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

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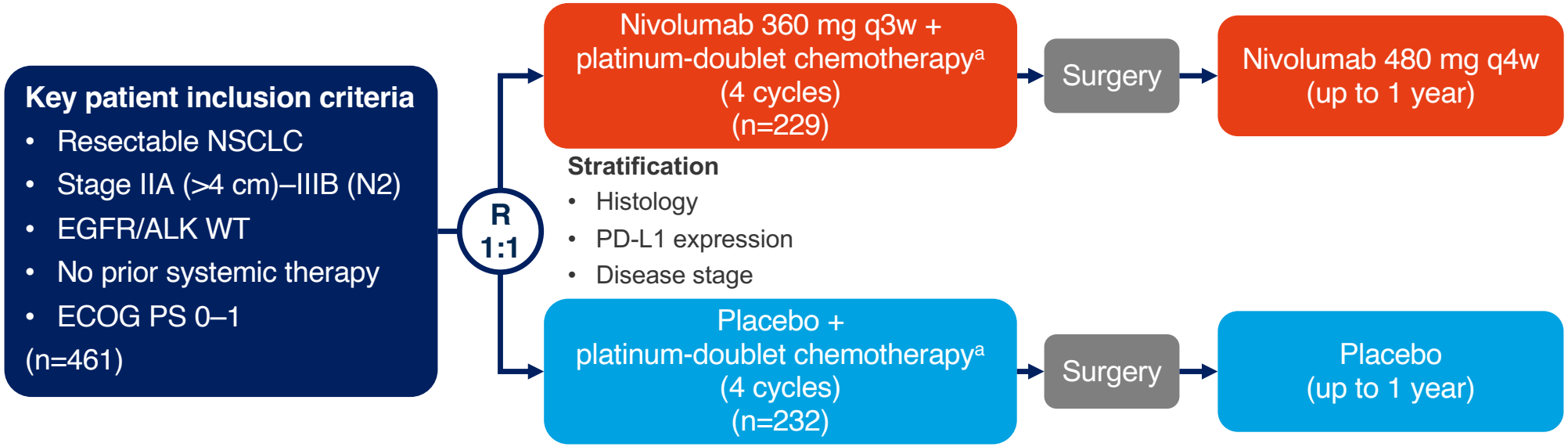
LBA1: CheckMate 77T: Phase 3 study comparing neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) vs neoadjuvant placebo plus chemo followed by surgery and adjuvant NIVO or placebo for previously untreated, resectable stage II–IIIB NSCLC – Cascone T, et al

- **Study objective**
  - To evaluate the efficacy and safety of neoadjuvant nivolumab + chemotherapy followed by adjuvant nivolumab in treatment-naïve patients with resectable stage II–IIIB NSCLC in the phase 3 CheckMate 77T study



Primary endpoint

- EFS (RECIST v1.1, BICR)

Secondary endpoints

- pCR, MPR, OS, safety

[a]Nonsquamous: cisplatin + pemetrexed, carboplatin + pemetrexed, or carboplatin + paclitaxel; squamous: cisplatin + docetaxel or carboplatin + paclitaxel.

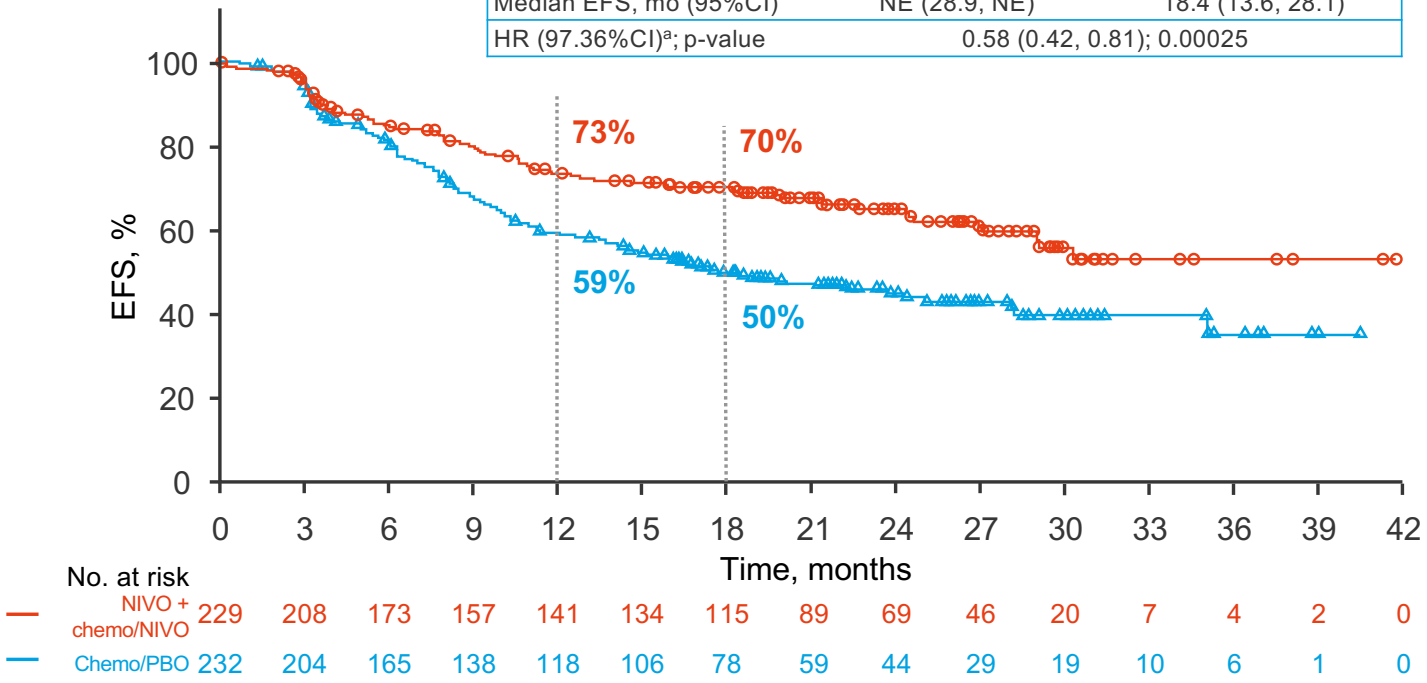
Cascone T, et al. Ann Oncol 2023;34(suppl):Abstr LBA1

LBA1: CheckMate 77T: Phase 3 study comparing neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) vs neoadjuvant placebo plus chemo followed by surgery and adjuvant NIVO or placebo for previously untreated, resectable stage II–IIIB NSCLC – Cascone T, et al

- **Key results (cont.)**

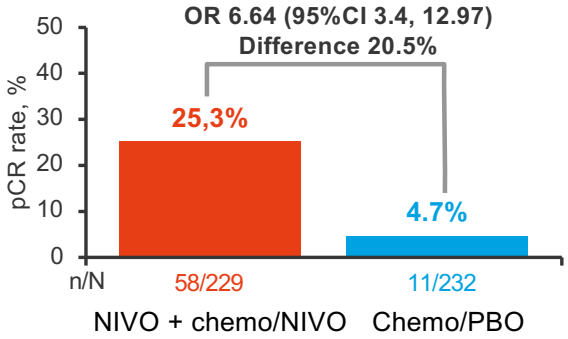
EFS[a] per BICR

	NIVO + chemo/NIVO (n=229)	Chemo/PBO (n=232)
Median EFS, mo (95%CI)	NE (28.9, NE)	18.4 (13.6, 28.1)
HR (97.36%CI)[a]; p-value	0.58 (0.42, 0.81); 0.00025	

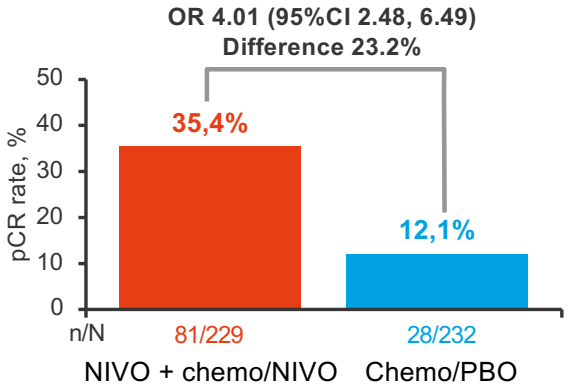


[b]Unstratified HR 0.59 (95%CI 0.44, 0.79).

pCR (BIPR)



MPR (BIPR)

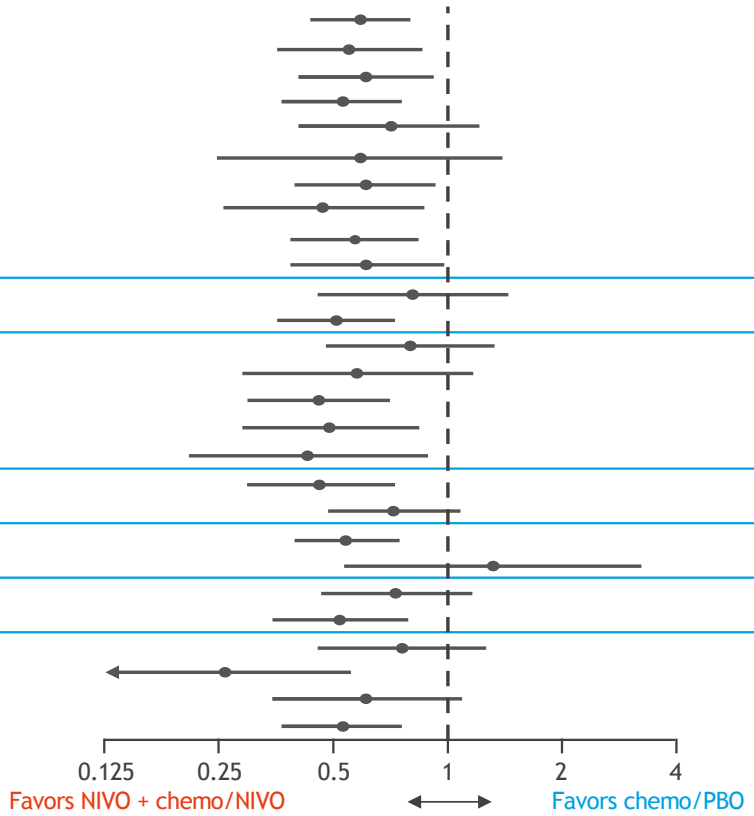


Cascone T, et al. Ann Oncol 2023;34(suppl):Abstr LBA1

LBA1: CheckMate 77T: Phase 3 study comparing neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) vs neoadjuvant placebo plus chemo followed by surgery and adjuvant NIVO or placebo for previously untreated, resectable stage II–IIIB NSCLC – Cascone T, et al

- **Key results (cont.)**

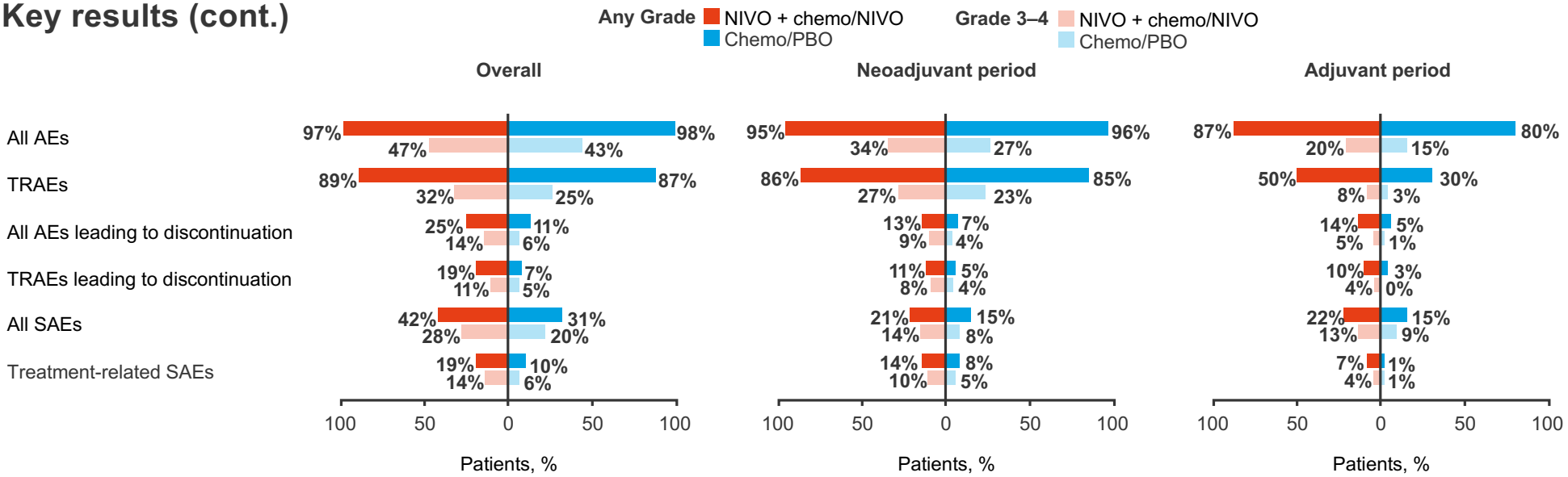
	Median EFS, mo		Unstratified HR (95%CI)
	NIVO + chemo/NIVO (n=229)	Chemo/PBO (n=232)	
Overall (N=461)	NR	18.4	0.59 (0.44, 0.79)
<65 years (n=202)	NR	16.7	0.55 (0.36, 0.85)
≥65 years (n=259)	NR	20.1	0.61 (0.41, 0.91)
Male (n=327)	NR	16.7	0.53 (0.37, 0.75)
Female (n=134)	30.2	18.8	0.71 (0.41, 1.20)
North America (n=44)	30.2	9.4	0.59 (0.25, 1.38)
Europe (n=250)	NR	23.7	0.61 (0.40, 0.92)
Asia (n=115)	NR	13.9	0.47 (0.26, 0.86)
ECOG PS 0 (n=288)	NR	20.1	0.57 (0.39, 0.83)
ECOG PS 1 (n=173)	29.0	17.3	0.61 (0.39, 0.97)
Stage II (n=162)	NR	NR	0.81 (0.46, 1.43)
Stage III (n=297)	30.2	13.4	0.51 (0.36, 0.72)
N0 (n=167)	NR	NR	0.80 (0.48, 1.32)
N1 (n=108)	NR	28.1	0.58 (0.29, 1.16)
N2 (n=182)	30.2	10.0	0.46 (0.30, 0.70)
Single-station (n=112)	30.2	10.0	0.49 (0.29, 0.84)
Multi-station (n=69)	NR	10.0	0.43 (0.21, 0.88)
Squamous (n=234)	NR	17.0	0.46 (0.30, 0.72)
Nonsquamous (n=227)	28.9	18.4	0.72 (0.49, 1.07)
Current/former smoker (n=417)	NR	17.0	0.54 (0.40, 0.74)
Never smoker (n=44)	19.7	25.0	1.32 (0.54, 3.20)
PD-L1 <1% (n=186)	29.0	19.8	0.73 (0.47, 1.15)
PD-L1 ≥1% (n=256)	NR	15.8	0.52 (0.35, 0.78)
PD-L1 1–49% (n=159)	30.2	28.1	0.76 (0.46, 1.25)
PD-L1 ≥50% (n=97)	NR	8.0	0.26 (0.12, 0.55)
Cisplatin (n=97)	27.0	15.8	0.61 (0.35, 1.08)
Carboplatin (n=347)	NR	17.3	0.53 (0.37, 0.75)



Cascone T, et al. Ann Oncol 2023;34(suppl):Abstr LBA1

LBA1: CheckMate 77T: Phase 3 study comparing neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) vs neoadjuvant placebo plus chemo followed by surgery and adjuvant NIVO or placebo for previously untreated, resectable stage II–IIIB NSCLC – Cascone T, et al

- **Key results (cont.)**

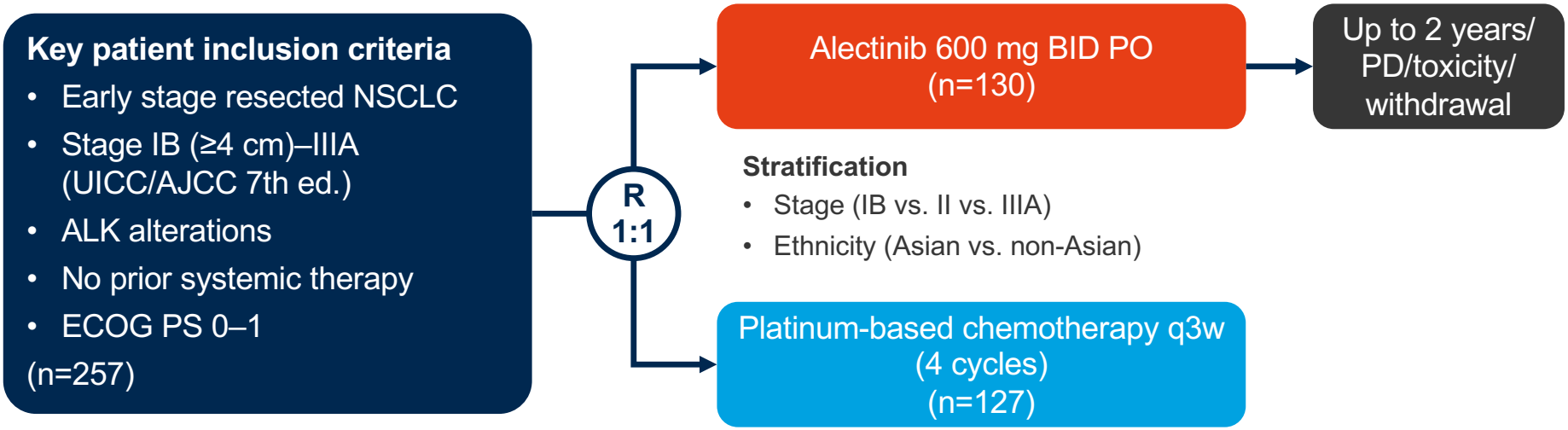


- **Conclusions**
  - In patients with resectable stage II–IIIB NSCLC, perioperative nivolumab + chemotherapy demonstrated a significant improvement in EFS compared with chemotherapy alone and no new safety signals were observed

Cascone T, et al. Ann Oncol 2023;34(suppl):Abstr LBA1

LBA2: ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage ALK+ non-small cell lung cancer (NSCLC) – Solomon BJ, et al

- **Study objective**
  - To evaluate the efficacy and safety of adjuvant alectinib in patients with early stage NSCLC with ALK alterations in the ALINA study



Primary endpoint

- DFS (investigator assessed)

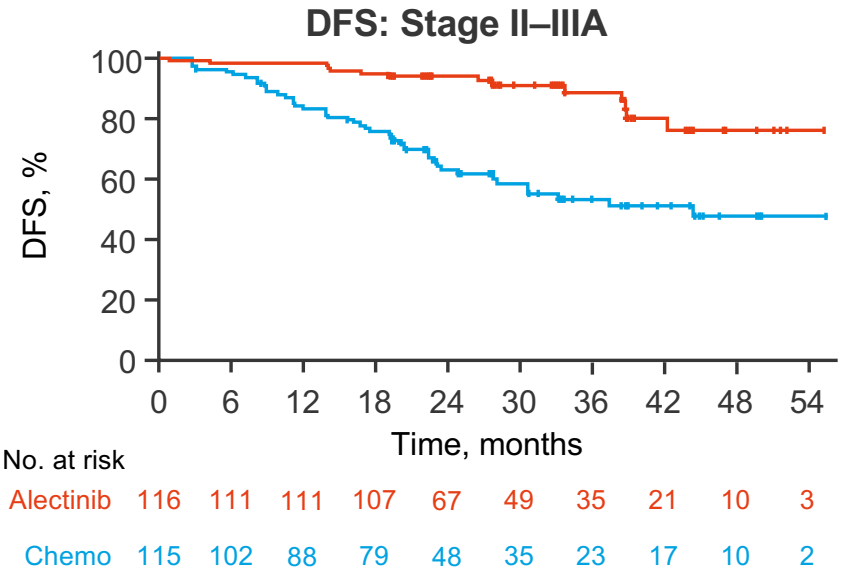
Secondary endpoints

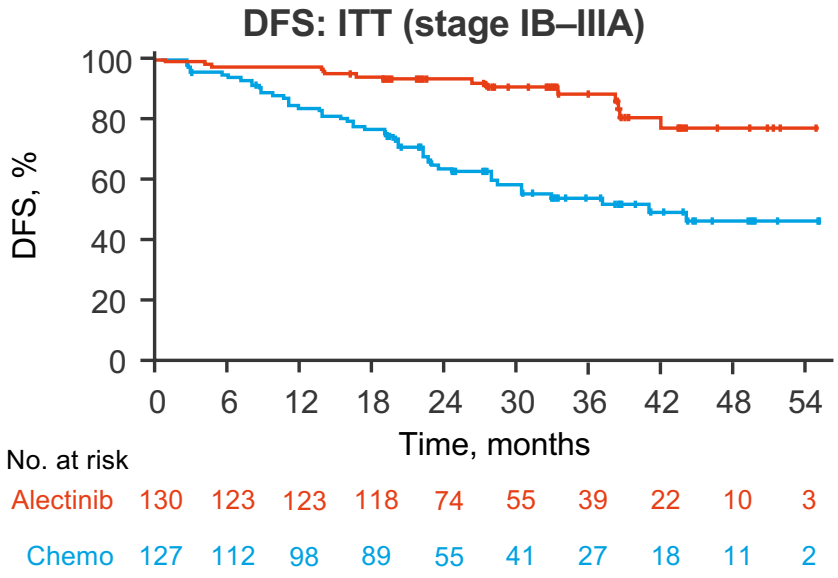
- CNS DFS, OS, safety

Solomon BJ, et al. Ann Oncol 2023;34(suppl):Abstr LBA2

LBA2: ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage ALK+ non-small cell lung cancer (NSCLC) – Solomon BJ, et al

- **Key results**





	Alectinib	Chemotherapy
Events, n (%)	14 (12)	45 (39)
Death, n	0	1
Recurrence, n	14	44
mDFS, mo (95%CI)	NR	44.4 (27.8, NE)
HR (95%CI); p-value[a]	0.24 (0.13, 0.45); <0.0001	
Median follow-up, mo	27.9	27.8

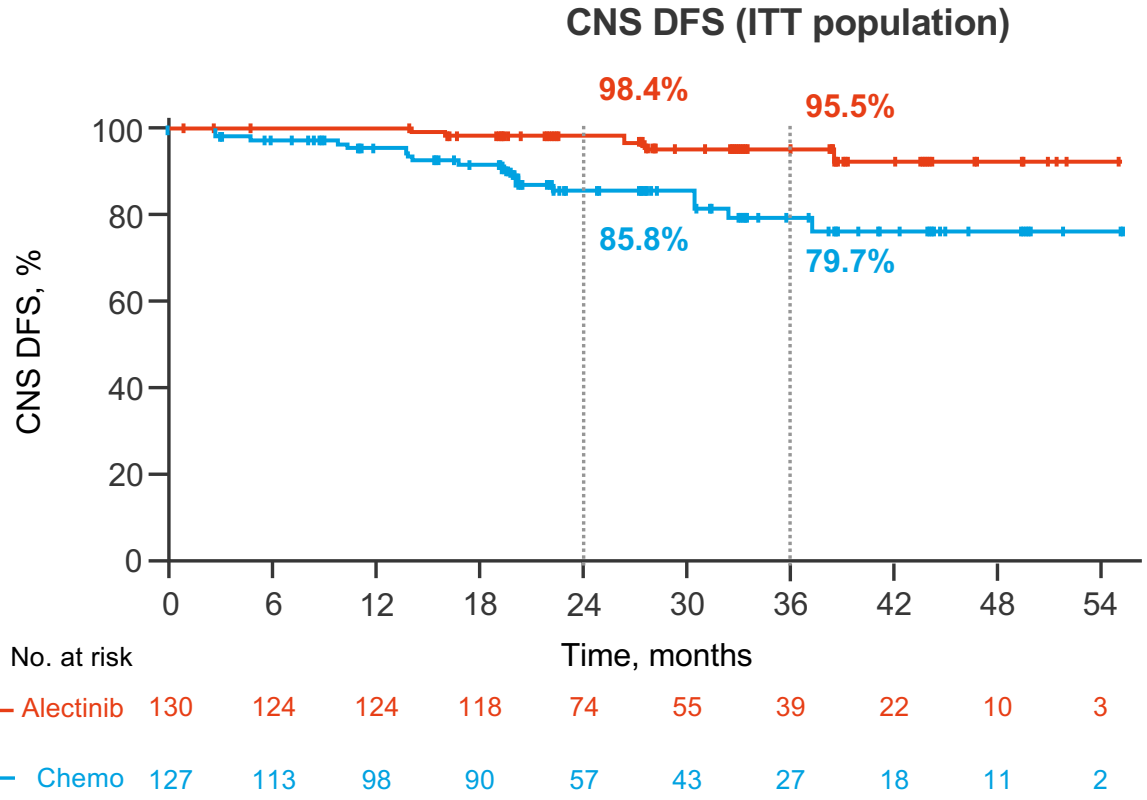
	Alectinib	Chemotherapy
Events, n (%)	15 (12)	50 (39)
Death, n	0	1
Recurrence, n	15	49
mDFS, mo (95%CI)	NR	41.3 (28.5, NE)
HR (95%CI); p-value[a]	0.24 (0.13, 0.43); <0.0001	
Median follow-up, mo	27.8	28.4

[a]Stratified log rank.

Solomon BJ, et al. Ann Oncol 2023;34(suppl):Abstr LBA2

LBA2: ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage ALK+ non-small cell lung cancer (NSCLC) – Solomon BJ, et al

- **Key results (cont.)**



	Alectinib	Chemotherapy
Events, n	5	18
Death, n	1	4
Brain recurrence, n	4	14
CNS DFS HR (95%CI)	0.22 (0.08, 0.58)	
Median follow-up, mo	27.8	28.4

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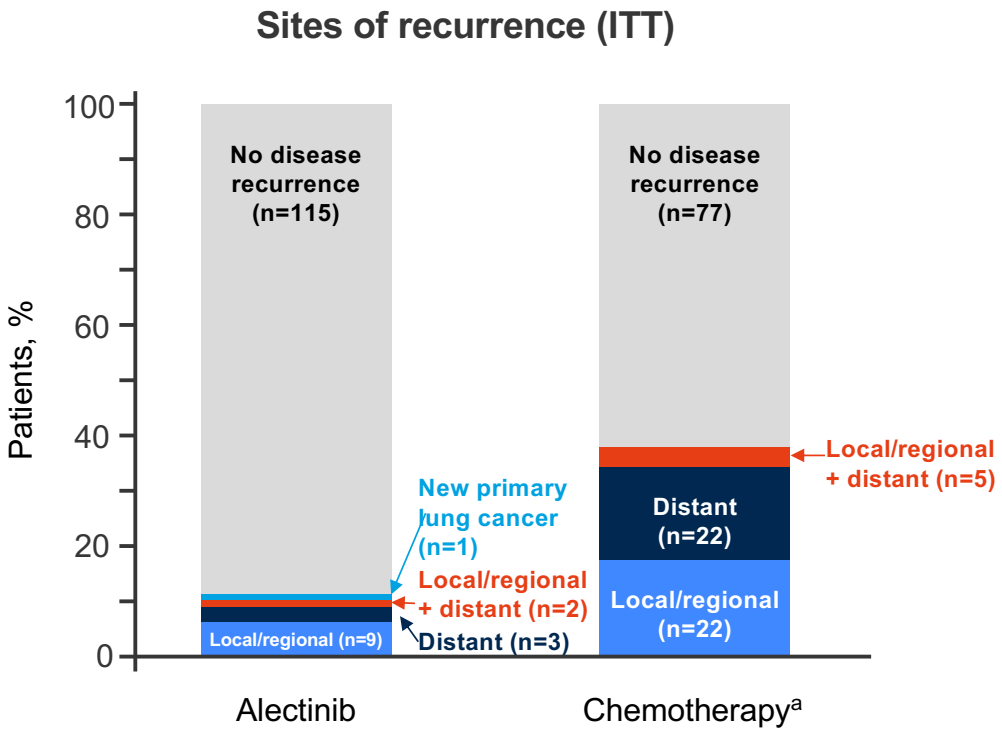
LBA2: ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage ALK+ non-small cell lung cancer (NSCLC) – Solomon BJ, et al

- **Key results**



Sites of recurrence[b]	Alectinib (n=130)	Chemotherapy (n=127)
Brain	4	14
Bone	1	8
Adrenal gland	0	3
Lymph node	0	2
Kidney	0	1
Peritoneum	0	1
Other	1	0

Patients with disease recurrence, n (%)	Alectinib (n=15)	Chemotherapy (n=49)
Patients with any subsequent therapy	13 (87)	43 (88)
Systemic therapy	13 (87)	38 (78)
ALK TKI	7 (47)	37 (76)
Alectinib	4 (27)	29 (59)
Brigatinib	4 (27)	4 (8)
Crizotinib	0	4 (8)
Lorlatinib	0	2 (4)
Ceritinib	0	1 (2)
Chemotherapy	6 (40)	2 (4)
Immunotherapy	1 (7)	1 (2)
Other anti-cancer therapy	1 (7)	1 (2)
Radiotherapy	5 (33)	9 (18)
Surgery	1 (7)	3 (6)

[a]One patient died without a recurrence event reported. [b]At disease assessment where first recurrence detected; patients may have multiple sites of disease recurrence counted.

Solomon BJ, et al. Ann Oncol 2023;34(suppl):Abstr LBA2

LBA2: ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage ALK+ non-small cell lung cancer (NSCLC) – Solomon BJ, et al

- **Key results (cont.)**

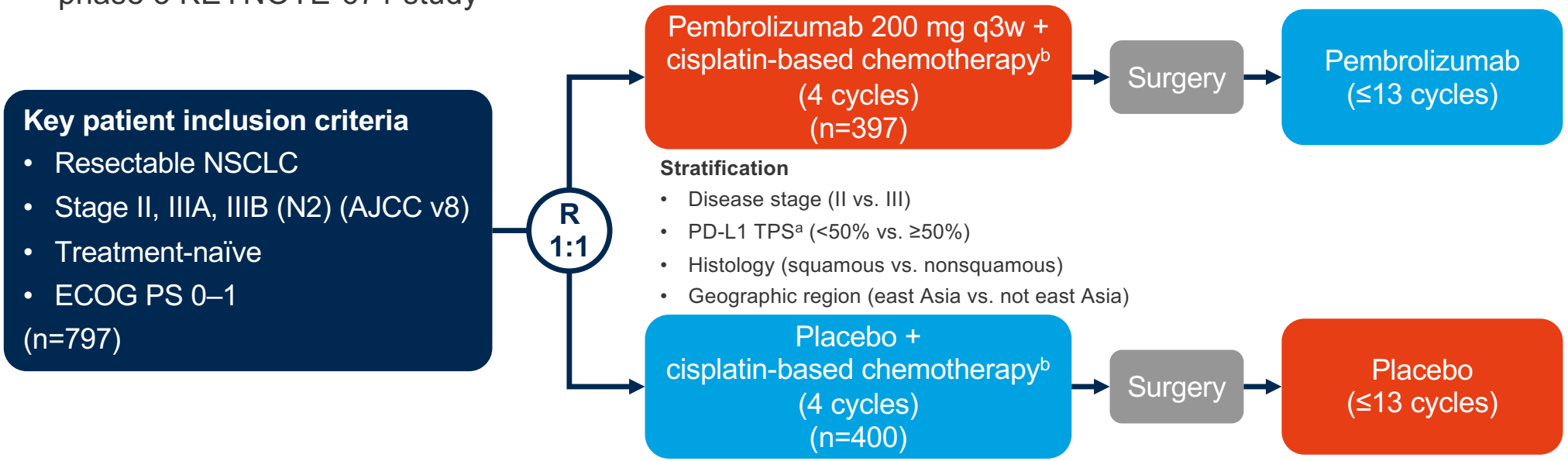
AEs, %	Alectinib (n=128)	Chemotherapy (n=127)
Median treatment duration, mo	23.9	2.1
Patients with any AEs	98	93
Grade 3/4	30	31
Grade 5	0	0
SAEs	13	8
Treatment-related	2	7
Led to dose reduction	26	10
Led to dose interruption	27	18
Led to discontinuation	5	13

- **Conclusions**
  - In patients with early stage ALK + NSCLC, adjuvant alectinib was associated with significant DFS benefit in the ITT (stage IB–IIIA) population and CNS DFS benefit compared with chemotherapy across all stages of disease

Solomon BJ, et al. Ann Oncol 2023;34(suppl):Abstr LBA2

LBA56: Overall survival in the KEYNOTE-671 study of perioperative pembrolizumab for early-stage non-small-cell lung cancer (NSCLC) – Spicer JD, et al

- **Study objective**
  - To evaluate the overall survival of perioperative pembrolizumab in patients with early stage NSCLC in the phase 3 KEYNOTE-671 study



Dual primary endpoints

- EFS (investigator assessed), OS

Secondary endpoints

- MPR, pCR safety

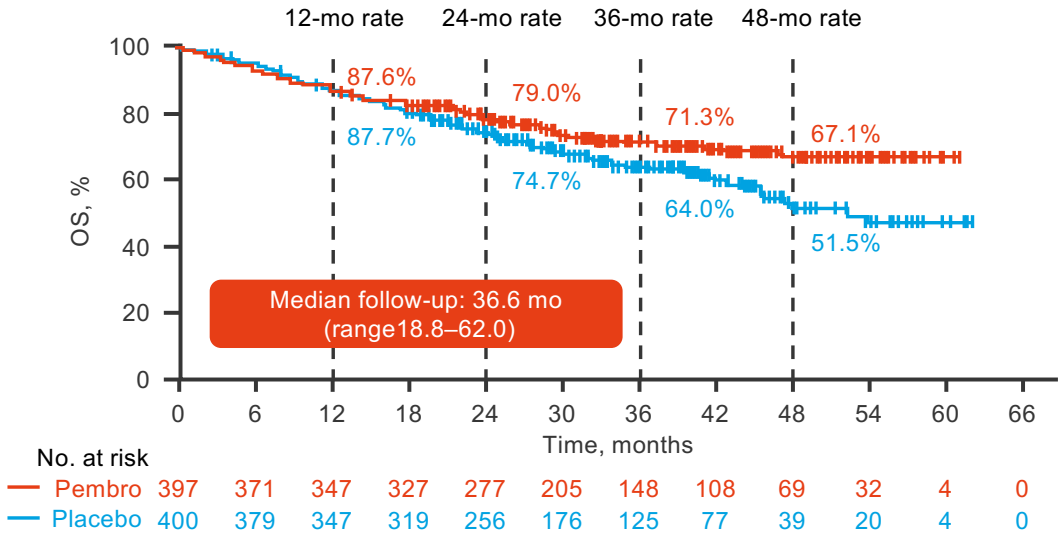
[a]Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx.
[b]Squamous: cisplatin 75 mg/m^2 IV q3w + gemcitabine 1000 mg/m^2 IV D1, 8 q3w; nonsquamous: cisplatin 75 mg/m^2 IV q3w + pemetrexed 500 mg/m^2 IV q3w.

Spicer JD, et al. Ann Oncol 2023;34(suppl):Abstr LBA56

LBA56: Overall survival in the KEYNOTE-671 study of perioperative pembrolizumab for early-stage non-small-cell lung cancer (NSCLC) – Spicer JD, et al

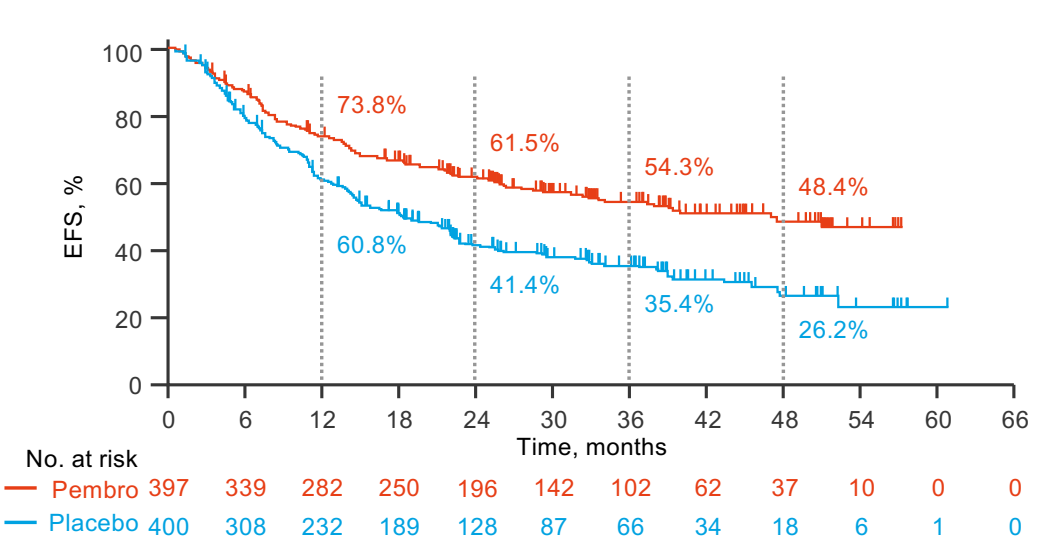
- **Key results**

Overall survival (IA2)



	Pembrolizumab (n=397)	Placebo (n=400)
Events, %	27.7	36.0
mOS, mo (95%CI)	NR (NR, NR)	52.4 (45.7, NR)
HR (95%CI); p-value	0.72 (0.56, 0.93); 0.00517[a]	

Event-free survival (IA2)



	Pembrolizumab (n=397)	Placebo (n=400)
Events, %	43.8	62.0
mEFS, mo (95%CI)	47.2 (32.9, NR)	18.3 (14.8, 22.1)
HR (95%CI)	0.59 (0.48, 0.72)	

[a]Significance boundary at IA2, one-sided p=0.00543.
Data cutoff date for IA2: July 10, 2023.

Spicer JD, et al. Ann Oncol 2023;34(suppl):Abstr LBA56

LBA56: Overall survival in the KEYNOTE-671 study of perioperative pembrolizumab for early-stage non-small-cell lung cancer (NSCLC) – Spicer JD, et al

- **Key results (cont.)**

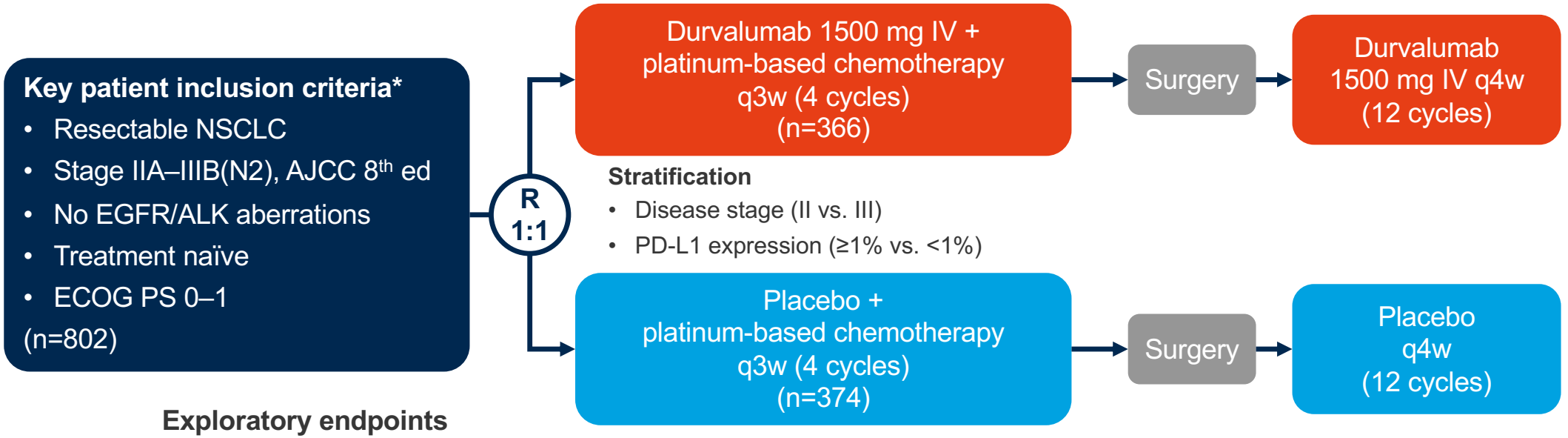
AEs, n (%)	Pembrolizumab (n=396)	Placebo (n=399)
TRAEs	383 (96.7)	381 (95.5)
Grade 3–5	179 (45.2)	151 (37.8)
Serious	73 (18.4)	58 (14.5)
Led to death	4 (1.0)	3 (0.8)
Led to discontinuation of all study treatment	54 (13.6)	21 (5.3)
irAEs and infusion reactions	103 (26.0)	36 (9.0)
Grade 3-5	26 (6.6)	6 (1.5)
Serious	24 (6.1)	6 (1.5)
Led to death	1 (0.3)	0
Led to discontinuation of all study treatment	23 (5.8)	3 (0.8)

- **Conclusions**
  - In patients with early stage NSCLC, perioperative pembrolizumab demonstrated a significant benefit in OS and EFS compared with chemotherapy and no new safety signals were observed

Spicer JD, et al. Ann Oncol 2023;34(suppl):Abstr LBA56

LBA59: Associations of ctDNA clearance and pathological response with neoadjuvant treatment in patients with resectable NSCLC from the phase 3 AEGEAN trial – Reck M, et al

- **Study objective**
  - To investigate the associations between ctDNA clearance and pathological response during neoadjuvant therapy in patients with resectable NSCLC in the phase 3 AEGEAN trial



Exploratory endpoints

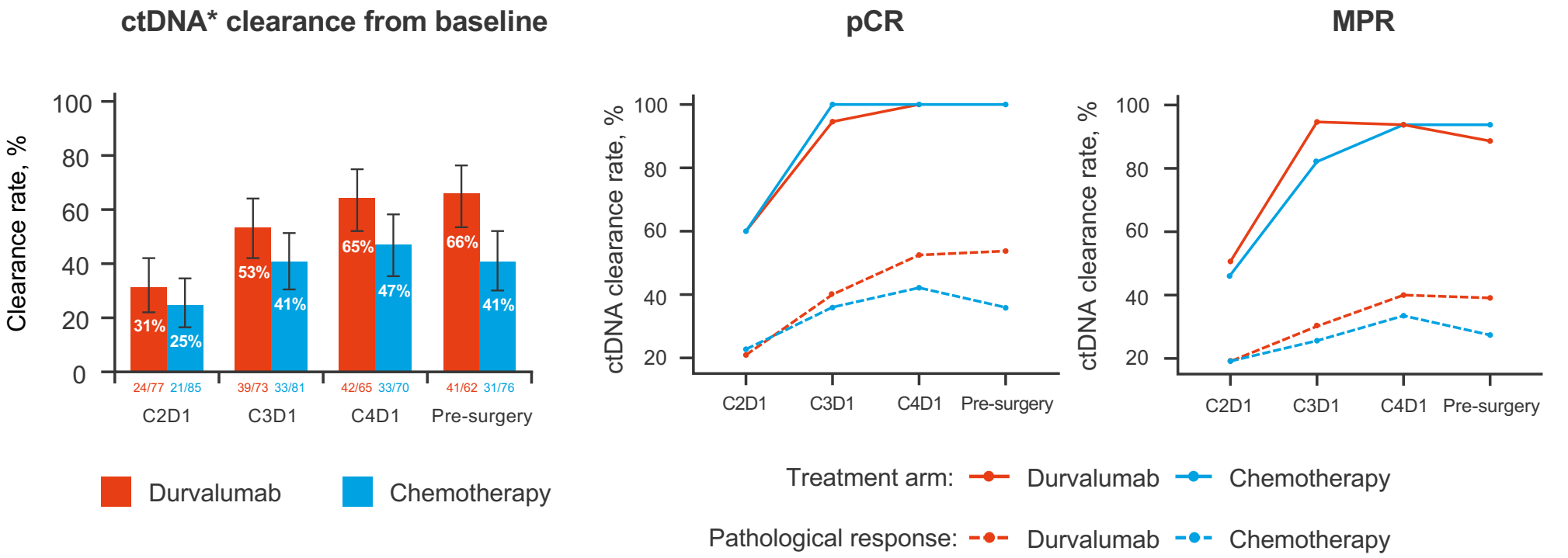
- Association between ctDNA clearance and pCR and MPR

*Protocol was amended while enrollment was ongoing to exclude patients with: tumors classified as T4 for any reason other than size; planned pneumonectomies; or documented EGFR/ALK aberrations.

Reck M, et al. Ann Oncol 2023;34(suppl):Abstr LBA59

LBA59: Associations of ctDNA clearance and pathological response with neoadjuvant treatment in patients with resectable NSCLC from the phase 3 AEGEAN trial – Reck M, et al

- **Key results**

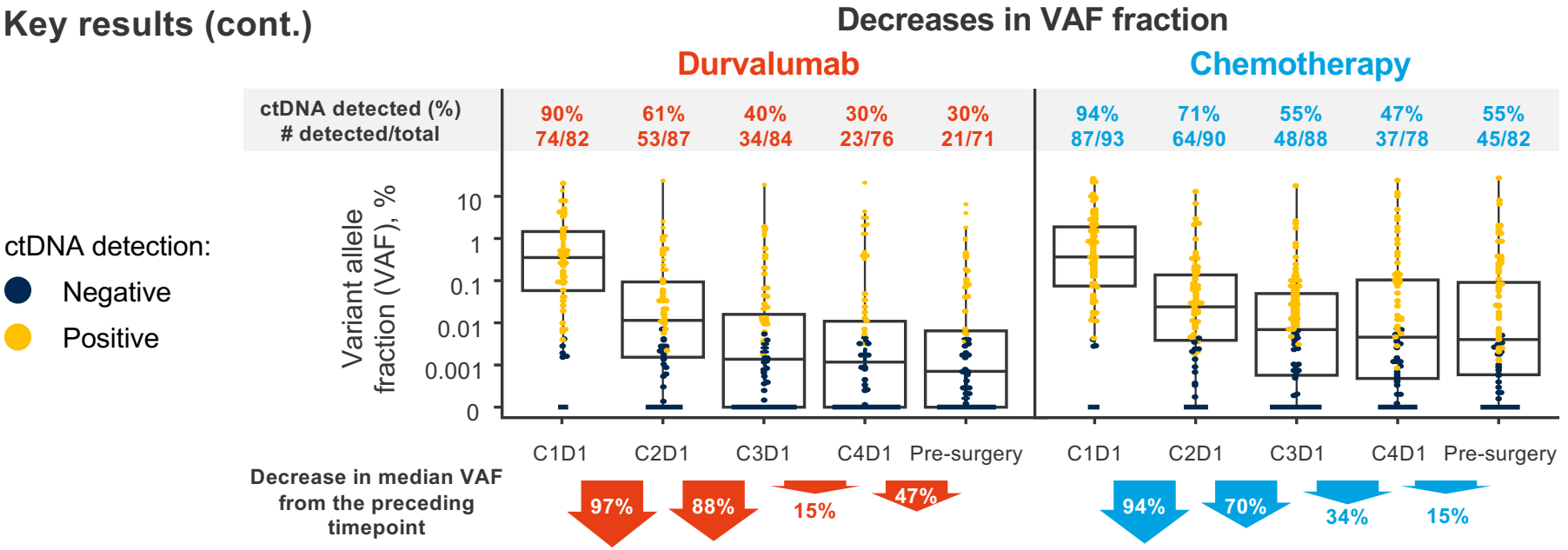


*ctDNA analysis was performed using patient-specific tumour-informed panels designed to include 16–50 variants, identified by whole exome sequencing of treatment-naïve diagnostic biopsies only.

Reck M, et al. Ann Oncol 2023;34(suppl):Abstr LBA59

LBA59: Associations of ctDNA clearance and pathological response with neoadjuvant treatment in patients with resectable NSCLC from the phase 3 AEGEAN trial – Reck M, et al

- **Key results (cont.)**

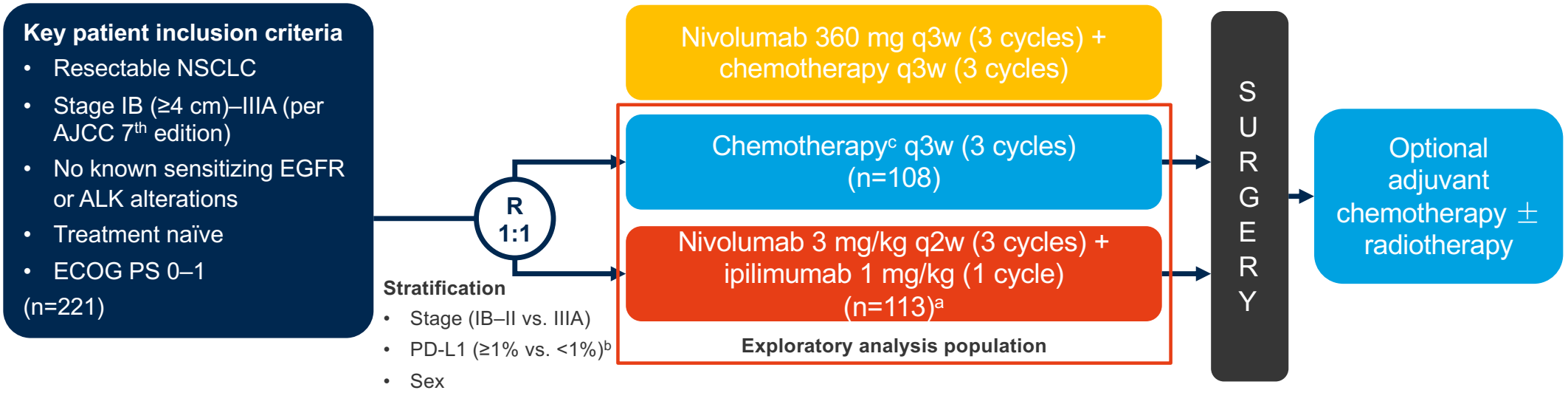


- **Conclusions**
  - In patients with resectable NSCLC, neoadjuvant treatment with durvalumab + chemotherapy provided greater ctDNA clearance and pathological response compared with chemotherapy alone. Patients without ctDNA clearance after neoadjuvant treatment were unlikely to achieve a pathological response

Reck M, et al. Ann Oncol 2023;34(suppl):Abstr LBA59

1261O: Neoadjuvant nivolumab (N) + ipilimumab (I) vs chemotherapy (C) in the phase 3 CheckMate 816 trial – Awad MM, et al

- **Study objective**
  - To evaluate the efficacy and safety of neoadjuvant nivolumab + ipilimumab in patients with resectable NSCLC with and without definitive surgery in an exploratory analysis of the phase 3 CheckMate 816 study



Primary endpoints

- pCR (0% viable tumor cells in lung and lymph nodes), EFS (BICR)

Exploratory endpoints

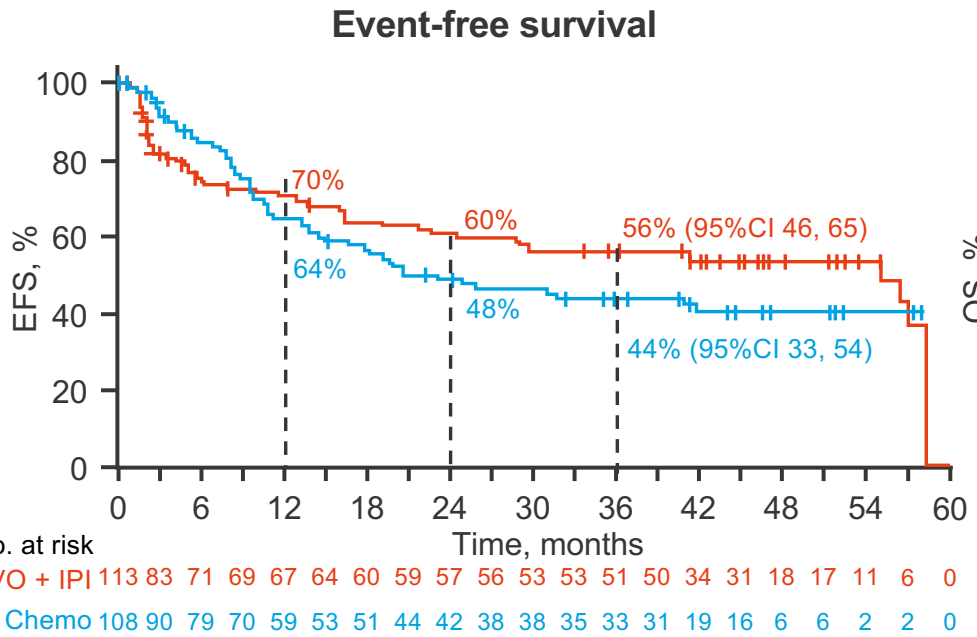
- EFS (BICR), pCR, MPR (10% viable tumor cells in lung and lymph nodes), OS

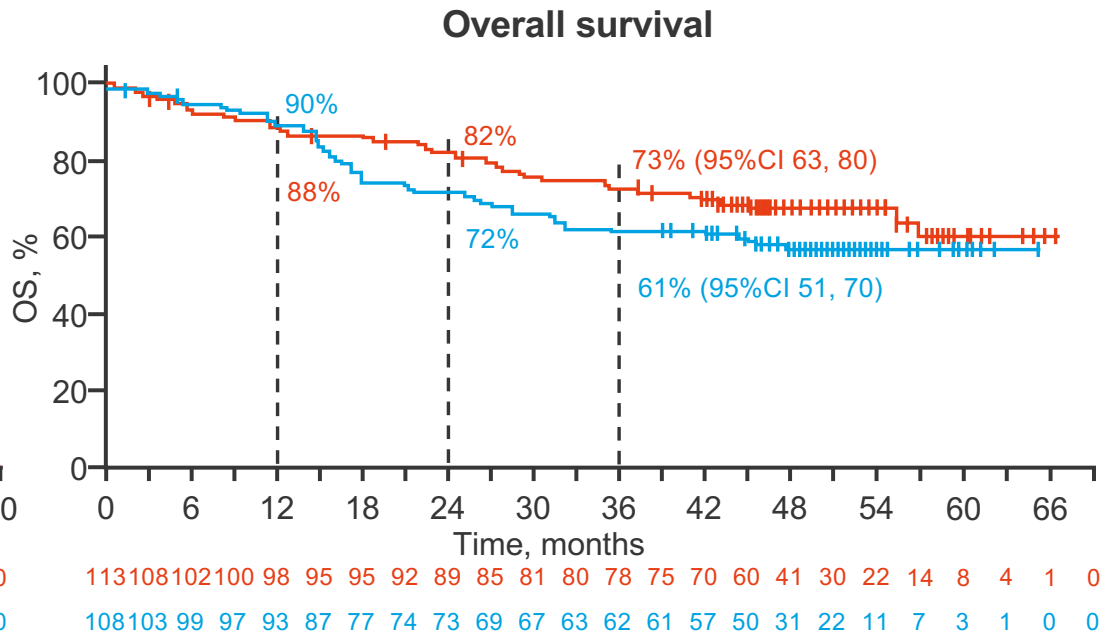
[a]Arm closed early after primary analysis population was changed to nivolumab + chemotherapy based on evolving external trial data. [b]Determined by the PD-L1 28-8 pharmDx assay. [c]Paclitaxel + carboplatin; or cisplatin + vinorelbine or docetaxel or gemcitabine for squamous and cisplatin + pemetrexed for nonsquamous.

Awad MM, et al. Ann Oncol 2023;34(suppl):Abstr 1261O

1261O: Neoadjuvant nivolumab (N) + ipilimumab (I) vs chemotherapy (C) in the phase 3 CheckMate 816 trial – Awad MM, et al

- **Key results**





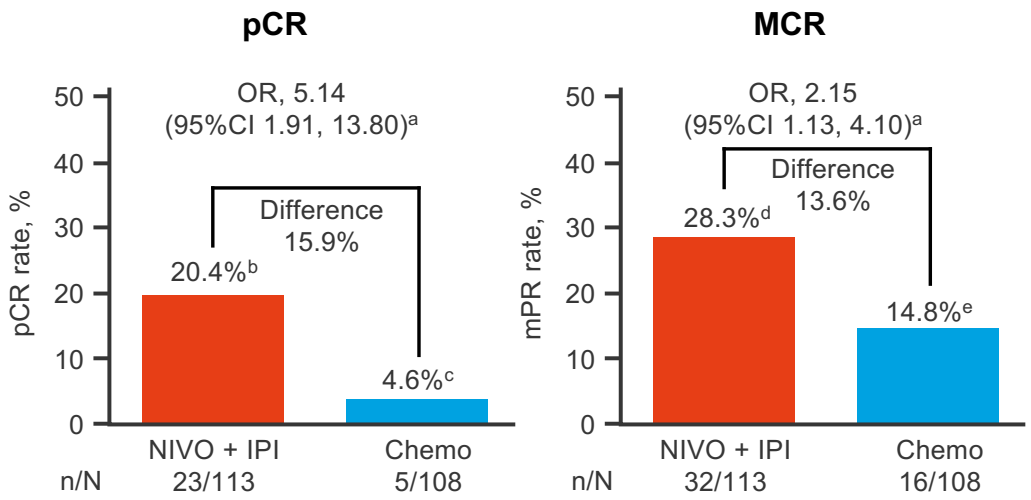
	NIVO + IPI (n=113)	Chemotherapy (n=108)
mEFS, mo (95%CI)	54.8 (24.4, NR)	20.9 (14.2, NR)
HR (95%CI)	0.77 (0.51, 1.15)	

	NIVO + IPI (n=113)	Chemotherapy (n=108)
mOS, mo (95%CI)	NR (56.5, NR)	NR (41.8, NR)
HR (95%CI)	0.73 (0.47, 1.14)	

Awad MM, et al. Ann Oncol 2023;34(suppl):Abstr 1261O

1261O: Neoadjuvant nivolumab (N) + ipilimumab (I) vs chemotherapy (C) in the phase 3 CheckMate 816 trial – Awad MM, et al

- **Key results (cont.)**



AEs, n (%)	NIVO + IPI (n=111)		Chemotherapy (n=104)	
	Any grade	Grade 3–4	Any grade	Grade 3–4
All AEs	97 (87)	22 (20)	103 (99)	47 (45)
TRAEs	72 (65)	15 (14)	96 (92)	38 (36)
AEs led to discontinuation	6 (5)	5 (4)	10 (10)	5 (5)
TRAEs led to discontinuation	6 (5)	5 (4)	7 (7)	4 (4)
All SAEs	15 (14)	11 (10)	21 (10)	17 (16)
Treatment-related SAEs	10 (9)	6 (5)	15 (14)	13 (12)
Surgery-related AEs	45 (55)	12 (15)	37 (45)	12 (14)
Treatment-related deaths	0		1 (1)	

- **Conclusions**
  - In patients with resectable NSCLC, neoadjuvant nivolumab + ipilimumab showed promising antitumour activity in an exploratory analysis with a similar rate of definitive surgery compared with chemotherapy and had a manageable safety profile

[a]Calculated using stratified Cochran-Mantel-Haenszel method.
[b]95%CI 13.4,29.0; [c]95%CI 1.5, 10.5; [d]95%CI 20.2, 37.6; [e]95%CI 8.7, 22.9.

Awad MM, et al. Ann Oncol 2023;34(suppl):Abstr 1261O