University of Colorado Cancer Center
University of Colorado Hospital
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Early Stage and Locally Advanced NSCLC

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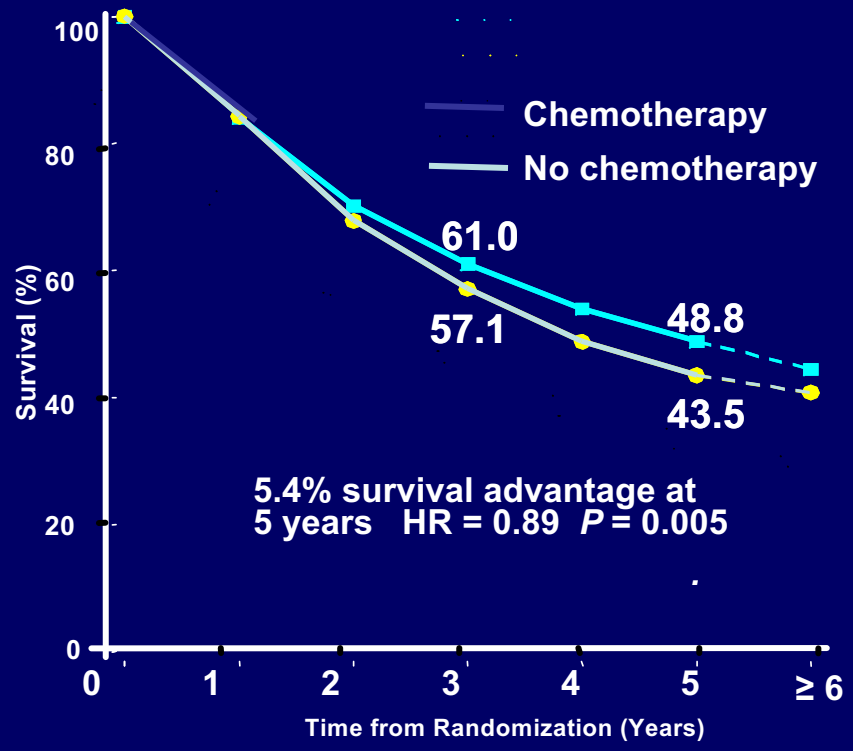
Meta-analyses of Adjuvant CT and Neoadjuvant CT

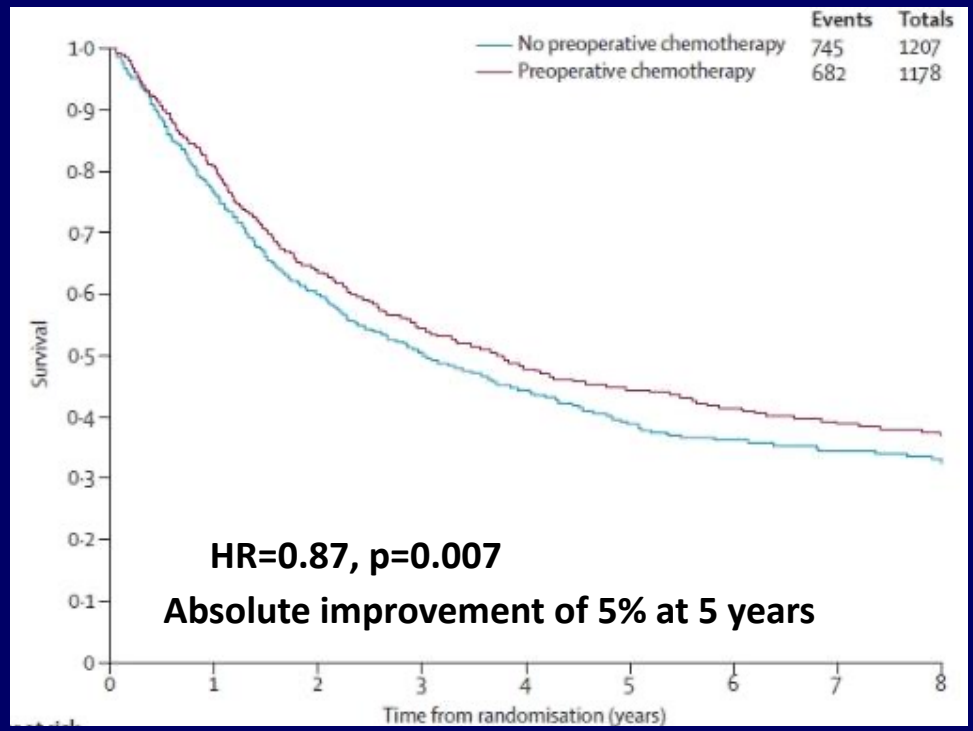
LACE: Pooled Adjuvant Data Overall Survival



Pignon JP, et al. J Clin Oncol. 2008;26:3552-3559

Path CR Rates <5%

NSCLC Neoadjuvant Collaborative Group meta-analysis



Lancet 2014;303:1561-71

Efficacy of Preoperative Immunotherapy

Path CR Rates 10-15%

Study	Total n= Squam, %	Stage I/II III	Drug # of preoperative cycles	# taken to surgery(%) #R0	ORR DCR	pCR^	MPR^	Biomarker Correlation with MPR
			PD-(L)1 Monotherapy					
Forde NEJM 2018	21 6 (29%)	66% 33%	Nivo 3 mg/kg x 2	21 (100) 20 R0	10% 95%	10%	45%	PD-L1: No correlation TMB: Correlation (+)
Gao JTO 2021	40 33 (83%)	55% 45%	Sintilimab 200 mg x 2	37 (92.5) 36 R0	20% 90%	16.2%	40.5%	PD-L1: Correlation (+)* TMB: NR
LCMC3	181 69 (38%)	51% 49%	Atezo 1200 mg x 2	159 (88) 145 R0	7%** 95%	7%	21%	PD-L1: No correlation TMB: No correlation
NEOSTAR	23 10 (43%)	78% 22%	Nivo 3 mg/kg x 3	22 (96) 22 R0	22% 87%	10%	19%	PD-L1: Correlation (+) TMB: NR
MK3475-223	15 NR	100% 0%	Pembro 200 mg x 1-2	13 (87) NR	13% NR	15%	31% 40% (2 doses)	PD-L1: No correlation TMB: NR
IFCT-1601 IONESCO	50 21 (42%)	96% 4%	Durva 750 mg x 3	43 (93) 41 R0	9% 87%	7%	18.6%	PD-L1: NR TMB: NR
PRINCEPS	30 NR	70% 30%	Atezo 1200 mg x 1	30 (100) 29 R0	7% 100%	0%	14%	PD-L1: Correlation (+) TMB: NR
			Dual Checkpoint Inhibitors					
Reuss JITC 2020	9 1 (11%)	33% 66%	Nivo 3 mg/kg x3, Ipi 1 mg/kg x 1	6 (67%) R0 NR	11% 55%	33%	33% (all pCR)	PD-L1: Correlation (+) TMB: No correlation
NEOSTAR	21 7 (33%)	81% 19%	Nivo 3 mg/mg x 3 Ipi 1 mg/kg x 1	17 (81) 17 R0	19% 81%	38%	44%	PD-L1: Correlation (+) TMB: NR

Squam: squamous; ORR: objective response rate; DCR: disease control rate; pCR: pathologic complete response; MPR: major pathologic response; TMB: tumor mutation burden; nivo: nivolumab; atezo: atezolizumab; pembro: pembrolizumab; durva: durvalumab; ipi: ipilimumab; NR: not reported

^Specimens with pCR also included among those with MPR. The denominator is patients undergoing resection. *Correlation in stromal cells only; **Based on data reported for 82 patients

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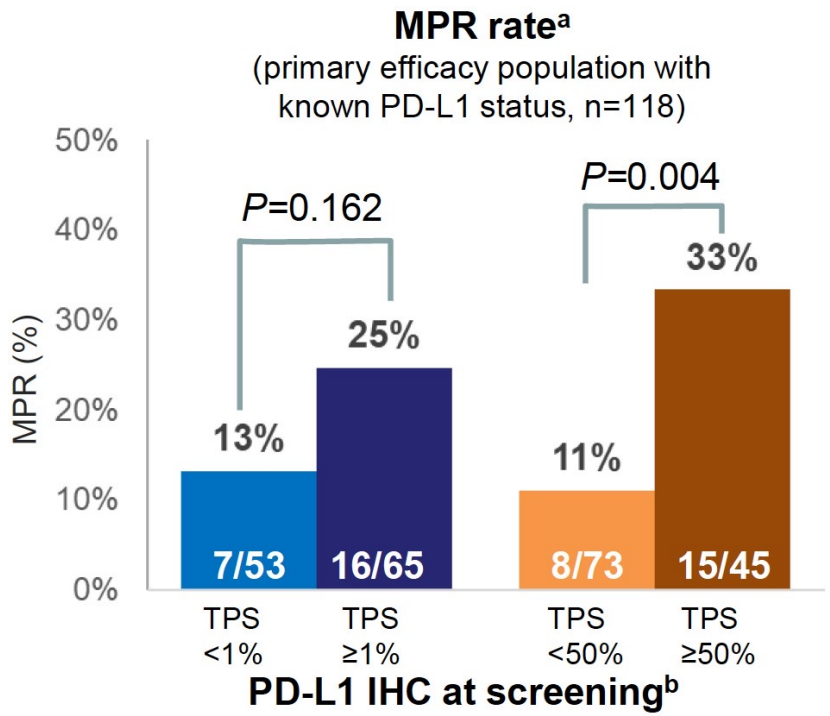
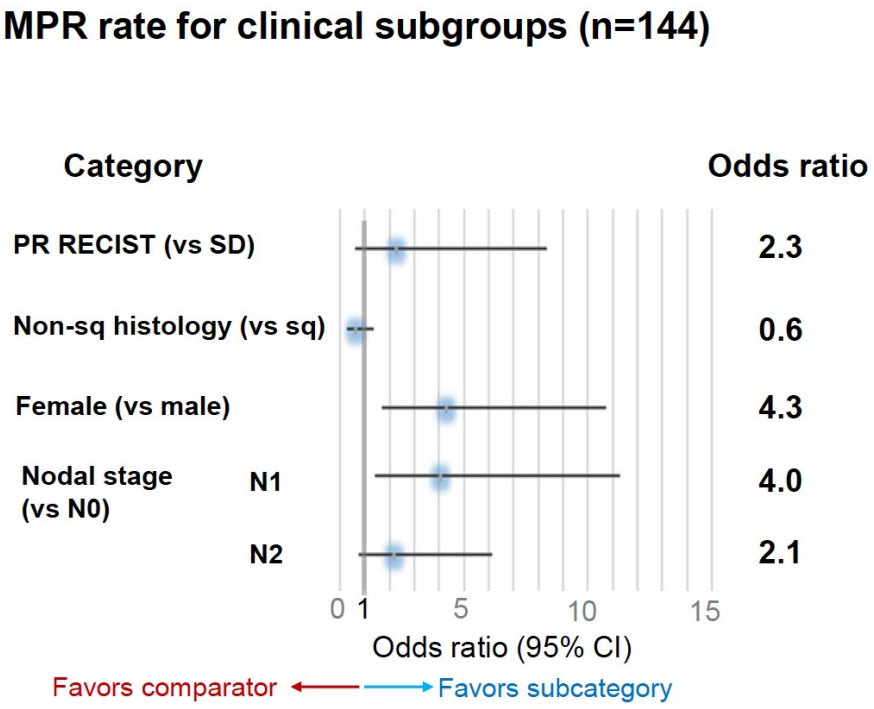
PD-L1 important with neo-adjuvant atezolizumab – LCMC3

MPR by PD-L1 status at screening and selected patient categories LCMC3



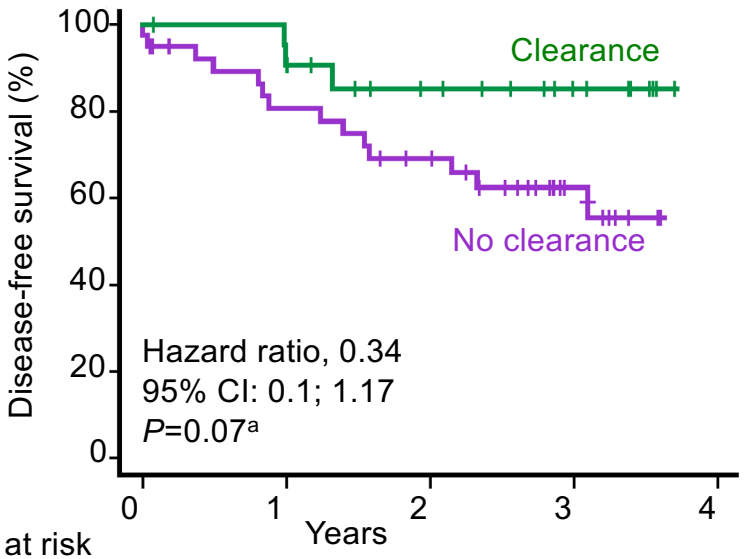


sq, squamous.

[a] Analysis population excluded of EGFR and ALK positive patients. [b] Local TPS score used if central score was not available.

LCMC 3 Atezo Neoadj.:Preliminary results showed improved disease-free survival in patients with ctDNA clearance

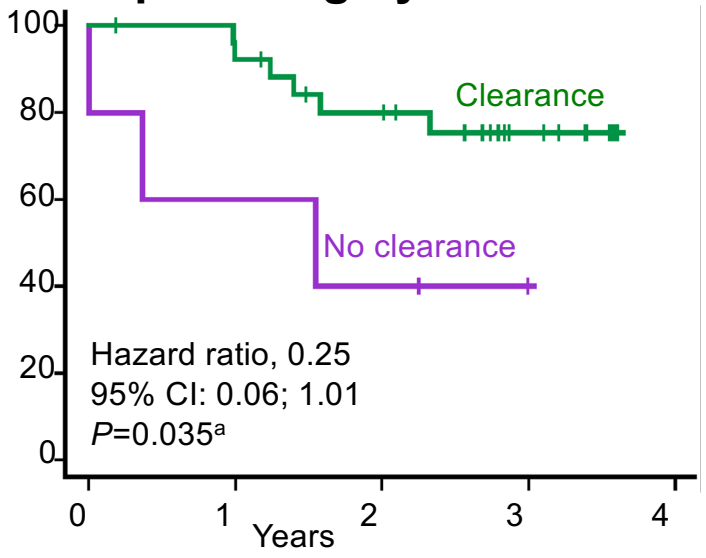
Disease-free survival by baseline to post-atezo clearance



No. at risk					
Clearance	22	19	13	7	0
No clearance	39	28	22	9	0

Years	Clearance		No clearance	
	DFS rate, %	At risk, n	DFS rate, %	At risk, n
1	91	19	81	28
2	85	13	69	22
3	85	7	62	9

Disease-free survival by baseline to post-surgery clearance

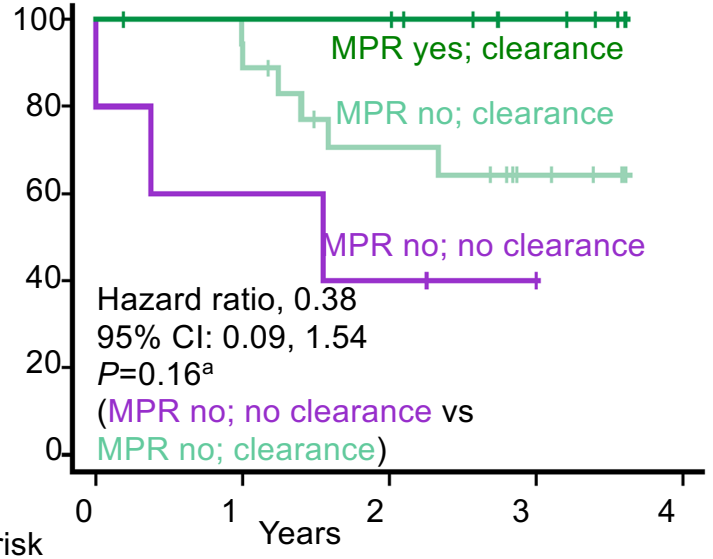


No. at risk					
Clearance	27	24	19	10	0
No clearance	5	3	2	0	0

Years	Clearance		No clearance	
	DFS rate, %	At risk, n	DFS rate, %	At risk, n
1	92	24	60	3
2	80	19	40	2
3	75	10	–	–

Disease-free survival by baseline to post-surgery clearance and MPR

Stratify by MPR



No. at risk					
MPR yes; clearance	8	8	8	4	0
MPR no; clearance	19	16	11	6	0
MPR no; no clearance	5	3	2	0	0

Years	MPR yes; clearance		MPR no; clearance		MPR no; no clearance	
	DFS rate, %	At risk, n	DFS rate, %	At risk, n	DFS rate, %	At risk, n
1	100	8	89	16	60	3
2	100	8	71	11	40	2
3	100	4	64	6	–	–

[a] Log-rank test.

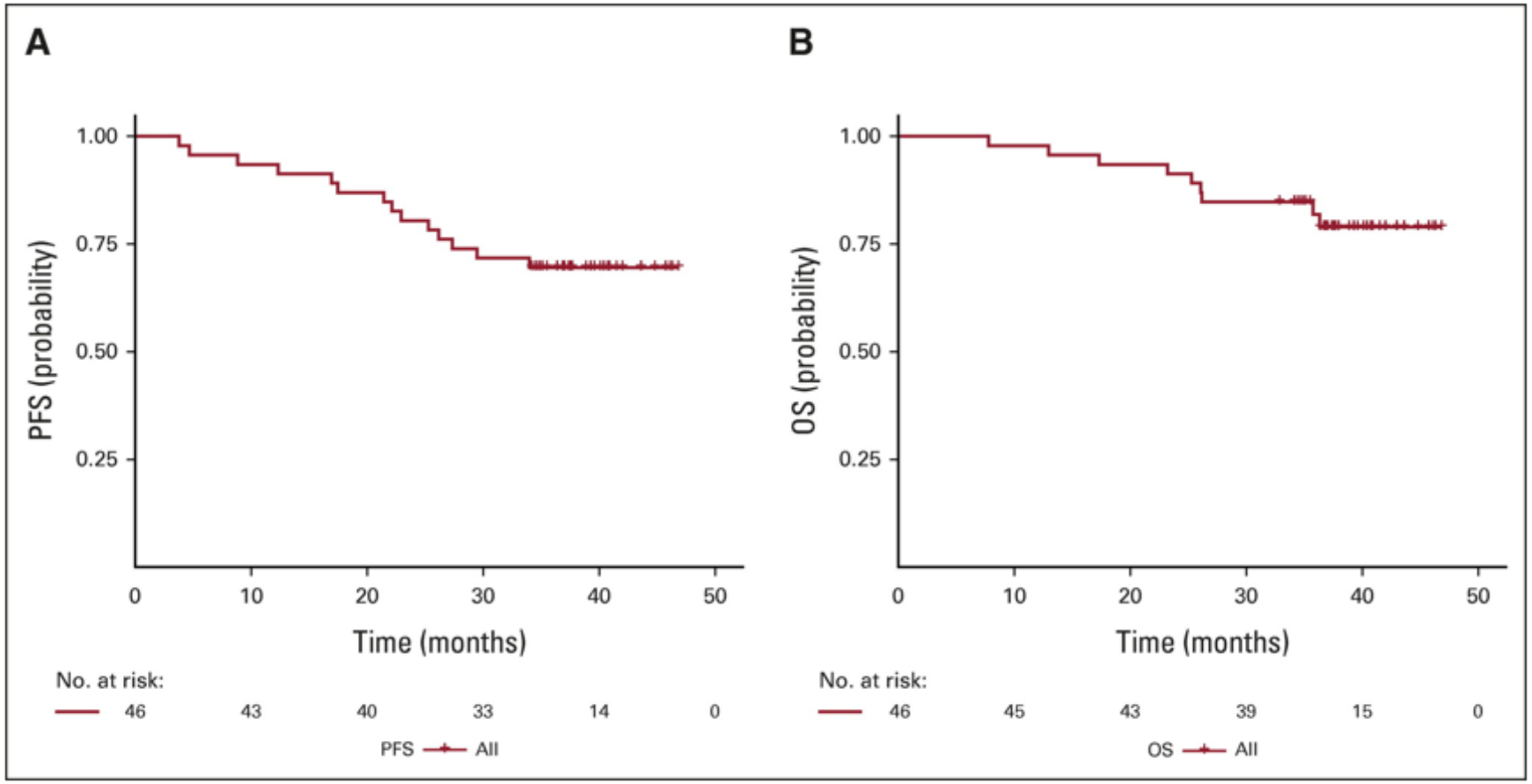
Neoadjuvant immuno-chemotherapy clinical trials

Trial	Phase	Enrollment	Stage	Neoadjuvant treatment	MPR	pCR
NCT02716038	II	30	IB-IIIA*	Atezolizumab + platinum doublet × 4 cycles	57%	33%
NADIM	II	46	IIIA*	Nivolumab + platinum doublet × 3 cycles	83%	63%
NCT04304248	II	33	IIIA, T3-4N2 IIIB**	Toripalimab + platinum doublet × 3 cycles	67%	50%
SAKK16/14	II	68	T1-3N2M0, IIIA(N2)*	Platinum doublet × 3 cycles, followed by durvalumab × 2 cycles	62%	18%
CheckMate816	III	358	IB-IIIA*	Nivolumab + platinum doublet vs platinum doublet × 3 cycles	36.9% vs 8.9%	24% vs 2.2%

*, per American Joint Committee on Cancer 7th edition
**, per American Joint Committee on Cancer 8th edition
pCR, complete pathology response.

Path CR 37-83%

NADIM Phase II (Nivo +CT):PFS & OS



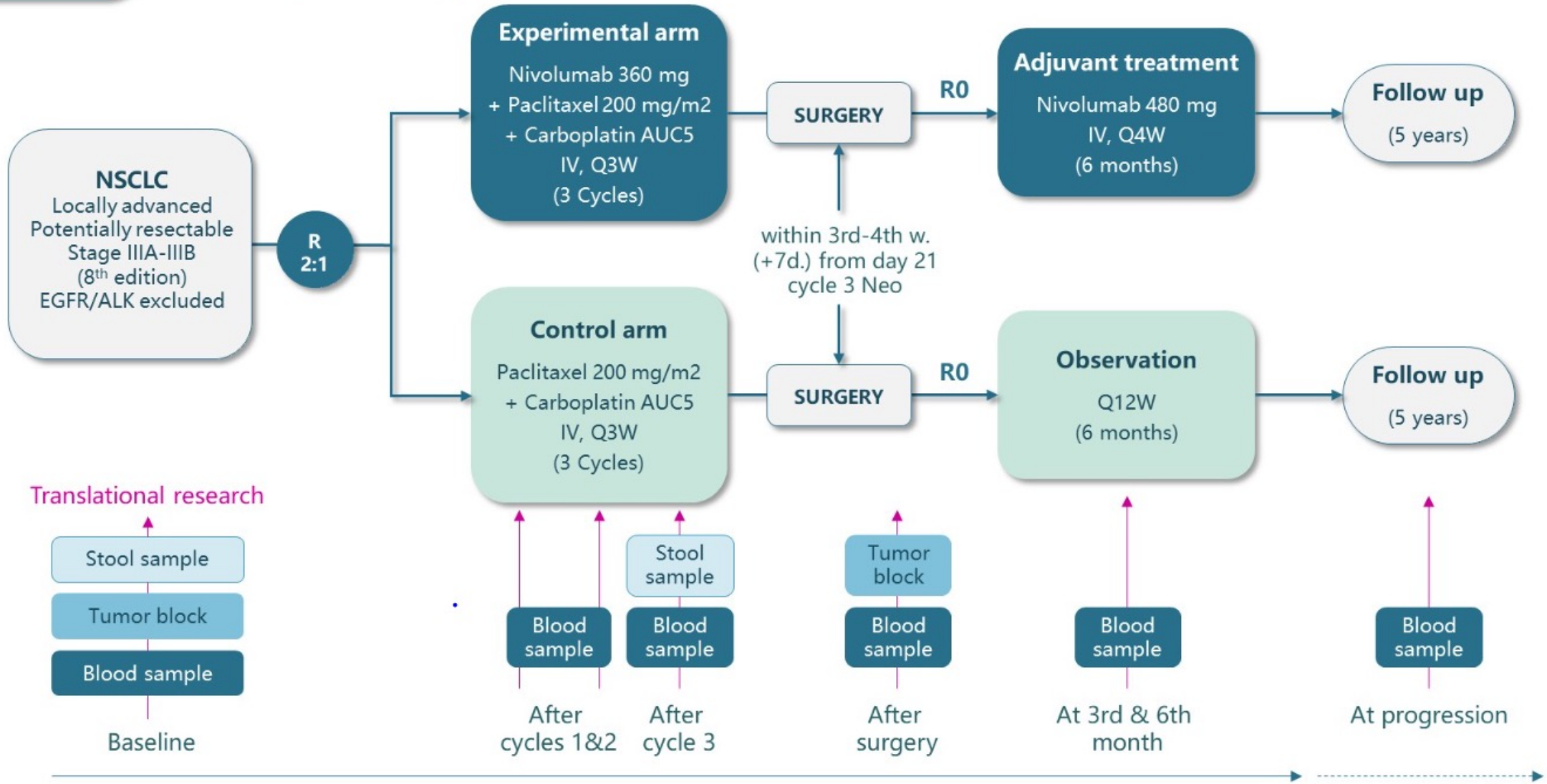
G 1. Kaplan-Meier curves for (A) PFS and (B) OS in the ITT population (N = 46). ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival.

Provencia M et al: JCO 40: 2924-33, 2022

Randomized neoadjuvant trials: CT+ IO vs CT

CANOPY N	NCT 03968419	Canakinumab or pembrolizumab (200 mg) or Canakinumab + Pembrolizumab x 2 cycles → S	IB-IIIA	110	II	MPR
KEYNOTE 617	NCT 03425643	CT + Pembrolizumab (200 mg) / placebo x 4 cycles → S → Pembrolizumab / Placebo x 13 cycles	IIB-IIIA	786	III	EFS, OS
CheckMate 816*	NCT 02998528	CT + Nivolumab (360 mg) x 3 cycles → S *vs.* CT x 3 cycles → S	IB-IIIA	350	III	EFS, MPR
IMpower 030	NCT 03456063	CT + Atezolizumab (1200 mg) / placebo x 4 cycles → S → Atezolizumab / Placebo x 16 cycles	II-IIIB (cT3N2)	374	III	MPR
AEGEAN	NCT 03800134	CT + Durvalumab (1500 mg) / Placebo Q3W x 4 cycles → S → Durvalumab / Placebo Q4W x 12 cycles	IIA-IIIB	300	III	MPR

NADIM II Study design



NADIM II (NCT03838159) is a randomized, phase 2, open-label, multicentre study evaluating nivolumab + chemotherapy vs chemotherapy as neoadjuvant treatment for potentially resectable NSCLC

PRESENTED BY: **Mariano Provencio MD, PhD.**
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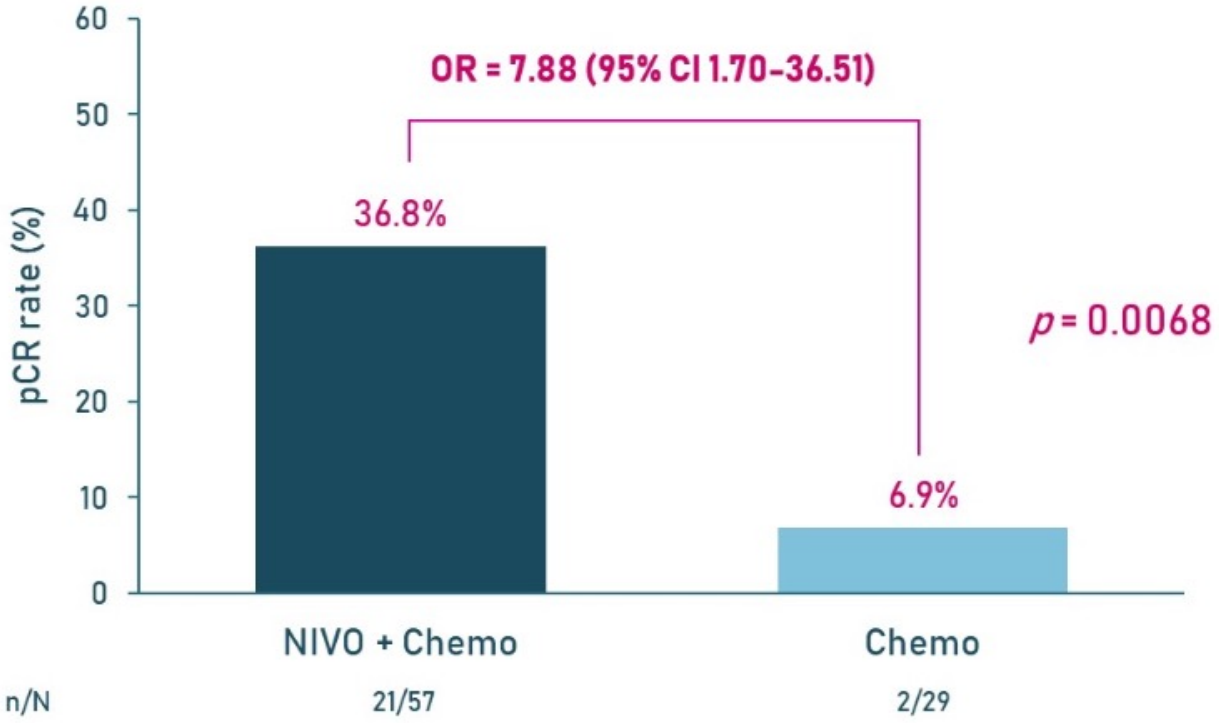
NADIM II Primary endpoint - pCR

pCR[a] rate with neoadjuvant NIVO + CT vs CT in the ITT population[b]



[a]pCR was defined as 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; [b]Patients who did not undergo surgery were considered as non-responders
Chemo, chemotherapy; ITT, intention-to-treat; Nivo, nivolumab; pCR, pathological complete response; RR, risk ratio

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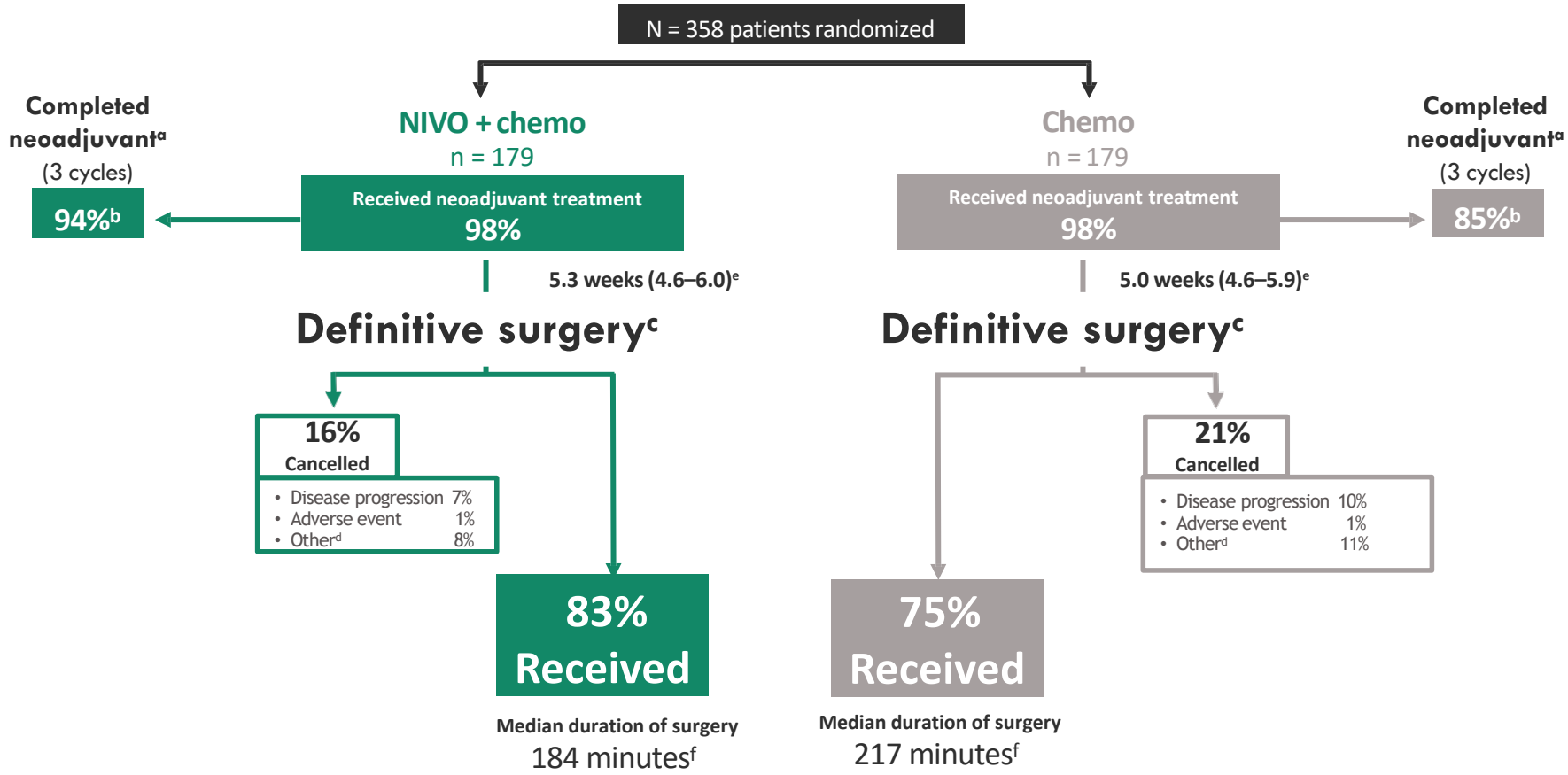
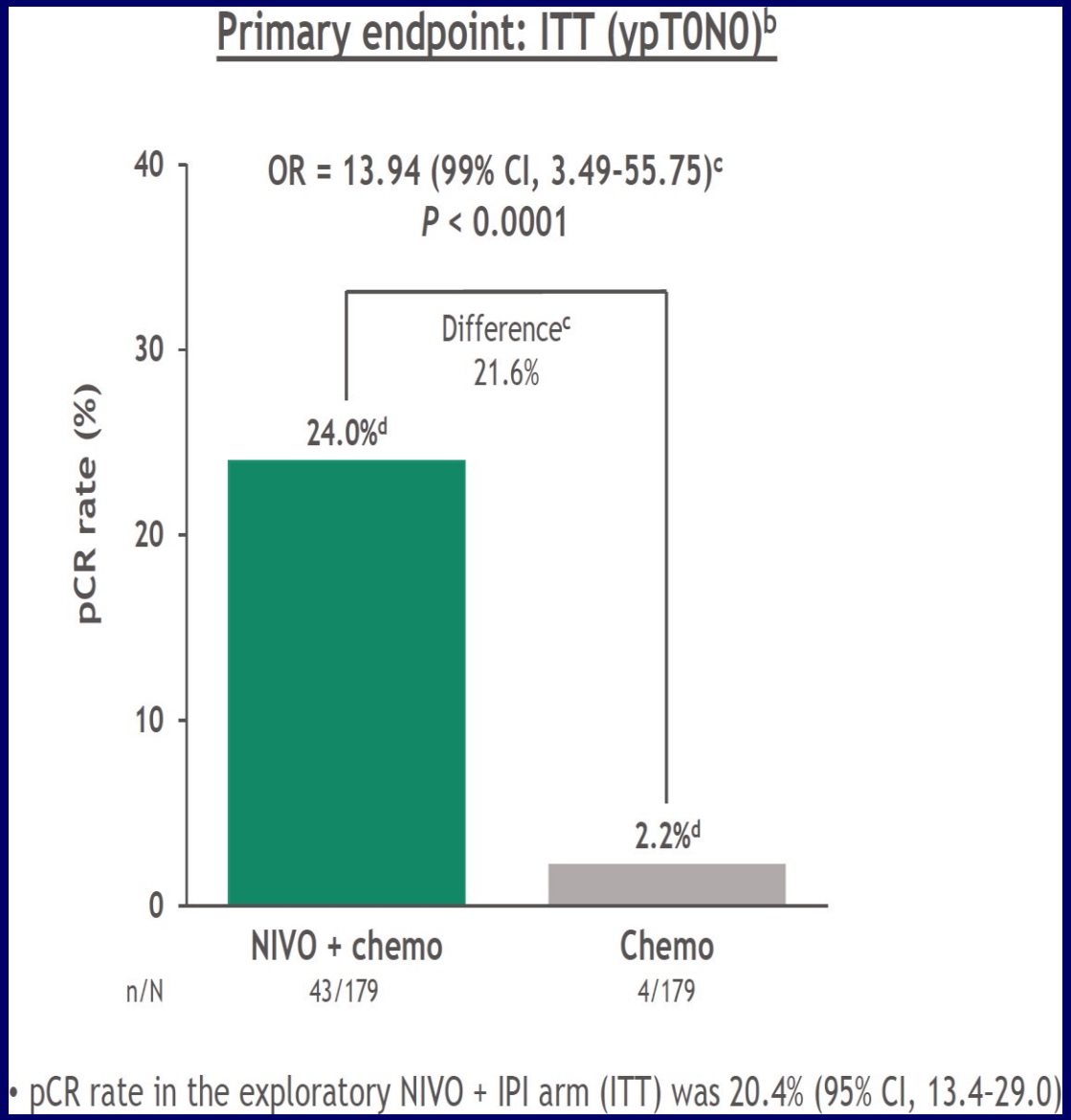
CM816: Treatment and surgery summary: all randomized patients

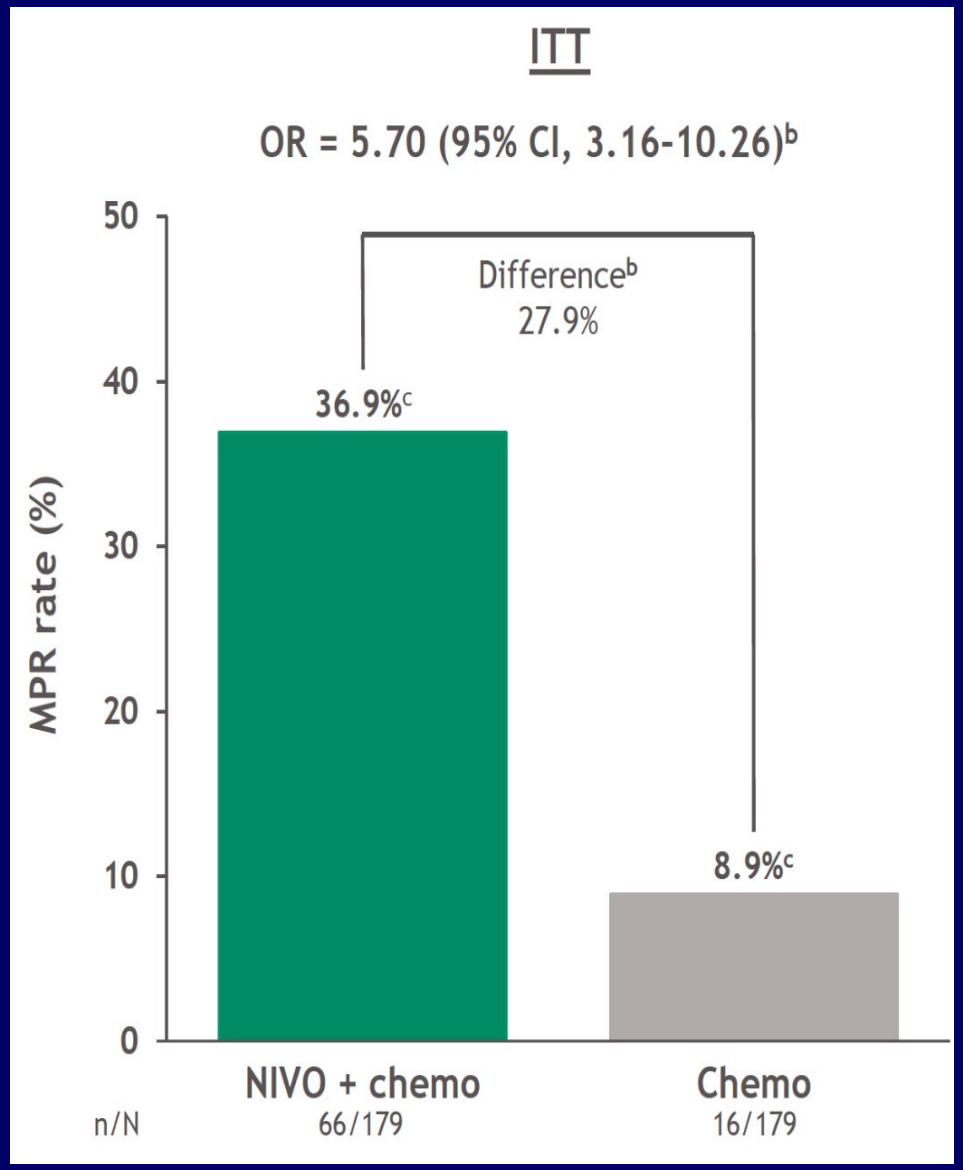


[a]Reasons for patients not completing neoadjuvant treatment: study drug toxicity (6% in the NIVO + chemo and 7% in the chemo arm), disease progression (1% in each arm), and other reasons (7% in the chemo arm only; this included AEs unrelated to study drug, patient request to discontinue treatment, patient withdrew consent, and patient no longer meeting study criteria); [b]Denominator based on patients with neoadjuvant treatment; [c]Definitive surgery not reported: NIVO + chemo, 1%; chemo, 3%; [d]Other reasons included patient refusal, unresectability, and poor lung function; [e]Median (IQR) time from last dose to definitive surgery; [f]Patients (n) with reported duration of surgery: NIVO + chemo, 122; chemo, 121; IQR for median duration of surgery: NIVO + chemo, 130.0-252.0 minutes; chemo, 150.0–283.0 minutes.

Spicer ASCO 2021 abstr 8503

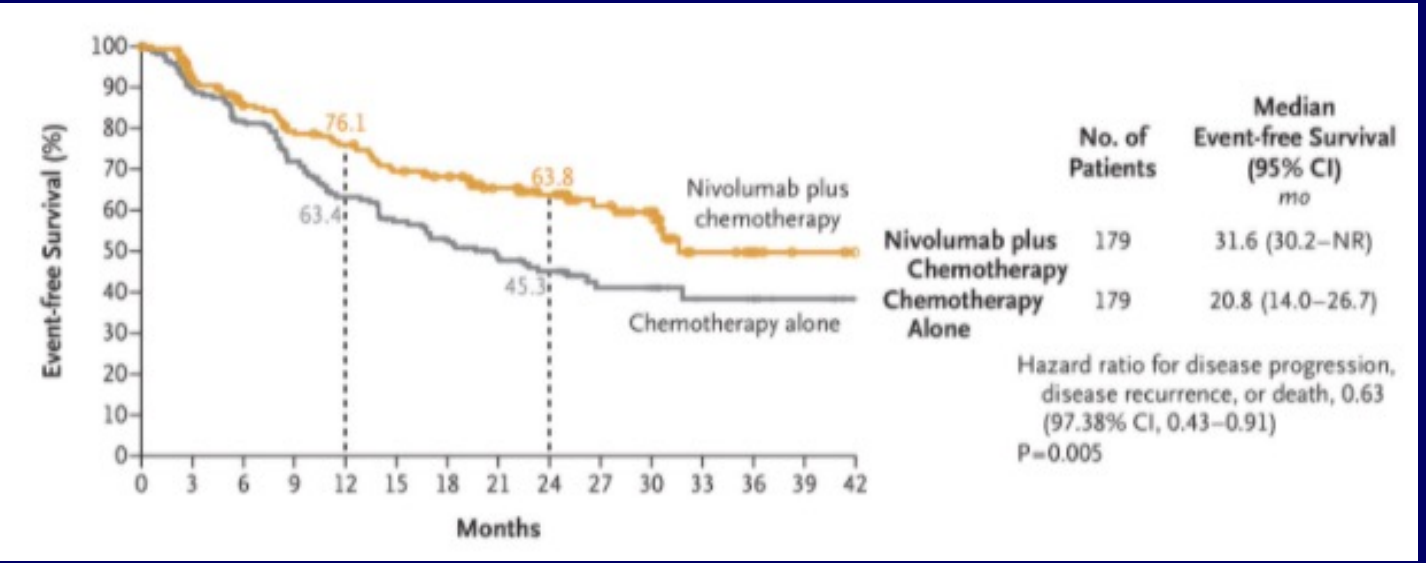
CM816 – pCR and MPR in ITT population





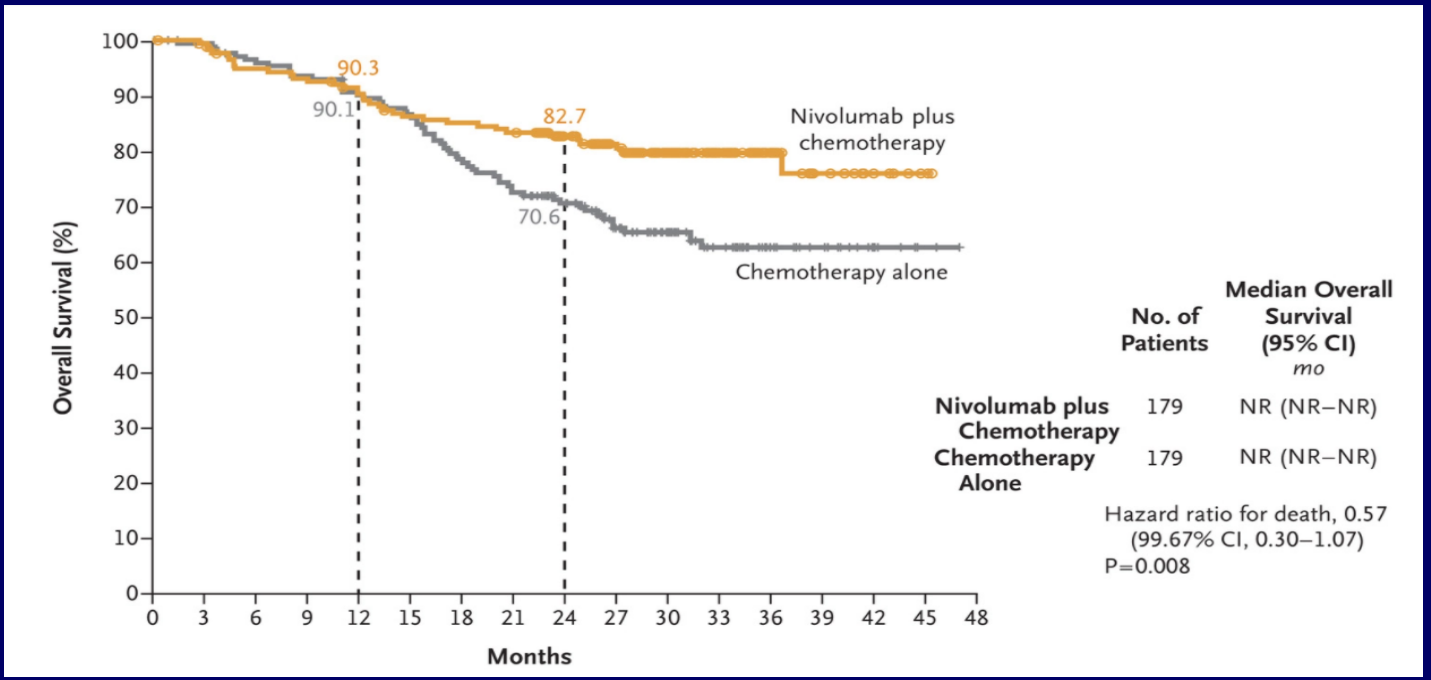
Forde CM816, AACR2021

Neoadjuvant Nivo +CT in Early Stage NSCLC



	No. of Patients	Median Event-free Survival (95% CI) mo
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

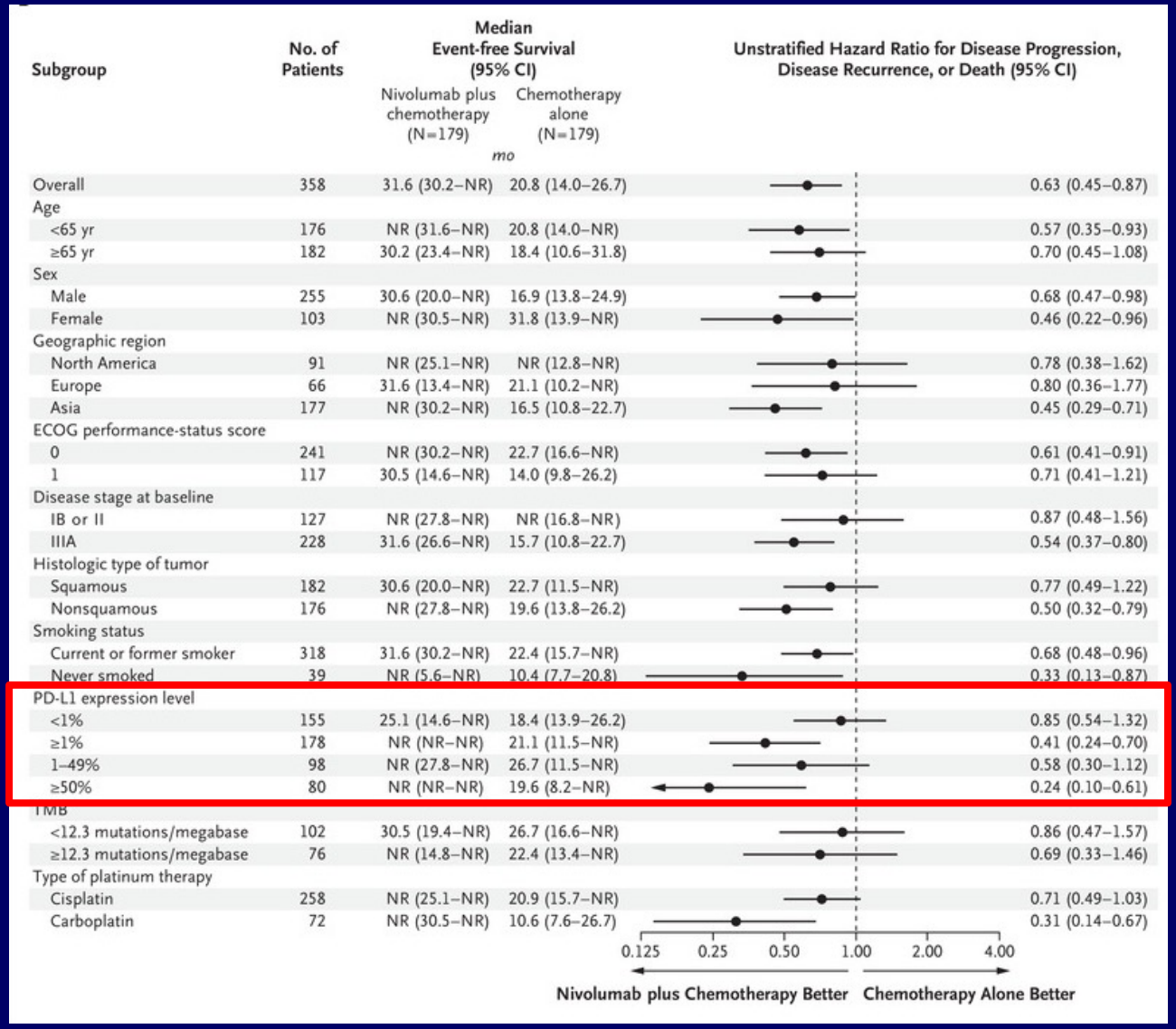


	No. of Patients	Median Overall Survival (95% CI) mo
Nivolumab plus Chemotherapy	179	NR (NR–NR)
Chemotherapy Alone	179	NR (NR–NR)

Hazard ratio for death, 0.57 (99.67% CI, 0.30–1.07)
P=0.008

Forde PM et al: Neoadjuvant Nivolumab plus Chemotherapy in resectable lung cancer. NEJM2022

Forest plot of EFS in CM816

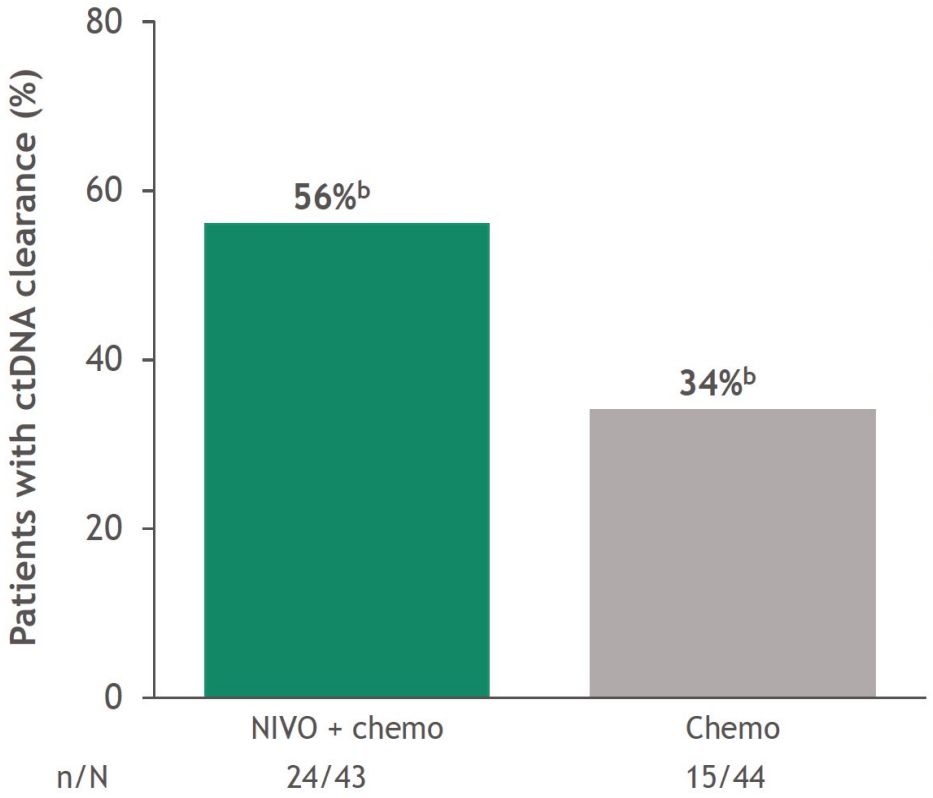


Subgroup	No. of Patients	Median Event-free Survival (95% CI)	
		Nivolumab plus chemotherapy (N=179)	Chemotherapy alone (N=179)
		mo	
Overall	358	31.6 (30.2–NR)	20.8 (14.0–26.7)
Age			
<65 yr	176	NR (31.6–NR)	20.8 (14.0–NR)
≥65 yr	182	30.2 (23.4–NR)	18.4 (10.6–31.8)
Sex			
Male	255	30.6 (20.0–NR)	16.9 (13.8–24.9)
Female	103	NR (30.5–NR)	31.8 (13.9–NR)
Geographic region			
North America	91	NR (25.1–NR)	NR (12.8–NR)
Europe	66	31.6 (13.4–NR)	21.1 (10.2–NR)
Asia	177	NR (30.2–NR)	16.5 (10.8–22.7)
ECOG performance-status score			
0	241	NR (30.2–NR)	22.7 (16.6–NR)
1	117	30.5 (14.6–NR)	14.0 (9.8–26.2)
Disease stage at baseline			
IB or II	127	NR (27.8–NR)	NR (16.8–NR)
IIIA	228	31.6 (26.6–NR)	15.7 (10.8–22.7)
Histologic type of tumor			
Squamous	182	30.6 (20.0–NR)	22.7 (11.5–NR)
Nonsquamous	176	NR (27.8–NR)	19.6 (13.8–26.2)
Smoking status			
Current or former smoker	318	31.6 (30.2–NR)	22.4 (15.7–NR)
Never smoked	39	NR (5.6–NR)	10.4 (7.7–20.8)
PD-L1 expression level			
<1%	155	25.1 (14.6–NR)	18.4 (13.9–26.2)
≥1%	178	NR (NR–NR)	21.1 (11.5–NR)
1–49%	98	NR (27.8–NR)	26.7 (11.5–NR)
≥50%	80	NR (NR–NR)	19.6 (8.2–NR)
TMB			
<12.3 mutations/megabase	102	30.5 (19.4–NR)	26.7 (16.6–NR)
≥12.3 mutations/megabase	76	NR (14.8–NR)	22.4 (13.4–NR)
Type of platinum therapy			
Cisplatin	258	NR (25.1–NR)	20.9 (15.7–NR)
Carboplatin	72	NR (30.5–NR)	10.6 (7.6–26.7)

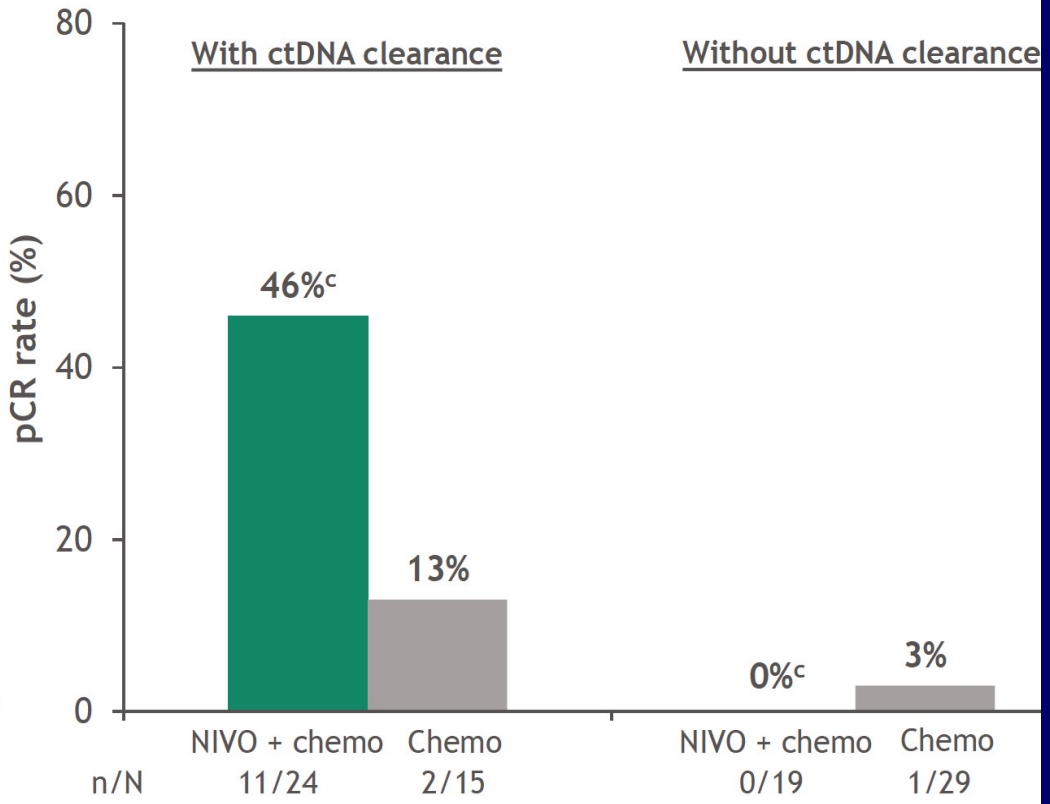
CM816 ctDNA data

ctDNA clearance and association with pathological response

ctDNA clearance rate (C1D1 to C3D1)[a]

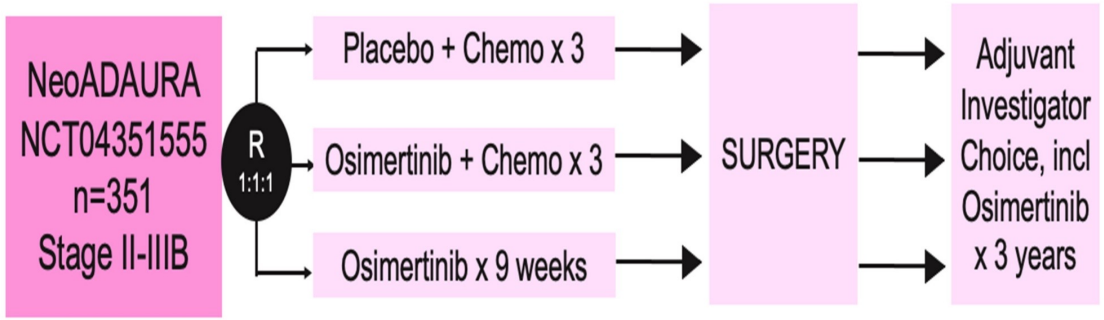


ctDNA clearance and pCR rates



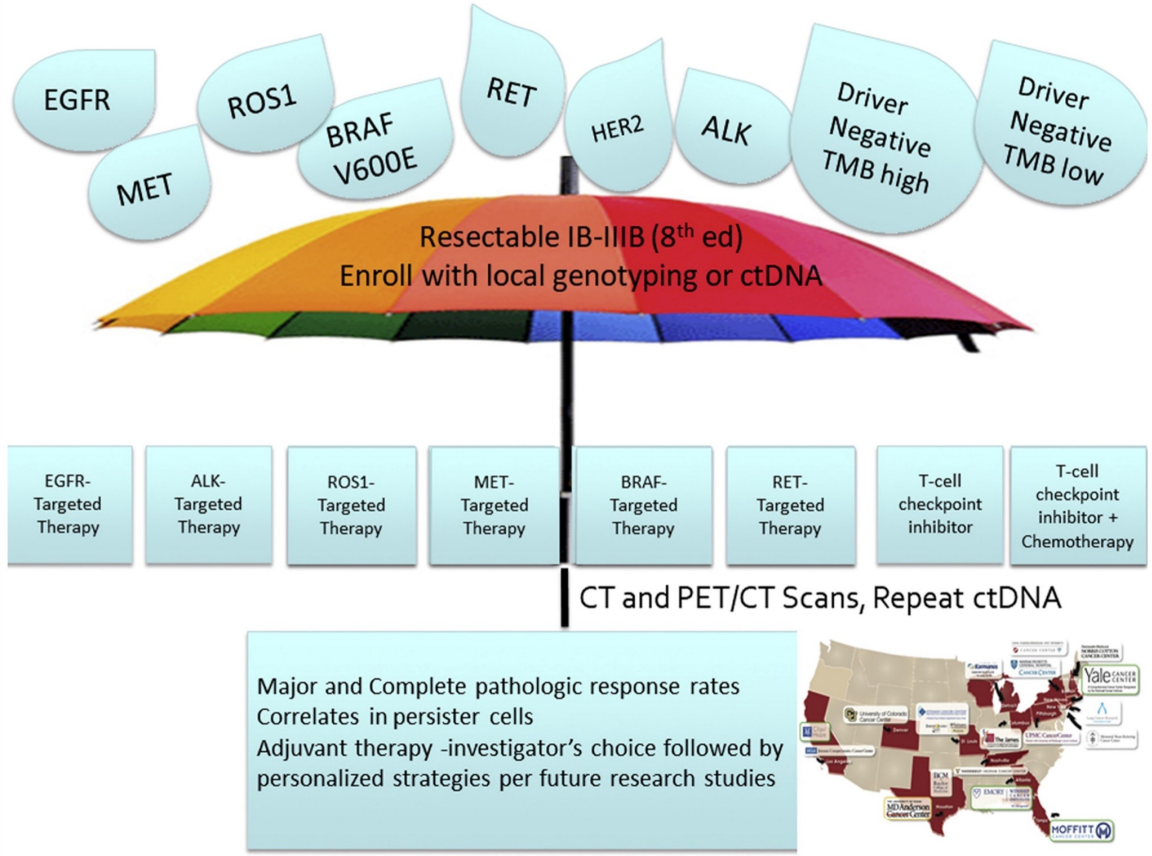
[a]Performed using tumor-guided personalized ctDNA panel (ArcherDX Personalized Cancer Monitoring); 90 patients were ctDNA evaluable and 87 had detectable ctDNA at C1D1; main reason for sample attrition were lack of tissue for WES and lack of quality control pass for tissue and plasma; [b]ctDNA clearance 95% CI: NIVO + chemo, 40-71; chemo, 20-50; [c]pCR rates 95% CI for NIVO + chemo: with ctDNA clearance, 26-67; without ctDNA clearance, 0-18.

Ongoing Studies Exploring Neoadjuvant Targeted Therapy



The primary endpoint is pCR

LCRF LEADER/LCMC4 Study



Major and Complete pathologic response rates
Correlates in persister cells
Adjuvant therapy -investigator's choice followed by personalized strategies per future research studies

Tsuboi JTO 2021, Blumenthal JTO 2018

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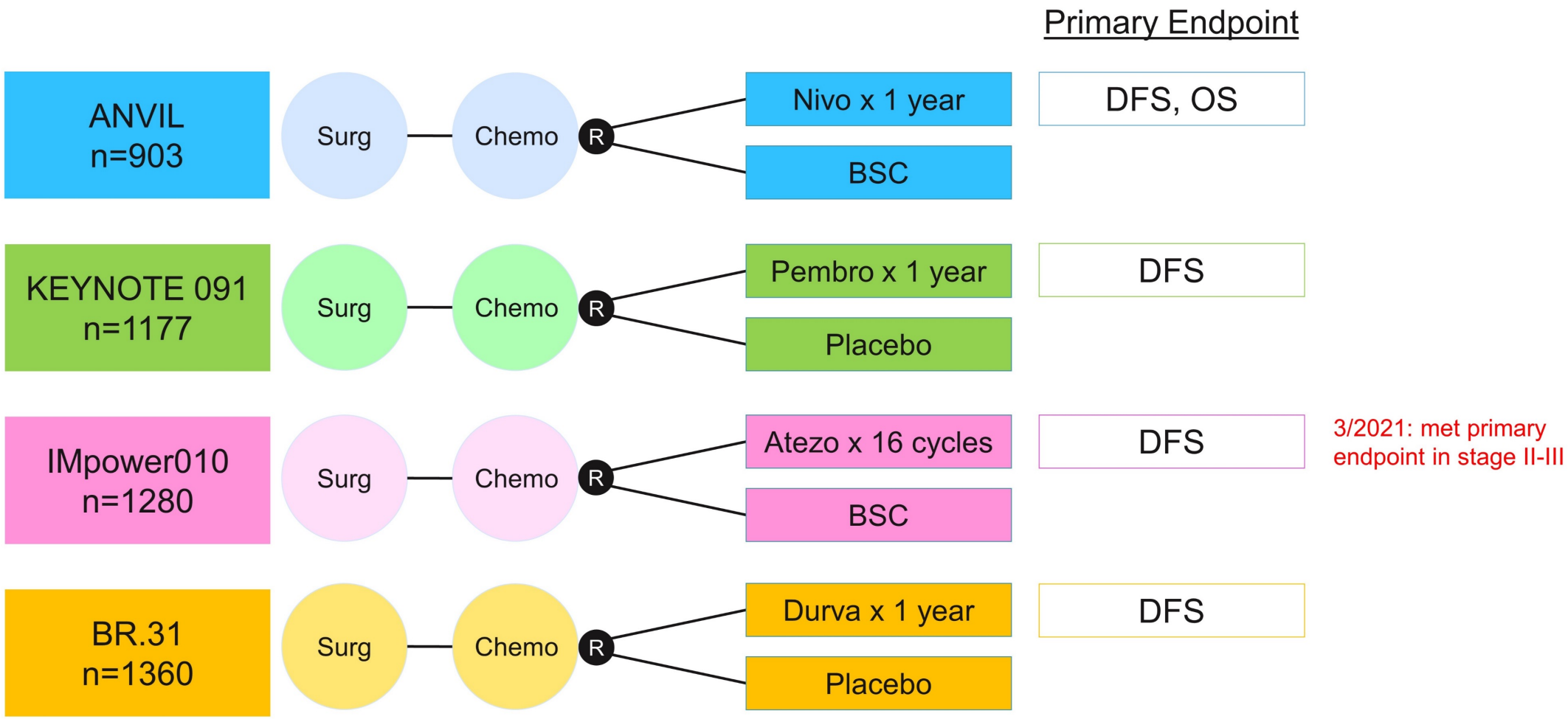
Major Remaining Questions: Neoadjuvant IO+CT & TKI Rx

- How many pre-op cycles? 2 vs 3
- Need for post-op adjuvant IO?
  - Does pCR matter?
  - Does ctDNA matter?
- Stage 1B included?
- Does PD-L1 status matter?
- Should patients with genetic alterations receive neoadjuvant TKI or CT/IO?

Phase III Studies Exploring Adjuvant Checkpoint Inhibitors



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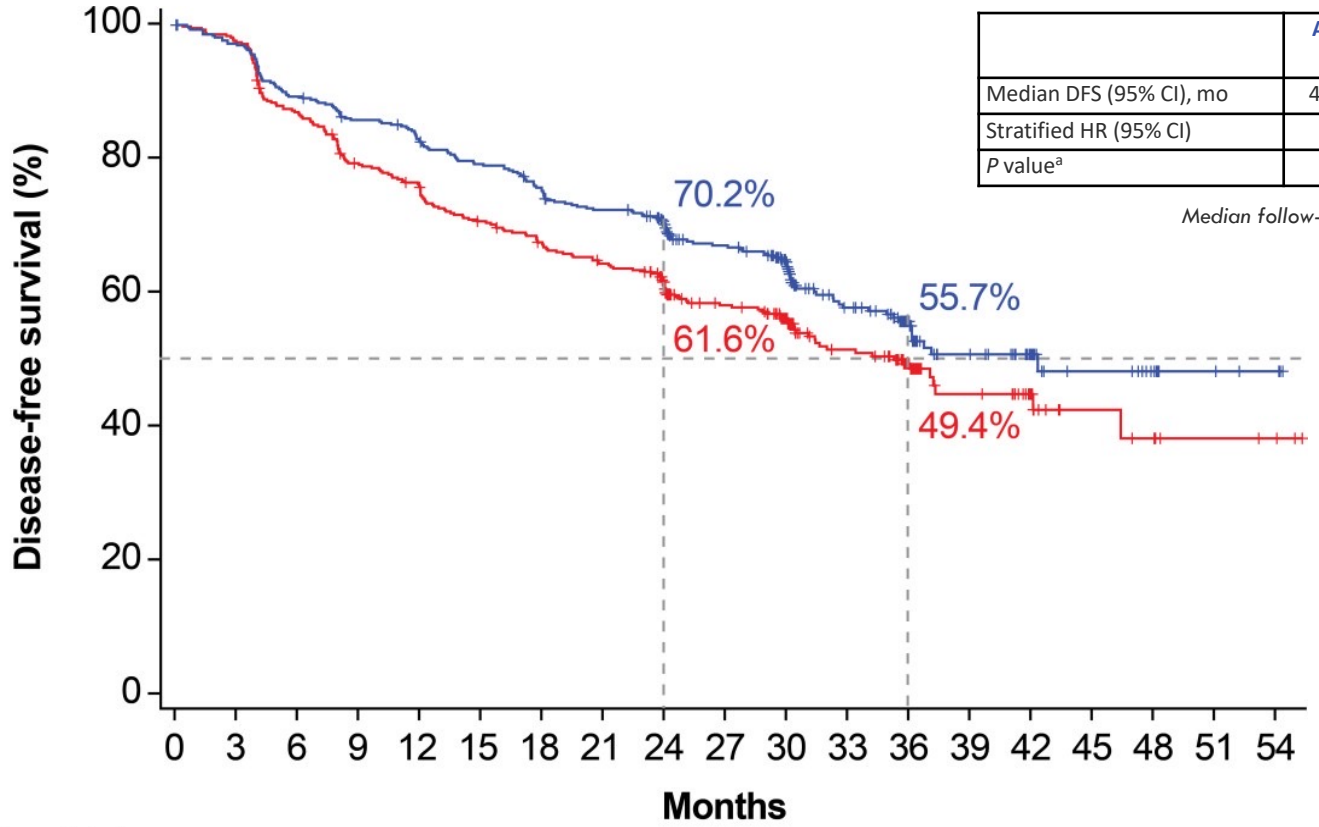
IMpower010: DFS in the all-randomized stage II-IIIA population (primary endpoint)



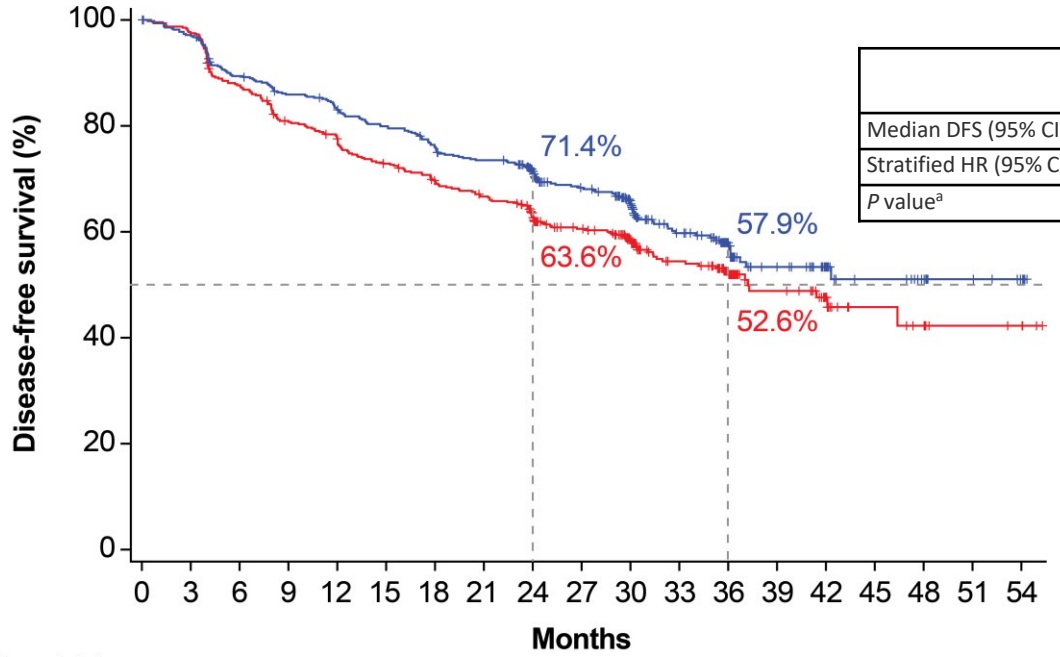
	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[a]	0.02[b]	

Median follow-up: 32.2 mo (range, 0-57.5)

Dr. Heather A. Wakelee ASCO 2021, abstr 8500 IMpower010 Interim Analysis https://bit.ly/33t6JJP

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] Crossed the significance boundary for DFS.

Impower 010: DFS in the ITT population- Exploratory (stage IB-IIIA; primary endpoint)



	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[a]	0.04[b]	

Median follow-up: 32.2 mo (range, 0-58.8)

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] The statistical significance boundary for DFS was not crossed.

- DFS in the ITT population did not cross the significance boundary at this interim DFS analysis

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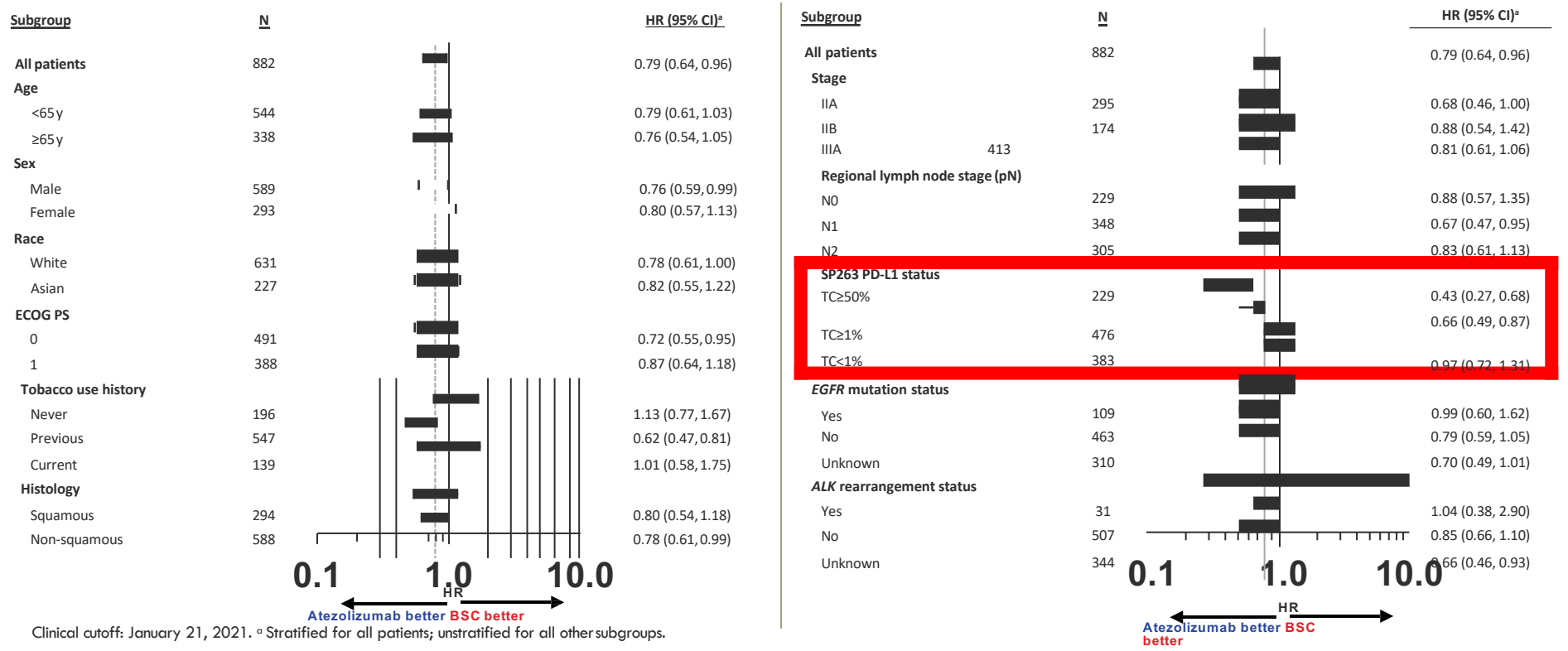
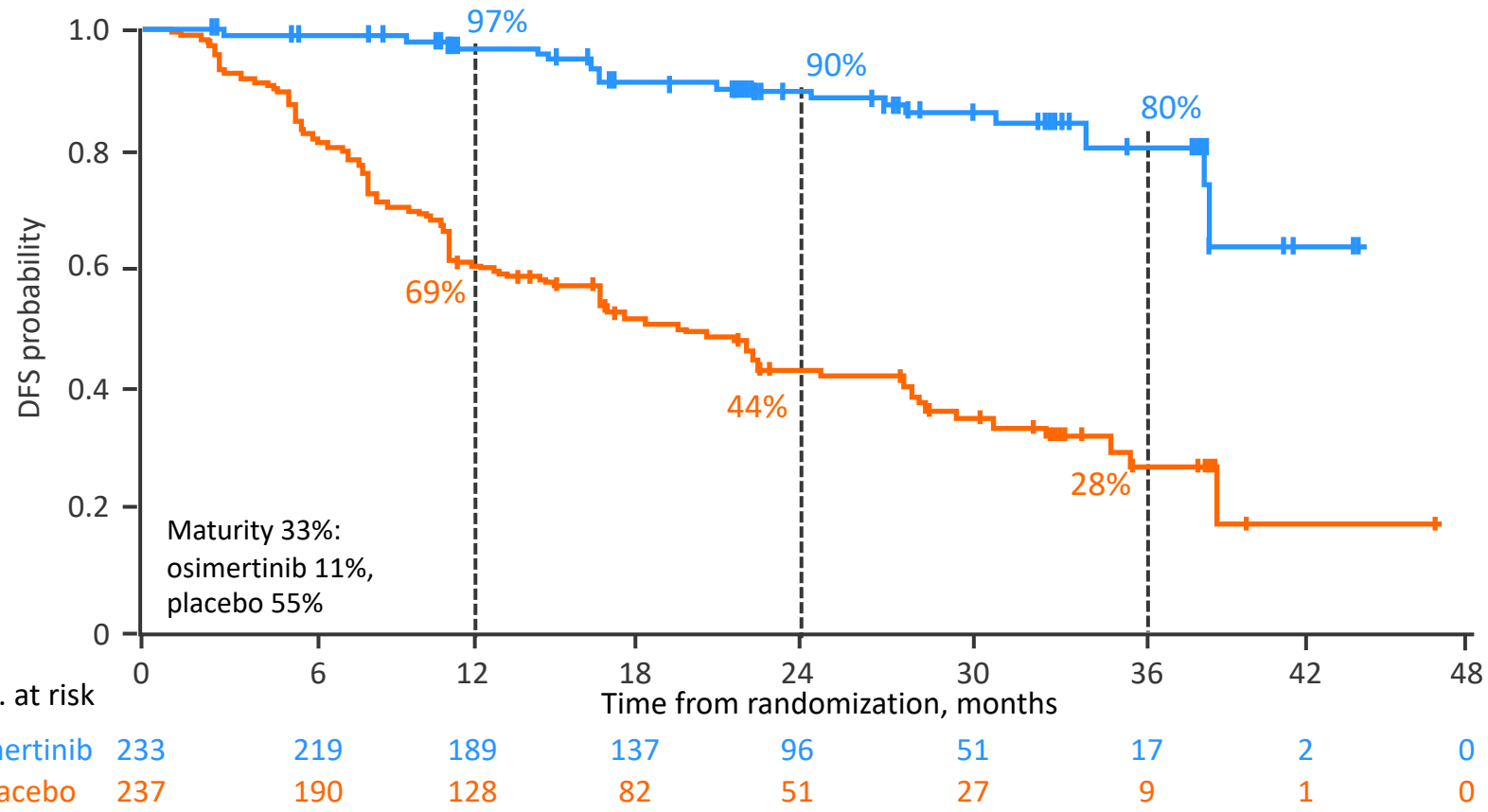
Impower 010: DFS in key subgroups of the all-randomized stage II-IIIA population



Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups.

Dr. Heather A. Wakelee ASCO 2021, abstr 8500
IMpower010 Interim Analysis
https://bit.ly/33t6JJP

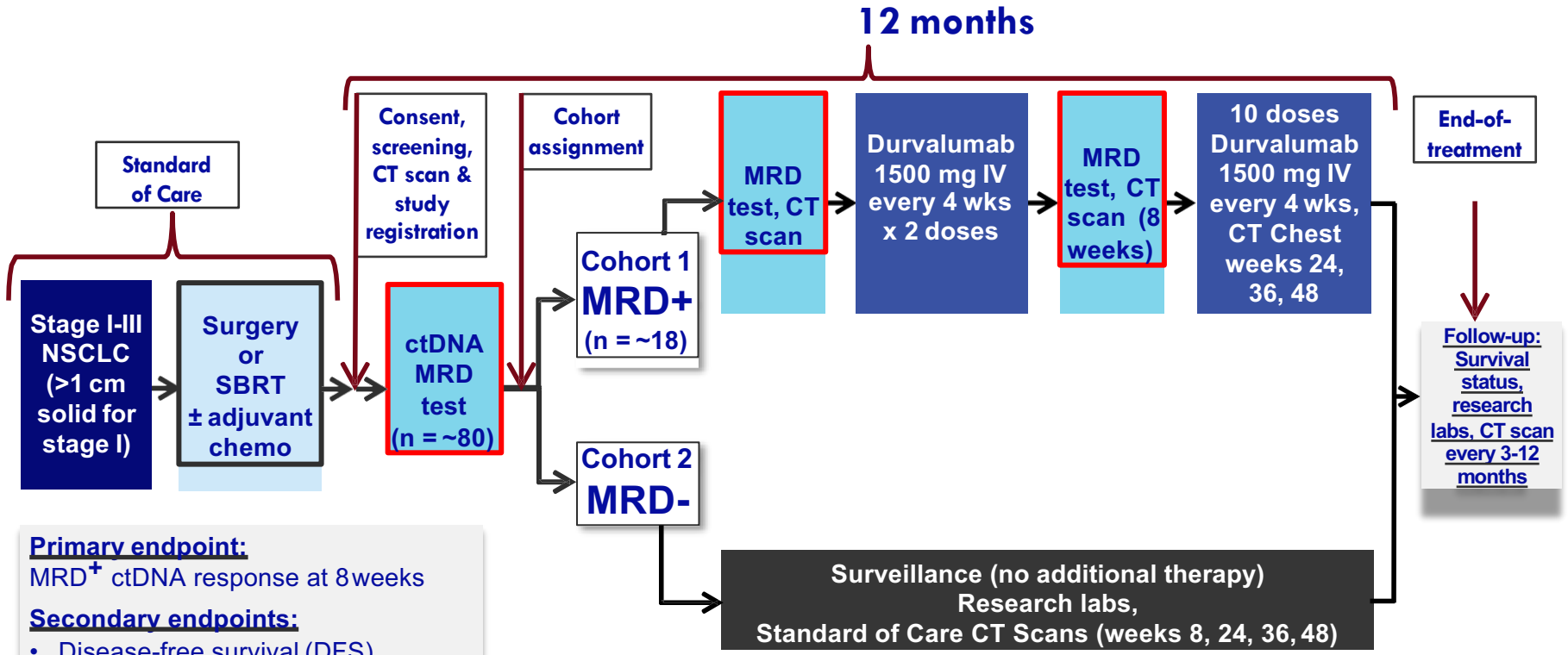
ADURA OS Results



Median DFS, months (95% CI)	
– Osimertinib	NR (38.8, NC)
– Placebo	20.4 (16.6, 24.5)
HR (95% CI)	**0.17 (0.12, 0.23); p<0.0001**

Maturity 33%:
osimertinib 11%, placebo 55%

Adjuvant Durvalumab for Early Stage NSCLC with ctDNA MRD after surgery – ongoing trial



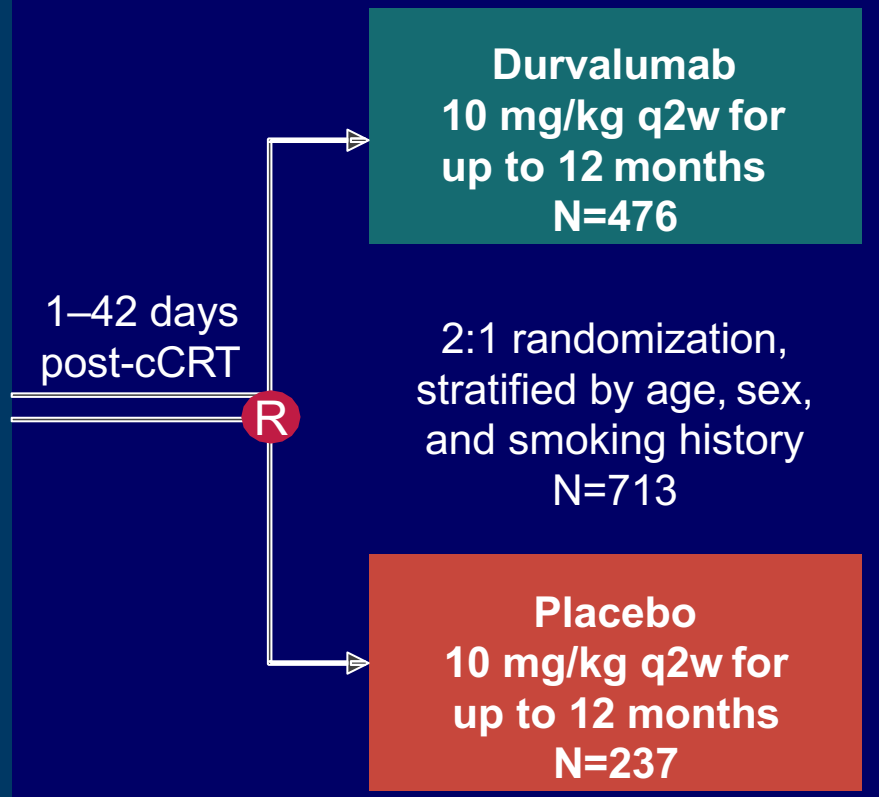
Major Remaining Questions: Adjuvant IO+CT & TKI Rx

- Should patients with ctDNA neg receive any adjuvant IO?
- Optimal duration of IO?
- What about PD-L1 negative?
- What about stage IB?
- What to do for those with other molecular alterations?

PACIFIC: Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study in unresectable stage III NSCLC

- Patients with stage III, locally advanced, unresectable NSCLC who have not progressed following definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- Estimated life expectancy of ≥12 weeks
- Archived tissue was collected

All-comers population



Co-primary endpoints

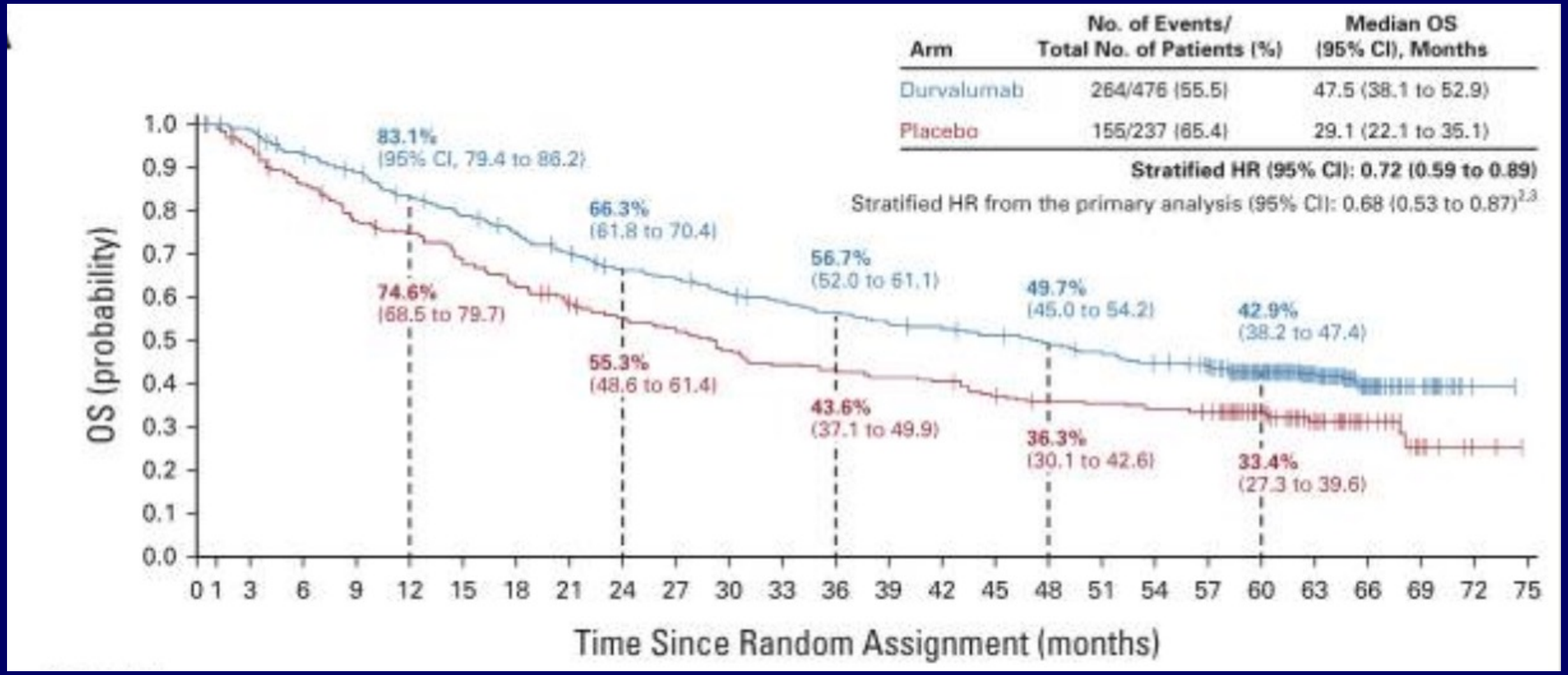
- PFS by BICR using RECIST v1.1*
- OS

Key secondary endpoints

- ORR (per BICR)
- DoR (per BICR)
- Safety and tolerability
- PROs

*Defined as the time from randomization (which occurred up to 6 weeks post-cCRT) to the first documented event of tumor progression or death in the absence of progression.
ClinicalTrials.gov number: NCT02125461 BICR, blinded independent central review; cCRT, concurrent chemoradiation therapy; DoR, duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q2w, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization

PACIFIC: OS (ITT)



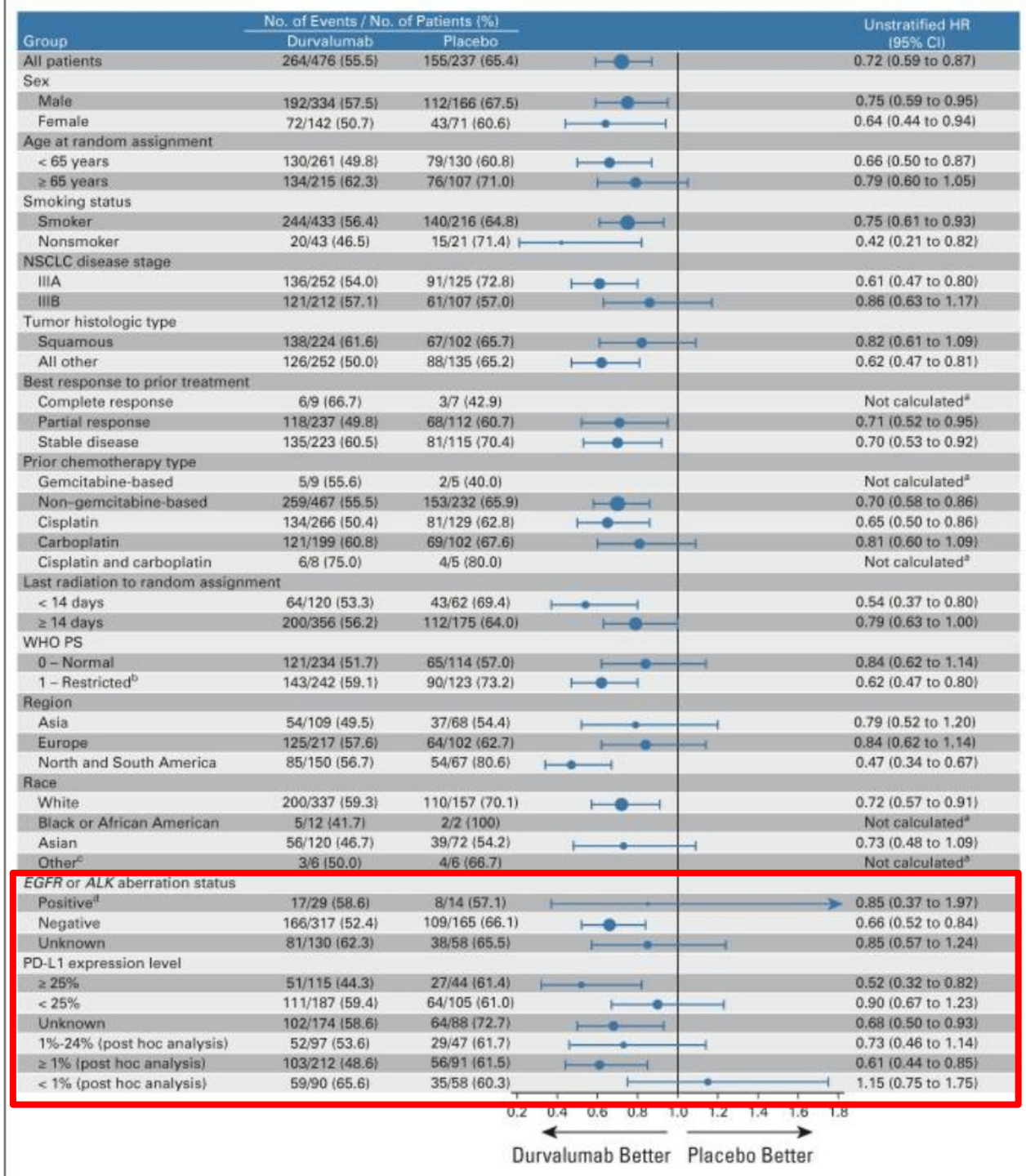
PACIFIC: updated safety summary

	Durvalumab (N=475)	Placebo (N=234)
Any-grade all-causality AEs, n (%)	460 (96.8)	222 (94.9)
Grade 3/4	145 (30.5)	61 (26.1)
Outcome of death	21 (4.4)	15 (6.4)
Leading to discontinuation	73 (15.4)	23 (9.8)
Serious AEs, n (%)	138 (29.1)	54 (23.1)
Any-grade pneumonitis/radiation pneumonitis, n (%)	161 (33.9)	58 (24.8)
Grade 3/4	17 (3.6)	7 (3.0)
Outcome of death	5 (1.1)	5 (2.1)
Leading to discontinuation	30 (6.3)	10 (4.3)

Antonia NEJM 18

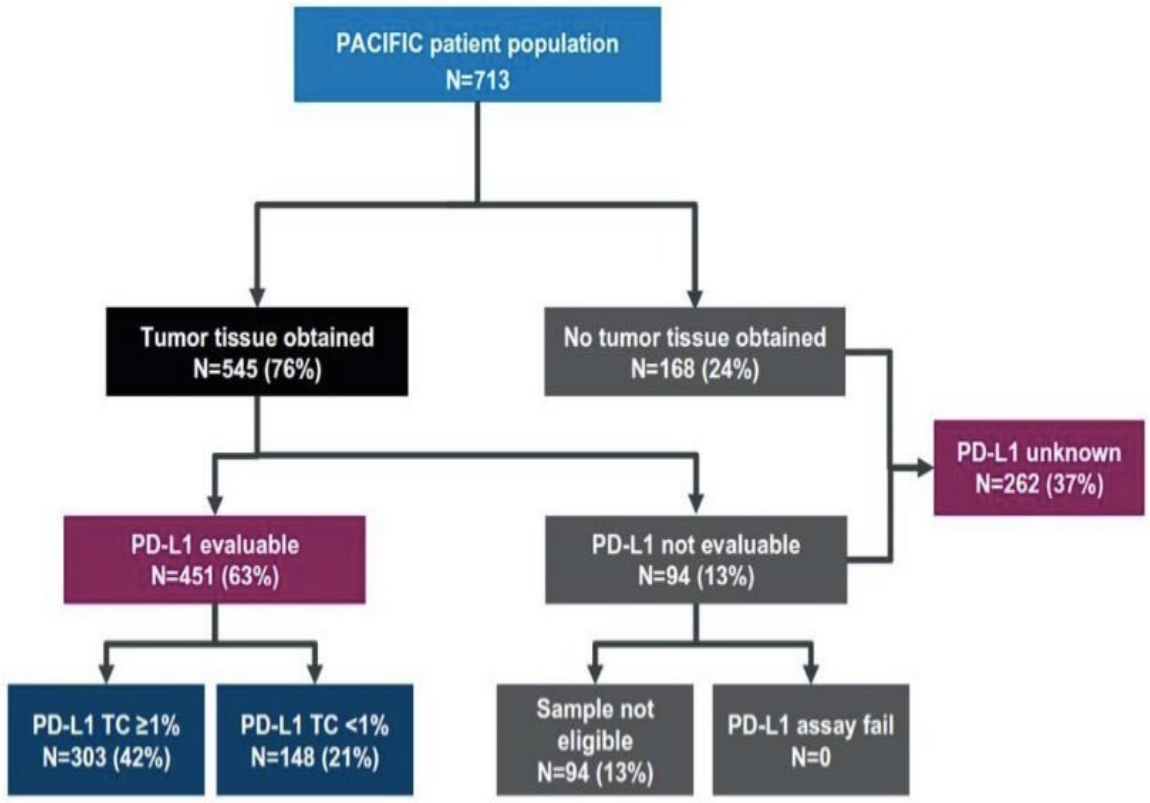
Forest Plot of OS results From Pacific Trial

Spigel DR et al
JCO 40:1271-1274,2022



Group	No. of Events / No. of Patients (%) Durvalumab	Placebo	Unstratified HR (95% CI)
All patients	264/476 (55.5)	155/237 (65.4)	0.72 (0.59 to 0.87)
Sex			
Male	192/334 (57.5)	112/166 (67.5)	0.75 (0.59 to 0.95)
Female	72/142 (50.7)	43/71 (60.6)	0.64 (0.44 to 0.94)
Age at random assignment			
< 65 years	130/261 (49.8)	79/130 (60.8)	0.66 (0.50 to 0.87)
≥ 65 years	134/215 (62.3)	76/107 (71.0)	0.79 (0.60 to 1.05)
Smoking status			
Smoker	244/433 (56.4)	140/216 (64.8)	0.75 (0.61 to 0.93)
Nonsmoker	20/43 (46.5)	15/21 (71.4)	0.42 (0.21 to 0.82)
NSCLC disease stage			
IIIA	136/252 (54.0)	91/125 (72.8)	0.61 (0.47 to 0.80)
IIIB	121/212 (57.1)	61/107 (57.0)	0.86 (0.63 to 1.17)
Tumor histologic type			
Squamous	138/224 (61.6)	67/102 (65.7)	0.82 (0.61 to 1.09)
All other	126/252 (50.0)	88/135 (65.2)	0.62 (0.47 to 0.81)
Best response to prior treatment			
Complete response	6/9 (66.7)	3/7 (42.9)	Not calculated[a]
Partial response	118/237 (49.8)	68/112 (60.7)	0.71 (0.52 to 0.95)
Stable disease	135/223 (60.5)	81/115 (70.4)	0.70 (0.53 to 0.92)
Prior chemotherapy type			
Gemcitabine-based	5/9 (55.6)	2/5 (40.0)	Not calculated[a]
Non-gemcitabine-based	259/467 (55.5)	153/232 (65.9)	0.70 (0.58 to 0.86)
Cisplatin	134/266 (50.4)	81/129 (62.8)	0.65 (0.50 to 0.86)
Carboplatin	121/199 (60.8)	69/102 (67.6)	0.81 (0.60 to 1.09)
Cisplatin and carboplatin	6/8 (75.0)	4/5 (80.0)	Not calculated[a]
Last radiation to random assignment			
< 14 days	64/120 (53.3)	43/62 (69.4)	0.54 (0.37 to 0.80)
≥ 14 days	200/356 (56.2)	112/175 (64.0)	0.79 (0.63 to 1.00)
WHO PS			
0 – Normal	121/234 (51.7)	65/114 (57.0)	0.84 (0.62 to 1.14)
1 – Restricted[b]	143/242 (59.1)	90/123 (73.2)	0.62 (0.47 to 0.80)
Region			
Asia	54/109 (49.5)	37/68 (54.4)	0.79 (0.52 to 1.20)
Europe	125/217 (57.6)	64/102 (62.7)	0.84 (0.62 to 1.14)
North and South America	85/150 (56.7)	54/67 (80.6)	0.47 (0.34 to 0.67)
Race			
White	200/337 (59.3)	110/157 (70.1)	0.72 (0.57 to 0.91)
Black or African American	5/12 (41.7)	2/2 (100)	Not calculated[a]
Asian	56/120 (46.7)	39/72 (54.2)	0.73 (0.48 to 1.09)
Other[c]	3/6 (50.0)	4/6 (66.7)	Not calculated[a]
EGFR or *ALK* aberration status			
Positive[d]	17/29 (58.6)	8/14 (57.1)	0.85 (0.37 to 1.97)
Negative	166/317 (52.4)	109/165 (66.1)	0.66 (0.52 to 0.84)
Unknown	81/130 (62.3)	38/58 (65.5)	0.85 (0.57 to 1.24)
PD-L1 expression level			
≥ 25%	51/115 (44.3)	27/44 (61.4)	0.52 (0.32 to 0.82)
< 25%	111/187 (59.4)	64/105 (61.0)	0.90 (0.67 to 1.23)
Unknown	102/174 (58.6)	64/88 (72.7)	0.68 (0.50 to 0.93)
1%-24% (post hoc analysis)	52/97 (53.6)	29/47 (61.7)	0.73 (0.46 to 1.14)
≥ 1% (post hoc analysis)	103/212 (48.6)	56/91 (61.5)	0.61 (0.44 to 0.85)
< 1% (post hoc analysis)	59/90 (65.6)	35/58 (60.3)	1.15 (0.75 to 1.75)

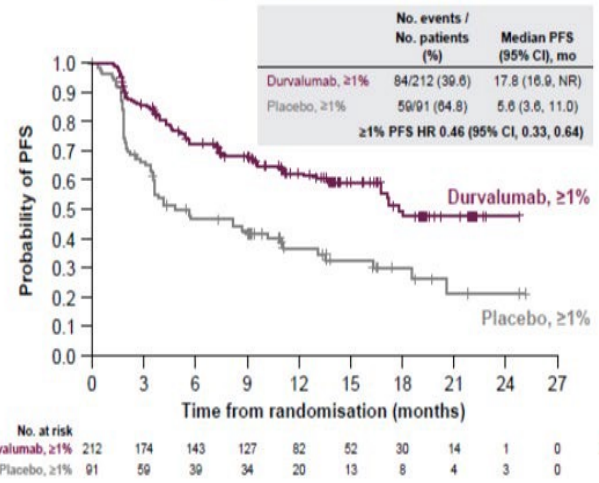
Subgroup analysis by PD-L1 status



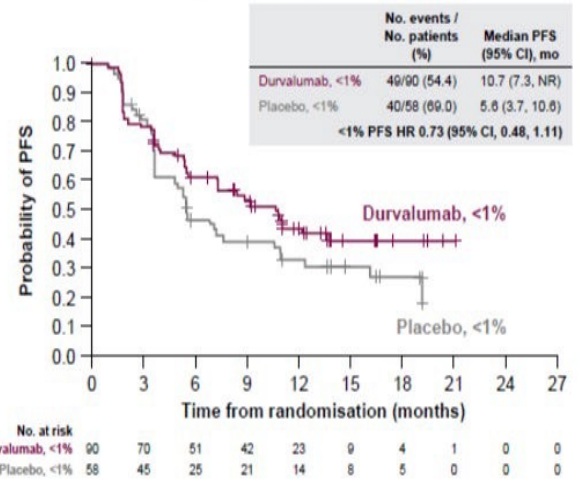
PD-L1 TC, PD-L1 expression on tumor cells.

- PD-L1 testing was not required
- 37% of patients with unknown PD-L1 status
- PD-L1 expression-level cutoff of 1% was part of an unplanned post-hoc analysis requested by a health authority

PFS (BICR) by PD-L1 TC ≥1%

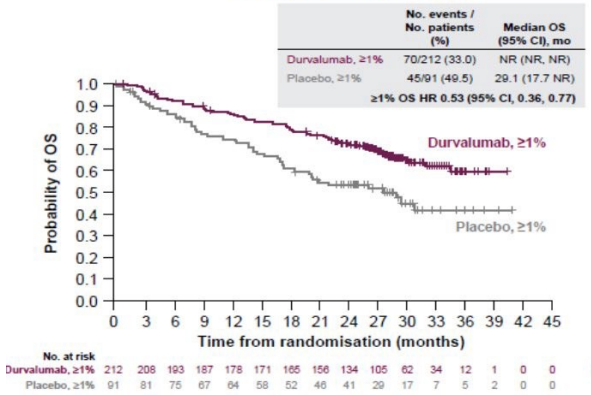


PFS (BICR) by PD-L1 TC <1%

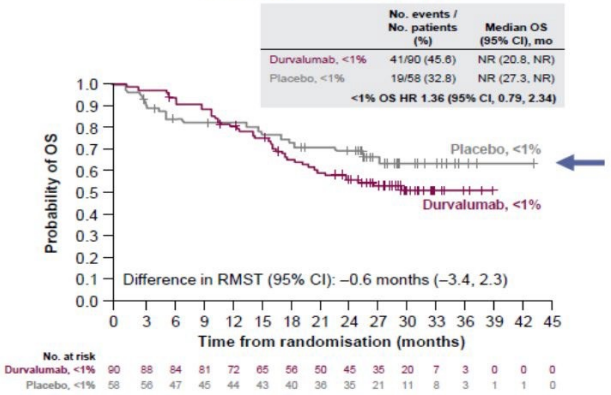


mo, months; NR, not reached; TC, tumour cell

OS by PD-L1 TC ≥1%



OS by PD-L1 TC <1%



RMST, restricted mean survival time

- In the PD-L1 TC <1% subgroup, the number of events are low and overall the subgroup is small
- Imbalances in baseline characteristics

PFS DCO: 13 February 2017; OS DCO: 22 March 2018

Faivre-Finn ESMO 18

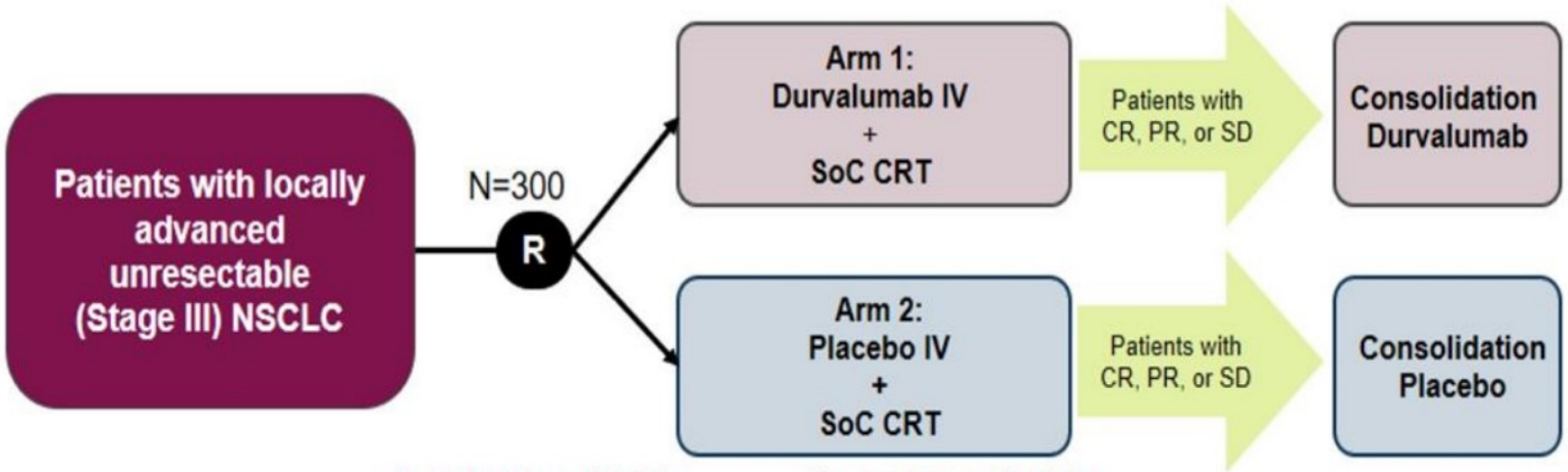
Concurrent CT-RT + immunotherapy in unresectable stage III

- ETOP-NICOLAS Phase II nivolumab
- KEYNOTE-799 Phase II pembrolizumab
- DETERRED Phase II atezolizumab
- PACIFIC-2 Phase III durvalumab
- CheckMate73L Phase III nivolumab
- NCT03840902 Phase II M7824

UPFRONT DURVALUMAB WITH CONCURRENT CHEMO/XRT

PACIFIC 2: Study Design[1,2]

- Phase 3, randomized, double-blind, placebo-controlled, multicenter, global study



Co-primary endpoints
- PFS
- ORR

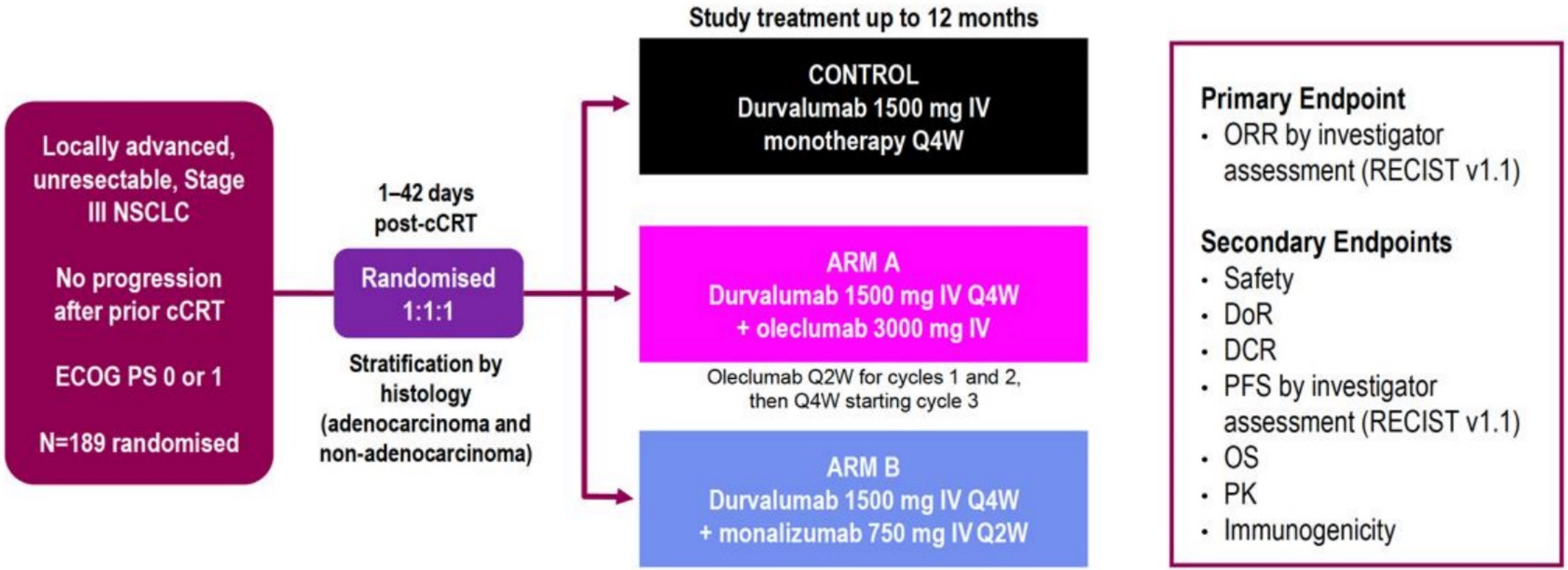
Secondary endpoints
- OS
- PK of durva in blood in combo with CRT
- Immunogenicity
- HRQoL
- DoR
- PFS2
- TTDM
- Rate of complete response

- Activated: 4/18
- N: 300
- Ex-US
- Treat until PD

- Upfront CRT & durva
- Dosing Interval/length
- PD-L1 Status

- COMPLETED ACCRUAL

COAST: Phase 2, randomised open-label study

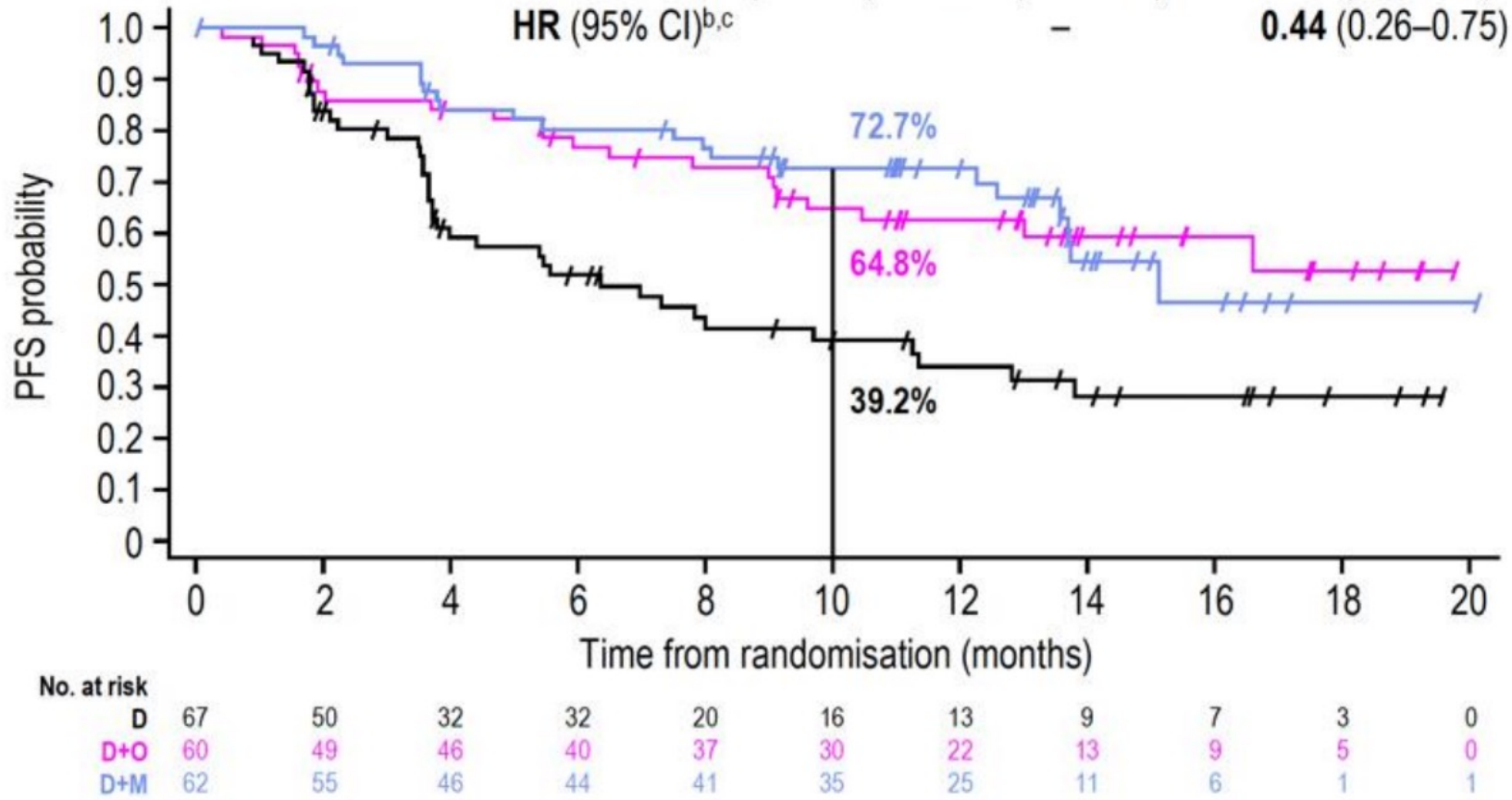


- A planned sample size of 60 patients per arm was designed to provide acceptable precision in estimating antitumour activities in an early phase setting
- Between Jan 2019 and Jul 2020, 189 patients were randomised of whom 186 received D (n=66), D+O (n=59) or D+M (n=61)
- As of 17 May 2021, all patients had a minimum of 10 months potential follow-up and the median actual follow-up was 11.5 months (range, 0.4–23.4; all patients)

D, durvalumab; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; IV, intravenously; M, monalizumab; O, oleclumab;

PFS by investigator assessment
(interim analysis; ITT population)

	D	D+O	D+M
Events/patients, n	38/67	22/60	21/62
mPFS, months (95% CI)[a]	**6.3** (3.7–11.2)	**NR** (10.4–NE)	**15.1** (13.6–NE)
HR (95% CI)[b,c]	–	**0.44** (0.26–0.75)	**0.65** (0.49–0.85)



No. at risk											
D	67	50	32	32	20	16	13	9	7	3	0
D+O	60	49	46	40	37	30	22	13	9	5	0
D+M	62	55	46	44	41	35	25	11	6	1	1

Data cutoff: 17 May 2021 (median follow-up of 11.5 months; range, 0.4–23.4)

[a]Interim analysis was performed when all patients had a 10-month minimum potential follow-up; Kaplan-Meier estimates for PFS, PFS rate and 95% CIs

[b]PFS HR and 95% CI estimated by Cox regression model, stratified by histology (adenocarcinoma and non-adenocarcinoma)

[c]Compared with the 67 and 64 patients in the D arm enrolled concurrently with patients in the D+O and D+M arms, respectively

CI, confidence interval; HR, hazard ratio; ITT, intention to treat; mPFS, median PFS; NE, not estimable; NR, not reached

CheckMate 73L

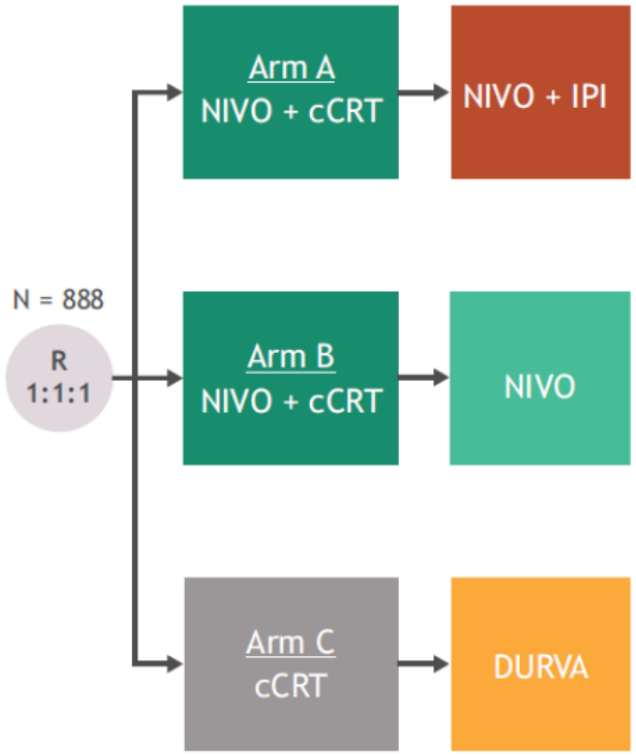
A phase 3 study comparing nivolumab plus concurrent CRT followed by nivolumab ± ipilimumab versus cCRT followed by durvalumab for previously untreated, locally advanced stage III NSCLC

Key eligibility criteria

- Locally advanced, unresectable stage III NSCLC
- ECOG performance status 0-1
- No prior treatment

Stratified by:

- Age
- PD-L1 expression
- Disease stage



Primary endpoints:
NIVO + cCRT followed by NIVO + IPI (Arm A) vs
cCRT followed by DURVA (Arm C)

- PFS
- OS

Study Design KEYLYNK 012

Patients:
- Stages IIIA, IIIB, and IIIC NSCLC
- ECOG PS 0-1
- Adequate pulmonary function (PFT)

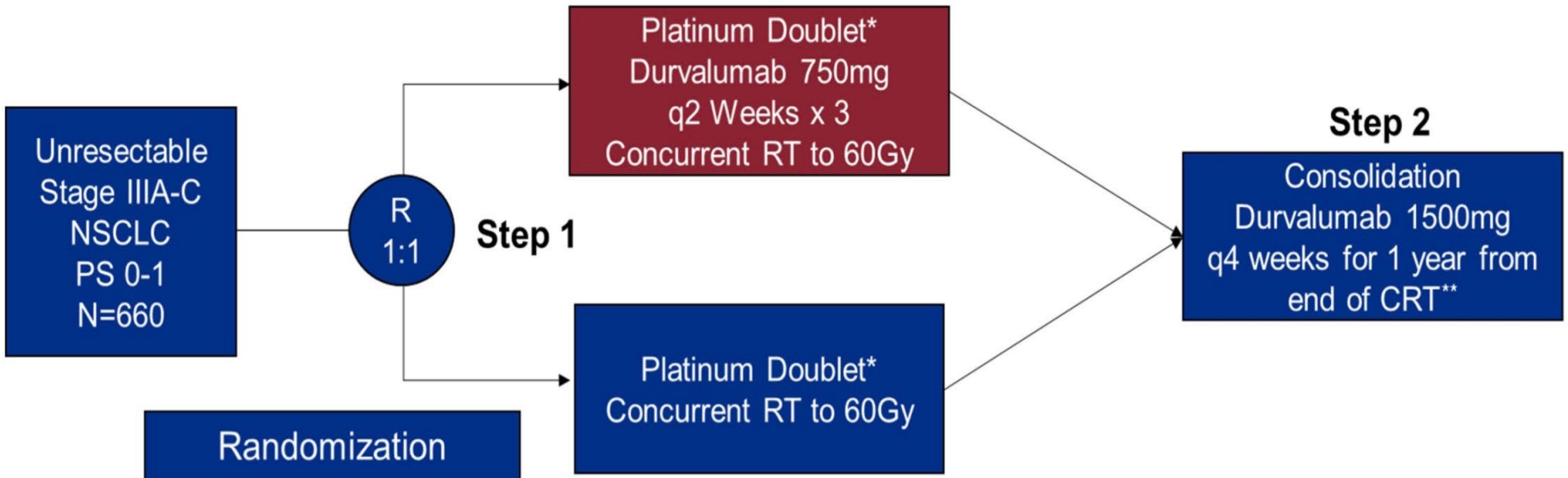
Stratification:
- Stage (IIIA vs IIIB/IIIC)
- Tumor histology (squamous vs nonsquamous)
- PD-L1 tumor proportion score (≥50% vs <50%)
- Region (East Asia vs North America/Western Europe/UK vs other)

Randomization
1:1
N = 870

	Thoracic Radiotherapy		Follow
Arm A: Platinum doublet + Pembrolizumab 200 mg X1 cycles	Platinum doublet + Pembrolizumab 200 mg Q3W X 2 cycles	Pembrolizumab 200 mg Q3W X 17 cycles + Olaparib Placebo X 12 Months	
Arm B: Platinum doublet + Pembrolizumab 200 mg X1 cycles	Platinum doublet+ Pembrolizumab 200 mg Q3W X 2 cycles	Pembrolizumab 200 mg Q3W X 17 cycles + Olaparib 300mg BID X 12 Months	
Arm C: Platinum doublet + Placebo X1 cycles	Platinum doublet + Placebo x 2 cycles	Durvalumab 10 mg/kg Q2W X 12 Months	

Primary Endpoints: PFS/OS
Secondary Endpoints: ORR, DOR, PRO
Exploratory Endpoints: Biomarker evaluation, PDL1 and outcomes, TTST and TTR

Randomized Phase III Trial of MEDI4736 (durvalumab) as Concurrent and Consolidative Therapy Alone for Unresectable Stage 3 NSCLC: A trial of the ECOG-ACRIN Research Group (EA5181)



***Investigator choice**

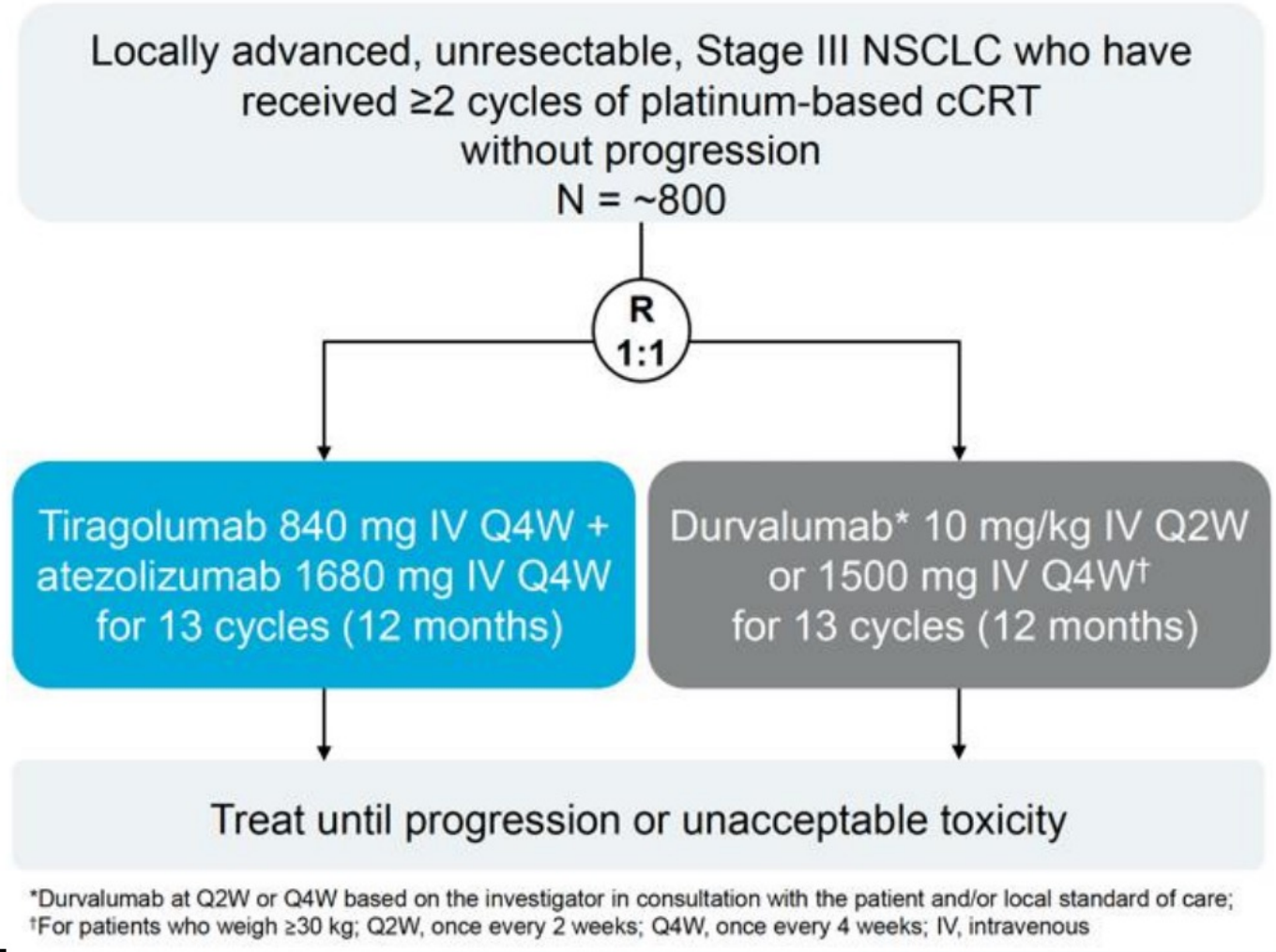
Cisplatin 50 mg/m2 D1, 8, 29, 36; etoposide 50 mg/m2 D1-5, 29-33

Cisplatin 75 mg/m2 D1, 22; pemetrexed 500 mg/m2 D1, 22 (nonsquamous only)

Carboplatin AUC 2 D1, 8, 15, 22, 29, 36; paclitaxel 45 mg/m2 D1, 8, 15, 22, 29, 36

**Starting within 14 days of CRT unless toxicity has not resolved to ≤ grade 2, but not later than 45 days post-CRT

SKYSCRAPER-03:



Primary endpoint: PFS by independent review facility assessment per RECIST v1.1

Key secondary endpoints: OS, investigator-assessed PFS, ORR, DOR, PFS and OS rates at 12, 18 and 24 months

Safety, pharmacokinetics, immunogenicity and biomarkers will also be evaluated

Stage I NSCLC: SBRT + IO Combinations

Study Name	Phase	Arm I SBRT	Arm II SBRT + IO	Placebo	Primary Endpoints
PACIFIC-4 N = 706	III	Standard of care 3, 4, 5 or 8 fraction regimens	SBRT followed by Durvalumab 1500 mg Q 4 w x 24 months	Yes	PFS
SWOG/NRG S1914 N = 480	III	Standard of care 3-5 fractions	Atezolizumab x Q 3 w x 2 → SBRT + Atezolizumab → Atezolizumab (8 cycles total)	No	EFS, OS
KEYNOTE-867 N = 530	III	Standard of care 3 – 5 fractions	SBRT followed by Pembrolizumab 200 mg Q 3 week x 12 months	Yes	OS