2025

DEBATES AND DIDACTICS in Hematology and Oncology

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Updates in the Management of Locally Advanced Unresectable Stage III NSCLC

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Disclosures

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Employee*	*Other (please specify)*
Emory University				x	
Varian/Siemens Healthineers			x		
Genentech		x			
Merck via RTOG Foundation	x	x			
RefleXion Medical			x		
BioAscend	x				

PACIFIC

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

- **Unresectable, Stage III NSCLC without progression and without G2+ toxicity after definitive platinum-based cCRT (≥2 cycles)**
- **18 years or older**
- **WHO PS score 0 or 1**
- **If available, archived pre-cCRT tumor tissue for PD-L1 testing***

All-comers population (i.e. irrespective of PD-L1 status)

N=713 randomized

1-42 days post-cCRT

R

Durvalumab
10 mg/kg q2w for up to 12 months
N=476

2:1 randomization, stratified by age, sex, and smoking history

Placebo
for up to 12 months
N=237

Primary endpoints
- PFS by BICR using RECIST v1.1†
- OS

Key secondary endpoints
- ORR, DoR and TTDM by BICR
- PFS2 by investigator
- Safety
- PROs

†Defined as the time from randomization until the date of objective disease progression or death by any cause in the absence of progression. BICR, blinded independent central review; cCRT, concurrent CRT; PFS2, time to second progression;
RECIST, Response Evaluation Criteria in Solid Tumors; TTDM, time to death or distant metastasis.

Antonia et al. NEJM 2017 & 2018

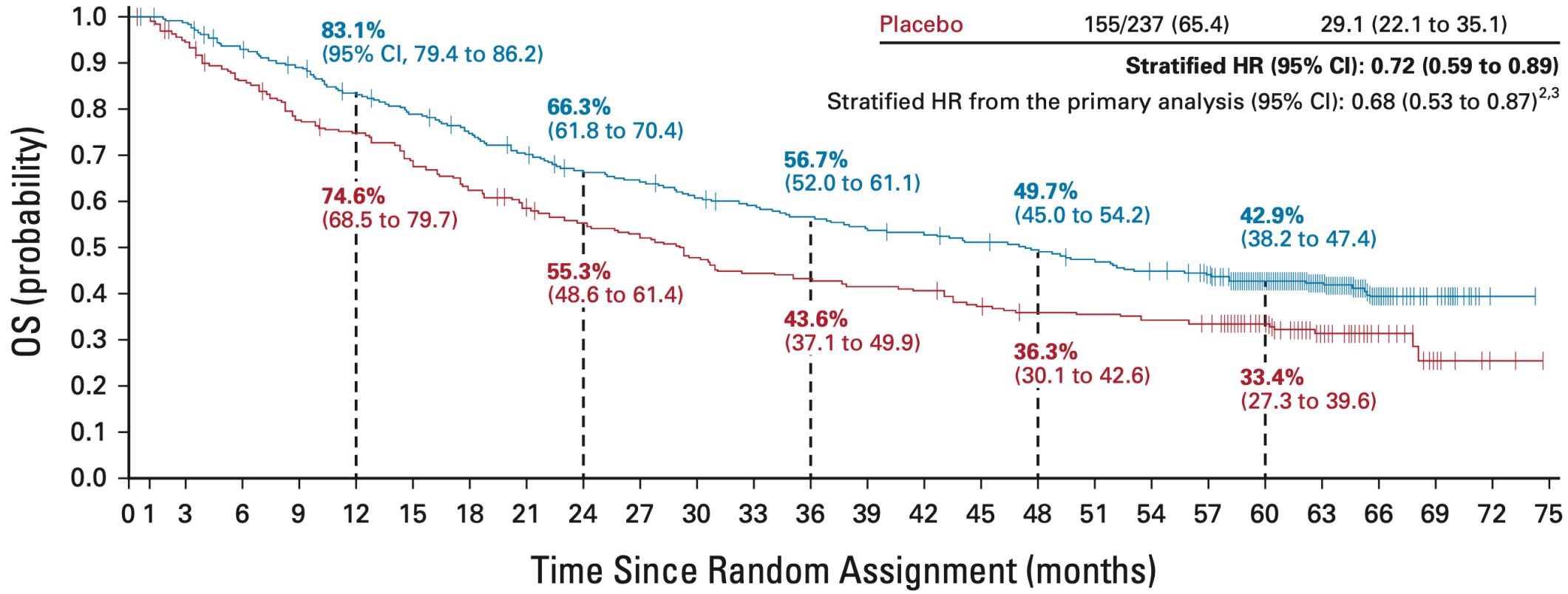
Antonia et al. *N Engl J Med*. 2018;379(24):2342-2350.

PACIFIC – 5 Year Outcomes

Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

Stratified HR (95% CI): 0.72 (0.59 to 0.89)

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]



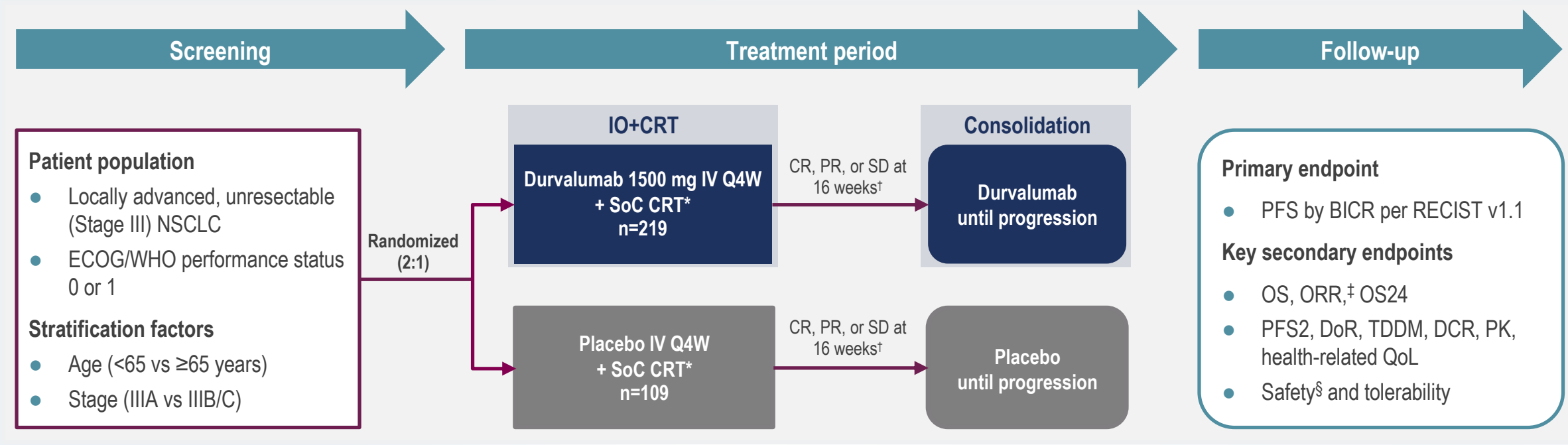
No. at risk:

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

Spigel et al. *J Clin Oncol*. 2022;40(12):1301-1311.

PACIFIC-2

PACIFIC-2 (NCT03519971) is a phase 3, randomized, double-blind, placebo-controlled, multicenter, global study of durvalumab + CRT followed by durvalumab versus placebo + CRT followed by placebo



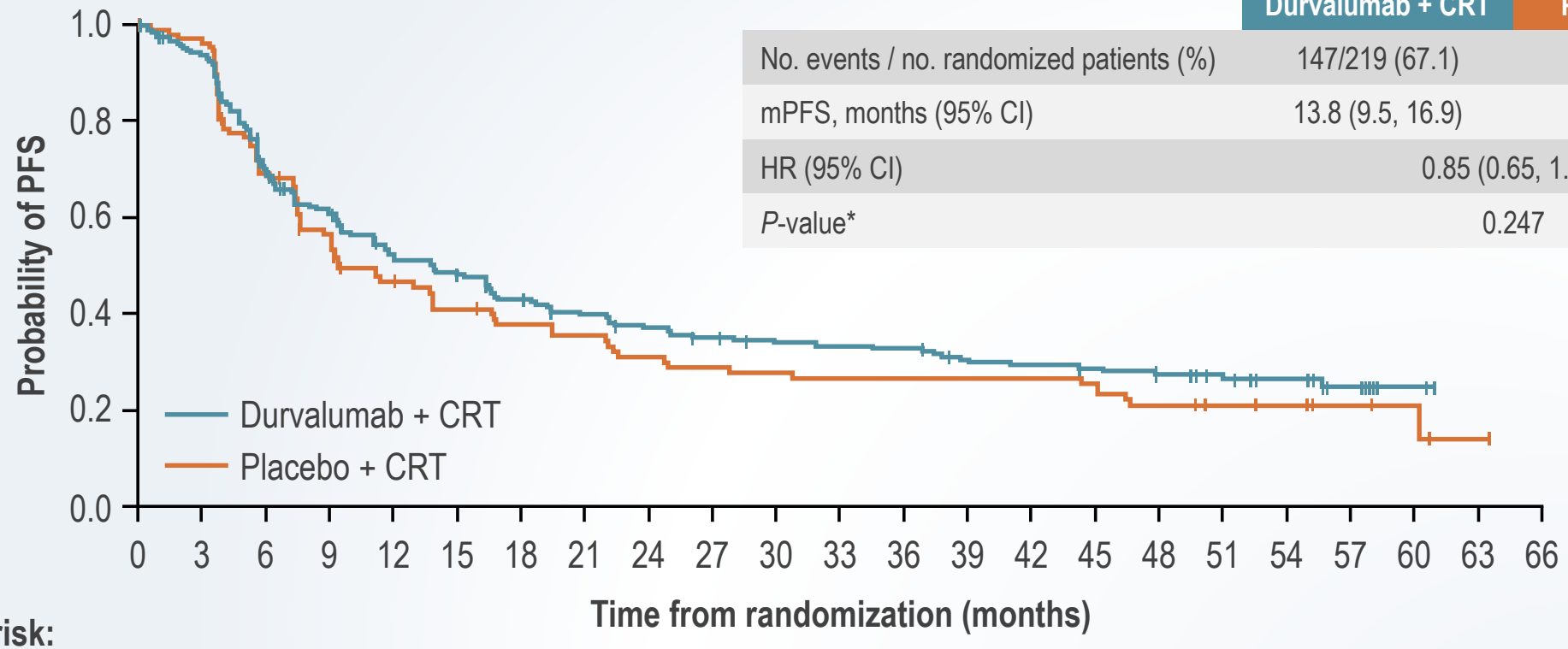
Patients were recruited from **29 March 2018** through **24 June 2019** across 106 sites in Asia, Eastern Europe, and the Americas, including: Brazil, Czech Republic, Hungary, India, Japan, Mexico, Peru, Philippines, Poland, Republic of Korea, Russia, Turkey, Thailand, and Vietnam.

BICR, blinded independent central review; CR, complete response; CRT, chemoradiotherapy; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; Gy, gray; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; OS24, overall survival at 24 months; PFS, progression-free survival; PFS2, time from randomization to second progression; PK, pharmacokinetics; PR, partial response; Q4W, once every 4 weeks; QoL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SoC, standard of care; TDDM, time to death or distant metastasis; WHO, World Health Organization.

*Platinum-based chemotherapy regimens include: cisplatin/etoposide, carboplatin/paclitaxel, pemetrexed/cisplatin (non-squamous only), or pemetrexed/carboplatin (non-squamous only), alongside radiation therapy (5 fractions/week for ~6 weeks [±3 days; total 60 Gy]). †Investigator assessed per RECIST v1.1. ‡Following a protocol amendment, ORR was moved from a primary endpoint to a key secondary endpoint. §Will be reviewed by an independent data monitoring committee in an unblinded manner.

PFS by BICR (ITT Population)

	Durvalumab + CRT	Placebo + CRT
No. events / no. randomized patients (%)	147/219 (67.1)	80/109 (73.4)
mPFS, months (95% CI)	13.8 (9.5, 16.9)	9.4 (7.5, 16.6)
HR (95% CI)	0.85 (0.65, 1.12)	
P-value*	0.247	



No. at risk:																						
Durvalumab + CRT	219	199	145	124	102	94	83	75	69	64	60	59	58	50	49	47	43	28	24	10	2	0	0
Placebo + CRT	109	104	72	58	44	38	34	32	28	26	25	24	24	24	24	23	19	15	12	7	3	1	0

elcc European Lung Cancer Congress 2024

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mPFS, median PFS; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

Per RECIST v1.1. Tick marks on the curves indicate censored observations.
*Based on the Lan and DeMets approach that approximates the O'Brien Fleming spending functions; the 2-sided p-value boundary for declaring statistical significance is 0.0416 for an overall 5% alpha.

Summary of Adverse Events (Safety Population)

AE category, n (%)	Durvalumab + CRT (n=219)	Placebo + CRT (n=108)
Any AE	216 (98.6)	108 (100)
Maximum grade 3 or 4*	117 (53.4)	64 (59.3)
Outcome of death	30 (13.7)	11 (10.2)
SAE	103 (47.0)	56 (51.9)
Any AE leading to discontinuation of durvalumab/placebo†	56 (25.6)	13 (12.0)
0 to ≤4 months from start of treatment **(approximates the duration of IO+CRT and ends at the first post-baseline scan)**	31 (14.2)	6 (5.6)
>4 to ≤16 months from start of treatment (approximates the duration of consolidation IO in the SoC PACIFIC regimen)	12 (5.5)	6 (5.6)
>16 months from start of treatment (approximates treatment beyond the duration of consolidation IO in the SoC PACIFIC regimen)	13 (5.9)	1 (0.9)

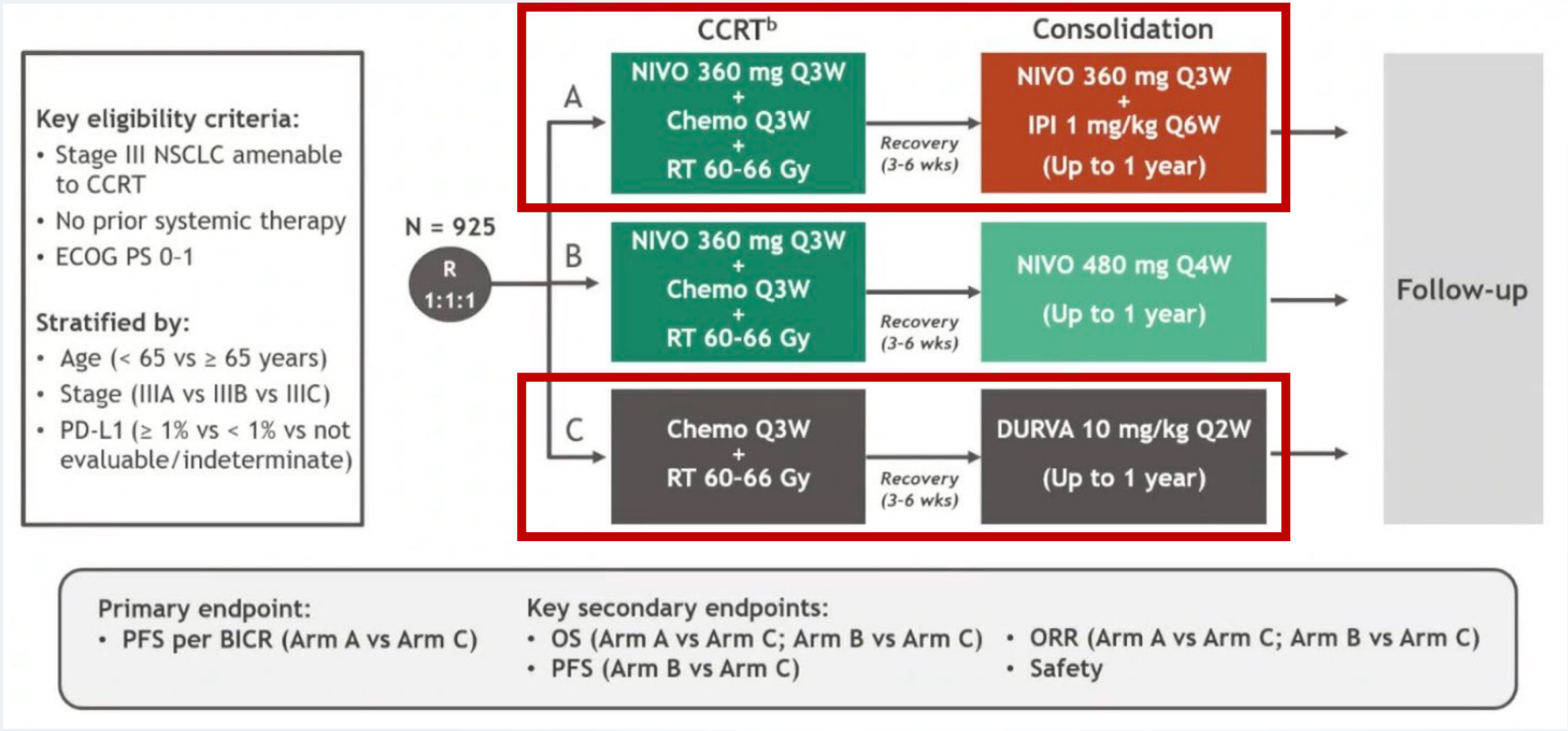
- The most common treatment-emergent AEs with **durvalumab** + SoC CRT were:
  - Anemia (42.0%), pneumonitis or radiation pneumonitis (28.8%), neutropenia (27.4%), and nausea (25.6%)
- The most common treatment-emergent AEs with **placebo** + SoC CRT were:
  - Anemia (38.0%), constipation (28.7%), pneumonitis or radiation pneumonitis (28.7%), and neutropenia (25.9%)
- Combined rates of pneumonitis or radiation pneumonitis were similar in the **durvalumab** arm (28.8%) and **placebo** arm (28.7%)
  - Grade ≥3 pneumonitis or radiation pneumonitis occurred in 10 patients (4.6%) in the **durvalumab** arm and 6 (5.6%) in the **placebo** arm

AE, adverse event; CRT, chemoradiotherapy; CTCAE, Common Terminology Criteria for Adverse Events; IO, immunotherapy; SAE, serious adverse event; SoC, standard of care.

Per CTCAE v5.0.
*Excludes any patients who experienced any AE of maximum CTCAE grade 5.
†At any time, regardless of discontinuation of CRT.

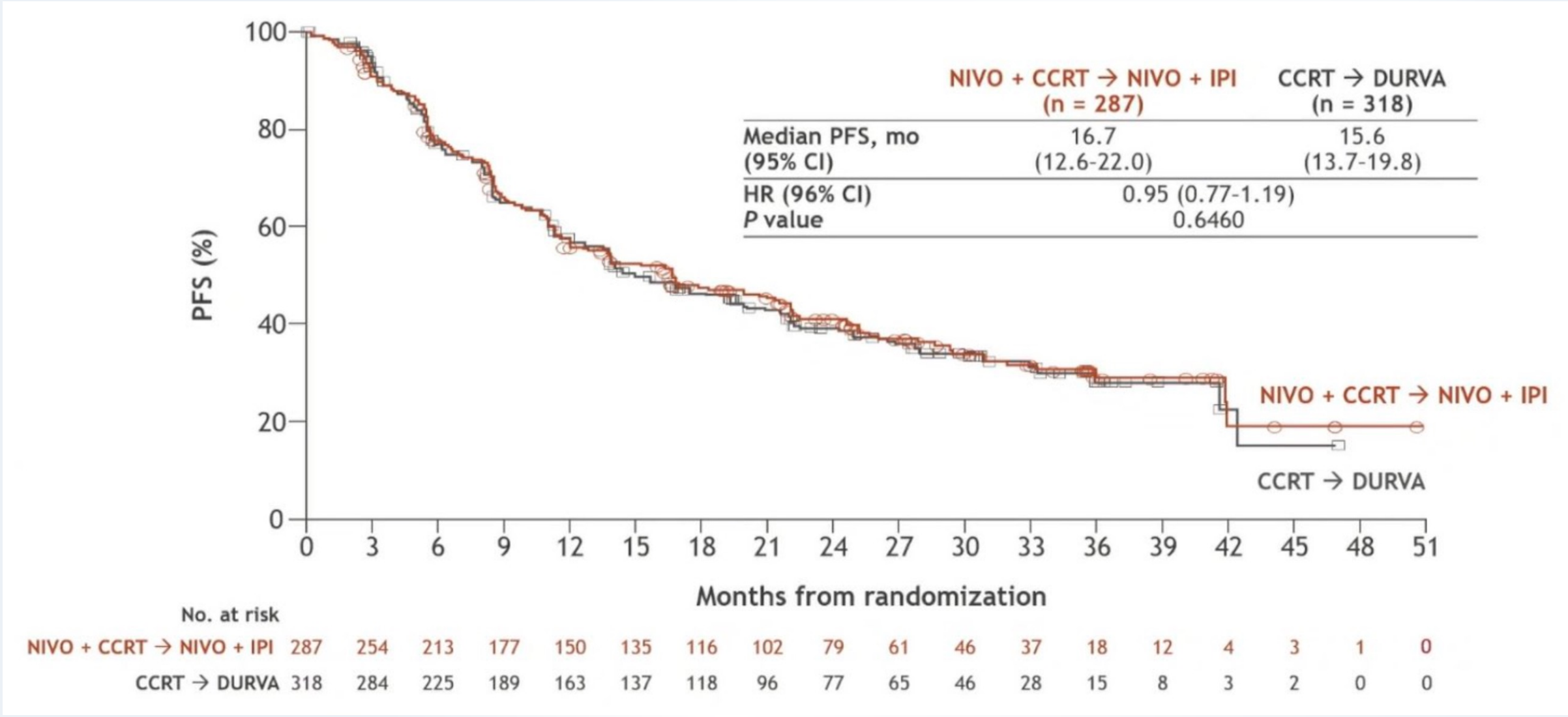
CheckMate 73L

Phase 3 Study Comparing Nivolumab Plus Concurrent Chemoradiotherapy Followed by Nivolumab With or Without Ipilimumab Versus Concurrent Chemoradiotherapy Followed by Durvalumab for Previously Untreated, Locally Advanced Stage III NSCLC



NCT04026412

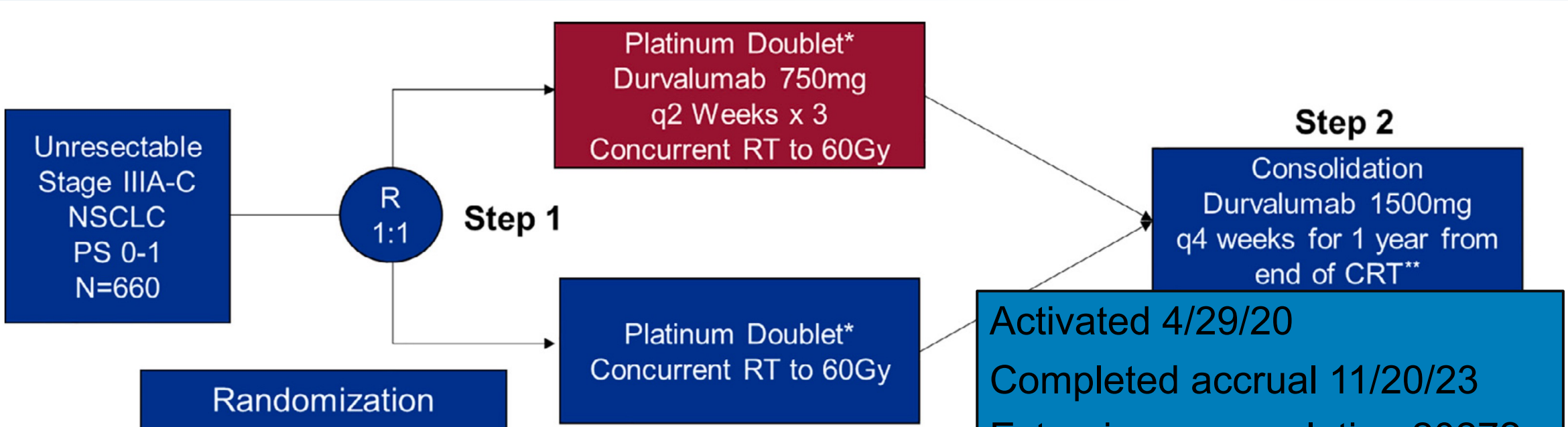
PFS – CRT + Nivo -> Nivo/Ipi vs CRT -> Durva (BICR)



Peters et al. Abstract 650 ESMO IO 2024

EA5181

Randomized Phase III Trial of MEDI4736 (durvalumab) as Concurrent and Consolidative Therapy or Consolidative Therapy Alone for Unresectable Stage 3 NSCLC



***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

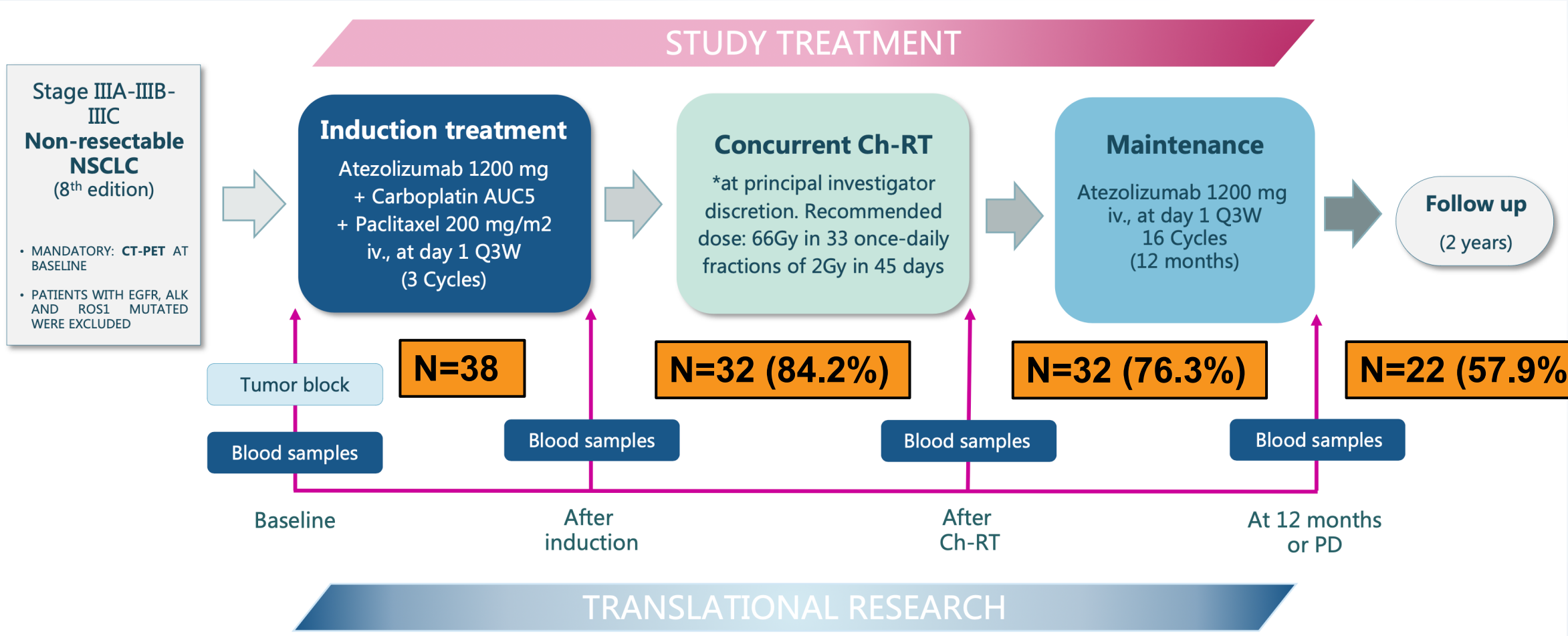
NCT04092283

Summary of Selected CRT + Concurrent IO Studies

Study	Control	Experimental	1° Endpoint	Endpoint Met?
PACIFIC-2	CRT	CRT w/ IO -> IO	PFS	✗
CheckMate 73L (arm C vs A)	CRT -> IO	CRT w/ IO -> IO/IO	PFS	✗
EA5181	CRT -> IO	CRT w/ IO -> IO	OS	Pending 2027?

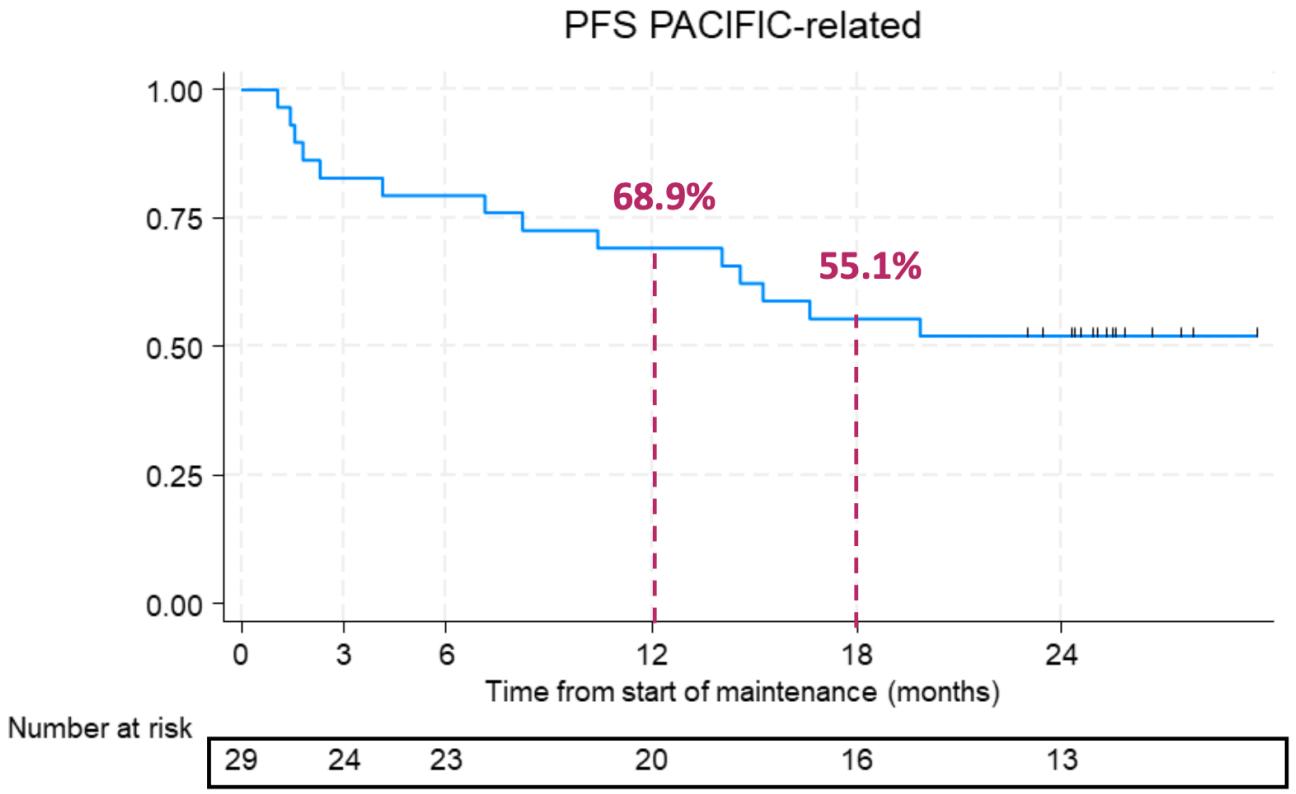
APOLO

Atezolizumab + induction chemotherapy + chemo-radiotherapy and atezolizumab maintenance in non-resectable stage IIIA-IIIB-IIIC NSCLC



Provencio et al. OA12.05 WCLC 2024

'PACIFIC-related' PFS



PFS from the start of maintenance treatment starting time in ITT population was **68.9%** (95%CI: 48.8-82.4%) **at 12 months** and **55.1%** (95%CI: 35.6-71%) **at 18 months.**

Median for follow-up: 29.6 months (95%CI: 28.8-29.8)

PACIFIC

12-mo PFS 55.9%

18-mo PFS 44.2%

NCT04776447

PACIFIC-BRAZIL (LACOG 2218)

Intensified chemo-immuno-radiotherapy with durvalumab for stage III NSCLCs: a single arm phase II study

ELIGIBILITY CRITERIA

- ✓ Non-small cell lung cancer
- ✓ Stage III (TNM 8th ed.)†
- ✓ PS 0-1
- ✓ FEV1 ≥ 1.2 liters/second (or ≥ 50% predicted value)
- ✓ Predicted lung V20 <35%, cardiac V50 ≤25%
- ✓ No previous local or systemic therapy

INDUCTION CHEMO-IMMUNOTHERAPY

Carboplatin AUC 6 IV+
Paclitaxel 200mg/m² IV+
Durvalumab 1500mg/m² IV q3w for 2 cycles

CONCURRENT CHEMO-IMMUNO-RADIOTHERAPY

Carboplatin AUC 2 IV weekly for 6 weeks +
Paclitaxel 50 mg/m² IV weekly for 6 weeks +
Durvalumab 1500mg/m² q3w for 2 cycles +
Intensity-modulated radiation therapy to 60 Gy in 30 fractions over 6 weeks‡

CONSOLIDATION IMMUNOTHERAPY

Durvalumab 1500mg/m² IV q4w for 12 cycles

PRIMARY ENDPOINT:	**12-month progression-free survival**
SECONDARY ENDPOINTS:	Overall survival, overall response rate, duration of response, patterns of failure, efficacy (iRECIST as opposed to RECIST version 1.1), toxicity (CTCAE version 5)
EXPLORATORY ENDPOINTS:	Predictive biomarkers of response/survival

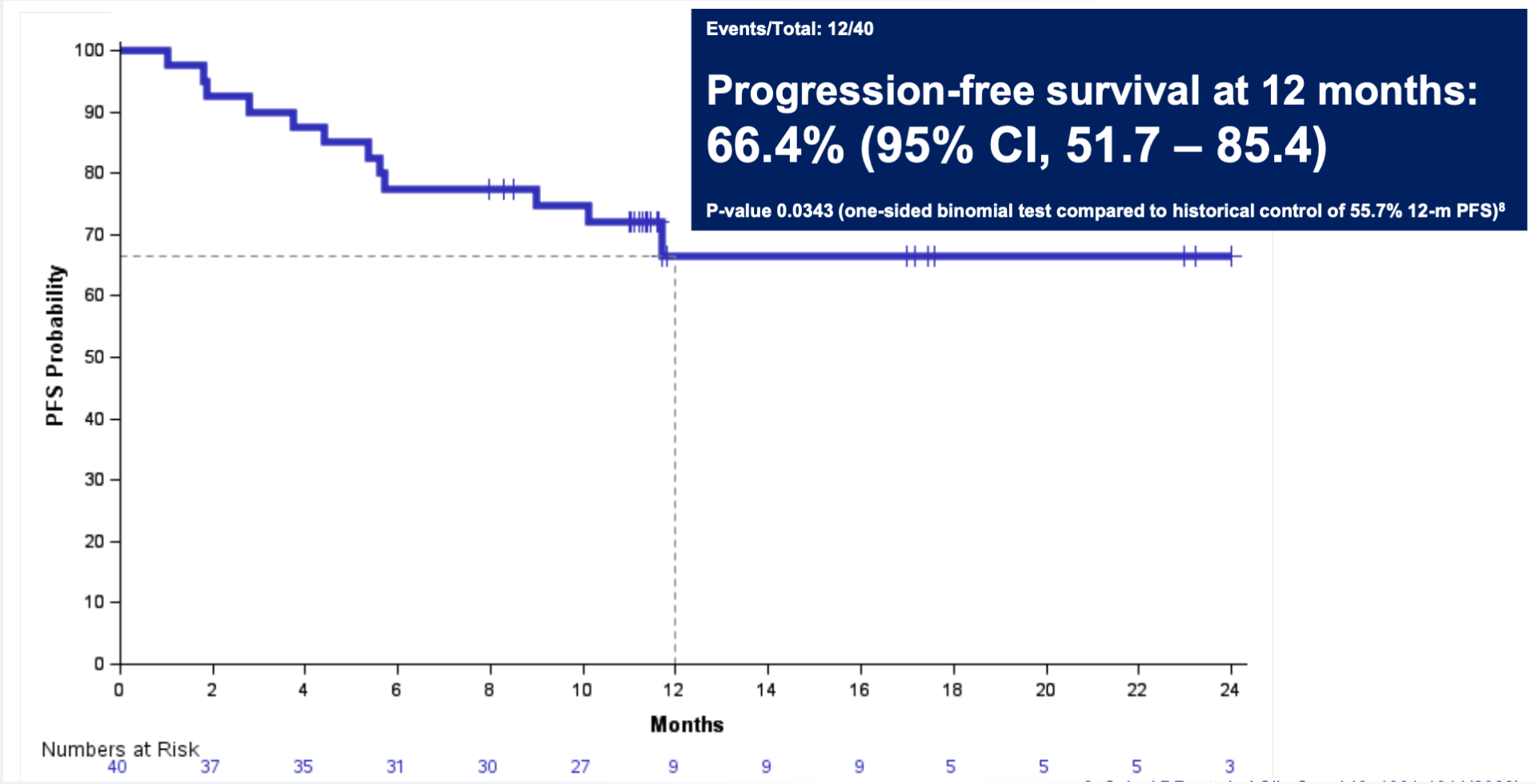
N= 49

†PET-CT was mandatory, invasive mediastinal staging was strongly encouraged. ‡Image guided radiation therapy (IGRT) was strongly encouraged.

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA

William et al. OA12.06 WCLC 2024

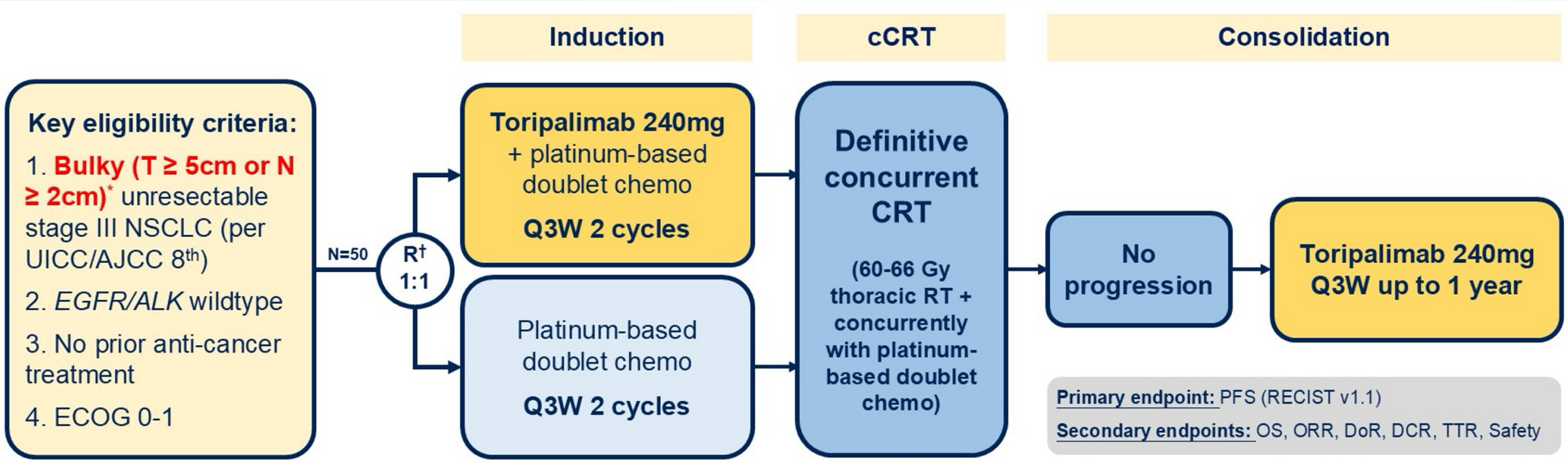
Pre-planned sensitivity landmark analysis: PFS from consol. IO



NCT04230408

InTRist (GCOG0074)

Randomized Phase II trial evaluating induction toripalimab plus chemotherapy followed by concurrent chemoradiotherapy and consolidation toripalimab in bulky unresectable stage III NSCLC



* Primary tumor ≥5 cm in the greatest dimension, or metastatic lymph nodes ≥2 cm in the shortest diameter
† Stratification factor: squamous vs non-squamous

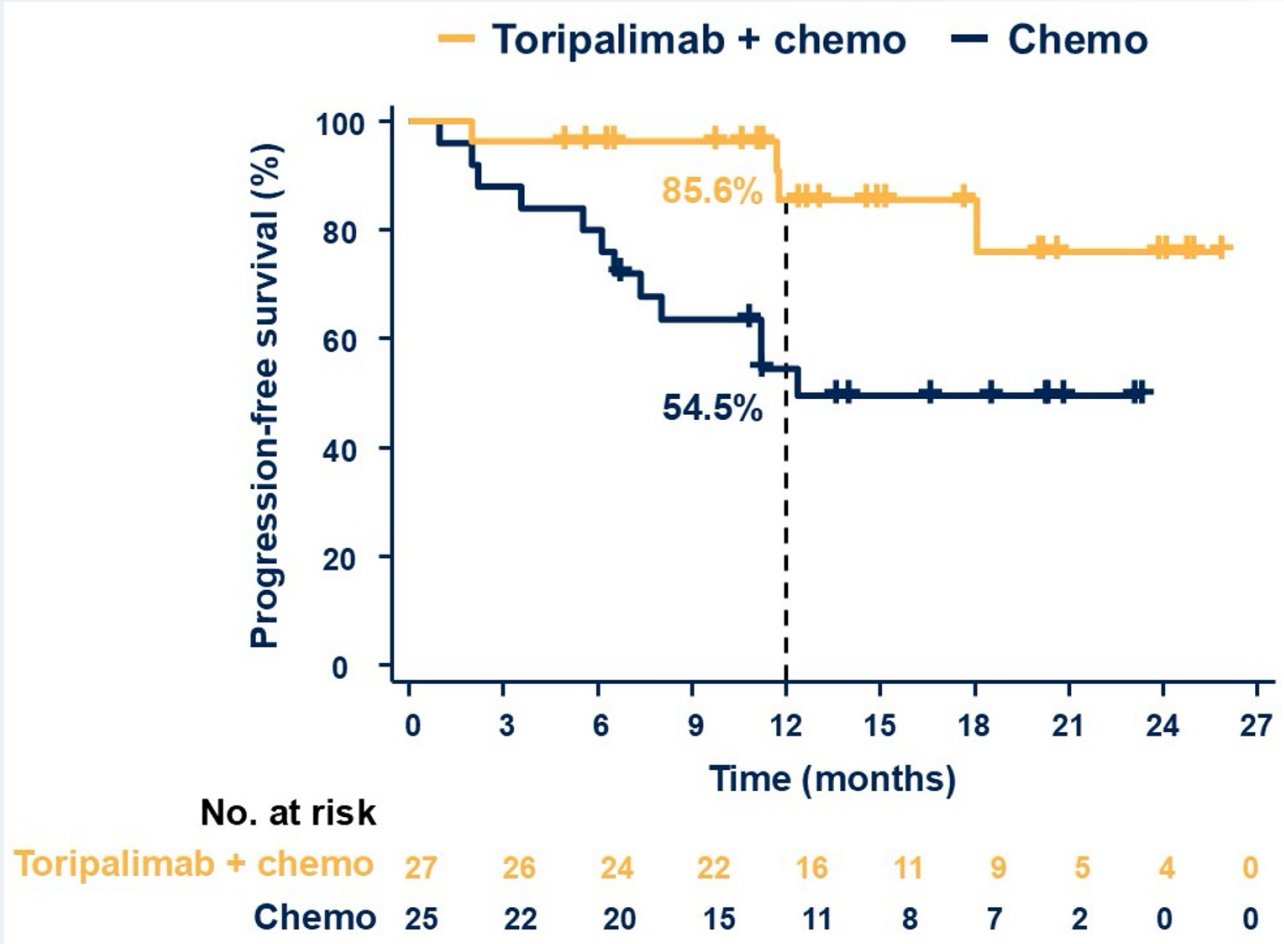
cCRT, concurrent CRT; RT, radiotherapy; PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DoR, duration of response; DCR, disease control rate; TTR, time to response

2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Yu Wang, MD

NCT05888402

Primary Endpoint – PFS



	Toripalimab + chemo	Chemo
Median PFS, mo (95% CI)	NR (NR-NR)	12.4 (8.0-NR)
1-yr PFS, % (95% CI)	85.6 (71.6-100.0)	54.5 (37.7-78.7)
HR (95% CI)	0.26 (0.08-0.81)	
Log-rank *P*	0.012	

Median follow-up 14.7 months

ORR after induction tx

77.8 vs 40 % (p=0.006)

G3+ pneumonitis

11.1 vs 4%

2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Yu Wang, MD

Selected Induction ChemoImmunotherapy (ICIO) Studies

Study	N	Treatment	Arm (s)	1º Endpoint	Outcome
APOLO	38	ICIO -> CRT -> IO (1yr atezo)		PFS	12-mo PFS 68.4%
PACIFIC-BRAZIL	49	ICIO -> CRT + IO -> IO (1yr durva)		PFS	12-mo PFS 68.1%
InTRist	52	IC -> CRT -> IO	ICIO -> CRT -> IO	PFS	12mo PFS 85.6 vs 54.5%
AFT-57	158	Atezo x2 -> CRT -> atezo (1 yr)	Atezo/tira x2 -> CRT -> atezo/tira (1 yr)	PFS	Enrolling

LAURA

Patients with locally advanced, unresectable stage III* EGFRm NSCLC with no progression during / following definitive CRT† treatment

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R‡
- Maximum interval between last dose of CRT and randomization: 6 weeks

Osimertinib 80 mg, once daily

Randomization 2:1 (N=216)

Stratification by:
Concurrent vs sequential CRT
Stage IIIA vs stage IIIB/IIIC
China vs non-China

Placebo, once daily

Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Open-label osimertinib after BICR-confirmed progression offered to both treatment arms§

Tumor assessments:
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

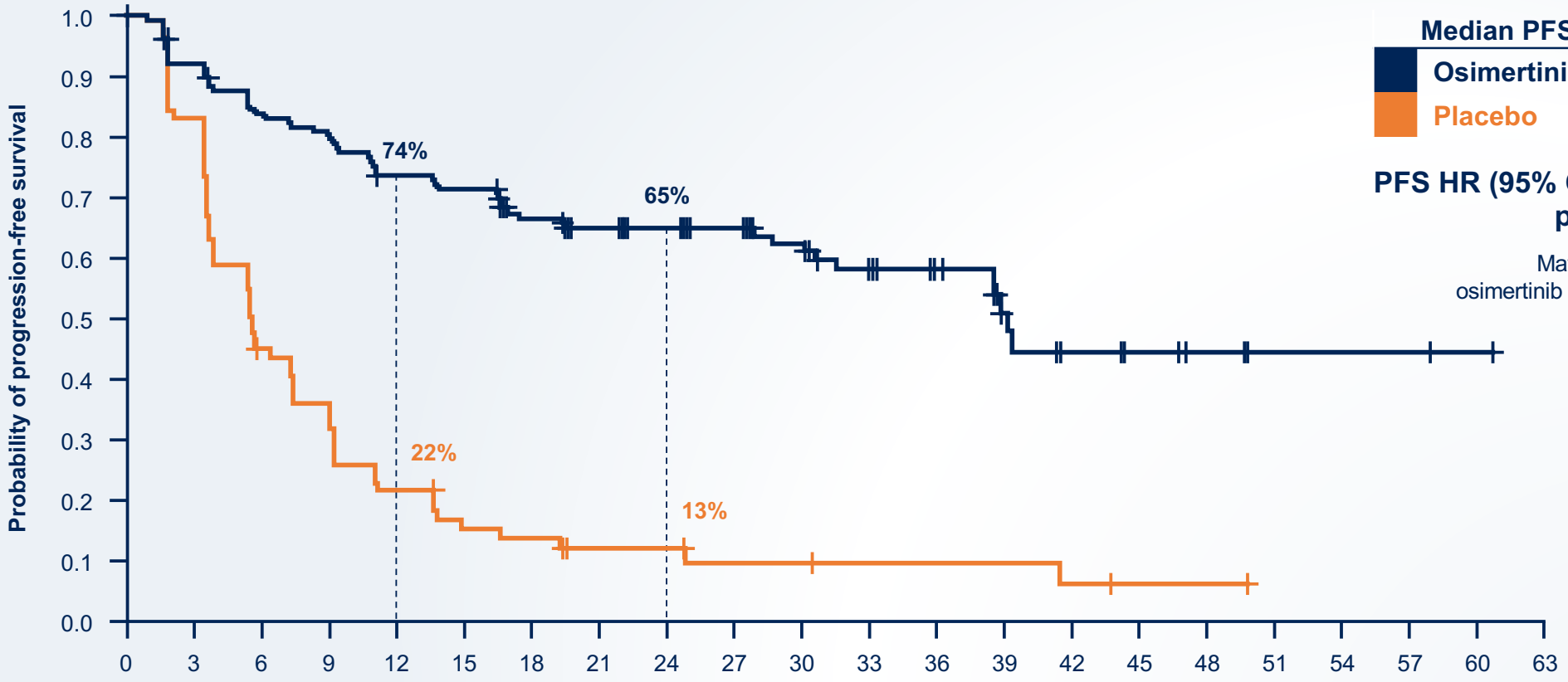
Endpoints

- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

*According to AJCC / UICC staging (8th edition);
†Concurrent or sequential CRT comprising ≥2 cycles of platinum-based chemotherapy (or 5 doses of weekly platinum-based chemotherapy) and a total dose of radiation of 60 Gy ±10%;
‡Central or FDA-approved local testing (from a CLIA-approved laboratory, or accredited local laboratory for sites outside of USA) based on tissue;
§If deriving clinical benefit (osimertinib arm); by the judgement of treating physician (placebo arm).

PRESENTED BY: Dr Suresh S. Ramalingam

Progression-Free Survival (BICR)



Median PFS, months (95% CI)	
Osimertinib	39.1 (31.5, NC)
Placebo	5.6 (3.7, 7.4)

PFS HR (95% CI): 0.16 (0.10, 0.24), p<0.001

Maturity 56%:
osimertinib 40%, placebo 86%

No. at risk																						
Osimertinib	143	127	114	109	99	96	83	76	69	61	49	37	28	16	9	6	4	2	2	2	1	0
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

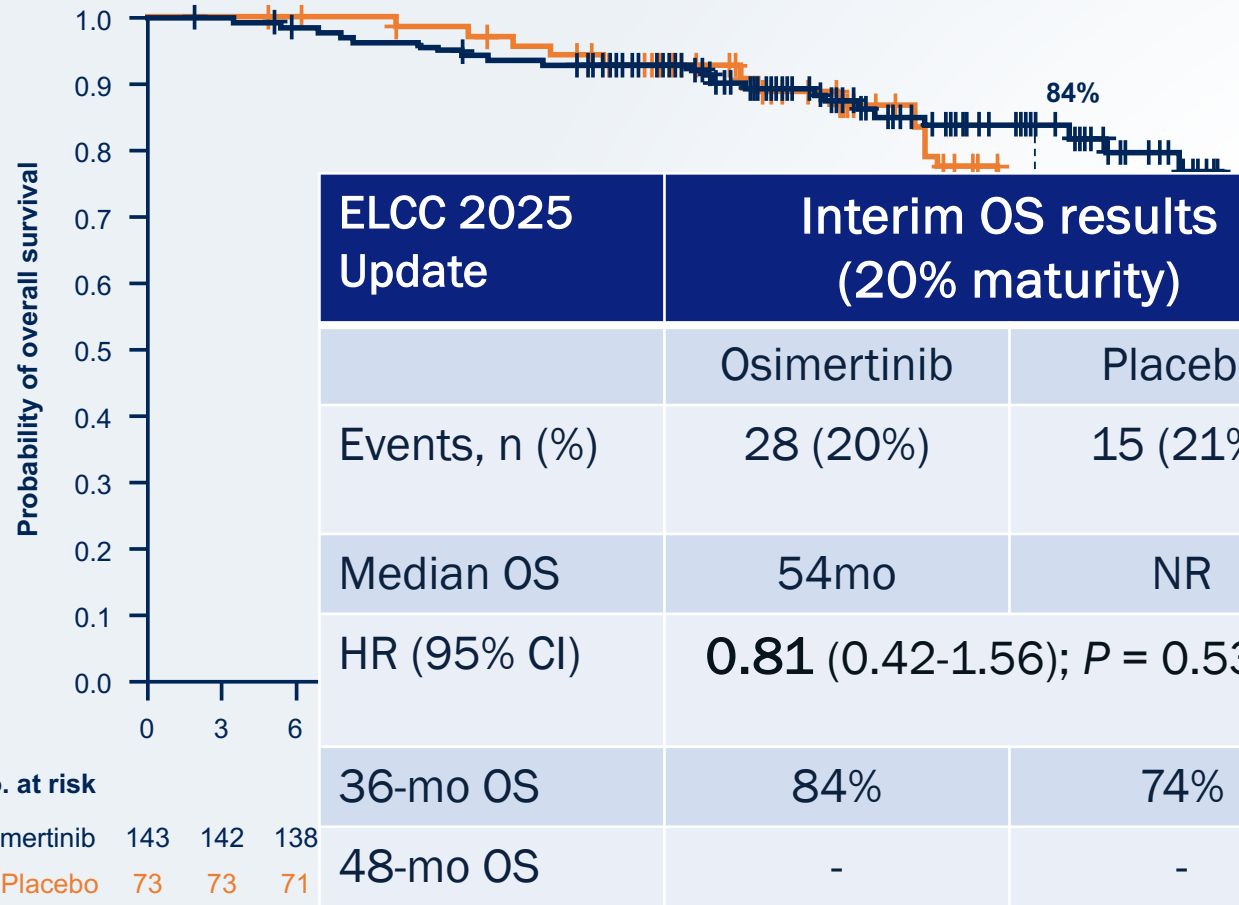
Data cut-off: January 5, 2024.

Tick marks indicate censored data. Median follow-up for PFS (all patients): osimertinib 22.0 months, placebo 5.6 months. Median follow-up for PFS (censored patients): osimertinib 27.7 months, placebo 19.5 months.

PRESENTED BY: Dr Suresh S. Ramalingam

Overall Survival (OS)

- In the placebo arm, 81% of patients with BICR-confirmed progression crossed over to osimertinib



Median OS, months (95% CI)

Osimertinib	54.0 (46.5, NC)
Placebo	NR (42.1, NC)

2, 1.56),

%

ELCC 2025 Update	Interim OS results (20% maturity)		Updated OS results (31% maturity)	
	Osimertinib	Placebo	Osimertinib	Placebo
Events, n (%)	28 (20%)	15 (21%)	40 (28%)	26 (36%)
Median OS	54mo	NR	58.8	54
HR (95% CI)	**0.81** (0.42-1.56); *P* = 0.530*		**0.67** (0.40-1.14); *P* = 0.140	
36-mo OS	84%	74%	82%	73%
48-mo OS	-	-	70%	52%

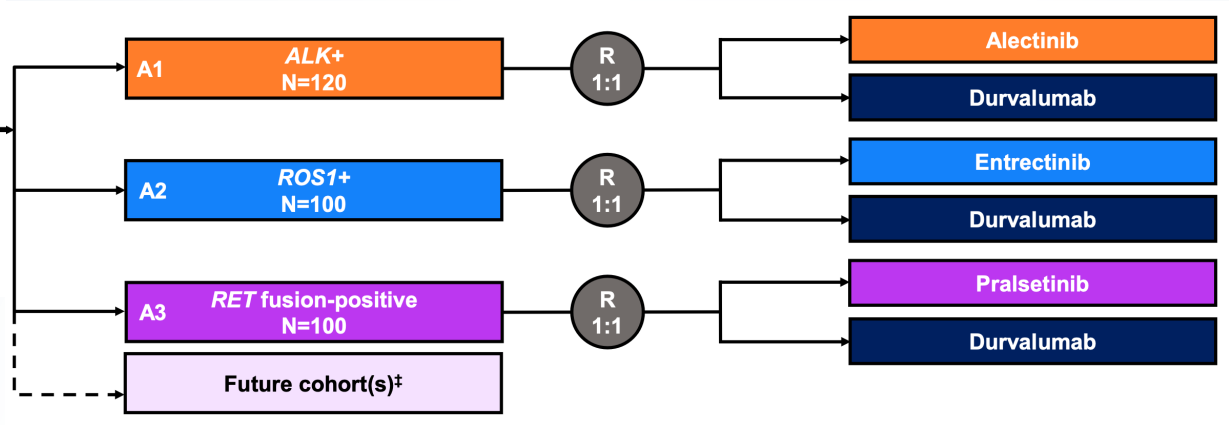
f: January 5, 2024.

Tick marks indicate censored data. *For statistical significance at this interim analysis, a p-value of <0.00036 was required;
Median follow-up for OS (all patients): osimertinib 29.5 months, placebo 28.1 months. Median follow-up for OS (censored patients): osimertinib 30.9 months, placebo 28.1 months.

HORIZON-01

A phase I–III platform study evaluating the safety and efficacy of multiple therapies in patients with biomarker-defined locally advanced, unresectable, stage III non-small cell lung cancer (NSCLC)

- Locally advanced, unresectable, stage III NSCLC
- ≥18 years
- Prior cCRT / sCRT
- ECOG PS 0–2
- Tumour tissue required from all patients
- Documented PD-L1 status†



Biomarker eligibility determined in BIOSTART master screening study or per available and acceptable local tissue-based test result*

Primary endpoint – PFS
Target enrollment N=320

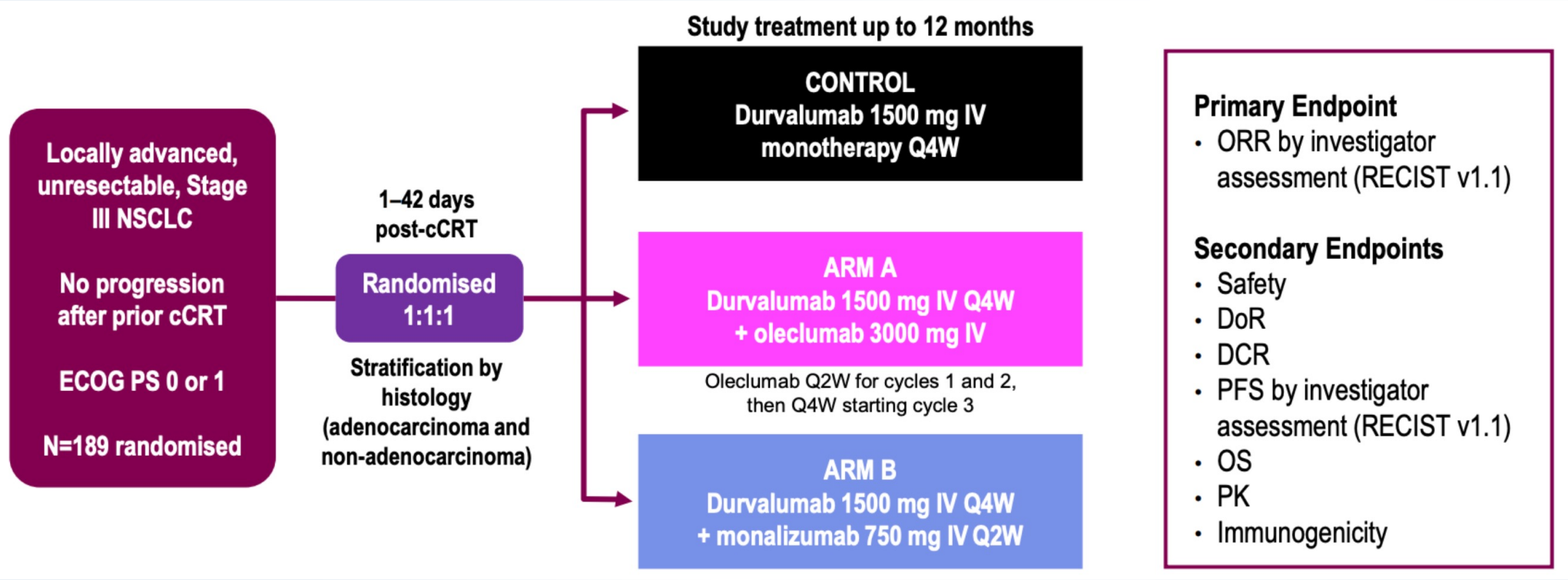
Stratification factors:
- Disease staging (stage IIIA vs. stage IIIB or IIIC)
- Type of CRT (cCRT vs. sCRT)
- PD-L1 expression (TC score <1% vs. ≥1% vs. unknown)†

Therapeutic	Administration	Dose*
Alectinib	Oral†	600 mg BID in 28-day cycles for ≤3 years
Entrectinib	Oral	600 mg QD in 28-day cycles for ≤3 years
Pralsetinib	Oral	400 mg QD in 28-day cycles for ≤3 years
Durvalumab	IV infusion	1500 mg Q4W in 28-day cycles for ≤1 year

NCT05170204

COAST

An Open-Label, Phase II, Multidrug Platform Study of Durvalumab Alone or in Combination With Oleclumab or Monalizumab in Patients With Unresectable, Stage III NSCLC

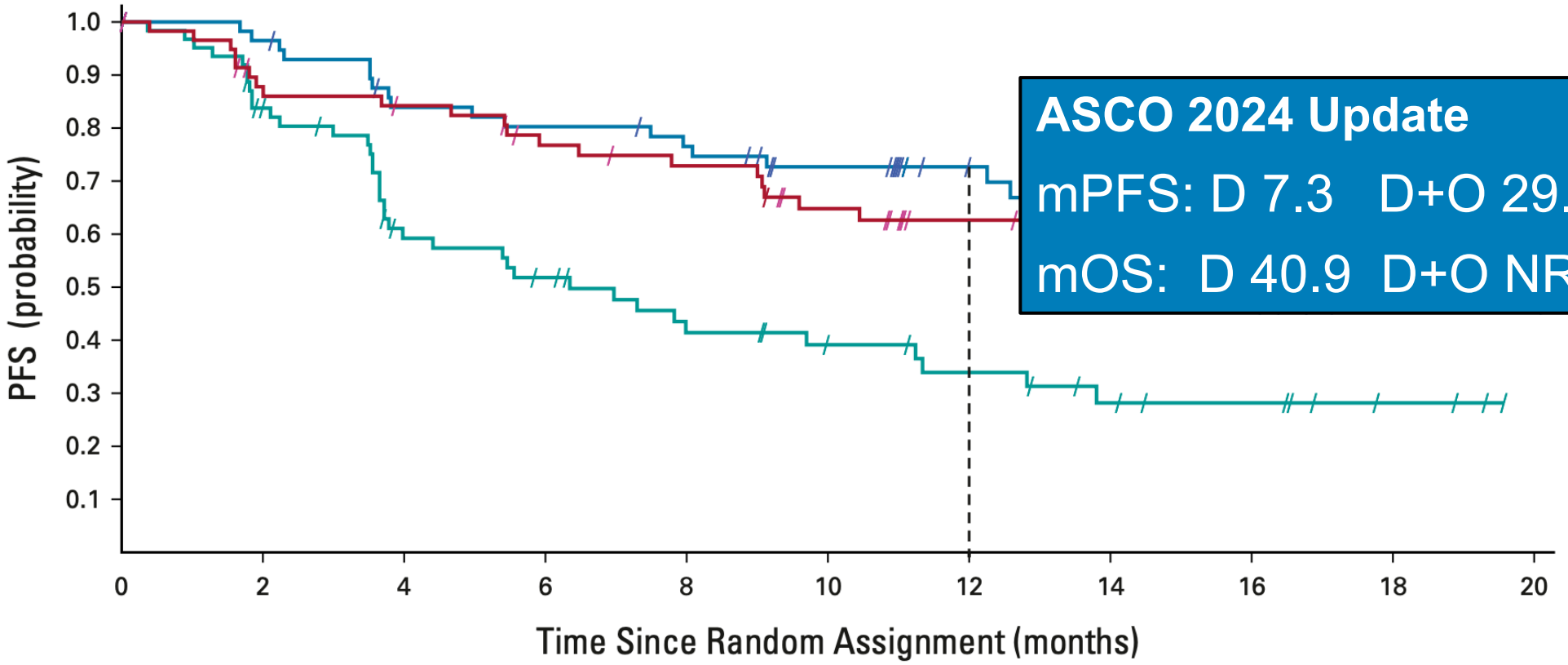


- A planned sample size of 60 patients per arm was designed to provide acceptable precision in estimating antitumor activities in an early phase setting
- Between Jan 2019 and Jul 2020, 189 patients were randomized of whom 186 received D (n = 66), D+O (n = 59) or D+M (n = 61)

Herbst et al. *J Clin Oncol* 2022;40(29):3383-3393.

COAST Results

Treatment Arm	No. of Events/ Total No. of Patients (%)	Median PFS, Months (95% CI)[a]	12-Month PFS Rate, % (95% CI)	HR, % (95% CI)[b,c]
Durvalumab + monalizumab	21/62 (33.9)	15.1 (13.6 to NE)	72.7 (58.8 to 82.6)	0.42 (0.24 to 0.72)
Durvalumab + oleclumab	22/60 (36.7)	NR (10.4 to NE)	62.6 (48.1 to 74.2)	0.44 (0.26 to 0.75)
Durvalumab	38/67 (56.7)	6.3 (3.7 to 11.2)	33.9 (21.2 to 47.1)	–



ASCO 2024 Update

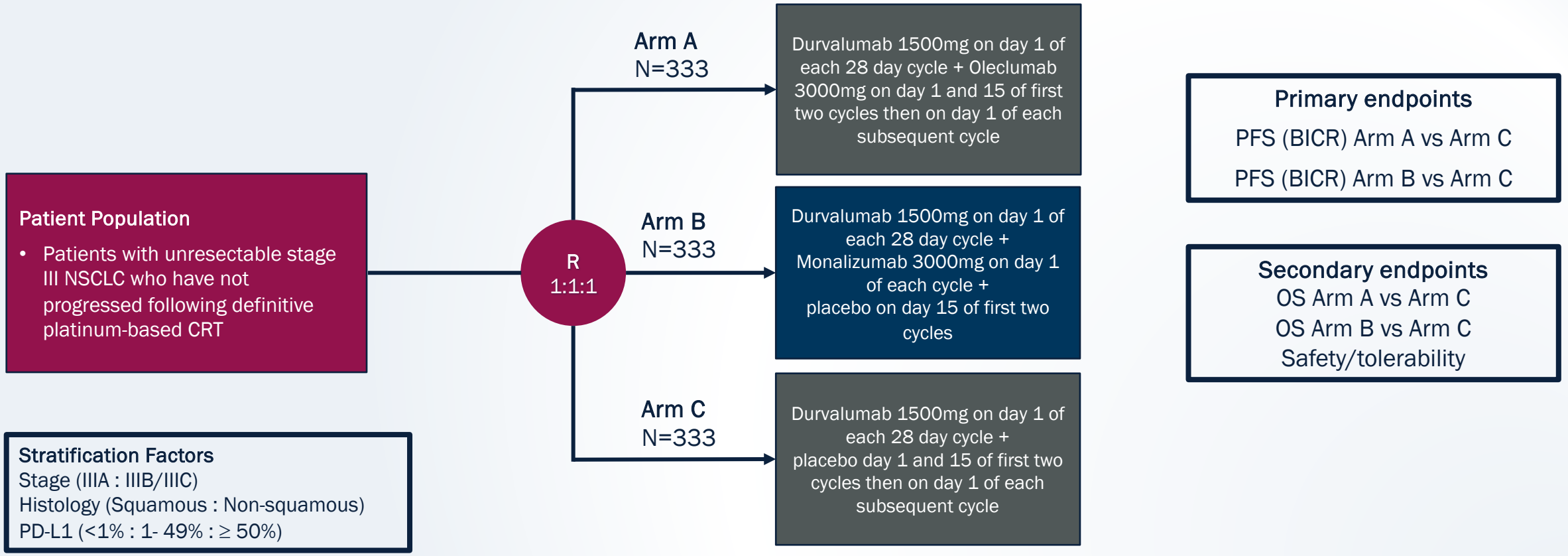
mPFS: D 7.3 D+O 29.9 D+M 23

mOS: D 40.9 D+O NR D+M NR

Herbst et al. *J Clin Oncol* 2022;40(29):3383-3393.

PACIFIC-9

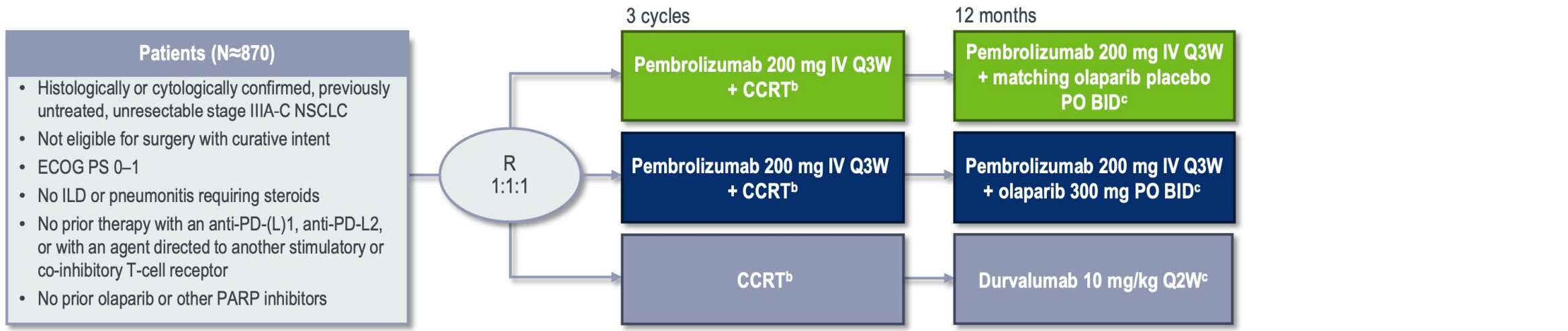
Phase III, double-blind, multicenter international study of durvalumab + oleclumab and durvalumab + monalizumab for the treatment of patients who have not progressed following concurrent chemoradiation treatment for locally-advanced, unresectable NSCLC



NCT05221840

KEYLYNK-012

Phase 3, randomized, double-blind, placebo-controlled study of pembrolizumab in combination with concurrent CRT followed by pembrolizumab ± olaparib vs CCRT followed by durvalumab in patients with unresectable, locally advanced, stage III NSCLC



Stratification Factors[a]

- Stage (IIIA vs IIIB/IIIC)
- Tumor histology (SQ vs NSQ)
- PD-L1 expression (TPS <50% vs ≥50%)
- Geographic region (East Asia vs North America/ Western Europe/UK vs other)

Primary End Points

- PFS[d]
- OS

Secondary End Points

- Safety
- ORR[d]
- DOR[d]
- HRQoL

Exploratory End Points

- Assess ctDNA and its correlation with efficacy end points
- Identifiy molecular biomarkers of response, safety, and activity
- Efficacy outcomes by PD-L1 levels
- Efficacy by iRECIST (investigator assessement)
- PFS2 (per RECIST v1.1 by investigator assessement), time to first subsequent therapy (TFST), and time to second subsequent therapy (TSST)
- Characterize health utility for use in economic models

Estimated primary completion: July 6, 2026[e]

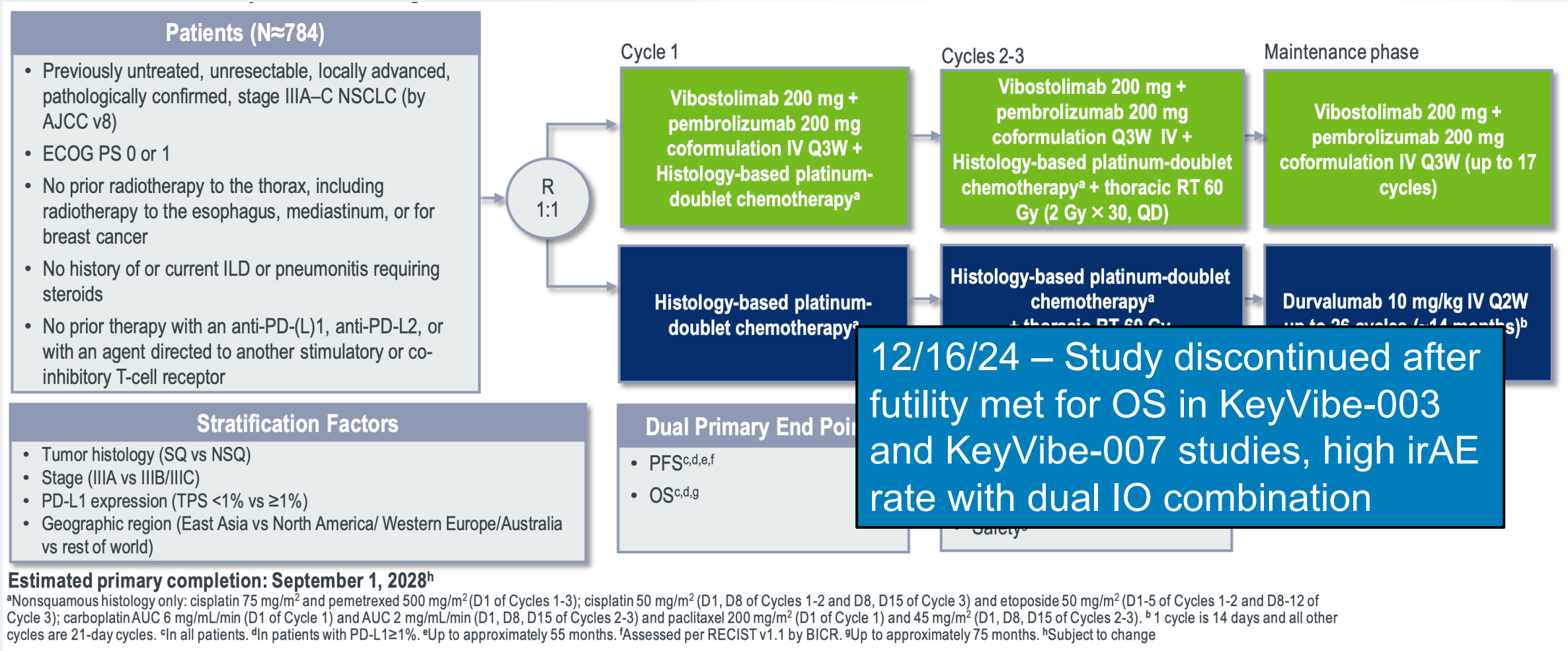
[a]Stratification occurs at randomization. [b]Platinum doublet chemotherapy and concurrent standard thoracic radiotherapy (60 Gy in 2 Gy fractions; during cycles 2 and 3). [b]Platinum doublet options (per investigator's choice) include cisplatin + pemetrexed (NSQ histology only), cisplatin + etoposide, and carboplatin + paclitaxel. [c]Patients in Groups A and B may receive a maximum of 20 cycles of pembrolizumab (Q3W) and patients in Group C may receive a maximum of 26 cycles of durvalumab (Q2W).[d]Assessed per RECIST v1.1 by BICR. [e]Subject to change.

ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04380636. Accessed June 22, 2022. Jabbour et al. Presented at ASCO 2021. Abstract TPS8580. Jabbour et al. *Clin Lung Cancer*. 2022;23(6):e342-e346.

NCT04380636

KEYVIBE-006

Phase 3, randomized, open-label study evaluating vibostolimab + pembrolizumab coformulation + CCRT vs CCRT followed by durvalumab in patients with unresectable, locally advanced, stage III NSCLC



Estimated primary completion: September 1, 2028[h]

[a]Nonsquamous histology only: cisplatin 75 mg/m^2 and pemetrexed 500 mg/m^2 (D1 of Cycles 1-3); cisplatin 50 mg/m^2 (D1, D8 of Cycles 1-2 and D8, D15 of Cycle 3) and etoposide 50 mg/m^2 (D1-5 of Cycles 1-2 and D8-12 of Cycle 3); carboplatin AUC 6 mg/mL/min (D1 of Cycle 1) and AUC 2 mg/mL/min (D1, D8, D15 of Cycles 2-3) and paclitaxel 200 mg/m^2 (D1 of Cycle 1) and 45 mg/m^2 (D1, D8, D15 of Cycles 2-3). [b] 1 cycle is 14 days and all other cycles are 21-day cycles. [c]In all patients. [d]In patients with PD-L1≥1%. [e]Up to approximately 55 months. [f]Assessed per RECIST v1.1 by BICR. [g]Up to approximately 75 months. [h]Subject to change

NCT05298423

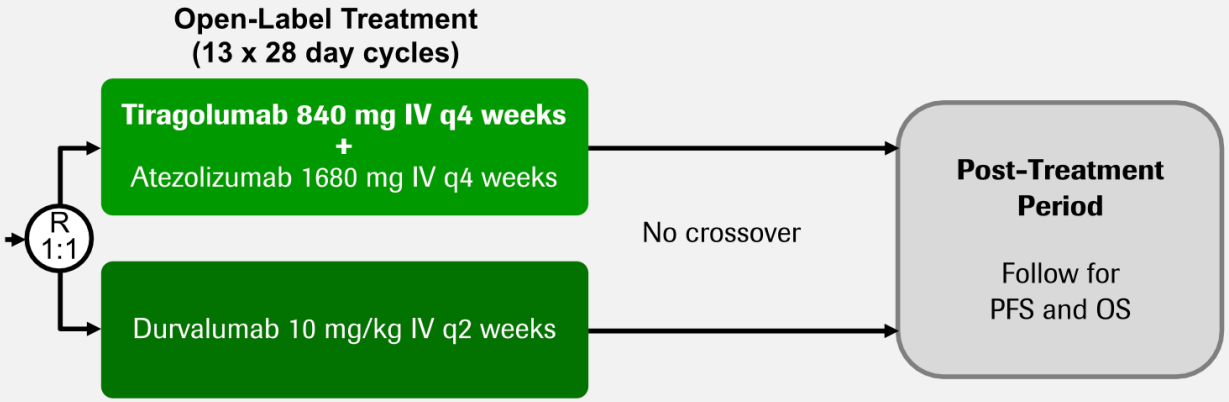
SKYSCRAPER-03

Phase III, Open-Label Randomised Study of Atezolizumab + Tiragolumab vs Durvalumab in Patients with Locally Advanced, Unresectable, Stage III NSCLC Who Have Not Progressed After Platinum-based Concurrent Chemoradiation

Study Schema

N~800

- Unresectable Stage III NSCLC without progression after definitive platinum-based cCRT (≥ 2 cycles)
- 18 years or older
- Known PD-L1 status
- ECOG PS 0 or 1
- No EGFR/Alk+ patients



Stratification Factors:

- PD-L1 expression (<1% vs ≥1%)
- Staging (IIIA vs IIIB vs IIIC)
- Histology (Squamous vs Non-Squamous)
- ECOG PS (0 vs 1)

Safety Run-in:

- iDMC review after a minimum of 24 patients (approximately 12 patients per arm) have completed 2 cycles of study treatment
- Enrollment will not be paused

Co-Primary Endpoints:

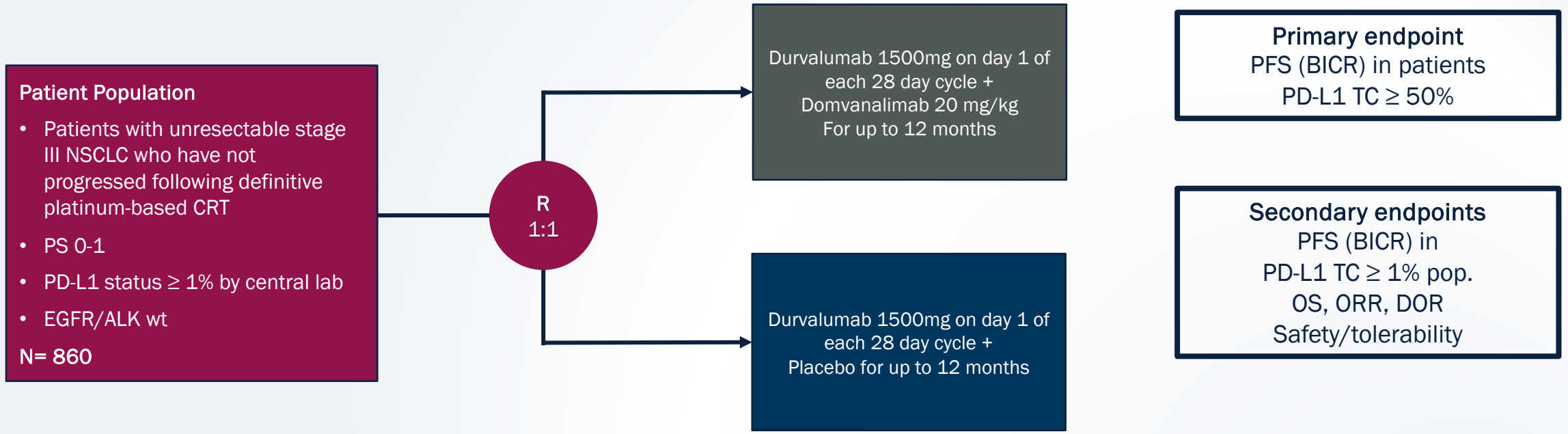
IRF-assessed PFS in the

- PD-L1 positive population
- ITT population

NCT04513925

PACIFIC-8

A Phase III, Randomized, Double blind, Placebo-controlled, Multicentre, International Study of Durvalumab plus Domvanalimab (AB154) in Participants with Locally Advanced (Stage III), Unresectable NSCLC



Domvanalimab (AB154) is a Fc-silent humanized IgG1 monoclonal antibody that blocks interaction of the T cell immunoreceptor with Ig and ITIM domains (TIGIT; upregulated by immune cells) with CD112 and CD155

NCT05211895

CONCORDE

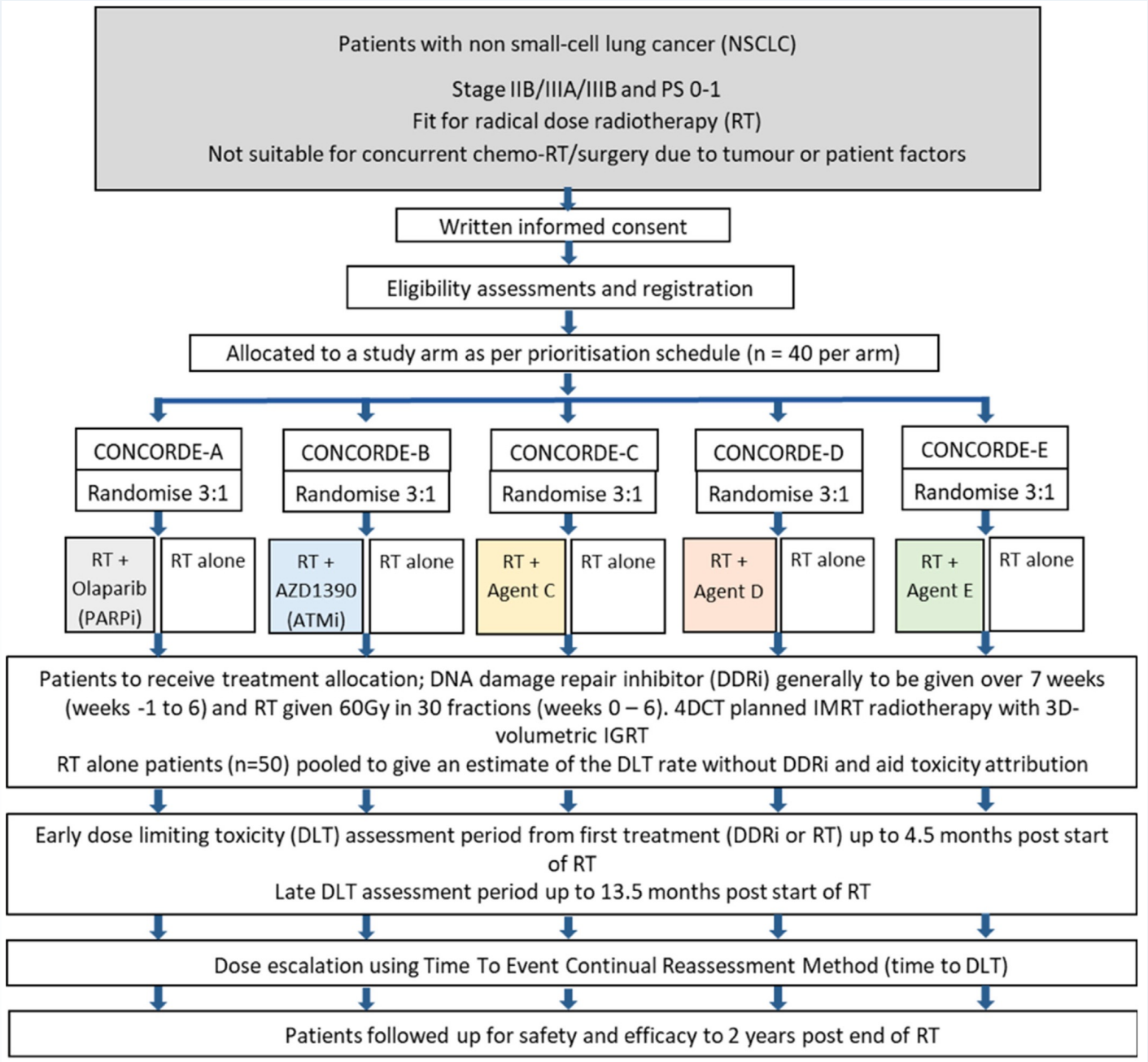
A Phase Ib Platform Study of DNA Damage Repair Inhibitors (DDRis) in Combination With Conventional Radiotherapy in NSCLC

Primary endpoint: DLT occurring between first dose of RT and 13.5mo post RT

2025 update: N=78 randomized

N=16 Olaparib + RT
N=14 AZD1390 + RT
N=9 Ceralasertib + RT
N=11 Saruparib + RT
N=25 RT alone

Arm B closed due to esophageal toxicity



CANCER RESEARCH UK

NCT04550104

NRG RTOG 1308

Phase III Randomized Trial Comparing Overall Survival After Photon vs Proton Chemoradiotherapy for Inoperable Stage II-IIIB NSCLC

STRATIFY	RANDOMIZE		
Stage 1.II 2.IIIA 3.IIIB Histology 1.Squamous 2.Non-Squamous Concurrent Chemotherapy Doublet Type 1.Carboplatin/paclitaxel 2.Cisplatin/etoposide 3. carboplatin/ pemetrexed	Arm 1: Photon dose—70 Gy*, at 2 Gy (RBE) once daily plus platinum-based doublet chemotherapy** Arm 2: Proton dose—70 Gy (RBE), at 2 Gy once daily plus platinum-based doublet chemotherapy**	Both Arms: Durvalumab or Consolidation chemotherapy x 2 cycles required for patients who receive concurrent carboplatin and paclitaxel***

Co-Primary: OS, Cardiac AE + lymphocyte reduction

2/3/14 Activated

9/26/23 Closed to accrual

Primary endpoint result anticipated late 2026

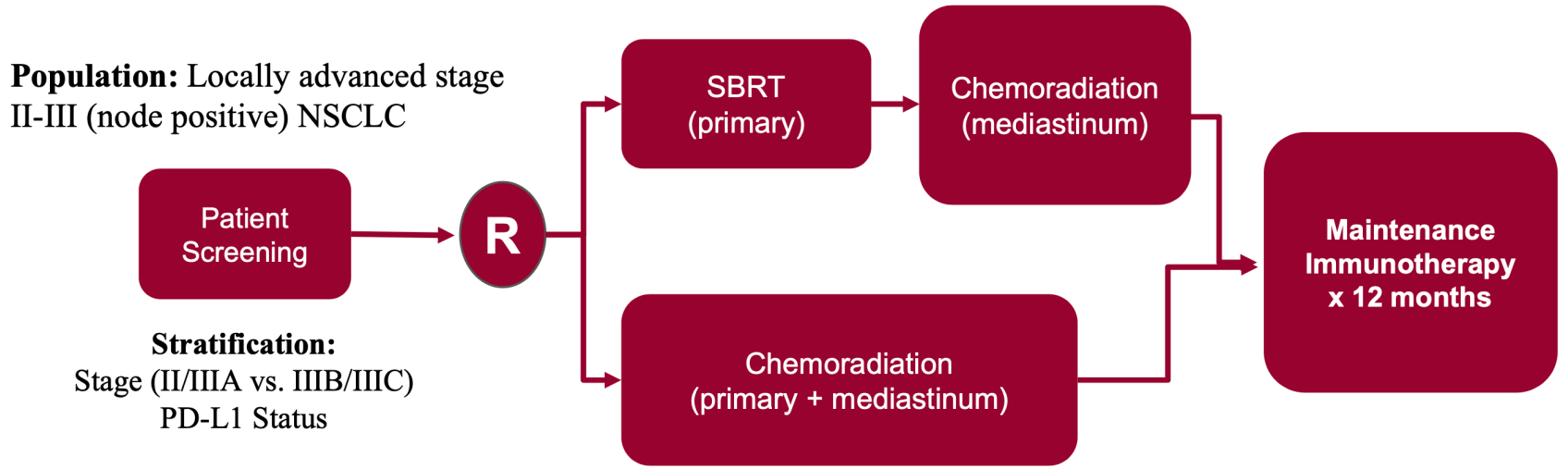
PI: Zhongxing Liao

*The highest total prescribed dose will be 70 Gy (Relative Biological Effectiveness (RBE)) **without exceeding tolerance dose-volume limits of all critical normal structures**. The dose range can be 60-70Gy provided the dose constraints of OARs are met.

NCT01993810

NRG-LU008

Phase III Prospective Randomized Trial of Primary Lung Tumor Stereotactic Body Radiation Therapy Followed by Concurrent Mediastinal Chemoradiation for Locally-Advanced Non-Small Cell Lung Cancer



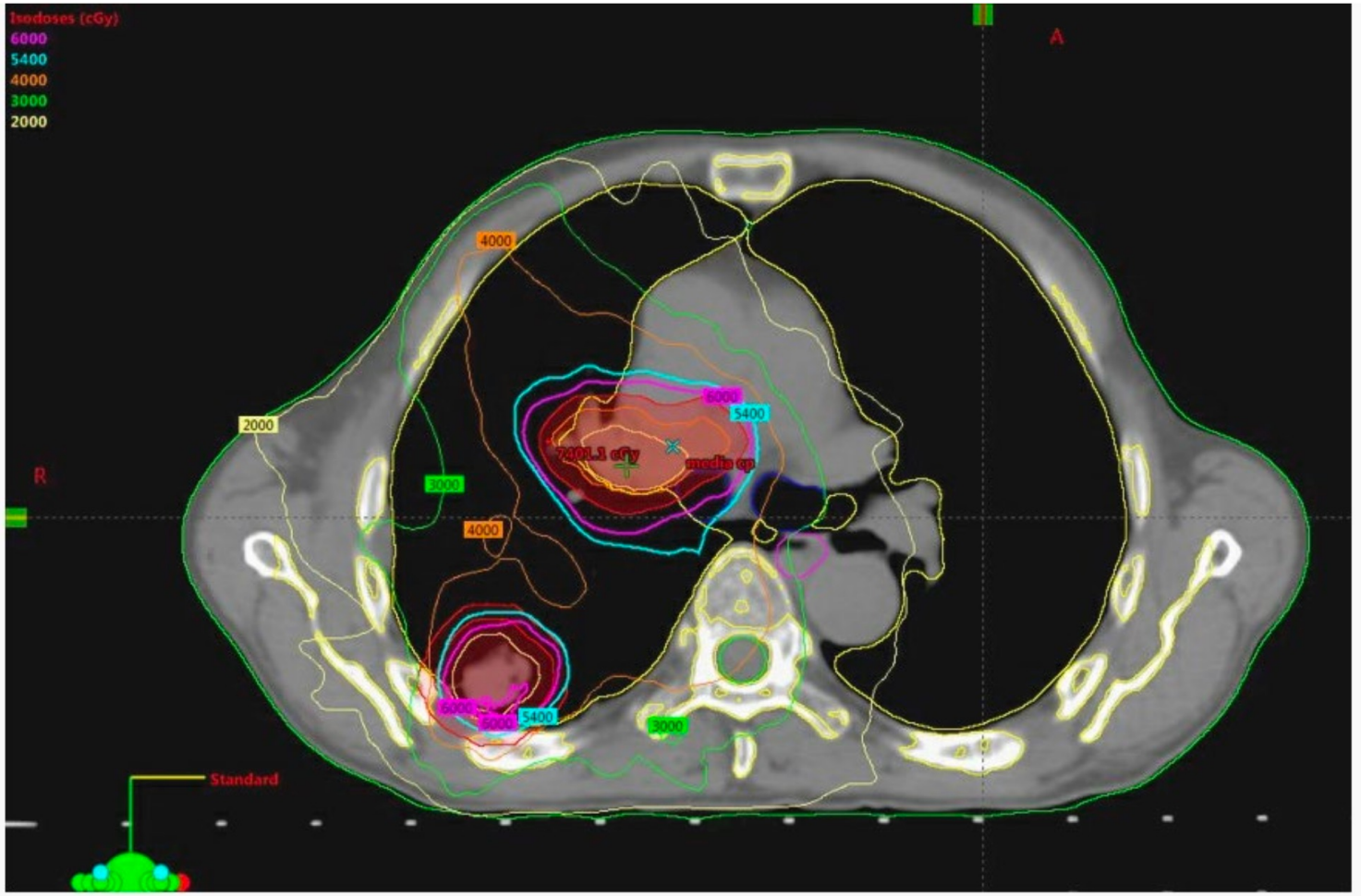
- Control arm: chemoradiation to the primary and mediastinal disease (60 Gy/2 Gy) → immu
- Experimental arm: SBRT to the primary (standard BED ≥100 Gy dose regimen) → chemor Gy) → immunotherapy maintenance x 12 months
  - SBRT to primary tumor:
    - 3 fractions to 54 Gy (BED10 of 151.2 Gy) [peripheral]
    - 4 fractions to 50 Gy (BED10 of 112.5 Gy) [peripheral]
    - 5 fractions to 50 Gy (BED10 of 100 Gy) [peripheral or central]
  - Radiation to involved hilar/mediastinal lymph nodes: 2 Gy x 30 fx to 60 Gy, IMRT or proton therapy
  - Concurrent chemotherapy: carboplatin + paclitaxel, cisplatin + etoposide, cisplatin + pemetrexed, or carboplatin + pemetrexed
  - Maintenance immunotherapy: durvalumab x 12 months [if durvalumab is NOT given, carbo/paclitaxel pts receive 2 cycles of consolidation]

Co-primary: OS and PFS
Activated 5/10/23
N = 171 of 474 planned

NRG ONCOLOGY™

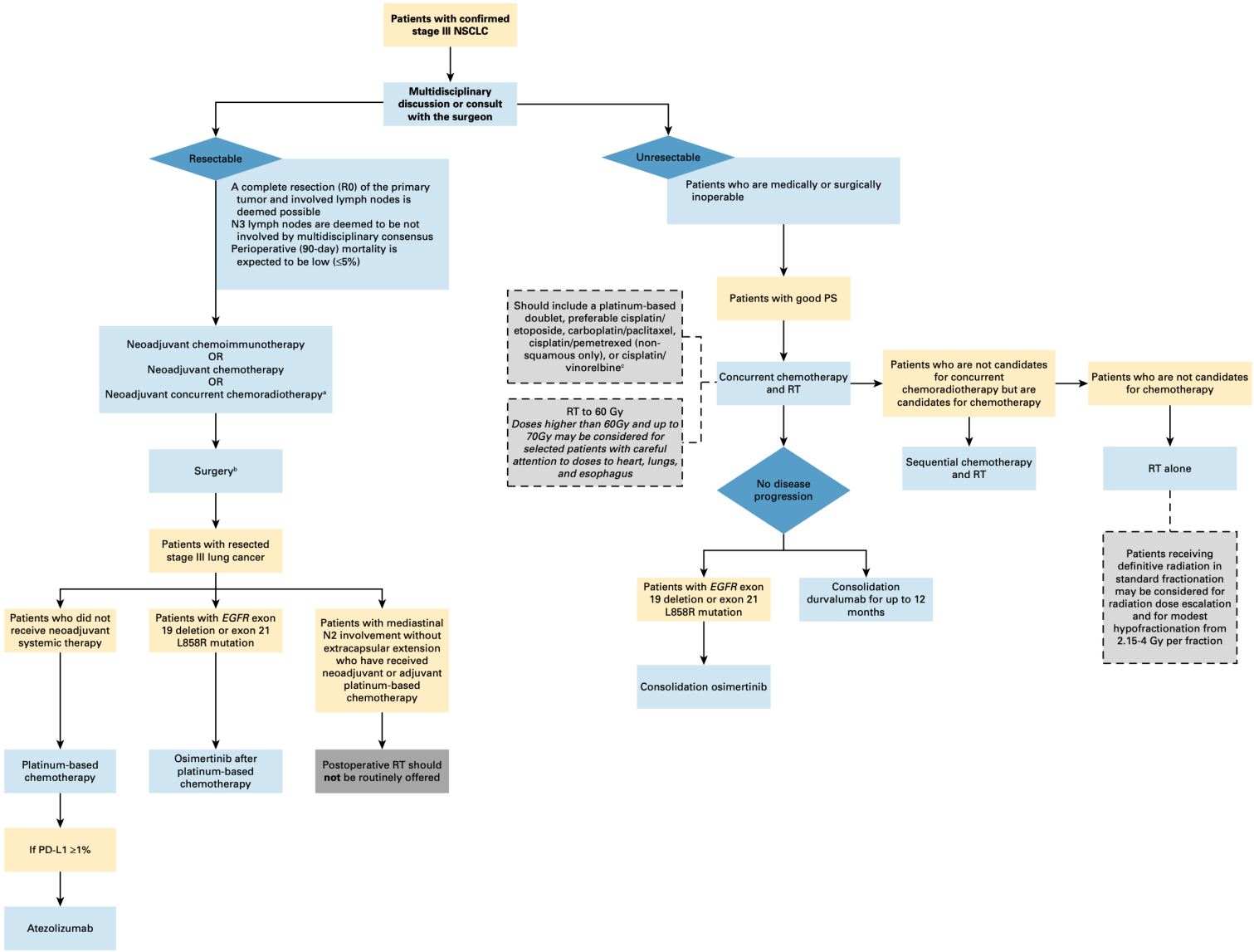
NCT05624996

NRG-LU008 Representative Case



Total volume of lung receiving 40 Gy= 332 cc (compared to 590 cc, 44% reduction)
Total volume of lung receiving 20 Gy=922 cc (compared to1300 cc, 29% reduction)
Total volume of lung receiving 10 Gy=2168 cc (compared to 2360, 8% reduction)

Management of Stage III NSCLC Algorithm



This algorithm is derived from recommendations in *Management of Stage III Non—Small-Cell Lung Cancer: ASCO Guideline, Management of Stage III NSCLC: ASCO Guideline Rapid Recommendation Update, and Management of Stage III Non-Small Cell Lung Cancer: ASCO Rapid Guideline Update*. This is a tool based on an ASCO Guideline and is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients. This tool does not purport to suggest any particular course of medical treatment. Use of the guideline and this tool are voluntary.

Daly et al. *J Clin Oncol.* 2024;42(25):3058-3060.

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