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Letter from Prof Rolf Stahel

Dear Colleagues

It is my pleasure to present this ETOP slide set which has been designed to highlight and summarise key findings in thoracic cancers from the major congresses in 2024. This slide set specifically focuses on the **ESMO Congress 2024** and is available in 3 languages – English, Chinese and Japanese.

The area of clinical research in oncology is a challenging and continually changing environment. Within this environment we all value access to scientific data and research which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in thoracic cancers of benefit to you in your practice. If you would like to share your thoughts with us, we would welcome your comments. Please send any correspondence to etop@etop.eu-org.

I would like to thank our ETOP members Drs Enriqueta Felip, Solange Peters, Martin Reck and Egbert Smit for their roles as Editors – for prioritising abstracts and reviewing slide content. The slide set you see before you would not be possible without their commitment and hard work.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this complex yet rewarding activity.

Yours sincerely,
Rolf Stahel
President, ETOP Foundation Council

ETOP Medical Oncology Slide Deck Editors 2024

Focus: biomarkers (all stages)

Dr Enriqueta Felip

Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain

Focus: early and locally advanced NSCLC (stages I–III)

Dr Egbert Smit

Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Focus: advanced NSCLC (not radically treatable stage III & stage IV)

Dr Solange Peters

Multidisciplinary Oncology Center, Lausanne Cancer Center, Lausanne, Switzerland

Focus: other malignancies, SCLC, mesothelioma, rare tumors

Dr Martin Reck

Department of Thoracic Oncology, Hospital Grosshansdorf, Grosshansdorf, Germany

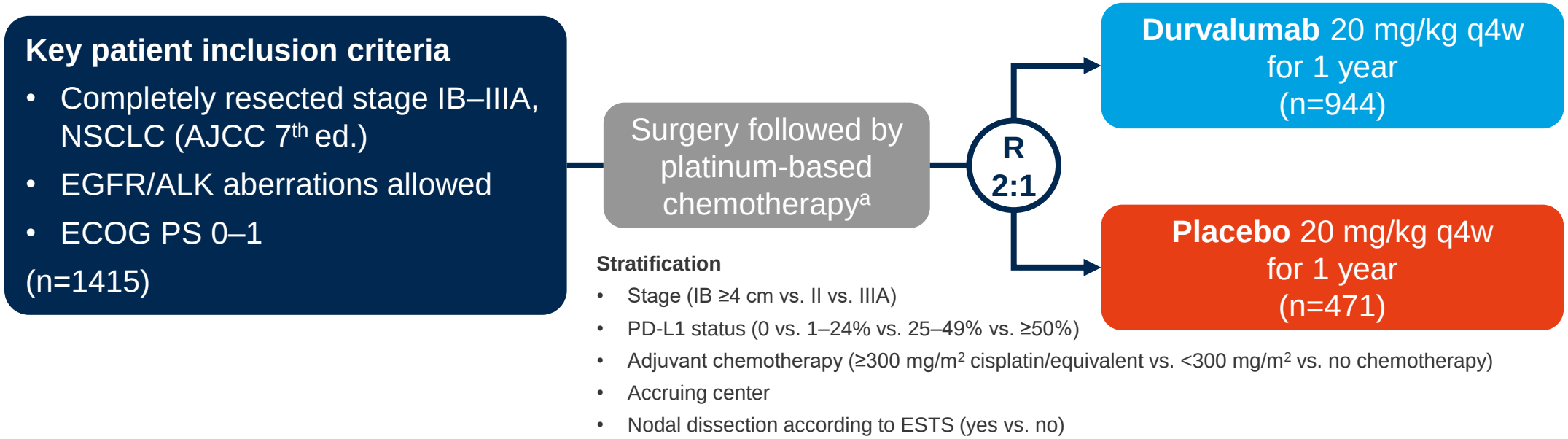
Contents

- Early stage and locally advanced NSCLC – Stages I, II and III
- Advanced NSCLC – Not radically treatable stage III and stage IV
  - Immunotherapy
  - Targeted therapies
- Other malignancies
  - SCLC, mesothelioma and thymic epithelial tumors

Early stage and locally advanced NSCLC – Stages I, II and III

LBA48: CCTG BR.31: A global, double-blind placebo-controlled, randomized phase III study of adjuvant durvalumab in completely resected non-small-cell lung cancer (NSCLC) – Goss G, et al

- **Study objective**
  - To evaluate the efficacy and safety of adjuvant durvalumab in patients with completely resected NSCLC in the phase 3 CCTG BR.31 study



Primary endpoint

- DFS in PD-L1 TC ≥25% EGFR-/ALK- (investigator assessed)

Secondary endpoints

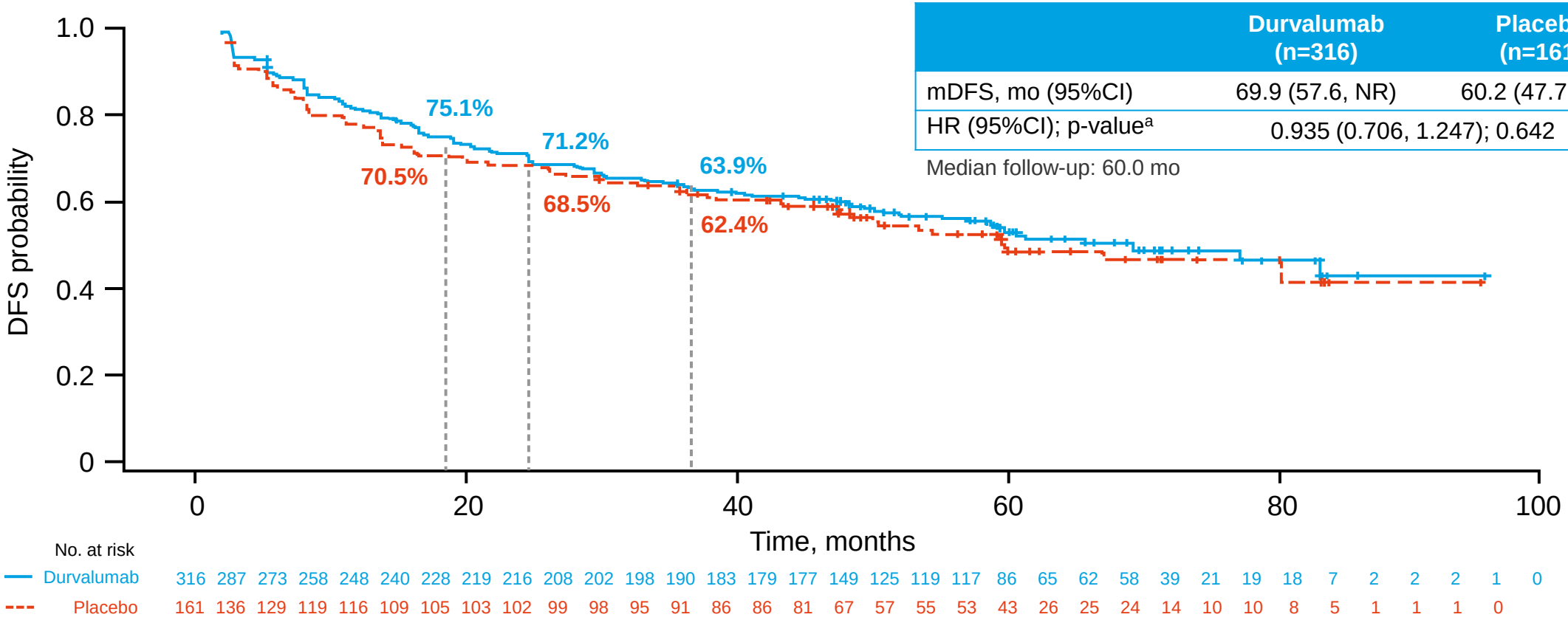
- DFS, OS, QoL, safety

[a]Patients not receiving chemotherapy may be included.

LBA48: CCTG BR.31: A global, double-blind placebo-controlled, randomized phase III study of adjuvant durvalumab in completely resected non-small-cell lung cancer (NSCLC) – Goss G, et al

- **Key results**

DFS in PD-L1 TC ≥25% EGFR-/ALK-



	Durvalumab (n=316)	Placebo (n=161)
mDFS, mo (95%CI)	69.9 (57.6, NR)	60.2 (47.7, NR)
HR (95%CI); p-value[a]	0.935 (0.706, 1.247); 0.642	

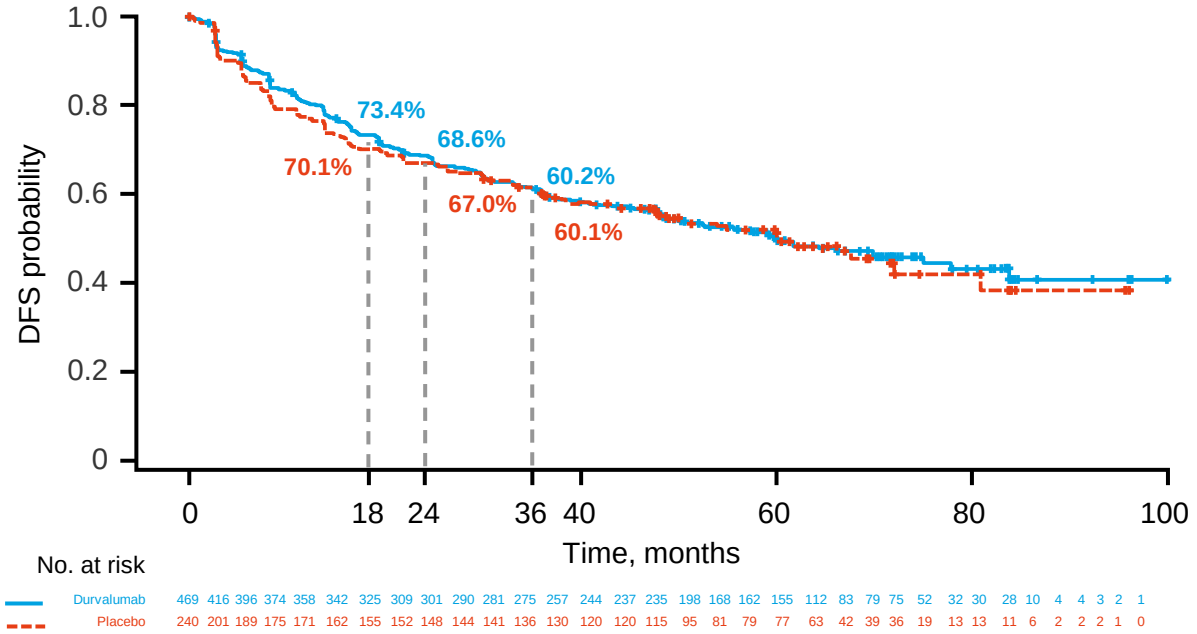
Median follow-up: 60.0 mo

[a]Two-sided.

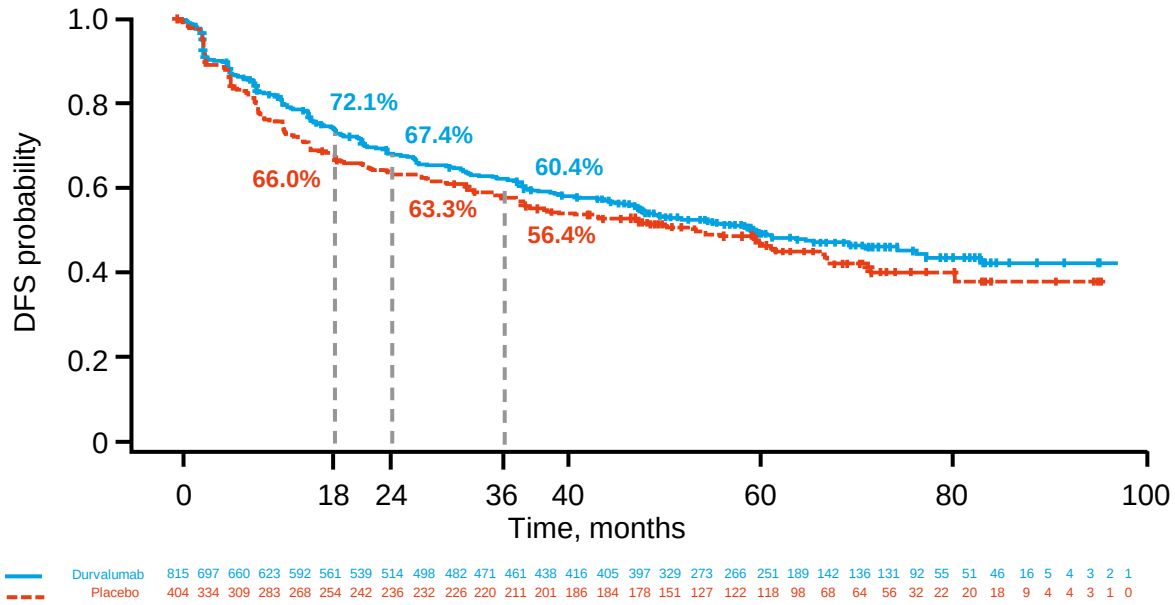
LBA48: CCTG BR.31: A global, double-blind placebo-controlled, randomized phase III study of adjuvant durvalumab in completely resected non-small-cell lung cancer (NSCLC) – Goss G, et al

- **Key results**

DFS in PD-L1 ≥1% EGFR-/ALK-



DFS in PD-L1 all comers EGFR-/ALK-



	Durvalumab (n=469)	Placebo (n=240)
mDFS, mo (95%CI)	59.9 (48.4, 77.9)	60.3 (43.8, 80.9)
HR (95%CI); p-value[a]	0.989 (0.788, 1.248); 0.926	

	Durvalumab (n=815)	Placebo (n=404)
mDFS, mo (95%CI)	60.0 (49.6, 74.9)	53.9 (36.7, 67.3)
HR (95%CI); p-value[a]	0.893 (0.752, 1.065); 0.207	

[a]Two-sided.

Goss G, et al. Ann Oncol 2024;35(suppl):Abstr LBA48

LBA48: CCTG BR.31: A global, double-blind placebo-controlled, randomized phase III study of adjuvant durvalumab in completely resected non-small-cell lung cancer (NSCLC) – Goss G, et al

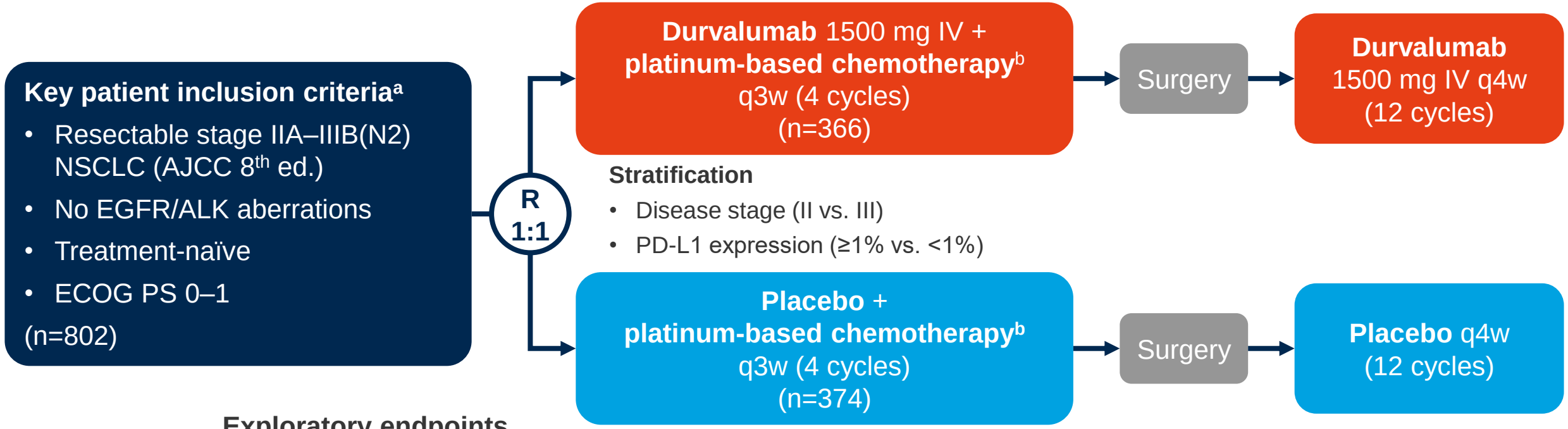
- **Key results (cont.)**

AEs, n (%)	Durvalumab (n=941)	Placebo (n=469)
Any AE	883 (93.8)	433 (92.3)
Possibly related to treatment	684 (72.7)	251 (53.5)
Grade 3/4	221 (23.5)	92 (19.6)
Possibly related to treatment	122 (13.9)	21 (4.5)
SAE	177 (18.8)	72 (15.4)
Possibly related to treatment	95 (10.1)	17 (3.6)
Led to discontinuation	132 (14.0)	24 (5.1)
Possibly related to treatment	118 (12.5)	13 (2.8)
Led to death	7 (0.7)	1 (0.2)
Possibly related to treatment	3 (0.3)	0
imAE	215 (22.8)	33 (7.0)
Possibly related to treatment	208 (22.1)	23 (4.9)

- **Conclusions**
  - In patients with completely resected NSCLC, adjuvant durvalumab failed to show improvement in DFS outcomes, regardless of the PD-L1 tumor score, and had a safety profile consistent with previous findings

LBA49: Associations of ctDNA clearance (CL) during neoadjuvant Tx with pathological response and event-free survival (EFS) in pts with resectable NSCLC (R-NSCLC): expanded analyses from AEGEAN – Reck M, et al

- **Study objective**
  - To evaluate the associations between ctDNA clearance and outcomes during neoadjuvant treatment in patients with resectable NSCLC in the AEGEAN study



Exploratory endpoints

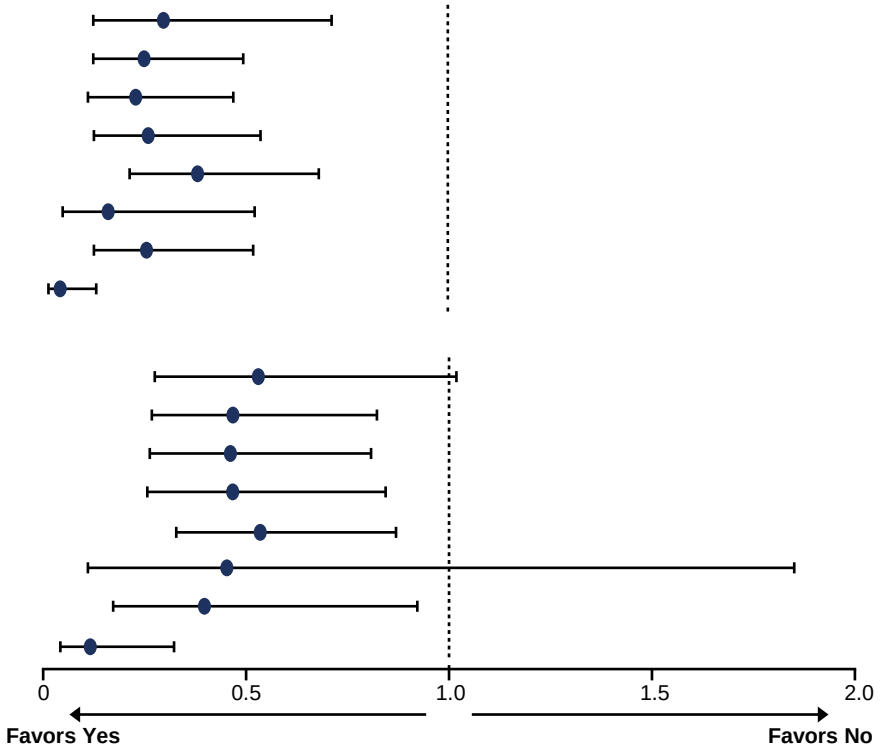
- Association between ctDNA clearance and pathological response[c] and EFS

[a]The protocol was amended to exclude patients with T4 tumors (not based on size, n=1); [b]Nonsquamous: cisplatin + pemetrexed or carboplatin + pemetrexed. Squamous: carboplatin + paclitaxel or cisplatin + gemcitabine (or carboplatin + gemcitabine for patients with comorbidities/unable to tolerate cisplatin); [c]pCR and MPR were evaluated centrally per IASLC recommendations.

LBA49: Associations of ctDNA clearance (CL) during neoadjuvant Tx with pathological response and event-free survival (EFS) in pts with resectable NSCLC (R-NSCLC): expanded analyses from AEGEAN – Reck M, et al

- **Key results**

Group[a,b,c]		Median EFS, mo (95%CI)		
Durvalumab	**Yes, n (%)**	**Yes**	**No**	**HR (95%CI)**
Neoadj. C2D1 ctDNA CL (n=121)	41 (33.9)	NR (NR, NR)	41.2 (18.2, NR)	0.30 (0.12, 0.71)
Neoadj. C3D1 ctDNA CL (n=115)	62 (53.9)	NR (NR, NR)	21.8 (11.3, NR)	0.25 (0.13, 0.49)
Neoadj. C4D1 ctDNA CL (n=102)	63 (61.8)	NR (NR, NR)	14.2 (9.0, NR)	0.23 (0.11, 0.47)
ctDNA CL at pre-surgery (n=100)	65 (65.0)	NR (NR, NR)	14.2 (9.8, NR)	0.26 (0.13, 0.54)
Pre-surgery OR (n=142)	89 (62.7)	NR (NR, NR)	14.9 (9.7, NR)	0.38 (0.21, 0.68)
pCR (n=142)	32 (22.5)	NR (NR, NR)	41.2 (21.8, NR)	0.16 (0.05, 0.52)
MPR (n=142)	59 (41.5)	NR (NR, NR)	31.9 (14.2, NR)	0.26 (0.13, 0.52)
Adj. C1D1 ctDNA CL (n=76)	66 (86.8)	NR (NR, NR)	9.7 (4.0, 14.2)	0.04 (0.01, 0.13)
Placebo				
Neoadj. C2D1 ctDNA CL (n=119)	27 (22.7)	40.4 (25.4, NR)	11.7 (7.3, NR)	0.53 (0.27, 1.02)
Neoadj. C3D1 ctDNA CL (n=115)	50 (43.5)	45.0 (30.0, NR)	9.4 (6.1, NR)	0.47 (0.27, 0.82)
Neoadj. C4D1 ctDNA CL (n=104)	51 (49.0)	42.6 (25.7, NR)	8.6 (6.1, 45.0)	0.46 (0.26, 0.81)
ctDNA CL at pre-surgery (n=108)	45 (41.7)	NE (25.7, NR)	10.1 (6.4, NR)	0.47 (0.26, 0.84)
Pre-surgery OR (n=141)	65 (46.1)	42.6 (20.6, NR)	11.0 (5.6, 45.0)	0.53 (0.33, 0.87)
pCR (n=141)	6 (4.3)	NE (7.0, NR)	30.0 (11.7, 45.0)	0.45 (0.11, 1.85)
MPR (n=141)	20 (14.2)	NE (20.6, NR)	22.8 (9.4, 42.6)	0.40 (0.17, 0.92)
Adj. C1D1 ctDNA CL (n=71)	64 (90.1)	NE (42.6, NR)	9.0 (6.1, 12.2)	0.12 (0.04, 0.32)



[a]ctDNA analysis was performed using Invitae Personalized Cancer Monitoring™; [b]the lower limit of detection for the assay was 0.008% VAF (80 parts per million); [c]ctDNA clearance: a change from ctDNA detected at baseline to undetected at the specified on-treatment timepoint. ctDNA non-clearance: ctDNA-positive at the specified timepoint, regardless of baseline status.

Reck M, et al. Ann Oncol 2024;35(suppl):Abstr LBA49

LBA49: Associations of ctDNA clearance (CL) during neoadjuvant Tx with pathological response and event-free survival (EFS) in pts with resectable NSCLC (R-NSCLC): expanded analyses from AEGEAN – Reck M, et al

- **Key results (cont.)**

Predictive value of ctDNA clearance at different timepoints for pCR

	Durvalumab		Placebo	
pCR, %	Positive predictive value	Negative predictive value	Positive predictive value	Negative predictive value
C2D1	49	89	11	98
C3D1	39	94	12	100
C4D1	40	100	12	100
Pre-surgery	40	100	13	100

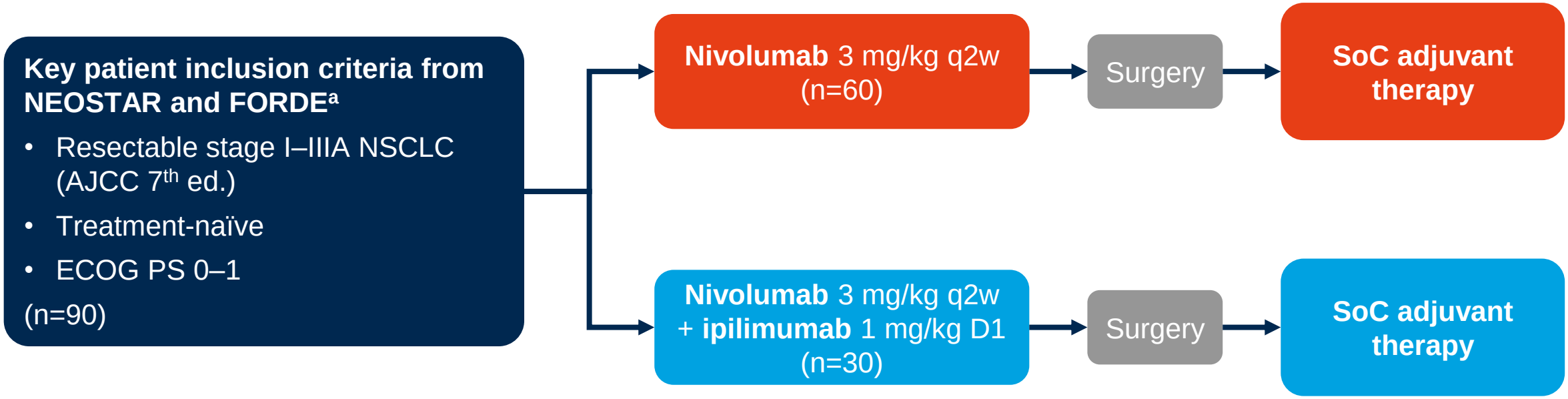
Associations of ctDNA clearance at neoadjuvant C2D1 with EFS and OS

	Durvalumab	Placebo
EFS, HR (95%CI)		
ctDNA CL vs no ctDNA CL	0.30 (0.12, 0.71)	0.53 (0.27, 1.02)
D vs PBO arm (ctDNA CL)	0.31 (0.11, 0.85)	
D vs PBO arm (no ctDNA CL)	0.62 (0.40, 0.97)	
OS, HR (95%CI)		
ctDNA CL vs no ctDNA CL	0.32 (0.14, 0.72)	0.61 (0.28, 1.31)
D vs PBO arm (ctDNA CL)	0.55 (0.20, 1.52)	
D vs PBO arm (no ctDNA CL)	1.07 (0.68, 1.69)	

- **Conclusions**
  - In patients with resectable NSCLC, pre-surgical ctDNA clearance was associated with improved pCR, EFS and OS, in both treatment arms

1209MO: Neoadjuvant nivolumab and nivolumab+ipilimumab in resectable non-small cell lung cancer: Combined analysis of 5-year outcomes from NEOSTAR and CA209-159 – Reuss J, et al

- **Study objective**
  - To evaluate the 5-year outcomes with neoadjuvant nivolumab ± ipilimumab in patients with resectable NSCLC in a combined analysis of NEOTAR and FORDE studies



Endpoints

- MPR[b], pCR, EFS, OS, safety

[a]Individual patient data meta-analyses were performed. Weighted Kaplan-Meier method was used to account for cohort effects; [b]≤10% viable tumour cells.

Reuss J, et al. Ann Oncol 2024;35(suppl):Abstr 1209MO

1209MO: Neoadjuvant nivolumab and nivolumab+ipilimumab in resectable non-small cell lung cancer: Combined analysis of 5-year outcomes from NEOSTAR and CA209-159 – Reuss J, et al

- **Key results**

Nivolumab

	Nivolumab (n=60)
36-mo EFS, % (95%CI)	65.0 (51.0, 75.9)
60-mo EFS, % (95%CI)	57.7 (43.1, 69.8)
36-mo OS, % (95%CI)	83.3 (71.0, 90.7)
60-mo OS, % (95%CI)	70.0 (55.1, 80.7)

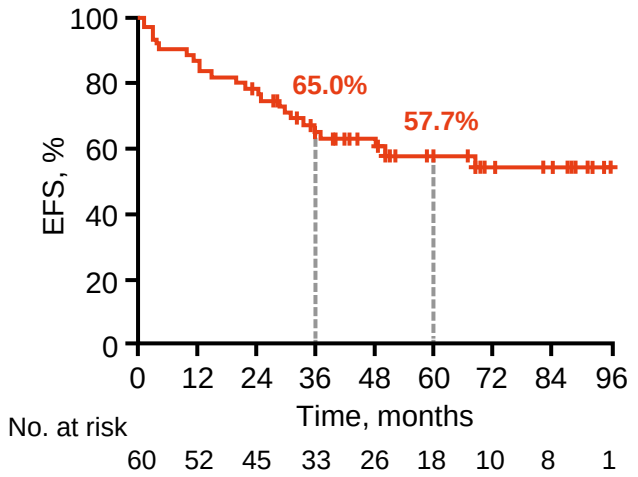
Median follow-up: 68.4 mo

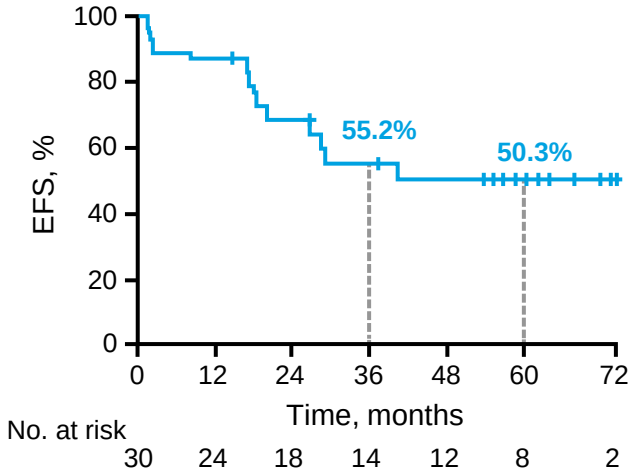
Nivolumab + ipilimumab

	Nivolumab + ipilimumab (n=30)
36-mo EFS, % (95%CI)	55.2 (34.4, 71.9)
60-mo EFS, % (95%CI)	50.3 (29.7, 67.8)
36-mo OS, % (95%CI)	69.0 (48.4, 82.7)
60-mo OS, % (95%CI)	66.9 (46.4, 81.0)

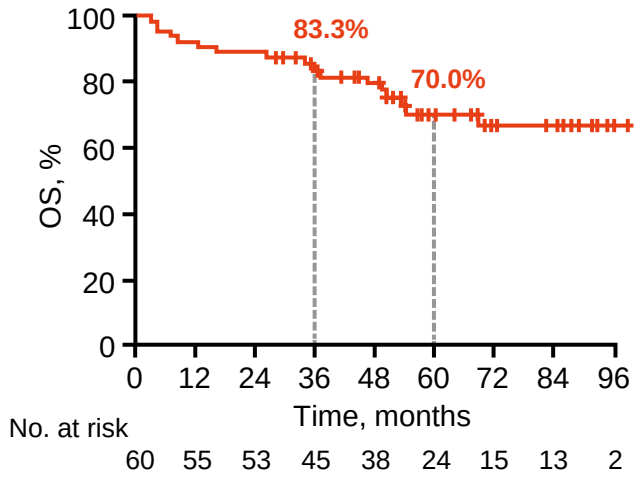
Median follow-up: 62.1 mo

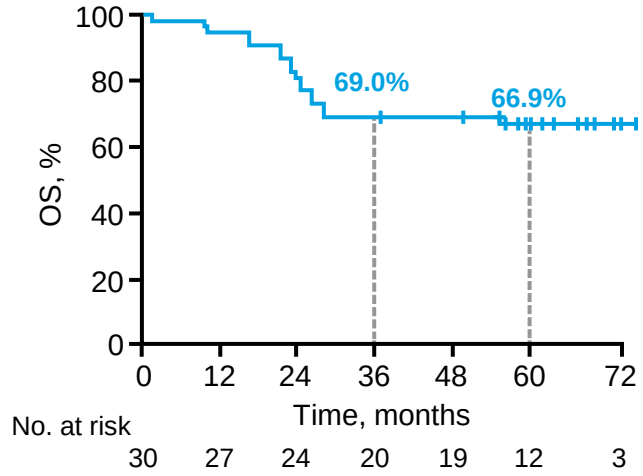
Event-free survival





Overall survival





Reuss J, et al. Ann Oncol 2024;35(suppl):Abstr 1209MO

1209MO: Neoadjuvant nivolumab and nivolumab+ipilimumab in resectable non-small cell lung cancer: Combined analysis of 5-year outcomes from NEOSTAR and CA209-159 – Reuss J, et al

- **Key results (cont.)**

	Nivolumab (n=60)	Nivolumab + ipilimumab (n=30)	All (n=90)
MPR, % (95%CI)	28.1 (17.4, 42.1)	33.3 (19.0, 51.7)	30.0 (21.5, 40.2)
pCR, % (95%CI)	8.3 (3.5, 18.5)	26.7 (13.9, 45.0)	13.5 (6.6, 25.7)

EFS and OS by pathological response	MPR	No MPR	pCR	No pCR
60-mo EFS, % (95%CI)	74.0 (52.9, 86.8)	54.4 (38.4, 67.9)	77.5 (44.9, 92.2)	56.9 (41.4, 69.8)
60-mo OS, % (95%CI)	81.7 (61.4, 92.0)	72.6 (56.1, 83.7)	85.5 (52.9, 96.2)	73.1 (57.4, 83.8)

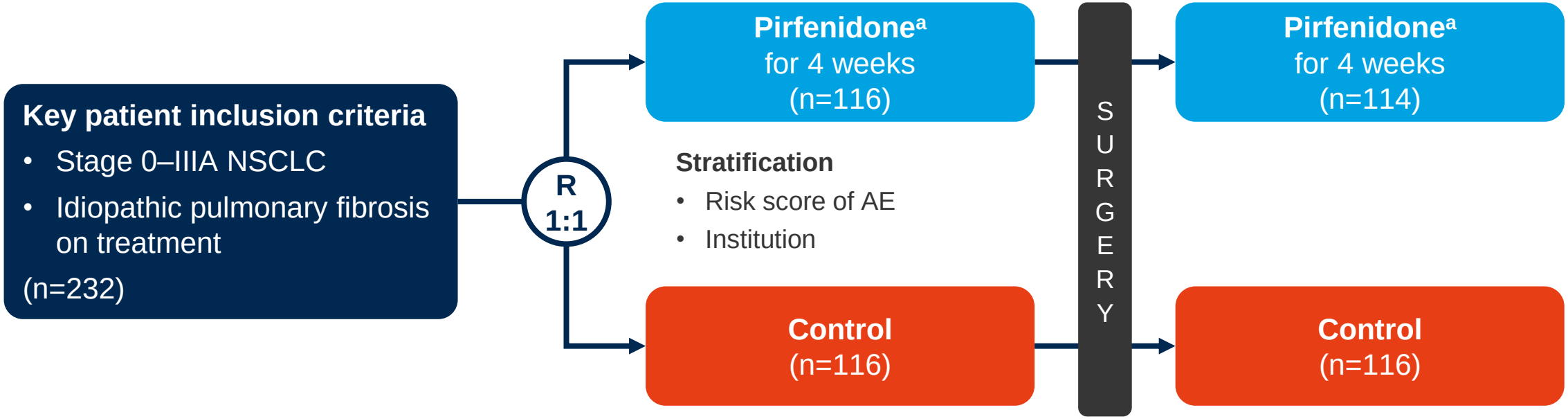
EFS by KRAS co-mutation with STK11, KEAP1 and/or SMARCA4	Nivolumab (n=60)		Nivolumab + ipilimumab (n=30)	
	Yes (n=5)	No (n=55)	Yes (n=5)	No (n=25)
Median follow-up, mo	68.4		62.1	
60-mo EFS, % (95%CI)	19.6 (0.8, 57.5)	64.0 (48.0, 76.2)	40.0 (5.2, 75.3)	53.2 (29.0, 72.4)

EFS by PD-L1 at baseline	Nivolumab (n=60)		Nivolumab + ipilimumab (n=30)	
	PD-L1 <1%	PD-L1 ≥1%	PD-L1 <1%	PD-L1 ≥1%
Event, n/N	11/18	4/21	7/14	6/11
HR (95%CI)	0.27 (0.08, 0.84)		1.02 (0.33, 3.20)	

- **Conclusions**
  - In patients with resectable NSCLC, neoadjuvant nivolumab ± ipilimumab demonstrated long-term survival benefit. EFS outcomes differed across PD-L1 expression levels and mutational subgroups

1208MO: Phase III trial of perioperative pirfenidone therapy for lung cancer with idiopathic pulmonary fibrosis (IPF): NEJ034 study – Goto Y, et al

- **Study objective**
  - To evaluate the efficacy and safety of perioperative pirfenidone (an antifibrotic and anti-inflammatory agent), in patients with lung cancer and idiopathic pulmonary fibrosis in the phase 3 NEJ034 study



Primary endpoint

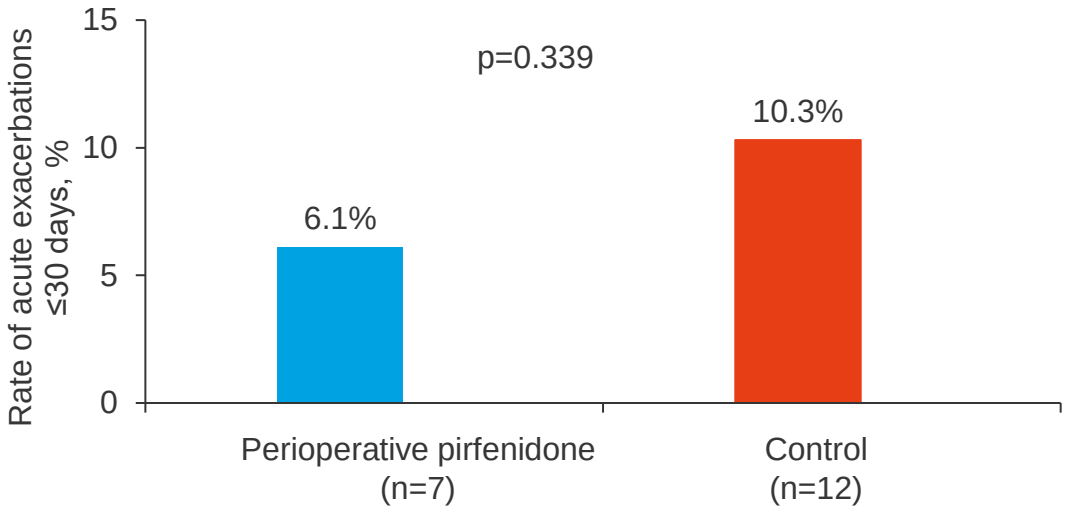
- Rate of acute exacerbations ≤30 days post-surgery

[a]Perfenidone 600 mg/day at start, then increased every 2 weeks up to 1200 mg/day.

Goto Y, et al. Ann Oncol 2024;35(suppl):Abstr 1208MO

1208MO: Phase III trial of perioperative pirfenidone therapy for lung cancer with idiopathic pulmonary fibrosis (IPF): NEJ034 study – Goto Y, et al

- **Key results (cont.)**

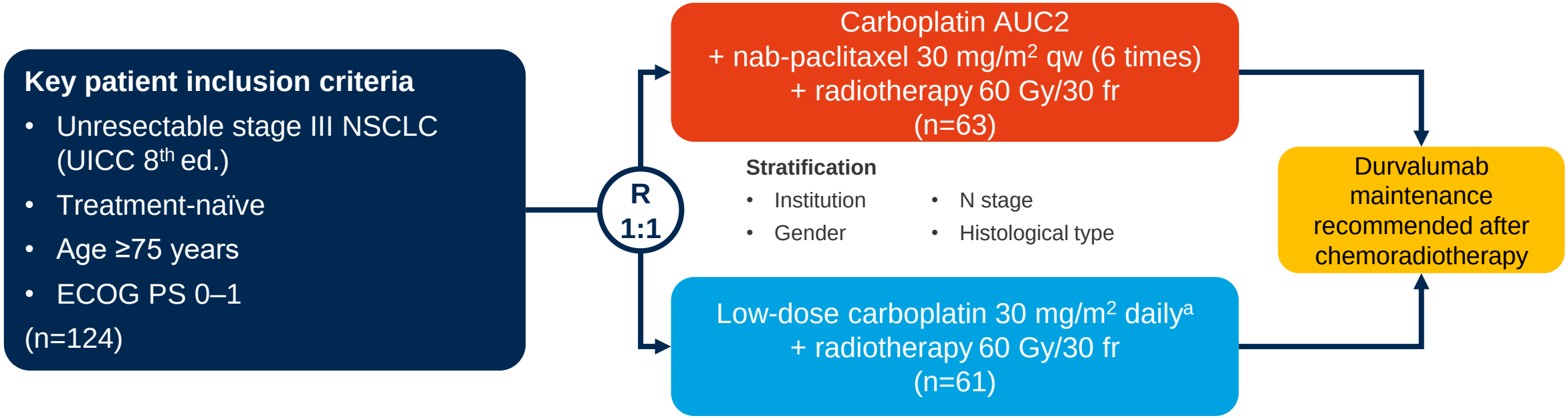


- **Conclusions**
  - In Japanese patients with lung cancer and idiopathic pulmonary fibrosis, perioperative pirfenidone failed to prevent the occurrence of acute exacerbations of interstitial lung diseases after pulmonary resection

Goto Y, et al. Ann Oncol 2024;35(suppl):Abstr 1208MO

1243MO: A phase III study comparing weekly carboplatin plus nab-paclitaxel and daily low-dose carboplatin for concurrent chemoradiotherapy in elderly patients (≥75 years) with unresectable locally advanced NSCLC: JCOG1914 – Omori S, et al

- **Study objective**
  - To evaluate the efficacy and safety of weekly carboplatin + nab-paclitaxel and daily low-dose carboplatin for concurrent chemoradiotherapy in elderly patients (age ≥75 years) with unresectable locally advanced NSCLC in the phase 3 JCOG1914 study



Primary endpoint

- OS

Secondary endpoints

- PFS, response, PROs, safety

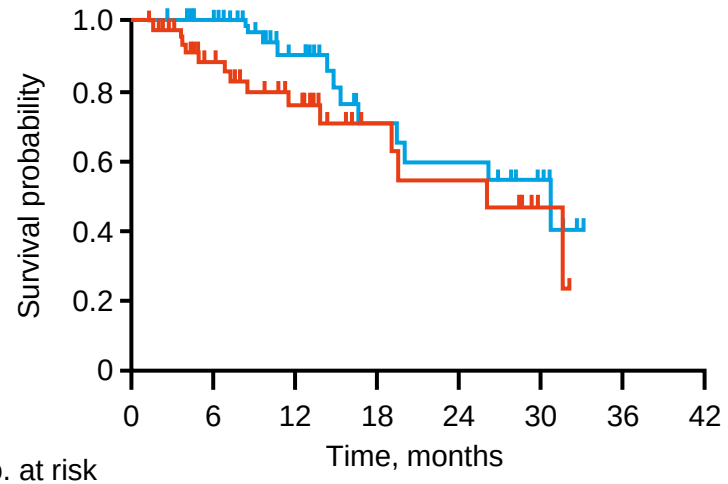
[a]Before radiotherapy for first 20 fr.

1243MO: A phase III study comparing weekly carboplatin plus nab-paclitaxel and daily low-dose carboplatin for concurrent chemoradiotherapy in elderly patients (≥75 years) with unresectable locally advanced NSCLC: JCOG1914 – Omori S, et al

- **Key results**

Interim OS

	CBDCA + RT (n=61)	CBDCA/nPAC + RT (n=63)
mOS, mo (95%CI)	30.8 (16.6, NE)	26.1 (19.1, NE)
1-year OS, % (95%CI)	90.8 (73.9, 97.0)	76.3 (58.8, 87.2)
HR (95%CI); p-value[a]	1.766 (0.800, 3.901); 0.1539	

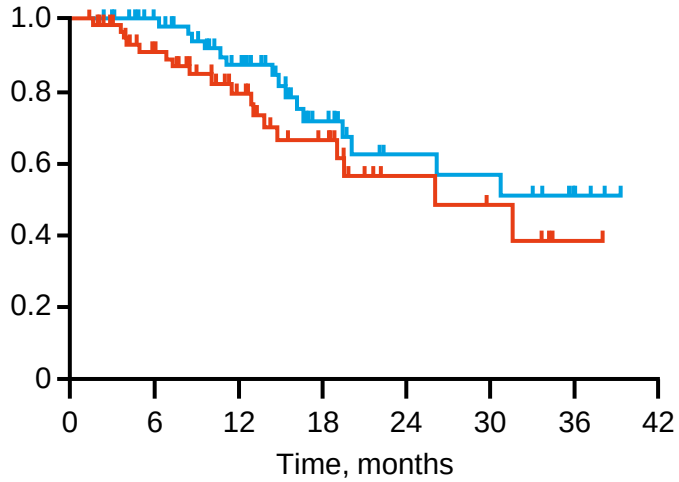


No. at risk

CBDCA + RT	50	44	24	13	11	6	0	0
CBDCA/nPAC + RT	50	34	20	9	7	2	0	0

Updated OS

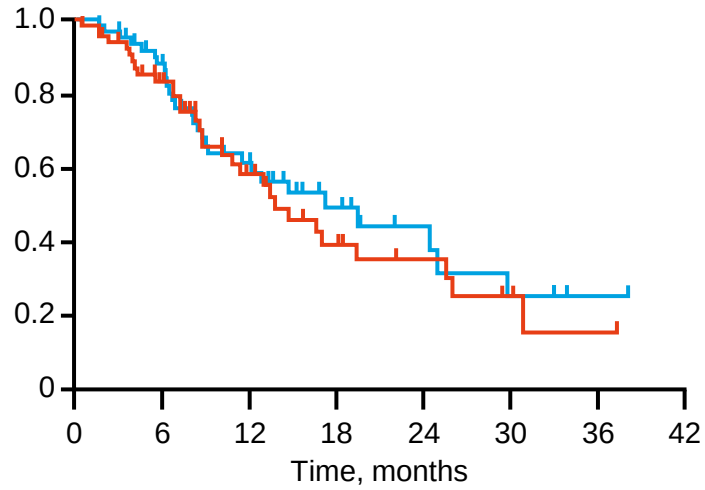
	CBDCA + RT (n=61)	CBDCA/nPAC + RT (n=63)
mOS, mo (95%CI)	NE (19.4, NE)	26.1 (14.8, NE)
1-year OS, % (95%CI)	87.3 (73.8, 94.1)	79.6 (65.0, 88.6)
HR (95%CI); p-value[a]	1.562 (0.786, 3.107); 0.1997	



CBDCA + RT	61	52	37	19	11	10	4	0
CBDCA/nPAC + RT	63	46	28	17	7	5	1	0

Updated PFS

	CBDCA + RT (n=61)	CBDCA/nPCA + RT (n=63)
mPFS, mo (95%CI)	17.3 (9.0, 25.0)	13.5 (8.8, 19.4)
1-year PFS, % (95%CI)	59.0 (43.6, 71.5)	55.5 (39.6, 68.8)
HR (95%CI); p-value[a]	1.188 (0.712, 1.982); 0.5101	



CBDCA + RT	61	44	23	11	6	3	1	0
CBDCA/nPCA + RT	63	39	19	10	6	3	1	0

[a]Unstratified Log-rank test, two-sided.

1243MO: A phase III study comparing weekly carboplatin plus nab-paclitaxel and daily low-dose carboplatin for concurrent chemoradiotherapy in elderly patients (≥75 years) with unresectable locally advanced NSCLC: JCOG1914 – Omori S, et al

- **Key results (cont.)**

Hematological AEs, n (%)	CBDCA + RT (n=61)		CBDCA/nPAC + RT (n=63)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Leukopenia	52 (85.2)	30 (49.2)	53 (84.1)	31 (49.2)
Neutropenia	48 (78.7)	26 (42.6)	45 (71.4)	20 (31.8)
Anemia	34 (55.7)	4 (6.6)	33 (52.4)	3 (4.8)
Thrombocytopenia	55 (90.2)	18 (29.5)	54 (85.7)	5 (7.9)
Febrile neutropenia	-	3 (4.9)	-	3 (4.8)

Deaths, n	CBDCA + RT (n=61)	CBDCA/nPAC + RT (n=63)
Treatment-related	0	2[a]
Non-cancer-related	0	7[b]

- **Conclusions**
  - In elderly Japanese patients with unresectable locally advanced NSCLC, carboplatin + nab-paclitaxel + radiotherapy failed to demonstrate superior survival benefit over low-dose carboplatin + radiotherapy

[a]Pneumonitis, sepsis; [b]aspiration pneumonia (n=4).

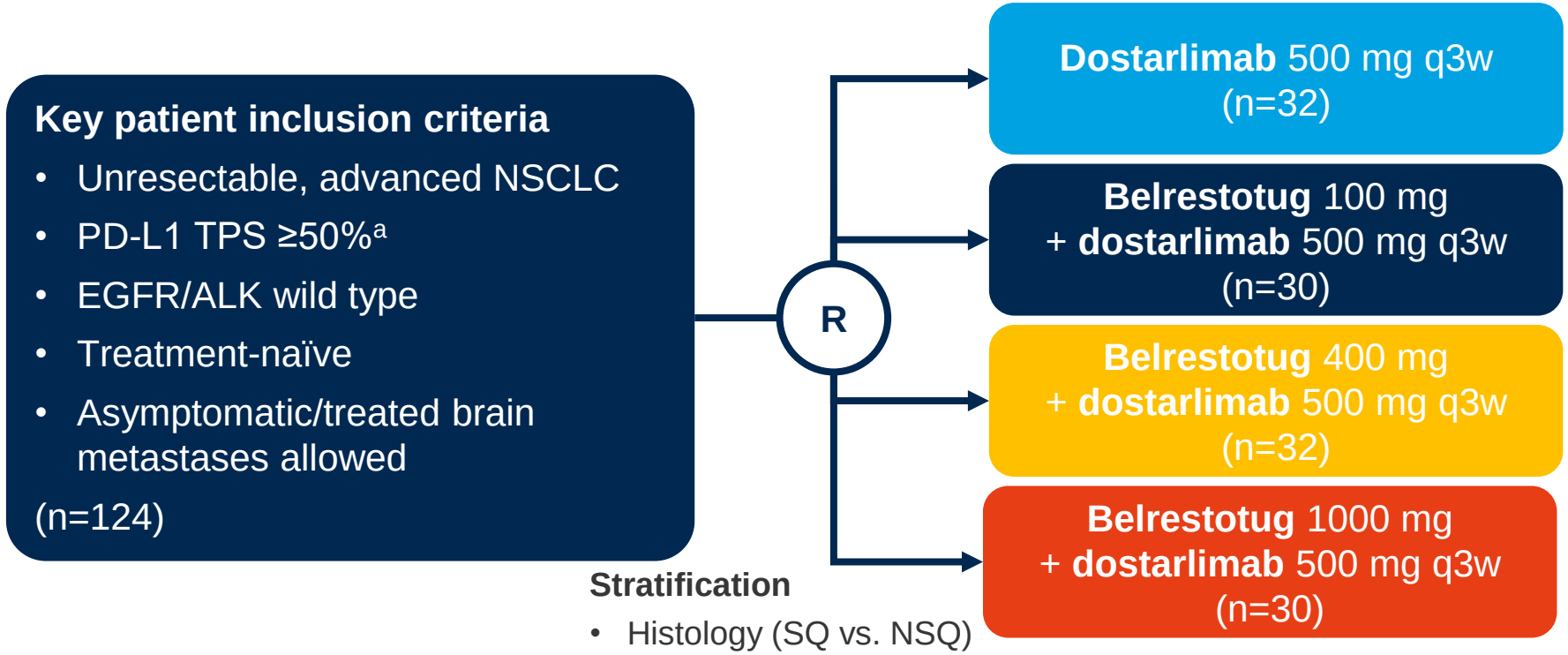
Omori S, et al. Ann Oncol 2024;35(suppl):Abstr 1243MO

Advanced NSCLC
Not radically treatable stage III and stage IV

Immunotherapy

LBA52: Interim analysis of GALAXIES Lung-201: Phase 2, randomized, open-label platform study of belrestotug plus dostarlimab in patients (pts) with previously untreated locally advanced/metastatic (LA/M) PD-L1 high (TPS ≥50%) non-small cell lung cancer (NSCLC) – Spigel DR, et al

- **Study objective**
  - To evaluate the efficacy and safety of belrestotug + dostarlimab in treatment-naïve patients with locally advanced or metastatic NSCLC and high PD-L1 (TPS ≥50%) in the phase 2 GALAXIES Lung-201 study



Primary endpoint

- ORR (RECIST v1.1)

Secondary endpoints

- PFS, OS, DoR, safety

[a]Locally or centrally assessed using DAK 22C3 or VENTANA SP263 assay.

LBA52: Interim analysis of GALAXIES Lung-201: Phase 2, randomized, open-label platform study of belrestotug plus dostarlimab in patients (pts) with previously untreated locally advanced/metastatic (LA/M) PD-L1 high (TPS ≥50%) non-small cell lung cancer (NSCLC) – Spigel DR, et al

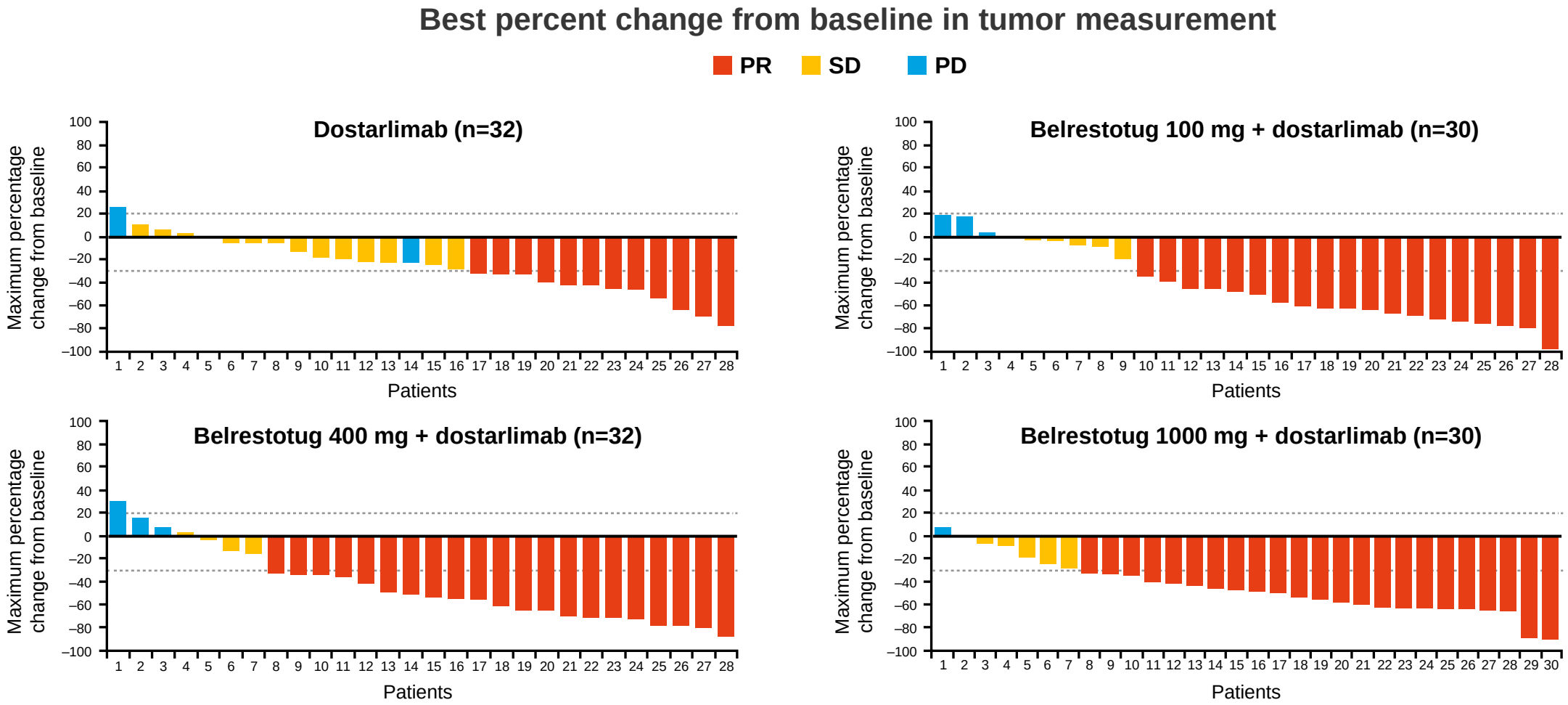
- **Key results**

Response measure in mITT	Dostarlimab (n=32)	Belrestotug 100 mg + dostarlimab (n=30)	Belrestotug 400 mg + dostarlimab (n=32)	Belrestotug 1000 mg + dostarlimab (n=30)
Median follow-up, mo (range)	7.0 (0.2–16.6)	8.5 (0.3–14.3)	8.5 (0.4–16.2)	6.7 (2.4–9.7)
ORR, n (%) [95%CI]	12 (37.5) [21.1, 56.3]	19 (63.3) [3.9, 80.1]	21 (65.6) [46.8, 81.4]	23 (76.7) [57.7, 90.1]
BOR, n (%)				
PR	12 (37.5)	19 (63.3)	21 (65.6)	23 (76.7)
SD	14 (43.8)	5 (16.7)	4 (12.5)	5 (16.7)
PD	2 (6.3)	4 (13.3)	3 (9.4)	2 (6.7)
NE/NA	4 (12.5)	2 (6.7)	4 (12.5)	0
Confirmed ORR, n (%) [95%CI]	9 (28.1) [13.7, 46.7]	18 (60.0) [40.6, 77.3]	19 (59.4) [40.6, 76.3]	19 (63.3) [43.9, 80.1]

Spigel DR, et al. Ann Oncol 2024;35(suppl):Abstr LBA52

LBA52: Interim analysis of GALAXIES Lung-201: Phase 2, randomized, open-label platform study of belrestotug plus dostarlimab in patients (pts) with previously untreated locally advanced/metastatic (LA/M) PD-L1 high (TPS ≥50%) non-small cell lung cancer (NSCLC) – Spigel DR, et al

- **Key results**



Spigel DR, et al. Ann Oncol 2024;35(suppl):Abstr LBA52

LBA52: Interim analysis of GALAXIES Lung-201: Phase 2, randomized, open-label platform study of belrestotug plus dostarlimab in patients (pts) with previously untreated locally advanced/metastatic (LA/M) PD-L1 high (TPS ≥50%) non-small cell lung cancer (NSCLC) – Spigel DR, et al

- **Key results (cont.)**

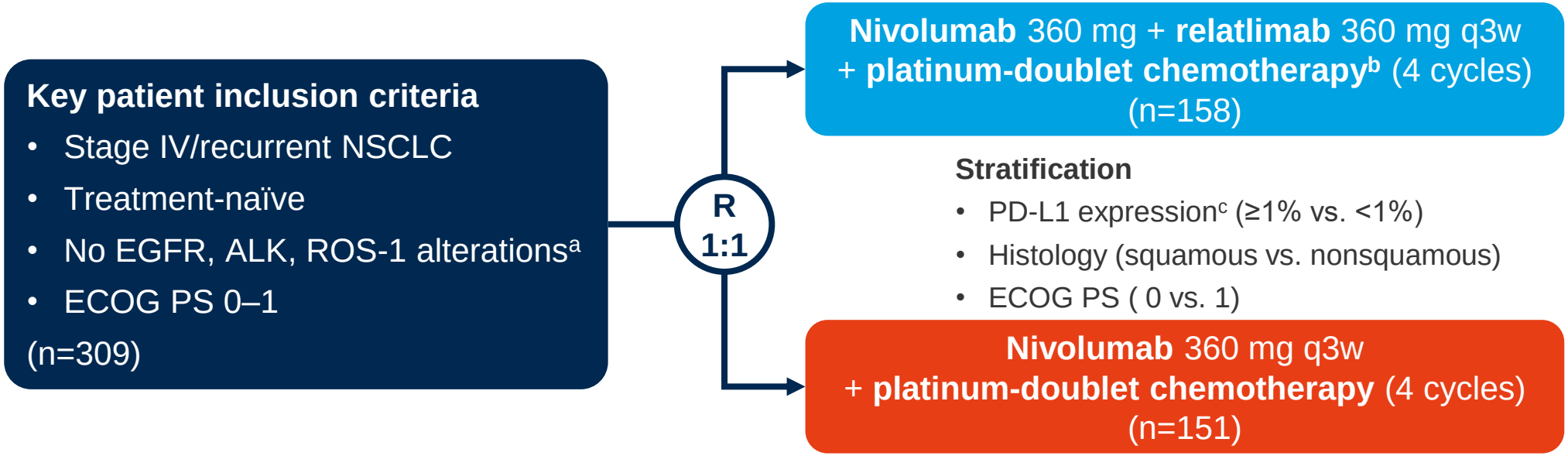
AEs, n (%)	Dostarlimab (n=32)	Belrestotug 100 mg + dostarlimab (n=30)	Belrestotug 400 mg + dostarlimab (n=32)	Belrestotug 1000 mg + dostarlimab (n=30)
TEAE	29 (91)	29 (97)	31 (97)	30 (100)
Grade ≥3	14 (44)	19 (63)	16 (50)	16 (53)
TRAE	19 (59)	24 (80)	27 (84)	29 (97)
Grade ≥3	5 (16)	10 (33)	7 (22)	13 (43)
Serious TRAE	3 (9)	10 (33)	8 (25)	11 (37)
Grade 5	0	2 (7)	1 (3)	0
TRAE led to discontinuation	2 (6)	7 (23)	5 (16)	12 (40)
TR-irAE	6 (19)	20 (67)	18 (56)	22 (73)
Grade ≥3	4 (13)	9 (30)	5 (16)	11 (37)
Infusion-related reactions	4 (13)	8 (27)	3 (9)	7 (23)

- **Conclusions**
  - In patients with locally advanced or metastatic PD-L1-high NSCLC, belrestotug + dostarlimab provided improvements in ORR across the cohorts compared with dostarlimab alone, but was associated with an increase in immune-related adverse events

Spigel DR, et al. Ann Oncol 2024;35(suppl):Abstr LBA52

LBA53: Nivolumab (NIVO) plus relatlimab with platinum-doublet chemotherapy (PDCT) vs NIVO + PDCT as first-line (1L) treatment (tx) for stage IV or recurrent NSCLC: results from the randomized phase 2 RELATIVITY-104 study – Girard N, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L nivolumab + relatlimab (a LAG-3 inhibitor) + platinum-doublet chemotherapy in patients with stage IV or recurrent NSCLC in the phase 2 RELATIVITY-104 study



Primary endpoint

- ORR (BICR)

Secondary endpoints

- PFS (BICR), ORR by PD-L1, PFS by PD-L1, DoR (BICR), safety

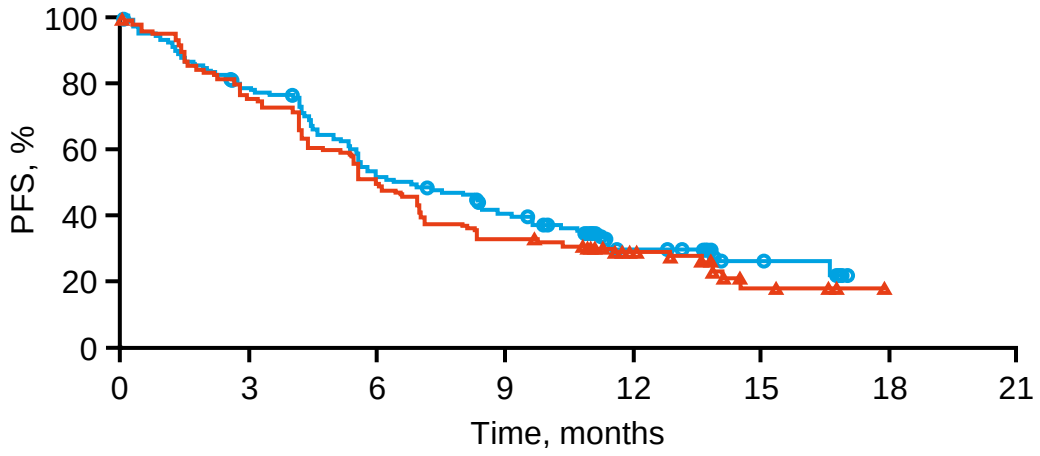
[a]Testing mandatory in patients with nonsquamous histology; [b]squamous: carboplatin AUC6 + paclitaxel 200 mg/m^2; nonsquamous: carboplatin AUC5 or cisplatin 75 mg/m^2 IV q3w + pemetrexed 500 mg/m^2; [c]assessed using the PD-L1 IHC 28-8 pharmDx assay.

Girard N, et al. Ann Oncol 2024;35(suppl):Abstr LBA53

LBA53: Nivolumab (NIVO) plus relatlimab with platinum-doublet chemotherapy (PDCT) vs NIVO + PDCT as first-line (1L) treatment (tx) for stage IV or recurrent NSCLC: results from the randomized phase 2 RELATIVITY-104 study – Girard N, et al

- **Key results**

PFS and ORR (BICR)



No. at risk

NIVO + RELA 360 mg + PDCT	158	123	80	61	26	7	0	0
NIVO + PDCT	151	112	74	49	26	6	0	0

	NIVO + RELA 360 mg + PDCT (n=158)	NIVO + PDCT (n=151)
mPFS, mo (90%CI)	6.7 (5.6, 8.4)	6.0 (5.5, 6.9)
HR (90%CI)	0.88 (0.71, 1.11)	

	NIVO + RELA 360 mg + PDCT (n=158)	NIVO + PDCT (n=151)
mDoR[a], mo (90%CI)	10.1 (7.4, NE)	9.1 (6.7, 13.4)
ORR, n (%)	81 (51.3)	66 (43.7)
Difference[b], % (90%CI)	7.6 (-1.3, 16.6)	

[a]Calculated using Kaplan-Meier curve; [b]calculated using the stratified Cochran-Haenszel method.

LBA53: Nivolumab (NIVO) plus relatlimab with platinum-doublet chemotherapy (PDCT) vs NIVO + PDCT as first-line (1L) treatment (tx) for stage IV or recurrent NSCLC: results from the randomized phase 2 RELATIVITY-104 study – Girard N, et al

- **Key results**

	PD-L1 ≥1%		PD-L1 <1%	
	NIVO + RELA 360 mg + chemotherapy (n=79)	NIVO + chemotherapy (n=71)	NIVO + RELA 360 mg + chemotherapy (n=70)	NIVO + chemotherapy (n=67)
mPFS, mo (90%CI)	9.8 (5.9,13.8)	6.1 (4.2, 7.0)	5.6 (5.3, 7.0)	5.8 (5.4, 7.0)
HR (90%CI)	0.63 (0.45, 0.88)		1.23 (0.89, 1.70)	
ORR, % (90%CI)	53.2 (43.3, 62.8)	40.8 (31.0, 51.3)	50.0 (39.6, 60.4)	44.8 (34.4, 55.5)

	Squamous		Nonsquamous	
	NIVO + RELA 360 mg + chemotherapy (n=51)	NIVO + chemotherapy (n=47)	NIVO + RELA 360 mg + chemotherapy (n=107)	NIVO + chemotherapy (n=104)
mPFS, mo (90%CI)	5.6 (5.3, 8.2)	5.8 (5.4, 7.1)	8.3 (5.6, 9.8)	6.0 (4.6, 7.0)
HR (90%CI)	0.97 (0.66, 1.43)		0.86 (0.65, 1.13)	
ORR, % (90%CI)	60.8 (48.3, 72.3)	55.3 (42.3, 67.8)	46.7 (38.5, 55.1)	38.5 (30.5, 47.0)

Girard N, et al. Ann Oncol 2024;35(suppl):Abstr LBA53

LBA53: Nivolumab (NIVO) plus relatlimab with platinum-doublet chemotherapy (PDCT) vs NIVO + PDCT as first-line (1L) treatment (tx) for stage IV or recurrent NSCLC: results from the randomized phase 2 RELATIVITY-104 study – Girard N, et al

- **Key results (cont.)**

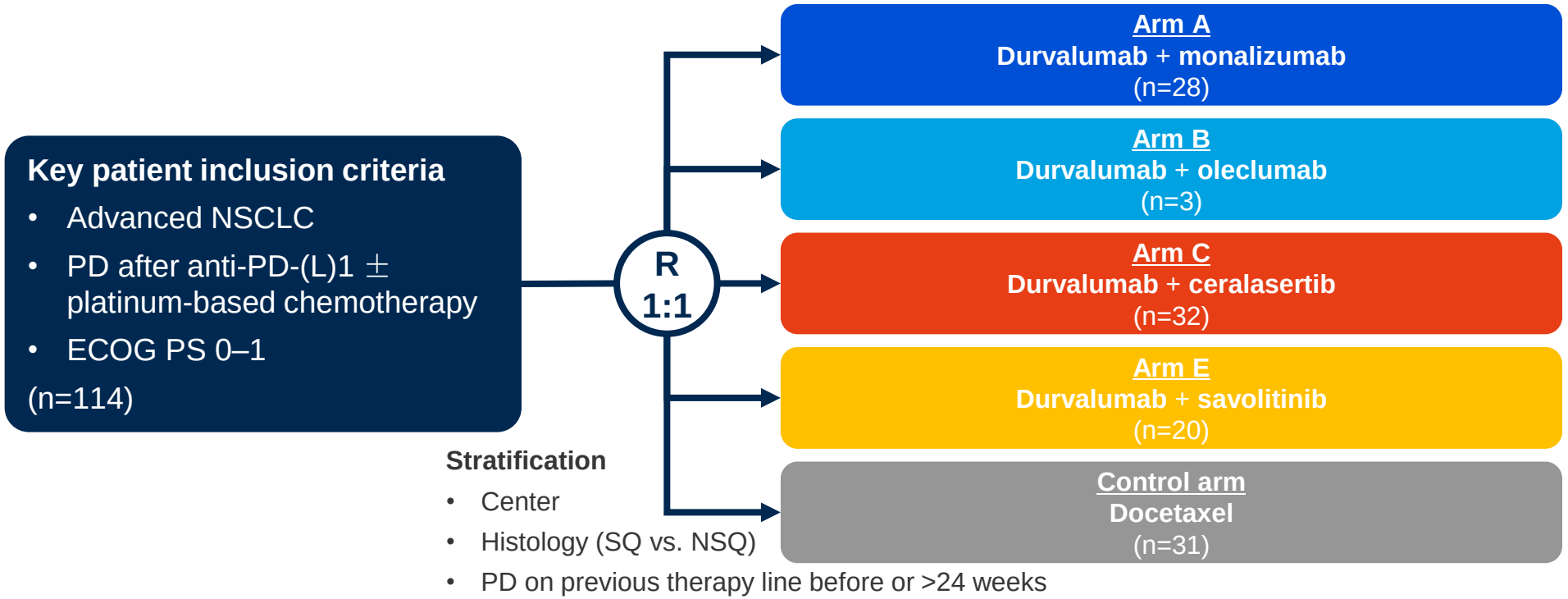
	NIVO + RELA 360 mg + chemotherapy (n=158)		NIVO + chemotherapy (n=149)	
AEs, n (%)	Any	Grade 3/4	Any	Grade 3/4
All-cause AEs	158 (100)	112 (71)	148 (99)	104 (70)
TRAE	147 (93)	86 (54)	138 (93)	82 (55)
Serious	37 (23)	33 (21)	36 (24)	32 (22)
Led to discontinuation	21 (13)	12 (8)	21 (14)	13 (9)
Led to death	6 (4)		5 (3)	

- **Conclusions**
  - In patients with stage IV/recurrent NSCLC, the addition of relatlimab to 1L nivolumab + platinum-doublet chemotherapy provided improvements in PFS and ORR, particularly in PD-L1+ and nonsquamous NSCLC, compared with nivolumab + platinum-doublet chemotherapy and had a safety profile consistent with previous findings for the individual components

Girard N, et al. Ann Oncol 2024;35(suppl):Abstr LBA53

LBA8: Precision Immuno-Oncology for advanced Non-small cell lung cancer (NSCLC) patients with PD-(L)1 inhibitors Resistance (PIONeeR): A phase Ib/IIa clinical trial targeting identified resistance pathways – Tomasini P, et al

- **Study objective**
  - To evaluate precision immuno-oncology targeting identified resistance pathways in patients with advanced NSCLC and PD-(L)1 inhibitor resistance in the phase 1b/2a PIONeeR study



Primary endpoint

- 12-week DCR (RECIST v1.1)

Secondary endpoints

- ORR, DoR, OS, PFS, safety

Bayesian approach to rule for experimental arms; arm closed if ≥90% probability 12-week DCR is ≤30%; arm considered for further evaluation if ≥90% probability 12-week DCR is ≥12-week DCR in control arm.

Tomasini P, et al. Ann Oncol 2024;35(suppl):Abstr LBA8

LBA8: Precision Immuno-Oncology for advanced Non-small cell lung cancer (NSCLC) patients with PD-(L)1 inhibitors Resistance (PIONeeR): A phase Ib/IIa clinical trial targeting identified resistance pathways – Tomasini P, et al

- **Key results**

	Arm A Durvalumab + monalizumab (n=28)	Arm B Durvalumab + oleclumab (n=3)	Arm C Durvalumab + ceralasertib (n=32)	Arm E Durvalumab + savolitinib (n=20)	Control arm Docetaxel (n=31)
Patients	6/27[a]	0/3	15/30[a]	2/20	11/20[a]
Median estimated 12-week DCR, % (95%CI)	21.1 (10.7, 41.0)	-	50 (33.1, 66.9)	13.6 (3.0, 30.4)	54.5 (34.0, 74.3)
Probability (12-week DCR-experimental ≥12-week DCR-control), %	1.2	0	36.8	-	-

[a]Non-evaluable patients.

Tomasini P, et al. Ann Oncol 2024;35(suppl):Abstr LBA8

LBA8: Precision Immuno-Oncology for advanced Non-small cell lung cancer (NSCLC) patients with PD-(L)1 inhibitors Resistance (PIONeeR): A phase Ib/IIa clinical trial targeting identified resistance pathways – Tomasini P, et al

- **Key results (cont.)**

	Arm A Durvalumab + monalizumab (n=28)	Arm B Durvalumab + oleclumab (n=3)	Arm C Durvalumab + ceralasertib (n=32)	Arm E Durvalumab + savolitinib (n=20)	Control arm Docetaxel (n=31)
Events, n (%)	28 (100)	-	25 (78.1)	18 (90)	18 (58)
mPFS, mo (95%CI)	1.6 (1.5, 3.1)	-	4.1 (2.8, 7.2)	1.4 (1.3, 2.9)	4.4 (1.6, 7.8)
Events, n (%)	25 (89.3)	-	21 (65.6)	16 (80)	18 (58)
mOS, mo (95%CI)	11.7 (6.6, 13.7)	-	17.4 (5.5, 21.7)	7.1 (3.3, 12.6)	13.8 (11.5, NE)
ORR (ITT), n (%) [95%CI]	0 (-) [0, 12.3]	0 (-) [0.0, 70.8]	5 (15.6) [5.3, 32.8]	0 (-) [0, 16.8]	5 (16.1) [5.5, 33.7]
BOR, n (%)					
PR	0	0	5 (17.9)	0	5 (25.0)
SD	12 (42.9)	2 (66.7)	16 (57.1)	6 (30.0)	10 (50.0)
DCR	12 (42.9)	2 (66.7)	21 (75.0)	6 (30.0)	15 (75.0)
PD	13 (46.4)	1 (33.3)	5 (17.9)	13 (65.0)	5 (25.0)
Early PD	3 (10.7)	0	2 (7.2)	1 (5.0)	0

Tomasini P, et al. Ann Oncol 2024;35(suppl):Abstr LBA8

LBA8: Precision Immuno-Oncology for advanced Non-small cell lung cancer (NSCLC) patients with PD-(L)1 inhibitors Resistance (PIONeeR): A phase Ib/IIa clinical trial targeting identified resistance pathways – Tomasini P, et al

- **Key results (cont.)**

AEs, n (%)	Arm A Durvalumab + monalizumab (n=28)	Arm B Durvalumab + oleclumab (n=3)	Arm C Durvalumab + ceralasertib (n=32)	Arm E Durvalumab + savolitinib (n=20)	Control arm Docetaxel (n=31)	ITT (n=114)
All AEs	28 (100.0)	3 (100)	31 (100)	20 (100)	23 (100)	105 (100)
TRAEs	23 (82.1)	3 (100)	29 (93.5)	19 (95.0)	23 (100)	97 (92.4)
Grade ≥3 AEs	12 (42.9)	2 (66.7)	23 (74.2)	12 (60.0)	19 (82.6)	69 (65.7)
Grade ≥3 TRAEs	2 (7.1)	1 (33.3)	17 (54.8)	6 (30.0)	10 (43.5)	36 (34.3)
Grade 5 AEs	5 (17.9)	1 (33.3)	3 (9.7)	2 (10.0)	1 (4.3)	12 (11.4)
Grade 5 TRAEs	0	0	1 (3.2)	0	0	1 (1.0)
Led to interruption	3 (10.7)	1 (33.3)	10 (32.3)	9 (45.0)	6 (26.1)	30 (28.6)
TRAE led to discontinuation	2 (7.1)	1 (33.3)	8 (25.8)	7 (35.0)	6 (26.1)	24 (22.9)
SAEs	11 (39.3)	1 (33.3)	12 (38.7)	8 (40.0)	15 (65.2)	47 (44.8)
Serious TRAEs	1 (3.6)	0	8 (25.8)	3 (15.0)	3 (13.0)	15 (14.3)

- **Conclusions**
  - In patients with advanced NSCLC and PD-(L)1 inhibitor resistance, durvalumab combinations did not provide improved survival outcomes compared with docetaxel
  - A comprehensive translational program will provide further insights into the mechanisms of resistance

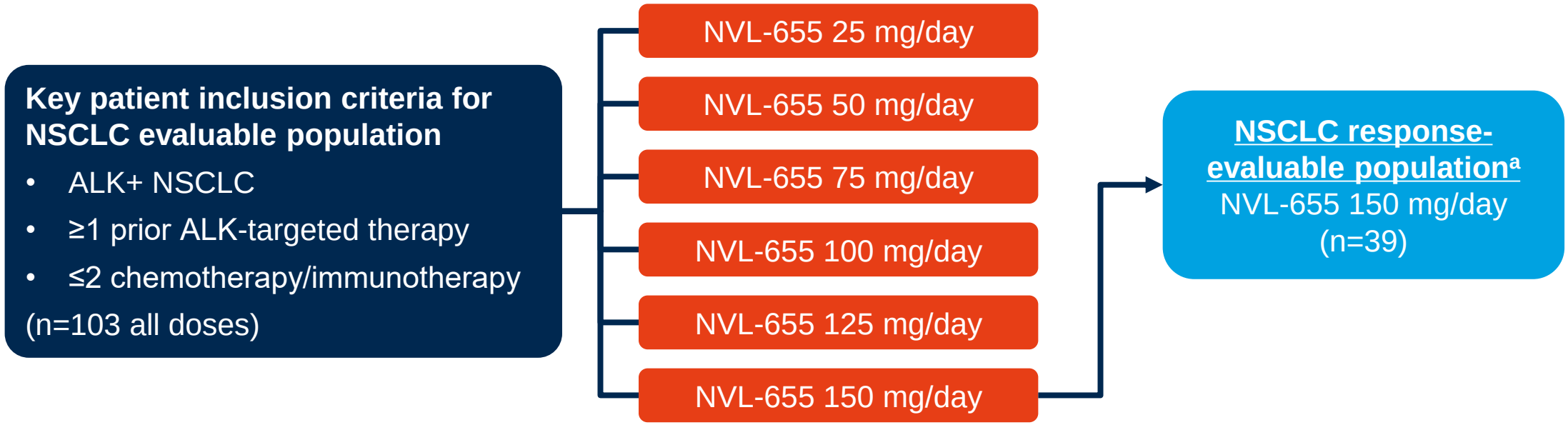
Tomasini P, et al. Ann Oncol 2024;35(suppl):Abstr LBA8

Advanced NSCLC
Not radically treatable stage III and stage IV

Targeted therapies

1253O: Phase 1/2 ALKOVE-1 study of NVL-655 in ALK-positive (ALK+) solid tumors – Drilon AE, et al

- **Study objective**
  - To evaluate the efficacy and safety of NVL-655 (an ALK-selective, TRK-sparing TKI) in patients with ALK+ solid tumors in a phase 1/2 study



Primary endpoint

- RP2D

Secondary endpoints

- Safety, PK, preliminary antitumor activity, intracranial activity

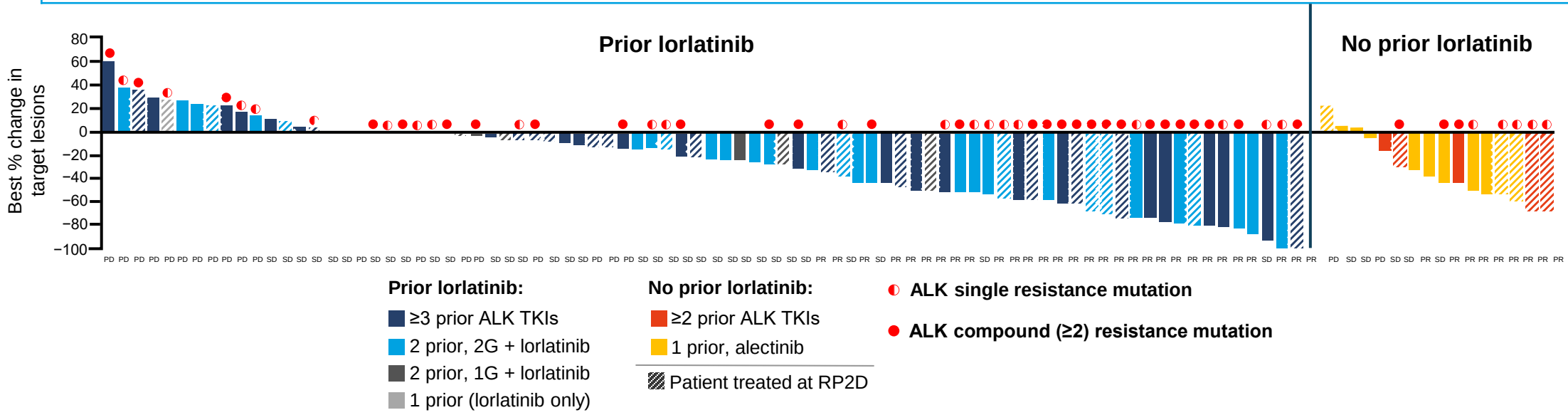
[a]Defined as all NSCLC patients with measurable disease, without concurrent oncogenic driver, and undergoing ≥1 response assessment.

Drilon AE, et al. Ann Oncol 2024;35(suppl):Abstr 1253O

1253O: Phase 1/2 ALKOVE-1 study of NVL-655 in ALK-positive (ALK+) solid tumors – Drilon AE, et al

- **Key results**

ORR (RECIST 1.1), n/N (%)	NSCLC response-evaluable (any prior ALK TKI, range 1−5)			Prior lorlatinib (≥2 ALK TKIs)			No prior lorlatinib (≥2 ALK TKIs)	
All patients ± chemotherapy	All	Any ALK mutation	G1202R	All	Any ALK mutation	Compound ALK mutation	All	Any ALK mutation
All doses	39/103 (38)	30/58 (52)	22/32 (69)	30/85 (35)	23/49 (47)	15/28 (54)	9/17 (53)	7/8 (88)
RP2D	15/39 (38)	12/22 (55)	10/14 (71)	11/31 (35)	8/16 (50)	7/11 (64)	4/7 (57)	4/5 (80)



Drilon AE, et al. Ann Oncol 2024;35(suppl):Abstr 1253O

1253O: Phase 1/2 ALKOVE-1 study of NVL-655 in ALK-positive (ALK+) solid tumors – Drilon AE, et al

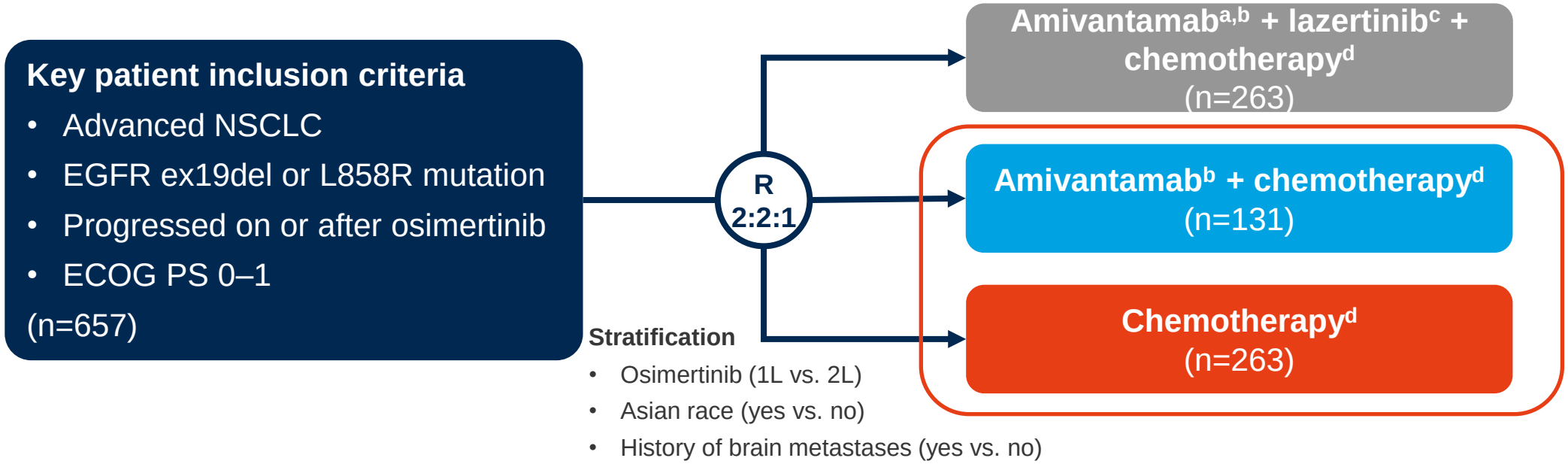
- **Key results (cont.)**

	All (n=133)				
TRAEs occurring in ≥10%, n (%)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Any grade**
ALT increased	21 (16)	6 (5)	17 (13)	1 (1)	45 (34)
AST increased	21 (16)	7 (5)	12 (9)	-	40 (30)
Constipation	15 (11)	6 (5)	-	-	21 (16)
Dysgeusia	15 (11)	2 (2)	-	-	17 (13)
Nausea	15 (11)	1 (1)	-	-	16 (12)

- **Conclusions**
  - In heavily pretreated (including lorlatinib exposure) patients with ALK+ NSCLC, NVL-655 showed encouraging antitumor activity with a highly manageable safety profile

LBA54: Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutated, advanced non-small cell lung cancer after disease progression on osimertinib: 2nd interim overall survival from MARIPOSA-2 – Popat S, et al

- **Study objective**
  - To evaluate the second interim OS with amivantamab + chemotherapy in patients with advanced EGFR-mutant NSCLC after progression on osimertinib in the MARIPOSA-2 study



Primary endpoint

- PFS (BICR, RECIST v1.1)

Secondary endpoints

- OS, TTSP, TTD, TTST, PFS2, safety

[a]The amivantamab + lazertinib + chemotherapy regimen was modified to start lazertinib after carboplatin completion due to hematologic toxicities; [b]amivantamab 1400 mg (1750 mg if ≥80 kg) q4w, then 1750 mg (2100 mg if ≥80 kg) q3w; [c]lazertinib 240 mg/day; [d]chemotherapy administered at the beginning of every cycle: carboplatin AUC5 (4 cycles); pemetrexed: 500 mg/m^2.

Popat S, et al. Ann Oncol 2024;35(suppl):Abstr LBA54

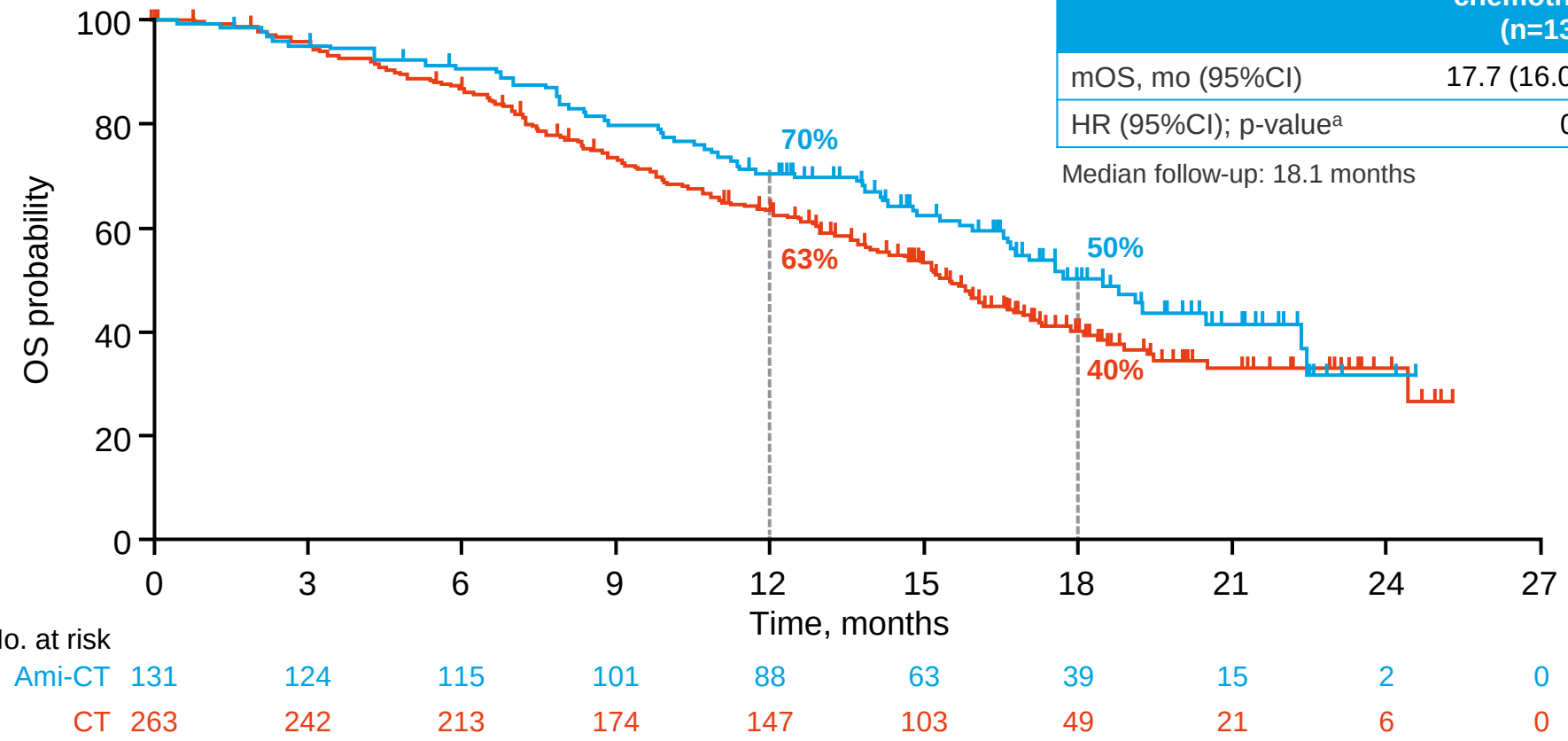
LBA54: Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutated, advanced non-small cell lung cancer after disease progression on osimertinib: 2nd interim overall survival from MARIPOSA-2 – Popat S, et al

- **Key results**

Overall survival

	Amivantamab + chemotherapy (n=131)	Chemotherapy (n=263)
mOS, mo (95%CI)	17.7 (16.0, 22.4)	15.3 (13.7, 16.8)
HR (95%CI); p-value[a]	0.73 (0.54, 0.99); 0.039	

Median follow-up: 18.1 months



[a]Log-rank test stratified by osimertinib line of therapy (1L vs. 2L), brain metastases (yes vs. no), Asian race (yes vs. no).

Popat S, et al. Ann Oncol 2024;35(suppl):Abstr LBA54

LBA54: Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutated, advanced non-small cell lung cancer after disease progression on osimertinib: 2nd interim overall survival from MARIPOSA-2 – Popat S, et al

- **Key results (cont.)**

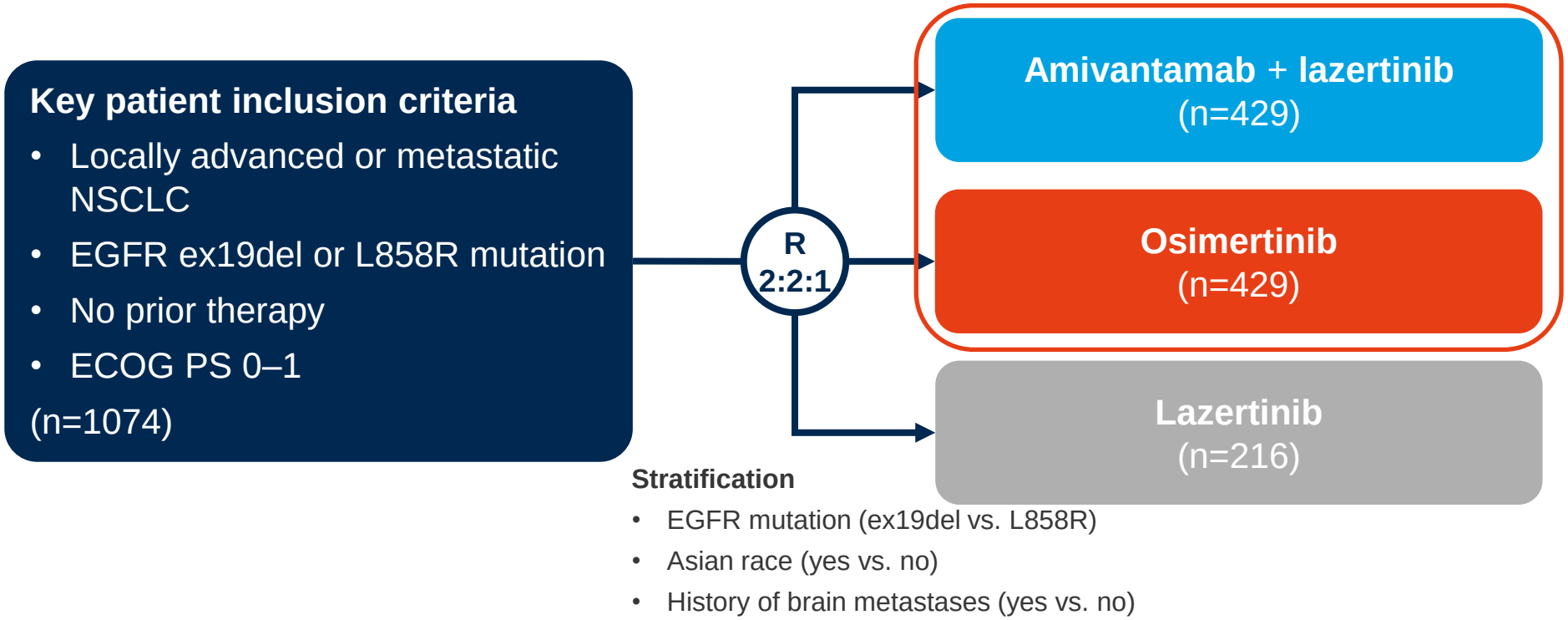
	Amivantamab + chemotherapy (n=131)	Chemotherapy (n=263)
Median TTSP, mo (95%CI)	16.0 (12.7, 19.4)	11.8 (8.9, 13.6)
HR (95%CI); p-value[a]	0.73 (0.55, 0.96); 0.026	
Median TTD, mo (95%CI)	10.4 (7.9, 11.6)	4.5 (4.2, 5.0)
HR (95%CI); p-value[a]	0.42 (0.33, 0.53); <0.0001	
Median TTSP, mo (95%CI)	12.2 (10.7, 14.3)	6.6 (6.1, 7.4)
HR (95%CI); p-value[a]	0.51 (0.39, 0.65); <0.0001	

- **Conclusions**
  - In patients with advanced EGFR-mutant NSCLC, amivantamab + chemotherapy continued to demonstrate an OS improvement at this second interim analysis in the post-osimertinib setting and provided prolonged benefits in post-progression outcomes over chemotherapy

[a]Log-rank test stratified by osimertinib line of therapy (1L vs. 2L), brain metastases (yes vs. no), Asian race (yes vs. no).

LBA55: Mechanisms of Acquired Resistance to First-line Amivantamab Plus Lazertinib Versus Osimertinib in Patients With EGFR-mutant Advanced Non-Small Cell Lung Cancer: An Early Analysis from the Phase 3 MARIPOSA Study – Besse B, et al

- **Study objective**
  - To evaluate mechanisms of acquired resistance to 1L amivantamab + lazertinib compared with osimertinib in patients with advanced EGFR-mutant NSCLC in the phase 3 MARIPOSA study



Primary endpoint

- PFS (BICR, RECIST v1.1)

Secondary endpoints

- OS, ORR, DoR, PFS2, safety

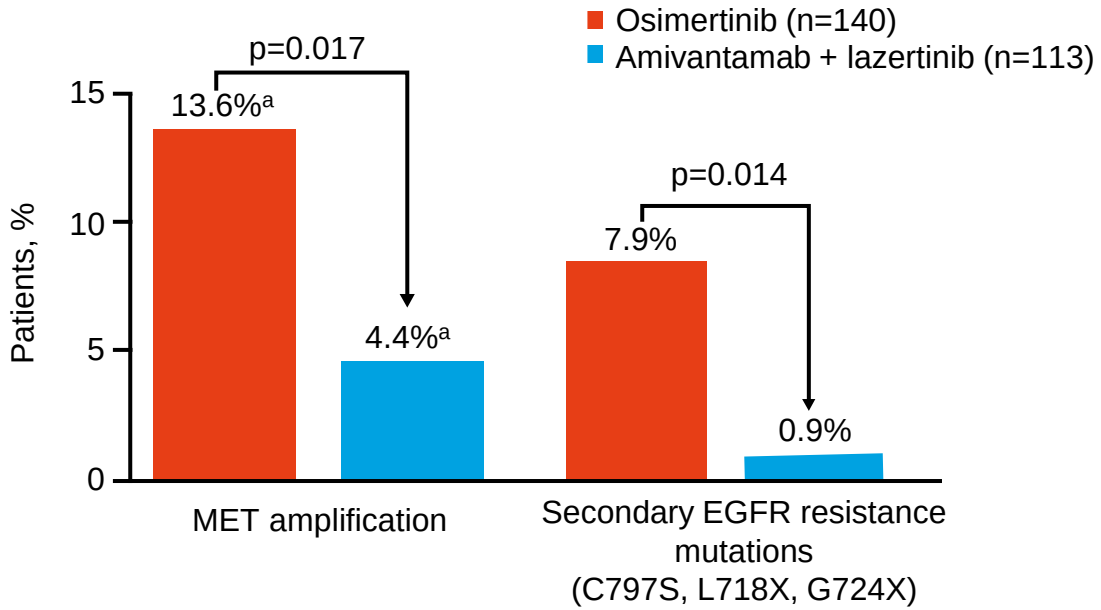
Analysis of ctDNA with Guardant 360® CDx NGS panel.

Besse B, et al. Ann Oncol 2024;35(suppl):Abstr LBA55

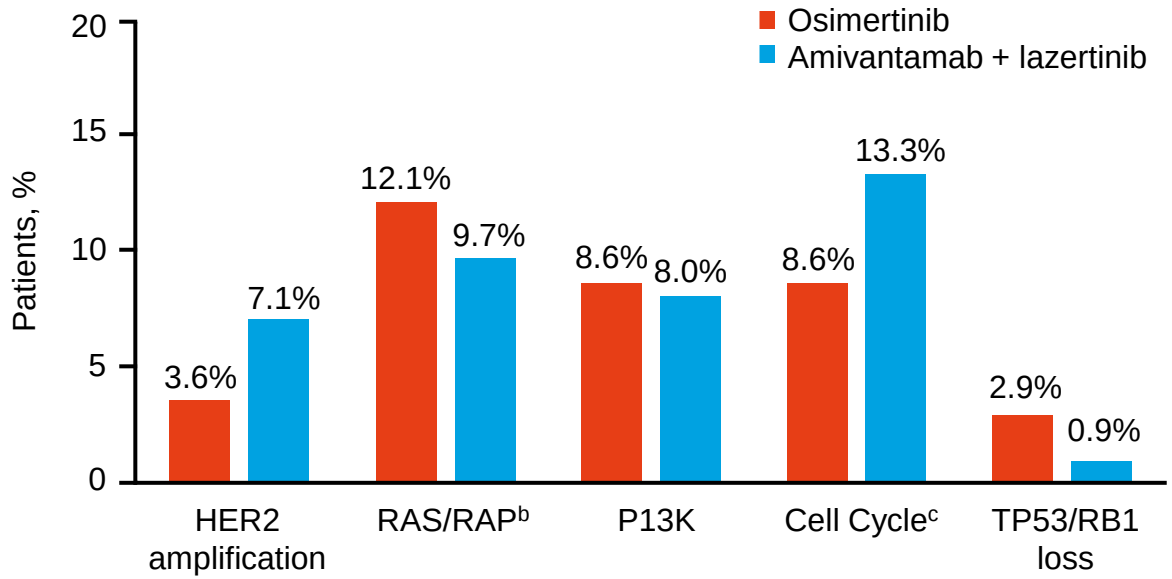
LBA55: Mechanisms of Acquired Resistance to First-line Amivantamab Plus Lazertinib Versus Osimertinib in Patients With EGFR-mutant Advanced Non-Small Cell Lung Cancer: An Early Analysis from the Phase 3 MARIPOSA Study – Besse B, et al

- **Key results**

MET- and EGFR-based resistance mechanisms



MET- and EGFR-independent resistance mechanisms

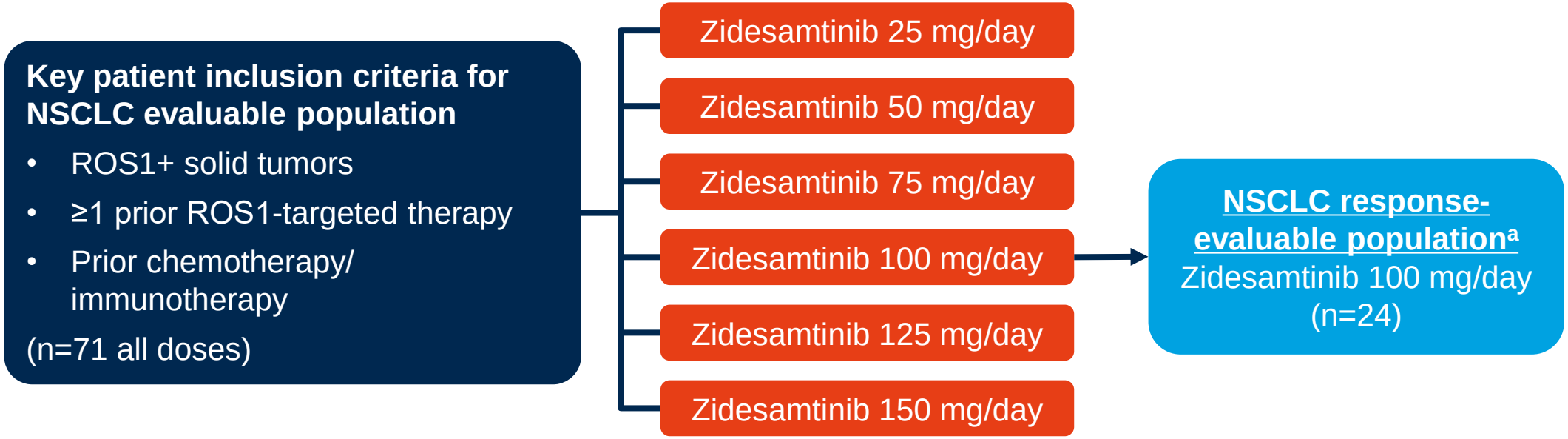


- **Conclusions**
  - In patients with advanced EGFR-mutant NSCLC, amivantamab + lazertinib significantly lowered the incidence of mechanisms of acquired resistance caused by EGFR and MET alterations

[a]MET amplification in 9.3% vs. 1.8% of patients in the osimertinib and amivantamab + lazertinib arms, respectively; [b]includes BRAF and KRAS; [c]includes CCNE1, CDKN2A, CDK4, CDK6, CCND2.

1256MO: Phase 1/2 ARROS-1 study of zidesamtinib (NVL-520) in ROS1 fusion-positive solid tumors – Besse B, et al

- **Study objective**
  - To evaluate the efficacy and safety of zidesamtinib (a ROS1 inhibitor) in patients with ROS1 fusion-positive solid tumors in the phase 1/2 ARROS-1 study



Primary endpoint

- RP2D

Secondary endpoints

- Safety, PK, preliminary antitumor activity, intracranial activity

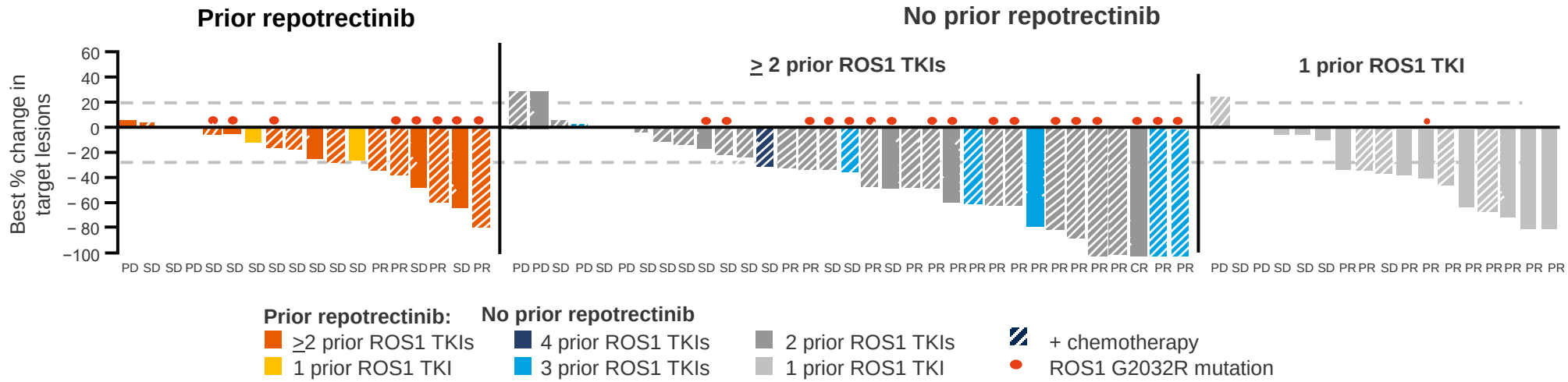
[a]Defined as all NSCLC patients with measurable disease, without concurrent oncogenic driver, and undergoing ≥1 response assessment.

Besse B, et al. Ann Oncol 2024;35(suppl):Abstr 1256MO

1256MO: Phase 1/2 ARROS-1 study of zidesamtinib (NVL-520) in ROS1 fusion-positive solid tumors – Besse B, et al

- **Key results**

All NSCLC response evaluable patients ± chemotherapy	Any prior ROS1 TKI (range 1–4)				≥2 prior ROS1 TKIs			1 prior ROS1 TKI (crizotinib)
			ROS1 G2032 resistance mutation[b]					
	All	No prior repotrectinib	Prior repotrectinib	No prior repotrectinib	All	Prior lorlatinib	No prior repotrectinib	
ORR, n/N (%)[a]	31/71 (44)	27/53 (51)	3/8 (38)	13/18 (72)	21/51 (41)	17/39 (44)	17/36 (47)	8/11 (73)
CR*	2	2	–	2	2	2	2	–



*2 confirmed CRs ongoing with DoR 19.3+ and 26.3+ mo. 5 additional CRs observed among patients without measurable disease (2 prior ROS1 TKIs [n=2], 1 prior ROS1 TKI [crizotinib (n=1), entrectinib (n=2)]), all ongoing with DoR 3.6+, 3.7+, 13.8+, 13.9+, and 18.5+ mo.

Besse B, et al. Ann Oncol 2024;35(suppl):Abstr 1256MO

1256MO: Phase 1/2 ARROS-1 study of zidesamtinib (NVL-520) in ROS1 fusion-positive solid tumors – Besse B, et al

- **Key results (cont.)**

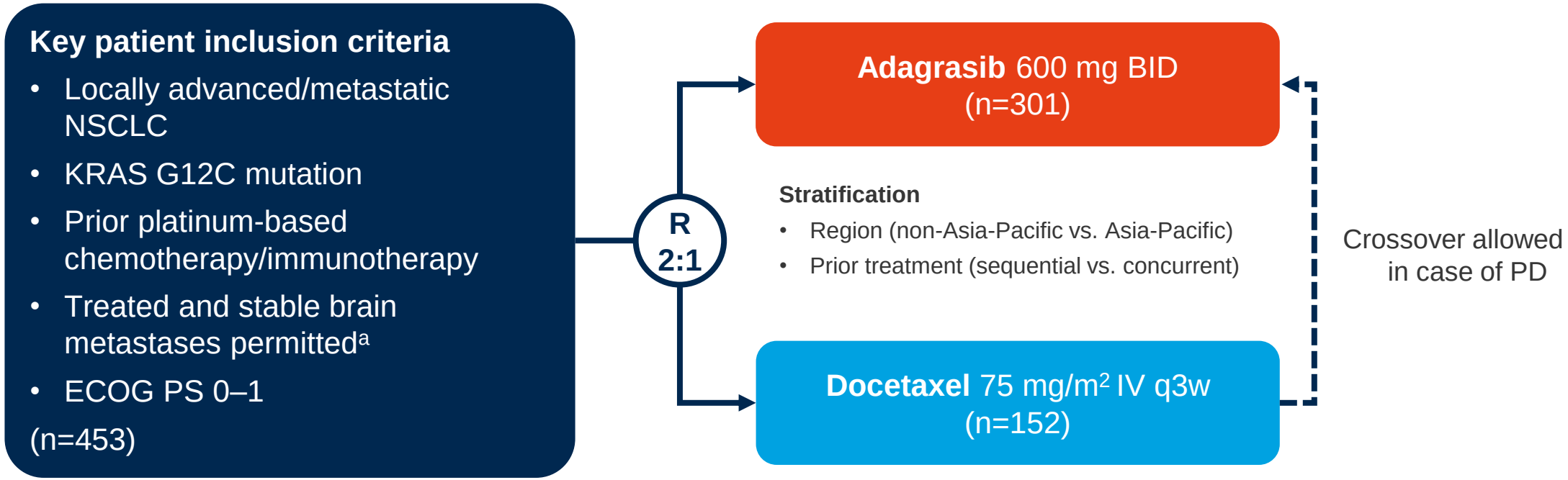
	All treated (n=104)			
TRAEs occurring in ≥10%, n (%)	**Grade 1**	**Grade 2**	**Grade 3**	**Any grade**
Peripheral edema	15 (14)	5 (5)	-	20 (19)
ALT increased	11 (11)	-	-	11 (11)
AST increased	11 (11)	-	-	11 (11)
Weight increased	7 (7)	3 (3)	1 (1)	11 (11)

- **Conclusions**
  - In heavily pretreated patients (including repotrectinib exposure) with ROS1+ NSCLC, zidesamtinib showed encouraging antitumor activity with a highly manageable safety profile

Besse B, et al. Ann Oncol 2024;35(suppl):Abstr 1256MO

LBA57: Adagrasib (ADA) vs docetaxel (DOCE) in patients (pts) with KRASG12C-mutated advanced NSCLC and baseline brain metastases (BM): Results from KRYSTAL-12 – Barlesi F, et al

- **Study objective**
  - To evaluate the efficacy and safety of adagrasib compared with docetaxel in patients with advanced KRAS G12C-mutant NSCLC and baseline brain metastases in the phase 3 KRYSTAL-12 study



Primary endpoint

- PFS (BICR, RECIST v1.1)

Secondary endpoints

- ORR, DoR, OS, PROs, safety

Exploratory endpoints

- Intracranial activity

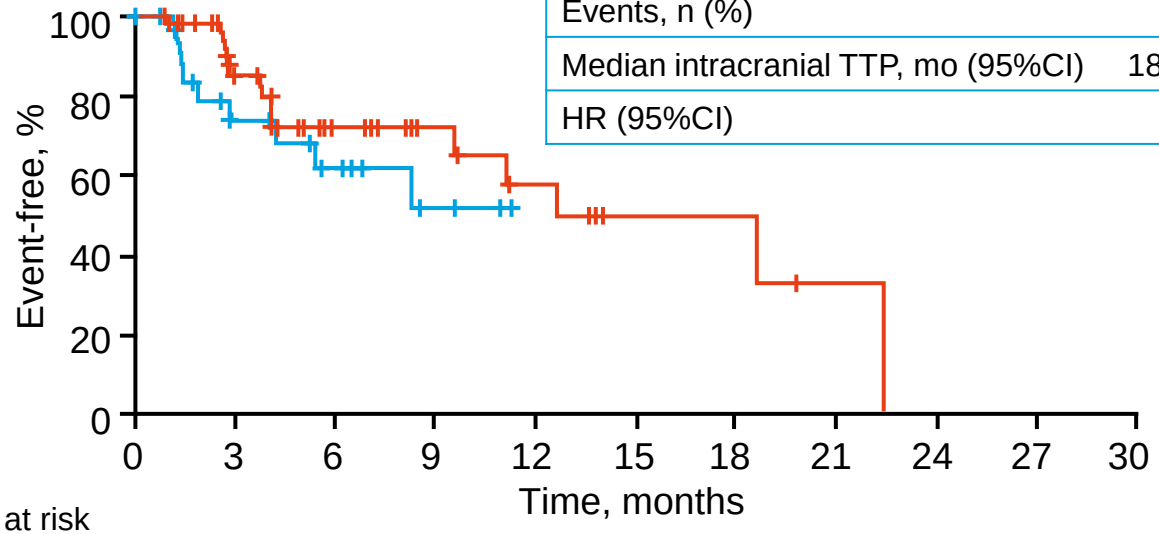
[a]Patients with baseline CNS metastases were reevaluated every 6 weeks for a year. If CNS were not found at baseline, patients were monitored every 12 weeks.

LBA57: Adagrasib (ADA) vs docetaxel (DOCE) in patients (pts) with KRASG12C-mutated advanced NSCLC and baseline brain metastases (BM): Results from KRYSTAL-12 – Barlesi F, et al

- **Key results**

Intracranial TTP in patients with baseline brain metastases

	Adagrasib (n=78)	Docetaxel (n=36)
Events, n (%)	17 (21.8)	9 (25.0)
Median intracranial TTP, mo (95%CI)	18.6 (9.6, NE)	NE (4.2, NE)
HR (95%CI)	0.60 (0.36, 1.40)	



Patients with baseline brain metastases	Adagrasib (n=78)	Docetaxel (n=36)
mPFS, mo (95%CI)	4.4 (3.1, 5.8)	2.9 (2.0, 6.2)
HR (95%CI)	0.70 (0.43, 1.20)	

Patients without baseline brain metastases	Adagrasib (n=223)	Docetaxel (n=116)
mPFS, mo (95%CI)	5.9 (4.8, 7.2)	3.9 (2.4, 5.6)
HR (95%CI)	0.54 (0.40, 0.73)	

LBA57: Adagrasib (ADA) vs docetaxel (DOCE) in patients (pts) with KRASG12C-mutated advanced NSCLC and baseline brain metastases (BM): Results from KRYSTAL-12 – Barlesi F, et al

- **Key results (cont.)**

	With baseline brain metastases		Without baseline brain metastases		All	
TRAEs, n (%)	Adagrasib (n=77)	Docetaxel (n=35)	Adagrasib (n=221)	Docetaxel (n=105)	Adagrasib (n=298)	Docetaxel (n=140)
All	72 (94)	30 (86)	208 (94)	91 (87)	280 (94)	121 (86)
Led to discontinuation	5 (7)	6 (17)	18 (8)	14 (13)	23 (8)	20 (14)
Led to dose reduction	36 (47)	12 (34)	107 (48)	21 (20)	143 (48)	33 (24)
Led to dose interruption	39 (51)	4 (11)	138 (62)	22 (21)	177 (59)	26 (19)
SAEs	13 (17)	8 (23)	49 (22)	15 (14)	62 (21)	23 (16)
Led to death	0	1 (3)	4 (2)	0	4 (1)	1 (<1)

- **Conclusions**
  - In patients with advanced KRAS G12C-mutant NSCLC and baseline treated brain metastases, adagrasib demonstrated CNS specific activity and favorable intracranial TTP compared with docetaxel, and continued to provide survival benefit regardless of baseline brain metastasis status

608O: Preliminary safety and clinical activity of ASP3082, a first-in-class, KRAS G12D selective protein degrader in adults with advanced pancreatic (PC), colorectal (CRC), and non-small cell lung cancer (NSCLC) – Park W, et al

- **Study objective**
  - To evaluate the efficacy and safety of ASP3082 (a KRAS G12D selective protein degrader) in patients with advanced NSCLC, pancreatic or colorectal cancer

Key patient inclusion criteria

- Advanced KRAS G12D-positive solid tumors (RECIST v1.1)
- No benefit from prior standard therapy
- ECOG PS 0–2

(n=111)

- **Cohort 1**: ASP3082 10 mg IV qw (n=20)
- **Cohort 2**: ASP3082 20 mg IV qw (n=44)
- **Cohort 3**: ASP3082 40 mg IV qw (n=20)
- **Cohort 4**: ASP3082 60 mg IV qw (n=30)
- **Cohort 5**: ASP3082 90 mg IV qw (n=12)
- **Cohort 6**: ASP3082 140 mg IV qw (n=10)
- **Cohort 7**: ASP3082 200 mg IV qw (n=20)
- **Cohort 8**: ASP3082 300 mg IV qw (n=30)
- **Cohort 9**: ASP3082 450 mg IV qw (n=12)
- **Cohort 10**: ASP3082 600 mg IV qw (n=10)

Primary endpoint

- Safety (DLT, MTD, RP2D)

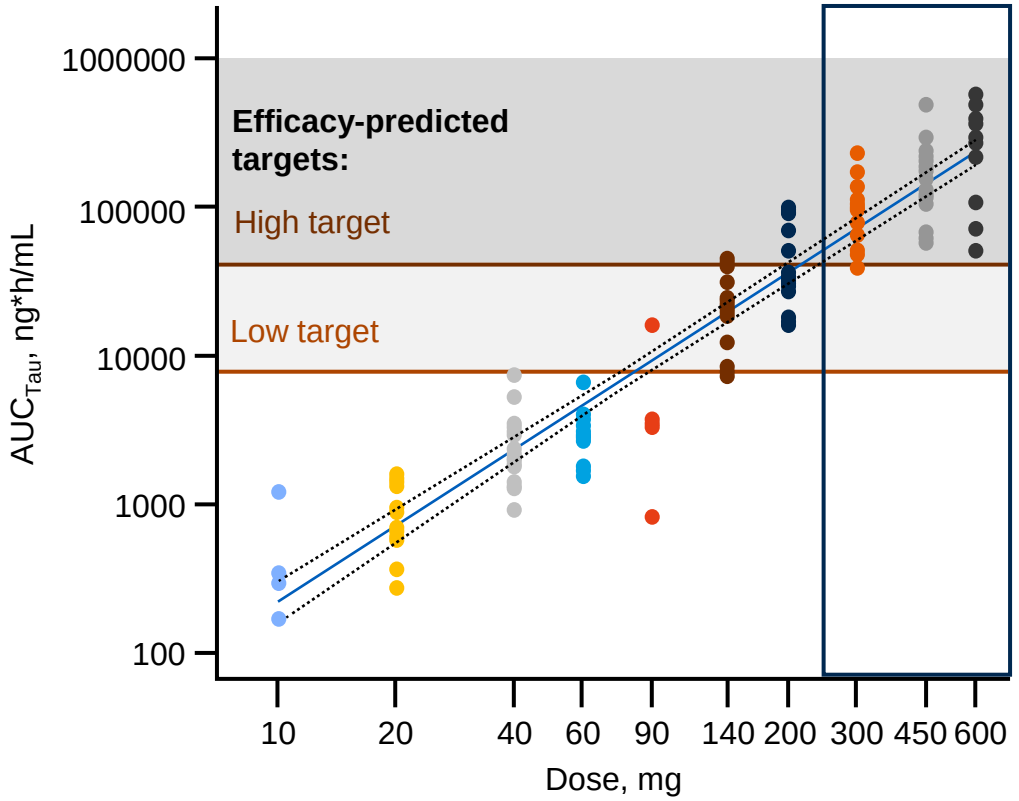
Secondary endpoints

- ORR, DCR, PK

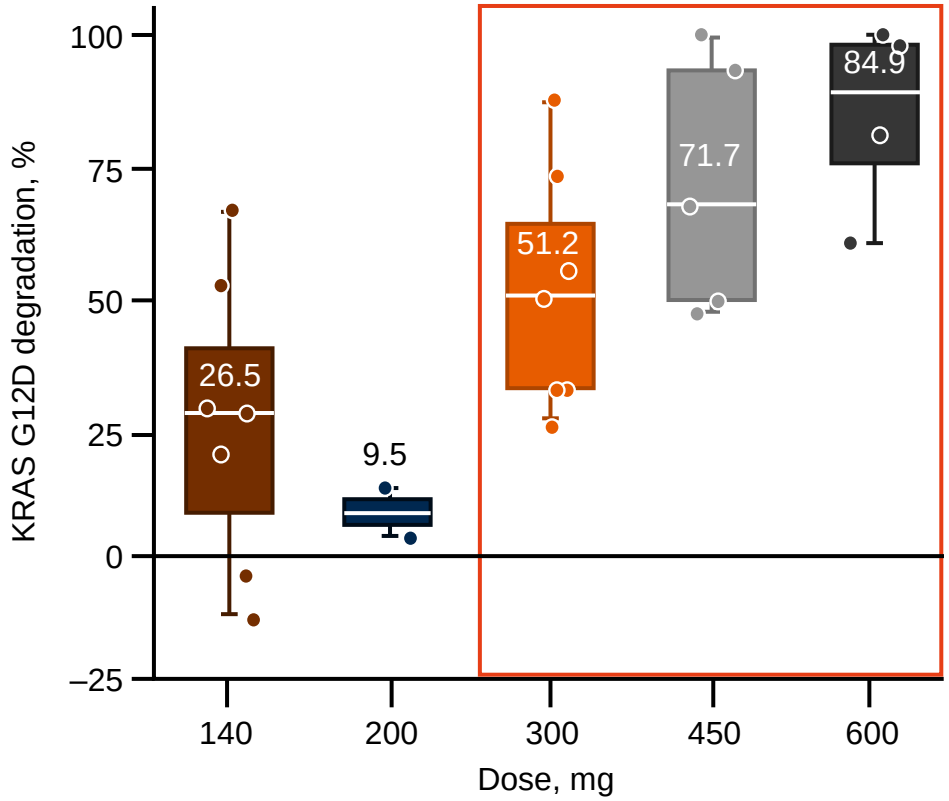
608O: Preliminary safety and clinical activity of ASP3082, a first-in-class, KRAS G12D selective protein degrader in adults with advanced pancreatic (PC), colorectal (CRC), and non-small cell lung cancer (NSCLC) – Park W, et al

- **Key results**

ASP3082 exposure in blood



KRAS G12D degradation by IHC



608O: Preliminary safety and clinical activity of ASP3082, a first-in-class, KRAS G12D selective protein degrader in adults with advanced pancreatic (PC), colorectal (CRC), and non-small cell lung cancer (NSCLC) – Park W, et al

- **Key results (cont.)**

Responses in patients with PDAC

	Response by prior lines of therapy		
	≤2 (n=17)	≥3 (n=10)	Overall (n=27)
ORR, n (%)	4 (23.5)	1 (10.0)	5 (18.5)
DCR, n (%)	8 (47.1)	5 (50.0)	13 (48.1)

Responses in patients with NSCLC

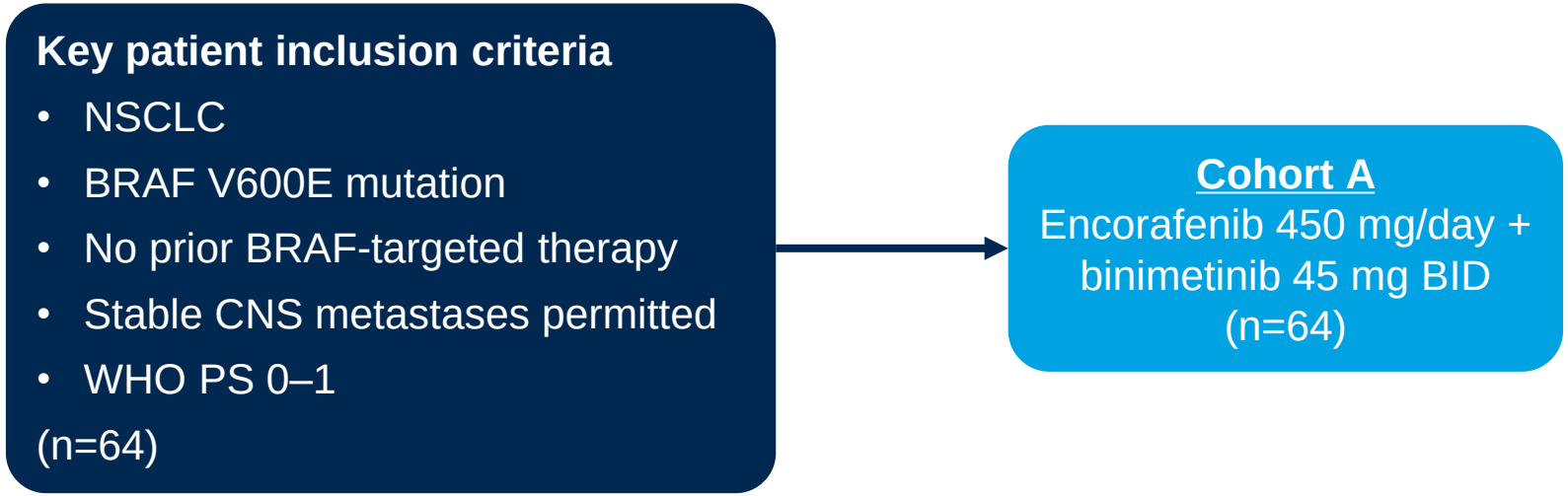
	ASP3082 monotherapy (n=13)
ORR, n (%)	3 (23.1)
DCR, n (%)	11 (84.6)

	Any grade		Grade 3	
AEs, n (%)	300–600 mg (n=48)	Overall (n=111)	300–600 mg (n=48)	Overall (n=111)
TRAEs	43 (89.6)	83 (74.8)	5 (10.4)	7 (6.3)
TRAEs occurring in ≥5%				
Infusion-related reaction	17 (35.4)	21 (18.9)	0	0
Fatigue	6 (12.5)	20 (18.0)	1 (2.1)	1 (0.9)
Rash	10 (20.8)	13 (11.7)	0	0
Urticaria	9 (18.8)	11 (9.9)	0	0
Nausea	5 (10.4)	10 (9.0)	0	0
Pruritus	6 (12.5)	9 (8.1)	0	0
AST increased	6 (12.5)	8 (7.2)	2 (4.2)	2 (1.8)
Vomiting	3 (6.3)	6 (5.4)	0	0

- **Conclusions**
  - In patients with advanced KRAS G12D-mutant NSCLC, pancreatic or colorectal cancer, ASP3082 showed promising antitumour activity with a manageable safety profile

1259MO: Encorafenib plus binimetinib in patients (pts) with previously untreated BRAF V600E-mutant advanced Non-Small Cell Lung Cancer (NSCLC): an open-label, multicenter phase 2 trial (IFCT-1904 ENCO-BRAF) – Planchard D, et al

- **Study objective**
  - To evaluate the efficacy and safety of encorafenib + binimetinib in treatment-naïve patients with advanced BRAF V600E-mutant NSCLC in the phase 2 IFCT-1904 ENCO-BRAF study



Primary endpoint

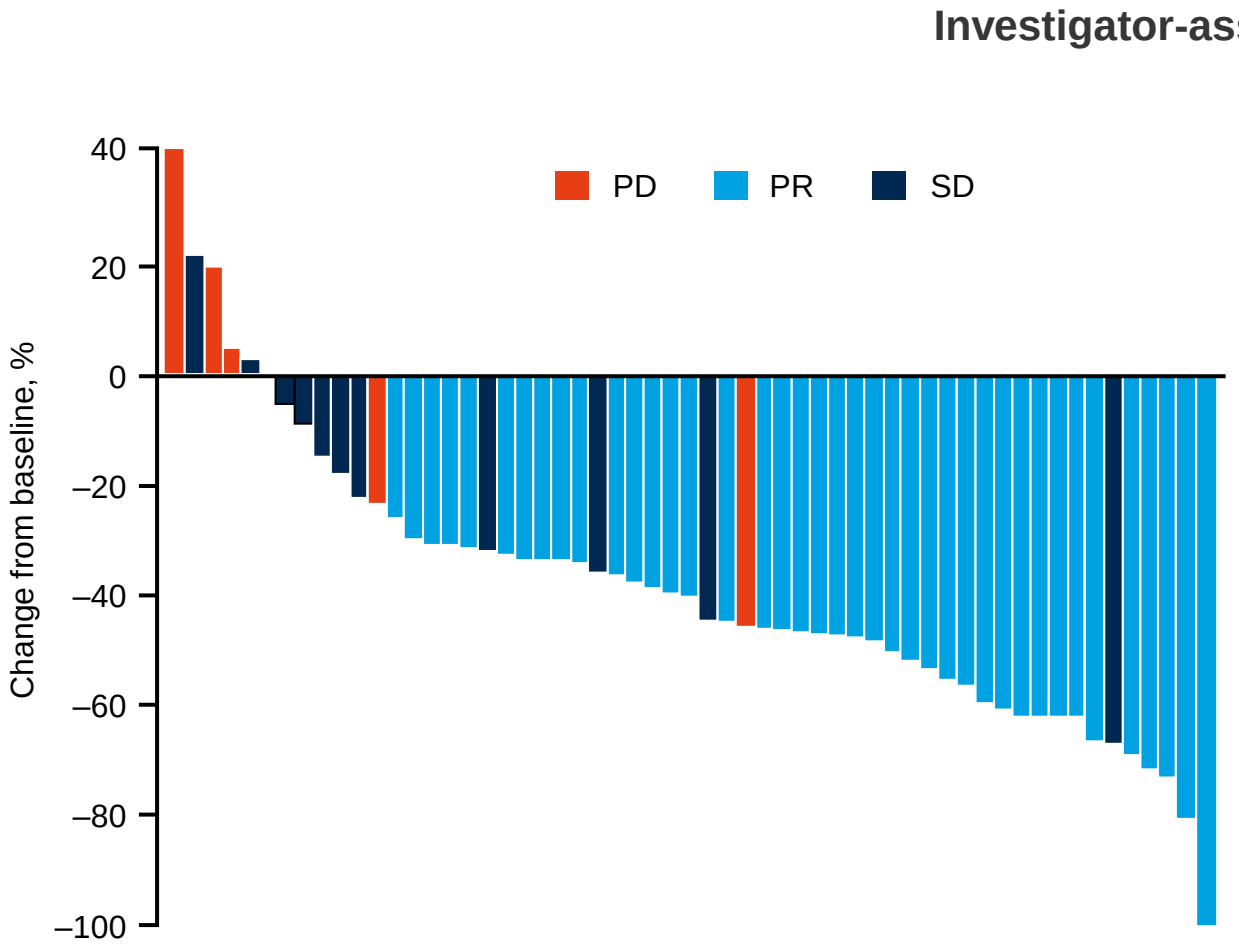
- ORR (RECIST v1.1)

Secondary endpoints

- PFS, DoR, OS, safety

1259MO: Encorafenib plus binimetinib in patients (pts) with previously untreated BRAF V600E-mutant advanced Non-Small Cell Lung Cancer (NSCLC): an open-label, multicenter phase 2 trial (IFCT-1904 ENCO-BRAF) – Planchard D, et al

- **Key results**



	Cohort A (n=61)
cORR, n (%) [95%CI]	40 (65.6) [53.7, 77.5]
BOR, n (%)	
PR	40 (65.6)
SD	12 (19.7)
PD	5 (8.2)
NE	4 (6.6)
mDoR, mo (95%CI)	13 (9.1, NR)
DCR, % (95%CI][a]	85.2 (76.3, 94.1)

[a]Four patients were not evaluable.

Planchard D, et al. Ann Oncol 2024;35(suppl):Abstr 1259MO

1259MO: Encorafenib plus binimetinib in patients (pts) with previously untreated BRAF V600E-mutant advanced Non-Small Cell Lung Cancer (NSCLC): an open-label, multicenter phase 2 trial (IFCT-1904 ENCO-BRAF) – Planchard D, et al

- **Key results (cont.)**

Patients, n (%)	All
Any grade TEAEs	64 (100)
Grade ≥3	47 (73.4)
Any grade TRAEs	59 (92.2)
Grade ≥3	32 (50.0)
Led to encorafenib/binimetinib discontinuation	6 (9.4)
Led to encorafenib/binimetinib dose interruption	21 (32.8)/23 (35.9)
Led to encorafenib/binimetinib dose reduction	22 (34.4)/21 (32.8)
Led to death	2 (3.1)

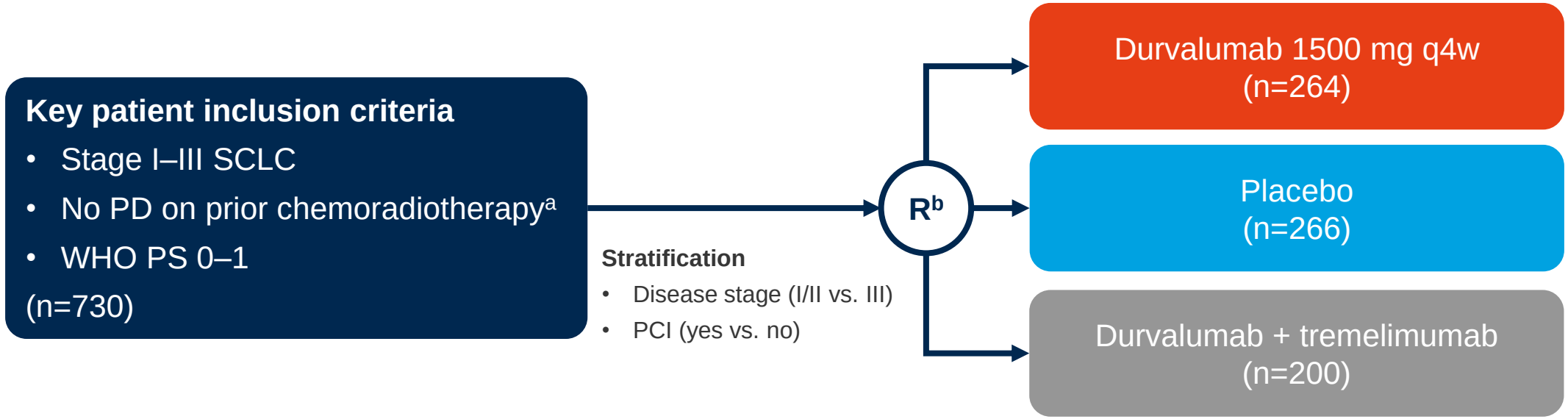
- **Conclusions**
  - In patients with advanced BRAF V600E-mutant NSCLC, 1L encorafenib + binimetinib showed promising antitumor activity and had a manageable safety profile

Other malignancies

SCLC, mesothelioma and thymic epithelial tumors

LBA81: Durvalumab (D) as consolidation therapy in limited-stage SCLC (LS-SCLC): outcomes by prior concurrent chemoradiotherapy (cCRT) regimen and prophylactic cranial irradiation (PCI) use in the ADRIATIC trial – Senan S, et al

- **Study objective**
  - To evaluate the outcomes with consolidation durvalumab according to prior concurrent chemoradiotherapy and prophylactic cranial irradiation use in patients with limited-stage SCLC in the ADRIATIC study



Dual primary endpoints

- OS, PFS (BICR, RECIST v1.1) for durvalumab vs. placebo

Secondary endpoints

- PFS, OS, safety

[a]If received, treatment must have been completed ≤42 days prior randomization;
[b]the first 600 patients were randomized 1:1:1, then 1:1 to either durvalumab or placebo.

Senan S, et al. Ann Oncol 2024;35(suppl):Abstr LBA81

LBA81: Durvalumab (D) as consolidation therapy in limited-stage SCLC (LS-SCLC): outcomes by prior concurrent chemoradiotherapy (cCRT) regimen and prophylactic cranial irradiation (PCI) use in the ADRIATIC trial – Senan S, et al

- **Key results**

	PCI yes		PCI no		ITT	
	Durvalumab (n=142)	Placebo (n=143)	Durvalumab (n=122)	Placebo (n=123)	Durvalumab (n=264)	Placebo (n=266)
mOS, mo (95%CI)	NR (43.9, NE)	42.5 (33.4, NE)	37.3 (24.3, NE)	24.1 (18.8, 31.1)	55.9 (37.3, NE)	33.4 (25.5, 39.9)
3-year OS, %	62.1	56.5	50.2	37.3	56.5	47.6
HR (95%CI)	0.75 (0.52, 1.07)[a]		0.71 (0.51, 0.99)[a]		0.73 (0.57, 0.93)[c]	
Multivariate HR (95%CI)	0.72 (0.50, 1.03)[b]		0.73 (0.52, 1.02)[b]		-	
mPFS, mo (95%CI)	28.2 (16.8, 44.2)	13.0 (9.2, 17.0)	9.1 (7.3, 14.3)	7.4 (5.7, 9.2)	16.6 (10.2, 28.2)	9.2 (7.4, 12.9)
2-year PFS, %	54.6	38.5	37.1	29.3	46.2	34.2
HR (95%CI)	0.73 (0.52, 1.00)[a]		0.80 (0.59, 1.09)[a]		0.76 (0.61, 0.95)[c]	
Multivariate HR (95%CI)	0.72 (0.52, 0.99)[b]		0.84 (0.61, 1.15)[b]		-	

	Carboplatin chemotherapy		Cisplatin chemotherapy		ITT	
OS by chemotherapy subgroups	Durvalumab (n=91)	Placebo (n=88)	Durvalumab (n=173)	Placebo (n=178)	Durvalumab (n=264)	Placebo (n=266)
mOS, mo (95%CI)	NR (42.5, NE)	33.4 (21.7, NE)	41.9 (27.7, NE)	34.3 (25.4, 40.7)	55.9 (37.3, NE)	33.4 (25.5, 39.9)
3-year OS, %	65.3	46.7	52.1	48.1	56.5	47.6
HR (95%CI)	0.56 (0.35, 0.89)[a]		0.82 (0.61, 1.10)[a]		0.73 (0.57, 0.93)[c]	
Multivariate HR (95%CI)	0.55 (0.35, 0.87)[b]		0.81 (0.60, 1.08)[b]		-	

[a]Unstratified Cox proportional hazards model; [b]Cox proportional hazard model stratified by receipt of PCI; [c]multivariate analysis interaction p=0.96.

Senan S, et al. Ann Oncol 2024;35(suppl):Abstr LBA81

LBA81: Durvalumab (D) as consolidation therapy in limited-stage SCLC (LS-SCLC): outcomes by prior concurrent chemoradiotherapy (cCRT) regimen and prophylactic cranial irradiation (PCI) use in the ADRIATIC trial – Senan S, et al

- **Key results (cont.)**

	BID RT		QD RT		ITT	
	Durvalumab (n=69)	Placebo (n=79)	Durvalumab (n=195)	Placebo (n=187)	Durvalumab (n=264)	Placebo (n=266)
mOS, mo (95%CI)	NR (NE, NE)	44.8 (29.4, NE)	41.9 (32.0, NE)	26.1 (21.7, 36.8)	55.9 (37.3, NE)	33.4 (25.5, 39.9)
3-year OS, %	65.8	57.4	53.1	43.3	56.5	47.6
HR (95%CI)	0.68 (0.40, 1.14)[a]		0.72 (0.55, 0.96)[a]		0.73 (0.57, 0.93)[c]	
Multivariate HR (95%CI)	0.71 (0.42, 1.18)[b]		0.73 (0.55, 0.96)[b]		-	
mPFS, mo (95%CI)	38.2 (22.7, NE)	14.3 (9.1, 28.1)	11.4 (9.0, 19.5)	7.8 (6.4, 11.5)	16.6 (10.2, 28.2)	9.2 (7.4, 12.9)
2-year PFS, %	60.5	42.9	41.0	30.3	46.2	34.2
HR (95%CI)	0.72 (0.45, 1.13)[a]		0.77 (0.60, 1.00)[a]		0.76 (0.61, 0.95)[c]	
Multivariate HR (95%CI)	0.73 (0.46, 1.14)[b]		0.79 (0.61, 1.03)[b]		-	

	PCI				Chemotherapy				Radiotherapy			
	PCI yes		PCI no		Carboplatin		Cisplatin		QD		BID	
TEAEs, %	Durvalumab	PBO	Durvalumab	PBO	Durvalumab	PBO	Durvalumab	PBO	Durvalumab	PBO	Durvalumab	PBO
Grade 3/4	28.4	29.6	19.8	17.9	31.5	31.8	20.8	20.3	18.8	22.8	26.4	24.7
Led to discontinuation	17.0	15.5	15.7	4.9	16.9	10.2	16.2	10.7	17.4	6.3	16.1	12.4

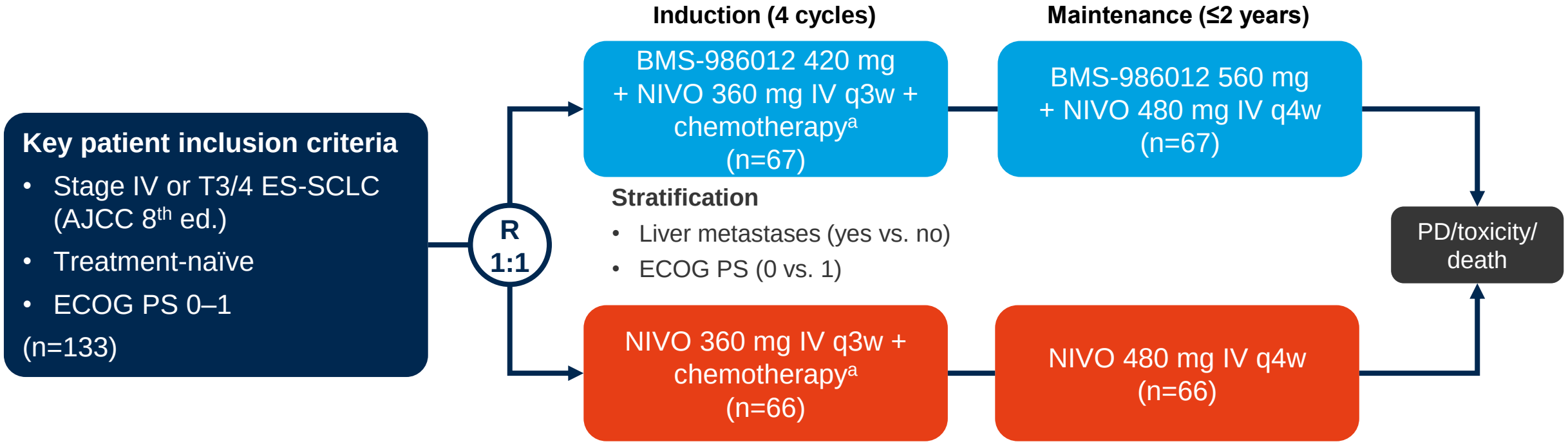
- **Conclusions**
  - In patients with limited-stage SCLC, consolidation with durvalumab was associated with statistically significant improvements in survival across subgroups compared with placebo and was well tolerated

[a]Unstratified Cox proportional hazards model; [b]Cox proportional hazard model stratified by receipt of PCI; [c]multivariate analysis interaction p=0.96.

Senan S, et al. Ann Oncol 2024;35(suppl):Abstr LBA81

1786O: BMS-986012 (anti-fucosyl-monosialoganglioside-1 [fuc-GM1]) with carboplatin + etoposide + nivolumab (CE/NIVO) as first-line (1L) therapy in extensive-stage small cell lung cancer (ES-SCLC): interim analysis (IA) of a randomized phase 2 study – Kalinka E, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L BMS-986012 (an anti-fucosyl-monosialoganglioside-1) + carboplatin + etoposide + nivolumab in patients with extensive-stage SCLC in a phase 2 study



Primary endpoints

- Safety, PFS (BICR, RECIST v1.1.)

Secondary endpoints

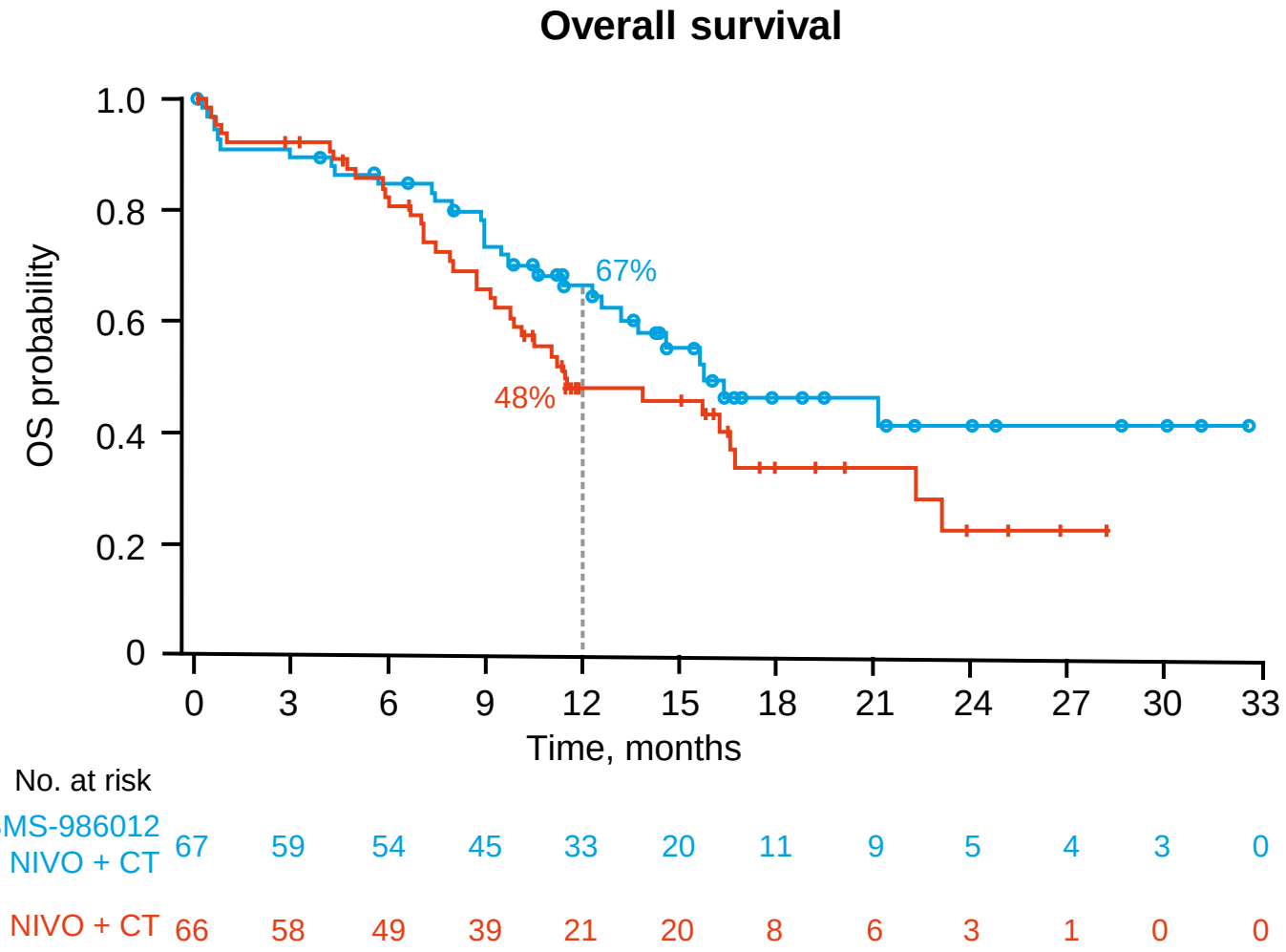
- OS, ORR, DoR, TTR

[a]Carboplatin AUC5 mg/mL/min IV D1 + etoposide 100 mg/m^2 IV D1, 2, 3.

Kalinka E, et al. Ann Oncol 2024;35(suppl):Abstr 1786O

1786O: BMS-986012 (anti-fucosyl-monosialoganglioside-1 [fuc-GM1]) with carboplatin + etoposide + nivolumab (CE/NIVO) as first-line (1L) therapy in extensive-stage small cell lung cancer (ES-SCLC): interim analysis (IA) of a randomized phase 2 study – Kalinka E, et al

- **Key result**



	BMS-986012 + NIVO + CT (n=67)	NIVO + CT (n=66)
mOS, mo (95%CI)	15.6 (12.5, NA)	11.4 (9.3, 16.6)
HR (95%CI)	0.71 (0.44, 1.16)	

Patients with baseline brain metastases	BMS-986012 + NIVO + CT (n=19)	NIVO + CT (n=15)
mOS, mo (95%CI)	16.3 (10.5, NA)	8.7 (6.6, 23.1)
HR (95%CI)	0.59 (0.24, 1.49)	

Patients without baseline brain metastases	BMS-986012 + NIVO + CT (n=48)	NIVO + CT (n=51)
mOS, mo (95%CI)	15.5 (11.3, NA)	13.8 (9.7, 16.6)
HR (95%CI)	0.72 (0.41, 1.28)	

1786O: BMS-986012 (anti-fucosyl-monosialoganglioside-1 [fuc-GM1]) with carboplatin + etoposide + nivolumab (CE/NIVO) as first-line (1L) therapy in extensive-stage small cell lung cancer (ES-SCLC): interim analysis (IA) of a randomized phase 2 study – Kalinka E, et al

- **Key results (cont.)**

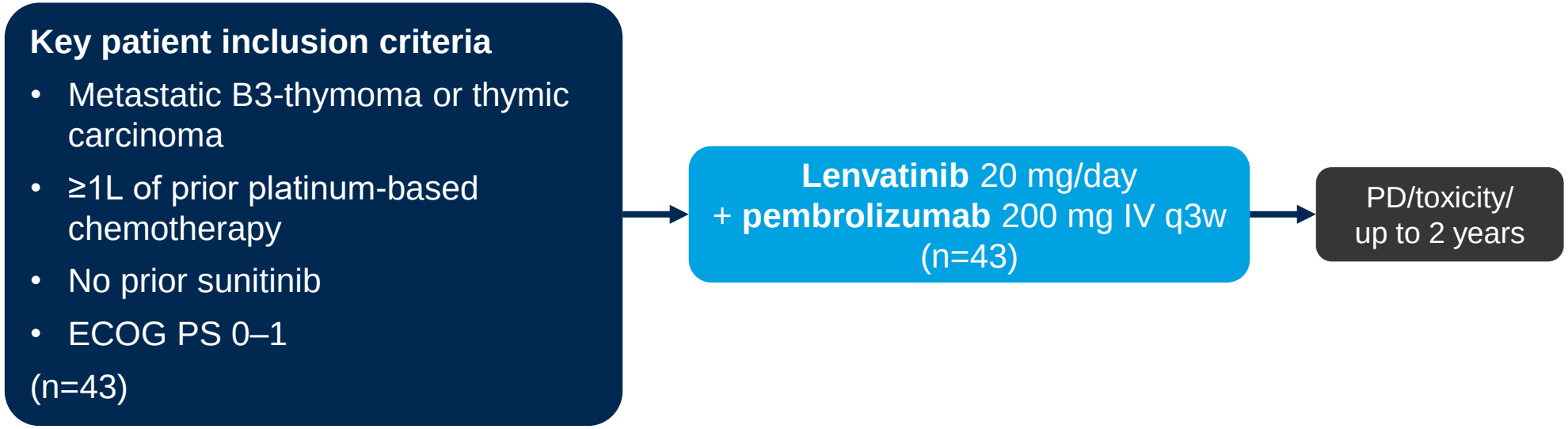
	BMS-986012 + NIVO + CT (n=67)	NIVO + CT (n=64)
mPFS, mo (95%CI)	5.8 (5.0, 7.9)	5.2 (4.8, 6.6)
HR (95%CI); p-value	0.89 (0.57, 1.40); p=0.61	
6-mo PFS rate, %	46	43
ORR, % (95%CI)	73 (61, 83)	68 (56, 79)
BOR, n (%)		
CR	5 (7)	2 (3)
PR	44 (66)	43 (65)
SD	9 (13)	13 (20)
PD	0	1 (2)
Not determined	9 (13)	7 (11)

	BMS-986012 + NIVO + CT (n=66)		NIVO + CT (n=64)	
AEs, n (%)	Any grade	Grade 3/4	Any grade	Grade 3/4
Any AE	66 (100)	35 (53)	63 (98)	36 (56)
SAE	35 (53)	21 (32)	31 (49)	19 (30)
TRAE	61 (92)	33 (50)	60 (94)	29 (45)
AE led to discontinuation	11 (17)	7 (11)	14 (22)	9 (14)
TRAE led to discontinuation	5 (8)	4 (6)	9 (14)	6 (9)
Treatment-related death	2 (3)		3 (5)	

- **Conclusions**
  - At an interim analysis, in patients with extensive-stage SCLC, 1L BMS-986012 combined with carboplatin + etoposide + nivolumab did not demonstrate an improvement in PFS, although there was a non-significant numerical OS superiority, and had a manageable safety profile

LBA83: PECATI: A phase 2 trial to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma – Masip JR, et al

- **Study objective**
  - To evaluate the efficacy and safety of lenvatinib + pembrolizumab in previously treated patients with B3-thymoma and thymic carcinoma in the phase 2 PECATI study



Primary endpoint

- 5-mo PFS (investigator assessed, RECIST v1.1)

Secondary endpoints

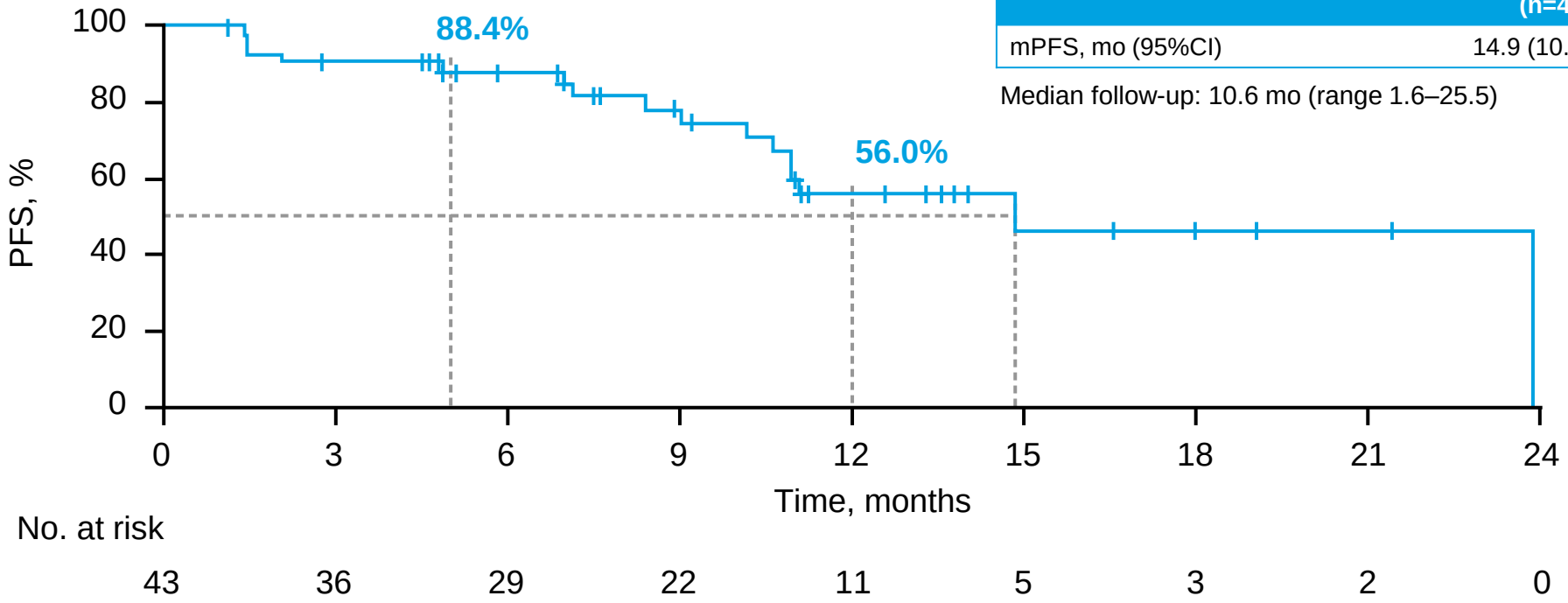
- ORR, OS, safety

Masip JR, et al. Ann Oncol 2024;35(suppl):Abstr LBA83

LBA83: PECATI: A phase 2 trial to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma – Masip JR, et al

- **Key results**

Progression-free survival



	Lenvatinib + pembrolizumab (n=43)
mPFS, mo (95%CI)	14.9 (10.6, NA)

Median follow-up: 10.6 mo (range 1.6–25.5)

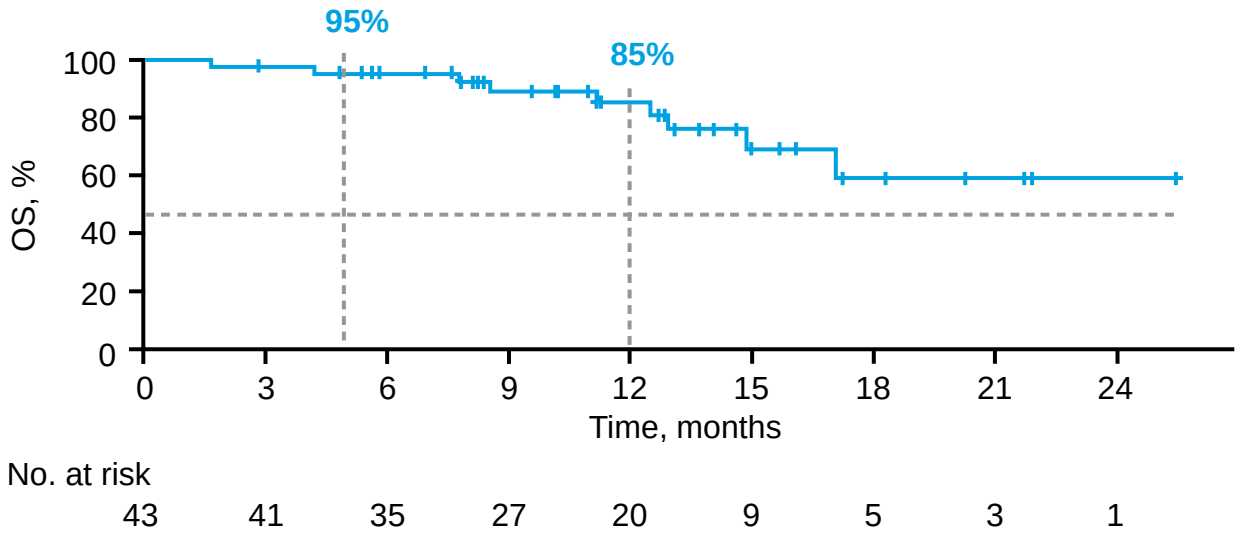
LBA83: PECATI: A phase 2 trial to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma – Masip JR, et al

- **Key results**

Overall survival

	Lenvatinib + pembrolizumab (n=43)
mOS, mo (95%CI)	NR

Median follow-up: 10.6 mo (range 1.6−25.5)



	Lenvatinib + pembrolizumab (n=43)
ORR, % (95%CI)	23.3 (11.8, 38.6)
BOR, n (%)	
PR	10 (23.3)
PD	2 (4.7)
NE	1 (2.3)
SD≥24 week	22 (51.2)
SD<24 week	8 (18.6)
mDoR, mo (95%CI)	8.2 (6.1, NE)

Masip JR, et al. Ann Oncol 2024;35(suppl):Abstr LBA83

LBA83: PECATI: A phase 2 trial to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma – Masip JR, et al

- **Key results (cont.)**

AEs, n (%)	Lenvatinib + pembrolizumab (n=43)
Any AEs	42 (97.7)
Grade ≥3 TEAEs	20 (46.5)
Grade ≥3 TRAEs	16 (37.2)
Treatment-related grade ≥3 SAEs	7 (16.3)
TRAE led to discontinuation	11 (25.6)

AEs, n (%)	Lenvatinib	Pembrolizumab
Median number of cycles administered, range	13 (1–35)	12 (1–35)
irAEs	-	6 (13.9)[a]
Grade ≥3 TRAEs	8 (18.6)	4 (9.3)
TRAEs led to temporary dose interruption	25 (58.1)	21 (48.8)
TRAEs led to discontinuation	10 (23.3)	8 (18.6)

- **Conclusions**
  - In pretreated patients with B3-thymoma and thymic carcinoma, lenvatinib + pembrolizumab showed promising PFS and OS benefit and had a manageable safety profile although close monitoring is recommended

[a]n=22, pneumonitis, myocarditis, encephalitis, myositis, cardiac dysfunction, cytolysis.

Masip JR, et al. Ann Oncol 2024;35(suppl):Abstr LBA83