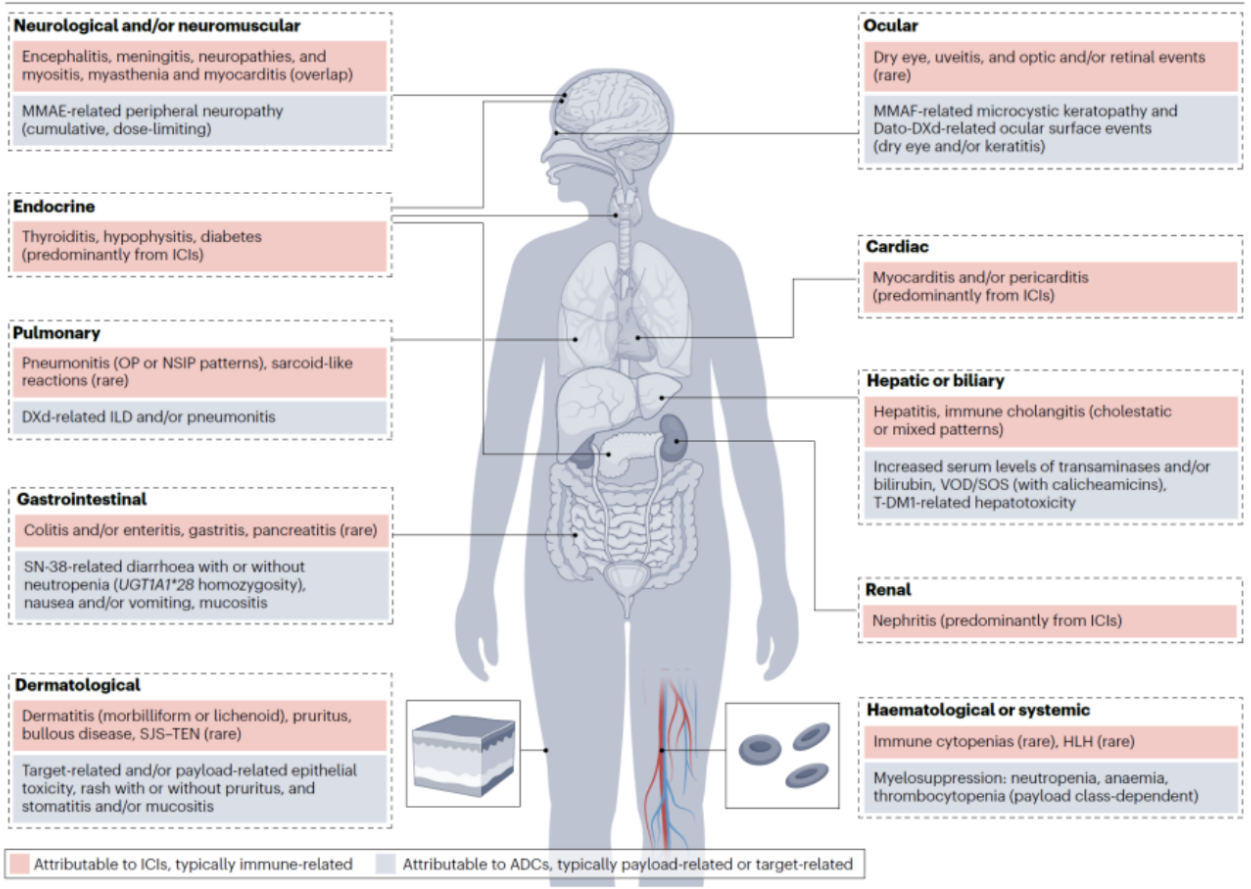
Due to sensitivity advantages, tumor-informed assays have emerged as the preferred approach for detecting ctDNA MRD

Toxicidades de ICI + ADCs



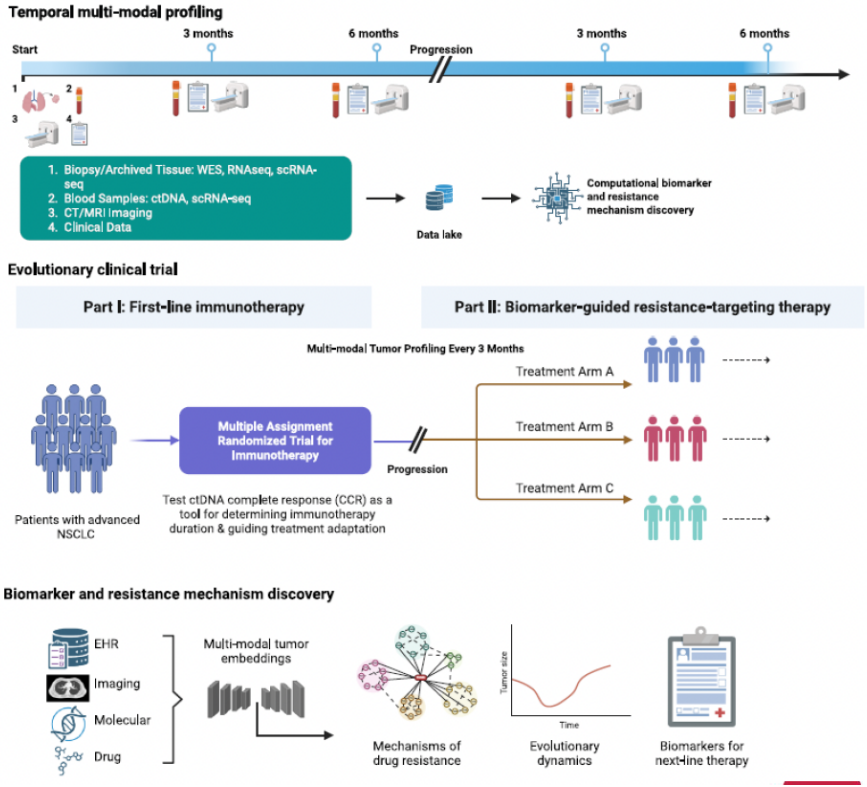
payload-independent effects to organ-level toxicity signatures.

Peters S. NRCo 2026



Peters S. NRCo 2026

IMMUNO-BIOMAP - *An adaptive multimodal framework*



Nath A, et al. Cell Rep Med. 2026

TRAcking NSCLC Evolution through therapy (
TRACERx
)

fDrug Tolerant Presister Cells (DTPC) serve as a reservoir where
acquired resistance develops

New clinical frameworks and methods must be developed to

TRAcking NSCLC Evolution through therapy (
TRACERx
)

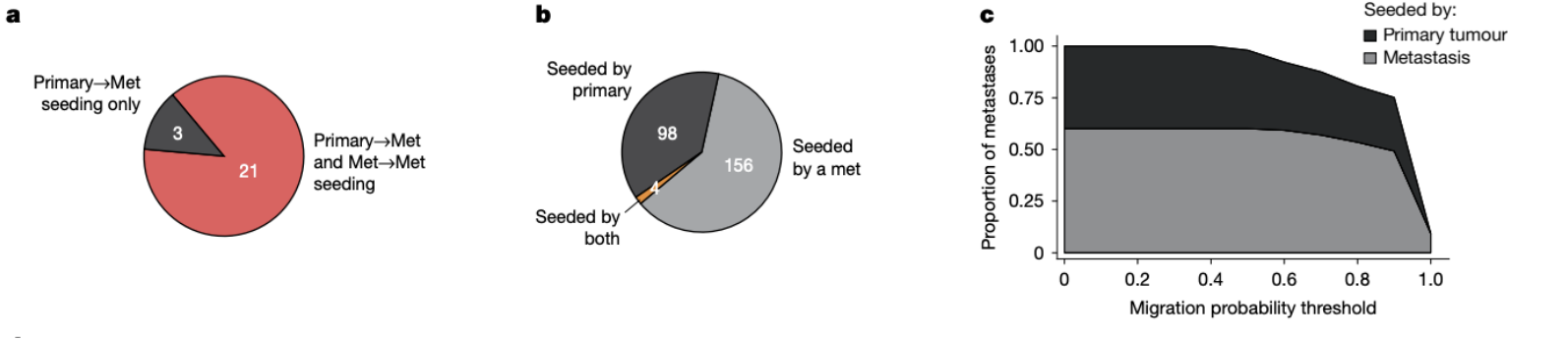


Fig. 3 | Metastatic seeding patterns. a, Number of patients whose metastases were seeded exclusively by the primary tumour (Primary->Met seeding only, black) or by both the primary tumour and other metastases (Primary->Met and Met->Met seeding, red). b, Number of metastases seeded by the primary tumour (black), by another metastasis (grey) or by both sources (yellow). c, Proportion of metastases seeded by other

Nature | Vol 653 | 21 May 2026 |

Currently 2 US FDA approved ctDNA assays for MRD detection
CLIA/CAP certified clinical tests are covered by Medicare for solid tumors
Many More Coming Globally
But not in NCCN Guidelines yet
Tumor Informed Assays Proven to Detect Relapse
Data from other Diseases
Data from “Real-World”
Data from Randomized Trials
Is that data Useful/Predictive? Or Just Prognostic?
In current Stage: Positive test mean very high risk and more therapy needed (but what?)
Negative test means better prognosis, but does NOT mean cure, more sensitivity needed

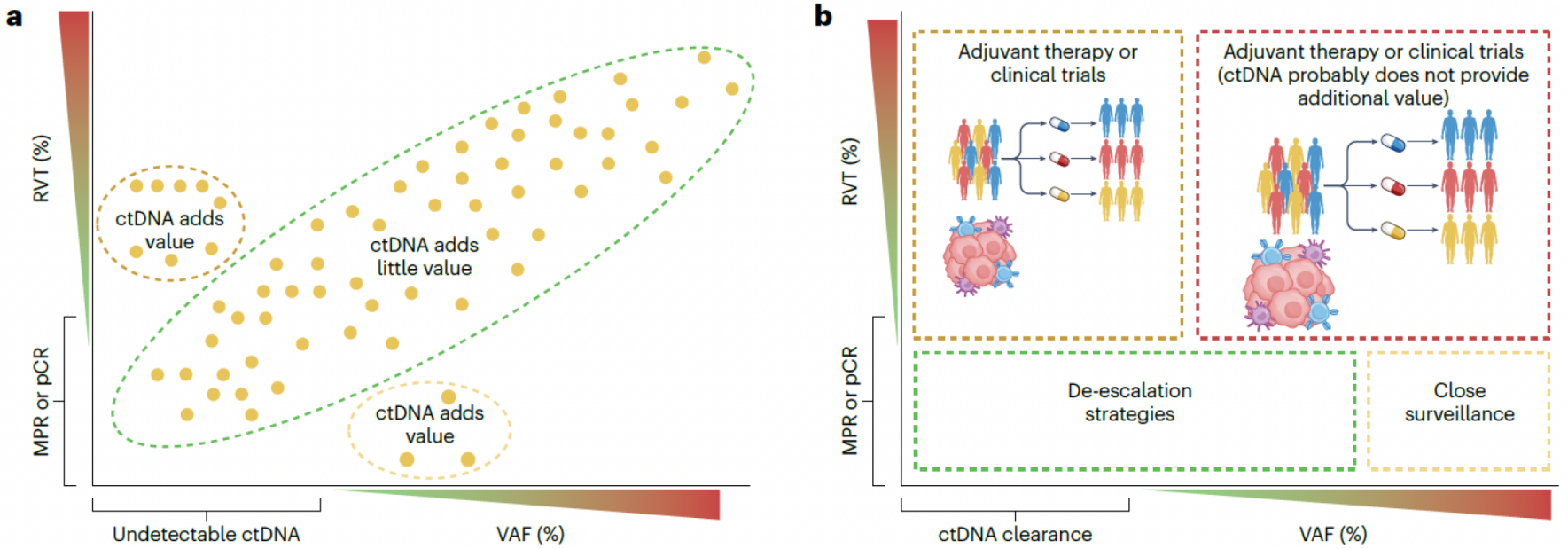
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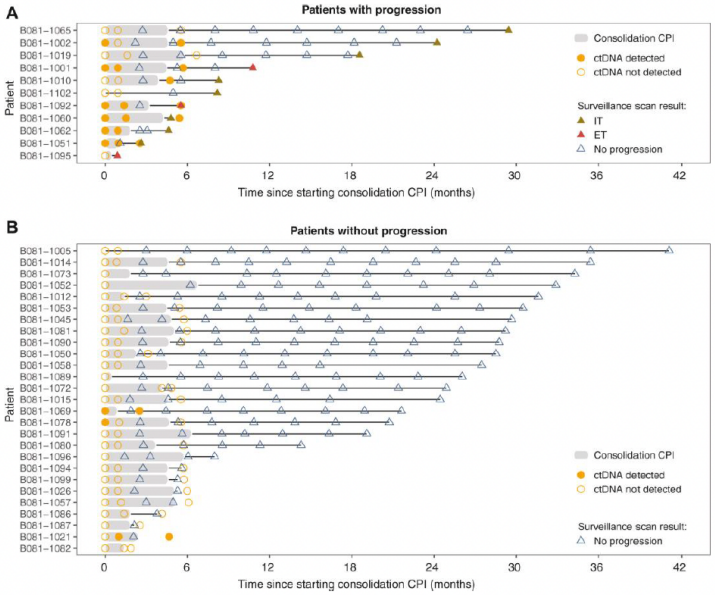
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- Discussion of these challenging scenarios at MDT is encouraged along with clinical trials addressing opportunities for treatment de-escalation and intensification



GaritaonaindiaY, et al. Nat Rev Clin Oncol. 2026;23:712–729.

Persistence of ctDNA in liquid biopsy is highly correlated with progression



Source: Jun, Shukla, Durm et al. (2024) J Thorac Oncol (NCT03285321)

Case Study

- Characterization of the relationship between ctDNA and clinical outcomes in patients with unresectable locally advanced NSCLC after a short-course of immunotherapy after CRT (NCT03285321)
- Detection of ctDNA predicted significantly inferior PFS

Key Lessons

- Patients with detectable ctDNA may need earlier intervention or benefit from treatment intensification

Ongoing Study

- Risk-stratified comparison of osimertinib versus osimertinib plus chemotherapy for patients with persistent EGFRm ctDNA (**SHEDDER** - NCT04410796)

Jun, Shukla, Durm et al. (2024) J Thorac Oncol (NCT03285321