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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 2023. This slide set specifically focuses on the **2023 ASCO® ANNUAL MEETING** 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 and Solange Peters 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 2023



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

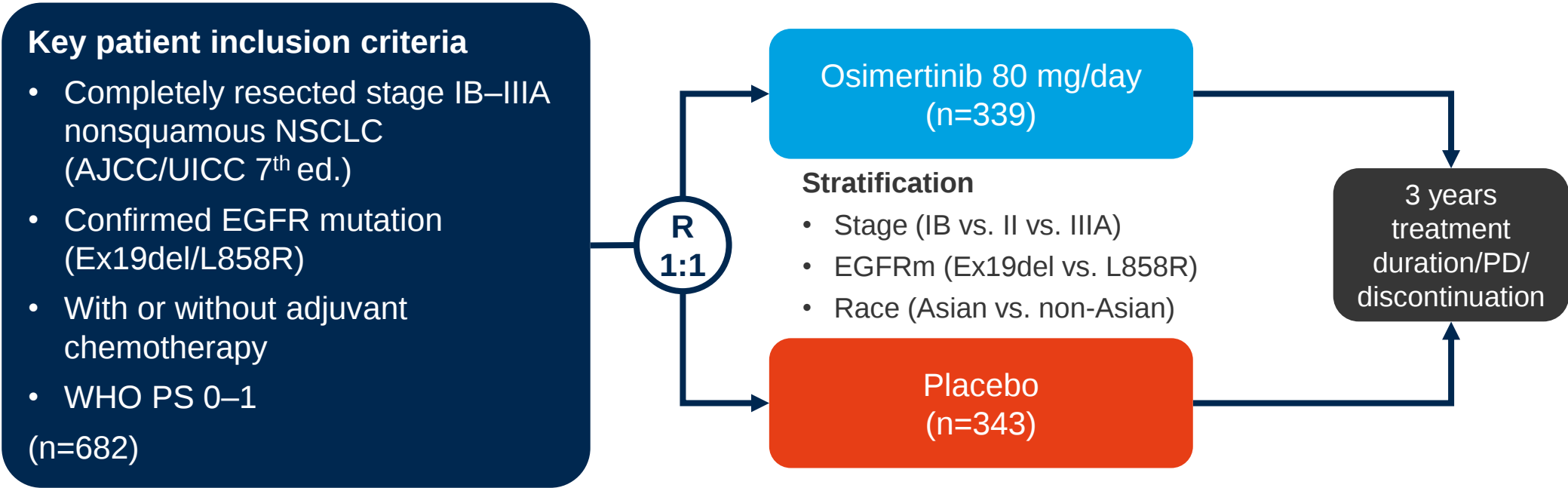
Contents

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

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

LBA3: Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC) – Herbst RS, et al

- Study objective
 - To evaluate the overall survival with adjuvant osimertinib in patients with resected EGFR-mutated NSCLC in the ADAURA study



Primary endpoint

- DFS (investigator assessed in stage II/IIIA)

Secondary endpoints

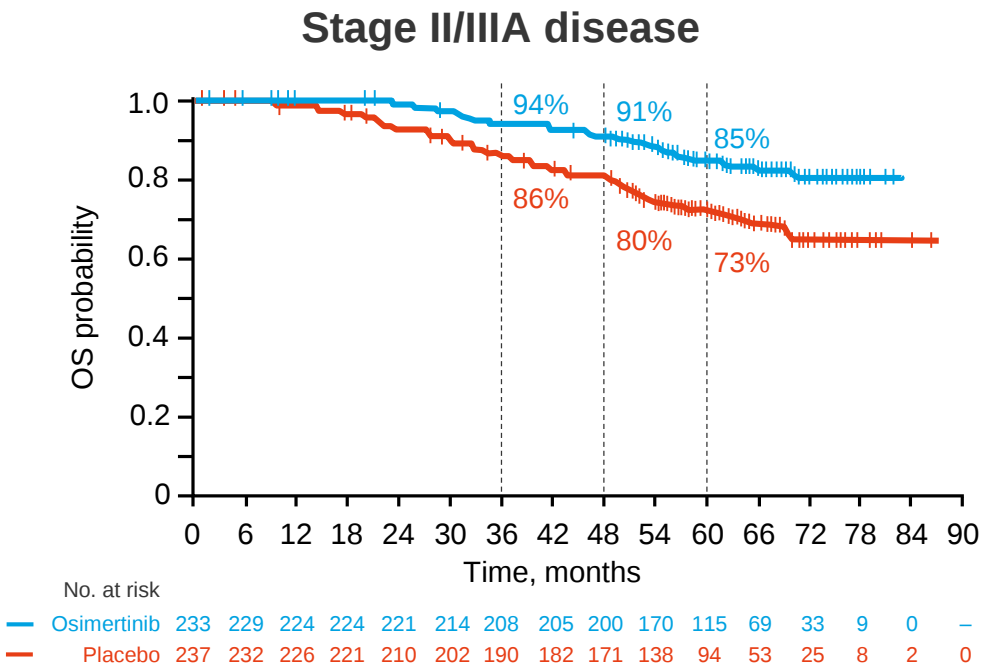
- DFS (overall population^a), OS, HRQoL, safety

^aStage IB, II and IIIA.

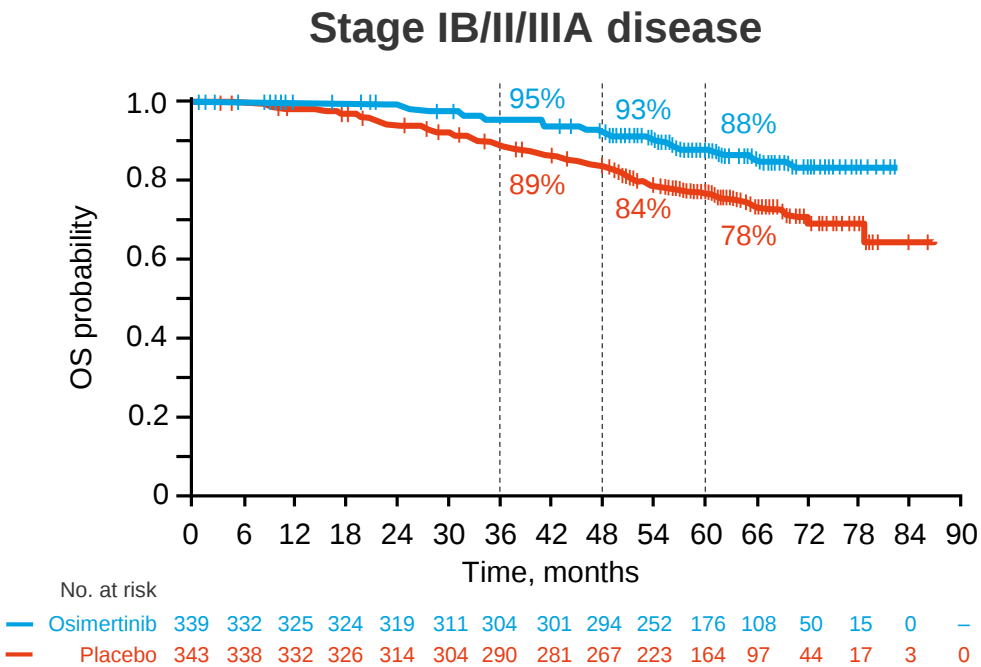
LBA3: Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC) – Herbst RS, et al

- Key results

Overall survival



	Osimertinib (n=233)	Placebo (n=237)
Median follow-up, months	61.7	60.4
5-year OS rate, % (95%CI)	85 (79, 89)	73 (66, 78)
HR (95%CI); p-value	0.49 (0.33, 0.73); 0.0004	

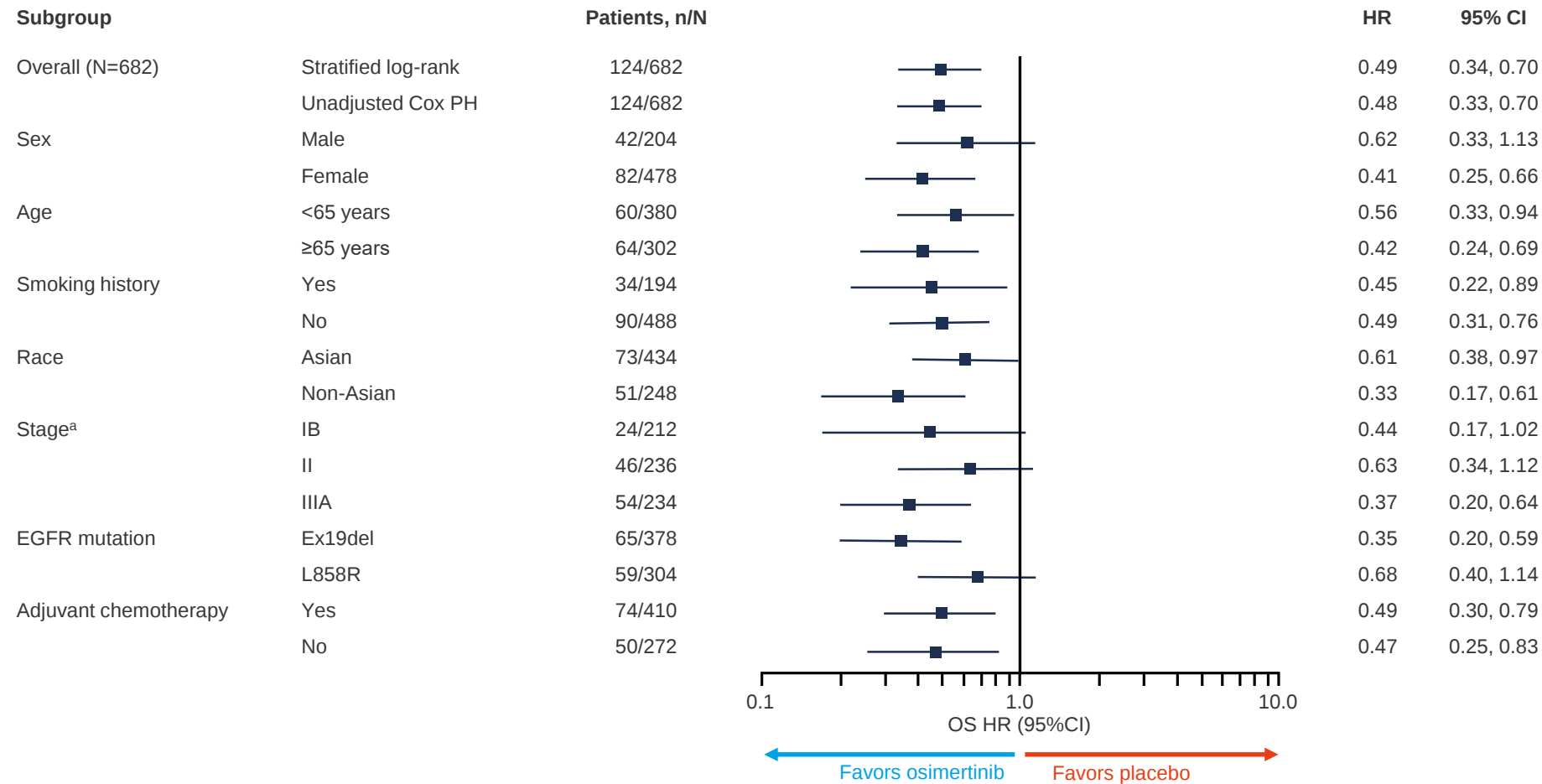


	Osimertinib (n=339)	Placebo (n=343)
Median follow-up, months	61.5	61.5
5-year OS rate, % (95%CI)	88 (83, 91)	78 (73, 82)
HR (95%CI); p-value	0.49 (0.34, 0.70); <0.0001	

LBA3: Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC) – Herbst RS, et al

- **Key results (cont.)**

OS across subgroups: patients with stage IB/II/IIIA disease



LBA3: Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC) – Herbst RS, et al

- Key results (cont.)

AEs, n (%)	Osimertinib (n=337)	Placebo (n=343)
Any	330 (98)	309 (90)
Grade ≥3	79 (23)	48 (14)
Serious	68 (20)	47 (14)
Led to dose reduction	42 (12)	3 (1)
Led to dose interruption	91 (27)	43 (13)
Led to discontinuation	43 (13)	9 (3)
Led to death	1 (>1)	2 (1)

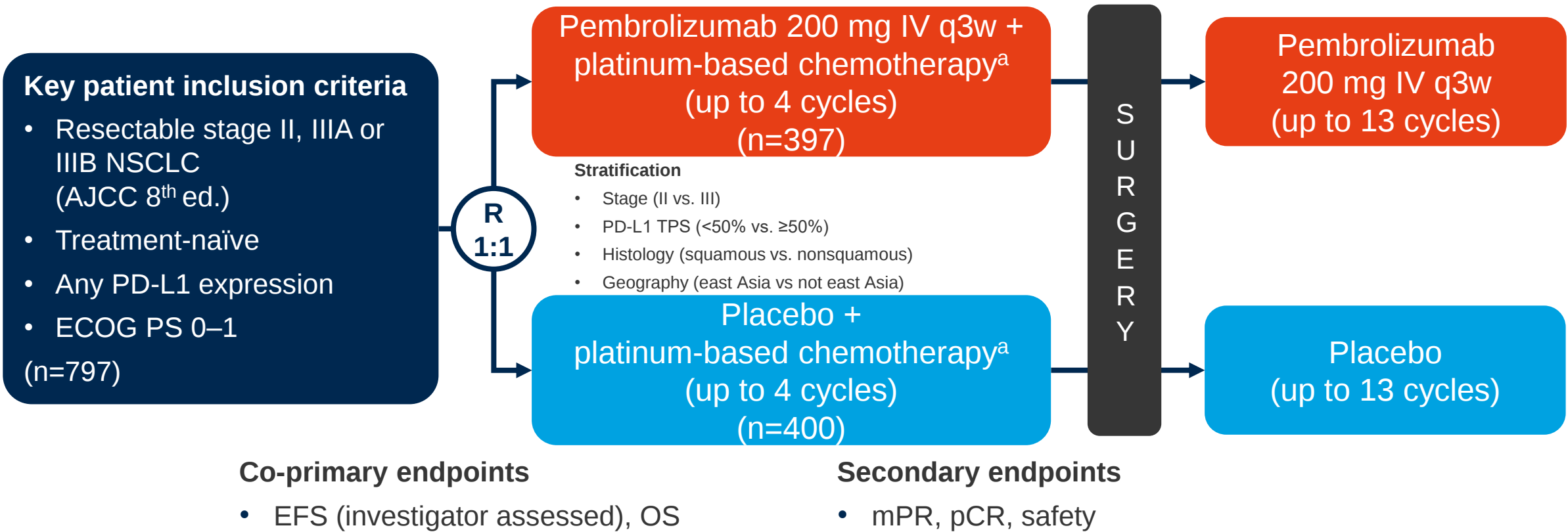
TRAEs, n (%)	Osimertinib (n=337)	Placebo (n=343)
Any	308 (91)	199 (58)
Grade ≥3	36 (11)	7 (2)
Serious	10 (3)	2 (1)
Led to death	0	0

- Conclusions

- In patients with resected EGFR-mutated NSCLC, adjuvant osimertinib showed significant OS benefit compared with placebo with no new safety signals observed

LBA100: KEYNOTE-671: Randomized, double-blind, phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early stage NSCLC – Wakelee HA, et al

- Study objective
 - To evaluate the efficacy and safety of pembrolizumab + platinum-based chemotherapy prior to surgery followed by pembrolizumab in patients with early stage NSCLC in the KEYNOTE-671 study

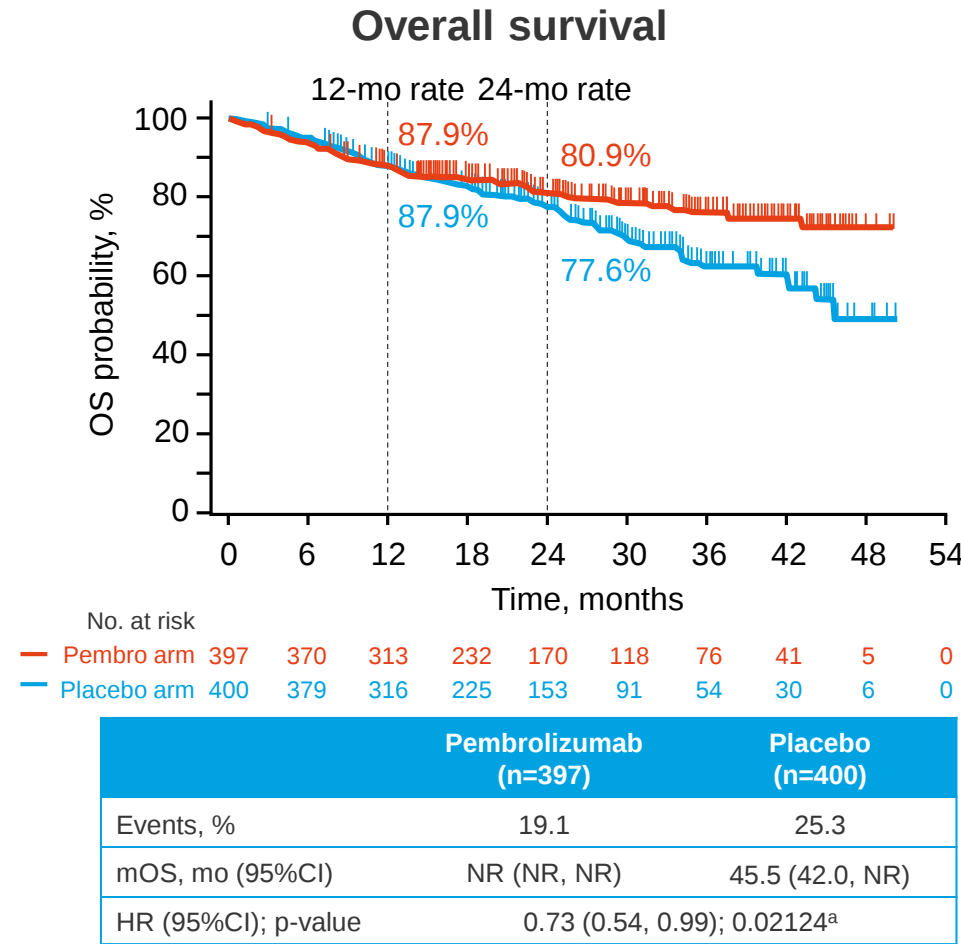
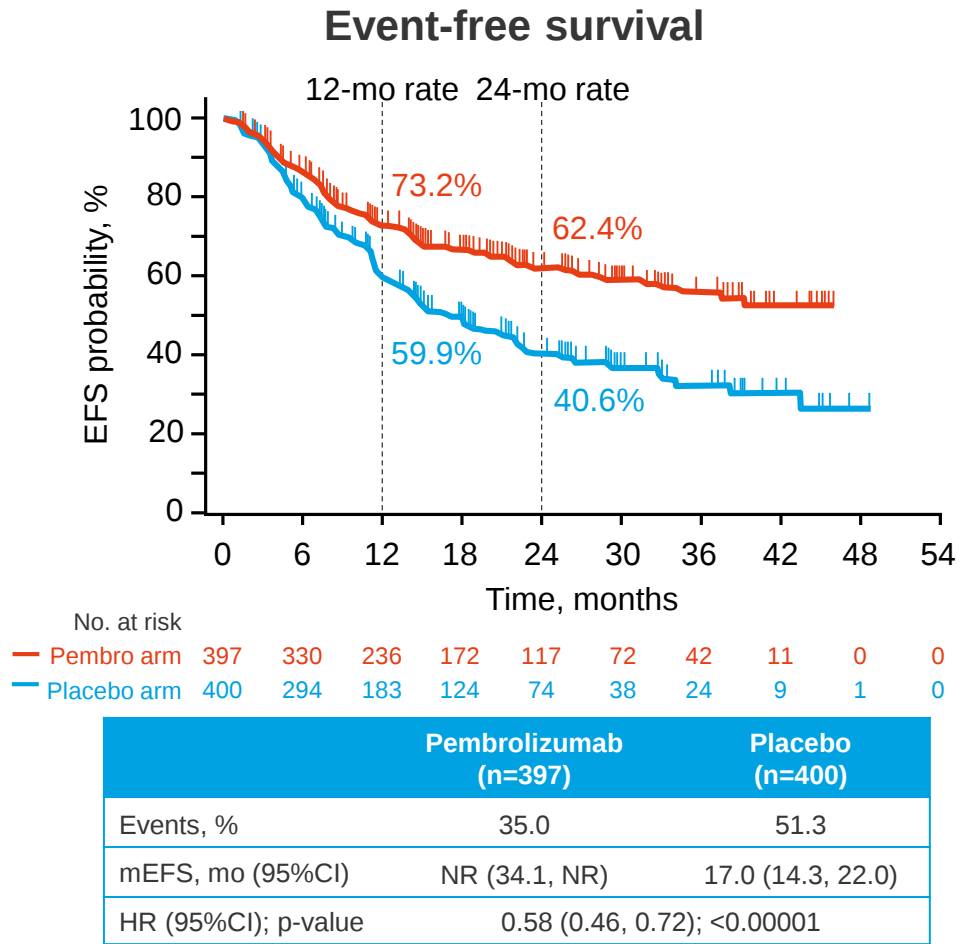


^a**Cisplatin** 75 mg/m² q3w + gemcitabine 1000 mg/m² IV D1, 8 q3w for squamous and **cisplatin** 75 mg/m² q3w + pemetrexed 500 mg/m² IV q3w for nonsquamous.

Wakelee HA, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA100 10

LBA100: KEYNOTE-671: Randomized, double-blind, phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early stage NSCLC – Wakelee HA, et al

- Key results

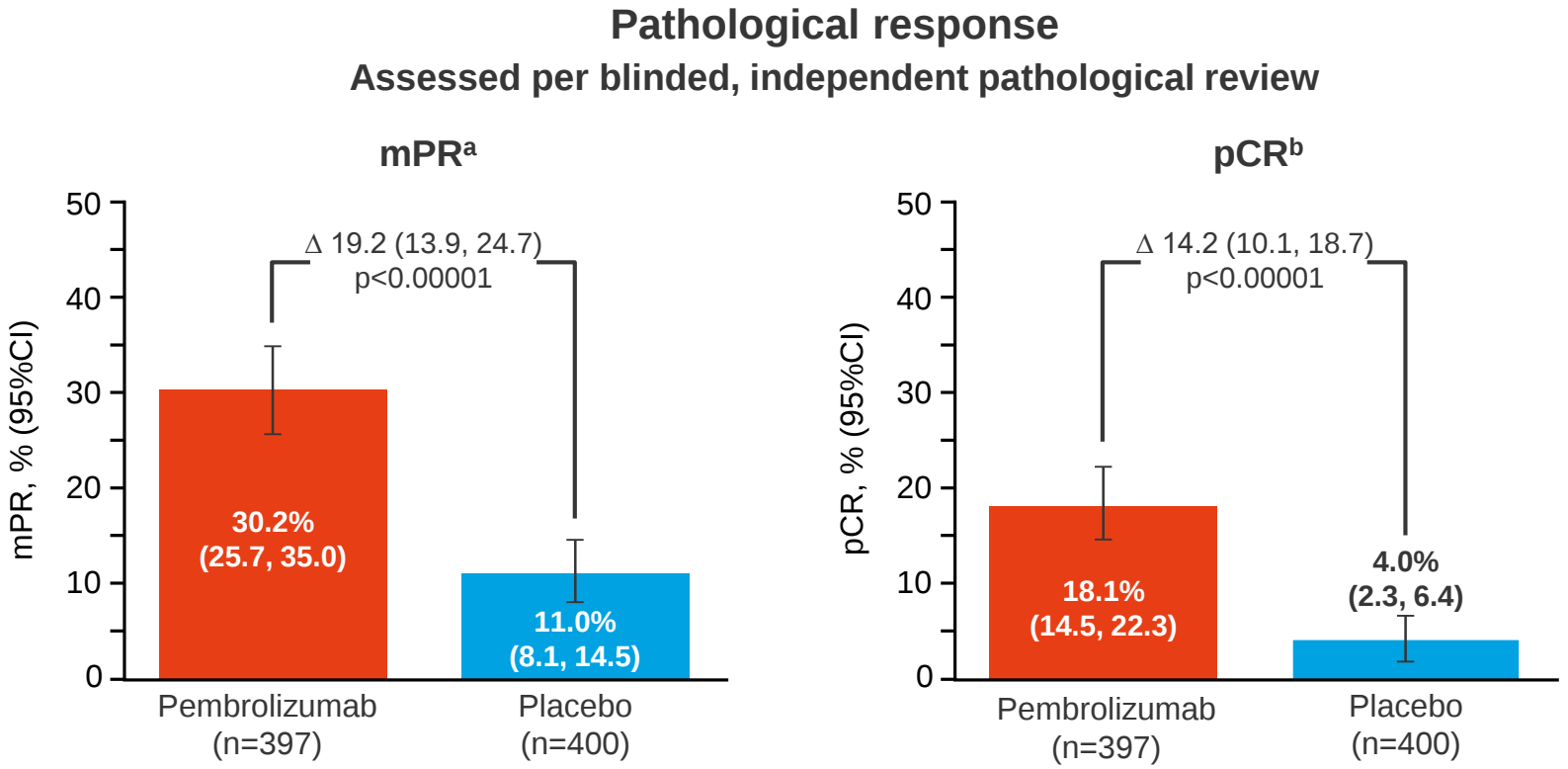


Median follow-up: 25.2 mo (7.5–50.6)

^aSignificant boundary was not met at IA1. OS will continue to be tested according to the analysis plan. Data cut-off date (IA1): July 29, 2022.

LBA100: KEYNOTE-671: Randomized, double-blind, phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early stage NSCLC – Wakelee HA, et al

- Key results (cont.)



^aDefined as ≤10% viable tumor cells in resected primary tumor and lymph nodes;
^bdefined as absence of residual invasive cancer in resected primary tumor and lymph nodes.

LBA100: KEYNOTE-671: Randomized, double-blind, phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early stage NSCLC – Wakelee HA, et al

- Key results (cont.)

AEs, n (%)	Pembrolizumab (n=396)	Placebo (n=399)
TRAEs	383 (96.7)	379 (95.0)
Grade 3–5	178 (44.9)	149 (37.3)
Serious	70 (17.7)	57 (14.3)
Led to death	4 (1.0)	3 (0.8)
Led to treatment discontinuation	50 (12.6)	21 (5.3)
irAEs and infusion reactions	100 (25.3)	42 (10.5)
Grade 3–5	23 (5.8)	6 (1.5)
Serious	21 (5.3)	6 (1.5)
Led to death	1 (0.3)	0
Led to treatment discontinuation	20 (5.1)	3 (0.8)

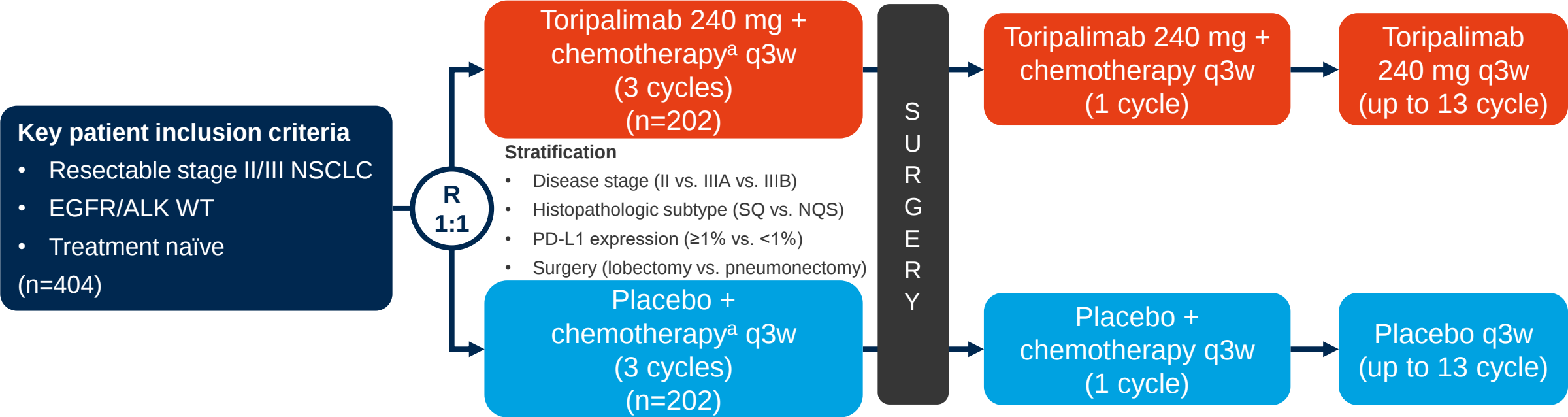
- Conclusions

- In patients with early stage NSCLC, pembrolizumab + cisplatin-based chemotherapy prior to surgery followed by adjuvant pembrolizumab demonstrated improvement in EFS and higher pathological response than neoadjuvant chemotherapy and surgery alone with a safety profile consistent with previously reported data

8501: Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study – Lu S, et al

- Study objective

- To evaluate the efficacy and safety of perioperative toripalimab + platinum-based chemotherapy in patients with resectable stage II/III NSCLC at an interim analysis of the NEOTORCH study



Primary endpoints

- EFS (investigator assessed), MPR (BICR) in stage II and II/III populations^b

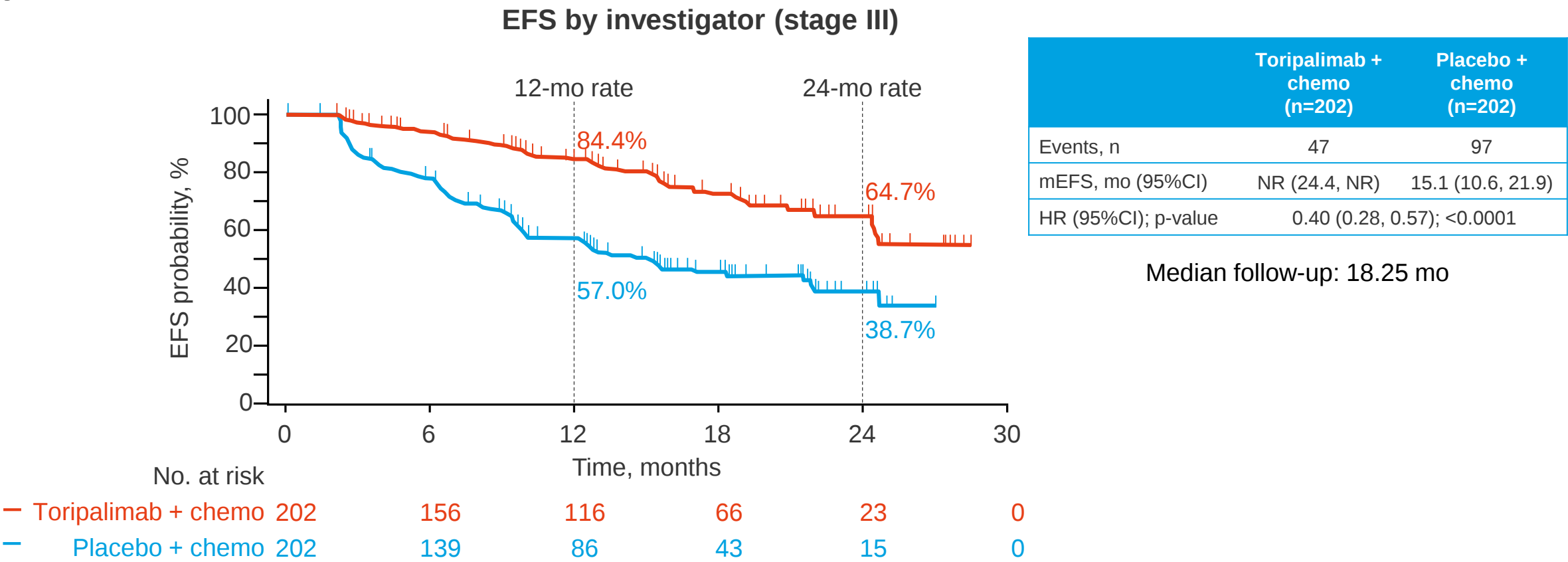
Secondary endpoints

- OS, pCR, safety

^aCisplatin 75 mg/m² IV q3w D1 or carboplatin AUC5 IV q3w D1 + pemetrexed 500 mg/m² IV q3w D1 (for nonsquamous only) or paclitaxel 175 mg/m² q3w or docetaxel 60–75 mg/m² q3w; ^bonly stage III results were reported.

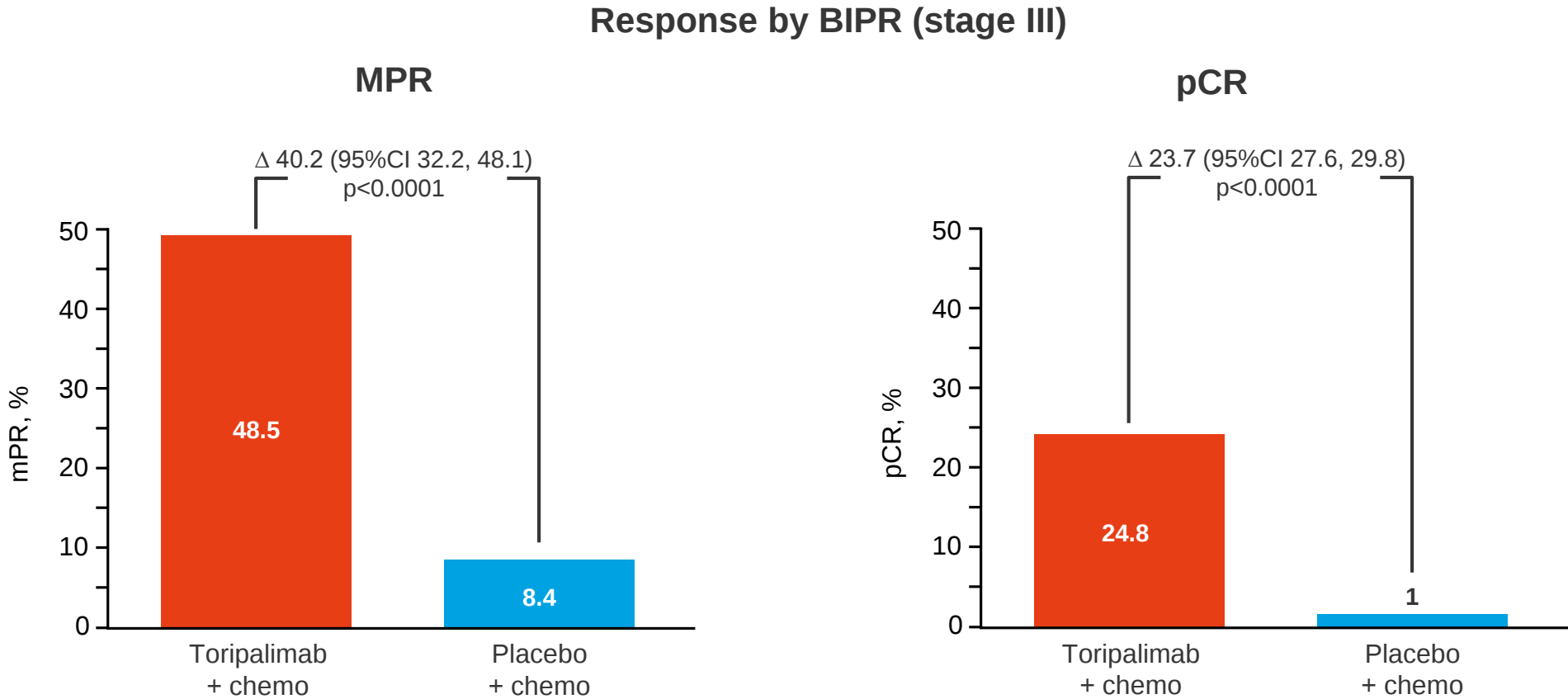
8501: Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study – Lu S, et al

- Key results



8501: Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study – Lu S, et al

- Key results (cont.)



8501: Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study – Lu S, et al

• Key results (cont.)

	Toripalimab + chemo	Placebo + chemo
PD-L1 <1% or NE, n	69	70
mEFS, mo	NE	15.3
HR (95%CI)	0.59 (0.327, 1.034)	
PD-L1 1–49%, n	69	67
mEFS, mo	24.6	12.7
HR (95%CI)	0.31 (0.176, 0.554)	
PD-L1 ≥50%, n	64	64
mEFS, mo	NE	15.5
HR (95%CI)	0.31 (0.152, 0.618)	
Nonsquamous (n=45) events, n	12	21
mEFS, mo (95%CI)	NE (17.5, NE)	21.9 (9.7, NE)
HR (95%CI); p-value	0.54 (0.265, 1.096); 0.0827	
Squamous (n=157) events, n	35	75
mEFS, mo (95%CI)	NE (24.4, NE)	12.9 (9.9, 21.6)
HR (95%CI); p-value	0.35 (0.236, 0.528); <0.0001	

AEs, n (%)	Toripalimab + chemo (n=202)	Placebo + chemo (n=202)
Any	201 (99.5)	199 (98.5)
Grade ≥3	128 (63.4)	109 (54.0)
Serious	82 (40.6)	57 (28.2)
Led to death	6 (3.0)	4 (2.0)
Treatment related	1 (0.5)	0
Led to interruption	57 (28.2)	29 (14.4)
Led to discontinuation	19 (9.4)	15 (7.4)
Any investigator-determined irAEs	85 (42.1)	46 (22.8)
Grade ≥3	24 (11.9)	6 (3.0)
Any infusion-related reactions	7 (3.5)	13 (6.4)

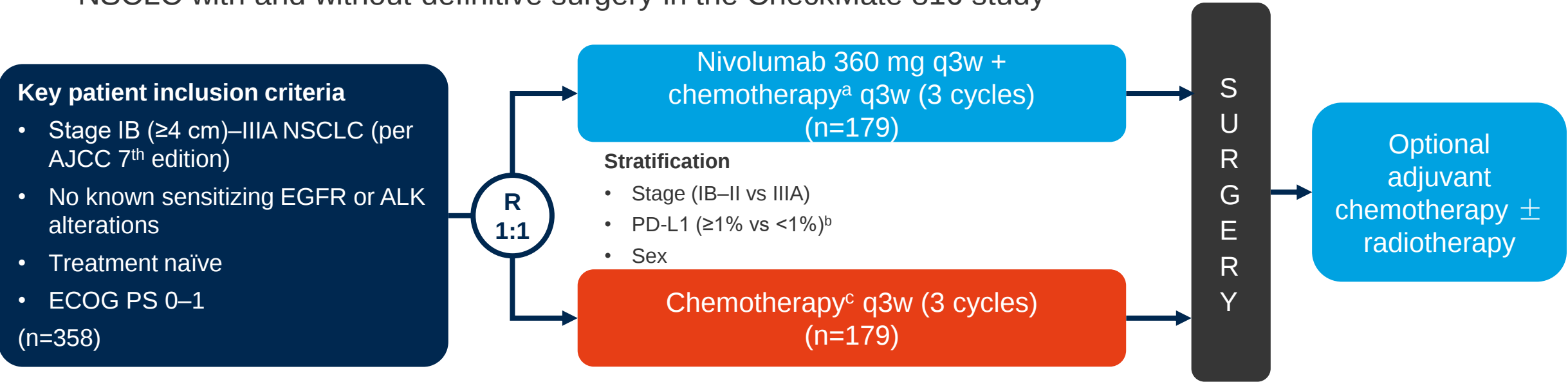
• Conclusions

- In patients with resectable stage III NSCLC, perioperative toripalimab + chemotherapy provided longer EFS and higher pathological response rates compared with chemotherapy alone and was generally well-tolerated

8521: Clinical outcomes with neoadjuvant nivolumab (N) + chemotherapy (C) vs C by definitive surgery in patients (pts) with resectable NSCLC: 3-y results from the phase 3 CheckMate 816 trial – Spicer J, et al

- Study objective

- To evaluate the efficacy and safety of neoadjuvant nivolumab + chemotherapy in patients with resectable NSCLC with and without definitive surgery in the CheckMate 816 study



Primary endpoints

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

Secondary endpoints

- MPR, OS, time to death or distant metastases, safety

^aGemcitabine + cisplatin or paclitaxel + carboplatin for squamous and pemetrexed + cisplatin or paclitaxel + carboplatin for nonsquamous; ^bdetermined by the PD-L1 28-8 pharmDx assay; ^cpaclitaxel + carboplatin; or cisplatin + vinorelbine or docetaxel or gemcitabine for squamous and cisplatin + pemetrexed for nonsquamous.

8521: Clinical outcomes with neoadjuvant nivolumab (N) + chemotherapy (C) vs C by definitive surgery in patients (pts) with resectable NSCLC: 3-y results from the phase 3 CheckMate 816 trial – Spicer J, et al

• Key results

With definitive surgery	Nivolumab + chemo (n=149)	Chemo (n=135)
mEFS, mo (95%CI)	NR (44.4, NR)	31.8 (18.0, NR)
HR (95%CI)	0.67 (0.47, 0.95)	
mTTDM, mo (95%CI)	NR (NR, NR)	46.8 (34.3, NR)
HR (95%CI)	0.55 (0.36, 0.84)	
mEFS2, mo (95%CI)	NR (NR, NR)	NR (NR, NR)
HR (95%CI)	0.60 (0.39, 0.95)	

Without definitive surgery	Nivolumab + chemo (n=30)	Chemo (n=44)
mEFS, mo (95%CI)	6.7 (2.7, 24.8)	4.1 (2.5, 11.2)
HR (95%CI)	0.75 (0.44, 1.28)	
mTTDM, mo (95%CI)	21.8 (6.7, 37.8)	15.6 (11.2, 18.6)
HR (95%CI)	0.63 (0.34, 1.16)	
mEFS2, mo (95%CI)	12.3 (8.4, 37.8)	15.5 (10.2, 18.6)
HR (95%CI)	0.94 (0.53, 1.66)	

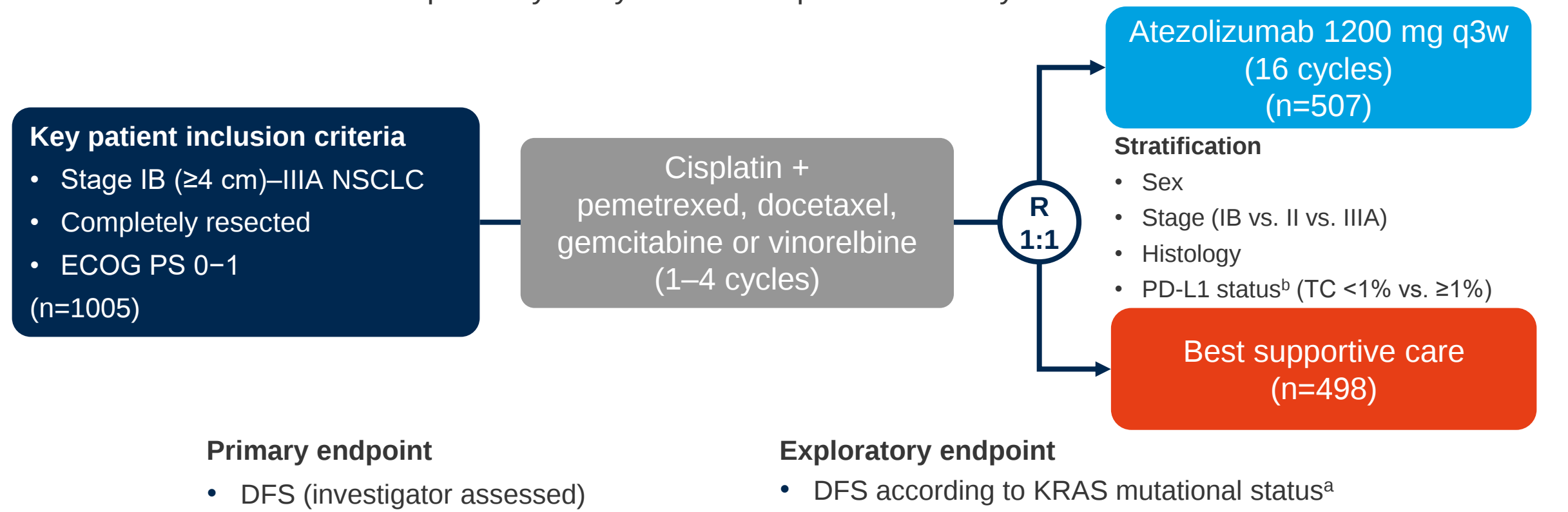
	With definitive surgery		Without definitive surgery	
Grade 3–4 TRAEs, n (%)	Nivolumab + chemo (n=149)	Chemo (n=135)	Nivolumab + chemo (n=27)	Chemo (n=41)
Any	56 (38)	48 (36)	7 (26)	19 (46)
Serious	13 (9)	9 (7)	2 (7)	5 (12)
Led to discontinuation	8 (5)	5 (4)	2 (7)	1 (2)
Led to death	0	1 (1)	0	2 (5)
Related to surgery	17 (11)	20 (15)	-	-

• Conclusions

- In patients with resectable NSCLC, neoadjuvant nivolumab + chemotherapy continued to provide long-term EFS in patients with resection with no additional safety findings and there was a trend towards improved outcomes in patients without definitive surgery

8522: IMpower010: Exploratory analysis of disease-free survival by KRAS status in patients with stage II-IIIa NSCLC treated with adjuvant atezolizumab vs best supportive care – Reck M, et al

- **Study objective**
 - To evaluate the efficacy of adjuvant atezolizumab in patients with stage II–IIIa NSCLC according to KRAS mutational status in an exploratory analysis of the IMpower010 study

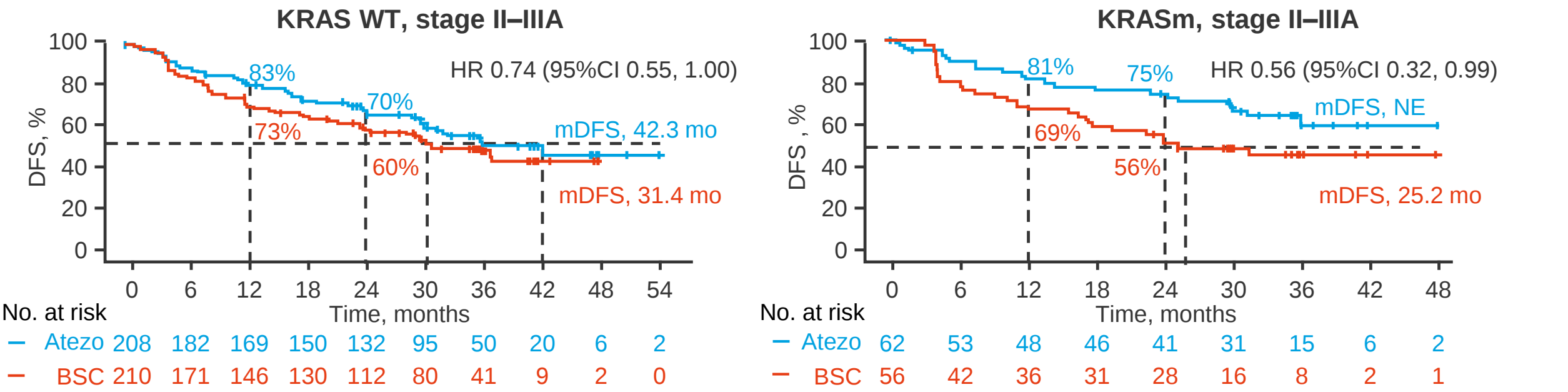


^aKRAS mutational status was assessed retrospectively in the whole-exome sequencing biomarker-evaluable population (WES-BEP); ^bby SP142.

Reck M, et al. J Clin Oncol 2023;41(suppl 16):Abstr 8522 20

8522: IMpower010: Exploratory analysis of disease-free survival by KRAS status in patients with stage II-IIIa NSCLC treated with adjuvant atezolizumab vs best supportive care – Reck M, et al

- Key results



- Atezolizumab provided DFS benefit in KRASm patients regardless of PD-L1 status (PD-L1 TC <1%, HR 0.67 [95%CI 0.26, 1.73]; PD-L1 TC ≥1%, HR 0.52 [95%CI 0.25, 1.08])

- Conclusions

- In patients with stage II-IIIa NSCLC, atezolizumab showed improvement in DFS regardless of KRAS mutation status and PD-L1 expression compared with BSC in this exploratory analysis

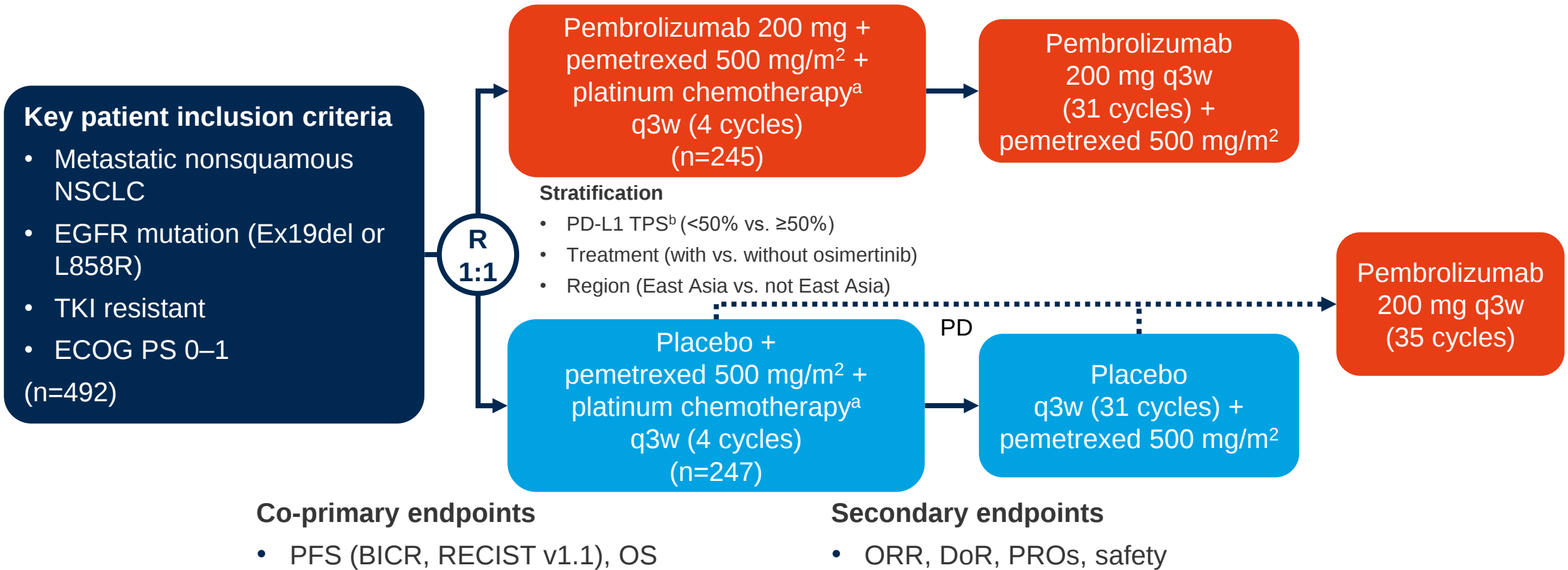
Advanced NSCLC

Not radically treatable stage III and stage IV

Immunotherapy

LBA9000: Pemetrexed and platinum with or without pembrolizumab for tyrosine kinase inhibitor (TKI)-resistant, EGFR-mutant, metastatic nonsquamous NSCLC: Phase 3 KEYNOTE-789 study – Yang JC, et al

- Study objective
 - To evaluate the efficacy and safety of pembrolizumab + pemetrexed + platinum chemotherapy in patients with TKI-resistant, EGFR mutant metastatic nonsquamous NSCLC in the KEYNOTE-789 study

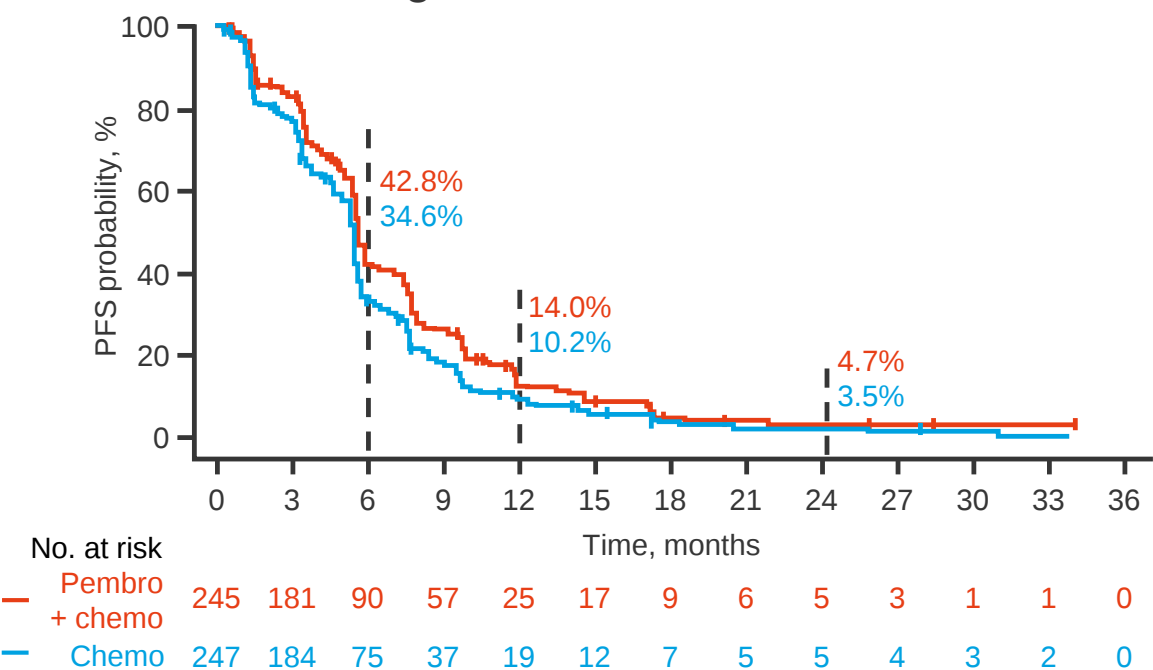


^aCarboplatin AUC5 or cisplatin 75 mg/m²; ^bassessed using PD-L1 IHC 22C3 pharmDx. Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000 23

LBA9000: Pemetrexed and platinum with or without pembrolizumab for tyrosine kinase inhibitor (TKI)-resistant, EGFR-mutant, metastatic nonsquamous NSCLC: Phase 3 KEYNOTE-789 study – Yang JC, et al

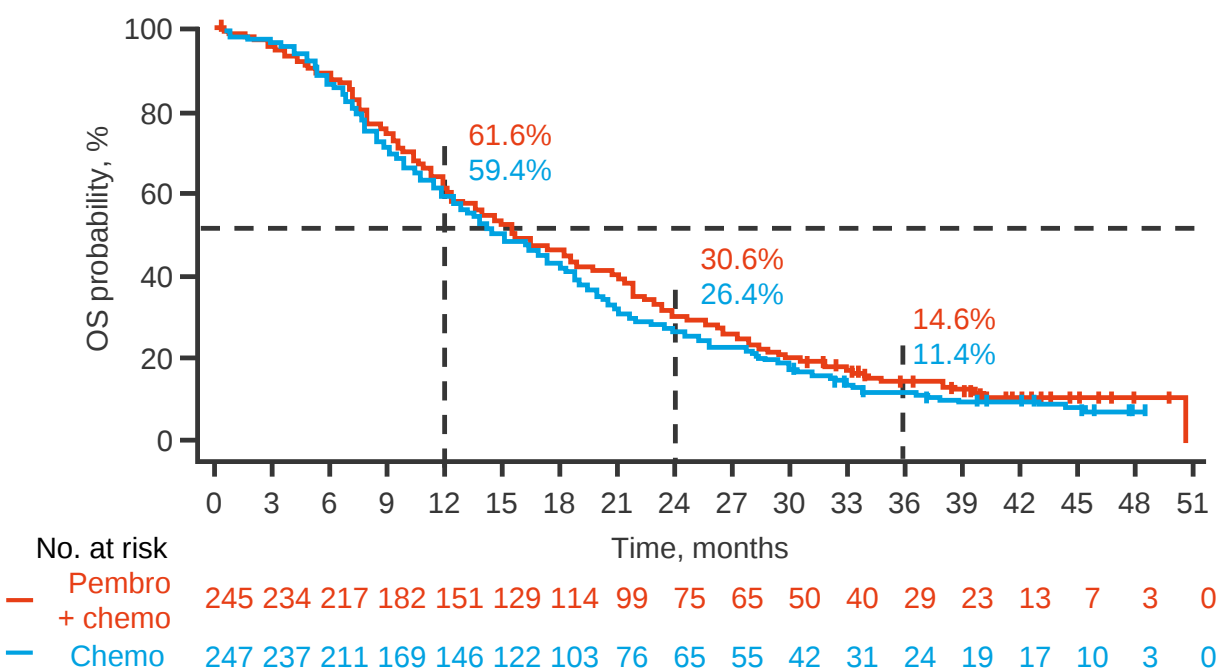
- Key results

Progression-free survival at IA2



	Pembro + chemo (n=245)	Chemo (n=247)
Events, n (%)	198 (80.8)	214 (86.6)
mPFS, mo (95%CI)	5.6 (5.5, 5.8)	5.5 (5.4, 5.5)
HR (95%CI); p-value	0.80 (0.65, 0.97); 0.0122	

Overall survival at FA

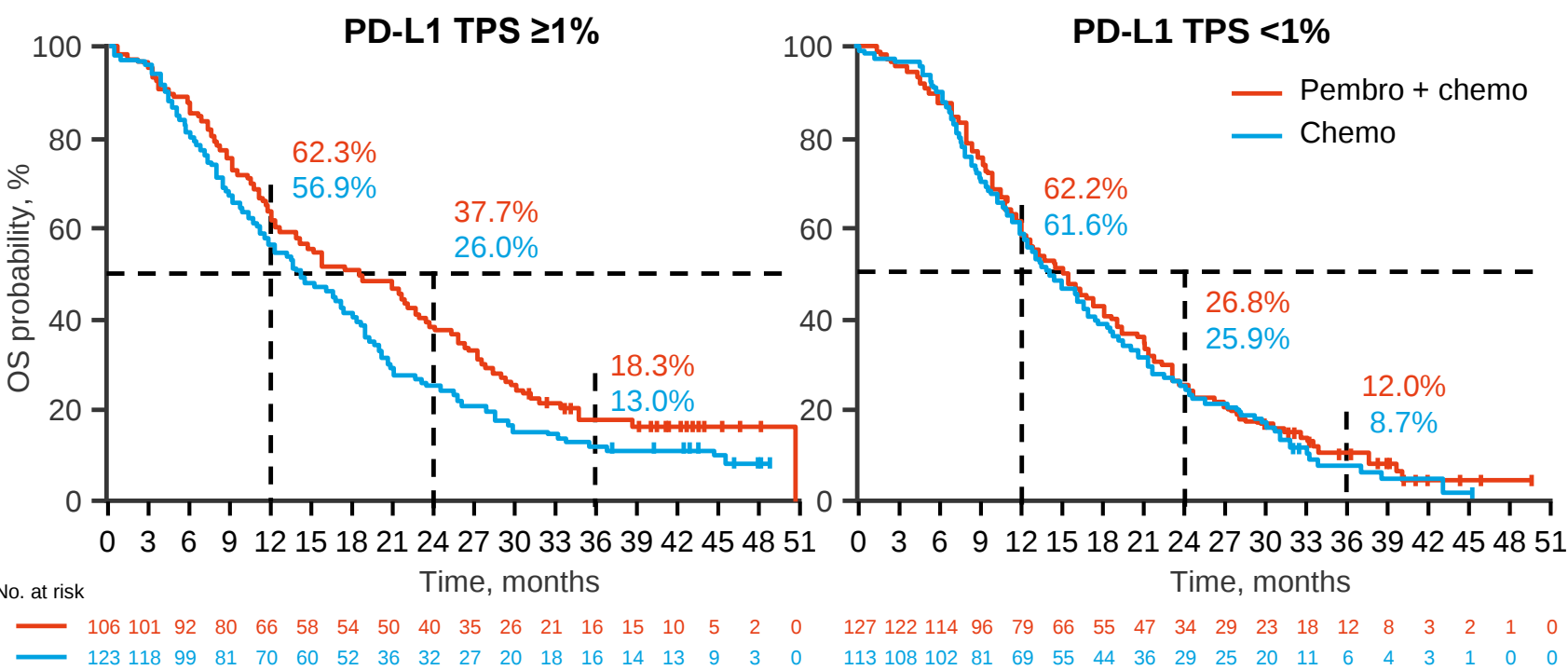


	Pembro + chemo (n=245)	Chemo (n=247)
Events, n (%)	214 (87.3)	224 (90.7)
mOS, mo (95%CI)	15.9 (13.7, 18.8)	14.7 (12.7, 17.1)
HR (95%CI); p-value	0.84 (0.69, 1.02); 0.0362	

LBA9000: Pemetrexed and platinum with or without pembrolizumab for tyrosine kinase inhibitor (TKI)-resistant, EGFR-mutant, metastatic nonsquamous NSCLC: Phase 3 KEYNOTE-789 study – Yang JC, et al

• Key results (cont.)

Overall survival at FA



	Pembrolizumab + chemotherapy (n=245)	Chemotherapy (n=247)
Response		
ORR, % (95%CI)	29.0 (23.4, 35.1)	27.1 (21.7, 33.1)
BOR, n (%)		
CR	5 (2.0)	3 (1.2)
PR	66 (26.9)	64 (25.9)
SD	121 (49.4)	117 (47.4)
PD	37 (15.1)	52 (21.1)
NE	8 (3.3)	5 (2.0)
No assessment	8 (3.3)	6 (2.4)
9-mo DoR rate at FA,%	34.0	22.9
mDoR at FA, mo (95%CI)	6.3 (2.3, 40.8+)	5.6 (1.8+, 40.6+)

	Pembro + chemo (n=106)	Chemo (n=123)
Events, n (%)	88 (83.0)	110 (89.4)
mOS, mo (95%CI)	18.6 (12.5, 22.9)	14.1 (11.4, 18.1)
HR (95%CI)	0.77 (0.58, 1.92)	

	Pembro + chemo (n=127)	Chemo (n=113)
Events, n (%)	115 (90.6)	104 (92.0)
mOS, mo (95%CI)	15.7 (12.4, 18.8)	14.7 (12.2, 17.3)
HR (95%CI)	0.91 (0.70, 1.19)	

LBA9000: Pemetrexed and platinum with or without pembrolizumab for tyrosine kinase inhibitor (TKI)-resistant, EGFR-mutant, metastatic nonsquamous NSCLC: Phase 3 KEYNOTE-789 study – Yang JC, et al

- Key results (cont.)

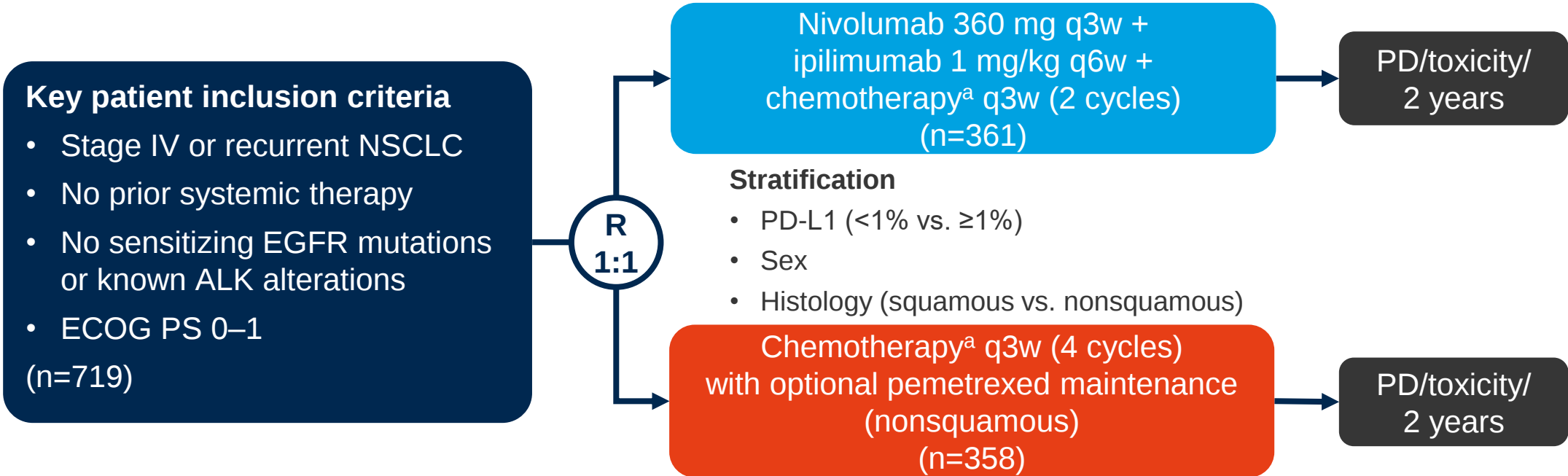
AEs, n (%)	Pembrolizumab + chemotherapy (n=245)	Chemotherapy (n=246)
Any AEs	239 (97.6)	241 (98.0)
Grade 3–5	137 (55.9)	143 (58.1)
Led to death	5 (2.0)	12 (4.9)
TRAE	220 (89.8)	212 (86.2)
Led to death	107 (43.7)	95 (38.6)
Led to discontinuation of any treatment component	40 (16.3)	29 (11.8)
Led to discontinuation of pembrolizumab or placebo	24 (9.8)	11 (4.5)
Led to discontinuation of any chemotherapy	31 (12.7)	29 (11.8)
Led to discontinuation of all treatment component	7 (2.9)	5 (2.0)
Immune-mediated AEs and infusion reactions	49 (20.2)	20 (8.1)
Grade 3–5	11 (4.5)	5 (2.0)

- Conclusions

- In patients with TKI-resistant, EGFR mutant metastatic nonsquamous NSCLC, the combination of pembrolizumab and chemotherapy provided numerically longer, but not statistically significant, PFS and OS compared with chemotherapy alone and had a manageable safety profile

LBA9023: First-line (1L) nivolumab (N) + ipilimumab (I) + chemotherapy (C) vs C alone in patients (pts) with metastatic NSCLC (mNSCLC) from CheckMate 9LA: 4-y clinical update and outcomes by tumor histologic subtype (THS) – Carbone DP, et al

- Study objective
 - To evaluate the long-term efficacy and outcomes by tumor histologic subtype of 1L nivolumab + ipilimumab + chemotherapy in patients with advanced NSCLC in the CheckMate 9LA study



Primary endpoint

- OS

Secondary endpoints

- PFS (BICR), ORR (BICR), safety

Exploratory endpoints

- OS by tumor histologic subtype

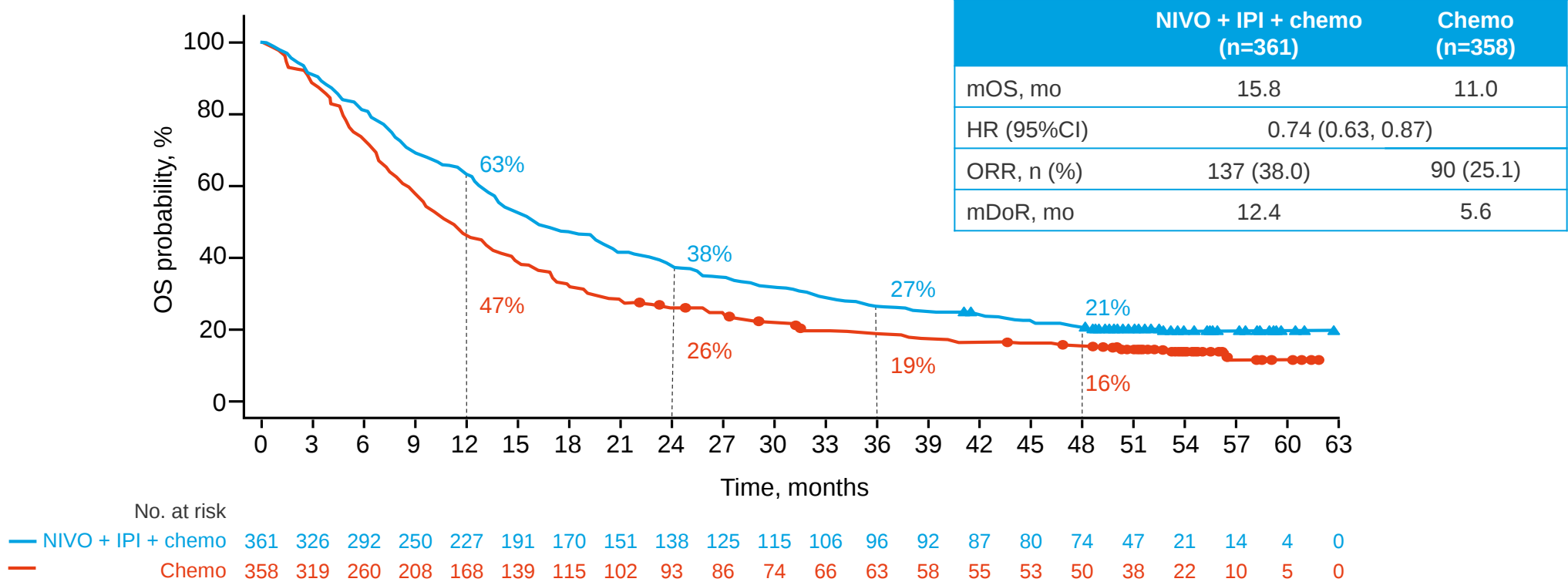
^aPemetrexed + cisplatin or carboplatin for nonsquamous and paclitaxel + carboplatin for squamous;

^bassessed using PD-L1 IHC 22C3 pharmDx.

LBA9023: First-line (1L) nivolumab (N) + ipilimumab (I) + chemotherapy (C) vs C alone in patients (pts) with metastatic NSCLC (mNSCLC) from CheckMate 9LA: 4-y clinical update and outcomes by tumor histologic subtype (THS) – Carbone DP, et al

- Key results

4-year update: OS in all randomized patients



LBA9023: First-line (1L) nivolumab (N) + ipilimumab (I) + chemotherapy (C) vs C alone in patients (pts) with metastatic NSCLC (mNSCLC) from CheckMate 9LA: 4-y clinical update and outcomes by tumor histologic subtype (THS) – Carbone DP, et al

- Key results (cont.)

	NIVO + IPI + chemo	Chemo
PD-L1 <1%, n	135	129
mOS, mo	17.7	9.8
HR (95%CI)	0.66 (0.50, 0.86)	
ORR, n (%)	42 (31.1)	26 (20.2)
mDoR, mo	17.5	4.3
PD-L1 ≥1%, n	204	204
mOS, mo	15.8	10.9
HR (95%CI)	0.74 (0.60, 0.92)	
ORR, n (%)	87 (42.6)	56 (27.5)
mDoR, mo	11.8	5.6

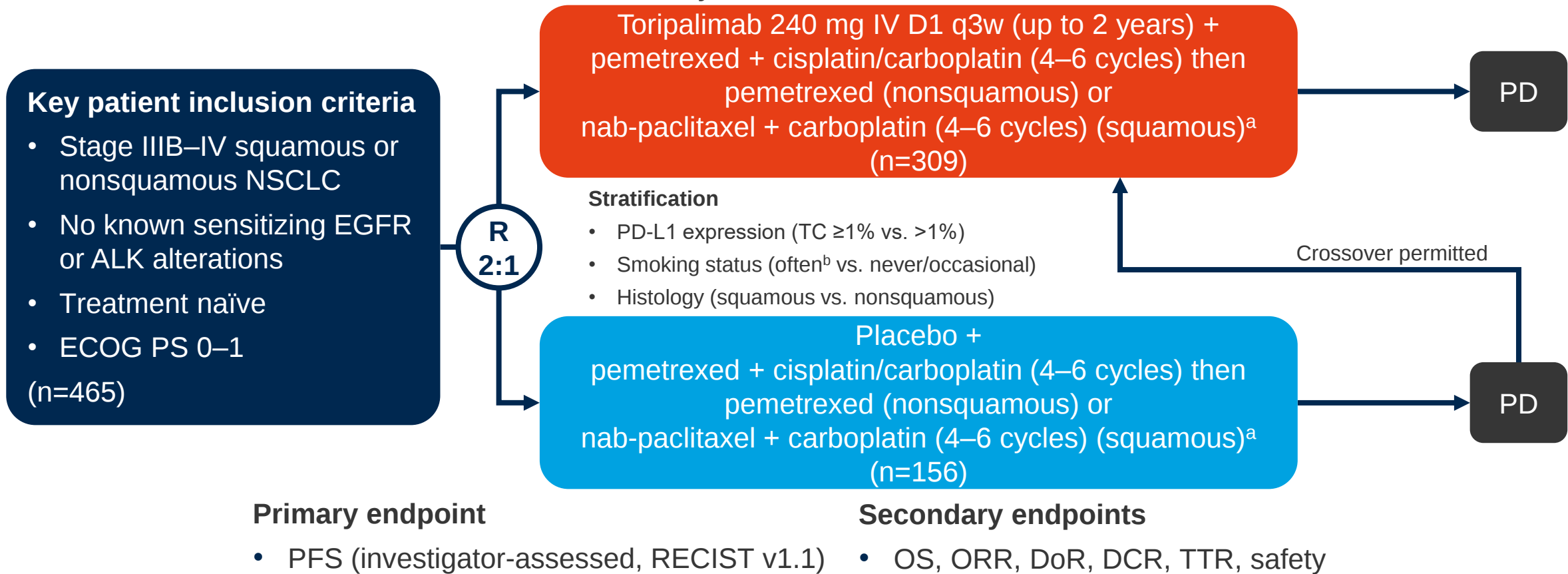
	NIVO + IPI + chemo	Chemo
Squamous, n	115	112
mOS, mo	14.5	9.1
HR (95%CI)	0.64 (0.48, 0.84)	
Nonsquamous, n	246	246
mOS, mo	17.8	12.0
HR (95%CI)	0.80 (0.66, 0.97)	
Solid tumors, n	80	87
mOS, mo	17.9	9.5
HR (95%CI)	0.70 (0.49, 0.99)	
Acinar tumors, n	63	53
mOS, mo	18.7	12.7
HR (95%CI)	0.77 (0.51, 1.15)	

- Conclusions

- In patients with advanced NSCLC, 1L nivolumab + ipilimumab + chemotherapy continued to provide survival benefit over chemotherapy alone, regardless of PD-L1 expression and tumor histologic subtype

9003: Final overall survival and biomarker analyses of CHOICE-01: A double-blind randomized phase 3 study of toripalimab versus placebo in combination chemotherapy for advanced NSCLC without EGFR/ALK mutations – Wu L, et al

- Study objective
 - To evaluate the final OS of 1L toripalimab + chemotherapy in patients with advanced NSCLC without EGFR/ALK mutations in the CHOICE-01 study

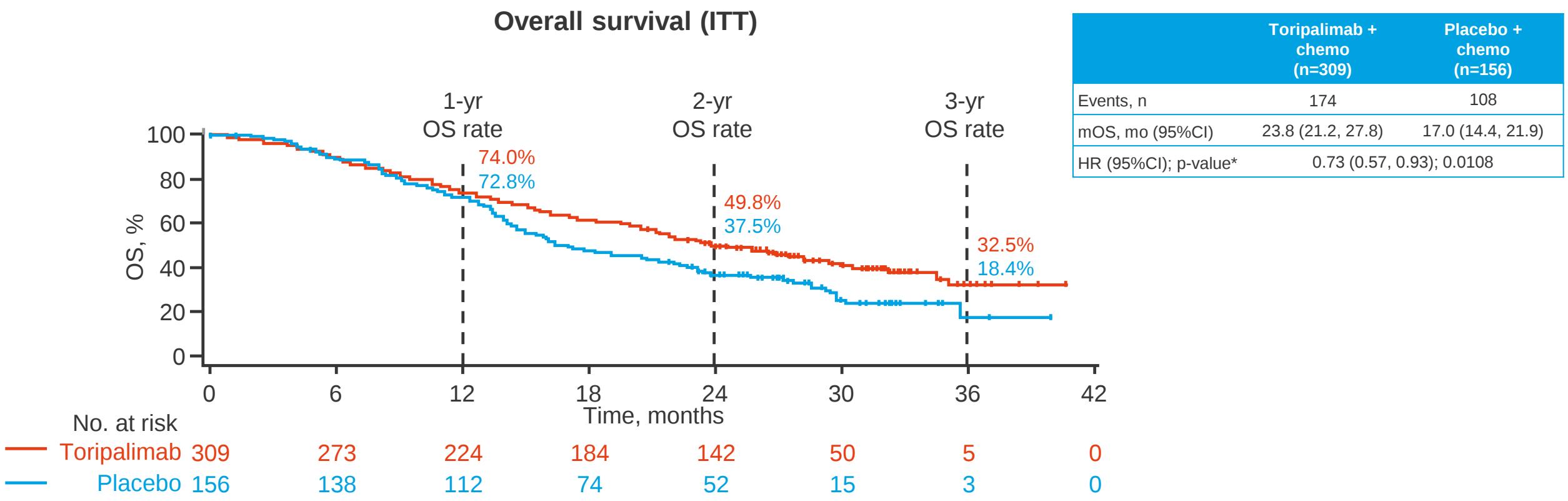


^aPemetrexed 500 mg/m² IV D1; cisplatin 75 mg/m² IV D1; carboplatin AUC5 IV D1; nab-paclitaxel 100 mg/m² IV D1, 8, 15; ^b≥400 cigarettes/year.

Wu L, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9003 30

9003: Final overall survival and biomarker analyses of CHOICE-01: A double-blind randomized phase 3 study of toripalimab versus placebo in combination chemotherapy for advanced NSCLC without EGFR/ALK mutations – Wu L, et al

- Key results



9003: Final overall survival and biomarker analyses of CHOICE-01: A double-blind randomized phase 3 study of toripalimab versus placebo in combination chemotherapy for advanced NSCLC without EGFR/ALK mutations – Wu L, et al

- Key results (cont.)

	Toripalimab + chemotherapy	Placebo + chemotherapy
Nonsquamous, n	162	83
mOS, mo (95%CI)	27.8 (25.0, NE)	15.9 (12.7, 22.9)
HR (95%CI); p-value	0.46 (0.35, 0.69); <0.0001	
TMB-H, n	77	45
mOS, mo (95%CI)	NE	20.7
HR (95%CI)	0.68 (0.41, 1.14)	
TMB-L, n	187	85
mOS, mo (95%CI)	23.2	16.0
HR (95%CI); p-value	0.75 (0.55, 1.04)	
PD-L1 TC <1%, n	98	41
mOS, mo (95%CI)	21.2	16.0
HR (95%CI); p-value	0.79 (0.52, 1.24)	
PD-L1 TC 1 - <50%, n	128	75
mOS, mo (95%CI)	23.7	17.0
HR (95%CI)	0.72 (0.51, 1.03)	
PD-L1 ≥50%, n	72	28
mOS, mo (95%CI)	30.0	28.4
HR (95%CI); p-value	0.91 (0.49, 1.80)	

	Toripalimab + chemotherapy (n=308)	Placebo + chemotherapy (n=156)
AEs, %		
Any	99.0	100
Grade ≥3	78.9	82.1
Serious	46.4	35.3
Grade ≥3	35.1	28.2
Led to death	5.5	2.6
Led to discontinuation	15.3	3.2
Led to interruption	64.3	55.1
Any investigator-determined irAEs	50.6	21.2
Grade ≥3	16.9	3.2
Any infusion-related reactions	2.6	1.3

- Conclusions

- In patients with advanced NSCLC without EGFR/ALK mutations, 1L toripalimab + chemotherapy significantly improved OS compared with chemotherapy alone and had a safety profile consistent with previous findings

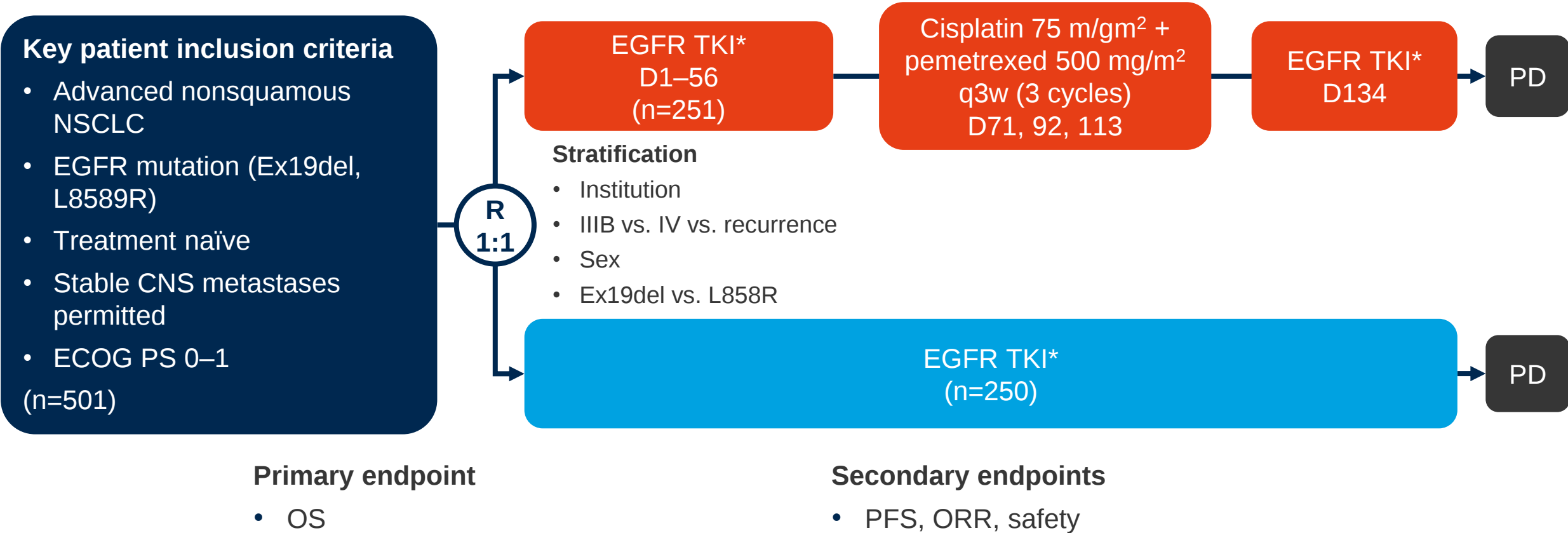
Advanced NSCLC

Not radically treatable stage III and stage IV

Targeted therapies

LBA9009: A phase III study comparing EGFR tyrosine kinase inhibitor (EGFR-TKI) monotherapy and EGFR-TKI with inserted cisplatin (CDDP) plus pemetrexed (PEM) as a first-line treatment in patients (pts) with advanced non-squamous non-small-cell lung cancer (NSqNSCLC) harboring EGFR activating mutation (EGFR-NSqNSCLC): JCOG1404/WJOG8214L, AGAIN study – Kanda S, et al

- **Study objective**
 - To evaluate the efficacy and safety of 1L EGFR TKI alone or combined with cisplatin + pemetrexed in patients with EGFR-mutant advanced nonsquamous NSCLC in the AGAIN study



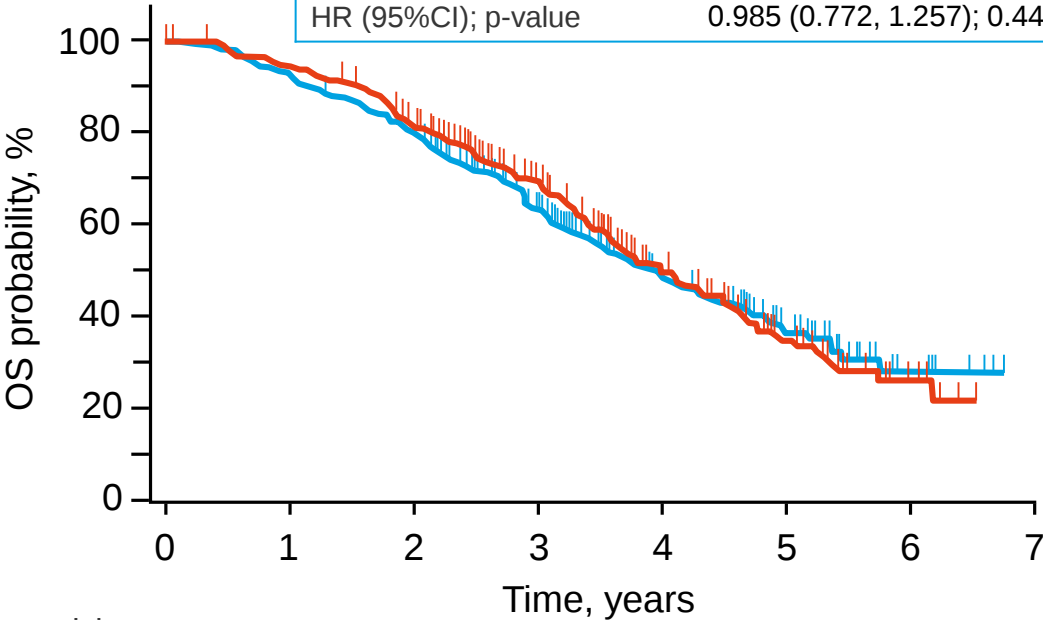
*Originally gefitinib 250 mg/day and changed to osimertinib 80 mg/day in October 2018. Kanda S, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9009 34

LBA9009: A phase III study comparing EGFR tyrosine kinase inhibitor (EGFR-TKI) monotherapy and EGFR-TKI with inserted cisplatin (CDDP) plus pemetrexed (PEM) as a first-line treatment in patients (pts) with advanced non-squamous non-small-cell lung cancer (NSqNSCLC) harboring EGFR activating mutation (EGFR-NSqNSCLC): JCOG1404/WJOG8214L, AGAIN study – Kanda S, et al

• Key results

Overall survival (ITT)

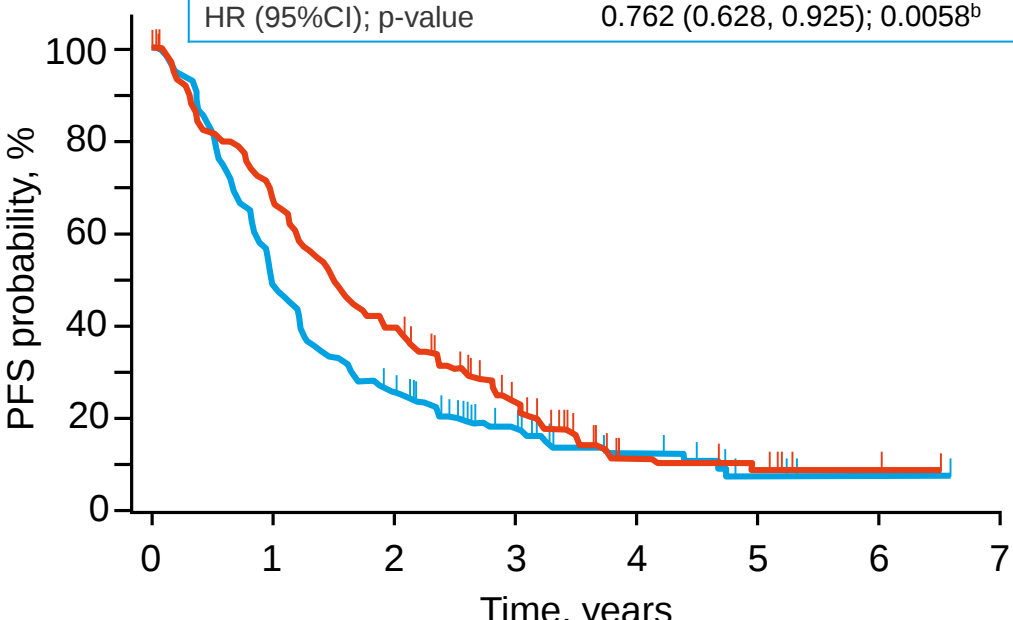
	EGFR TKI alone (n=250)	EGFR TKI + chemo (n=251)
mOS, mo (95%CI)	48.0 (40.8, 55.2)	48.0 (43.2, 54.0)
HR (95%CI); p-value	0.985 (0.772, 1.257); 0.4496 ^a	



No. at risk								
— EGFR TKI alone	250	232	200	124	70	36	7	0
— EGFR TKI + chemo	251	234	198	134	70	33	8	0

Progression-free survival (ITT)

	EGFR TKI alone (n=250)	EGFR TKI + chemo (n=251)
mPFS, mo (95%CI)	12.0 (10.8, 14.4)	18.0 (15.6, 20.4)
HR (95%CI); p-value	0.762 (0.628, 0.925); 0.0058 ^b	



	250	123	64	28	10	3	1	0
	251	166	97	46	11	7	2	0

^aOne-sided p-value calculated from log-rank test stratified by drug and sex and EGFR mutation subtype;
^btwo-sided p-value calculated from log-rank test.

LBA9009: A phase III study comparing EGFR tyrosine kinase inhibitor (EGFR-TKI) monotherapy and EGFR-TKI with inserted cisplatin (CDDP) plus pemetrexed (PEM) as a first-line treatment in patients (pts) with advanced non-squamous non–small-cell lung cancer (NSqNSCLC) harboring EGFR activating mutation (EGFR-NSqNSCLC): JCOG1404/WJOG8214L, AGAIN study – Kanda S, et al

• **Key results (cont.)**

AEs, %	EGFR TKI alone (n=250)				EGFR TKI + chemo (n=251)			
	Gefitinib (n=153)		Osimertinib (n=97)		Gefitinib (n=155)		Osimertinib (n=96)	
	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4
Neutrophil count decreased	22.0	1.3	36.8	3.2	65.6	11.3	70.2	18.1
Platelet count decreased	22.7	0	49.5	1.1	47.0	0.7	71.3	2.1
AST increased	82.0	15.3	43.2	3.2	80.1	15.2	69.1	3.2
ALT increased	80.7	26.7	44.2	4.2	83.4	27.8	72.3	8.5
Creatinine increased	28.0	0	35.8	0	36.4	0	53.2	1.1
Nausea	8.7	0	9.5	0	50.3	2.6	45.7	2.1
Anorexia	13.3	2.0	9.5	0	51.7	6.0	45.7	2.1
Diarrhea	38.7	2.0	52.6	0	41.1	0.7	44.7	1.1
Rash acneiform	82.0	2.0	58.9	2.1	80.8	1.3	58.5	1.1
Paronychia	38.7	2.0	44.2	1.1	23.2	0.7	40.4	0
ECG QTc prolonged	-	-	6.3	0	-	-	10.6	1.1
Pneumonitis	1.3	0	10.5	1.1	0.7	0.7	5.3	0
Led to discontinuation	14.4		11.3		8.4		14.6	
Led to death	0		1.0		0		0	

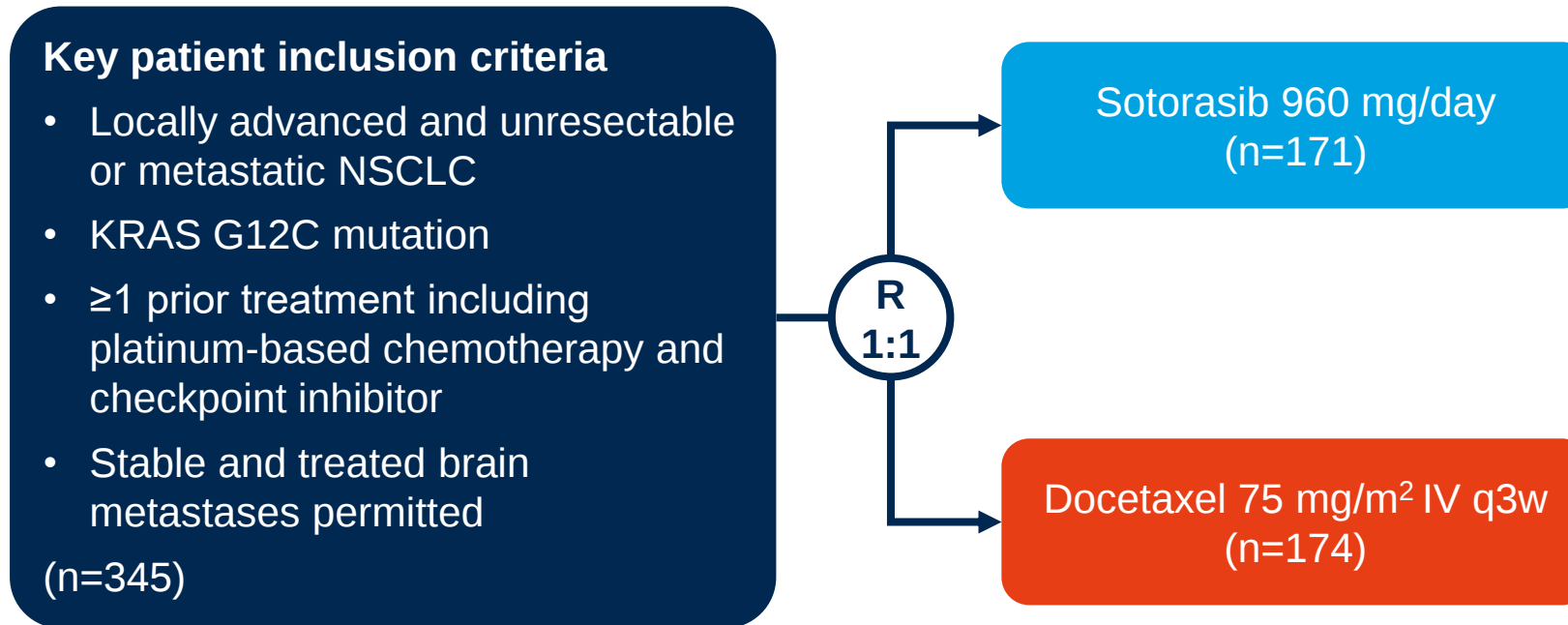
• **Conclusions**

- In patients with EGFR-mutant advanced nonsquamous NSCLC, using cisplatin + pemetrexed after initial response to EGFR TKI improved PFS, but not OS, compared with EGFR TKI alone and was associated with higher rates of TRAEs

LBA9016: Intracranial efficacy of sotorasib versus docetaxel in pretreated KRAS G12C-mutated advanced non-small cell lung cancer (NSCLC): Practice-informing data from a global, phase 3, randomized, controlled trial (RCT) – Dingemans AC, et al

- **Study objective**

- To evaluate the intracranial efficacy of sotorasib in previously treated patients with KRAS G12C-mutant advanced NSCLC a post-hoc analysis of the CodeBreak 200 study



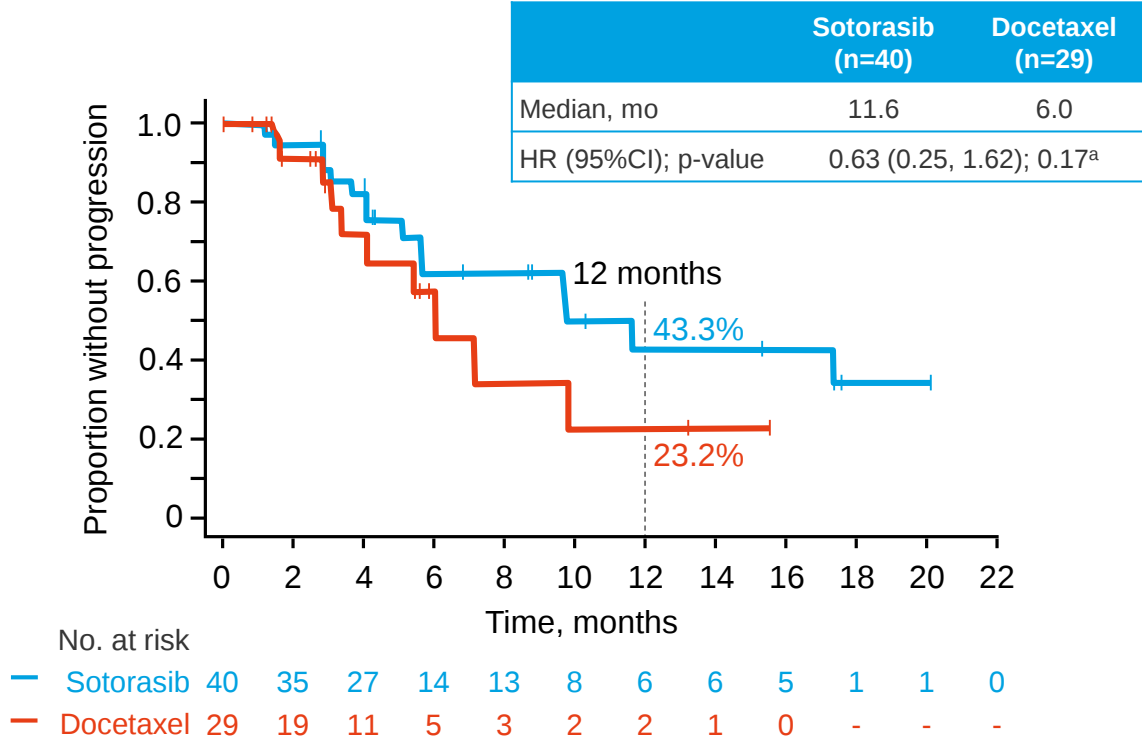
Endpoints

- CNS PFS/progression, intracranial ORR/DCR, safety

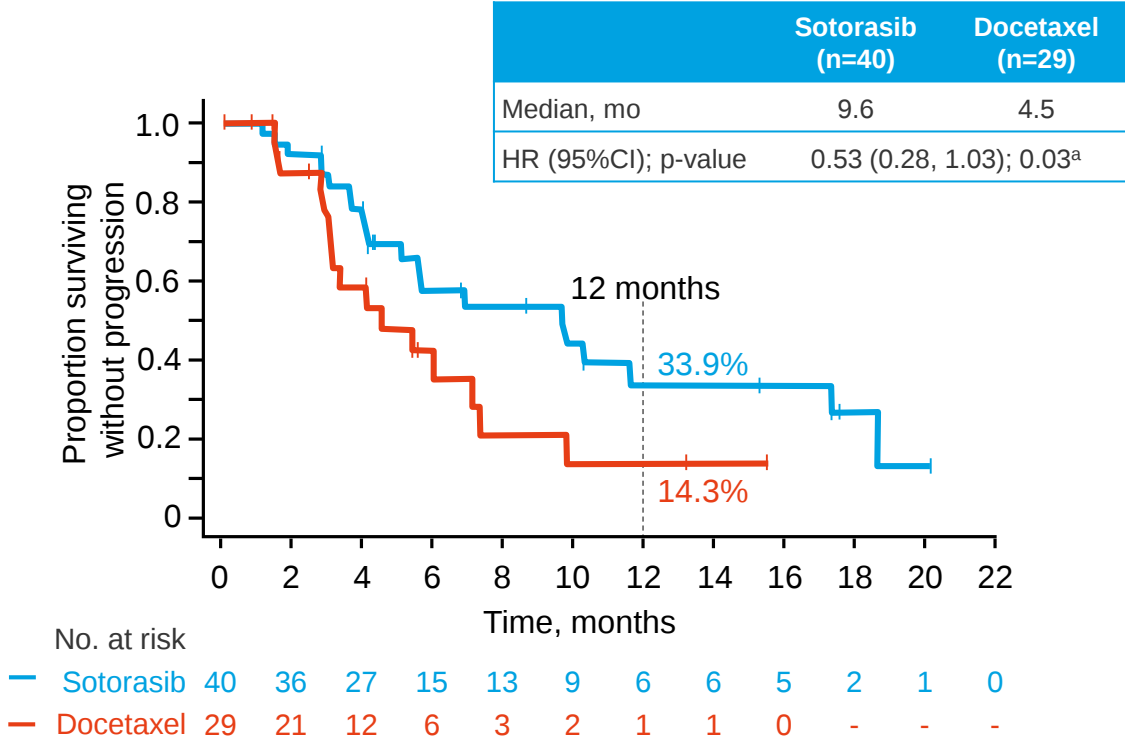
LBA9016: Intracranial efficacy of sotorasib versus docetaxel in pretreated KRAS G12C-mutated advanced non-small cell lung cancer (NSCLC): Practice-informing data from a global, phase 3, randomized, controlled trial (RCT) – Dingemans AC, et al

- Key results

Time to CNS progression in patients with CNS lesions at baseline



CNS progression-free survival in patients with CNS lesions at baseline



LBA9016: Intracranial efficacy of sotorasib versus docetaxel in pretreated KRAS G12C-mutated advanced non-small cell lung cancer (NSCLC): Practice-informing data from a global, phase 3, randomized, controlled trial (RCT) – Dingemans AC, et al

- Key results (cont.)

Intracranial response (RANO-BM criteria), n (%)	Patients with stable/pretreated CNS lesions at baseline ^a	
	Sotorasib (n=18)	Docetaxel (n=13)
Confirmed ORR	6 (33.3)	2 (15.4)
CR	1 (5.6)	1 (7.7)
PR	5 (27.8)	1 (7.7)
SD	9 (50.0)	9 (69.2)
PD	1 (5.6)	2 (15.4)
NE/not done	2 (11.2)	0
DCR	15 (83.3)	11 (84.6)
Unconfirmed/confirmed ORR	9 (50.0)	2 (15.4)

- Conclusions

- In previously treated patients with KRAS G12C-mutant advanced NSCLC, sotorasib demonstrated encouraging CNS specific activity compared with docetaxel

9001: Randomized phase 3 study of first-line AZD3759 (zorifertinib) versus gefitinib or erlotinib in EGFR-mutant (EGFRm+) non–small-cell lung cancer (NSCLC) with central nervous system (CNS) metastasis – Wu Y, et al

- **Study objective**

- To evaluate the efficacy and safety of 1L zorifertinib in previously treated patients with EGFR-mutant NSCLC and CNS metastases

Key patient inclusion criteria

- Advanced NSCLC
 - EGFR mutation (L858R and/or Ex19del)
 - No EGFR T790M, KRAS or cMET mutations
 - No prior 1L systemic therapy or brain radiotherapy
 - CNS metastases
 - ECOG PS 0–1
- (n=439)

R
1:1

Zorifertinib 200 mg BID
(n=220)

Gefitinib 250 mg/day or
erlotinib 150 mg/day
(n=219)

Primary endpoint

- PFS (BICR, RECIST v1.1)

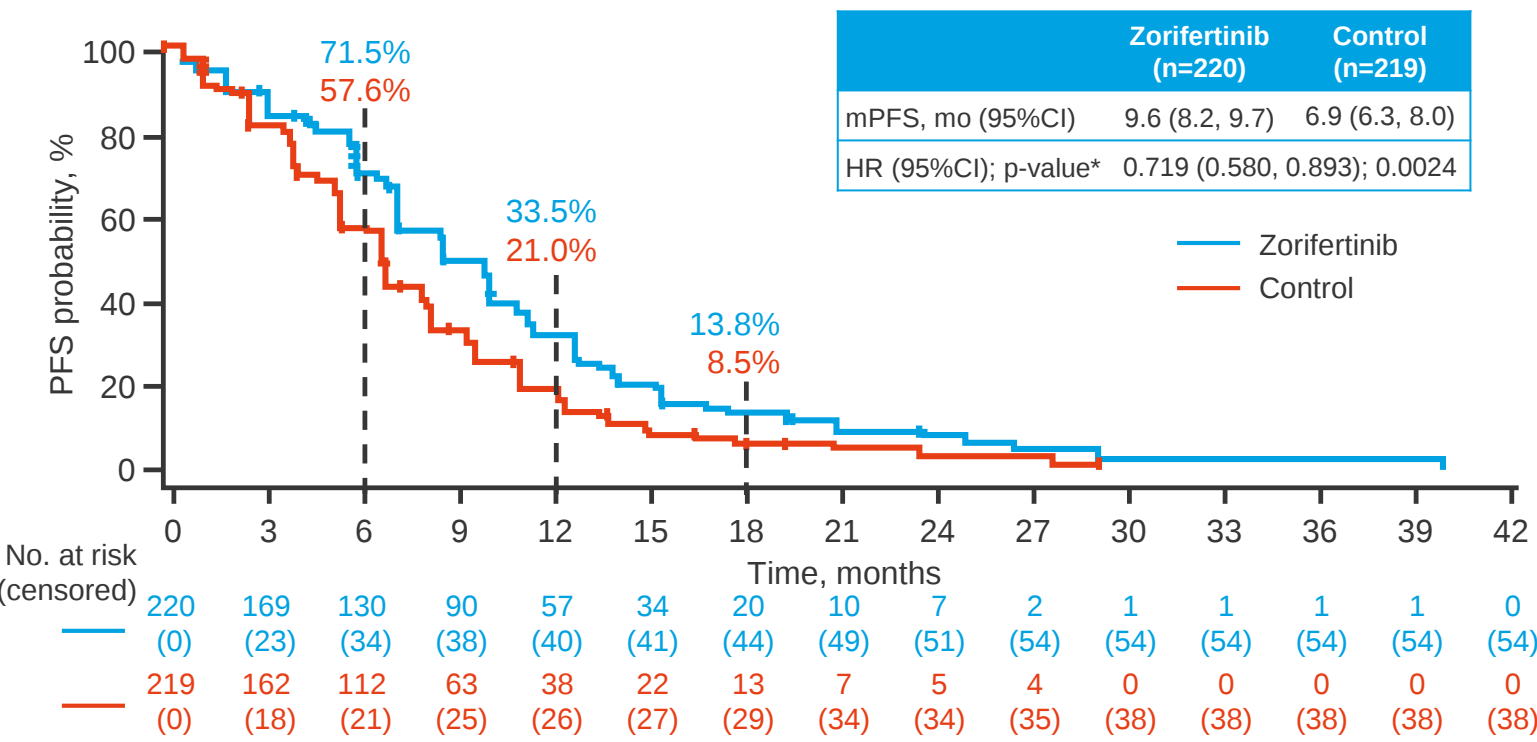
Secondary endpoints

- Cranial PFS, ORR, DoR, OS, safety

9001: Randomized phase 3 study of first-line AZD3759 (zorifertinib) versus gefitinib or erlotinib in EGFR-mutant (EGFRm+) non–small-cell lung cancer (NSCLC) with central nervous system (CNS) metastasis – Wu Y, et al

- Key results

PFS assessed by BICR per RECIST 1.1 (ITT)



Response	BICR per RECIST v1.1	
	Zorifertinib (n=220)	Control (n=219)
ORR, n (%)	151 (68.6)	128 (58.4)
OR (95%CI)	1.533 (1.051, 2.293)	
mDoR, mo (95%CI)	8.2 (6.9, 8.3)	6.8 (5.6, 7.0)
HR (95%CI); p-value*	0.801 (0.613, 1.047); 0.0997	
Intracranial ORR, n (%)	96 (75.6)	76 (62.3)
OR (95%CI)	1.904 (1.098, 3.302)	
mDoR, mo (95%CI)	13.8 (8.5, 22.1)	11.1 (8.3, 14.0)
HR (95%CI); p-value*	0.789 (0.501, 1.244); 0.3037	
Intracranial PFS, mo (95%CI)	15.2 (12.5, 19.4)	8.3 (8.0, 9.6)
HR (95%CI); p-value*	0.467 (0.352, 0.619); <0.0001	

– An exploratory analysis showed that EGFR T790M mutation was associated with resistance in 33.3% and 12.0% of patients in the zorifertinib and control arms, respectively

9001: Randomized phase 3 study of first-line AZD3759 (zorifertinib) versus gefitinib or erlotinib in EGFR-mutant (EGFRm+) non–small-cell lung cancer (NSCLC) with central nervous system (CNS) metastasis – Wu Y, et al

- Key results (cont.)

Grade 3–4* TRAEs in ≥5% of patients, n (%)	Zorifertinib (n=220)		Control (n=218)		TRAEs leading to dose modification in ≥5% of patients, n (%)	Zorifertinib (n=220)	Control (n=218)
	Grade 3	Grade 4	Grade 3	Grade 4			
Any	139 (63.2)	5 (2.3)	38 (17.4)	2 (0.9)	Any	155 (70.5)	38 (17.4)
AST increased	14 (6.4)	1 (0.5)	16 (7.3)	0	Rash	39 (17.7)	1 (0.5)
ALT increased	23 (10.5)	1 (0.5)	22 (10.1)	1 (0.5)	Diarrhea	38 (17.3)	1 (0.5)
Diarrhea	29 (13.2)	0	1 (0.5)	0	Dermatitis acneiform	33 (15.0)	3 (1.4)
Rash	30 (13.6)	0	1 (0.5)	0	ALT increased	31 (14.1)	26 (11.9)
Dermatitis acneiform	30 (13.6)	0	1 (0.5)	0	AST increased	30 (13.6)	23 (10.6)
γ-GT increased	12 (5.5)	2 (0.9)	5 (2.3)	0	Decreased appetite	18 (8.2)	0
Hypokalemia	13 (5.9)	1 (0.5)	0	0	Blood bilirubin increased	14 (6.4)	1 (0.5)
Any TRAE led to discontinuation	13 (5.9)		5 (2.3)				

- Conclusions

- In patients with EGFR-mutant NSCLC and CNS metastases, 1L zorifertinib demonstrated encouraging CNS antitumor efficacy compared with gefitinib or erlotinib, however, this is not compared with the current standard osimertinib and had a manageable safety profile

9002: Sunvozertinib for the treatment of NSCLC with EGFR Exon20 insertion mutations: The first pivotal study results – Wang M, et al

- **Study objective**

- To evaluate the efficacy and safety of sunvozertinib in patients with NSCLC and EGFR exon20 insertion mutations

Key patient inclusion criteria

- Locally advanced or metastatic NSCLC
- EGFR exon20 insertion mutation (local or central)
- 1–3 prior lines of systemic therapy
- PD on or after platinum-based chemotherapy

(n=104)

Sunvozertinib
300 mg/day

Primary endpoint

- ORR (IRC)

Secondary endpoints

- DoR, PFS, DCR, OS, safety

9002: Sunvozertinib for the treatment of NSCLC with EGFR Exon20 insertion mutations: The first pivotal study results – Wang M, et al

- Key results

Response	Sunvozertinib (n=97)
ORR, n (%) [95%CI]; p-value	59 (60.8) [50.4, 70.6]; <0.0001
BOR, n (%)	
PR (confirmed)	59 (60.8)
SD	26 (26.8)
PD	6 (6.2)
NR	6 (6.2)
DCR, n (%) [95%CI]	85 (87.6) [79.4, 93.4]

EGFR Ex20ins subtypes	Sunvozertinib (n=97)
C-helical, n	2
ORR, %	100
DCR, %	100
Near loop, n	71
ORR, %	62.0
DCR, %	88.7
Far loop, n	24
ORR, %	54.2
DCR, %	83.3

9002: Sunvozertinib for the treatment of NSCLC with EGFR Exon20 insertion mutations: The first pivotal study results – Wang M, et al

- Key results (cont.)

TEAEs, n (%)	Sunvozertinib (n=104)	
	All grade	Grade ≥3
Diarrhea	70 (67.3)	8 (7.7)
Blood CPK increased	60 (57.7)	18 (17.3)
Rash	56 (53.8)	1 (1.0)
Anemia	51 (49.0)	6 (5.8)
Blood creatine increased	39 (37.5)	0
Paronychia	34 (32.7)	2 (1.9)
Body weight decreased	30 (28.8)	1 (1.0)
WBC count decreased	27 (26.0)	0
Lipase increased	27 (26.0)	2 (1.9)
Vomiting	25 (24.0)	1 (1.0)
Appetite decreased	25 (24.0)	2 (1.9)
Mouth ulceration	24 (23.1)	0

- Conclusions

- In patients with NSCLC and EGFR exon20 insertion mutations, 2L sunvozertinib demonstrated promising antitumor activity regardless of the mutational subtypes with a manageable safety profile

9006: The primary endpoint analysis of SCARLET study: A single-arm, phase II study of sotorasib plus carboplatin-pemetrexed in patients with advanced non-squamous, non-small cell lung cancer with KRAS G12C mutation (WJOG14821L) – Akamatsu H, et al

- **Study objective**

- To evaluate the efficacy and safety of sotorasib + carboplatin-pemetrexed in patients with advanced nonsquamous NSCLC and KRAS G12C mutations in the SCARLET study

Key patient inclusion criteria

- Advanced nonsquamous NSCLC
 - KRAS G12C mutation
 - Cytotoxic chemotherapy and KRAS inhibitor naïve
 - Asymptomatic CNS metastases permitted
 - ECOG PS 0–1
- (n=29)

Sotorasib 960 mg/day +
carboplatin AUC5 +
pemetrexed 500 mg/m² q3w
(4 cycles)

Sotorasib +
pemetrexed
q3w

PD

Primary endpoint

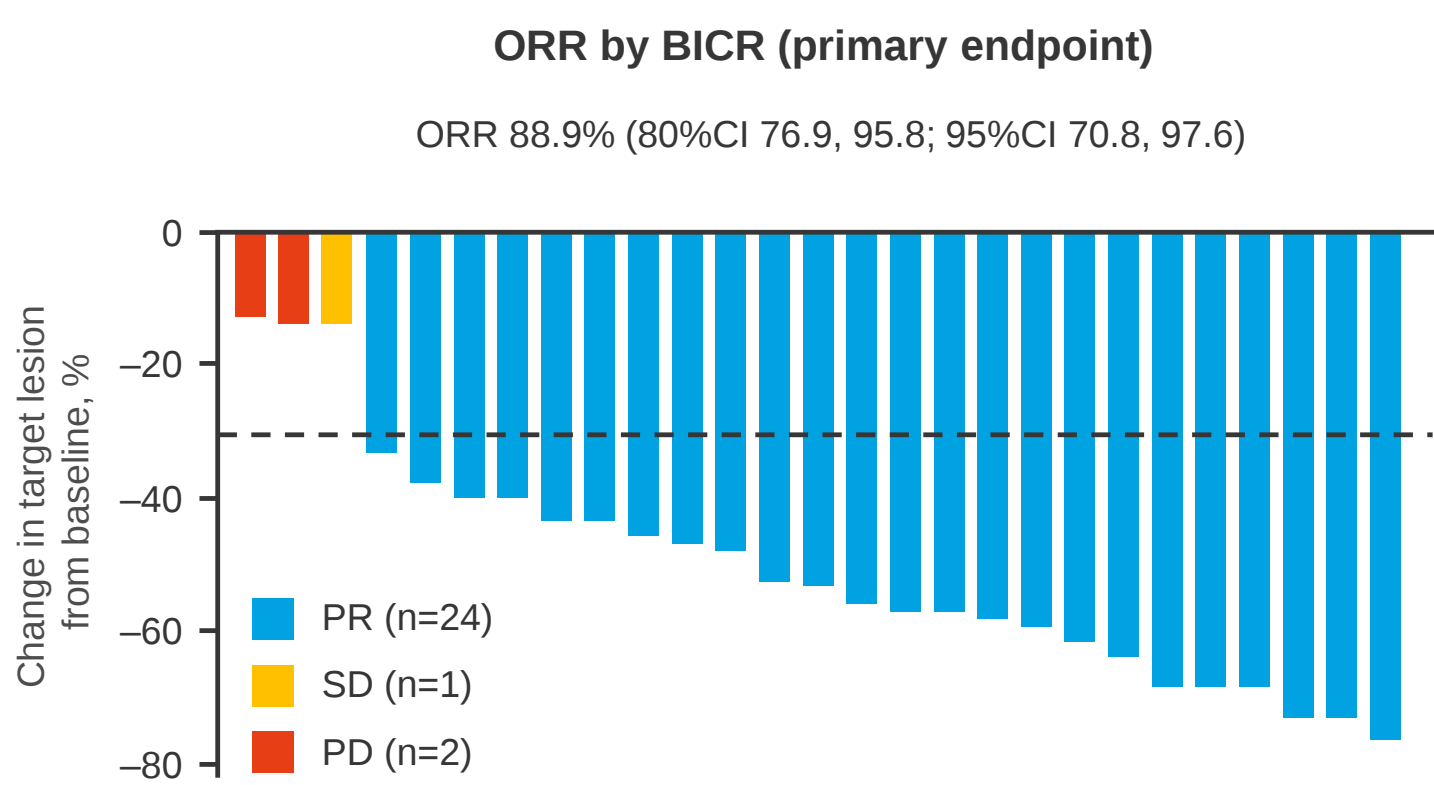
- ORR (BICR)

Secondary endpoints

- PFS, DCR, DoR, OS, safety

9006: The primary endpoint analysis of SCARLET study: A single-arm, phase II study of sotorasib plus carboplatin-pemetrexed in patients with advanced non-squamous, non-small cell lung cancer with KRAS G12C mutation (WJOG14821L) – Akamatsu H, et al

- Key results



Sotorasib + carboplatin-pemetrexed (n=27)	
mPFS, mo*	5.7
6-mo PFS rate, %	49.6
mOS, mo	NR
6-mo OS rate, %	87.3

	PD-L1 expression		
	Negative (<1%) (n=5)	Low (1–49%) (n=9)	High (≥50%) (n=13)
ORR, % (95%CI)	100 (47.8, 100)	100 (66.4, 100)	76.9 (46.2, 95.0)
mPFS, mo	7.5	5.7	NR

*Median follow-up: 4.1 mo (0.6–11.3).

9006: The primary endpoint analysis of SCARLET study: A single-arm, phase II study of sotorasib plus carboplatin-pemetrexed in patients with advanced non-squamous, non-small cell lung cancer with KRAS G12C mutation (WJOG14821L) – Akamatsu H, et al

- Key results (cont.)

Grade ≥3 TRAEs occurring in ≥5%, n (%)	Sotorasib + carboplatin-pemetrexed (n=29)
Any	21 (72.4)
Anemia	11 (37.9)
Platelet count decreased	7 (24.1)
Neutrophil decreased	7 (24.1)
WBC count decreased	6 (20.7)
Neutropenia	3 (10.3)
AST increased	2 (6.9)
Diarrhea	2 (6.9)

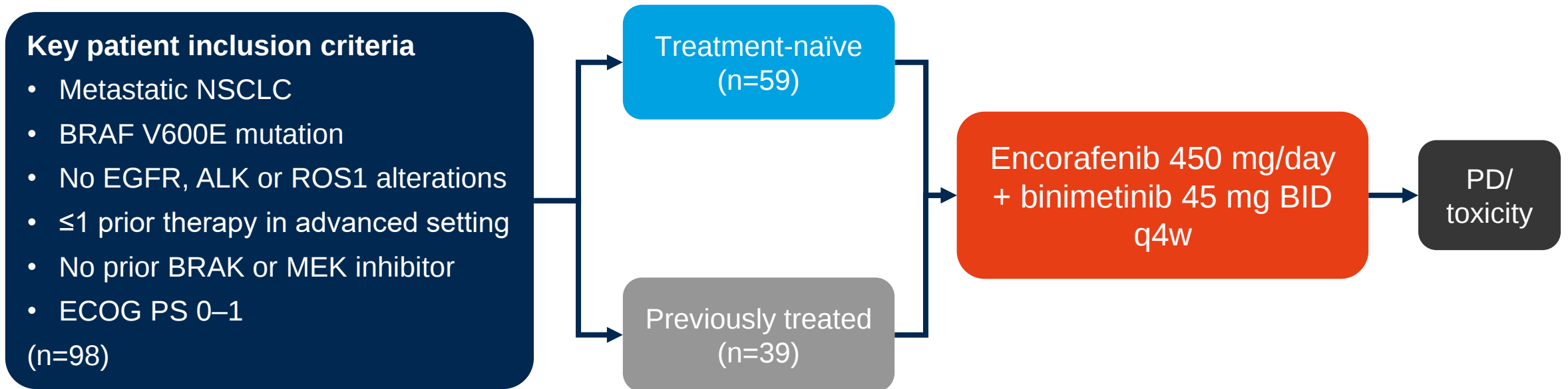
- Conclusions

- In patients with advanced nonsquamous NSCLC and KRAS G12C mutations, sotorasib + carboplatin-pemetrexed showed interesting antitumor activity and a manageable safety profile in this early analysis

9018: Efficacy and safety of encorafenib (enco) plus binimetinib (bini) in patients with BRAF V600E-mutant (BRAFFV600E) metastatic non-small cell lung cancer (NSCLC) from the phase 2 PHAROS study – Riely GJ, et al

- **Study objective**

- To evaluate the efficacy and safety of encorafenib + binimetinib in patients with metastatic BRAF V600E-mutant NSCLC in the phase 2 PHAROS study



Primary endpoint

- ORR (IRR)

Secondary endpoints

- DoR, DCR, PFS, TTR, OS, safety

9018: Efficacy and safety of encorafenib (enco) plus binimetinib (bini) in patients with BRAF V600E-mutant (BRAFFV600E) metastatic non-small cell lung cancer (NSCLC) from the phase 2 PHAROS study – Riely GJ, et al

- Key results

Response	Treatment-naïve (n=59)	Previously treated (n=39)
ORR, ^a % (95%CI)	75 (62, 85)	46 (30, 63)
BOR, n (%)		
CR	9 (15)	4 (10)
PR	35 (59)	14 (36)
SD	10 (17)	13 (33)
PD	2 (3)	3 (8)
DCR at 24 weeks, % (95%CI)	64 (51, 76)	41 (26, 58)
mDoR, mo (95%CI)	NE (23.1, NE)	16.7 (7.4, NE)
Duration of response ≥12 months, n/N (%)	26/44 (59)	6/18 (33)
mTTR, mo (range)	1.9 (1.1–19.1)	1.7 (1.2–7.3)
PFS events, n (%)	21 (36)	17 (44)
mPFS, mo (95%CI)	NE (15.7, NE)	9.3 (6.2, NE)

^aResponse was not evaluable in 3 patients in the treatment-naïve group and 5 in the treated group.

9018: Efficacy and safety of encorafenib (enco) plus binimetinib (bini) in patients with BRAF V600E-mutant (BRAFV600E) metastatic non-small cell lung cancer (NSCLC) from the phase 2 PHAROS study – Riely GJ, et al

- Key results (cont.)

TRAEs occurring in ≥10% of patients, n (%)	Overall (n=98)		
	Any grade	Grade 3	Grade 4
Any TRAEs ^a	92 (94)	37 (38)	3 (3)
Nausea	49 (50)	3 (3)	0
Diarrhea	42 (43)	4 (4)	0
Fatigue	31 (32)	2 (2)	0
Vomiting	28 (29)	1 (1)	0
Anemia	18 (18)	3 (3)	0
Vision blurred	17 (17)	1 (1)	0
Constipation	13 (13)	0	0
ALT increased	12 (12)	5 (5)	0
AST increased	12 (12)	7 (7)	0
Pruritus	12 (12)	0	0
Blood creatine phosphokinase increased	11 (11)	0	0
Edema peripheral	11 (11)	0	0

- Conclusions

- In patients with metastatic BRAF V600E-mutant NSCLC, encorafenib + binimetinib demonstrated promising antitumor activity and had an acceptable safety profile

^aOne patient died due to intracranial hemorrhage which was treatment-related.

Advanced NSCLC

Not radically treatable stage III and stage IV

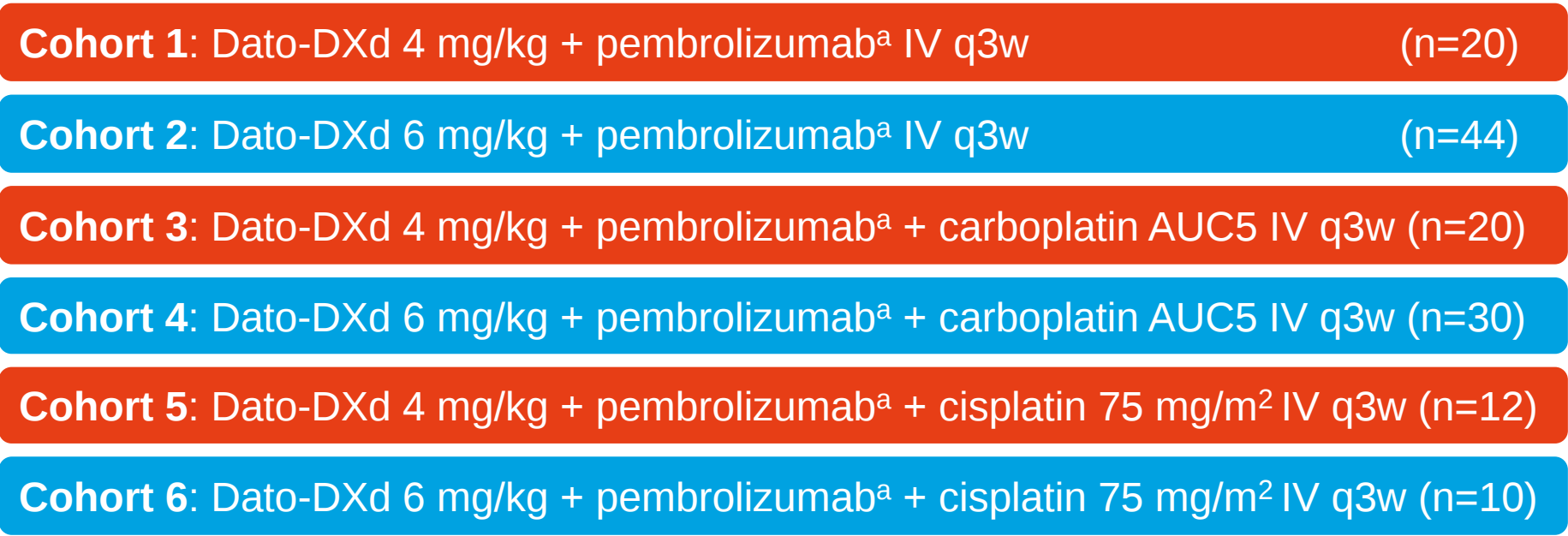
ADCs and other therapies

9004: TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab (pembro) with or without platinum chemotherapy (Pt-CT) in advanced non-small cell lung cancer (aNSCLC) – Goto Y, et al

- Study objective
 - To evaluate the efficacy and safety of datopotamab deruxtecan + pembrolizumab ± platinum chemotherapy in patients with advanced NSCLC in the TROPION-Lung02 study

Key patient inclusion criteria

- Advanced or metastatic NSCLC
- Dose confirmation: ≤2 lines of prior therapy
- Dose expansion: ≤1 line of platinum-based chemotherapy (Cohorts 1 and 2) and no prior therapy (Cohorts 3–6)



Primary endpoint

- Safety

Secondary endpoints

- Efficacy, PK, immunogenicity

9004: TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab (pembro) with or without platinum chemotherapy (Pt-CT) in advanced non-small cell lung cancer (aNSCLC) – Goto Y, et al

- Key results

AEs, n (%)	Doublet (n=64)	Triplet (n=72)
TEAEs	62 (97)	72 (100)
Treatment-related	58 (91)	72 (100)
Grade ≥3 TEAEs	34 (53)	55 (76)
Treatment-related	20 (31)	42 (58)
Serious TEAEs	20 (31)	29 (40)
Treatment-related	6 (9)	16 (22)
TEAEs led to:		
Death	3 (5)	5 (7)
Dose reduction of any drug	14 (22)	14 (19)
Dose reduction of Dato-DXd	14 (22)	11 (15)
Discontinuation of any drug	18 (28)	27 (38)
Discontinuation of Dato-DXd	15 (23)	20 (28)

Grade ≥3 TEAEs occurring in ≥5%, %	Doublet	Triplet
Stomatitis	8	4
Anemia	2	13
Fatigue	3	8
Appetite decreased	5	1
Platelet count decreased	0	7
Amylase increased	6	8
Neutrophil count decreased	0	14
Neutropenia	0	13

9004: TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab (pembro) with or without platinum chemotherapy (Pt-CT) in advanced non-small cell lung cancer (aNSCLC) – Goto Y, et al

- Key results (cont.)

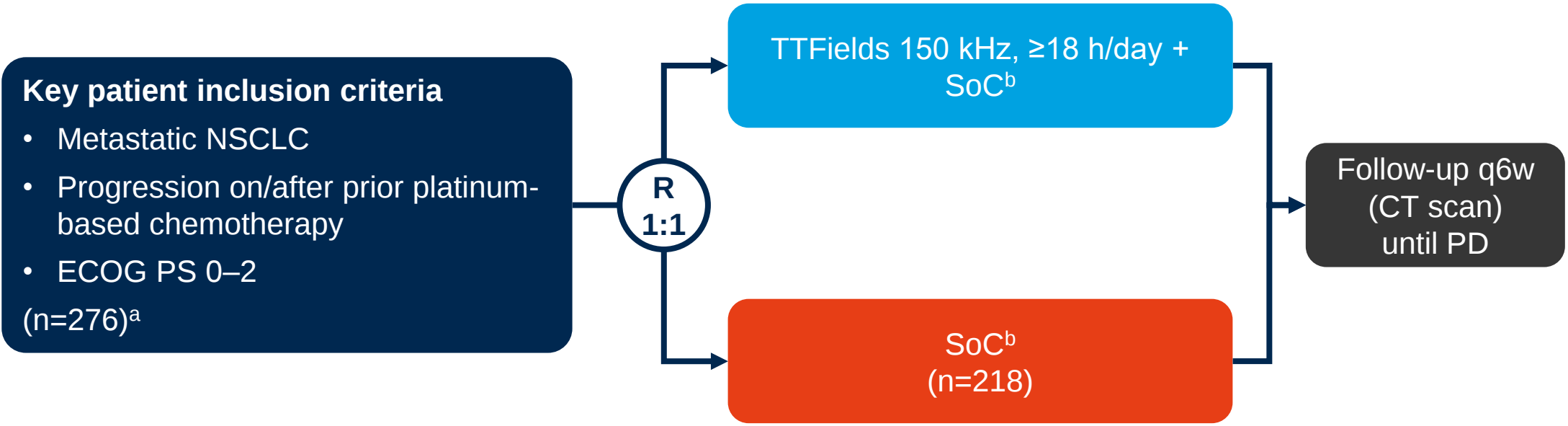
Response	All patients		1L patients	
	Doublet (n=61)	Triplet (n=71)	Doublet (n=61)	Triplet (n=71)
Confirmed + pending ORR, n (%) [95%CI]	23 (38) [26, 51]	35 (49) [37, 61]	17 (50) [32, 68]	30 (57) [42, 70]
Confirmed + pending BOR, n (%)				
Confirmed CR	0	1 (1)	0	1 (2)
Pending CR	0	0	0	0
Confirmed PR	21 (34)	34 (48)	15 (44)	29 (55)
Pending PR	2 (3)	0	2 (6)	0
SD, n (%)	30 (49)	27 (38)	16 (47)	18 (34)
DCR, n (%)	51 (84)	62 (87)	31 (91)	48 (91)
mDoR, mo (95%CI)	NE (8.8, NE)	NE (5.8, NE)	NE [5.5, NE]	NE (5.7, NE)
Preliminary mPFS, mo (95%CI)	8.3 (6.8, 11.8)	7.8 (5.6, 11.1)	-	-

- Conclusions

- In patients with advanced NSCLC, datopotamab deruxtecan + pembrolizumab ± platinum chemotherapy demonstrated promising antitumor activity with no new safety signals observed

LBA9005: Tumor Treating Field (TTFields) therapy with standard of care (SOC) in metastatic non-small cell lung cancer (mNSCLC) following platinum failure: Randomized, phase 3 LUNAR study – Leal T, et al

- Study objective
 - To evaluate the efficacy and safety of TTFields therapy + SoC in patients with metastatic NSCLC who have progressed on platinum therapy in the LUNAR study



Primary endpoint

- OS

Secondary endpoints

- OS (in ICI-treated and docetaxel-treated subgroups), PFS, ORR, safety

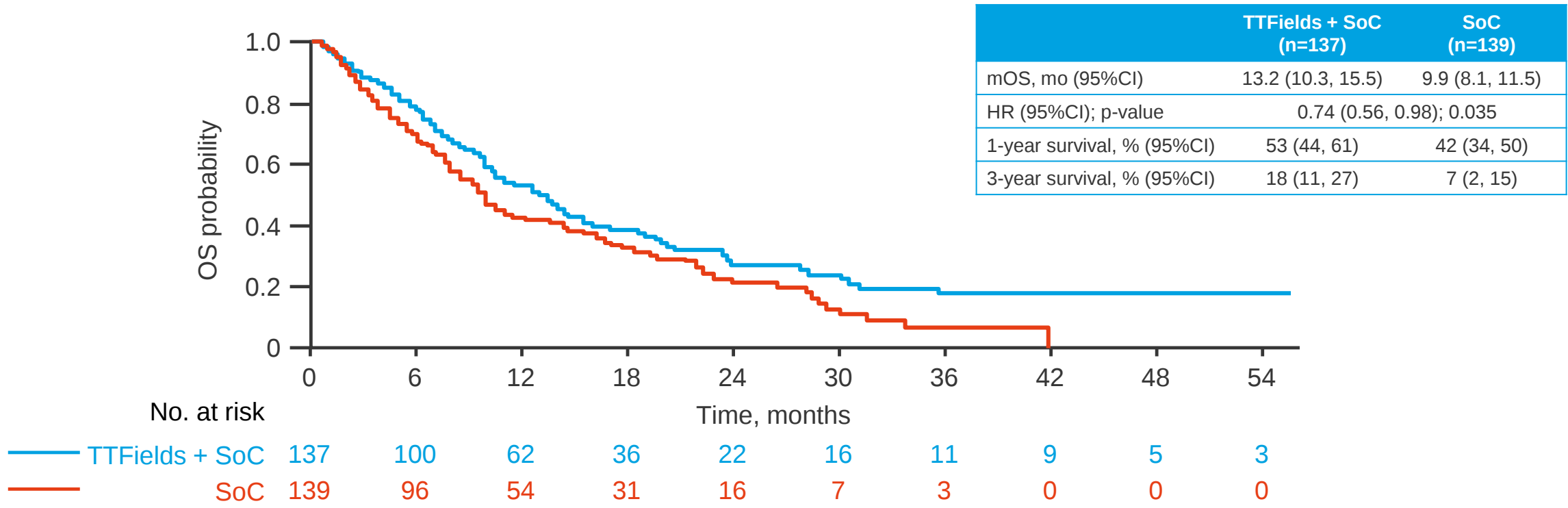
^aPatient accrual changed from 534 to 276 following DMC recommendation at planned interim analysis (March 2021); ^binvestigator's choice of docetaxel or ICI (pembrolizumab, or nivolumab, or atezolizumab).

Leal T, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9005 56

LBA9005: Tumor Treating Field (TTFields) therapy with standard of care (SOC) in metastatic non-small cell lung cancer (mNSCLC) following platinum failure: Randomized, phase 3 LUNAR study – Leal T, et al

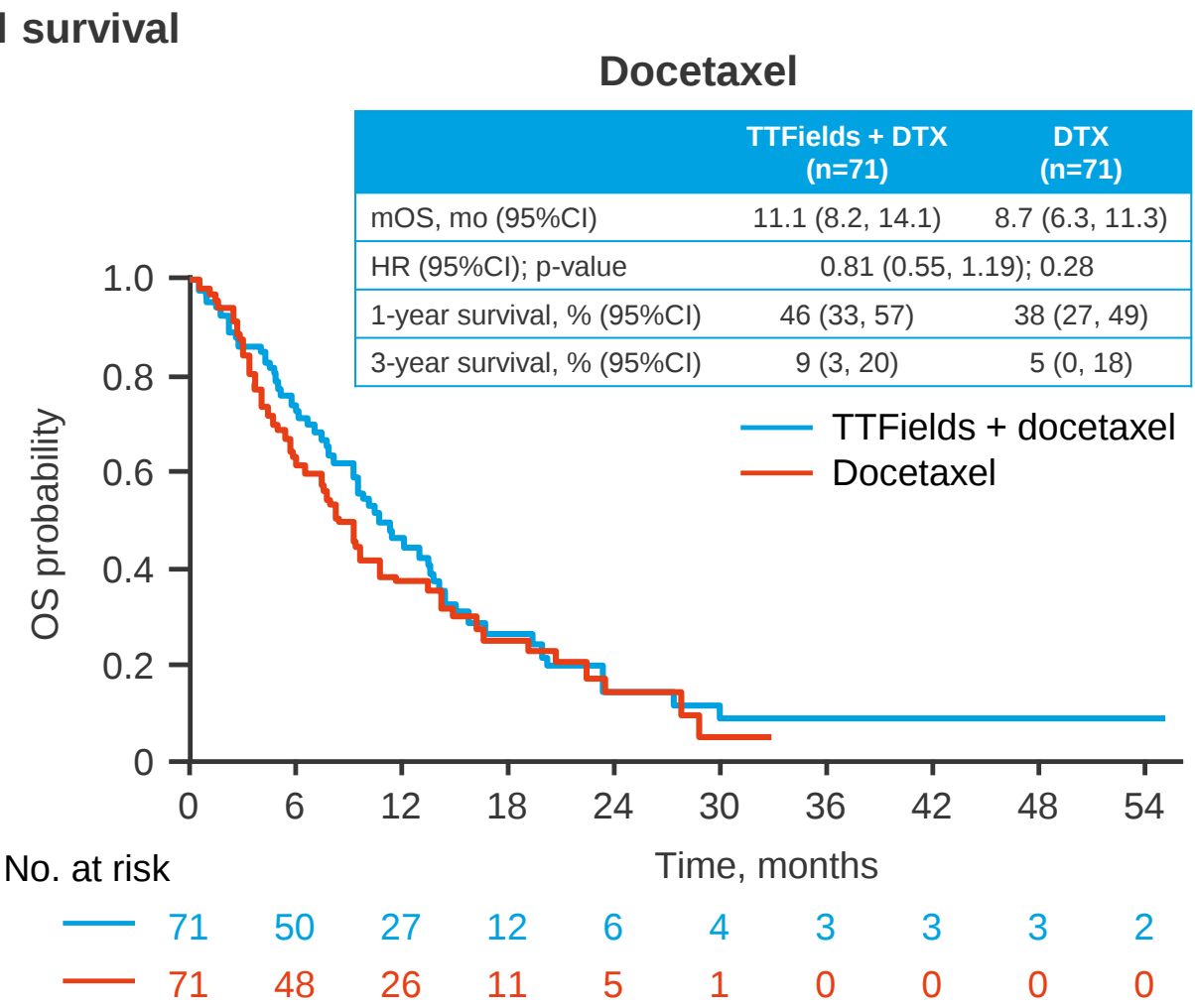
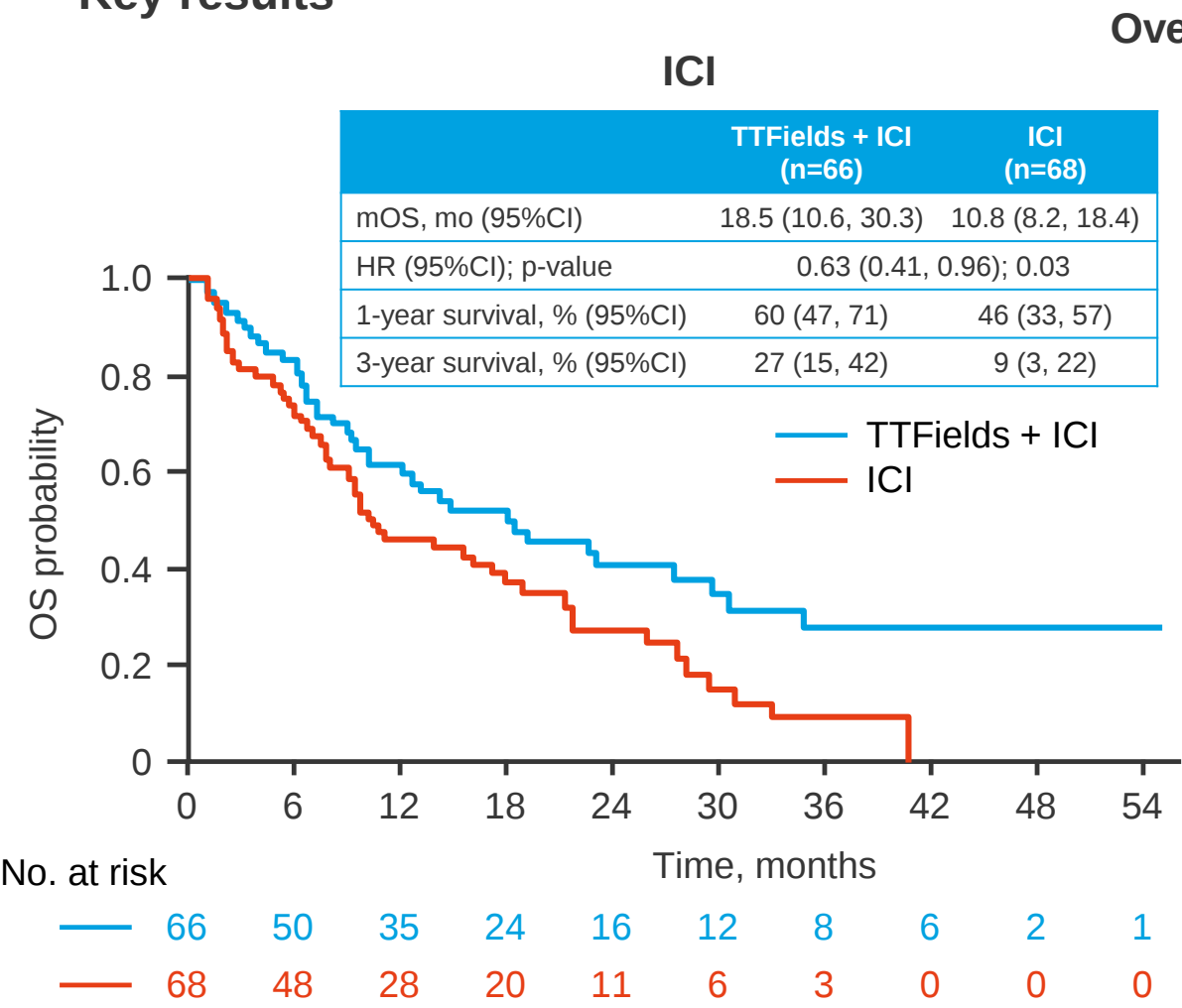
- Key results

Overall survival in the ITT population



LBA9005: Tumor Treating Field (TTFields) therapy with standard of care (SOC) in metastatic non-small cell lung cancer (mNSCLC) following platinum failure: Randomized, phase 3 LUNAR study – Leal T, et al

- Key results



LBA9005: Tumor Treating Field (TTFields) therapy with standard of care (SOC) in metastatic non-small cell lung cancer (mNSCLC) following platinum failure: Randomized, phase 3 LUNAR study – Leal T, et al

- Key results (cont.)

	TTFields + SoC (n=137)	SoC (n=139)
mPFS, mo (95%CI)	4.8 (4.1, 5.7)	4.1 (3.0, 4.6)
HR (95%CI); p-value	0.85 (0.67, 1.11); 0.23	
Patients with follow-up scan, n	122	127
ORR, % (95%CI)	20 (14, 28)	17 (11, 25)
Difference, % (95%CI); p-value	3 (-8.5, 14.9); 0.5	
BOR, %		
CR	3	1
PR	18	17
SD	49	47
PD	18	26
NE	2	1

	TTFields + SoC	SoC
Nonsquamous, n	79	77
mOS, mo (95%CI)	12.6 (8.8, 19.8)	9.9 (6.9, 16.4)
HR (95%CI); p-value	0.80 (0.54, 1.16); 0.28	
Squamous, n	58	62
mOS, mo (95%CI)	13.9 (9.7, 17.1)	10.1 (8.3, 14.3)
HR (95%CI); p-value	0.67 (0.44, 1.01); 0.05	

LBA9005: Tumor Treating Field (TTFields) therapy with standard of care (SOC) in metastatic non-small cell lung cancer (mNSCLC) following platinum failure: Randomized, phase 3 LUNAR study – Leal T, et al

- Key results (cont.)

AEs, %	TTFields + SoC (n=133)	SoC (n=134)
Any	97	91
Grade ≥3	59	56
Serious	53	38
Led to discontinuation	36	20
Led to death	10	8

TRAEs occurring in ≥5% of patients, %	TTFields + SoC (n=133)	SoC (n=134)
Leukopenia	14	14
Pneumonia	11	11
Anemia	8	8
Dyspnea	7	3
Fatigue	4	8

- Conclusions

- In patients with metastatic NSCLC who had progressed on platinum therapy, TTFields + SoC showed a significant improvement in OS, which was driven by ICI-naïve patients who received ICI in 2L, compared with SoC alone and was generally well-tolerated

Other malignancies

SCLC, mesothelioma and thymic epithelial tumors

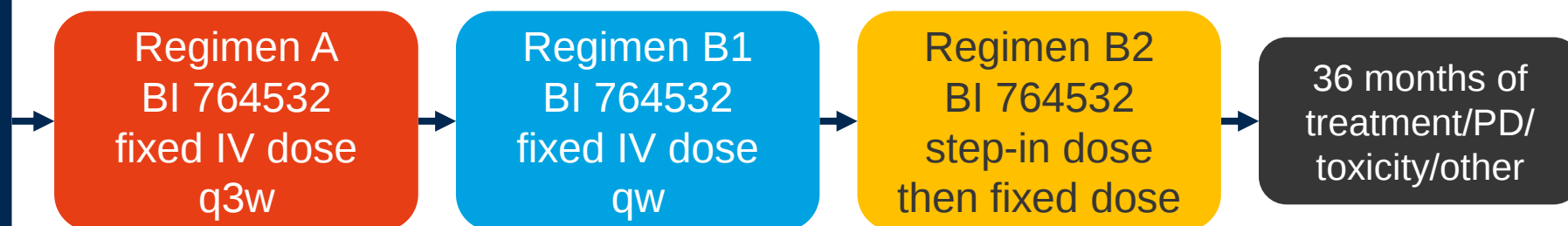
8502: First-in-human dose-escalation trial of the delta-like ligand 3 (DLL3)/CD3 bispecific T-cell engager BI 764532 in patients (pts) with DLL3-positive (DLL3+) small-cell lung cancer (SCLC) and neuroendocrine carcinoma (NEC) – Wermke M, et al

- **Study objective**

- To evaluate the safety and antitumor activity of BI 764532, a DLL3/CD3 bispecific T-cell engager, in patients with SCLC and neuroendocrine carcinoma

Key patient inclusion criteria

- Advanced SCLC or neuroendocrine carcinoma^a
 - DLL3+ (central)^b
 - Patients progressed or were ineligible for available standard treatments (≥1 line of platinum-based chemotherapy)
 - ECOG PS 0–1
- (n=107)



Primary endpoint

- MTD, DLTs

Secondary endpoints

- ORR, PK

^aIncluding extrapulmonary neuroendocrine carcinoma and large cell neuroendocrine carcinoma;

^barchived tissue or in-study biopsy using Ventana DLL3 (SP347) assay.

8502: First-in-human dose-escalation trial of the delta-like ligand 3 (DLL3)/CD3 bispecific T-cell engager BI 764532 in patients (pts) with DLL3-positive (DLL3+) small-cell lung cancer (SCLC) and neuroendocrine carcinoma (NEC) – Wermke M, et al

- Key results



8502: First-in-human dose-escalation trial of the delta-like ligand 3 (DLL3)/CD3 bispecific T-cell engager BI 764532 in patients (pts) with DLL3-positive (DLL3+) small-cell lung cancer (SCLC) and neuroendocrine carcinoma (NEC) – Wermke M, et al

- Key results (cont.)

TRAEs occurring in ≥10% of patients, n (%)	All grade	Grade 1–2	Grade 3–5
Any	92 (86)	63 (59)	29 (27)
Cytokine release syndrome	63 (59)	61 (57)	2 (2)
Lymphocyte count decreased	21 (20)	4 (3)	17 (16)
Dysgeusia	21 (20)	21 (20)	0
Asthenia	20 (19)	19 (18)	1 (<1)
Pyrexia	19 (18)	19 (18)	0
AST increased	15 (14)	13 (12)	2 (2)
Fatigue	15 (14)	14 (13)	1 (<1)
Nausea	13 (12)	13 (12)	0

DLTs, n	n=107
Any	5
Cytokine release syndrome, grade3–4	2
Confusional state, grade 3	1
Infusion-related reaction, grade 2	1
Nervous system disorder, grade 3	1

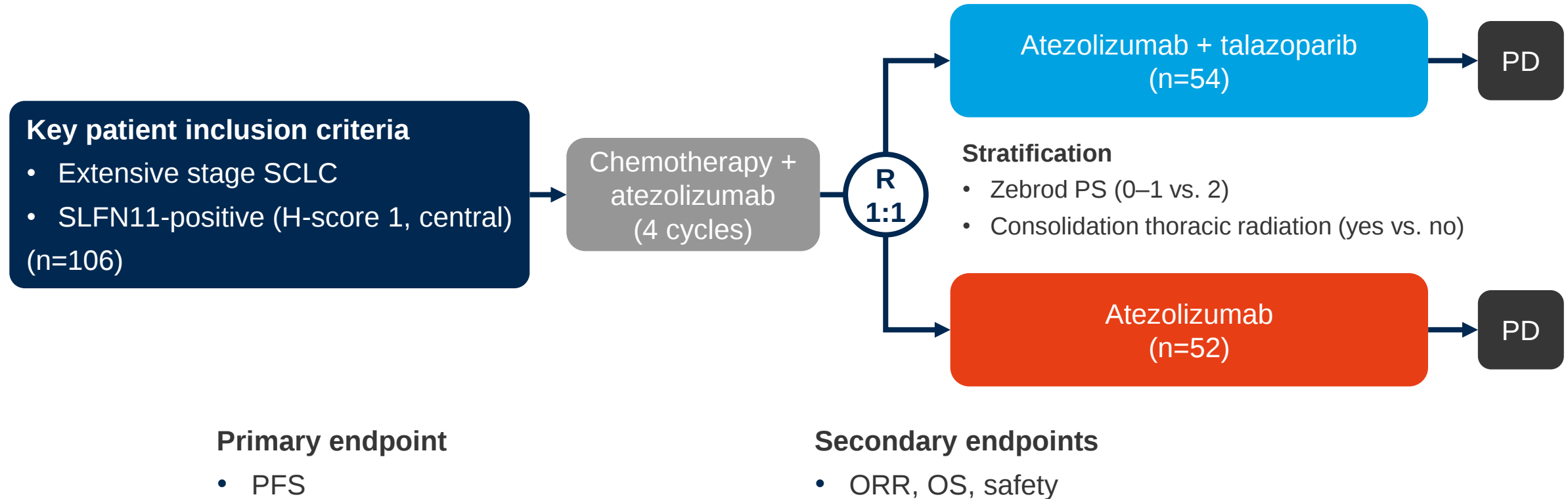
- Conclusions

- In patients with SCLC and neuroendocrine carcinoma, BI 764532 demonstrated encouraging antitumor activity at doses of ≥90 µg/kg with a manageable safety profile

8504: SWOG S1929: Phase II randomized study of maintenance atezolizumab (A) versus atezolizumab + talazoparib (AT) in patients with SLFN11 positive extensive stage small cell lung cancer (ES-SCLC) – Karim NA, et al

- **Study objective**

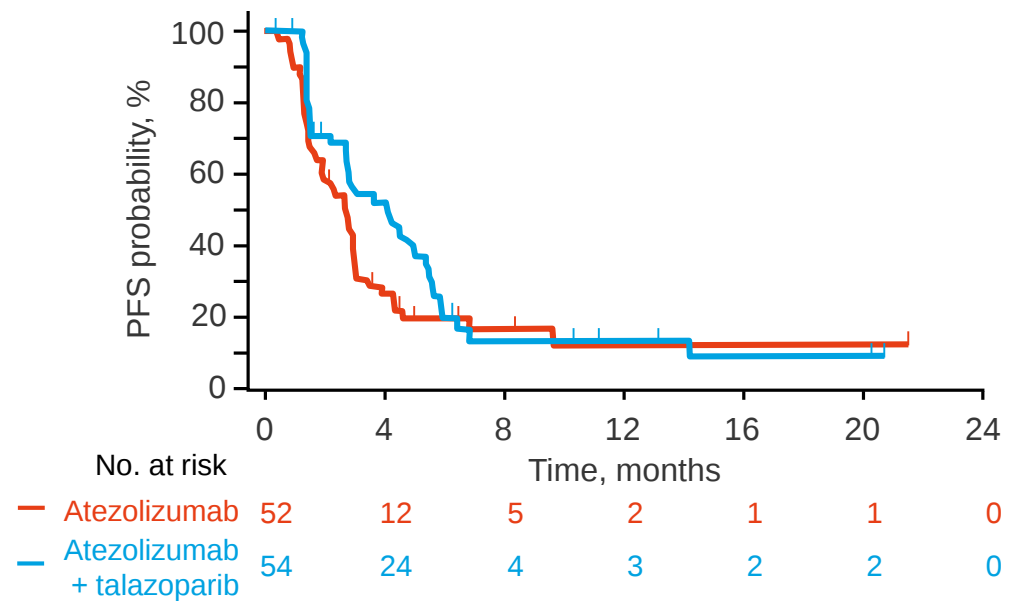
- To evaluate the efficacy and safety of maintenance atezolizumab ± talazoparib in patients with SLFN11-positive extensive stage SCLC in the SWOG S1929 study



8504: SWOG S1929: Phase II randomized study of maintenance atezolizumab (A) versus atezolizumab + talazoparib (AT) in patients with SLFN11 positive extensive stage small cell lung cancer (ES-SCLC) – Karim NA, et al

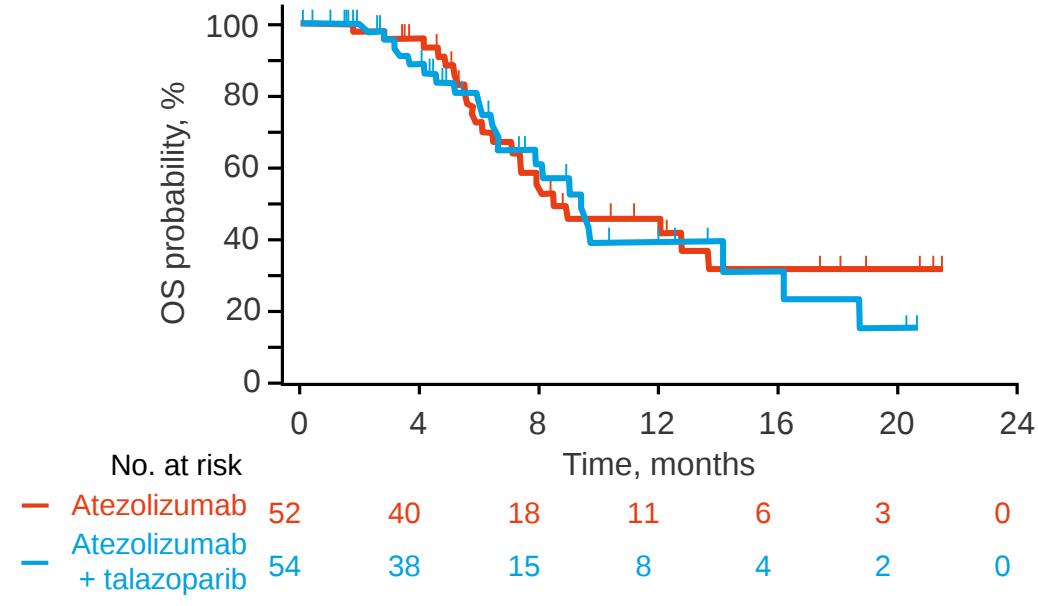
- Key results

Progression-free survival



	Atezolizumab (n=52)	Atezolizumab + talazoparib (n=54)
Events, n	41	39
mPFS, mo (80%CI)	2.8 (2.0, 2.9)	4.2 (2.8, 4.7)
HR (80%CI); p-value ^a	0.70 (0.52, 0.94); 0.056	

Preliminary overall survival



	Atezolizumab (n=52)	Atezolizumab + talazoparib (n=54)
Events, n	23	22
mOS, mo (80%CI)	8.5 (7.4, 12.7)	9.4 (8.1, 14.2)
HR (80%CI); p-value ^a	0.30 (0.80, 1.71); 0.30	

8504: SWOG S1929: Phase II randomized study of maintenance atezolizumab (A) versus atezolizumab + talazoparib (AT) in patients with SLFN11 positive extensive stage small cell lung cancer (ES-SCLC) – Karim NA, et al

• Key results (cont.)

Response in evaluable patients	Atezolizumab (n=32)	Atezolizumab + talazoparib (n=34)
ORR, % (80%CI); p-value	16 (8, 27)	12 (5, 22); 0.32
BOR, n (%)		
PR	5 (16)	4 (12)
SD	17 (53)	16 (47)
PD	10 (31)	12 (35)
NE	0	2 (6)
DCR, % (80%CI); p-value	69 (55, 80)	59 (46, 70); 0.27

Grade 3–4 TRAEs occurring in ≥3% of patients or grade 4 in any patient, n (%)	Atezolizumab (n=47)		Atezolizumab + talazoparib (n=52)	
	G3	G4	G3	G4
Hematologic				
Anemia	1 (2)	0	19 (37)	0
Lymphocyte count decreased	1 (2)	0	3 (6)	0
Neutrophil count decreased	0	0	0	1 (2)
Platelet count decreased	0	0	9 (17)	4 (8)
WBC count decreased	0	0	2 (4)	1 (2)
Non-hematologic				
AST increased	2 (4)	0	2 (4)	1 (2)
ALT increased	1 (2)	1 (2)	2 (4)	1 (2)
Hyperglycemia	0	0	0	1 (2)
Cardiac arrest	0	0	0	1 (2)
Lung infection	2 (4)	0	0	1 (2)

• Conclusions

- In patients with SLFN11-positive SCLC, maintenance atezolizumab + talazoparib prolonged PFS compared with atezolizumab alone and was associated with a higher incidence of hematologic AEs

8518: Phase II study of durvalumab plus olaparib as maintenance therapy in extensive-stage small-cell lung cancer (TRIDENT): Preliminary efficacy and safety results

– Huang Y, et al

- **Study objective**

- To evaluate the efficacy and safety of maintenance durvalumab + olaparib in patients with extensive stage SCLC in the TRIDENT study

Key patient inclusion criteria

- Extensive stage SCLC
- No prior therapy
- Asymptomatic or stable brain metastases permitted
- ECOG PS 0–2

(n=60)

Durvalumab 1500 mg +
platinum-etoposide* q3w
(4 cycles)

Durvalumab 1500 mg q4w +
olaparib 300 mg BID

PD/
toxicity

Primary endpoint

- 12-month PFS rate (RECIST v1.1)

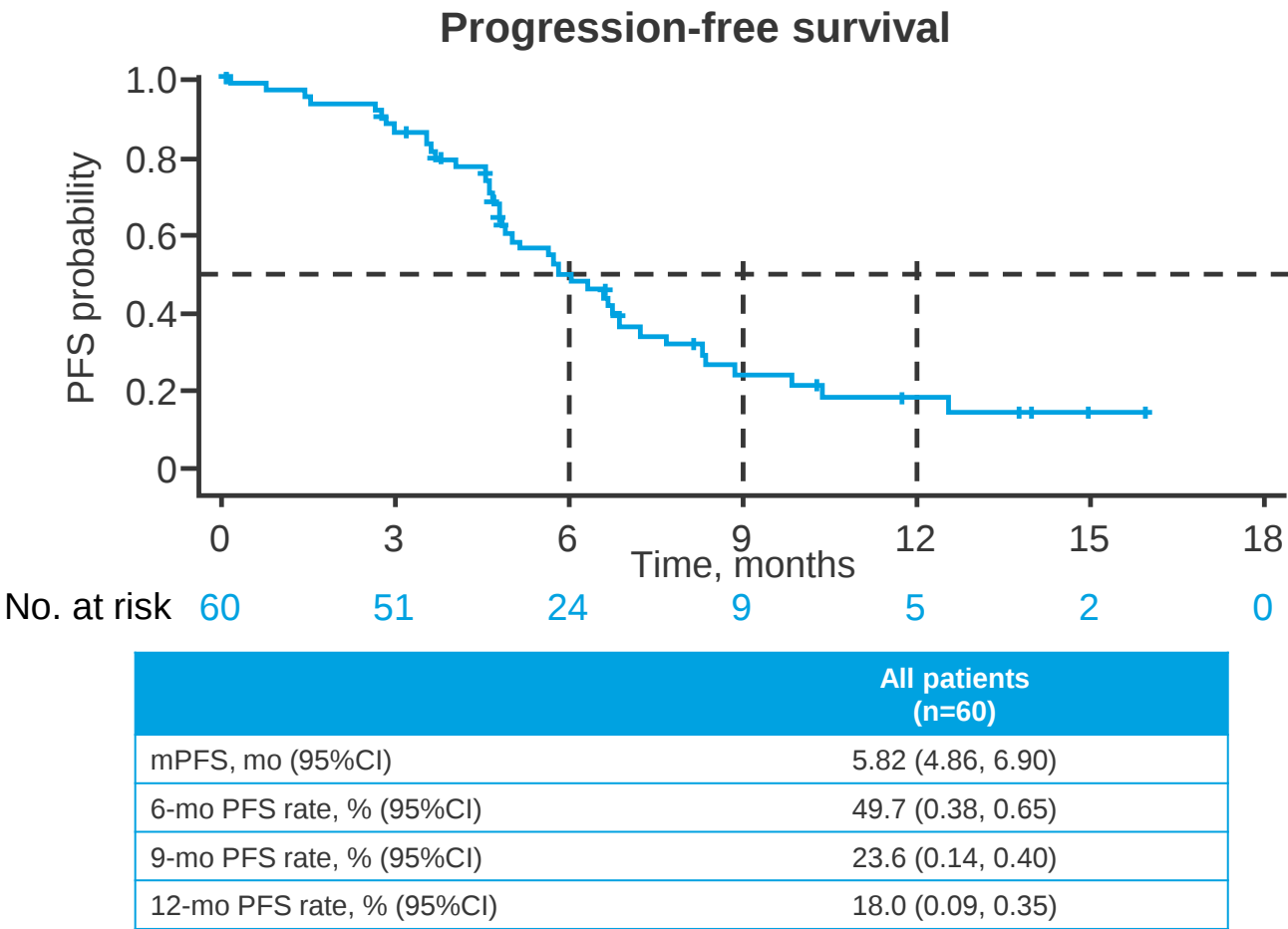
Secondary endpoints

- PFS, ORR, DoR, OS, safety

*Etoposide 80–100 mg/m² D1–3 + carboplatin AUC5–6 or cisplatin 75–80 mg/m².

8518: Phase II study of durvalumab plus olaparib as maintenance therapy in extensive-stage small-cell lung cancer (TRIDENT): Preliminary efficacy and safety results – Huang Y, et al

- Key results



Response	All patients (n=60)
ORR, % (95%CI)	73.4 (62, 85)
BOR, n (%)	
CR	1 (1.7)
PR	43 (71.7)
SD	6 (10)
PD	9 (15)
NE	1 (1.7)
DCR, % (95%CI)	81 (70, 90)
DoR, mo (95%CI)	5.36 (4.37, 7.56)
mOS, mo (95%CI)	NR (10.15, NR)

8518: Phase II study of durvalumab plus olaparib as maintenance therapy in extensive-stage small-cell lung cancer (TRIDENT): Preliminary efficacy and safety results

– Huang Y, et al

- Key results (cont.)

AEs, n (%)	Total (n=60)
Any	56 (93.3)
Grade ≥3	22 (36.7)
Serious	13 (21.7)
Treatment-related	11 (18.3)
Led to discontinuation	5 (8.3)
Led to death	1 (1.7)

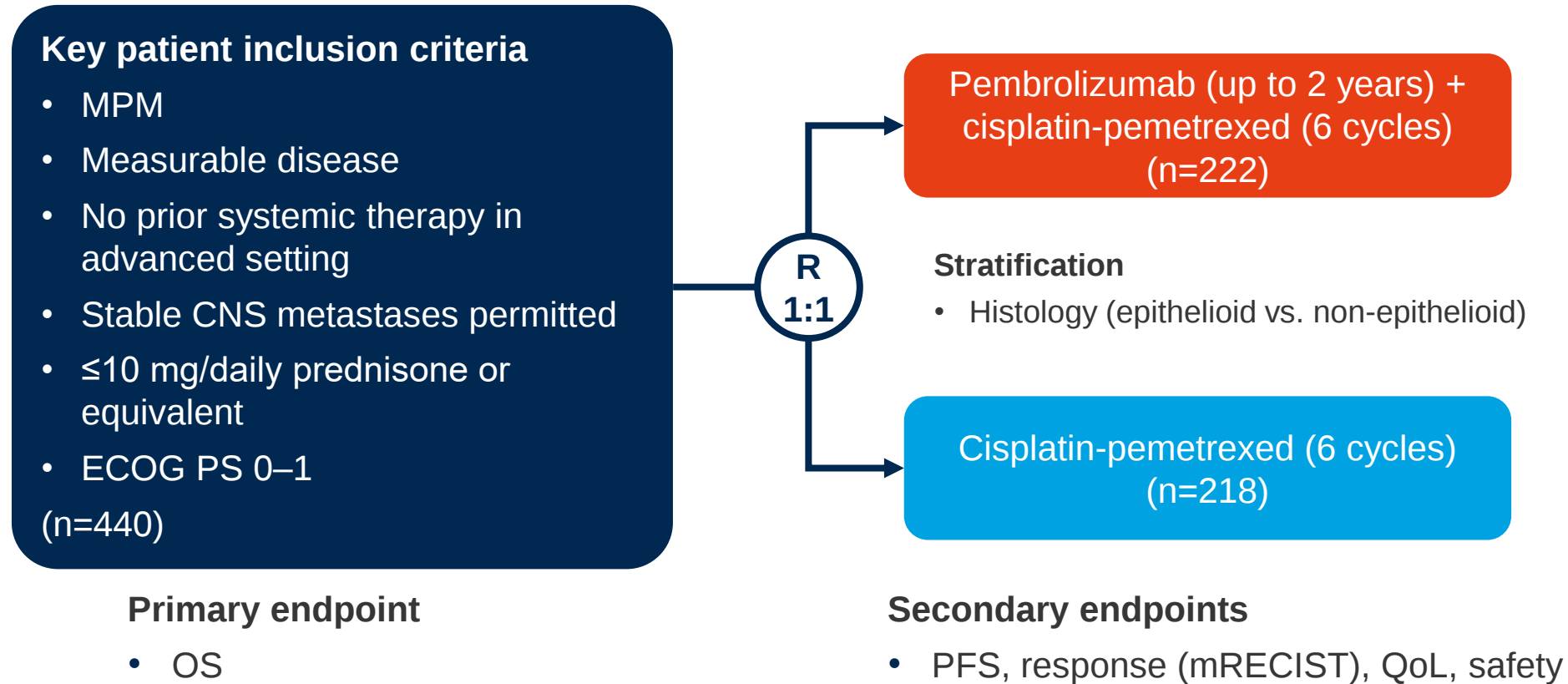
- Conclusions

- In patients with extensive stage SCLC, 2L durvalumab + olaparib demonstrated some signal of activity and was generally well-tolerated

LBA8505: IND227 phase III (P3) study of cisplatin/pemetrexed (CP) with or without pembrolizumab (Pembro) in patients (pts) with malignant pleural mesothelioma (PM): A CCTG, NCIN, and IFCT trial – Chu QS, et al

- **Study objective**

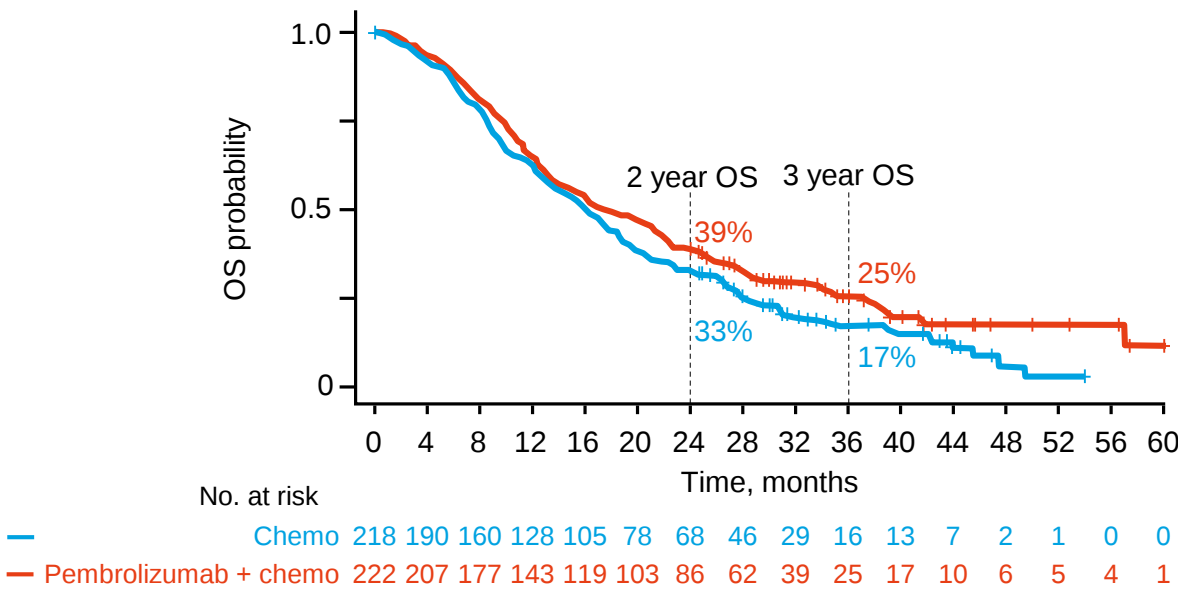
- To evaluate the efficacy and safety of pembrolizumab + cisplatin-pemetrexed in patients with MPM



LBA8505: IND227 phase III (P3) study of cisplatin/pemetrexed (CP) with or without pembrolizumab (Pembro) in patients (pts) with malignant pleural mesothelioma (PM): A CCTG, NCIN, and IFCT trial – Chu QS, et al

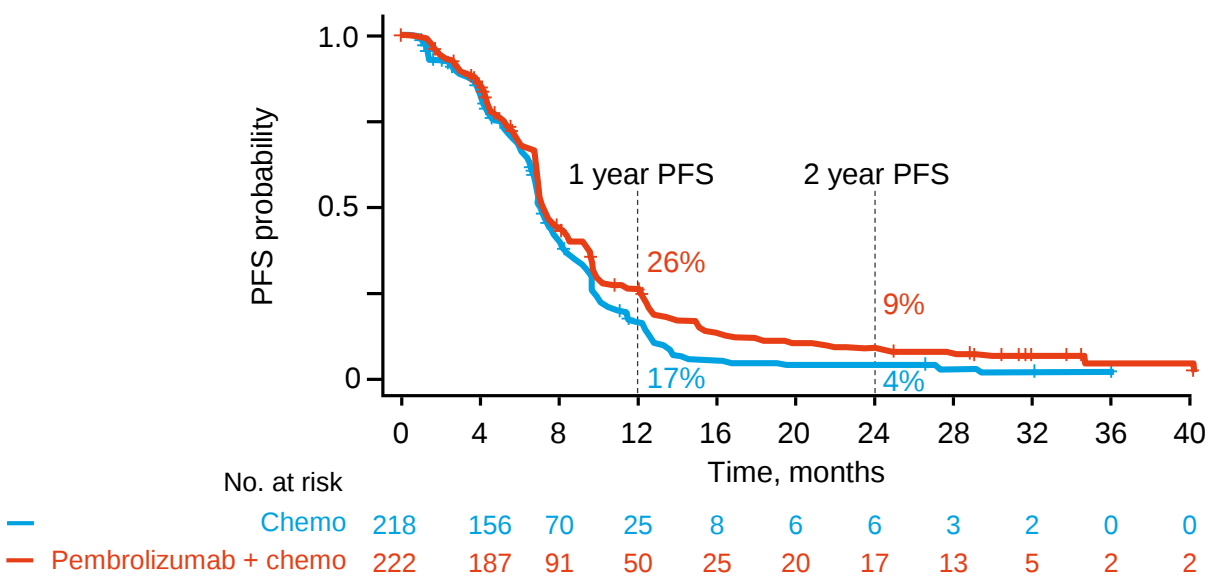
- Key results

Overall survival



	Chemotherapy (n=218)	Pembrolizumab + chemotherapy (n=222)
mOS, mo (95%CI)	16.13 (13.08, 18.17)	17.28 (14.36, 21.29)
HR (95%CI); p-value	0.79 (0.64, 0.98); 0.0324	

Progression-free survival



	Chemotherapy (n=218)	Pembrolizumab + chemotherapy (n=222)
mPFS, mo (95%CI)	7.16 (6.83, 7.69)	7.13 (6.93, 8.12)
HR (95%CI); p-values	0.80 (0.65, 0.99); 0.0372	

LBA8505: IND227 phase III (P3) study of cisplatin/pemetrexed (CP) with or without pembrolizumab (Pembro) in patients (pts) with malignant pleural mesothelioma (PM): A CCTG, NCIN, and IFCT trial – Chu QS, et al

- Key results (cont.)

Response	Chemotherapy (n=218)	Pembrolizumab + chemotherapy (n=222)	p-value
BOR, n (%)			
CR	0	2 (1)	<0.0001
PR	83 (38)	136 (61)	
SD/non-CR/PD	103 (47)	70 (32)	
PD	11 (5)	9 (4)	
Response could not be assigned, n (%)			
Total	21 (10)	5 (2)	
Never treated/withdrawal	7 (3)	0	
Other reasons	9 (4)	3 (1)	
No baseline images uploaded	5 (2)	2 (1)	
Median duration of CR/PR, mo (95%CI)	5.5 (4.2, 6)	5.8 (5.5, 7)	0.185

	Chemotherapy	Pembrolizumab + chemotherapy
Epithelioid, n	169	176
mOS, mo (95%CI)	18.2 (16.0, 20.4)	19.8 (16.0, 22.2)
HR (95%CI)	0.89 (0.70, 1.13)	
Non-epithelioid, n	49	46
mOS, mo (95%CI)	8.2 (5.9, 10.8)	12.3 (8.7, 21.2)
HR (95%CI)	0.57 (0.36, 0.89)	
PD-L1 negative, n	63	70
mOS, mo (95%CI)	18.5 (13.2, 23.7)	22.4 (14.4, 28.0)
HR (95%CI)	0.70 (0.47, 1.03)	
PD-L1 positive, n	132	131
mOS, mo (95%CI)	15.0 (12.0, 17.0)	16.2 (12.7, 20.3)
HR (95%CI)	0.84 (0.64, 1.10)	

LBA8505: IND227 phase III (P3) study of cisplatin/pemetrexed (CP) with or without pembrolizumab (Pembro) in patients (pts) with malignant pleural mesothelioma (PM): A CCTG, NCIN, and IFCT trial – Chu QS, et al

- Key results (cont.)

Grade 3–4 TRAEs occurring in ≥3% of patients or grade 4 in any patient, n (%)	Chemotherapy (n=211)		Pembrolizumab + chemotherapy (n=222)	
	G3	G4	G3	G4
Any	31 (15)	1 (<1)	50 (23)	10 (5)
Nausea	2 (1)	0	10 (5)	0
Fatigue	12 (6)	0	15 (7)	0
Anemia	0	0	4 (2)	1 (<1)
Febrile neutropenia	2 (1)	0	8 (4)	3 (1)

- Conclusions

- In patients with MPM, 1L pembrolizumab + cisplatin-pemetrexed provided significant improvements in survival compared with chemotherapy alone without any new safety signals