

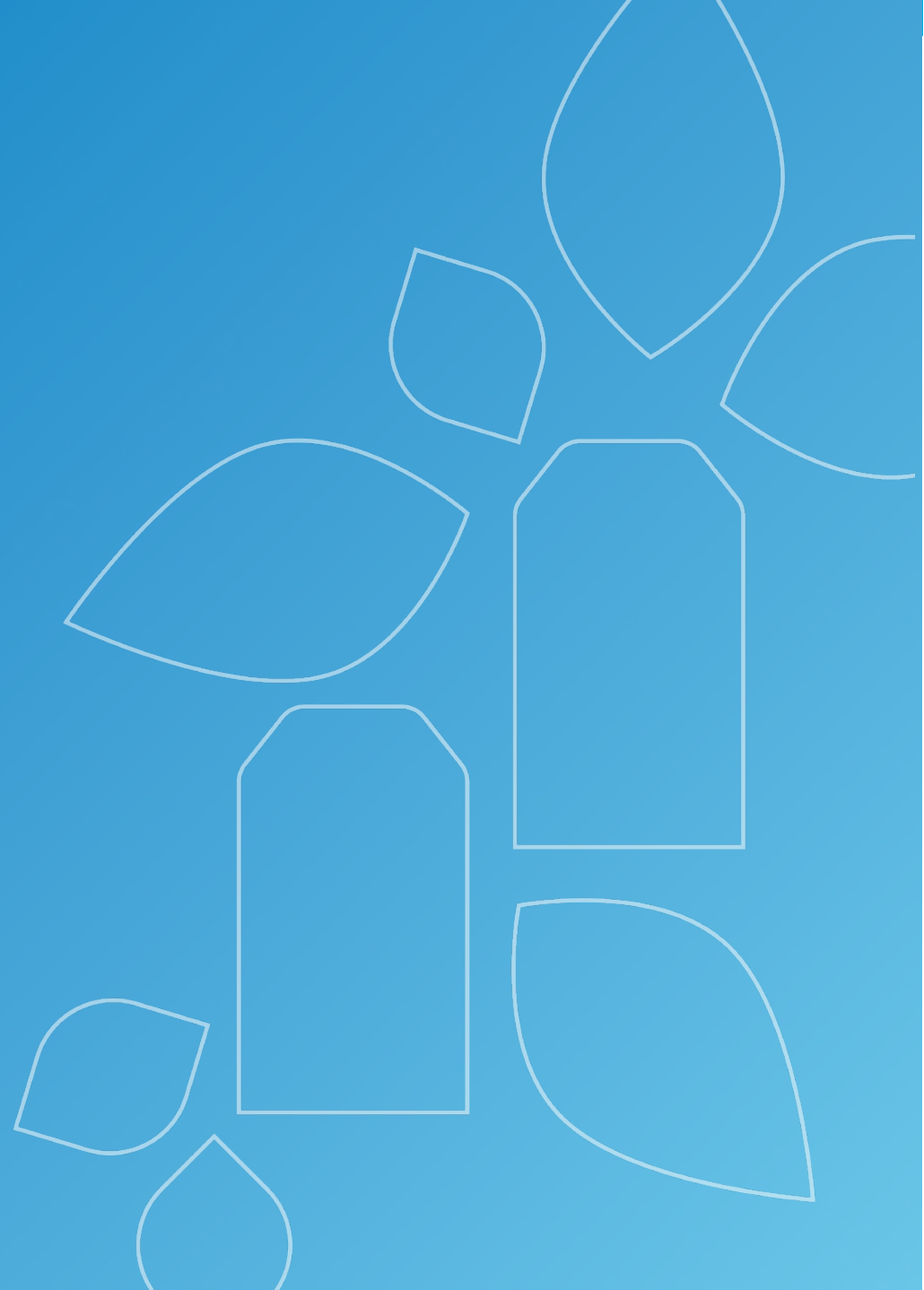


Southeastern Multidisciplinary Approaches to Cancer Symposium

Perioperative and Neoadjuvant Approaches in Early Stage, Resectable NSCLC

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City Of Hope



Disclosures

I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.



Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed [Assembly Bill \(AB\) 1195](#), which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed [AB 241](#), which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

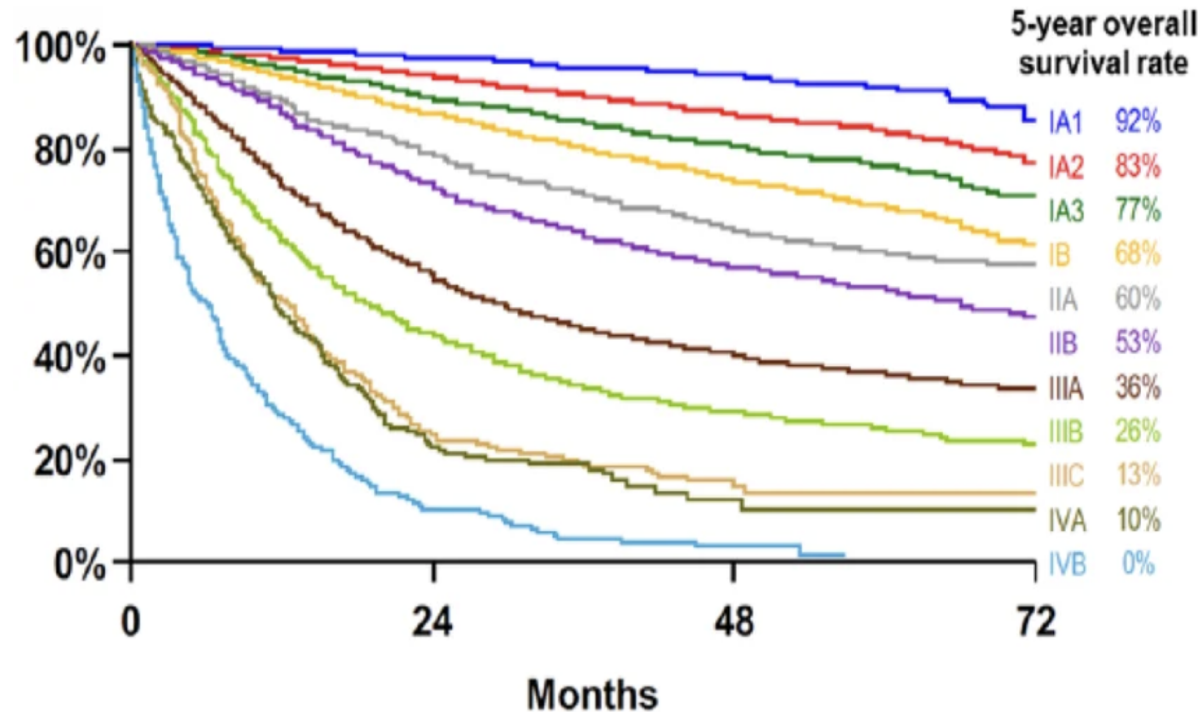
- *Access to targeted medication.*
- *Screening for lung cancer in smokers vs non smokers.*



Early-Stage Non-Small Cell Lung Cancer (NSCLC)

- Early-stage non–small cell lung cancer (NSCLC) accounts for **up to 40% of all newly** diagnosed lung cancer cases
- **Lung Cancer Screening** has improved the detection of early-stage NSCLC
- **Neoadjuvant, adjuvant, and perioperative therapies** have transformed the treatment landscape for resectable NSCLC over the last few years
- Optimal therapy for resectable early-stage NSCLC **continues to evolve...**

High recurrence rates after resection in early-stage lung cancer



5-year overall survival rates of patients with non-small cell lung cancer according to the 8th edition TNM staging.

- ~30%-60% recurrence risk after surgical resection for patients with stage IB – IIIA NSCLC^{1, 2}.
- Standard of care for several decades has been adjuvant cisplatin-based chemotherapy,
 - HR 0.89 (95% CI: 0.82-0.96)
 - 5.4% improvement in 5yr OS³
- More recently – paradigm shifts in **perioperative chemo-immunotherapy** and **adjuvant targeted therapy** have revolutionized care for patients with early stage NSCLC⁴.

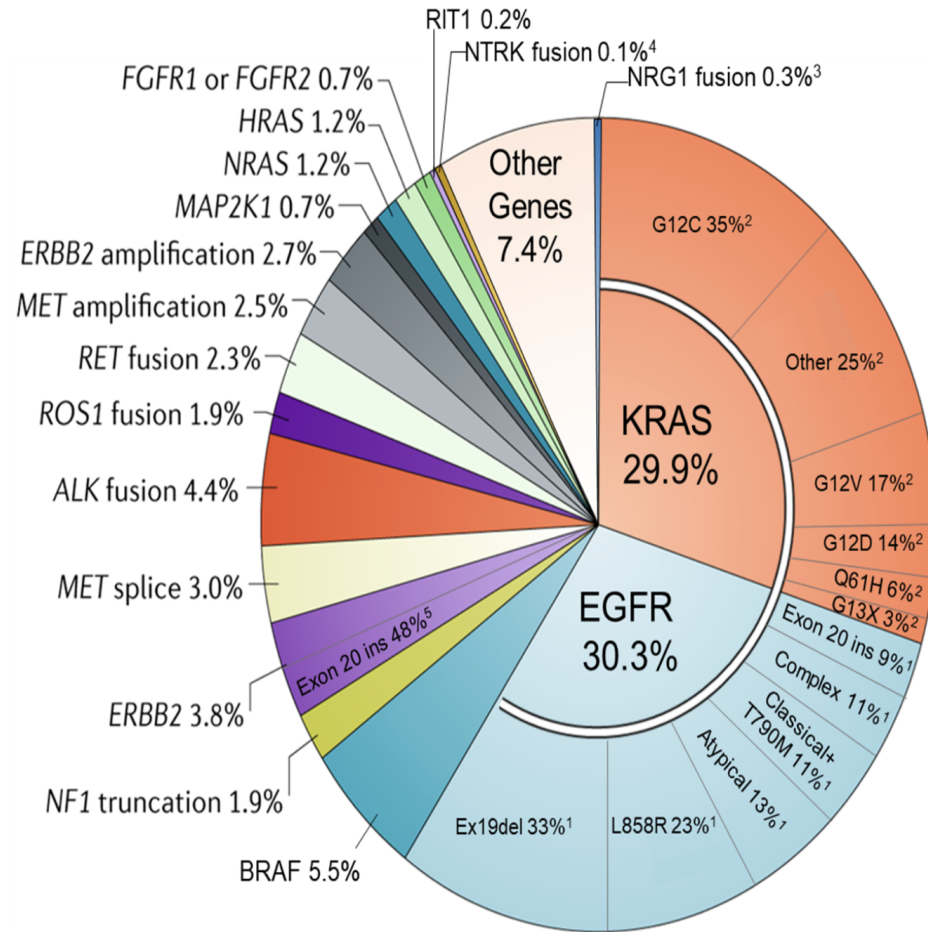
1) Goldstraw P. *J Thorac Oncol* 2016; 11:39-51

2) Deslypere G. *Ther Adv Med Oncol* 2018; 10:1-11

3) Pignon LP. *J Clin Oncol*. 2008; 26, 3552-3559.

4) Spicer JD. *J Thorac Oncol* 2024; 19, 1373-1414.

Biomarker Driven Care in Non-Small Cell Lung Cancer (2026)



Targets with FDA-approved biomarker driven therapies in advanced NSCLC

Gene biomarkers

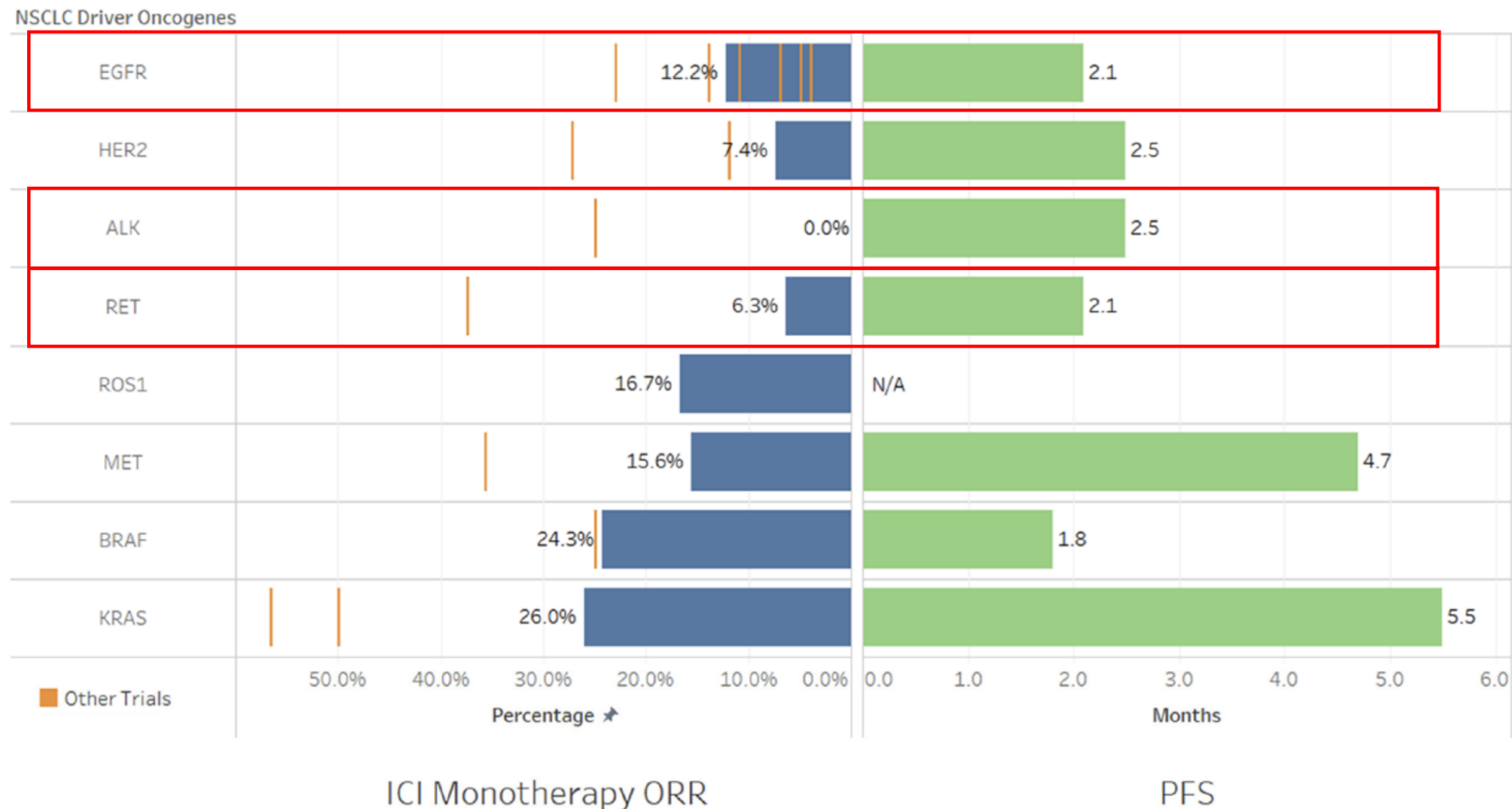
- ALK fusions
- BRAF p.V600E
- EGFR “classical” (ex19del, L858R)
- EGFR “non-classical” (L861Q, G719x, S786I)
- EGFR exon 20 insertions
- HER2 kinase domain
- KRAS p.G12C
- MET exon14 skipping alterations
- NRG1 fusions
- NRTK 1/2/3 fusions
- RET fusions
- ROS1 fusions

Only ALK and EGFR targeted therapies currently have approvals in early-stage NSCLC.

Proteins

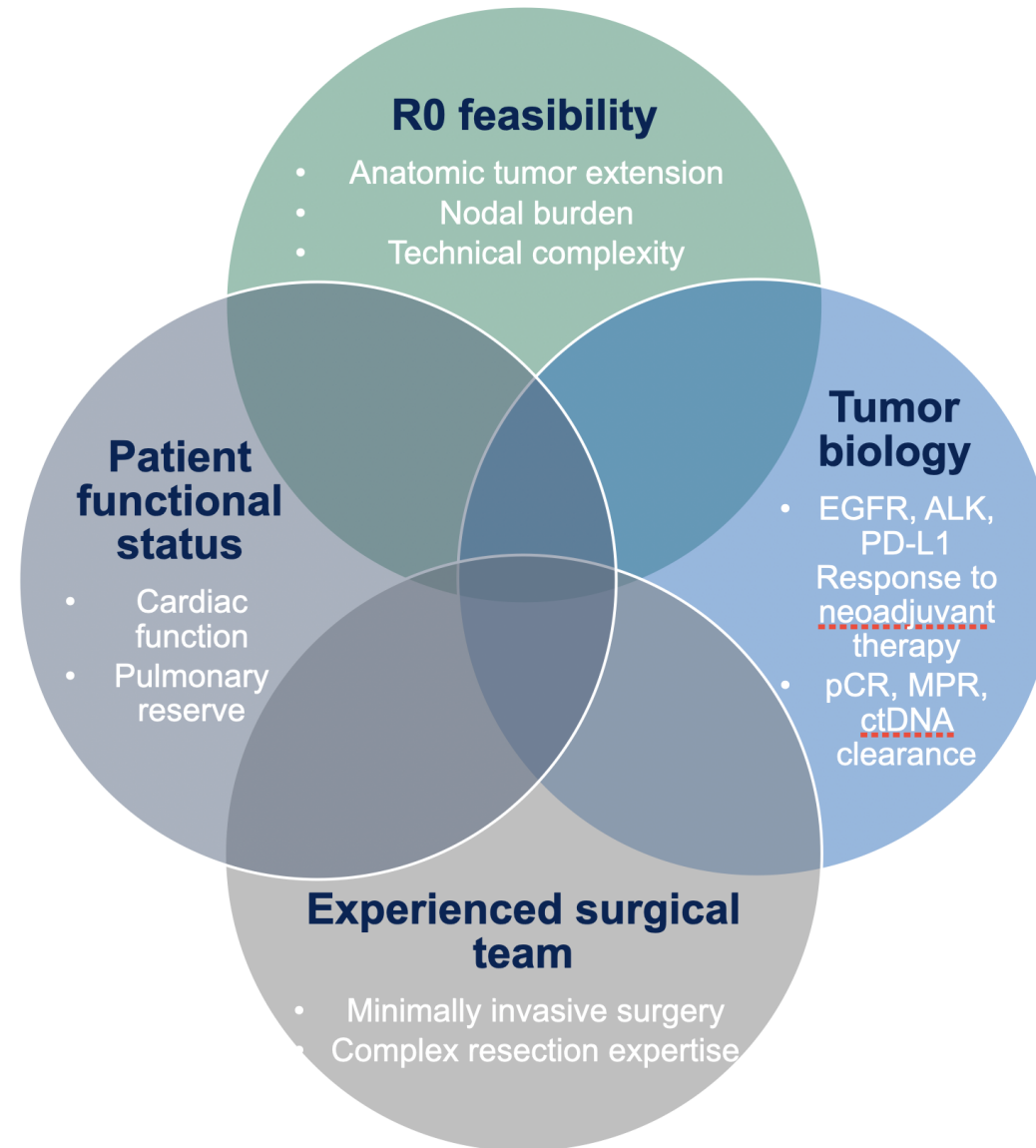
- PD-L1 expression (IHC)
- HER2 expression (IHC)
- MET expression (IHC)

Immunotherapy does not work for some Oncogene addicted NSCLC

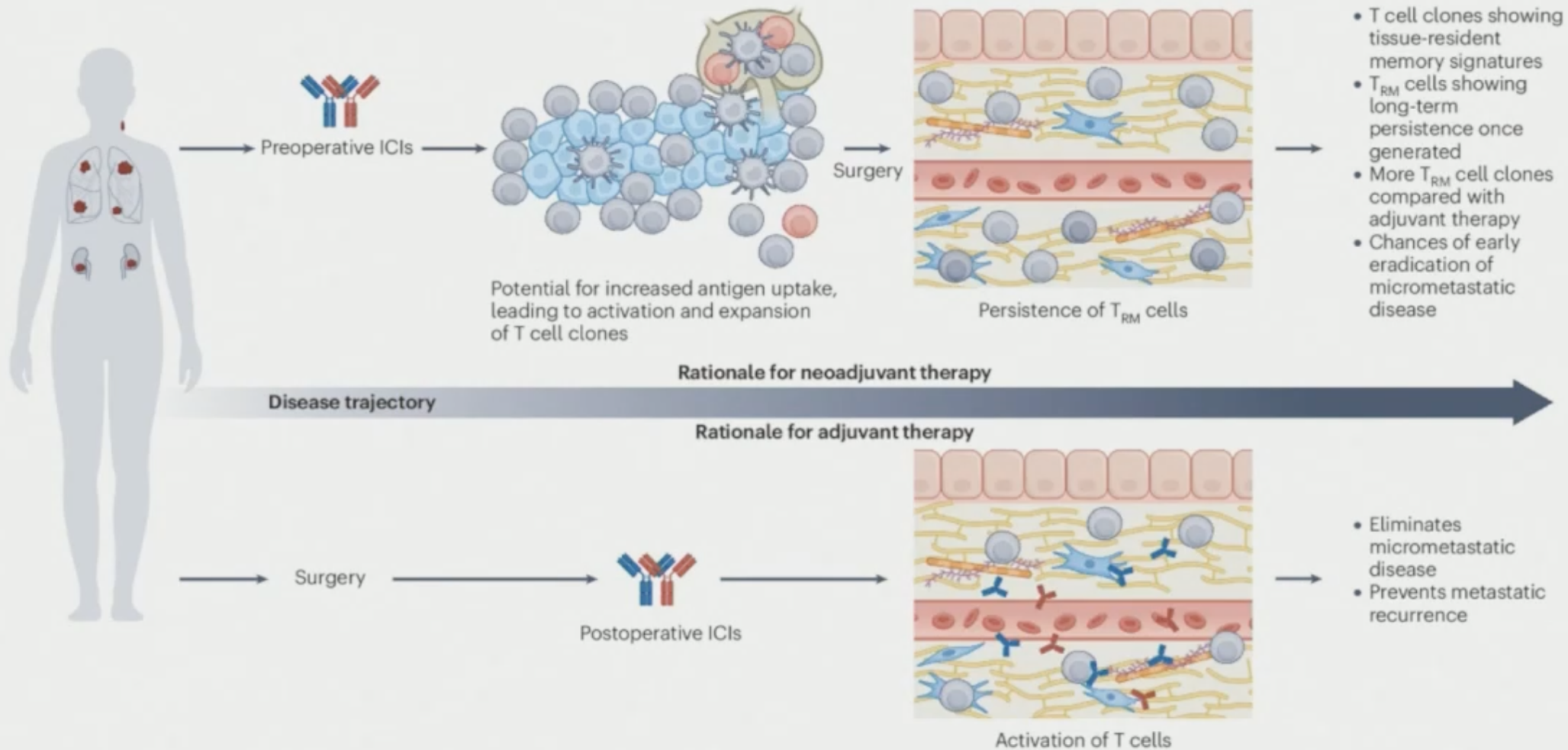


Resectability, redefined

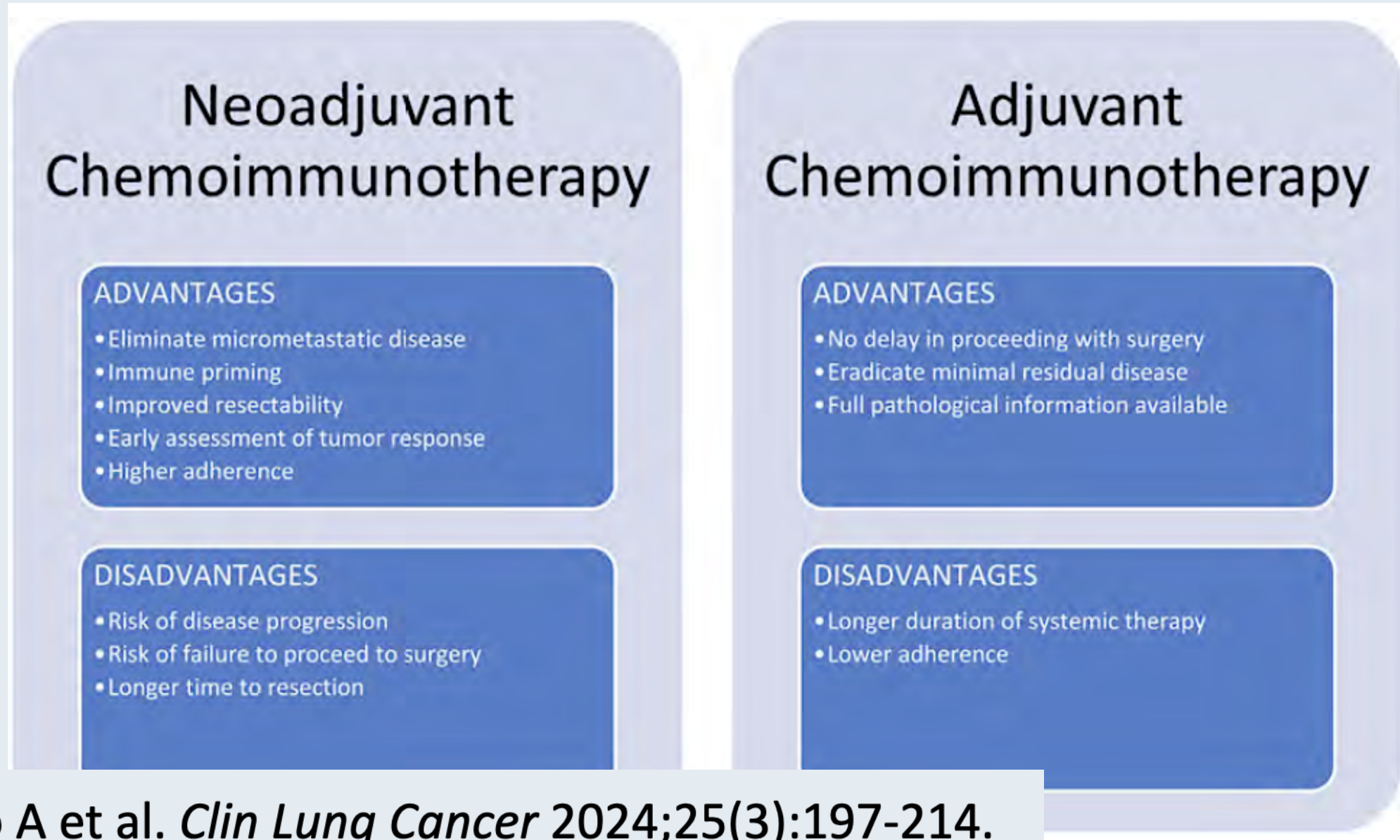
No longer a **radiographic definition**,
but a **multidimensional decision**



Rationale For ICI in Early-Stage NSCLC



Neoadjuvant and Adjuvant Advantages and Disadvantages



Neoadjuvant and Perioperative ICIs in Early-Stage NSCLC (Now with OS benefits!)

Neoadjuvant
treatment

ICI + Chemo
vs
Chemo



Surgery

Perioperative
treatment

ICI + Chemo vs
Chemo



Surgery

ICI
vs Placebo

TRIAL (Phase III)	POPULATION (Stage)	TREATMENT SCHEMA
CHECKMATE-816 <i>Nivolumab + Chemo (Neoadjuvant only)</i>	IB (≥4 cm) – IIIA Resectable NSCLC	NEOADJUVANT ONLY
KEYNOTE-671 <i>Pembrolizumab + Chemo (Perioperative)</i>	II – IIIB (N2) Resectable NSCLC	PERIOPERATIVE (NEOADJUVANT → ADJUVANT)
AEGEAN <i>Durvalumab + Chemo (Perioperative)</i>	II – IIIB (N2) Resectable NSCLC (includes IIIB)	PERIOPERATIVE (NEOADJUVANT → ADJUVANT)
CHECKMATE-77T <i>Nivolumab + Chemo (Perioperative)</i>	II – IIIB (N2) Resectable NSCLC (includes IIIB)	PERIOPERATIVE (NEOADJUVANT → ADJUVANT)

Johnson D, Nassar A...Naqash AR et al. *Nature Reviews Clin Onc* 2026; Forde P et al *ASCO* 2026; Wakelee H et al. *ESMO* 2025

Neoadjuvant and Perioperative ICIs in Early-Stage NSCLC (Now with **OS** benefits!)

Neoadjuvant
treatment

ICI + Chemo
vs
Chemo

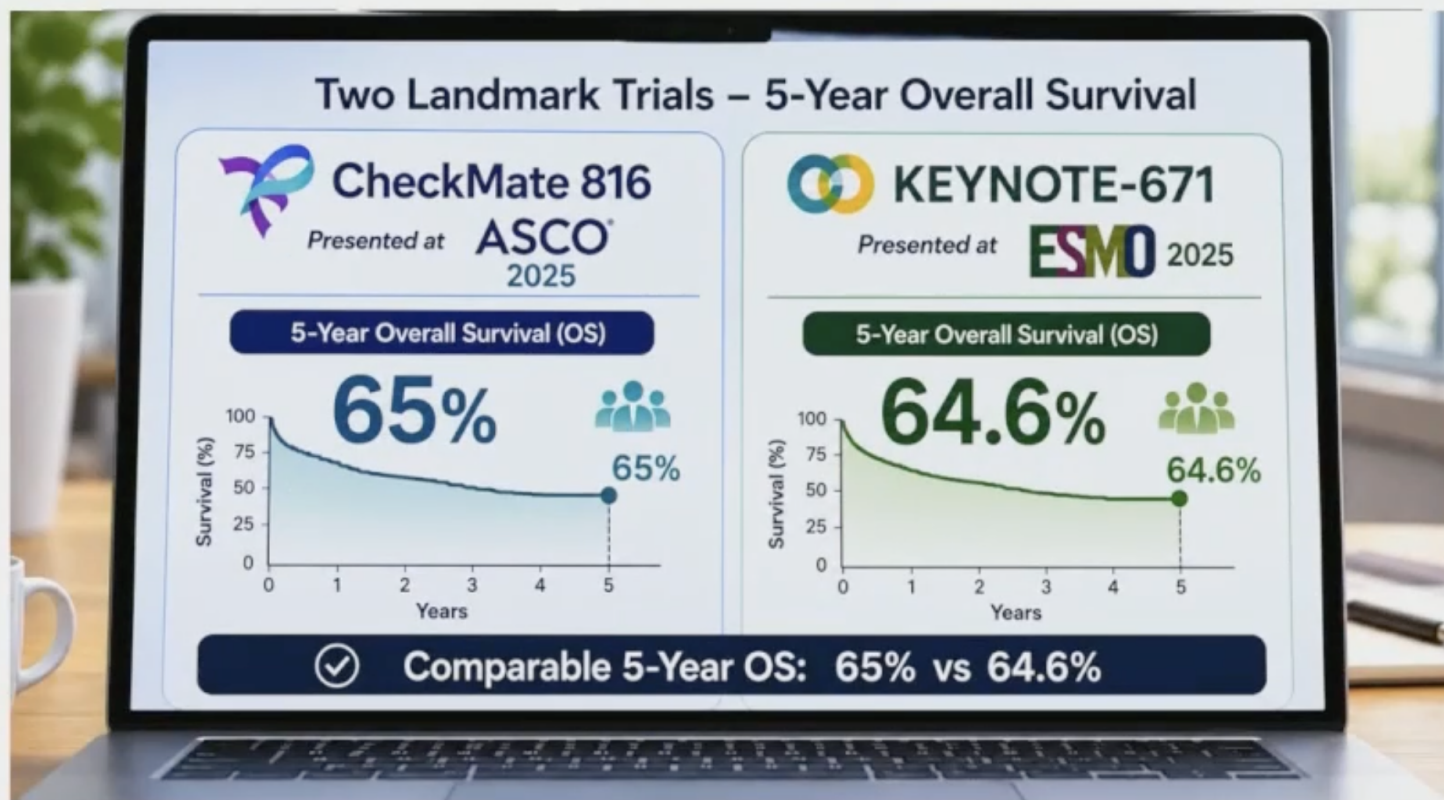
Surgery

Perioperative
treatment

ICI + Chemo vs
Chemo

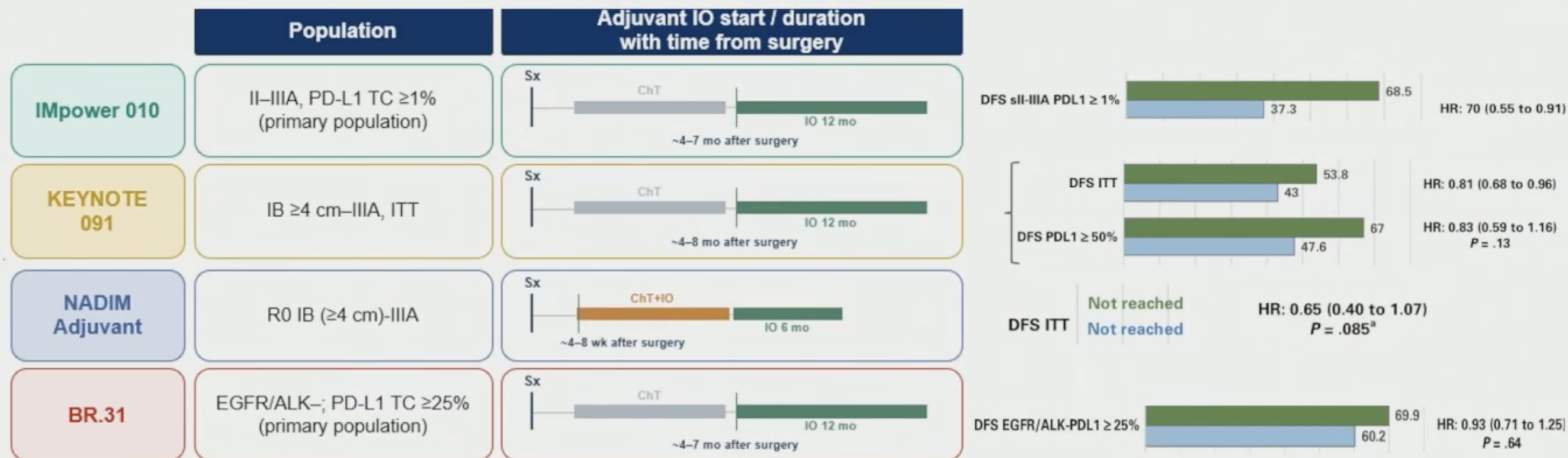
Surgery

ICI
vs Placebo



Johnson D, Nassar A...Naqash AR et al. Nature Reviews Clin Onc 2026; Forde P et al ASCO 2026; Wakelee H et al. ESMO 2025

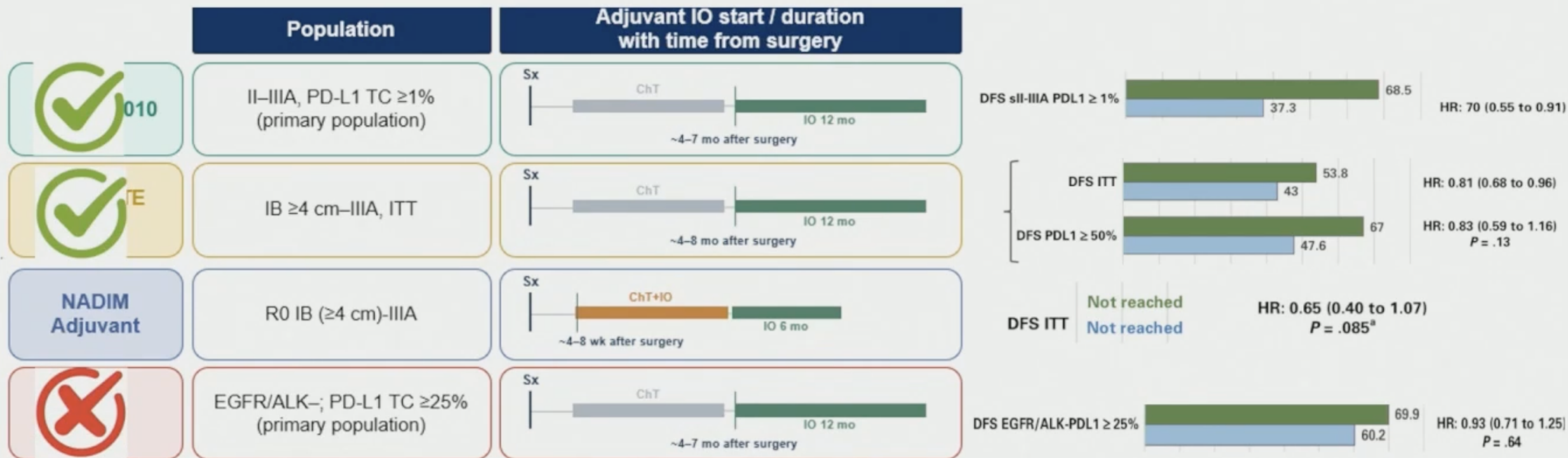
Landscape of Adjuvant ICI in Resected NSCLC



Adjuvant Chemotherapy: Mandated for IMpower 010; **NOT** for Keynote-091 or BR.31

Adapted from Provencio M, ASCO 2026, and Remon J et al. JCO 2026

Landscape of Adjuvant ICI in Resected NSCLC

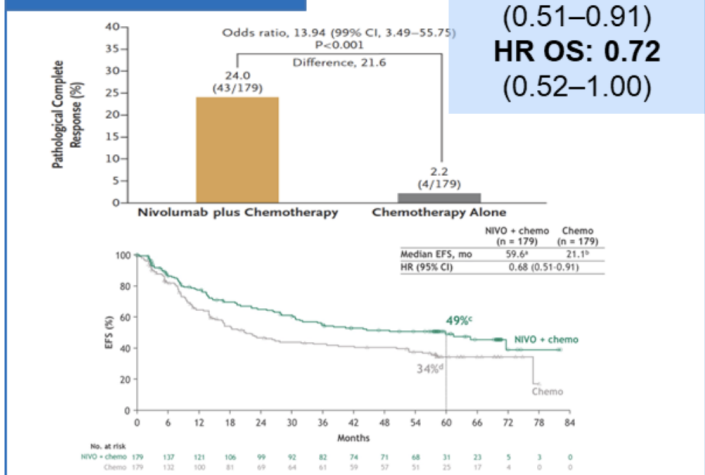


Adjuvant Chemotherapy: Mandated for IMpower 010; **NOT** for Keynote-091 or BR.31

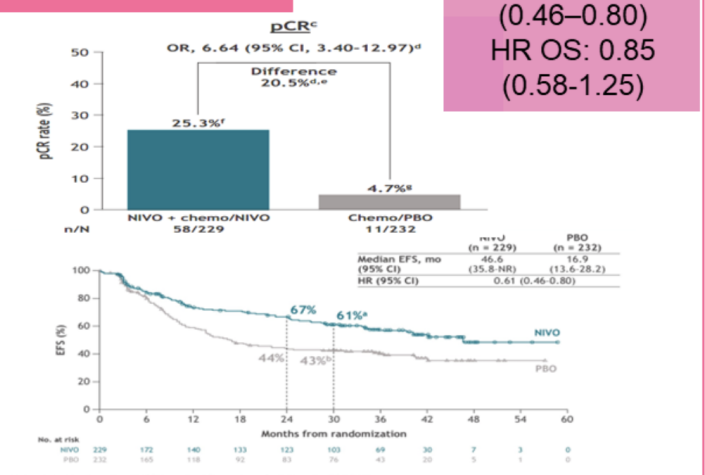
Adapted from Provencio M, ASCO 2026, and Remon J et al. JCO 2026

Efficacy of neoadjuvant and perioperative IO in NSCLC

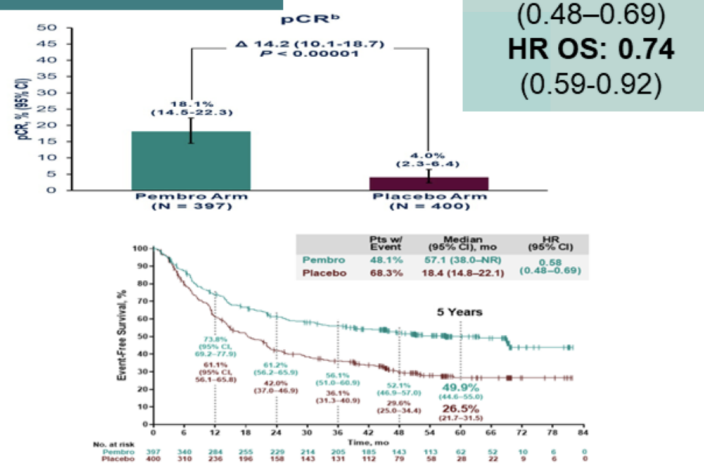
CheckMate-816



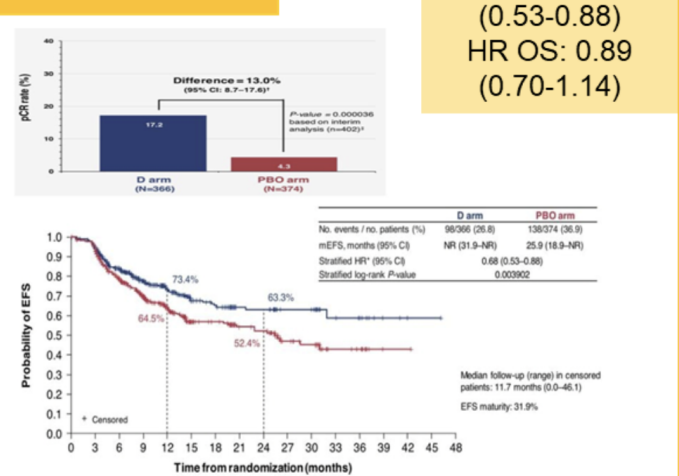
CheckMate-77T



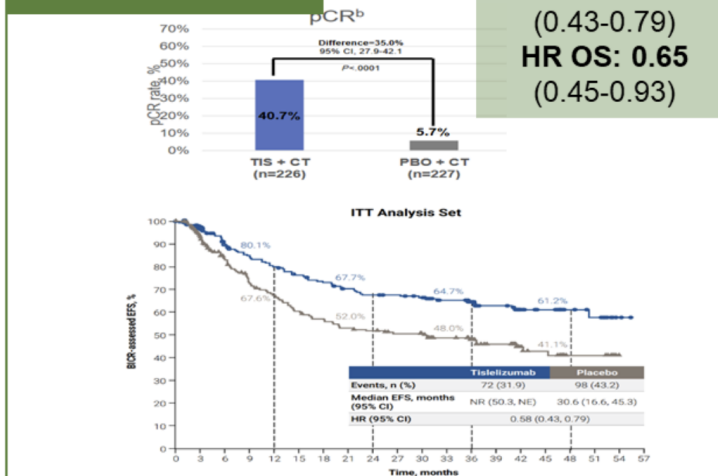
KEYNOTE-671



AEGEAN



RATIONALE-315



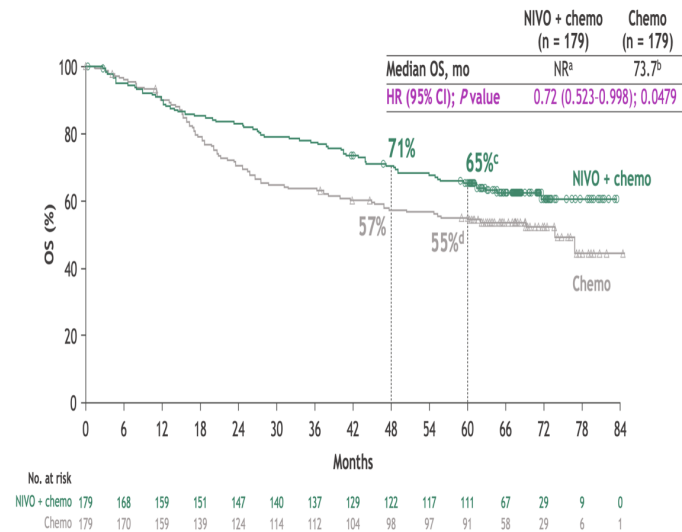
Adapted from Drs. S. Pei Li Saw and J. Remon

A defining moment in Surgical Oncology!

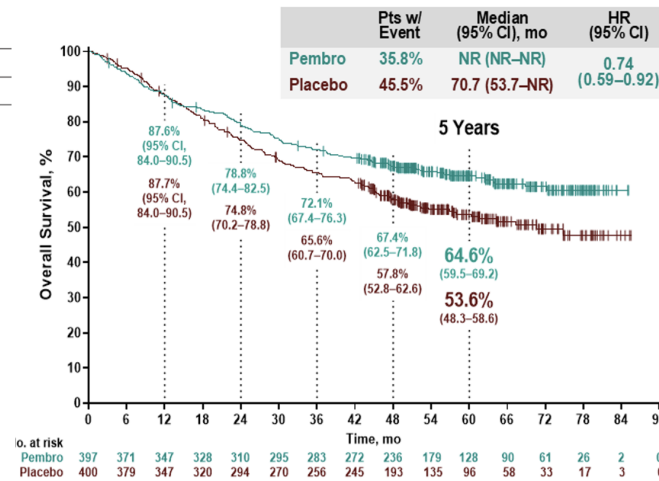
Overall survival benefit in neoadjuvant and perioperative IO trials

Neoadjuvant CT IO

CheckMate 816: Nivolumab

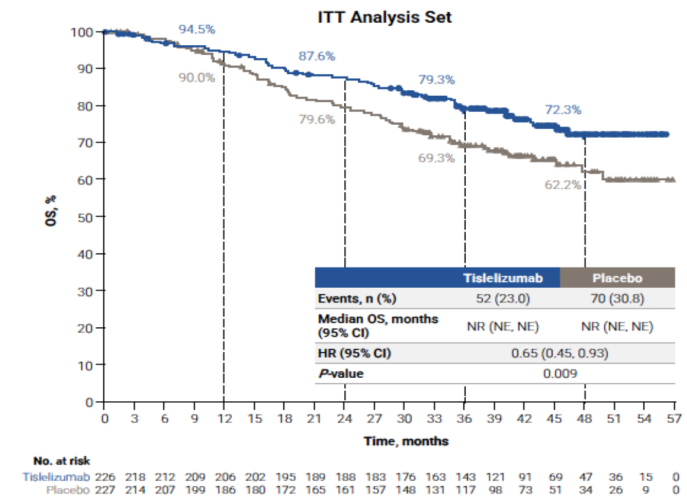


KEYNOTE 671: Pembrolizumab



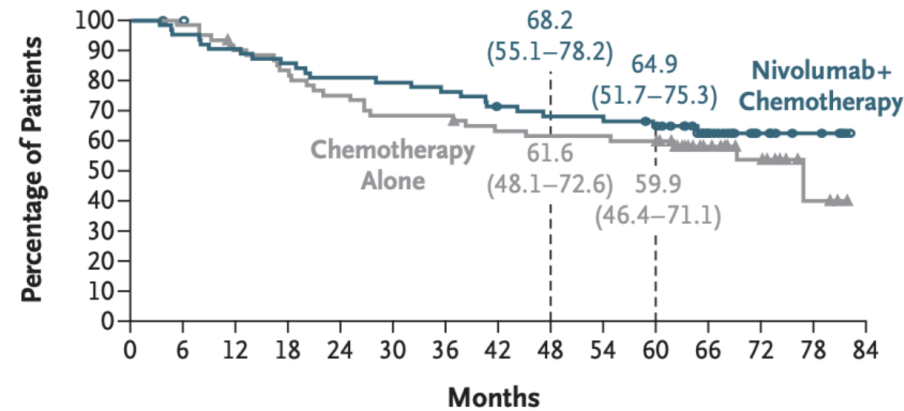
Perioperative IO

RATIONALE 315: Tislelizumab



Stage no longer stratifies!

A Overall Survival in Patients with Baseline Disease Stage IB to II

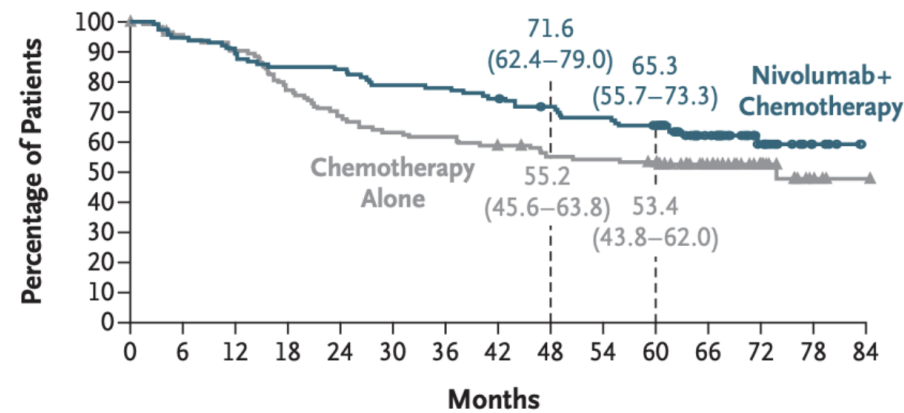


	Median Overall Survival (95% CI) mo
Nivolumab+Chemotherapy (N=65)	NR (64.7–NR)
Chemotherapy Alone (N=61)	76.8 (41.6–NR)
Hazard ratio for death, 0.77 (95% CI, 0.44–1.35)	

No. at Risk

Nivolumab+chemotherapy	65	60	57	54	51	50	48	44	42	41	39	21	11	4	0
Chemotherapy alone	61	60	54	50	45	41	41	37	36	36	34	20	12	3	0

B Overall Survival in Patients with Baseline Disease Stage IIIA



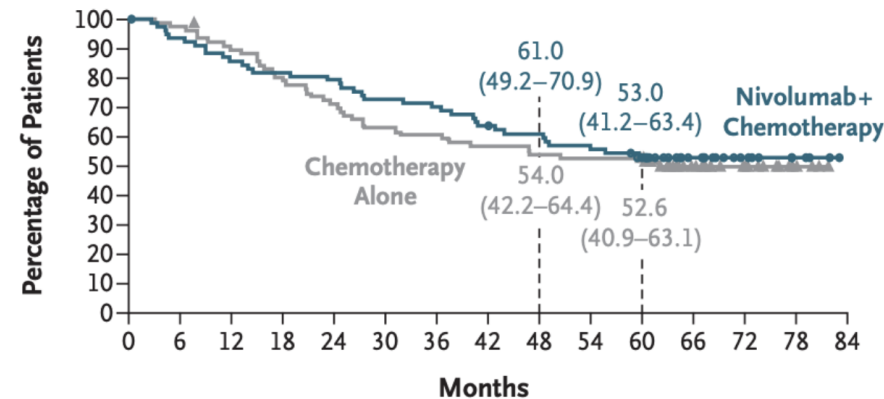
	Median Overall Survival (95% CI) mo
Nivolumab+Chemotherapy (N=113)	NR (71.6–NR)
Chemotherapy Alone (N=116)	73.7 (39.8–NR)
Hazard ratio for death, 0.70 (95% CI, 0.47–1.05)	

No. at Risk

Nivolumab+chemotherapy	113	107	101	96	95	89	88	84	79	75	71	46	18	5	0
Chemotherapy alone	116	108	103	88	78	72	70	66	61	60	57	38	17	3	1

PDL1 TPS and access to neoadj ICI redefine clinical staging

C Overall Survival in Patients with Tumor PD-L1 Expression <1%

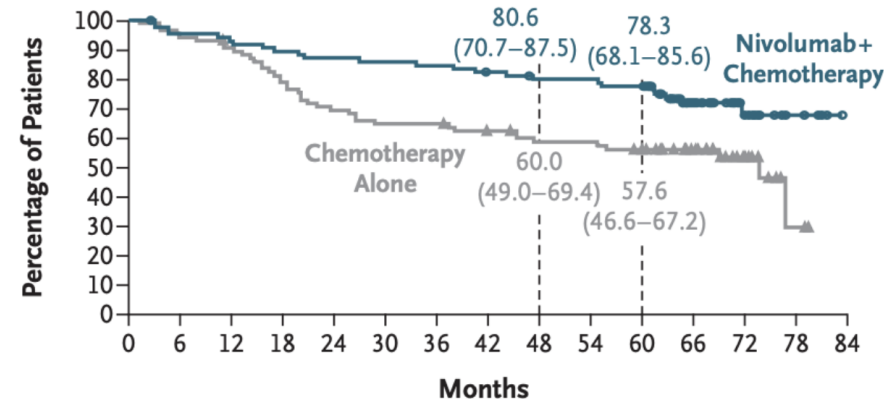


No. at Risk

Nivolumab+chemotherapy	78	72	66	63	61	56	54	49	46	42	38	23	12	4	0
Chemotherapy alone	77	74	68	61	54	48	46	43	41	40	39	23	13	3	0

	Median Overall Survival (95% CI)
	<i>mo</i>
Nivolumab+Chemotherapy (N=78)	NR (43.8-NR)
Chemotherapy Alone (N=77)	61.8 (31.2-NR)
	Hazard ratio for death, 0.89 (95% CI, 0.57-1.41)

D Overall Survival in Patients with Tumor PD-L1 Expression ≥1%



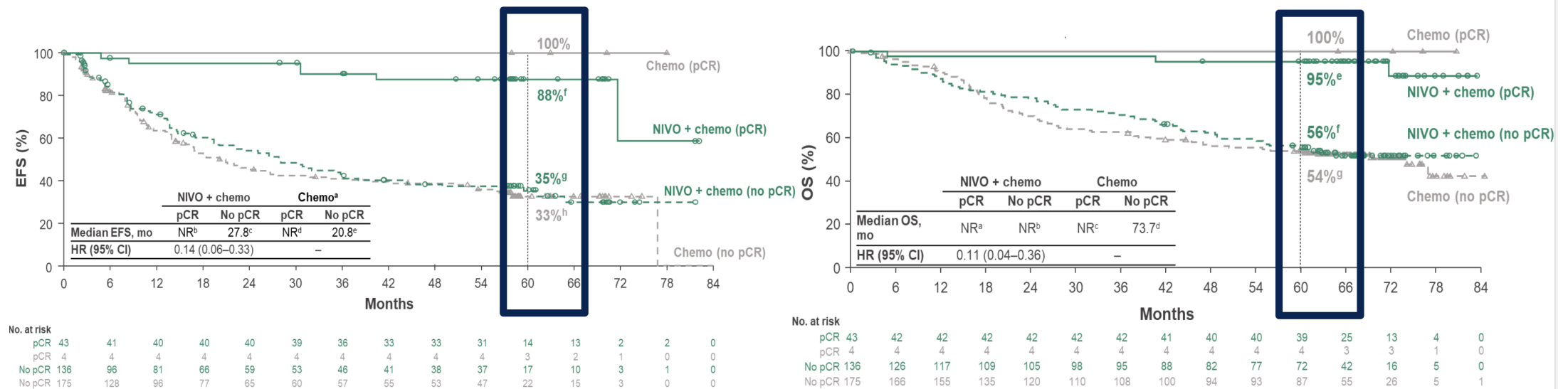
No. at Risk

Nivolumab+chemotherapy	89	84	82	79	77	76	75	72	69	69	67	40	16	5	0
Chemotherapy alone	89	84	80	70	62	58	58	54	50	50	46	31	15	2	0

	Median Overall Survival (95% CI)
	<i>mo</i>
Nivolumab+Chemotherapy (N=89)	NR (NR-NR)
Chemotherapy Alone (N=89)	73.7 (47.3-NR)
	Hazard ratio for death, 0.51 (95% CI, 0.31-0.84)

Path CR is an early and robust indicator of cure

CheckMate 816 exploratory analysis: EFS and OS by pCR status



In the NIVO + chemo arm:

- **pCR: 3 (7.0%)** had disease recurrence or relapse
- **No pCR: 57 (41.9%)** had disease recurrence or relapse

In the NIVO + chemo arm:

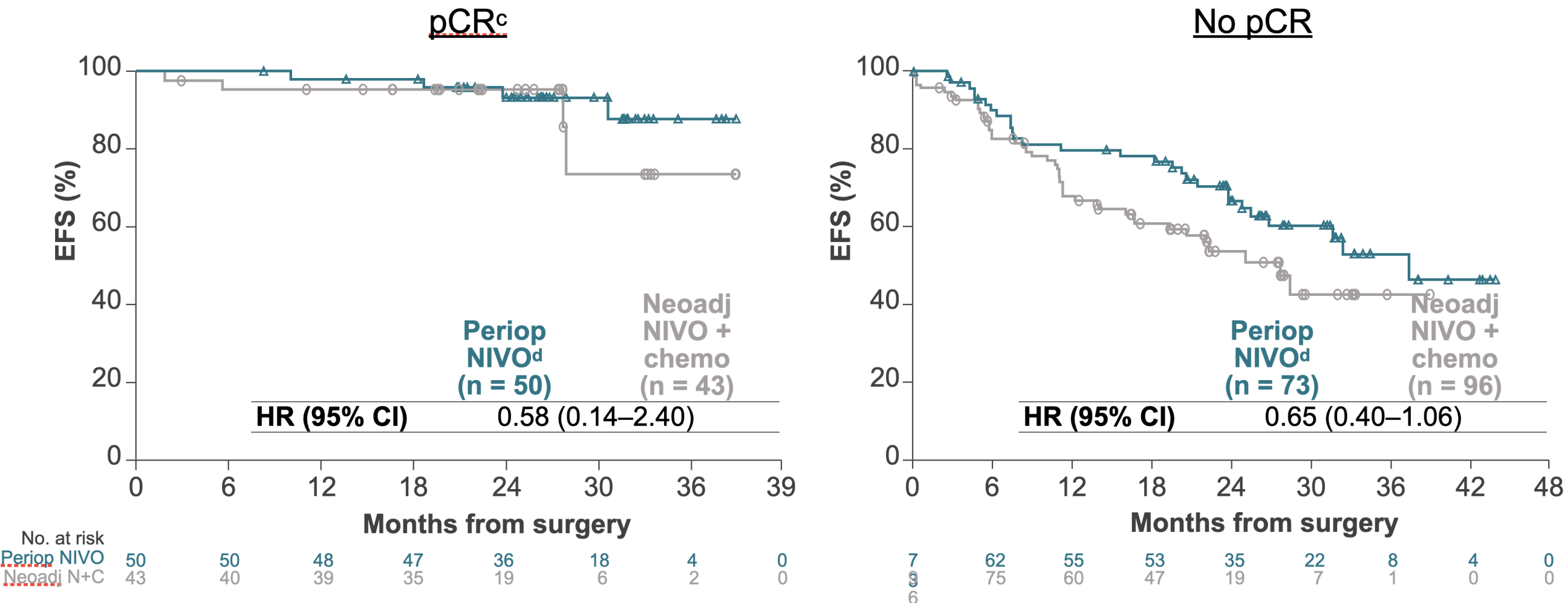
- **pCR: Death occurred in 3 pts; none were due to disease**
- **No pCR: 62 (46.6%)** deaths; 44 (33.1%) due to disease

Median follow-up: 68.4 months.

Neoadjuvant CT-IO perhaps enough for pts who achieve pCR?

Forde PM et al, *New Engl J Med* 2025

Exploratory landmark EFS from definitive surgery CheckMate 816 vs CheckMate 77T by pCR status



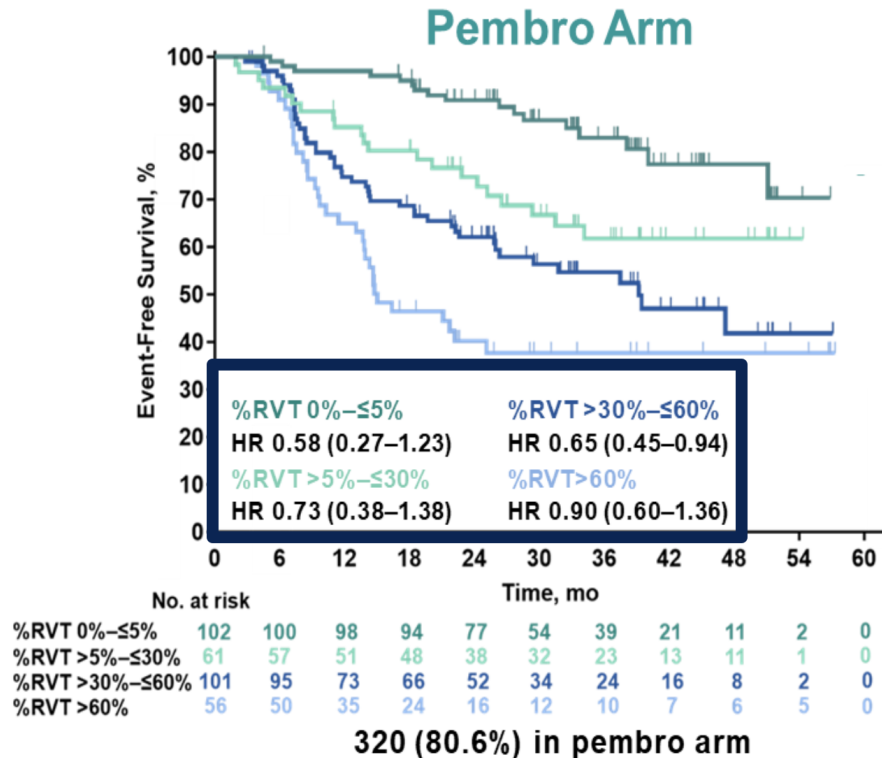
Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. ^aPatients with non-evaluable pCR status were excluded. ^bUnweighted analyses. ^cpCR rates in this analysis population: perioperative NIVO, 40.7%; neoadjuvant NIVO + chemo, 30.5%. ^dIncludes only patients who received ≥ 1 dose of adjuvant NIVO.

Forde P et al, Presidential Presentation WCLC 2024

Pathological response (%RVT) is the new ypTNM

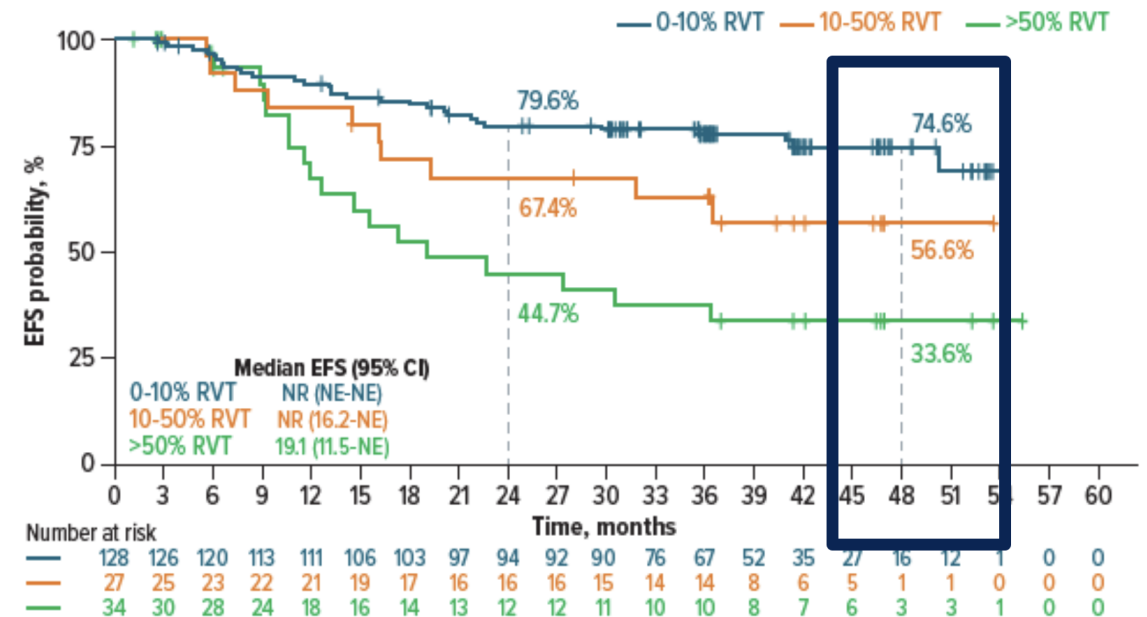
EFS according to %RVT in resected specimens in perioperative IO trials

KEYNOTE 671 CT plus pembro



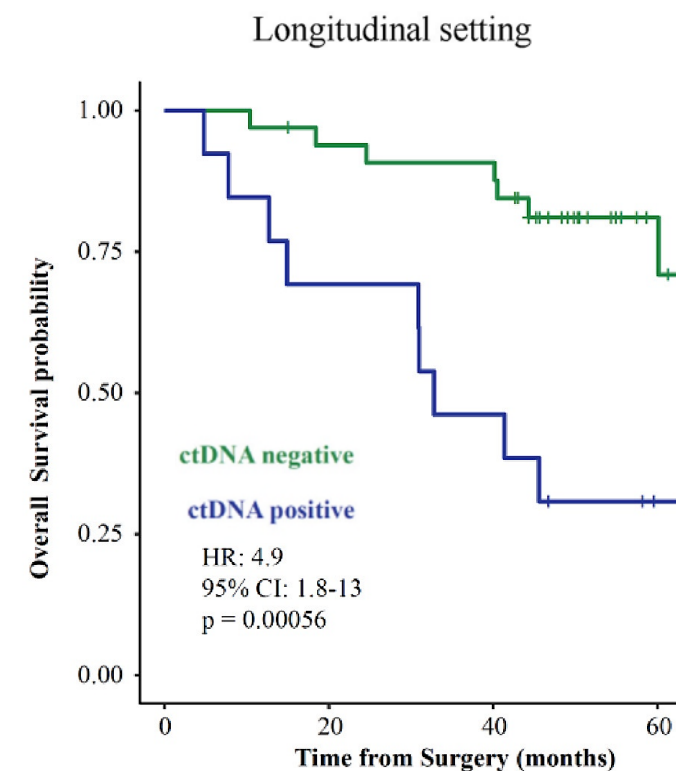
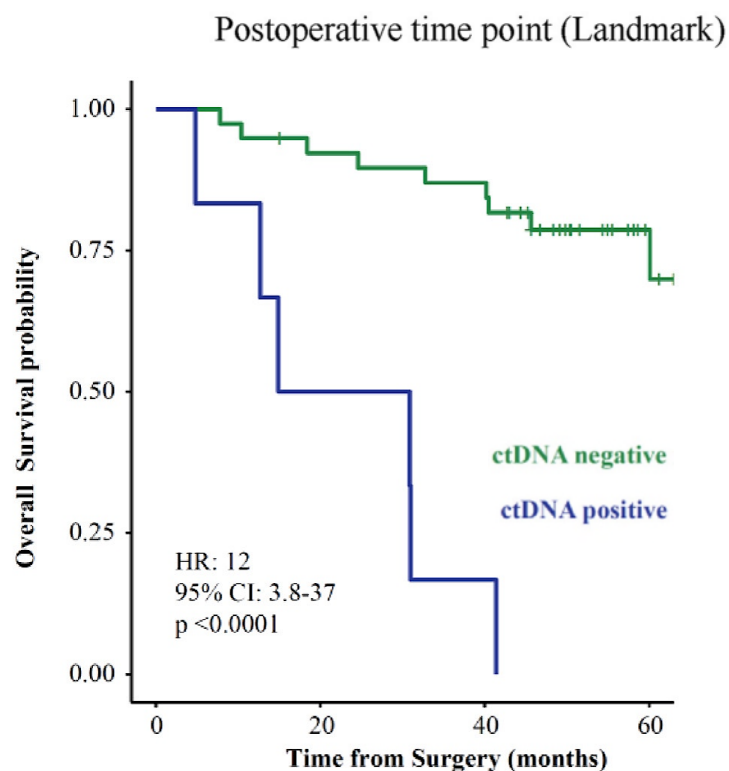
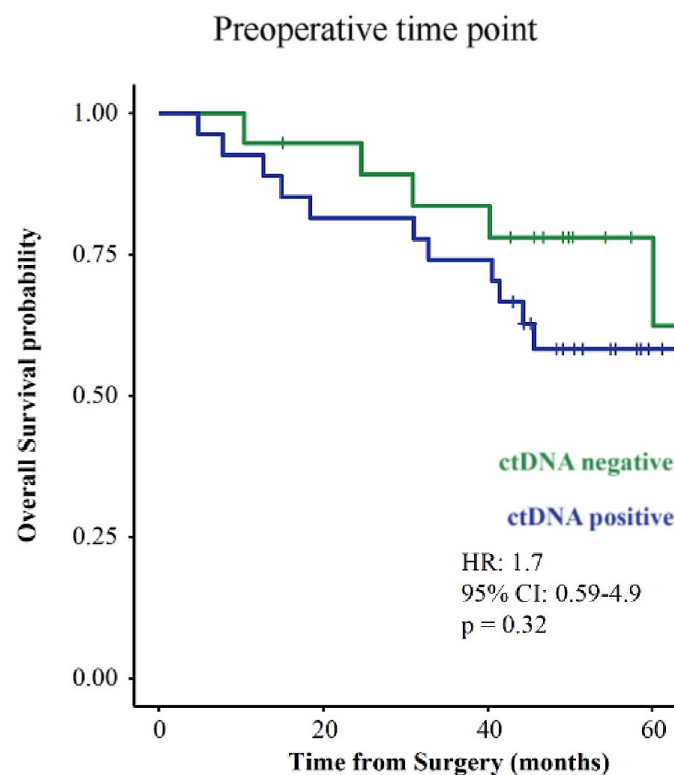
Jones D et al, WCLC 2024, Oral Presentation

RATIONALE-315 : CT plus Tisle Arm

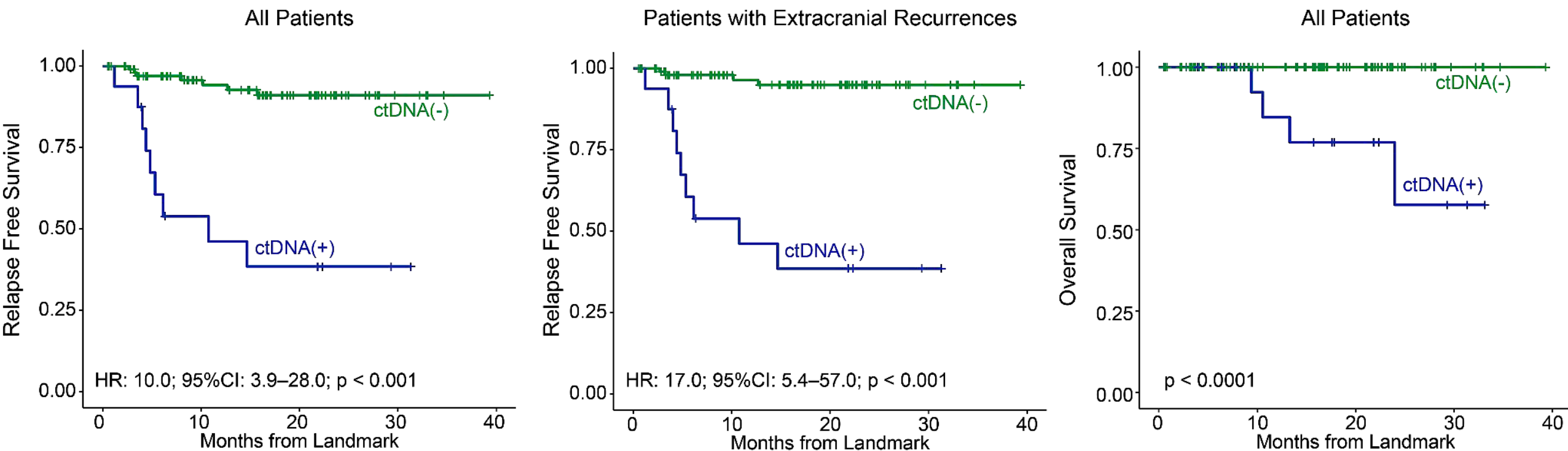


Schvartsman G et al, ELCC 2026, Poster Presentation

Overall Survival by ctDNA Positivity

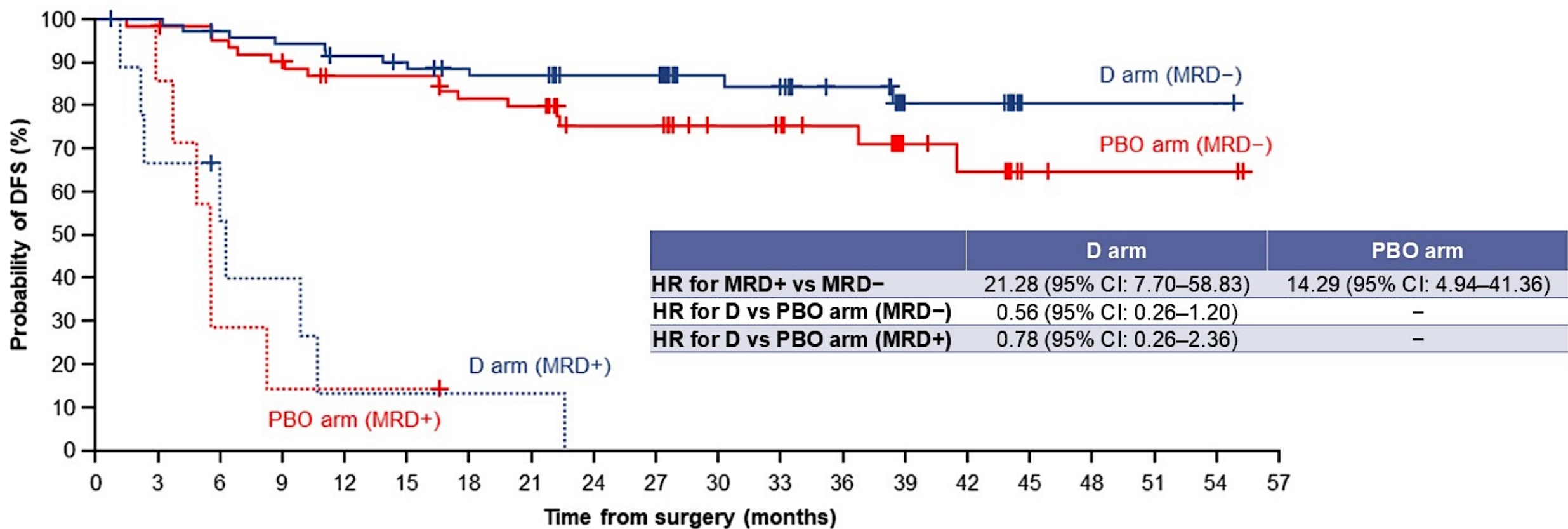


ctDNA Negativity During MRD Window*: RFS and Overall Survival

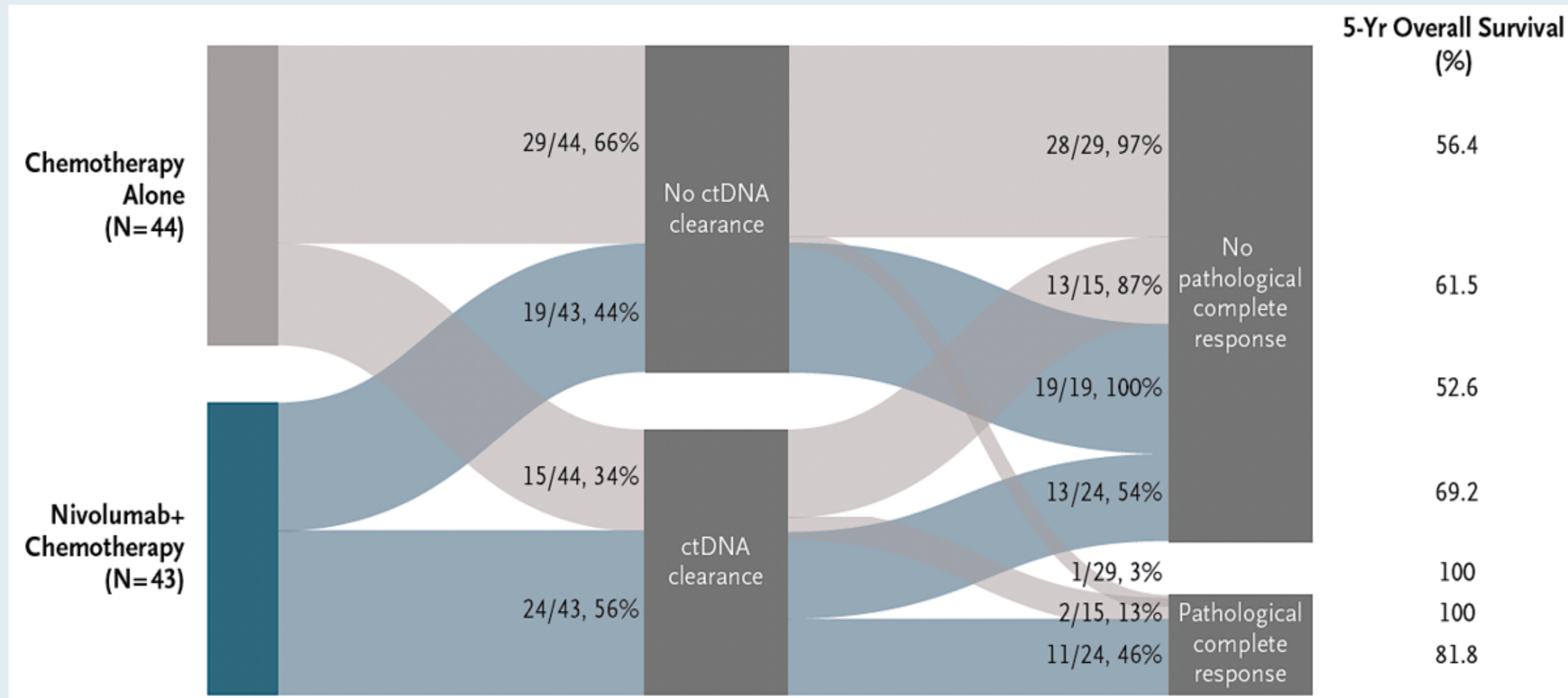


* MRD window was defined as 3 months after surgery (landmark) and prior to adjuvant treatment initiation

Phase III AEGEAN: Association of MRD After Surgery with DFS

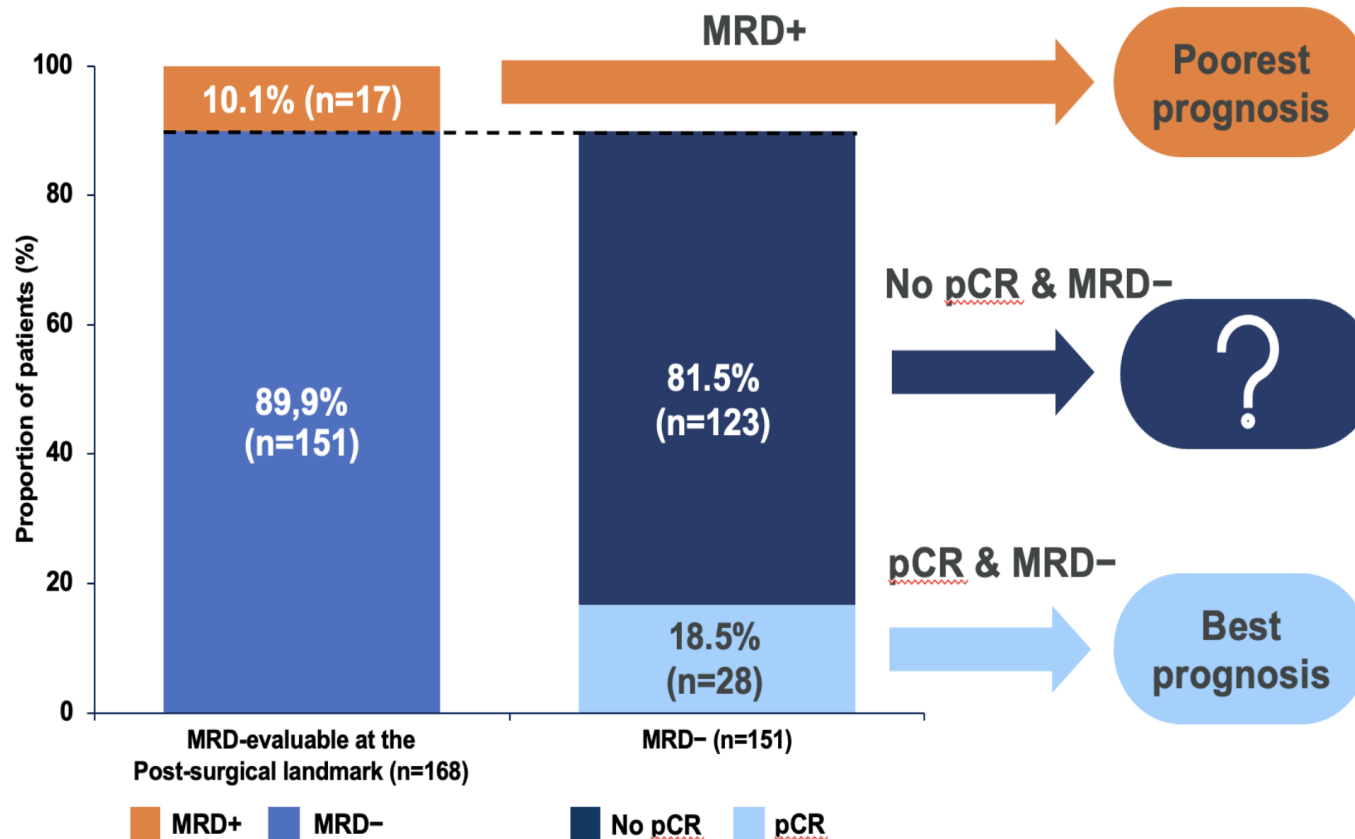


CheckMate 816: Association Between ctDNA Clearance and pCR



Should we stratify by pCR and MRD for adjuvant IO-based treatment decisions?

AEGEAN: Perioperative Durvalumab



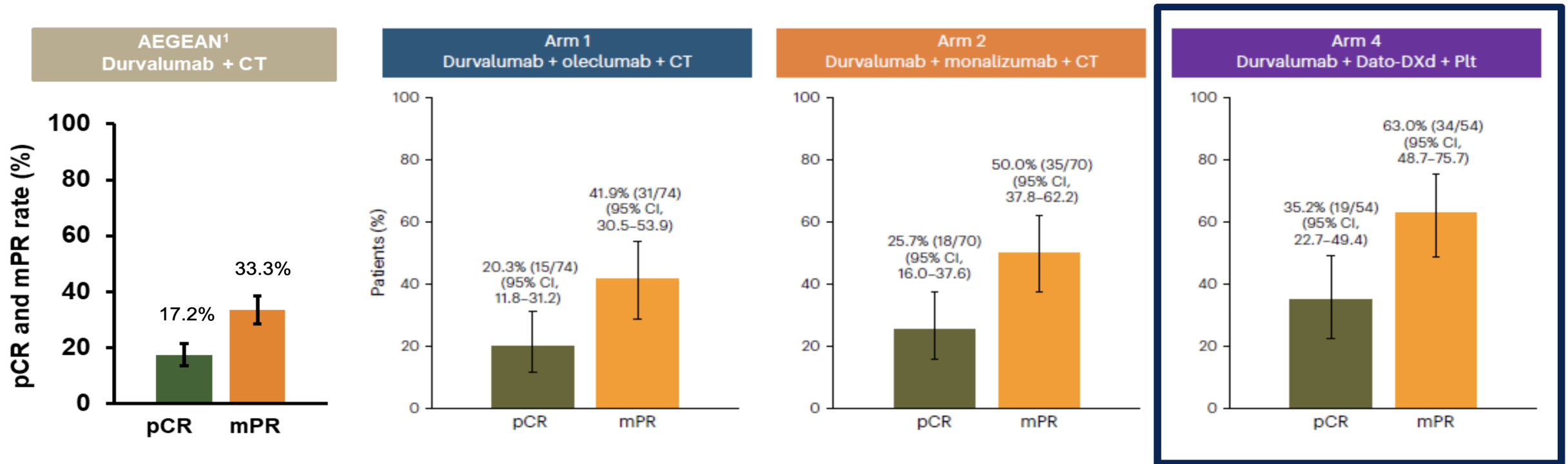
Will adjuvant IO post neoadjuvant CT-IO overcome the poor prognosis?
Treatment now or at PD?

Ideal for adjuvant treatment:
IO sufficient or escalation needed?

Overtreatment with adjuvant IO?

Surgery is still critical to outcome

Pathological response rates are the highest after neoadjuvant ADC plus IO and chemo treatment



ADOPT-Lung ETOP and INSIGHT SWOG trials

ADOPT-Lung trial, NCT06284317



INSIGHT Trial, NCT06498635

Design:

International, multicentre, open-label randomized phase III trial.

Sample size:

364 randomised patients (approx. 520 enrolled)

Trial chair:

Solange Peters

Trial co-chair:

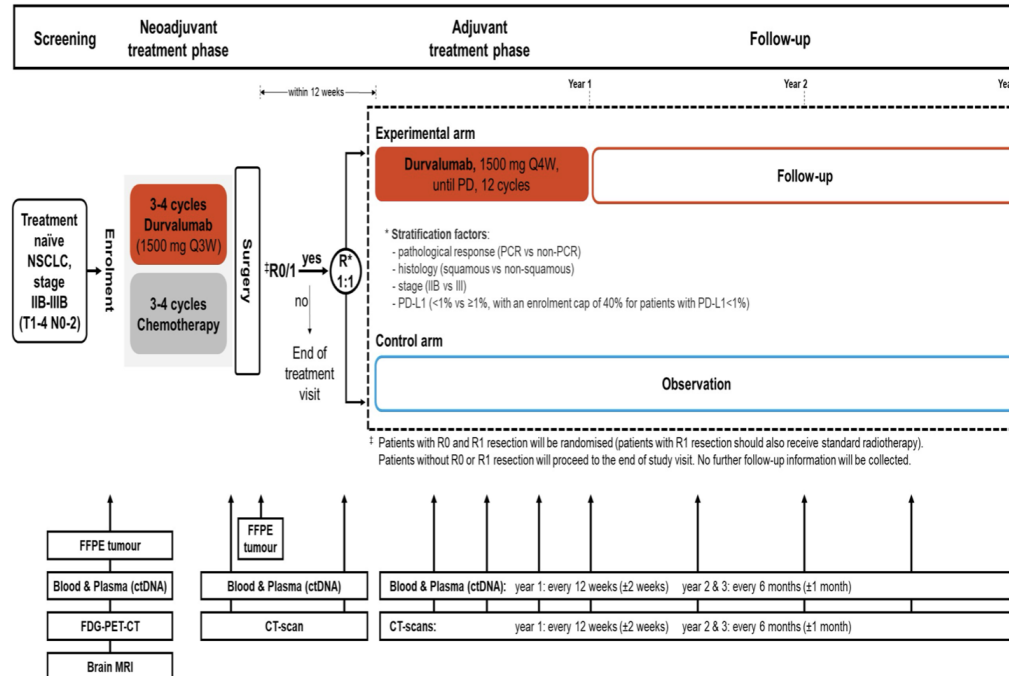
Sabine Schmid

Sponsor:

ETOP IBCSG Partners Foundation

Financial partner:

AstraZeneca



Stage II-IIIb (v.8/9) NSCLC
3-4 Cycles of Histology Specific Chemotherapy + Anti-PD-1/L1

Definitive resection

Endpoints:

- Primary: DFS
- Secondary: OS, toxicity, EFS

pCR
Local Pathology

Randomize 1:1

Durvalumab x 12 months

Surveillance

Inclusion:

- ECOG 0/1
- R0 resection
- No known EGFR/ALK
- Confirmed PD-L1 status

Stratification factors:

- N0/N1 v N2N3
- PD-L1 (<1% v ≥1%)
- Histology (Sq v NSq)

Exploratory Objectives

- AI based assessment
- ctDNA

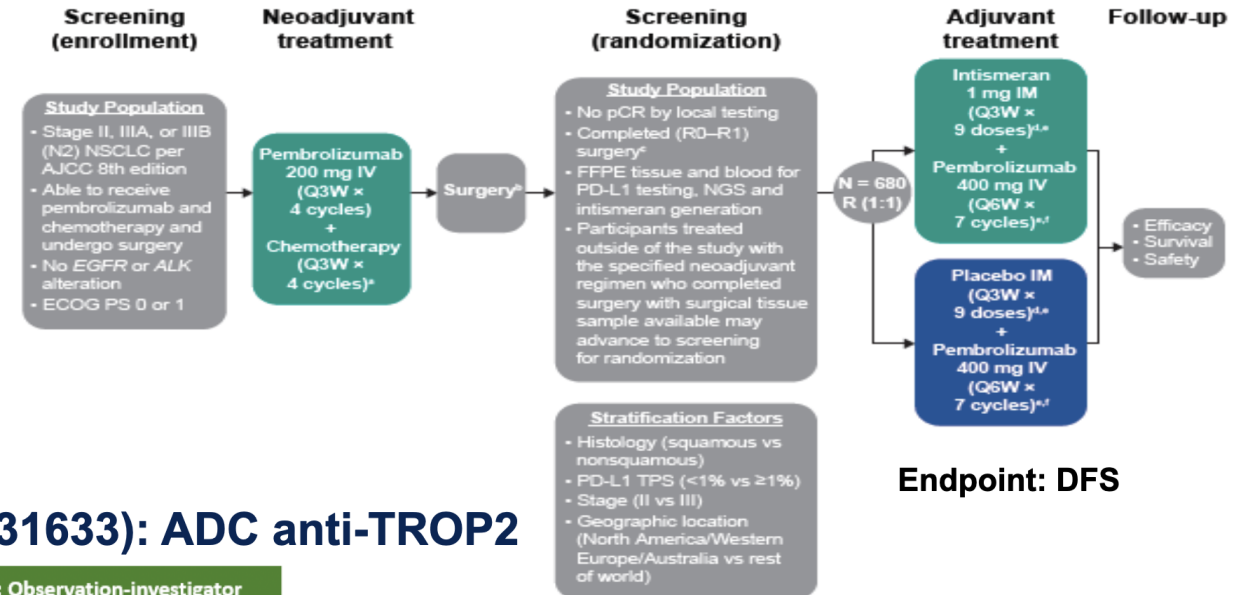
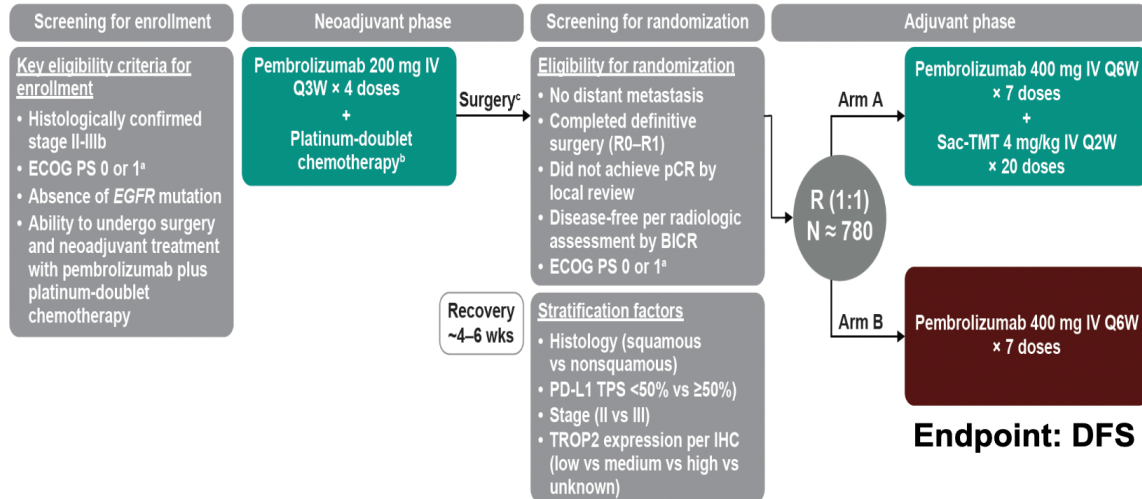
QOL Objectives:

- Primary: FACT-L TOI @ 6 months
- Secondary: FACT-BRM

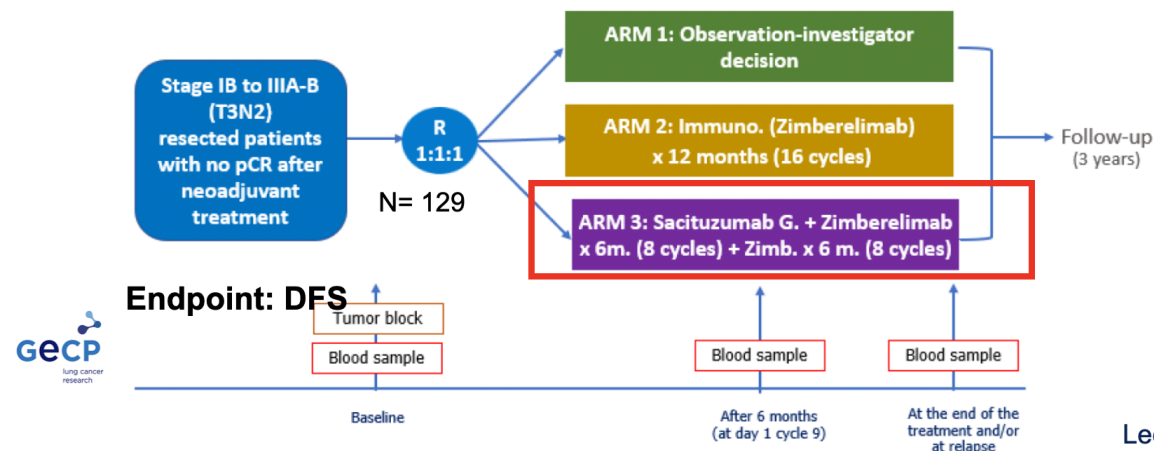
¹ Pts can enroll on optional pre-screening study

Adjuvant trials ADCs or vaccines in non-pCR

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

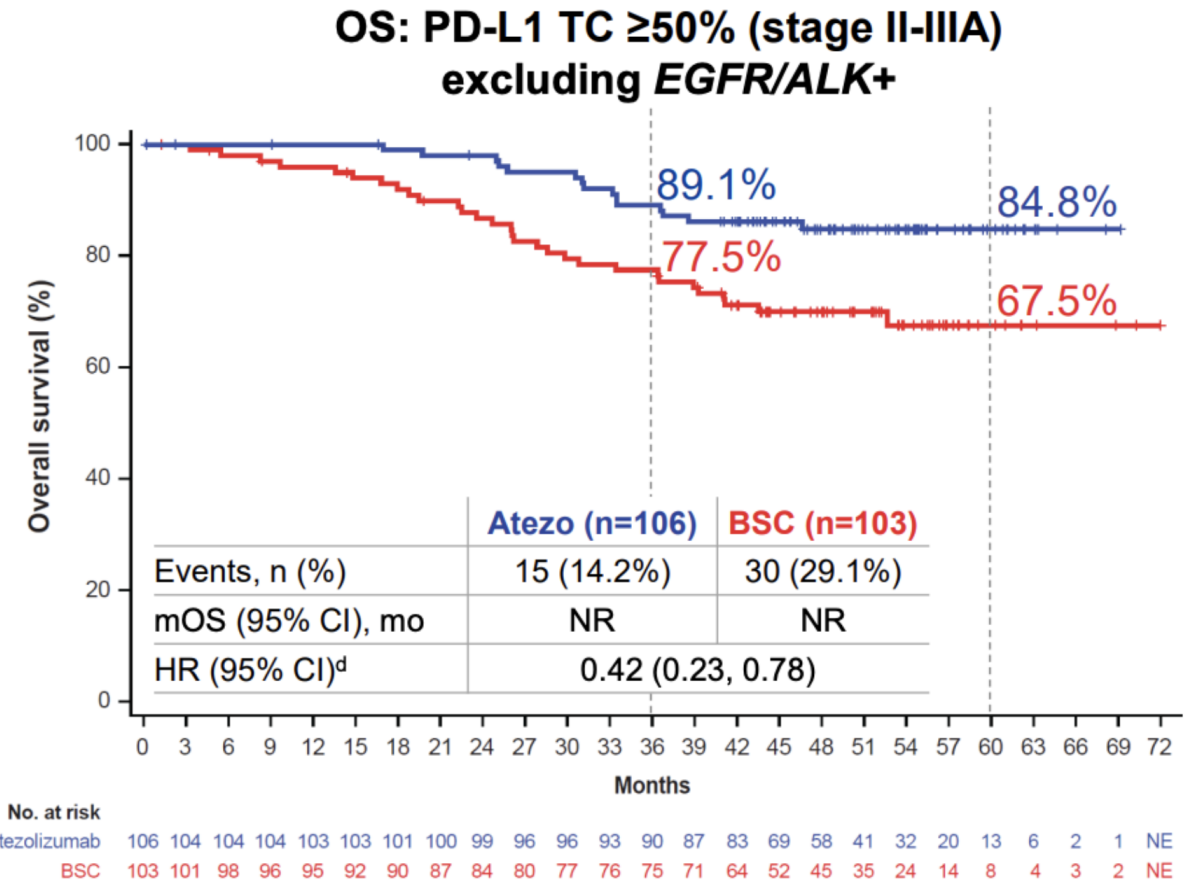
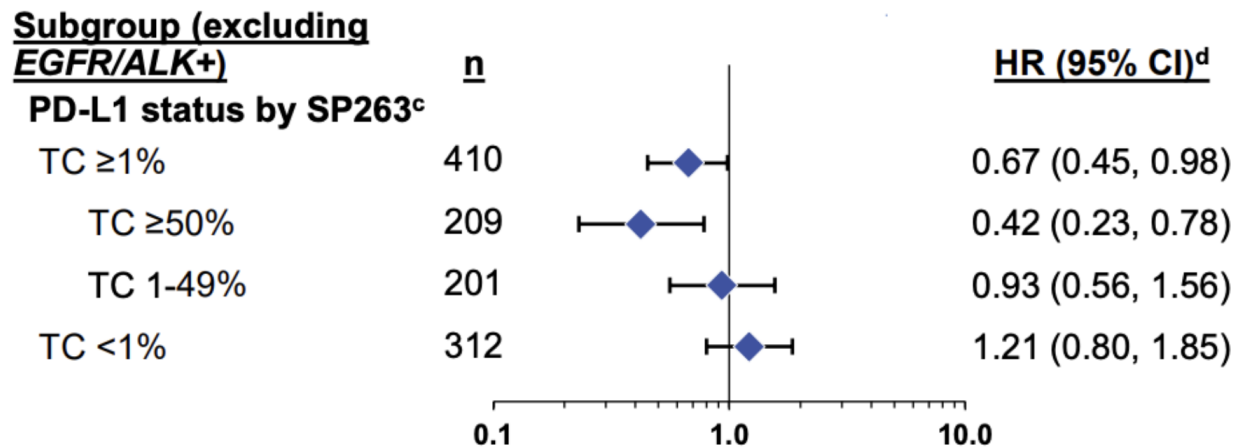
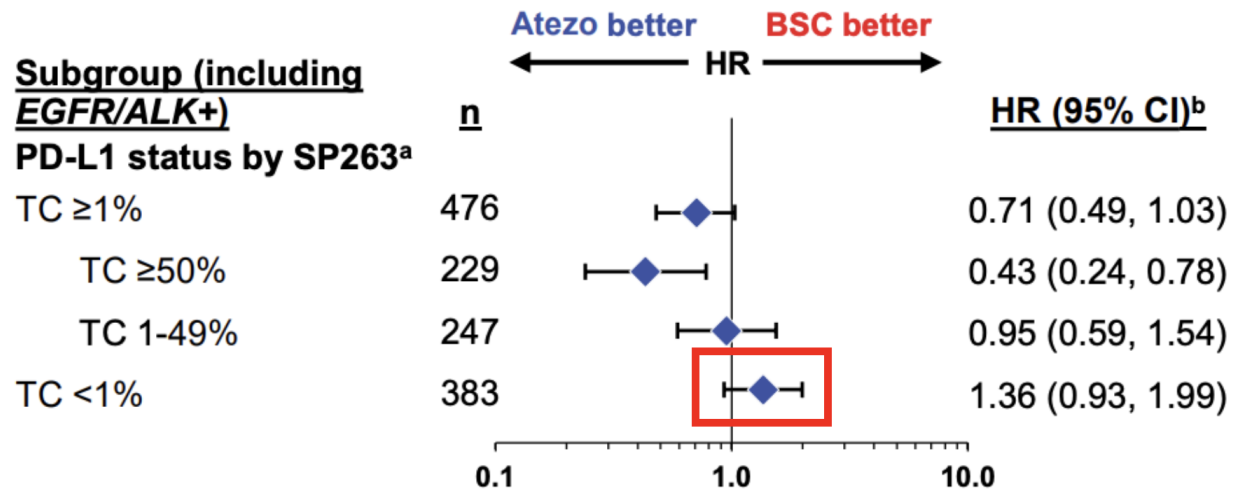


Phase III ARIAN trial (NCT06431633): ADC anti-TROP2



What do we know about adjuvant ICI therapy?

Adjuvant IO can have + AND – impact on OS

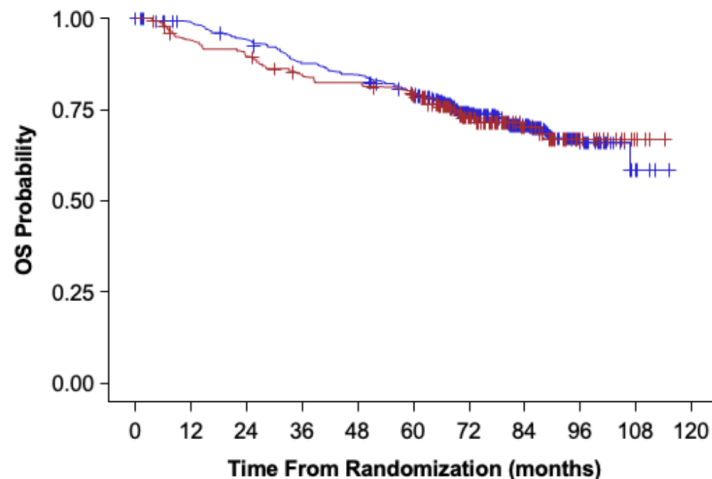


^a 23 patients had unknown PD-L1 status. ^b Stratified for PD-L1 TC ≥1%; unstratified for all other subgroups. ^c 21 patients had unknown PD-L1 status. ^d Unstratified.

Totality of data from adjuvant space suggests inconsistent utility

PD-L1 $\geq 25\%$ and *EGFR*-/*ALK*-

	D arm n=316	PBO arm n=161
No. of events (%)	88 (27.8)	45 (28.0)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	0.98 (0.69–1.42)	
P-value (2-sided)	0.93	

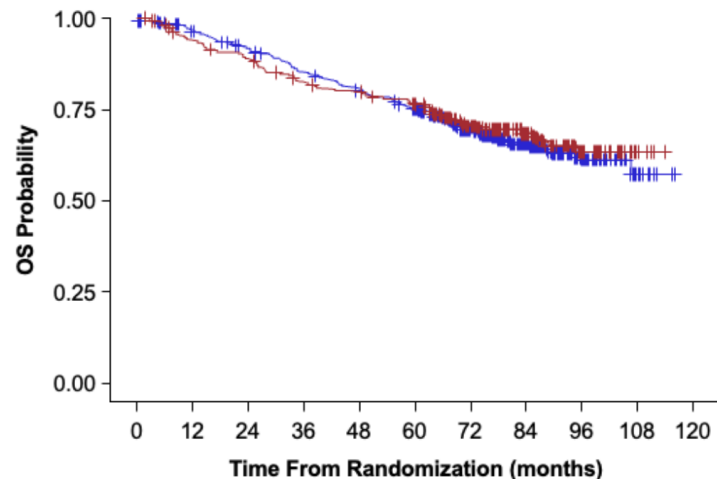


No. at risk:

D arm	316	301	286	266	256	237	172	100	40	6	0
PBO arm	161	147	140	129	126	121	84	44	20	4	0

PD-L1 $\geq 1\%$ and *EGFR*-/*ALK*-

	D arm n=469	PBO arm n=240
No. of events (%)	149 (31.8)	72 (30.0)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	1.10 (0.83–1.47)	
P-value (2-sided)	0.52	

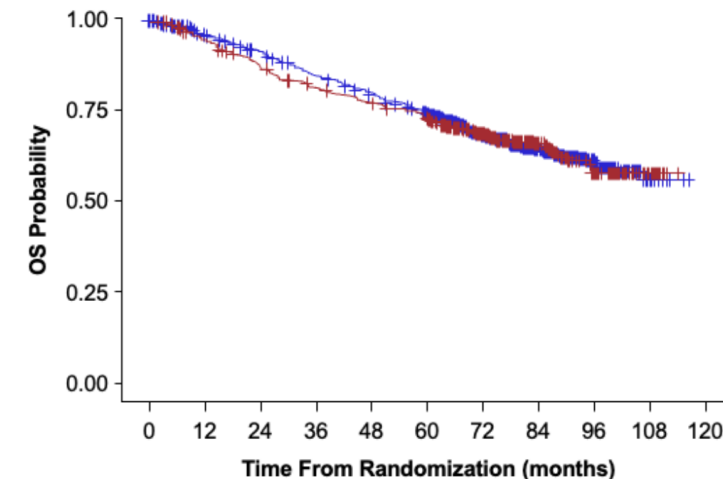


No. at risk:

D arm	469	439	409	378	356	326	236	133	58	10	0
PBO arm	240	219	205	188	181	173	123	66	30	5	0

PD-L1 All Comers and *EGFR*-/*ALK*-

	D arm n=815	PBO arm n=404
No. of events (%)	266 (32.6)	135 (33.4)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	1.00 (0.81–1.23)	
P-value (2-sided)	0.96	

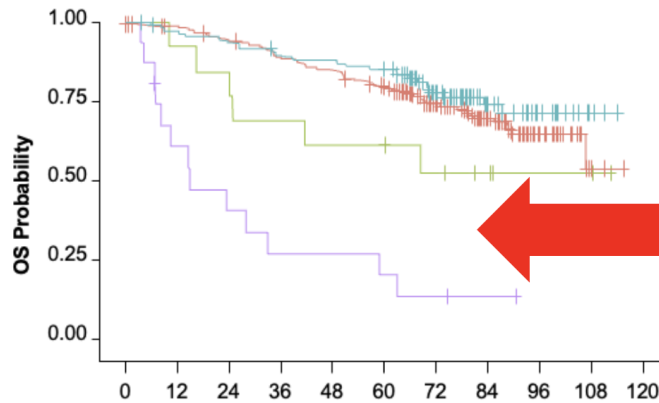


No. at risk:

D arm	815	748	699	643	604	556	390	229	103	14	0
PBO arm	404	371	337	313	296	278	201	111	49	8	0

Perhaps adjuvant IO only helps those who still have cancer when they are IO naive!

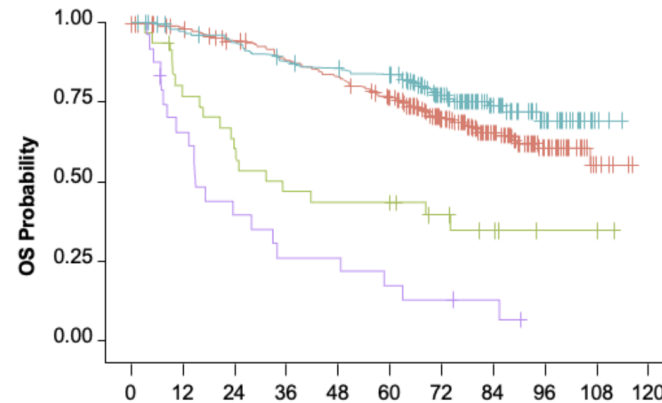
PD-L1 $\geq 25\%$ and *EGFR*-/*ALK*-



No. at risk:	Time From Randomization (months)										
D arm, MRD-	238	229	217	204	195	178	130	76	29	3	0
D arm, MRD+	13	12	11	9	8	8	6	4	2	2	0
PBO arm, MRD-	112	107	103	98	96	93	63	29	14	3	0
PBO arm, MRD+	16	9	6	4	4	3	2	1	0	0	0

MRD+		D arm n=13	PBO arm n=16
Median OS (95% CI), months		NR (24.0–NR)	14.9 (7.0–58.8)
Unstratified HR (95% CI)		0.30 (0.11–0.80)	
P-value (2-sided)		0.011	
MRD-		D arm n=238	PBO arm n=112
Median OS (95% CI), months		NR (106.8–NR)	NR (0–NR)
Unstratified HR (95% CI)		1.28 (0.82–2.01)	
P-value (2-sided)		0.28	
Interaction P-value		0.006	

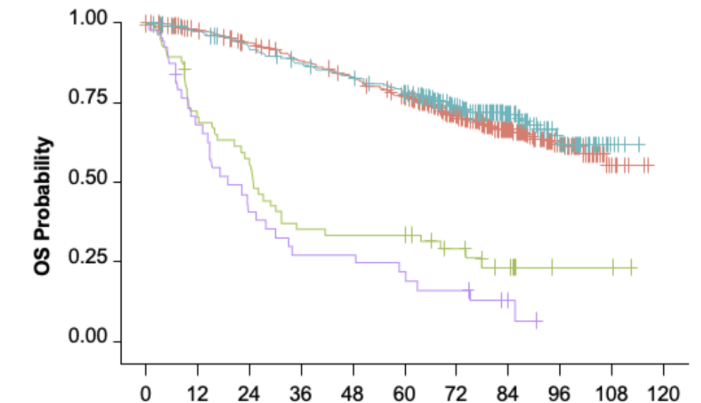
PD-L1 $\geq 1\%$ and *EGFR*-/*ALK*-



No. at risk:	Time From Randomization (months)										
D arm, MRD-	343	329	308	289	270	243	176	99	43	6	0
D arm, MRD+	31	23	19	14	13	13	9	6	2	2	0
PBO arm, MRD-	171	161	154	144	139	135	95	47	22	3	0
PBO arm, MRD+	24	15	9	6	6	4	3	2	0	0	0

MRD+		D arm n=31	PBO arm n=24
Median OS (95% CI), months		35.1 (20.6–NR)	14.9 (8.3–33.1)
Unstratified HR (95% CI)		0.49 (0.26–0.92)	
P-value (2-sided)		0.024	
MRD-		D arm n=343	PBO arm n=171
Median OS (95% CI), months		NR (106.8–NR)	NR (0–NR)
Unstratified HR (95% CI)		1.38 (0.97–1.97)	
P-value (2-sided)		0.080	
Interaction P-value		0.003	

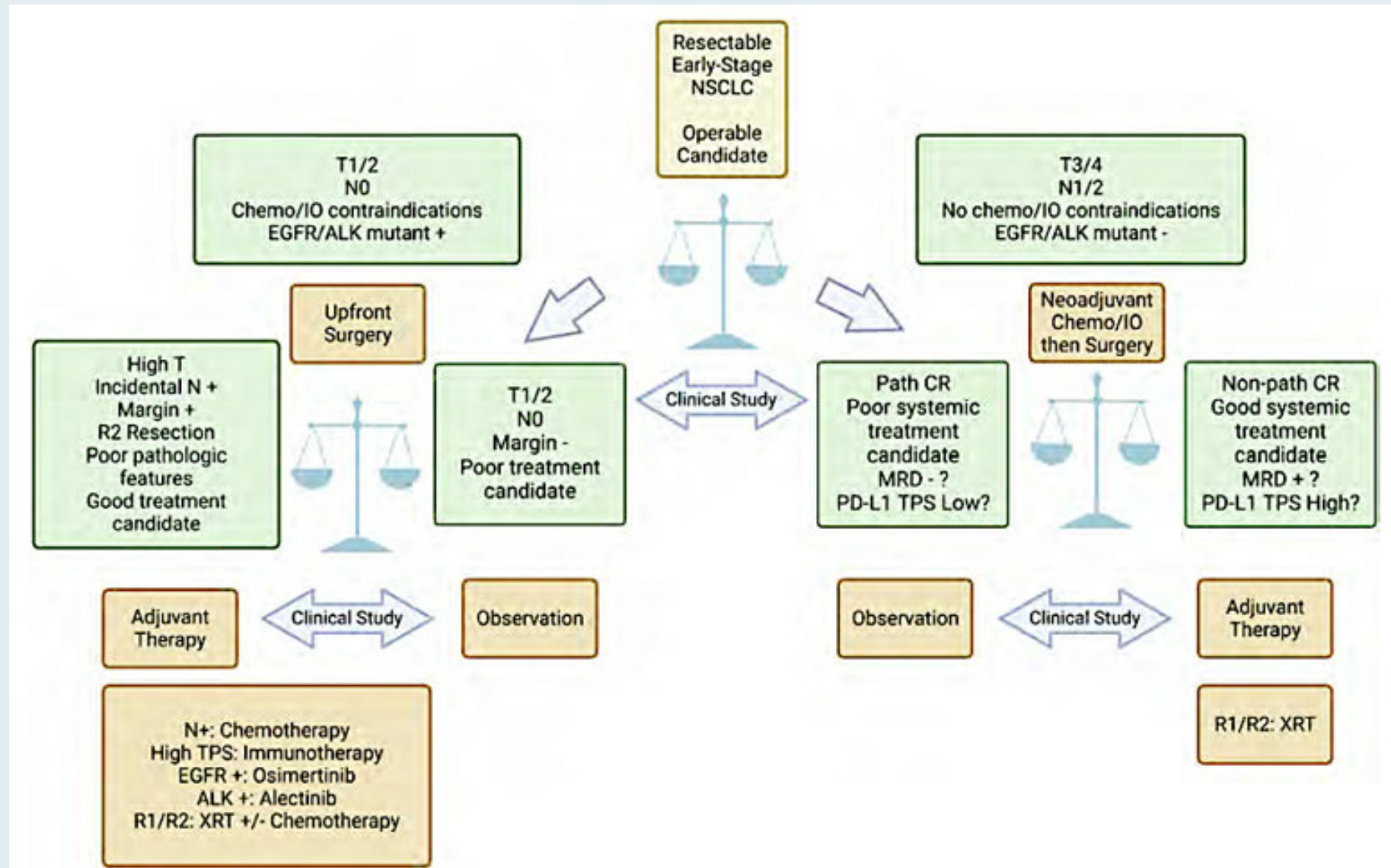
PD-L1 All Comers and *EGFR*-/*ALK*-



No. at risk:	Time From Randomization (months)										
D arm, MRD-	605	569	536	501	469	429	301	179	80	9	0
D arm, MRD+	58	38	31	19	18	18	12	7	2	2	0
PBO arm, MRD-	282	269	251	237	224	210	155	82	34	5	0
PBO arm, MRD+	39	25	15	10	10	8	6	3	0	0	0

MRD+		D arm n=58	PBO arm n=39
Median OS (95% CI), months		25.1 (16.6–31.5)	19.5 (13.3–30.1)
Unstratified HR (95% CI)		0.71 (0.45–1.12)	
P-value (2-sided)		0.14	
MRD-		D arm n=605	PBO arm n=282
Median OS (95% CI), months		NR (106.8–NR)	NR (0–NR)
Unstratified HR (95% CI)		1.12 (0.86–1.45)	
P-value (2-sided)		0.39	
Interaction P-value		0.044	

Practical Implementation and Patient Navigation for Perioperative Immunotherapy in NSCLC



Conclusions

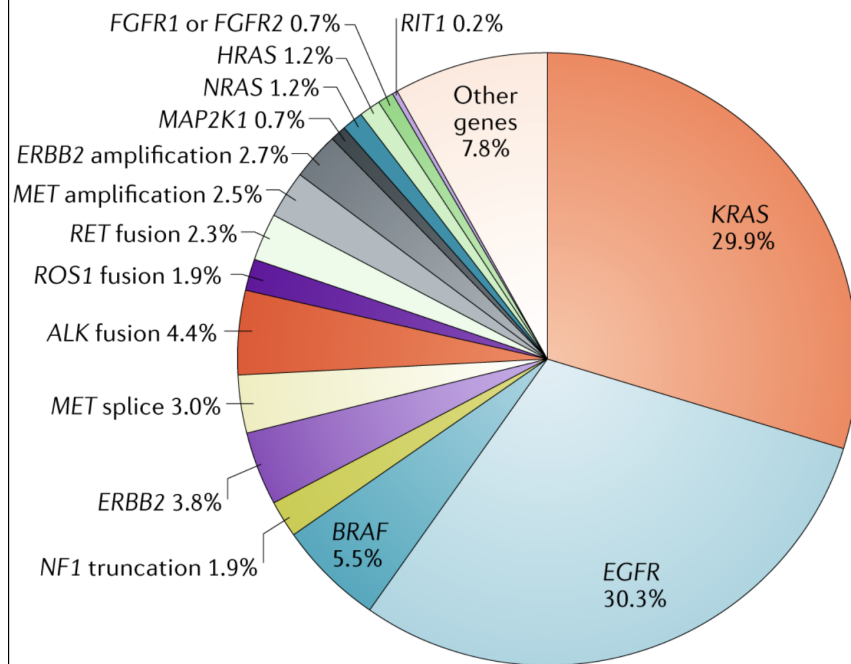
- Perioperative IO added to neoadjuvant CT improve pCR, EFS and OS compared with CT (plus PBO) alone.
- Benefit of adjuvant IO after neoadjuvant CT plus IO in subsets of non pCR patients, but those who receive adjuvant treatment have better prognosis.
- Patients with pCR benefit less from adjuvant IO, deintensification can be discussed but a subset may relapse.
- Whether adjuvant IO is the best strategy or escalation may be more appropriate for non pCR patients remains to be determined: Innovative adaptive trials and biomarkers are needed to tailor therapy rationally.

What Did We Learn in 2025-2026, And What Do We Need To Learn Beyond 2026?

- EA5142, like BR.31 **challenges the comfort**, not adjuvant ICI use per se in early-stage resected NSCLC: timing and context matter
- What **adjuvant ICI** adds in the perioperative **Chemotherapy-ICI paradigm** in early-stage resectable NSCLC..... ***debatable***, as current perioperative studies do not address the contribution of the effect of adjuvant ICI
- Ongoing trials (**PROSPECT-Lung; ETOP 25-23; INSIGHT**) will be important to better understand appropriate approaches in early-stage NSCLC

Not One size fits all anymore!

The diagnosis and management of NSCLC is complex and getting more complicated



Access, coverage, and adequate interpretation of NGS is imperative

PRINCIPLES OF BIOMARKER-DIRECTED THERAPY FOR ADVANCED OR METASTATIC DISEASE

Order does not imply preference. This is a listing for references.

EGFR Exon 19 Deletion or L858R Mutation

- First-line therapy
 - Afatinib¹
 - Erlotinib²
 - Dacomitinib³
 - Gefitinib^{4,5}
 - Osimertinib⁶
- (Carboplatin or Cisplatin)/Osimertinib/Pemetrexed (nonsquamous)⁷
- Erlotinib + Ramucirumab⁸
- Erlotinib + Bevacizumab (nonsquamous)⁹
- Lazertinib + Amivantamab-vmjw¹⁰
- Lazertinib¹⁰
- Subsequent therapy
 - Osimertinib¹¹
 - Carboplatin/Pemetrexed + Amivantamab-vmjw (nonsquamous)¹²
 - Datopotamab deruxtecan-dlnk (nonsquamous)¹³
 - Lazertinib + Amivantamab-vmjw^{14,15}

EGFR S768I, L861Q, and/or G719X Mutations

- First-line therapy
 - Afatinib^{1,16}
 - Erlotinib²
 - Dacomitinib³
 - Gefitinib^{4,5}
 - Osimertinib^{6,17}

EGFR S768I, L861Q, and/or G719X Mutations (continued)

- Subsequent therapy
 - Osimertinib¹¹
 - Datopotamab deruxtecan-dlnk (nonsquamous)¹³

EGFR Exon 20 Insertion Mutation

- First-line therapy
 - Carboplatin/Pemetrexed + Amivantamab-vmjw (nonsquamous)¹⁸
 - Sunvozertinib²⁰
- Subsequent therapy
 - Amivantamab-vmjw¹⁹
 - Sunvozertinib²⁰
 - Datopotamab deruxtecan-dlnk (nonsquamous)¹³

KRAS G12C Mutation^a

- Subsequent therapy
 - Sotorasib²¹
 - Adagrasib²²

ALK Gene Fusion

- First-line therapy
 - Alectinib^{23,24}
 - Brigatinib²⁵
 - Ceritinib²⁶
 - Crizotinib^{23,27}
 - Ensartinib²⁸
 - Lorlatinib²⁹
- Subsequent therapy
 - Alectinib^{30,31}
 - Brigatinib³²
 - Ceritinib³³
 - Ensartinib³⁴
 - Lorlatinib³⁵

ROS1 Gene Fusion

- First-line therapy
 - Crizotinib³⁶
 - Entrectinib³⁷
 - Repotrectinib³⁸
 - Taletrectinib³⁹
- Subsequent therapy
 - Lorlatinib⁴⁰
 - Entrectinib³⁷
 - Repotrectinib³⁸
 - Taletrectinib³⁹

BRAF V600E Mutation

- First-line therapy
 - Dabrafenib/Trametinib⁴¹
 - Binimetinib/Encorafenib⁴²
 - Dabrafenib⁴³
 - Vemurafenib
- Subsequent therapy
 - Dabrafenib/Trametinib^{43,44}
 - Binimetinib/Encorafenib⁴²

NTRK1/2/3 Gene Fusion

- First-line/Subsequent therapy
 - Larotrectinib⁴⁵
 - Entrectinib⁴⁶
 - Repotrectinib⁴⁷

MET Exon 14 Skipping Mutation^a

- First-line therapy/Subsequent therapy
 - Capmatinib⁴⁸
 - Crizotinib⁴⁹
 - Tepotinib⁵⁰

RET Gene Fusion

- First-line therapy
 - Selpercatinib⁵¹
 - Pralsetinib⁵²
- Subsequent therapy
 - Cabozantinib^{53,54}

ERBB2 (HER2) Mutation^a

- First-line therapy
 - Zongertinib⁵⁵
- Subsequent therapy
 - Fam-trastuzumab deruxtecan-nxki⁵⁶
 - Ado-trastuzumab emtansine⁵⁷
 - Zongertinib⁵⁸
 - Sevabertinib⁵⁹

NRG1 Gene Fusion

- Subsequent therapy
 - Zenocutuzumab-zbco⁶⁰

HER2-positive IHC 3+

- Subsequent therapy
 - Fam-trastuzumab deruxtecan-nxki⁶¹

HGF receptor (c-Met) (≥50% IHC 3+ and EGFR wild-type)

- Subsequent therapy
 - Telisotuzumab vedotin-tllv (nonsquamous)⁶²

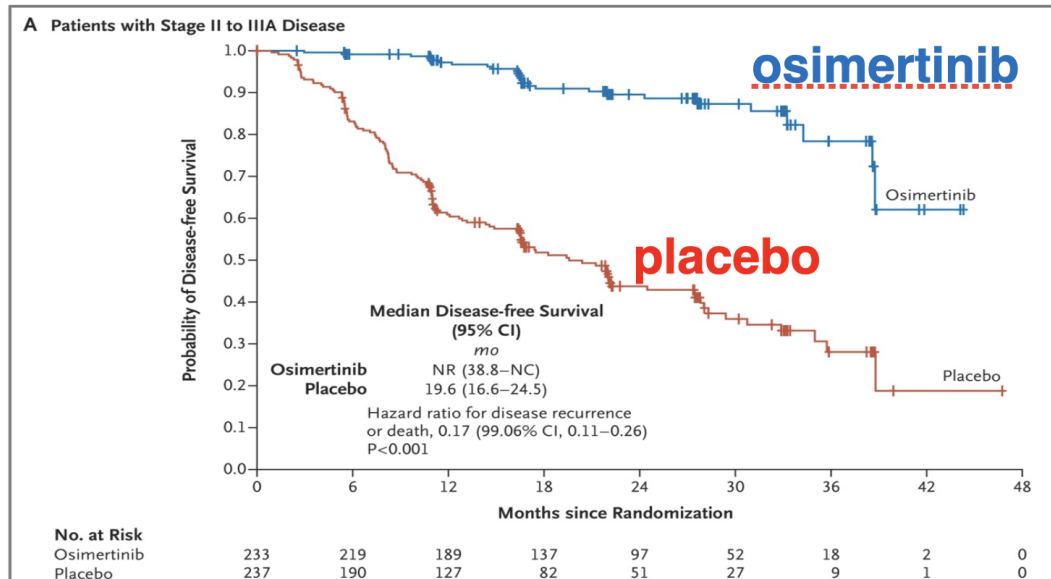
Precision adjuvant therapy for NSCLC

EGFR

ADAURA¹ trial - adjuvant EGFR targeted therapy

Practice changing standard

- Phase III: resected stage IB–IIIA EGFR-mutant NSCLC
- Classical mutations – exon 19 deletion, L858R
- Osimertinib × 3 years vs. placebo

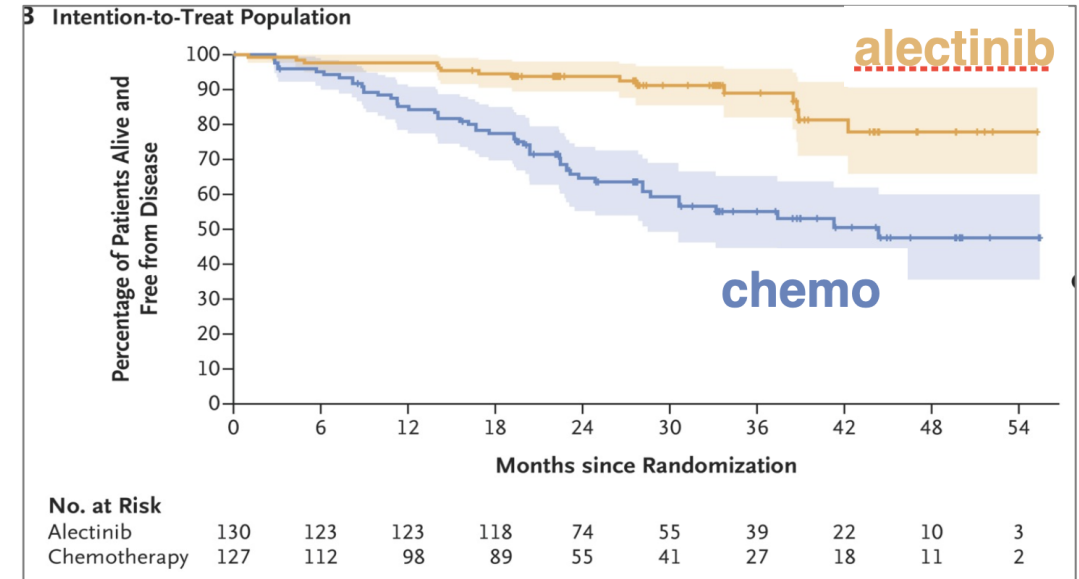


ALK

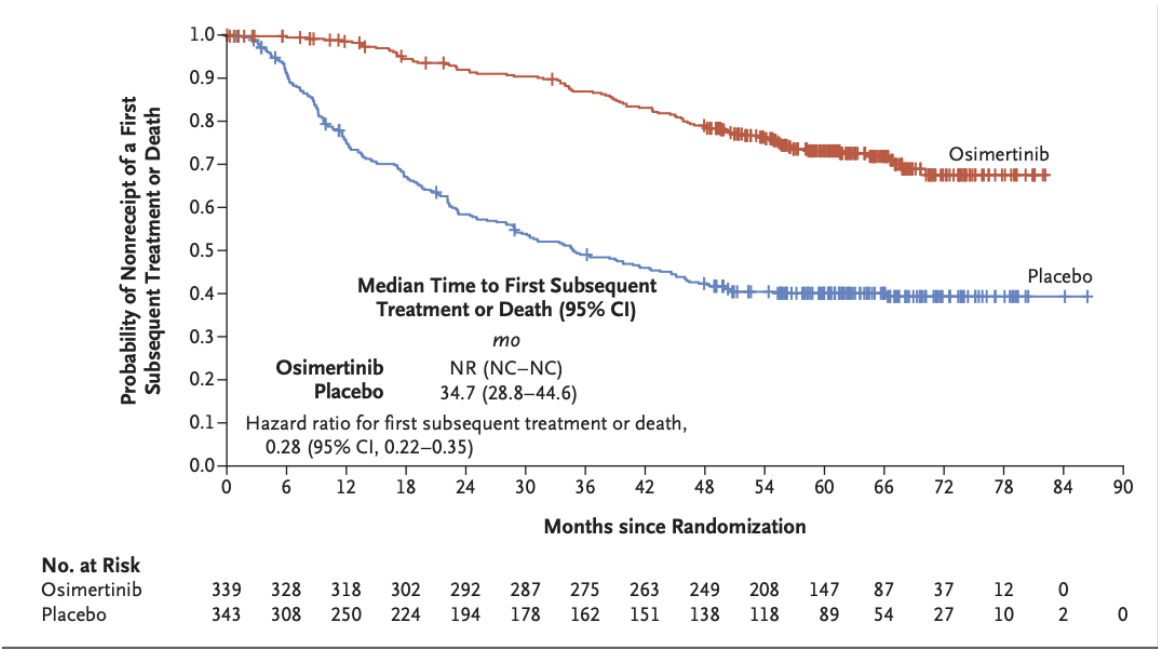
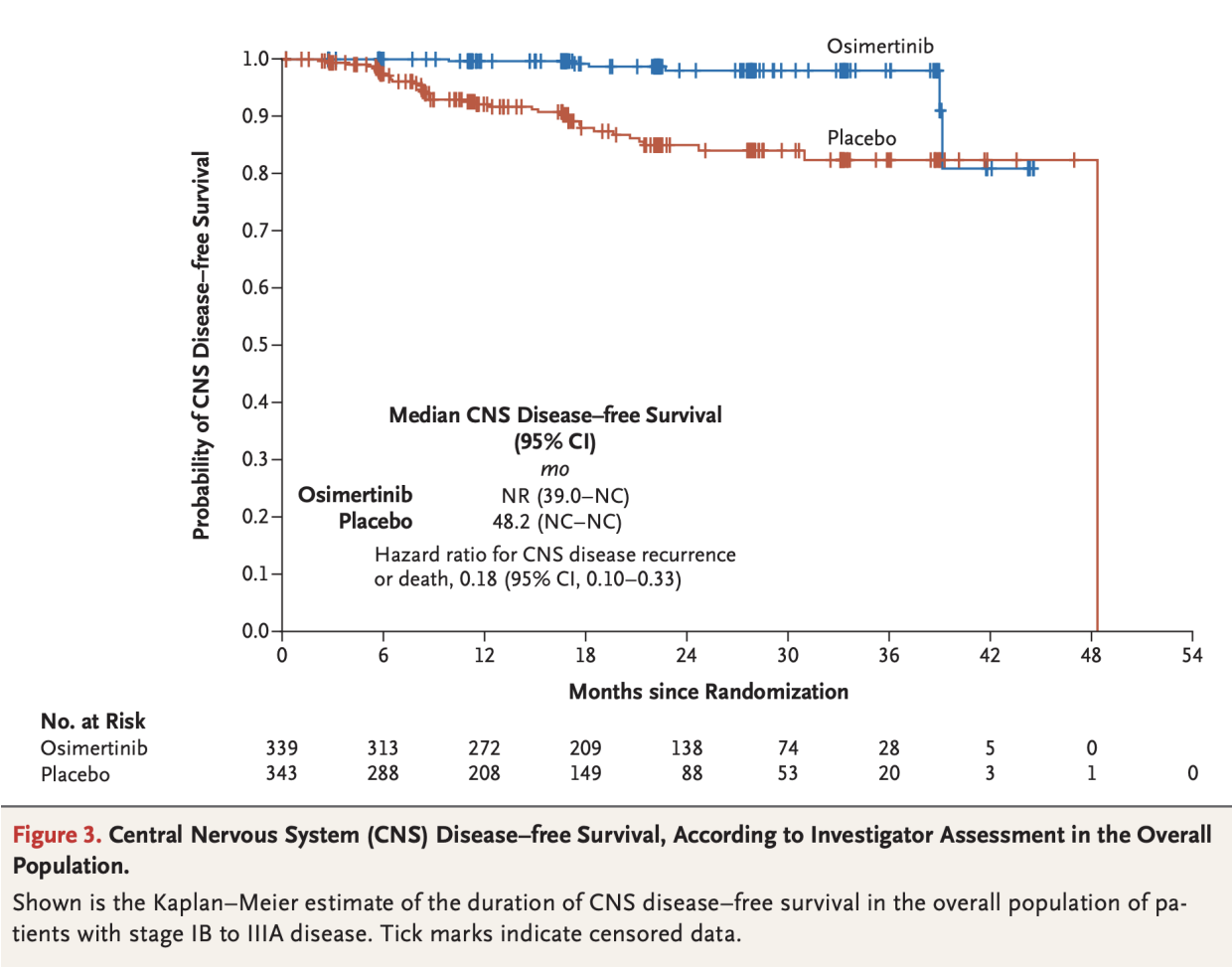
ALINA² trial - adjuvant ALK targeted therapy

Practice changing standard

- Phase III: resected stage IB–IIIA ALK fusion + NSCLC
- Alectinib × 2 years vs. chemotherapy

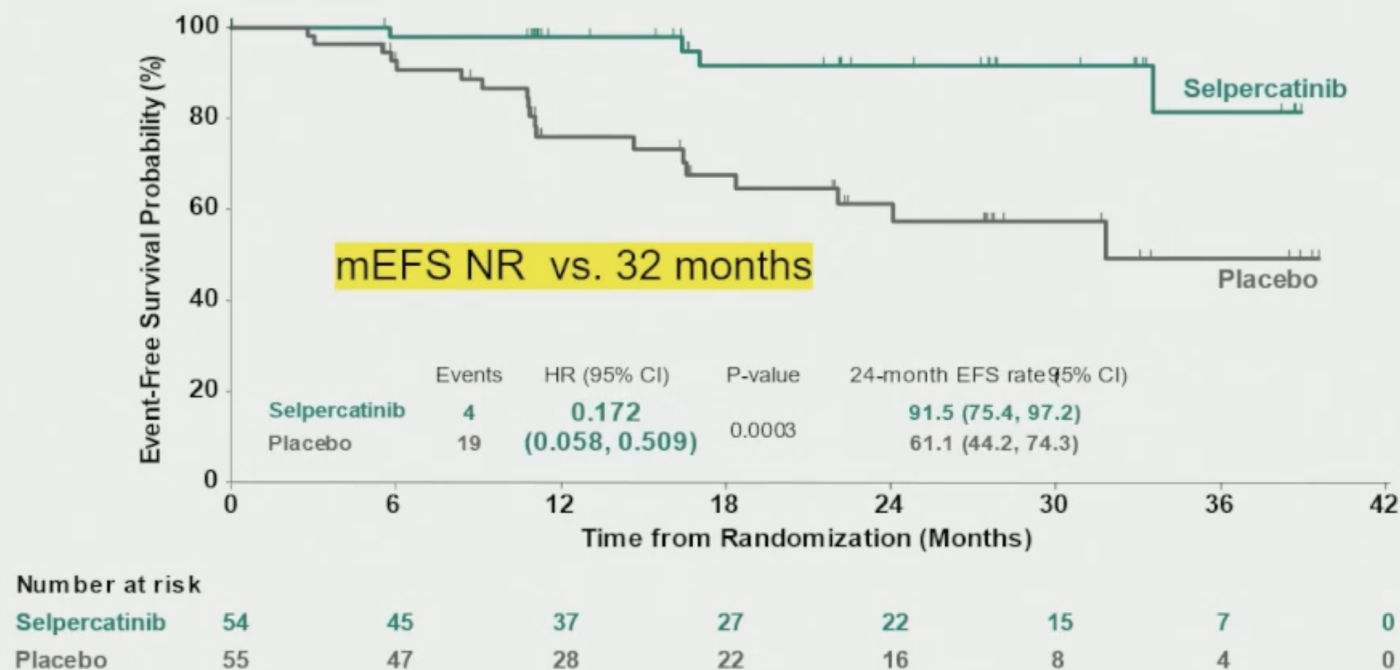


Prevention of brain metastases and OS benefit with adjuvant Osimertinib



2026 - RET fusion positive Early stage NSCLC

EFS Primary Endpoint Met...As Expected!



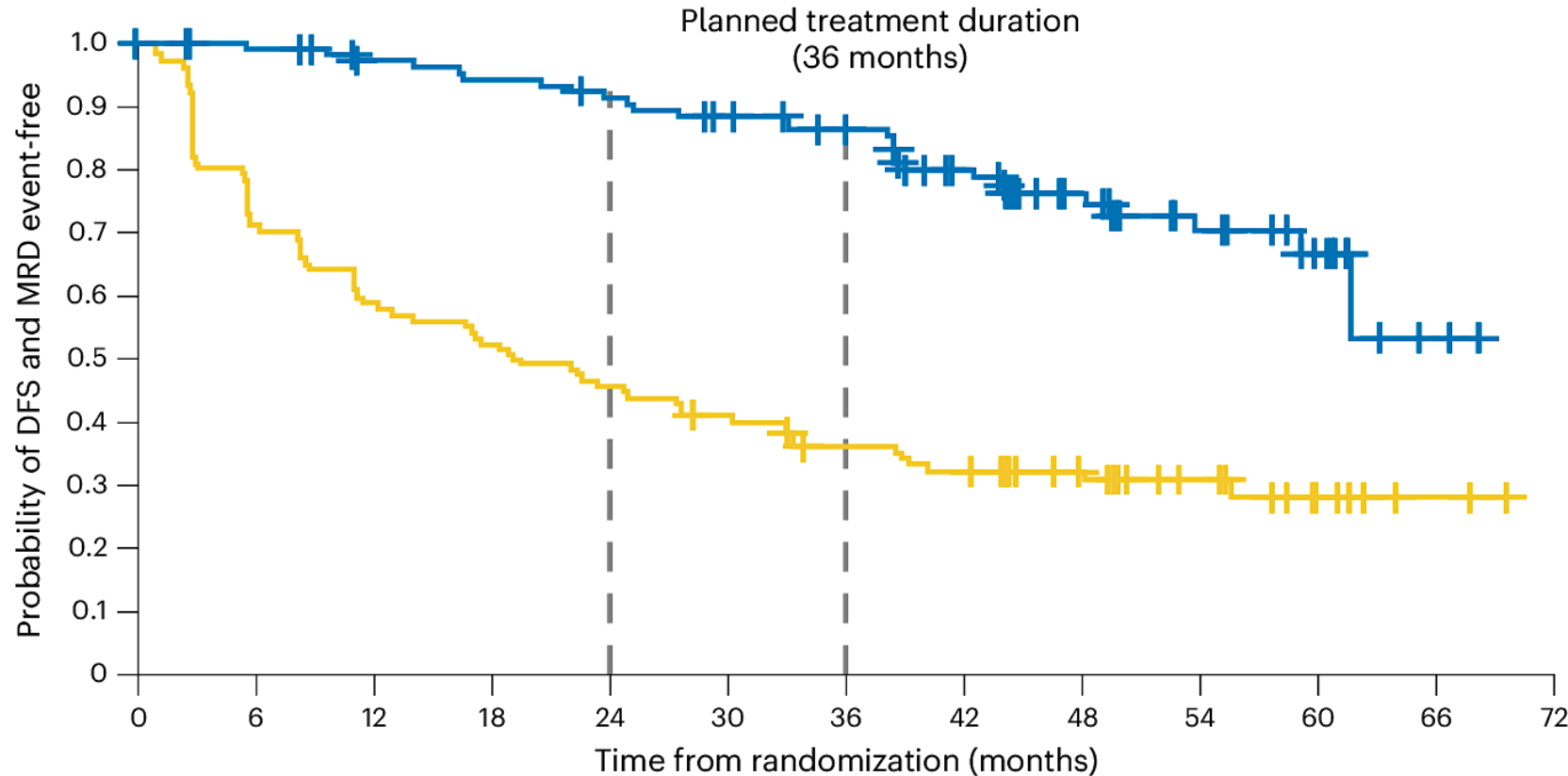
- Approx 90-92% of participants received prior anticancer systemic therapy
- Approx 17% participants d/c therapy due to TRAEs.

Primary Analysis Population, Stage II-III A *RET* fusion-positive NSCLC

- First and only randomized phase 3 study to evaluate a RET kinase inhibitor as adjuvant therapy in patients with early-stage *RET* fusion-positive lung cancer with acceptable safety profile

Presented By Goldman J et al ASCO 2026

Phase III ADAURA: DFS and MRD Event-Free Rate



Percent (95% CI)	DFS and MRD event-free rate	
	24 months	36 months
Osimertinib (n = 112)	91 (84–95)	86 (78–92)
Placebo (n = 108)	46 (36–55)	36 (27–45)
HR (95% CI) 0.23 (0.15–0.36)		

Median follow-up time, months (95% CI):
osimertinib: 44.2 (42.4–49.1), placebo: 19.1 (11.1–28.3)

Can We Find It—and Can We Fund It?

Early-Stage EGFR, ALK, and RET-positive NSCLC in LMICs

- **Reflex NGS is critical** to identifying targetable alterations in **early-stage NSCLC**
- ALK and RET fusions are **partner-diverse**—**NGS captures** the full actionable fusion landscape beyond the limits of RT-PCR and FISH
- **One month** of targeted therapy **out-of-pocket cost (approx. \$10-15K)** exceeds the annual income of many households in LMICs
- Precision oncology **advancement** is GREAT. Access **inequities** are BAD



Redefining Outcomes and Renewing Hope Through Precision Medicine

Key Priorities for Impact

- ✓ **Expand biomarker testing for early stage lung cancers.**
- ✓ **Develop risk stratification models to inform duration and intensity of therapy.**
- ✓ **Expand the reach of lung cancer screening.**
- ✓ **Focus on survivorship programs for lung cancer patients.**



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