Stage III NSCLC: Beyond the PACIFIC/Novel Approaches

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Lung Cancer Stage Grouping (AJCC 8th Edition)

5-Yr OS,* %	IA1	IA2	IA3	IB	IIA	IIB
Clinical	92	83	77	68	60	53
Pathologic	90	85	80	73	65	56

5-Yr OS,* %	IIIA	IIIB	IIIC	IVA	IVB
Clinical	36	26	13	10	0
Pathologic	41	24	12	-	-

Locally Advanced Stage III NSCLC

T/M	Subgroup†	N0	N1	N2	N3
T1	T1a ≤ *1*	IA1	IIB	IIIA	IIIB
	T1b > *1-2*	IA2	IIB	IIIA	IIIB
	T1c > *2-3*	IA3	IIB	IIIA	IIIB
T2	T2a *Cent, Visc Pl*	IB	IIB	IIIA	IIIB
	T2a > *3-4*	IB	IIB	IIIA	IIIB
	T2b > *4-5*	IIA	IIB	IIIA	IIIB
T3	T3 > *5-7*	IIB	IIIA	IIIB	IIIC
	T3 *Inv*	IIB	IIIA	IIIB	IIIC
	T3 *Satell*	IIB	IIIA	IIIB	IIIC
T4	T4 > *7*	IIIA	IIIA	IIIB	IIIC
	T4 *Inv*	IIIA	IIIA	IIIB	IIIC
	T4 *Ipsi Nod*	IIIA	IIIA	IIIB	IIIC
M1	M1a *Contra Nod*	IVA	IVA	IVA	IVA
	M1a *Pl Disem*	IVA	IVA	IVA	IVA
	M1b *Single*	IVA	IVA	IVA	IVA
	M1c *Multi*	IVB	IVB	IVB	IVB

*5-yr OS per IASLC global database for patients receiving NSCLC diagnoses from 1999-2010.

†All numbers in cm; other abbreviations defined in slidenotes.

Detterbeck. Chest. 2017;151:193. Goldstraw. J Thorac Oncol. 2016;11:39.

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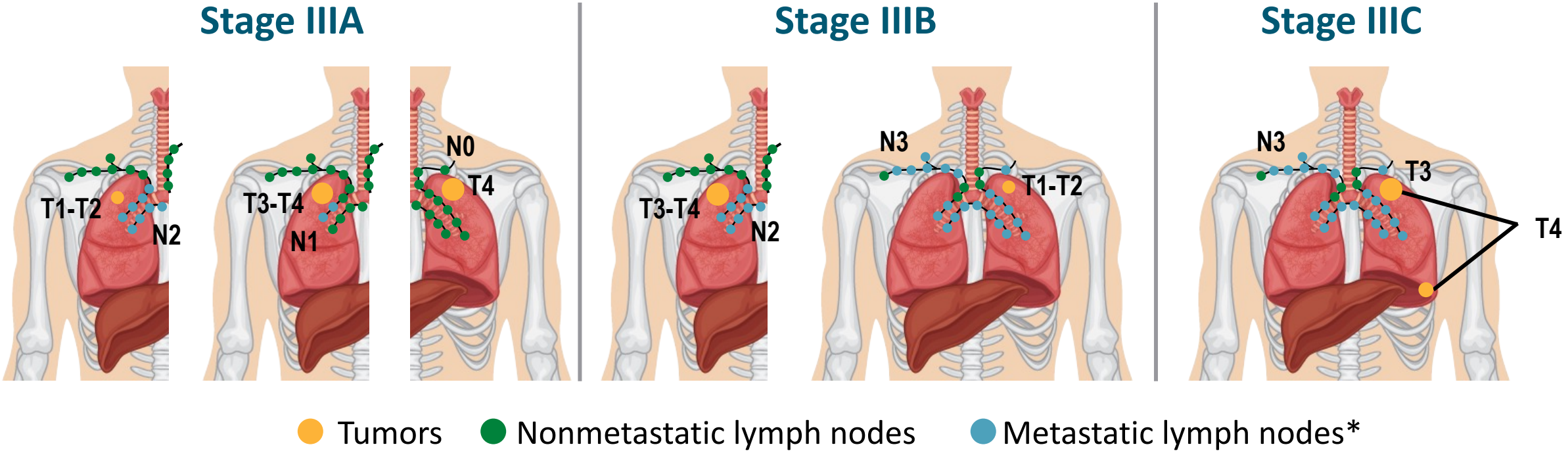
Stage III, Locally Advanced NSCLC is Heterogeneous With Majority Of Patients Having Unresectable Tumors



Detterbeck. Chest. 2017;151:193.

*Considered regional or local, not distant.
All numbers in cm; other abbreviations defined in slidenotes.

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Combined Modality Therapy in Stage III NSCLC: Meta-Analyses of Chemoradiotherapy Strategies

Strategy	No. of Trials	N	Absolute Benefit at Yr 3, %	HR for Survival (95% CI)	*P* Value
Sequential CRT vs RT alone[1]	22	3839	2.6	0.88 (0.82-0.94)	.0001
Concurrent CRT vs RT alone[1]	16	2910	3.2	0.88 (0.81-0.95)	.0008
Concurrent CRT vs Sequential CRT[2]	6	1205	5.7	0.84 (0.74-0.95)	.004

1. Rolland. J Thor Oncol. 2007;2:S309 (Abstract A1-04). 2. Aupérin. J Clin Oncol. 2010;28:2181.

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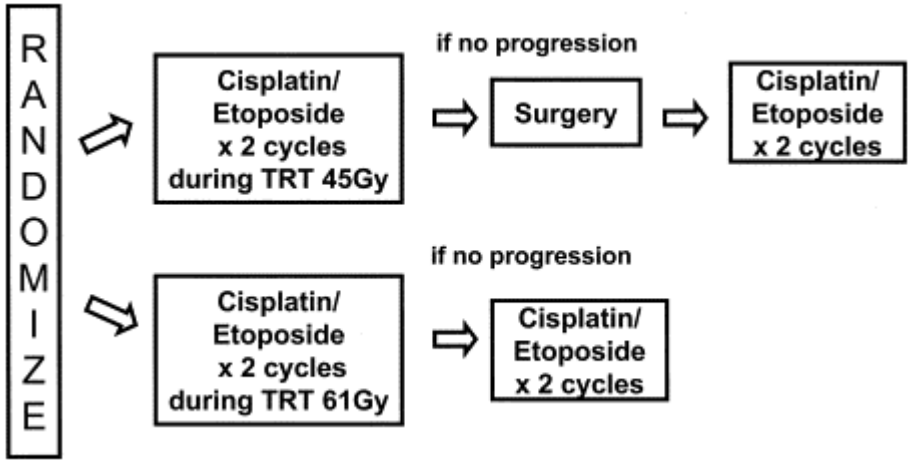
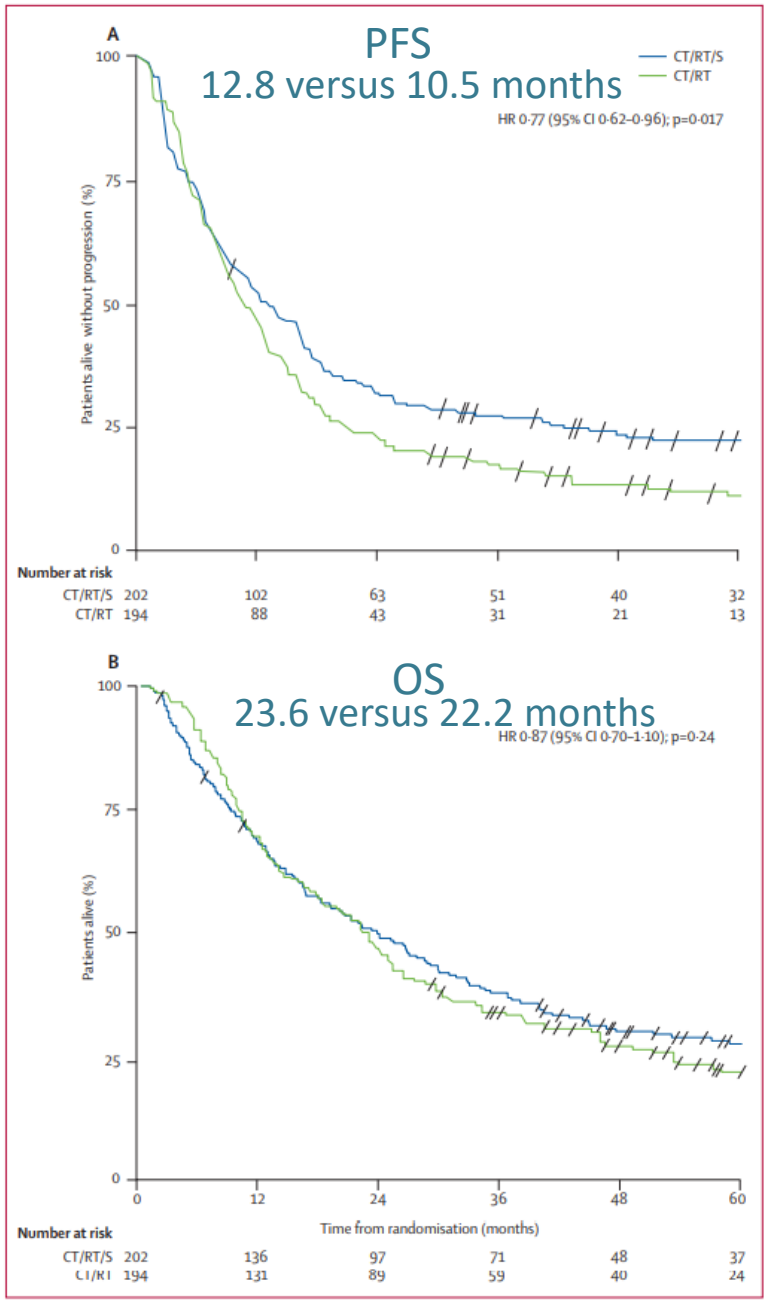
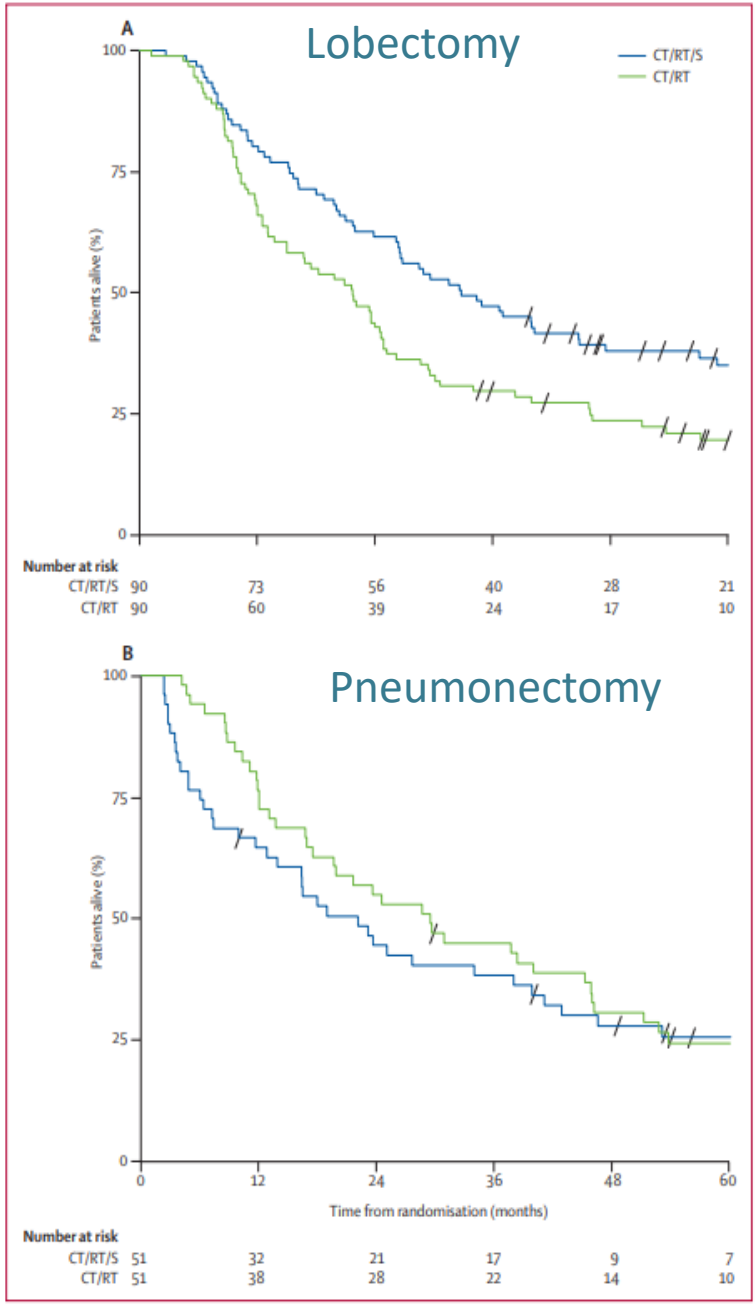
Intergroup 0139



429 Stage IIIA patients randomized

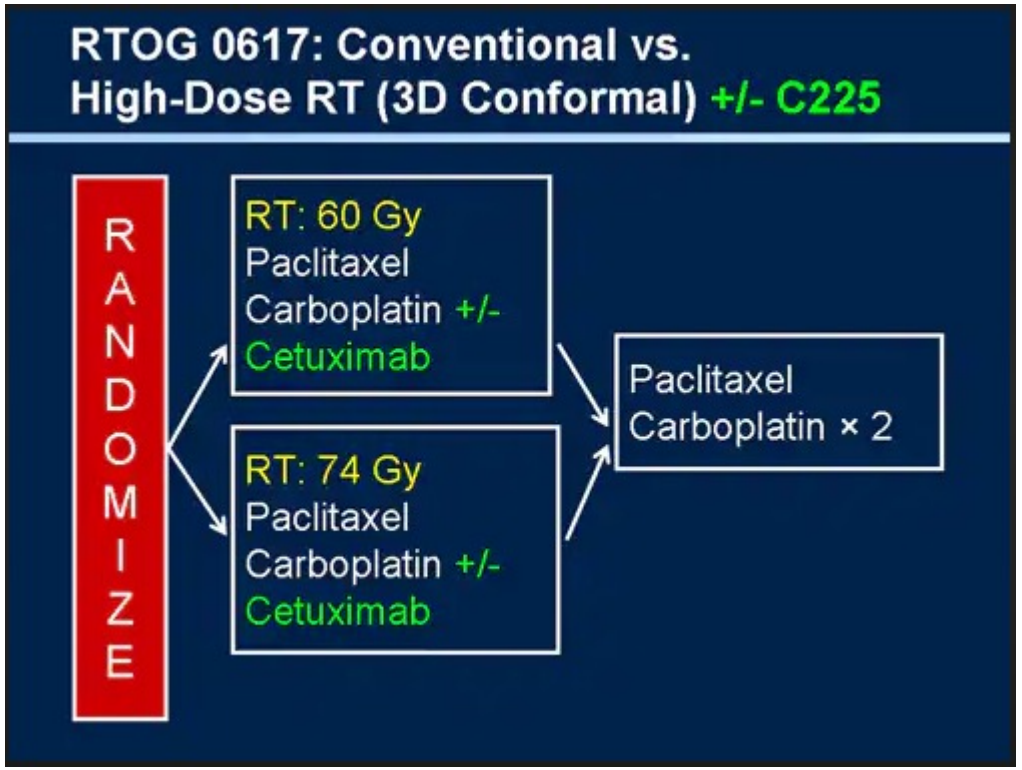
396 patients eligible for analysis

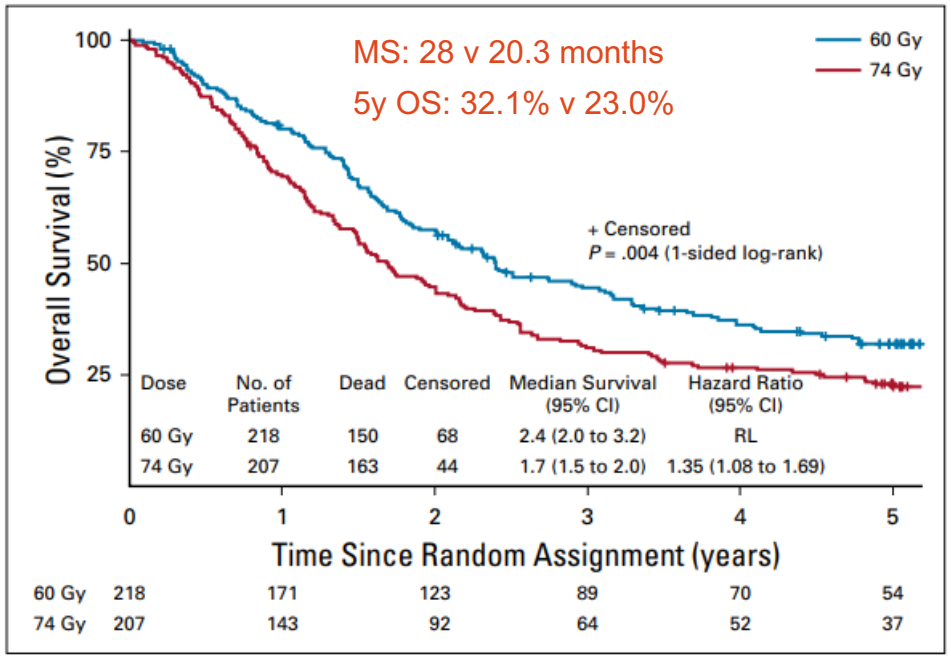


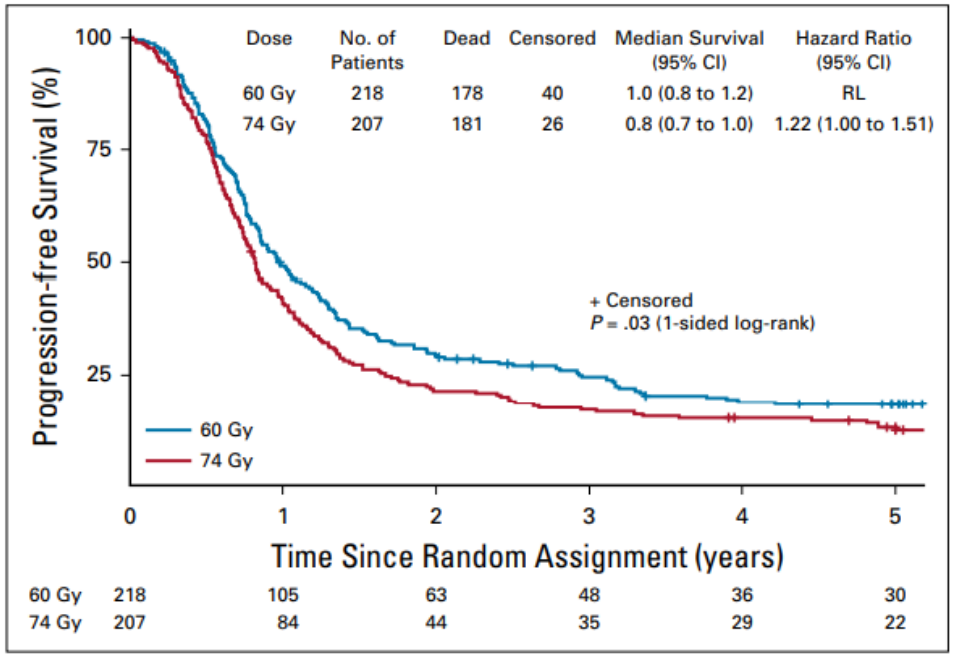


RTOG 0617

- 544 patients accrued
- 496 patients eligible for analysis (66% IIIA)







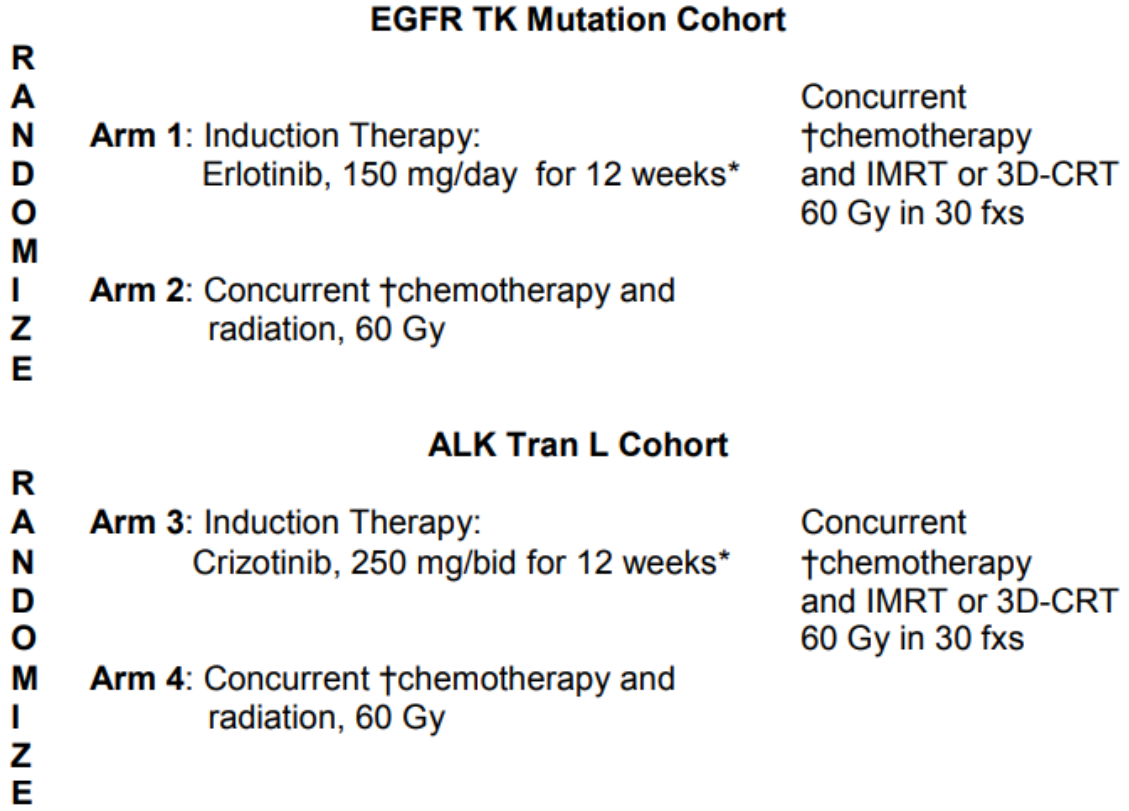
RTOG 0617

	60 Gy	74 Gy
Grade 5 events	2	10
Esophagitis Grade 3	7%	20.9%
Median survival	28.7 mo	19.5 mo
3 year PFS	36.6%	26.3%
Local failure	25.1%	34.3%

	Cetuximab	No Cetuximab
MS	23.1 mo	23.5 mo
Grade ≥3 tox	70.5%	50.7%
Grade 4 or 5 tox	35.8%	28.2%

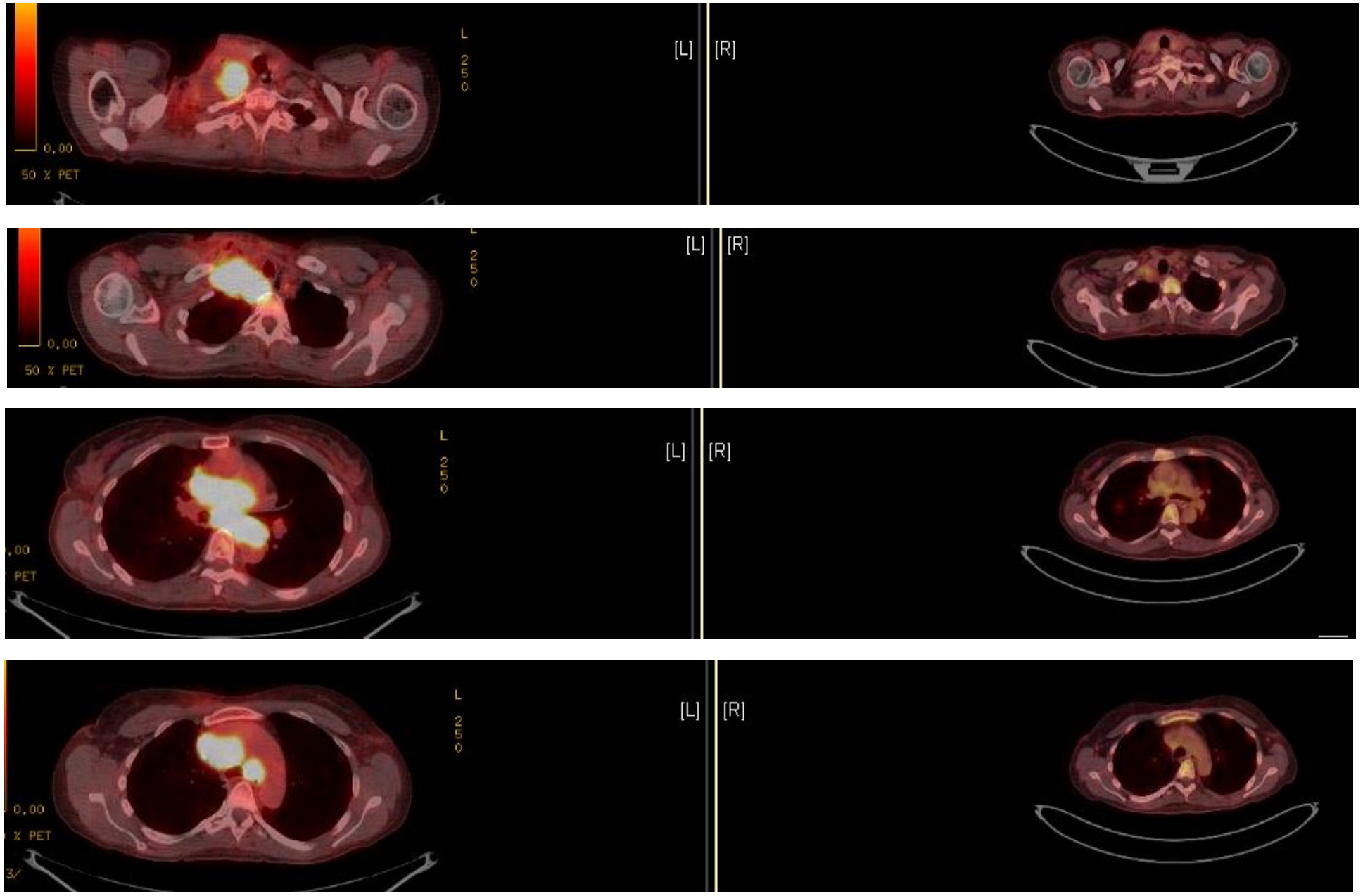
RTOG 1306

- Closed in 2017



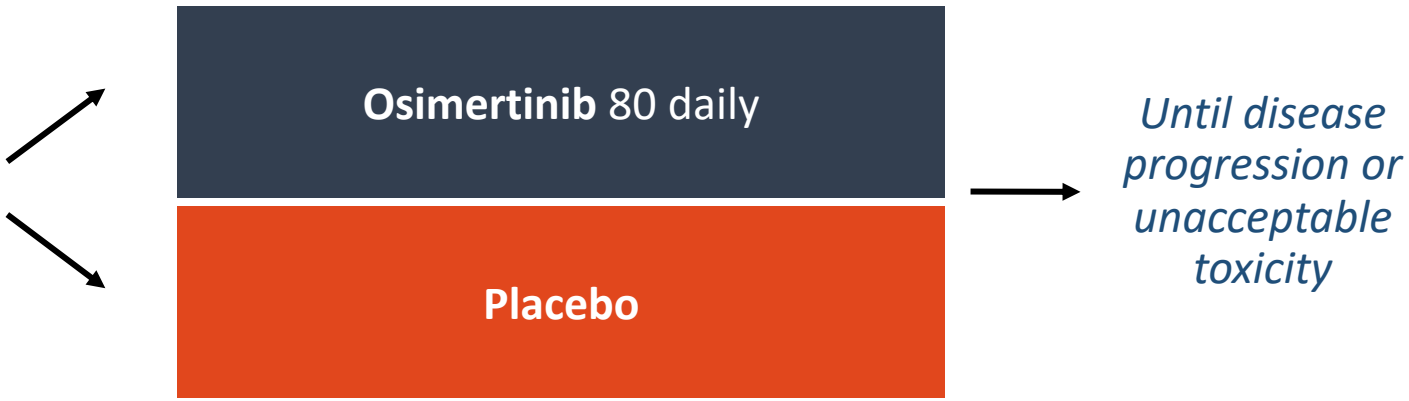
Pre-treatment

4 weeks



A Global Study to Assess the Effects of Osimertinib Following Chemoradiation in Patients With Stage III Unresectable Non-small Cell Lung Cancer (LAURA)

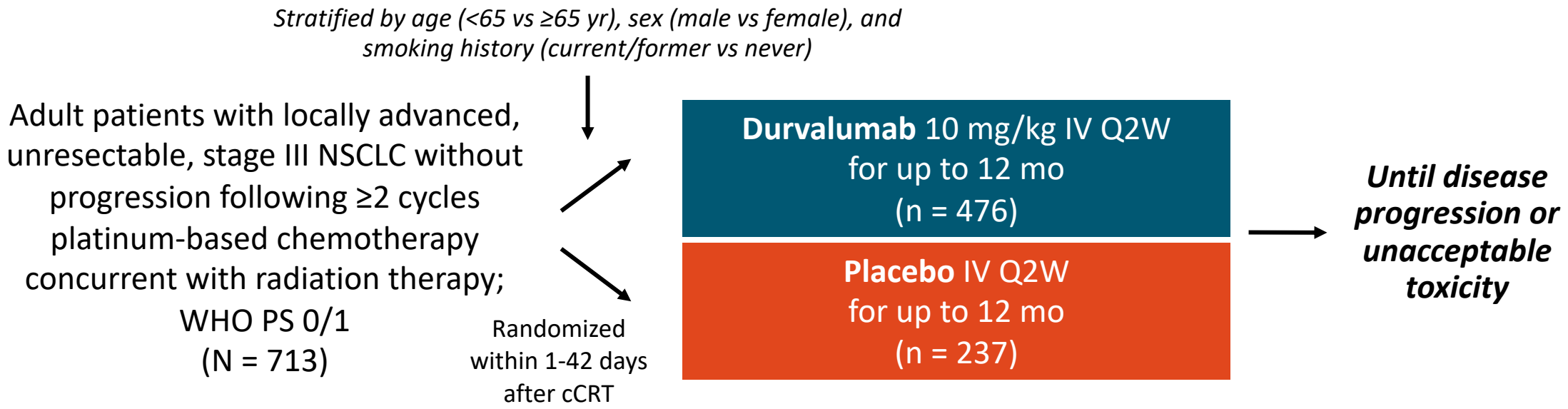
- Patients with locally advanced non-small cell lung cancer with EGFR (L858R, Ex19del) mutations receiving chemotherapy and radiation (concurrent or sequential)
- N=200



NCT03521154

PACIFIC 5-Yr Update: Study Design

- Randomized, double-blind, placebo-controlled phase III trial



Patients enrolled regardless of PD-L1 status. If available, pre-cCRT tumor tissue archived for PD-L1 testing.

- Primary endpoints: PFS by BICR per RECIST v1.1, OS
- Secondary endpoints: ORR, DoR, TTDM, safety, PROs

Spigel. ASCO 2021. Abstr 8511.

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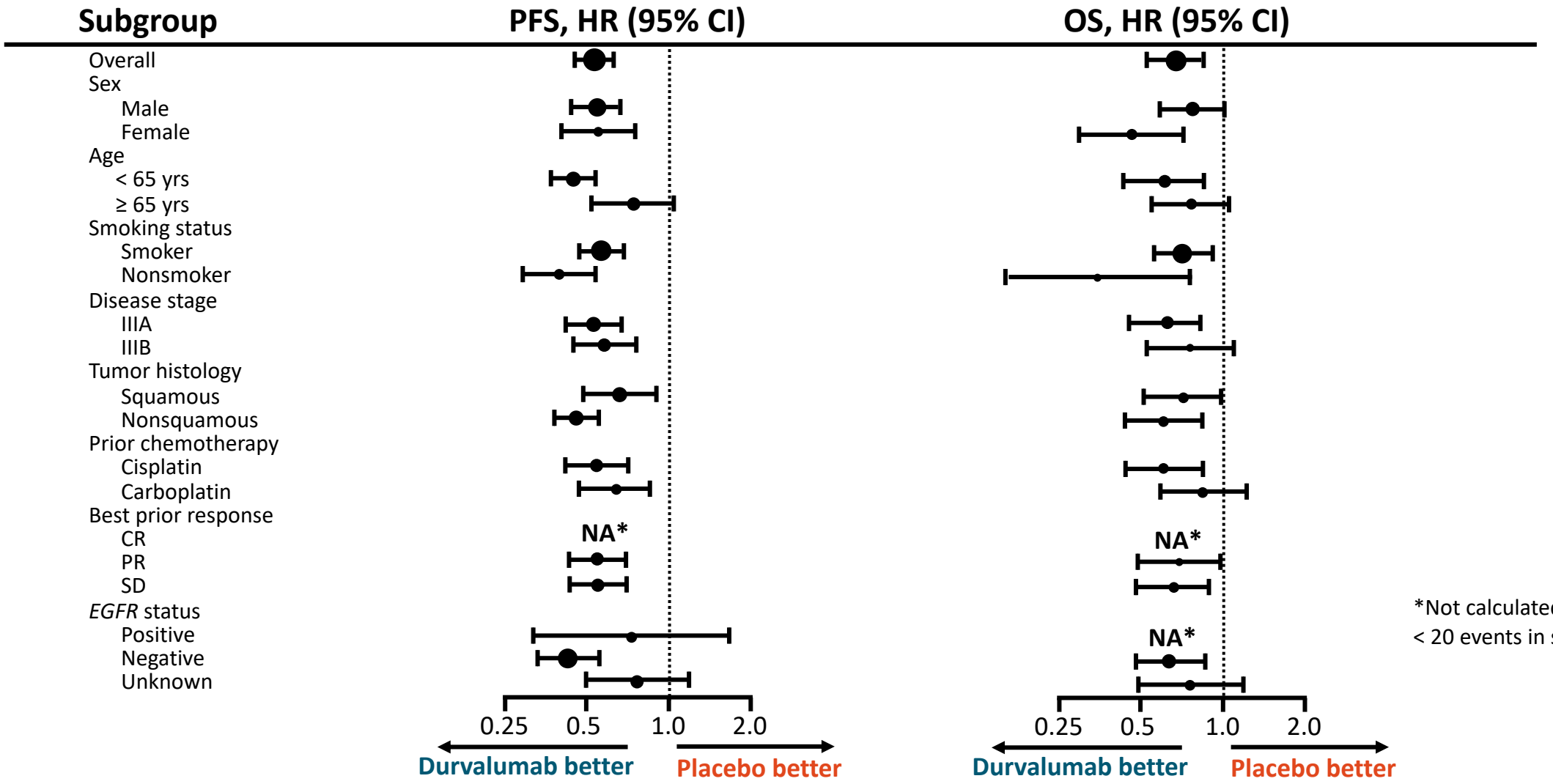
Table S2. Prior Definitive Chemotherapy Regimens (Intention-to-Treat population).

	Durvalumab (N=476)	Placebo (N=237)	Total (N=713)
Total – no. (%)	**473 (99.4)**	**236 (99.6)**	**709 (99.4)**
Cisplatin*	266 (55.9)	129 (54.4)	395 (55.4)
Cisplatin + etoposide	106 (22.3)	49 (20.7)	155 (21.7)
Cisplatin + vinorelbine	77 (16.2)	34 (14.3)	111 (15.6)
Cisplatin + vinorelbine ditartrate	26 (5.5)	14 (5.9)	40 (5.6)
Cisplatin + docetaxel	26 (5.5)	8 (3.4)	34 (4.8)
Cisplatin + paclitaxel	13 (2.7)	15 (6.3)	28 (3.9)
Cisplatin + pemetrexed	11 (2.3)	5 (2.1)	16 (2.2)
Cisplatin + nab-paclitaxel	1 (0.2)	0	1 (0.1)
Cisplatin + vinblastine	1 (0.2)	0	1 (0.1)
Cisplatin + other	1 (0.2)	0	1 (0.1)
Carboplatin†	199 (41.8)	102 (43.0)	301 (42.2)
Carboplatin + paclitaxel	158 (33.2)	84 (35.4)	242 (33.9)
Carboplatin + vinorelbine	8 (1.7)	4 (1.7)	12 (1.7)
Carboplatin + etoposide	8 (1.7)	2 (0.8)	10 (1.4)
Carboplatin + vinorelbine ditartrate	7 (1.5)	5 (2.1)	12 (1.7)
Carboplatin + pemetrexed	7 (1.5)	4 (1.7)	11 (1.5)
Carboplatin + docetaxel	2 (0.4)	1 (0.4)	3 (0.4)
Carboplatin + nab-paclitaxel	2 (0.4)	0	2 (0.3)
Carboplatin + pemetrexed disodium	1 (0.2)	0	1 (0.1)
Carboplatin + other	2 (0.4)	1 (0.4)	3 (0.4)
Cisplatin / carboplatin	8 (1.7)	5 (2.1)	13 (1.8)
Cisplatin / carboplatin + vinorelbine	2 (0.4)	1 (0.4)	3 (0.4)
Cisplatin / carboplatin + etoposide	2 (0.4)	0	2 (0.3)
Cisplatin / carboplatin + pemetrexed	1 (0.2)	1 (0.4)	2 (0.3)
Cisplatin / carboplatin + docetaxel	1 (0.2)	0	1 (0.1)
Cisplatin / carboplatin + vinorelbine ditartrate	1 (0.2)	0	1 (0.1)
Cisplatin / carboplatin + other	1 (0.2)	3 (1.3)	4 (0.6)

*Cisplatin alone was received by 4 patients in each group (0.8% and 1.7% in the durvalumab and placebo groups, respectively).
†Carboplatin alone was received by 4 patients (0.8%) in the durvalumab group and 1 patient (0.4%) in the placebo group.

PACIFIC: Prespecified Subgroup Analysis of Survival



*Not calculated if < 20 events in subgroup.

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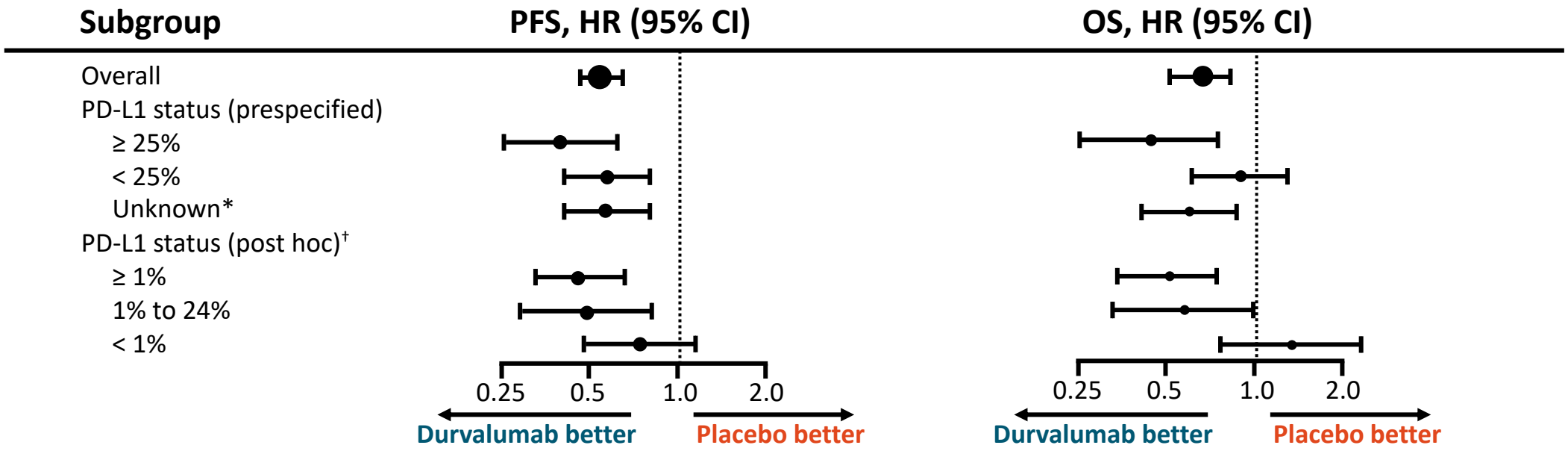
PACIFIC: Subgroup Analysis of Survival by PD-L1 Status



*Unknown PD-L1 status in 37% of patients; testing not required, obtained pre-CRT.
†1% cutoff used in unplanned post hoc analysis requested by a health authority.

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PACIFIC

Subgroup	Durvalumab	Placebo	Unstratified Hazard Ratio for Disease Progression or Death (95% CI)
	no. of patients		
All patients	476	237	0.55 (0.45–0.68)
Sex			
Male	334	166	0.56 (0.44–0.71)
Female	142	71	0.54 (0.37–0.79)
Age at randomization			
<65 yr	261	130	0.43 (0.32–0.57)
≥65 yr	215	107	0.74 (0.54–1.01)
Smoking status			
Smoker	433	216	0.59 (0.47–0.73)
Nonsmoker	43	21	0.29 (0.15–0.57)
NSCLC disease stage			
IIIA	252	125	0.53 (0.40–0.71)
IIIB	212	107	0.59 (0.44–0.80)
Tumor histologic type			
Squamous	224	102	0.68 (0.50–0.92)
Nonsquamous	252	135	0.45 (0.33–0.59)
Best response			
Complete response	9	7	—
Partial response	232	111	0.55 (0.41–0.75)
Stable disease	222	114	0.55 (0.41–0.74)
PD-L1 status			
≥25%	115	44	0.41 (0.26–0.65)
<25%	187	105	0.59 (0.43–0.82)
Unknown	174	88	0.59 (0.42–0.83)
EGFR mutation			
Positive	29	14	0.76 (0.35–1.64)
Negative	315	165	0.47 (0.36–0.60)
Unknown	132	58	0.79 (0.52–1.20)

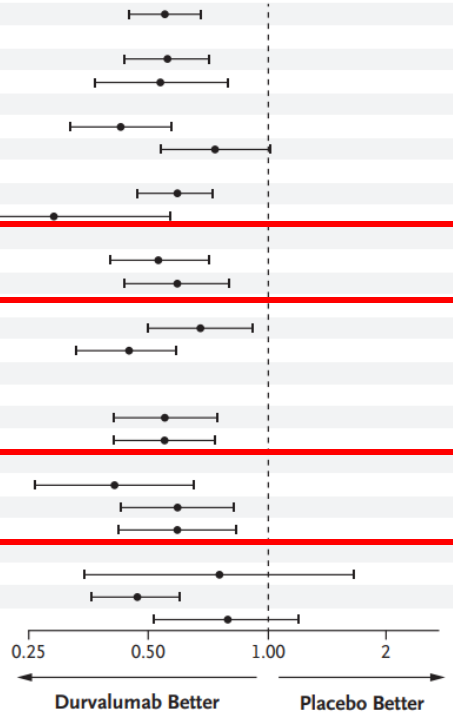

Figure 2. Subgroup Analysis of Prognostic Factors for Progression-free Survival in the Intention-to-Treat Population.

Progression-free survival was defined according to RECIST, version 1.1, and assessed by means of blinded independent central review. The hazard ratio and 95% confidence interval were not calculated for the complete response because this subgroup had less than 20 events. EGFR denotes epidermal growth factor receptor, and PD-L1 programmed death ligand 1.

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)

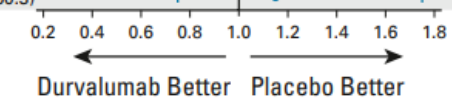

Table 1. Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.*

Characteristic	Durvalumab (N=476)	Placebo (N=237)	Total (N=713)
Age — yr			
Median	64	64	64
Range	31–84	23–90	23–90
Sex — no. (%)			
Male	334 (70.2)	166 (70.0)	500 (70.1)
Female	142 (29.8)	71 (30.0)	213 (29.9)
Race — no. (%)†			
White	337 (70.8)	157 (66.2)	494 (69.3)
Black	12 (2.5)	2 (0.8)	14 (2.0)
Asian	120 (25.2)	72 (30.4)	192 (26.9)
Disease stage — no. (%)			
IIIA	252 (52.9)	125 (52.7)	377 (52.9)
IIIB	212 (44.5)	107 (45.1)	319 (44.7)
Other‡	12 (2.5)	5 (2.1)	17 (2.4)
WHO performance-status score — no. (%)§			
0	234 (49.2)	114 (48.1)	348 (48.8)
1	240 (50.4)	122 (51.5)	362 (50.8)
Tumor histologic type — no. (%)			
Squamous	224 (47.1)	102 (43.0)	326 (45.7)
Nonsquamous	252 (52.9)	135 (57.0)	387 (54.3)
Smoking status — no. (%)			
Current smoker	79 (16.6)	38 (16.0)	117 (16.4)
Former smoker	354 (74.4)	178 (75.1)	532 (74.6)
Never smoked	43 (9.0)	21 (8.9)	64 (9.0)
Previous radiotherapy — no. (%)¶			
<54 Gy	3 (0.6)	0	3 (0.4)
≥54 to ≤66 Gy	442 (92.9)	217 (91.6)	659 (92.4)
>66 to ≤74 Gy	30 (6.3)	19 (8.0)	49 (6.9)
Previous chemotherapy — no. (%)‖			
Induction	123 (25.8)	68 (28.7)	191 (26.8)
Concurrent with radiation therapy	475 (99.8)	236 (99.6)	711 (99.7)
Best response to previous chemoradiotherapy — no. (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	232 (48.7)	111 (46.8)	343 (48.1)
Stable disease	222 (46.6)	114 (48.1)	336 (47.1)

PACIFIC 5-Yr Update: Patient Disposition

Characteristic, %	Durvalumab (n = 476)	Placebo (n = 237)
On study at data cutoff*	37.4	28.7
Terminated study	62.6	71.3
▪ Patient decision†	6.3	6.8
▪ Death	54.6	62.9
▪ Lost to follow-up	1.7	1.3
▪ Unknown	0	0.4

*Data cutoff: January 11, 2021.
†n = 9 have since died (n = 4: durvalumab; n = 5: placebo).

Characteristic, %‡	Durvalumab (n = 473)	Placebo (n = 236)
Completed 12 mo of study tx	49.0	34.7
Discontinued study tx	51.0	65.3
▪ Patient decision	3.0	5.1
▪ AE	15.4	9.7
▪ Severe protocol noncompliance	0.2	0.4
▪ Disease worsening	31.3	49.6
▪ Study-specific d/c criteria	0.2	0.4
▪ Other	0.8	0

‡Percentages calculated based on number of treated patients.

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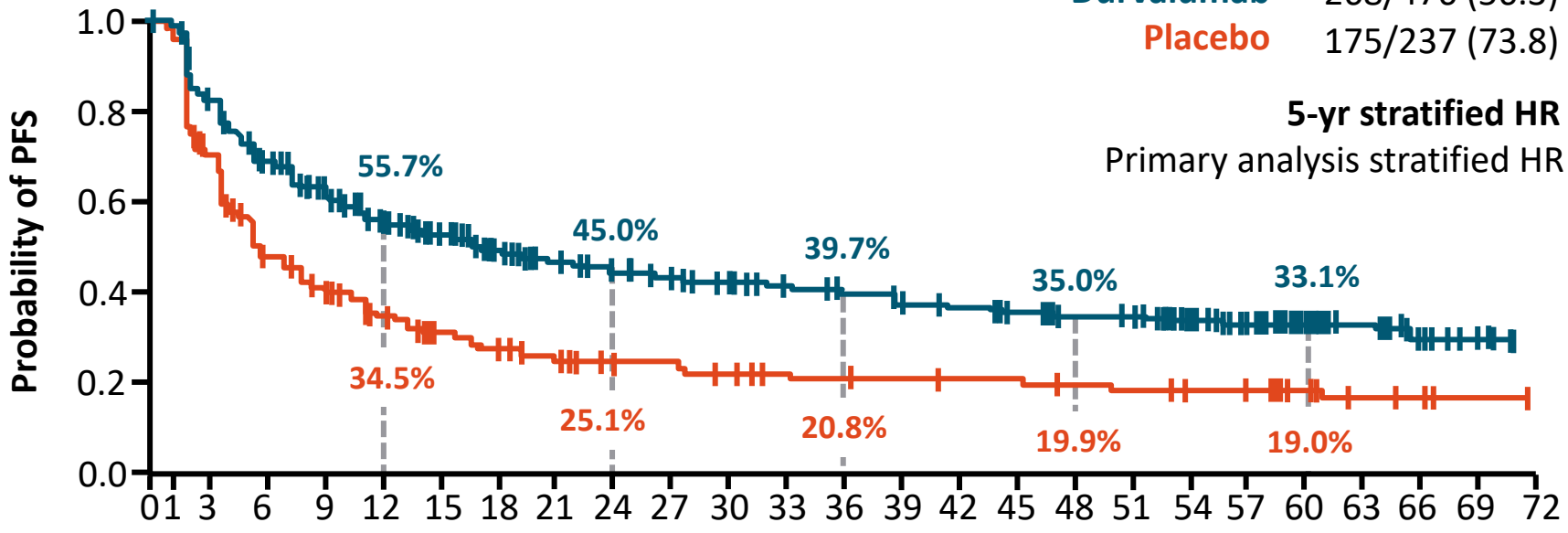
PACIFIC 5-Yr Update: PFS (ITT)

	Events/Patients, n/N (%)	Median PFS, Mo (95% CI)
Durvalumab	268/476 (56.3)	16.9 (13.0-23.9)
Placebo	175/237 (73.8)	5.6 (4.8-7.7)

5-yr stratified HR (95% CI): 0.55 (0.45-0.68)

Primary analysis stratified HR (95% CI): 0.52 (0.42-0.65)



Patients at Risk, n																									
Durvalumab	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

- 72 additional PFS events reported since time of primary analysis (data cutoff: February 13, 2017); updated results, including across patient subgroups, consistent with those from primary analysis

Spigel. ASCO 2021. Abstr 8511.

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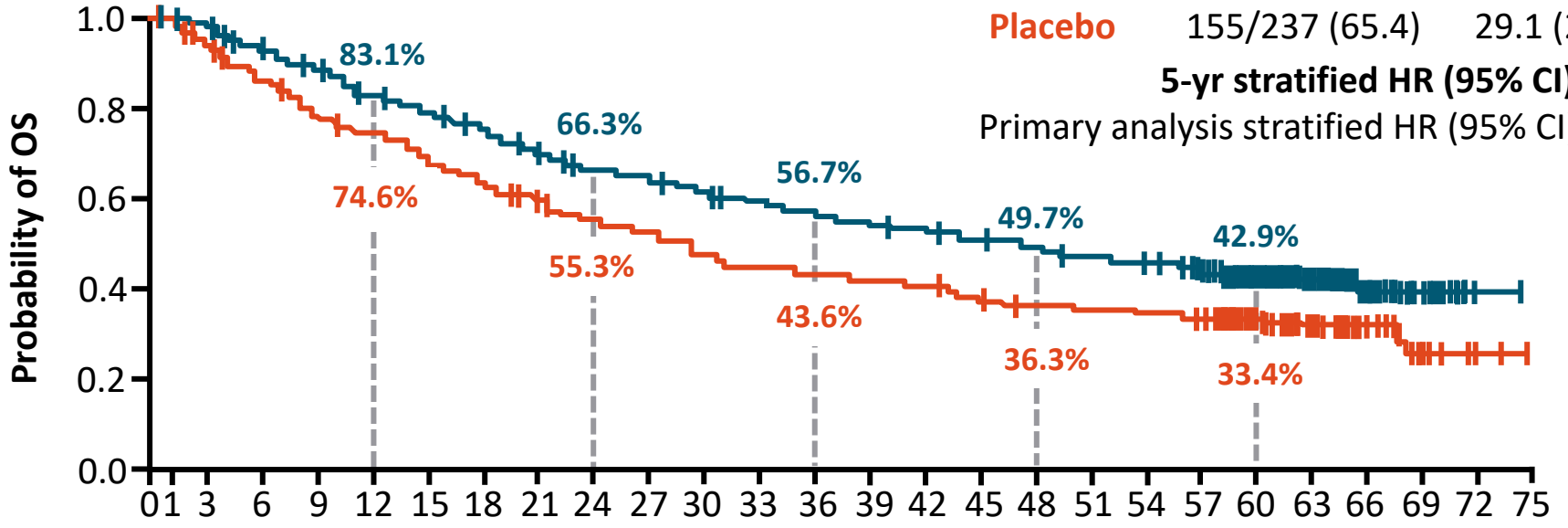
PACIFIC 5-Yr Update: OS (ITT)

	Events/Patients, n/N (%)	Median OS, Mo (95% CI)
Durvalumab	264/476 (55.5)	47.5 (38.1-52.9)
Placebo	155/237 (65.4)	29.1 (22.1-35.1)

5-yr stratified HR (95% CI): 0.72 (0.59-0.89)

Primary analysis stratified HR (95% CI): 0.68 (0.53-0.87)



Patients at Risk, n																									
Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

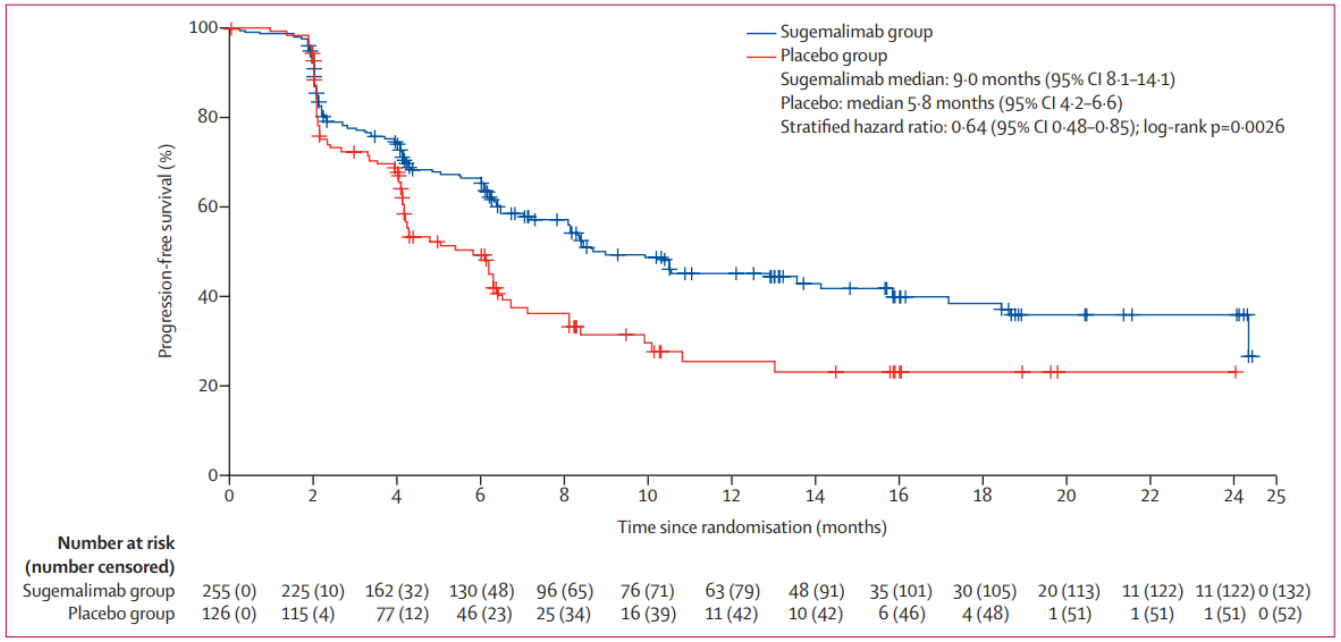
- 120 additional OS events reported since time of primary analysis (data cutoff: March 22, 2018); updated results, including across patient subgroups, consistent with those from primary analysis

Spigel. ASCO 2021. Abstr 8511.

Slide credit: clinicaloptions.com

Sugemalimab versus placebo after concurrent or sequential chemoradiotherapy in patients with locally advanced, unresectable, stage III non-small-cell lung cancer in China (GEMSTONE-301): interim results of a randomised, double-blind, multicentre, phase 3 trial

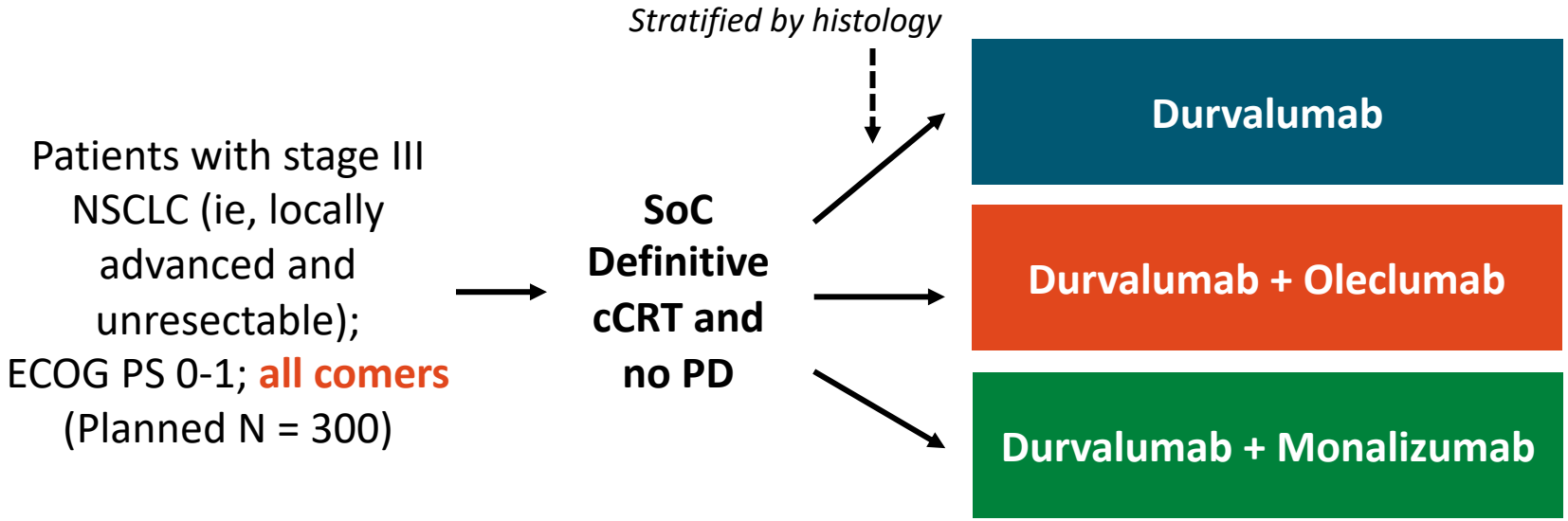
- 381 patients with stage III NSCLC
- Consolidation Sugemalumab(PDL-1)
- Expected toxicity



Zhou, Lancet Oncol 2022

COAST: Durvalumab + Oleclumab or Monalizumab vs Durvalumab Alone in Stage III NSCLC

- Randomized, open-label, multicenter phase II trial
  - Oleclumab: human IgG1 mAb to CD73, inhibits adenosine production
  - Monalizumab: human mAb to CD94/NKG2a, enhances antitumor effects of immune effector cells



- Primary endpoints: ORR
- Key secondary endpoints: safety, DoR, disease control, PFS, PFS12

ClinicalTrials.gov. NCT03822351.

Slide credit: clinicaloptions.com

COAST: Durvalumab + Oleclumab or Monalizumab vs Durvalumab Alone in Stage III NSCLC

ITT	D	D+O	D+M
N	67	60	62
ORR (95% CI), %[a,b]	25.4 (15.5, 37.5)	38.3 (26.1, 51.8)	37.1 (25.2, 50.3)
Objective responses, n[a]	17	23	23
CR, n (%)	2 (3.0)	1 (1.7)	3 (4.8)
PR, n (%)	15 (22.4)	22 (36.7)	20 (32.3)
Median PFS (95% CI), mo[c]	6.3 (3.7, 11.2)	NR (10.4, NE)	15.1 (13.6, NE)
PFS HR (95% CI)[d,e]	-	0.44 (0.26, 0.75)	0.65 (0.49, 0.85)
10-month PFS rate (95% CI), %[c]	39.2 (26.1, 52.0)	64.8 (50.4, 76.0)	72.7 (58.8, 82.6)

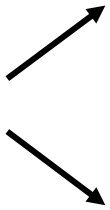
Chemoradiation strategies

- Concurrent checkpoint inhibitor and radiation
- Induction checkpoint inhibitor
- consolidation checkpoint inhibitor plus other immune mechanism

Concurrent RT + PD-1/PDL-1 Strategies

A Global Study to Assess the Effects of Durvalumab + Domvanalimab Following Concurrent Chemoradiation in Participants With Stage III Unresectable NSCLC (PACIFIC-8)

Adult patients with locally advanced, unresectable, stage III NSCLC without progression following ≥2 cycles platinum-based chemotherapy concurrent with radiation therapy; WHO PS 0/1
(N = 860)



Durvalumab + Domvanalimab
Q4W for up to 12 mo

Durvalumab + Placebo IV Q4W
for up to 12 mo

Until disease progression or unacceptable toxicity

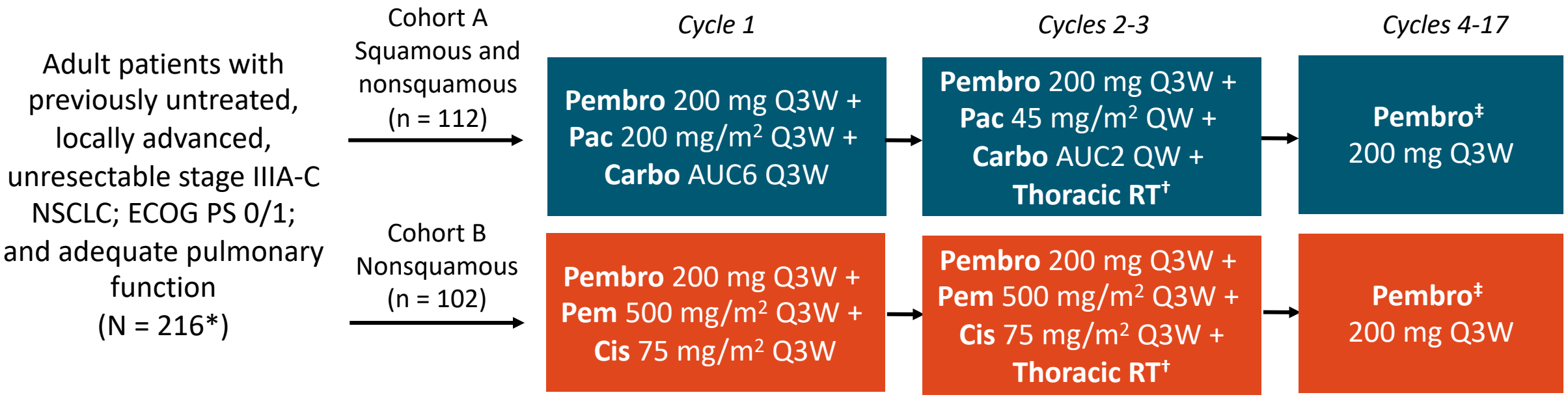
NCT05211895

Small trials of concurrent checkpoint inhibitor and radiation in non-small cell lung cancer

Trial	ICI	# of Patients	Unexpected AE
AFT-16	Atezolizumab	62	No
Tsao et al	Atezolizumab	30	No
Jabbour et al	Pembrolizumab	21	No
NICOLAS	Nivolumab	79	No
DETERRED	Atezolizumab	52	No

KEYNOTE-799: Study Design

- Nonrandomized, open-label phase II trial



*n = 2 did not receive treatment. †60 Gy in 30 daily 2-Gy fractions. ‡Until completion of cycle 17, PD, unacceptable AEs, or study withdrawal.

- Primary endpoints: ORR per RECIST 1.1 by BICR, grade ≥3 pneumonitis
- Secondary endpoints: PFS per RECIST 1.1 by BICR, OS, safety

Jabbour. ASCO 2021. Abstr 8512.

Slide credit: clinicaloptions.com

KEYNOTE-799: Efficacy Outcomes

Efficacy Outcome	Cohort A: Squamous and Nonsquamous (n = 112)	Cohort B: Nonsquamous (n = 102)
Median follow-up, mo (range)	18.5 (13.6-23.8)	13.7 (2.9-23.5)
ORR, % (95% CI)	70.5 (61.2-78.8)	70.6 (60.7-79.2)
▪ CR, n (%)	4 (3.6)	5 (4.9)
▪ PR, n (%)	75 (67.0)	67 (65.7)
▪ SD, n (%)	20 (17.9)	23 (22.5)
▪ PD, n (%)	1 (0.9)	0
▪ Not evaluable, n (%)	2 (1.8)	0
▪ No assessment, n (%)	10 (8.9)	7 (6.9)
Median DoR, mo (range)	NR (1.7+ to 19.7+)	NR (1.8+ to 21.4+)
▪ DoR ≥12 mo, %	79.7	75.6
Median PFS, mo (95% CI)	NR (16.6 to NR)	NR (NR to NR)
▪ 12-mo PFS, %	67.1	71.6
Median OS, mo (95% CI)	NR (NR to NR)	NR (21.9 to NR)
▪ 12-mo OS, %	81.3	87.0

- ORR results consistent regardless of whether PD-L1 TPS <1% vs ≥1%
  - Cohort A: 66.7% vs 75.8%
  - Cohort B: 71.4% vs 72.5%
- ORR results also consistent regardless of nonsquamous vs squamous histology
  - Cohort A: 69.2% vs 71.2%
  - Cohort B: 70.6% vs NA

Jabbour. ASCO 2021. Abstr 8512.

Slide credit: clinicaloptions.com

KEYNOTE-799: Safety Outcomes

Safety Outcome	Cohort A: Squamous and Nonsquamous (n = 112)	Cohort B: Nonsquamous (n = 102)
All-cause grade ≥3 pneumonitis, n (%) [95% CI]	9 (8.0) [3.7-14.7]	7 (6.9) [2.8-13.6]
Treatment-related AEs, n (%)	105 (93.8)	99 (97.1)
▪ Grades 3-5	72 (64.3)	51 (50.0)
▪ Leading to death*	4 (3.6)	1 (1.0)
▪ Leading to discontinuation of any treatment component	38 (33.9)	19 (18.6)
Immune-mediated AEs and infusion reactions, n (%)	58 (51.8)	42 (41.2)
▪ Grades 3-5	18 (16.1)	9 (8.8)
▪ Leading to death*	4 (3.6)	1 (1.0)
▪ Leading to discontinuation of any treatment component	21 (18.8)	11 (10.8)

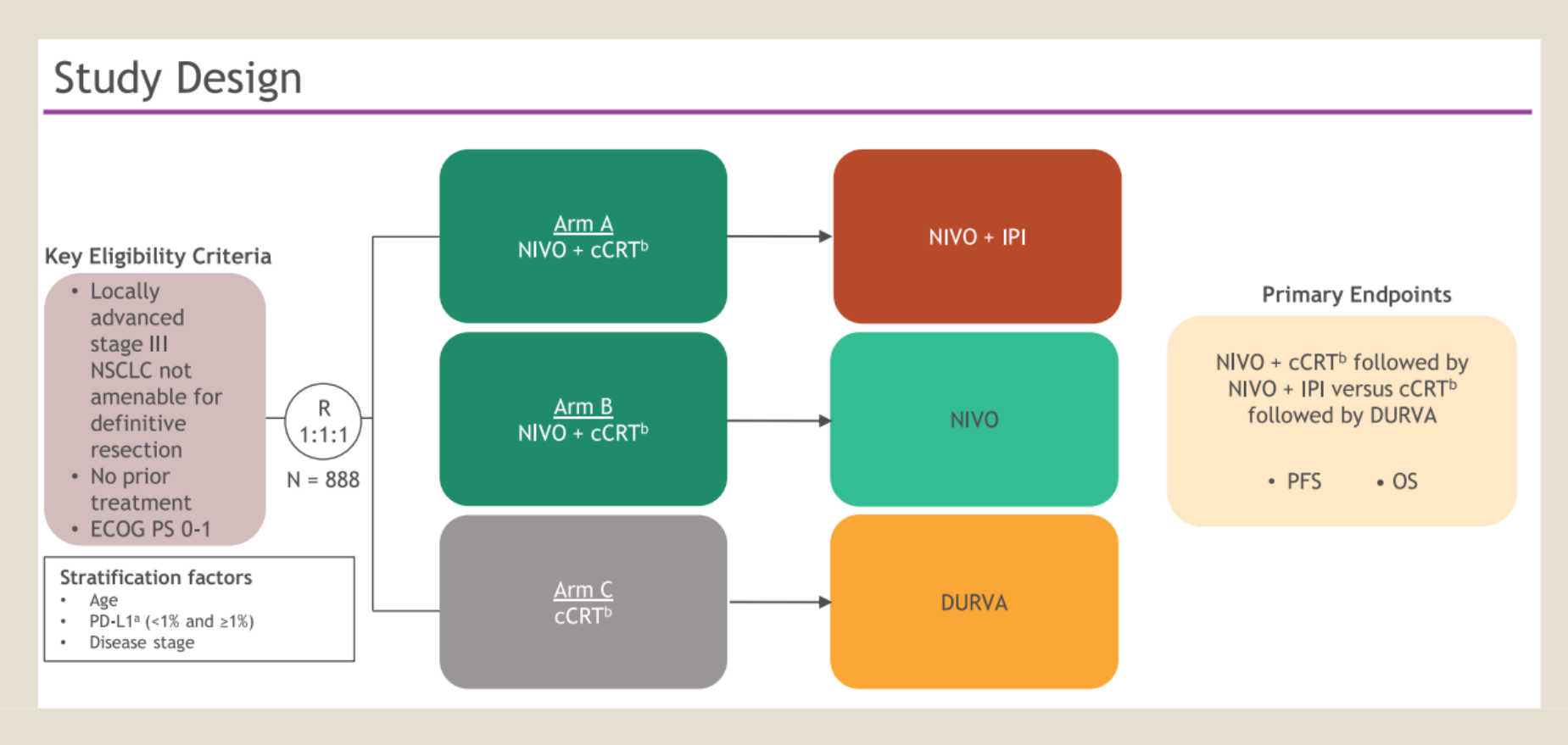
*Includes 4 patients (3.6%) with grade 5 pneumonitis in cohort A and 1 patient (1.0%) with grade 5 interstitial lung disease in cohort B.

Jabbour. ASCO 2021. Abstr 8512.

Slide credit: clinicaloptions.com

CheckMate 73L

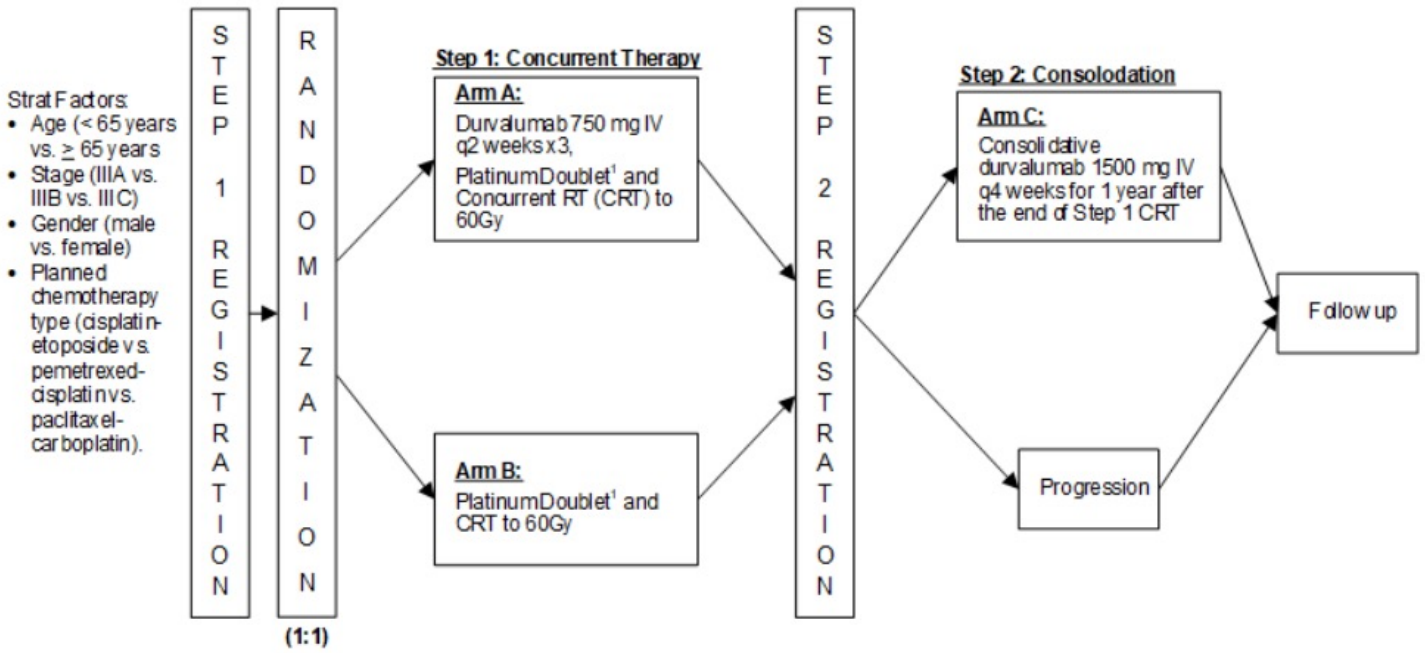
- 888 patients stage III
- Stratified by age, PDL-1, and stage



De Ruysscher, Clinical Lung Cancer 2021

EA 5181

Schema



N = 660

Cycle = Step 1 (Arms A & B): 28 days for patients receiving platinum doublet option #1 (see below)
21 days for patients receiving platinum doublet option #2 (see below)
7 days for patients receiving platinum doublet option #3 (see below)
Step 2 (Arm C): 28 days for patients on consolidative durvalumab (Arm C).

1. Investigator's Choice for Step 1 (see Section 5.1):
   a. Option #1: Cisplatin 50 mg/m2 IV on C1D1, C1D8, C2D1, C2D8; etoposide 50 mg/m2 IV C1D1-D5; C2D1-D5 (Cycle = 28 days)
   b. Option #2: pemetrexed 500 mg/m2 IV C1D1, C2D1; Cisplatin 75 mg/m2 IV on C1D1, C2D1 (Cycle = 21 days) (nonsquamous only)
   c. Option #3: paclitaxel 45 mg/m2 IV on D1 of each cycle for 6 cycles; Carboplatin AUC 2 IV on D1 of each cycle for 6 cycles (Cycle = 7 days)

KEYLYNK-012: A Phase 3 Study of Pembrolizumab With Concurrent Chemoradiation Therapy (CCRT) Followed by Pembrolizumab With or Without Olaparib vs. CCRT Followed by Durvalumab in Unresectable, Locally Advanced, Stage III Non–Small-Cell Lung Cancer

Adult patients with previously untreated, locally advanced, unresectable stage IIIA-C NSCLC; ECOG PS 0/1; and adequate pulmonary function (N = 870)

Chemoradiation + Pembrolizumab (60 Gy)

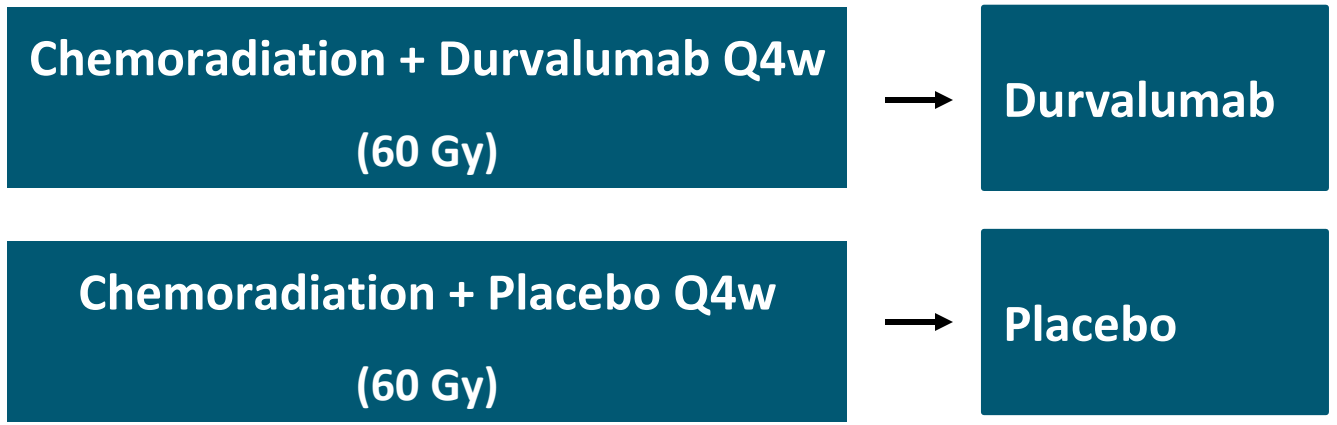
- **Pembrolizumab + Olaparib BID** Q3W for up to 12 mo
- **Pembrolizumab + Placebo** Q3W for up to 12 mo

PACIFIC

NCT04380636

PACIFIC-2: Phase 3 study of concurrent durvalumab and platinum-based chemoradiotherapy in patients with unresectable, stage III NSCLC. (ExUS)

Adult patients with locally advanced, unresectable, stage III NSCLC without progression following ≥2 cycles platinum-based chemotherapy concurrent with radiation therapy;
WHO PS 0/1
(N = 328)

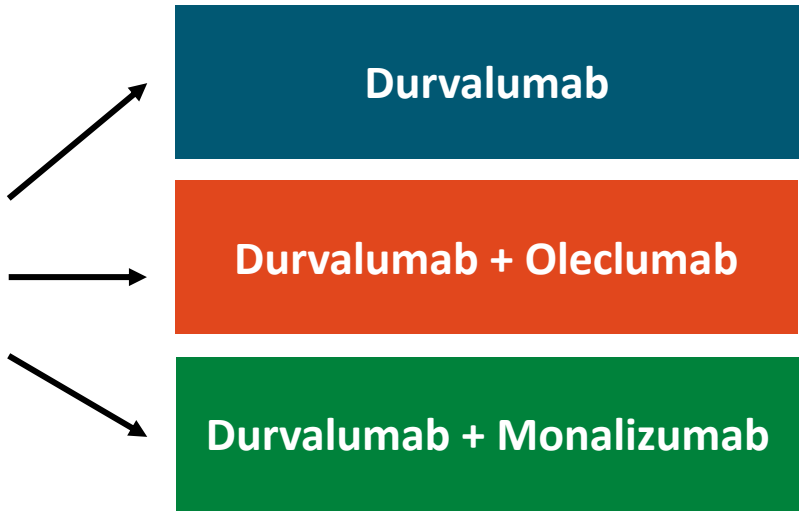


NCT03519971

New PD-1/PDL-1 Inhibitors And Combinations

A Global Study to Assess the Effects of Durvalumab With Oleclumab or Durvalumab With Monalizumab Following Concurrent Chemoradiation in Patients With Stage III Unresectable Non-Small Cell Lung Cancer (PACIFIC-9)

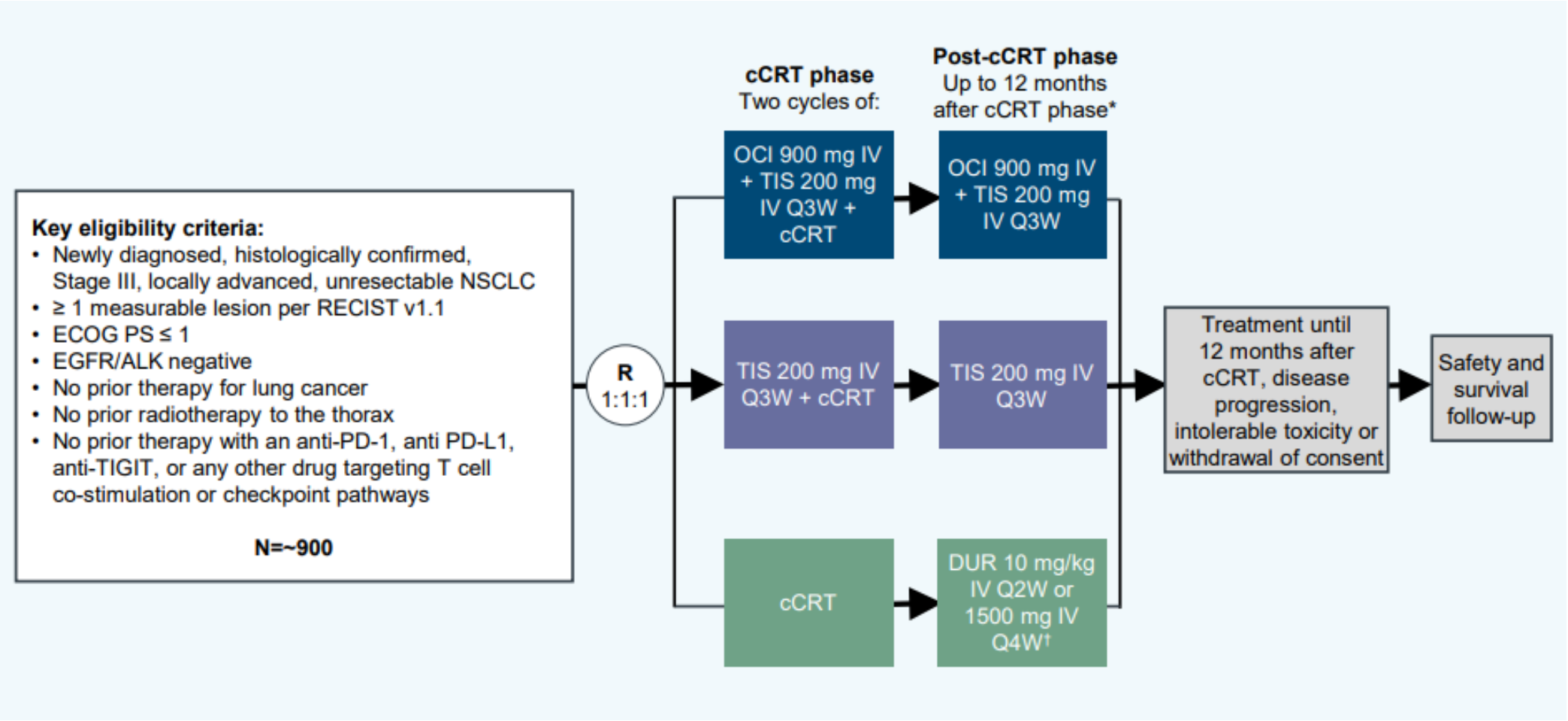
Patients with stage III NSCLC (ie, locally advanced and unresectable); ECOG PS 0-1; (Planned N = 999)



NCT05221840

Tislelizumab Plus Ociperlimab Versus Tislelizumab Versus Durvalumab When Co-administered With Concurrent Chemoradiotherapy (cCRT) in Lung Cancer

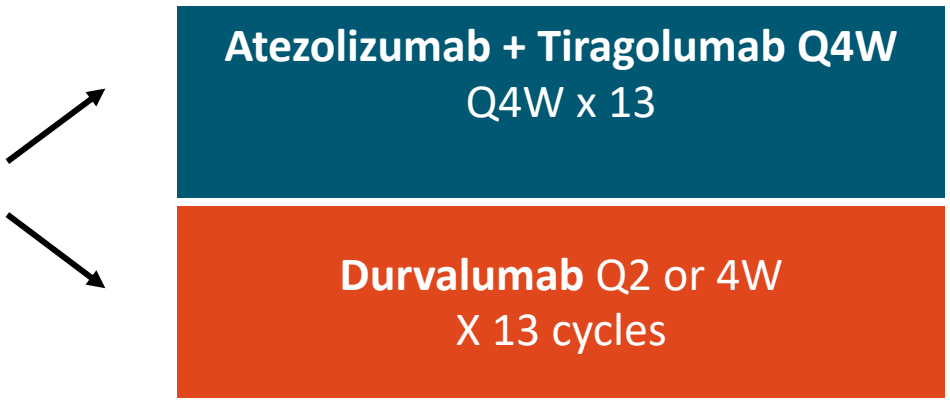
AdvanTIG-301



Xing, ESMO 2021

SKYSCRAPER-03: Phase III, open-label randomised study of atezolizumab + tiragolumab vs durvalumab in patients with locally advanced, unresectable, stage III non-small cell lung cancer (NSCLC) who have not progressed after platinum-based concurrent chemoradiation (cCRT)

Adult patients with locally advanced, unresectable, stage III NSCLC without progression following ≥2 cycles platinum-based chemotherapy concurrent with radiation therapy; WHO PS 0/1
(N = 800)



NCT04513925

Summary

- Before era of immunotherapy, concurrent CRT ± induction chemotherapy demonstrated 20% to 25% “cure” rate
- The addition of consolidation immunotherapy after concurrent chemoradiation has shown a 5 year overall survival of 42.9%
- Multiple strategies are being investigated to improve efficacy over the current standard of care.