

Innovative strategies for resectable and unresectable stage III NSCLC (part two)

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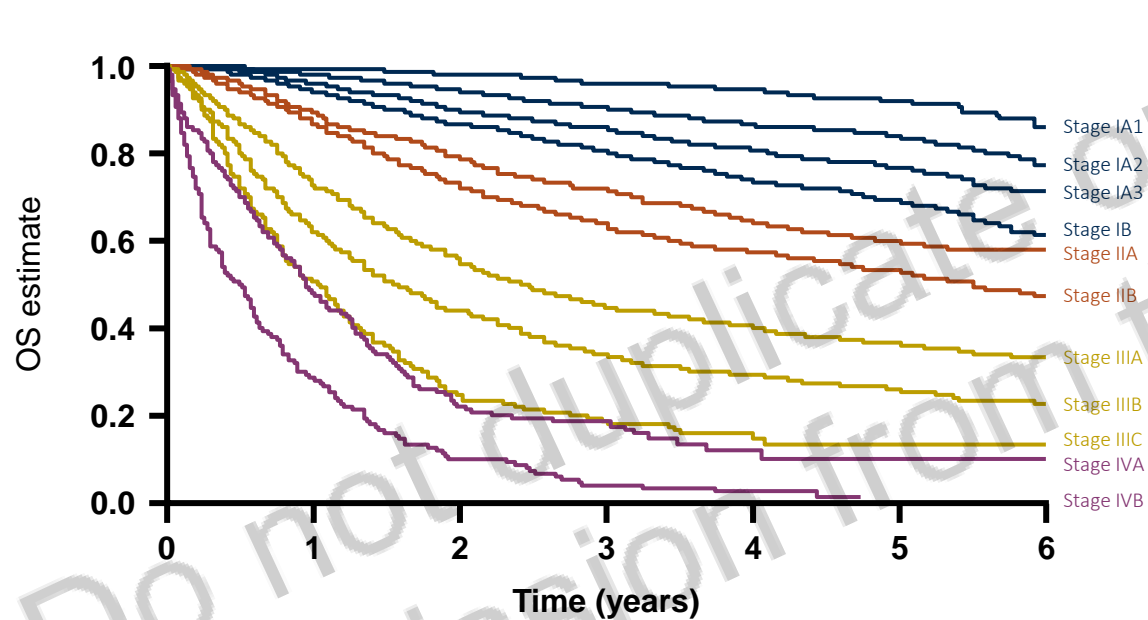
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Disclosures

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- Institutional grant: Astra Zeneca

Over half of all patients with NSCLC are initially diagnosed with stage I–III disease



5-year survival¹

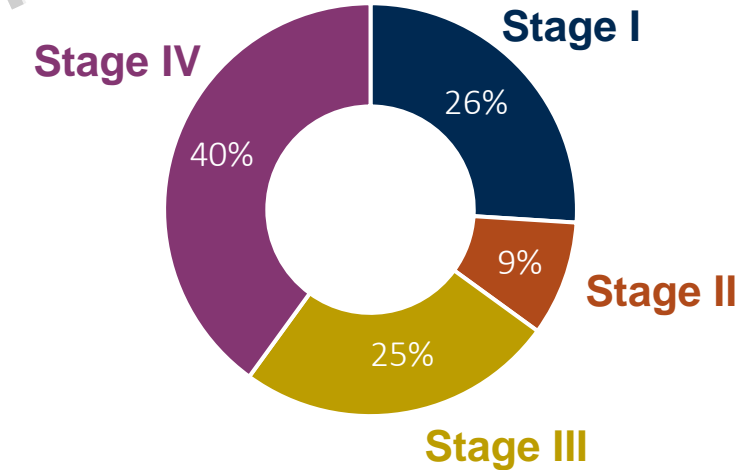
Stage I 68–92%

Stage II 53–60%

Stage III 13–36%

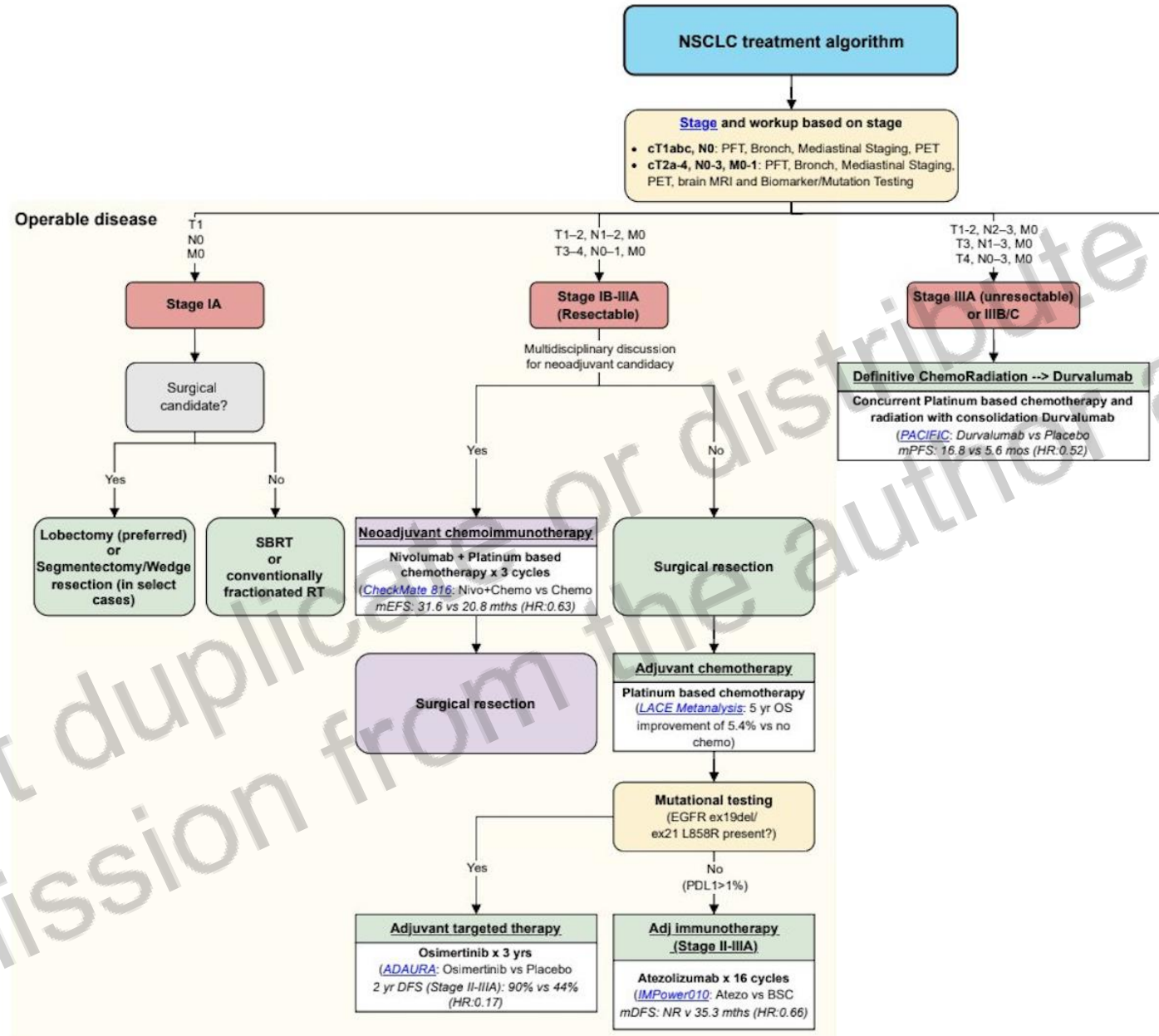
Stage IV 0–10%

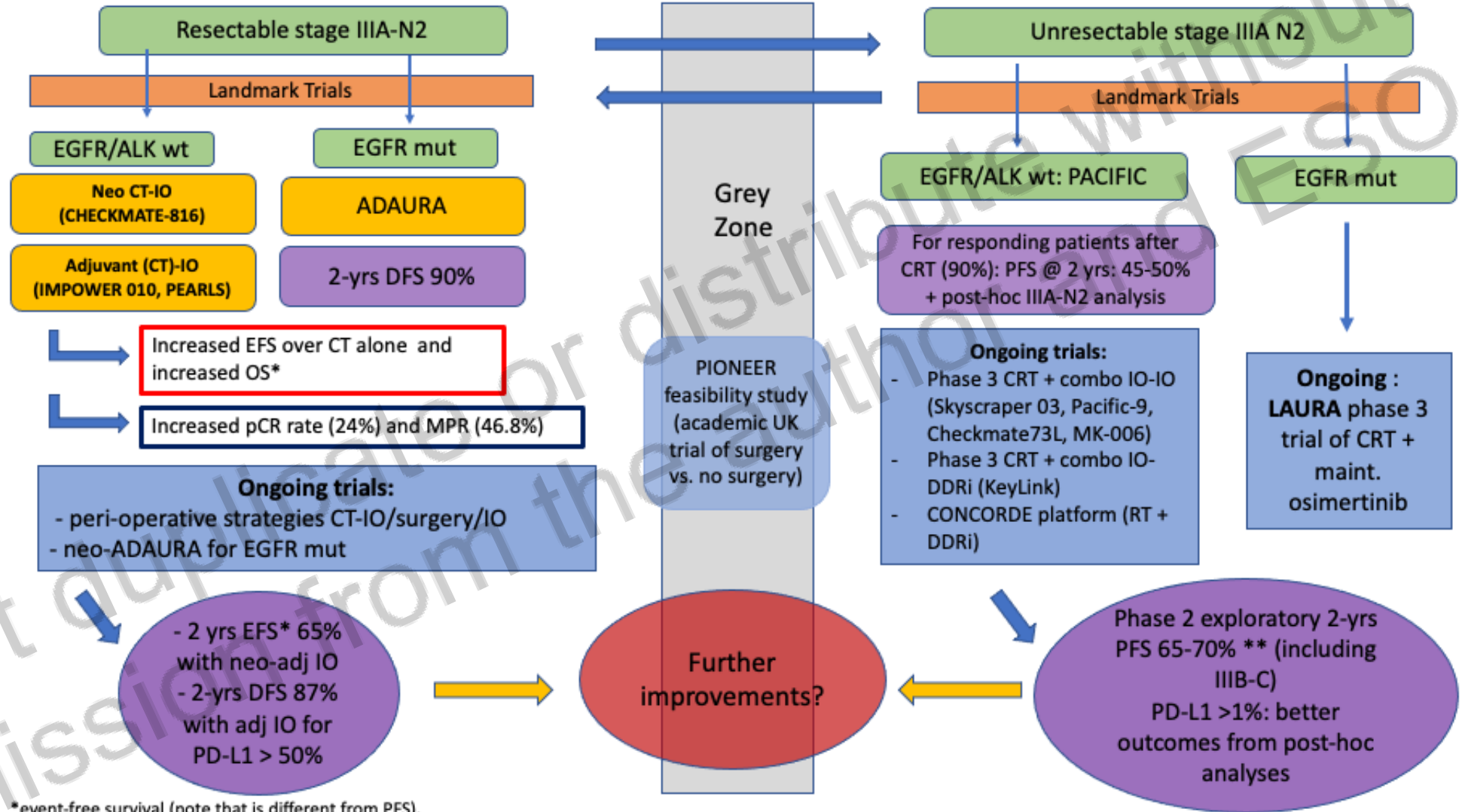
% at diagnosis^{2*}



*Data from: France, Germany, Japan, Italy, Spain, UK and US

1. [Goldstraw, et al. J Thorac Oncol 2016](#)
2. [EpiCast report: NSCLC Epidemiology Forecast to 2025. GlobalData. 2016](#)



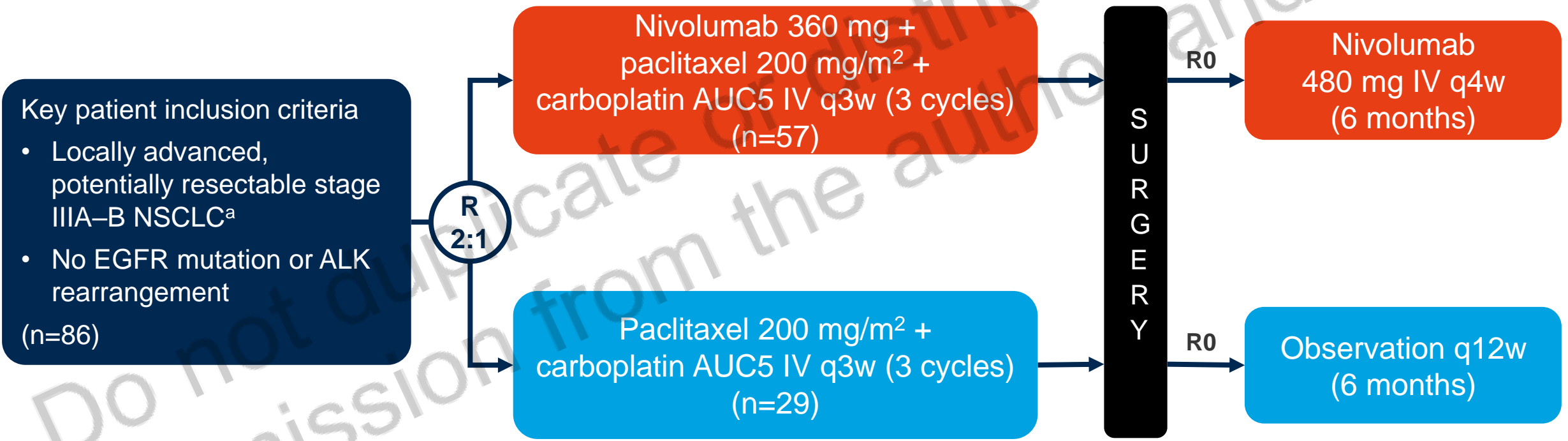


*event-free survival (note that is different from PFS).

Resectable/borderline resectable stage 3 NSCLC

PL03.12: Progression Free Survival and Overall Survival in NADIM II Study – Provencio M, et al

- Study objective
 - To evaluate the efficacy and safety of neoadjuvant nivolumab + chemotherapy in patients with resectable stage IIIA–B NSCLC in the NADIM II study



Primary endpoint

- pCR

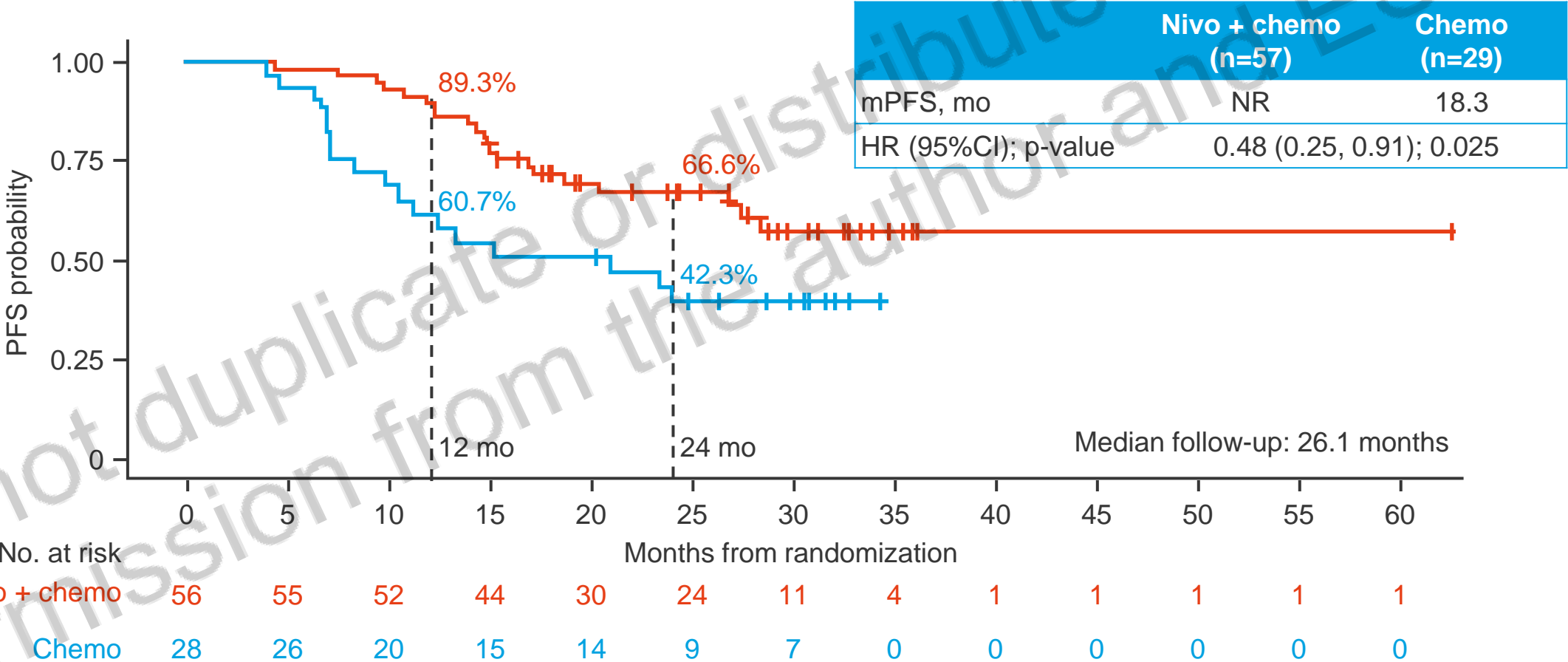
Secondary endpoints

- MPR, surgical outcomes, OS, PFS, safety

PL03.12: Progression Free Survival and Overall Survival in NADIM II Study – Provencio M, et al

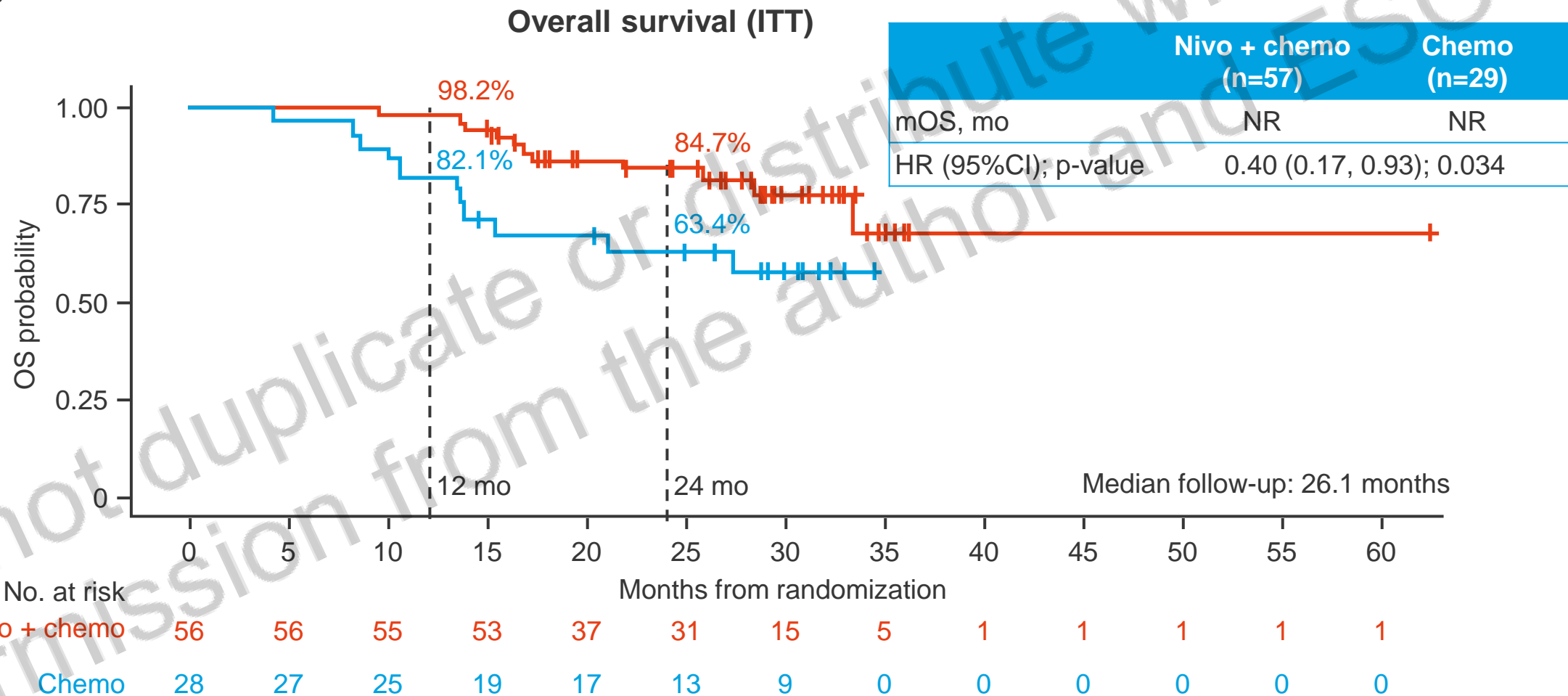
- Key results

Progression-free survival (ITT)



PL03.12: Progression Free Survival and Overall Survival in NADIM II Study – Provencio M, et al

- Key results



PL03.12: Progression Free Survival and Overall Survival in NADIM II Study – Provencio M, et al

- Key results (cont.)

Surgical outcomes	Nivo + chemo (n=57)	Chemotherapy (n=29)
R0, n (%)	49 (92.5)	13 (65.0)
OR (95%CI); p-value	6.60 (1.67, 26.02); 0.007	
Definitive surgery ^a , %	93.0	69.0
OR (95%CI); p-value	5.96 (1.65, 21.56); 0.008	
Downstaging, n (%)		
Yes	37 (69.8)	8 (40.0)
No	16 (30.2)	12 (60.0)
Downstaging rate, %	69.8	40.0
OR (95%CI); p-value	3.47 (1.19, 10.1); 0.04	

- Conclusions

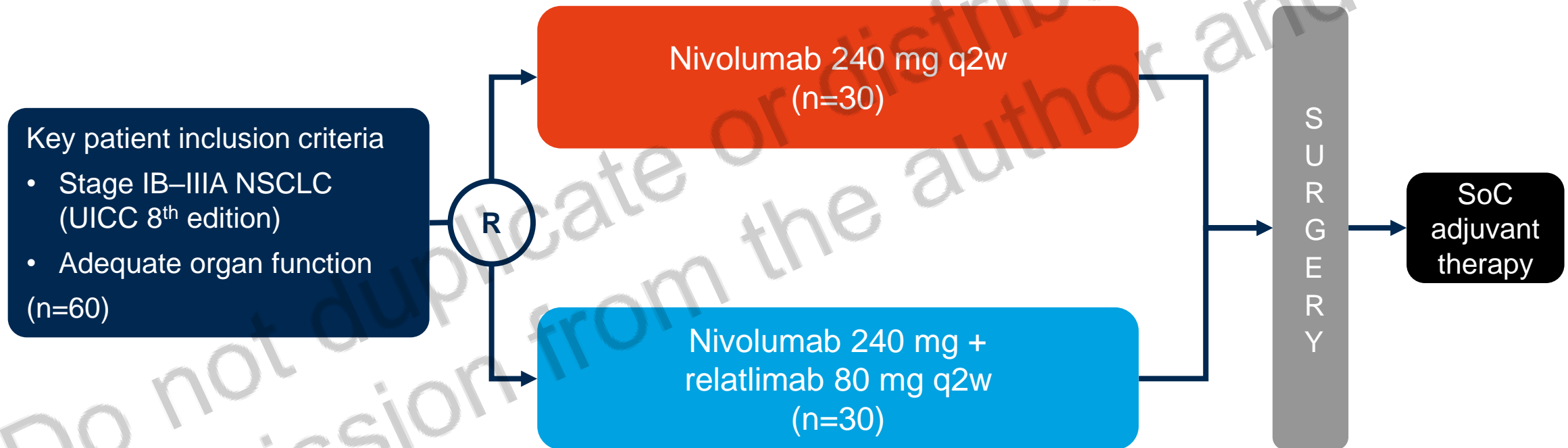
- In patients with potentially resectable stage IIIA–B NSCLC, neoadjuvant nivolumab + chemotherapy demonstrated significant improvements in surgical outcomes and survival

^aDefined as complete resection

LBA37: A randomized, multicentric phase II study of preoperative nivolumab plus relatlimab or nivolumab in patients with resectable non-small-cell lung cancer (NEOpredict-Lung) – Schuler MH, et al

- **Study objective**

- To evaluate the efficacy of nivolumab or nivolumab + relatlimab (a LAG-3 targeting mAb) prior to surgery in patients with NSCLC in the phase 2 NEOpredict-Lung study



Primary endpoint

- Feasibility (surgery \leq D43)

Secondary endpoints

- Histopathological response, radiological response, DFS, OS, safety

LBA37: A randomized, multicentric phase II study of preoperative nivolumab plus relatlimab or nivolumab in patients with resectable non-small-cell lung cancer (NEOpredict-Lung) – Schuler MH, et al

- Key results

	Nivolumab (n=30)	Nivolumab + relatlimab (n=30)
Feasibility (surgery ≤D43), %	100	100
ORR (RECIST v1.1), %	10	27
ORR (PERCIST v1.0), %	38	38
Complete/major pathological response*, %	27	30
12-mo DFS rate, % (95%CI)	92 (70, 98)	91 (66, 98)
12-mo OS rate, % (95%CI)	92 (70, 98)	100
R0 resection rate, %	100	97

*2 patients excluded at surgery

LBA37: A randomized, multicentric phase II study of preoperative nivolumab plus relatlimab or nivolumab in patients with resectable non-small-cell lung cancer (NEOpredict-Lung) – Schuler MH, et al

- Key results (cont.)

Grade ≥3 TRAEs, n (%)	Nivolumab (n=30)	Nivolumab + relatlimab (n=30)
Atrial fibrillation	1 (3)	-
Hyperthyroidism	1 (3)	-
Hepatic	1 (3)	1 (3)

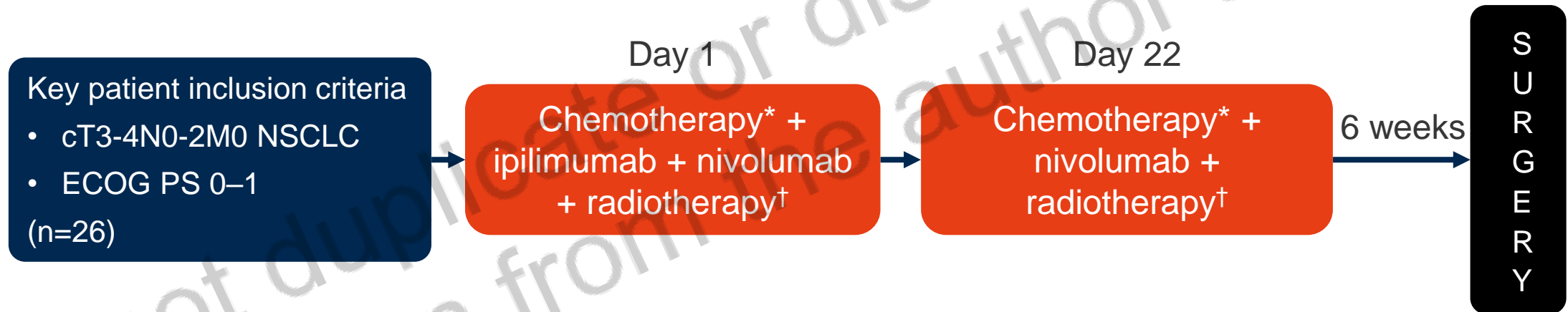
- Conclusions

- In patients with resectable NSCLC, preoperative treatment with nivolumab + relatlimab is safe and feasible and demonstrated a preliminary efficacy signal

950O: Ipilimumab plus nivolumab and chemoradiotherapy followed by surgery in patients with resectable and borderline resectable lung cancer: the INCREASE trial – Bahce I, et al

- **Study objective**

- To evaluate the efficacy and safety of neoadjuvant nivolumab + ipilimumab + chemoradiotherapy prior to surgery in patients with locally advanced NSCLC in the INCREASE study



Primary endpoints

- pCR/MPR,‡ safety

Secondary endpoints

- EFS, OS

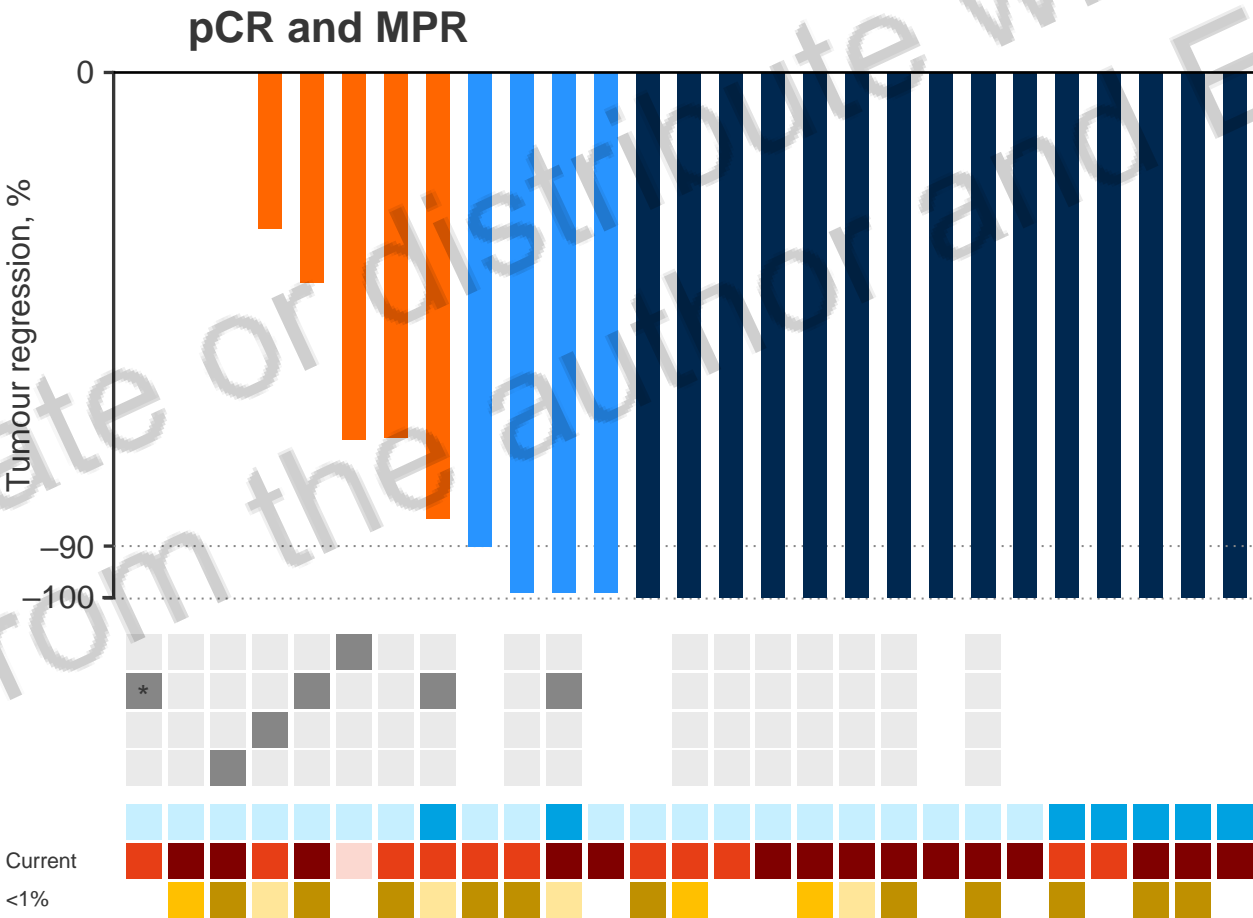
*Platinum-doublet chemotherapy; †once daily dose of 2 Gy;

‡defined as a residual viable tumour cells percentage of ≤10%

950O: Ipilimumab plus nivolumab and chemoradiotherapy followed by surgery in patients with resectable and borderline resectable lung cancer: the INCREASE trial – Bahce I, et al

• Key results

	pCR, n (%)	MPR, n (%)
Operated patients (n=24)	15 (63) (p<0.001) ^a	19 (79)
Received induction ^b (n=27)	15 (55) (p=0.003) ^a	19 (70)



^aBinomial probability using 30% pCR as historical reference; ^bexcluding patients on treatment.
*This patient developed pleural metastases during induction therapy and did not receive surgery

950O: Ipilimumab plus nivolumab and chemoradiotherapy followed by surgery in patients with resectable and borderline resectable lung cancer: the INCREASE trial – Bahce I, et al

- Key results (cont.)

	n (%)
Any TEAE	27 (100)
Grade 3–4	22 (81)
Serious AE	10 (37)
Grade 5	1 (4)
Any TRAE	21 (78)
Grade 3-4	18 (67)
Ir-AE grade 3–4	5 (19)
Grade 5	0
Led to IO discontinuation	2 (7)

Key ir-AEs	Any grade, n (%)	Grade 3–4, n
Dermatitis	11 (41)	2
Thyroid disorders	9 (33)	0
Pneumonitis	3 (11)	1
Hepatitis	2 (7)	2
Pancreatitis	1 (4)	1
Allergic reaction	1 (4)	0

- Conclusions

- In patients with locally advanced NSCLC, neoadjuvant nivolumab + ipilimumab + concurrent chemoradiotherapy provided promising antitumor activity with a manageable safety profile

LBA47: Osimertinib as adjuvant therapy in patients (pts) with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC): updated results from ADAURA – Tsuboi M, et al

- **Study objective**

- To evaluate the updated efficacy and safety of adjuvant osimertinib in patients with resected EGFR-mutated NSCLC in the ADAURA study

Key patient inclusion criteria

- Completely resected stage IB–IIIA NSCLC (AJCC/UICC 7th ed.)
 - With or without adjuvant chemotherapy
 - Confirmed EGFR mutation (Ex19del/L858R)
 - WHO PS 0–1
- (n=682)

R
1:1

Osimertinib 80 mg/day
(n=339)

PD/3 years/
discontinuation

Stratification

- Stage (IB vs. II vs. IIIA)
- EGFRm (Ex19del vs. L858R)
- Race (Asian vs. non-Asian)

Placebo
(n=343)

PD/3 years/
discontinuation

Primary endpoint

- DFS (in stage II/IIIA)

Secondary endpoints

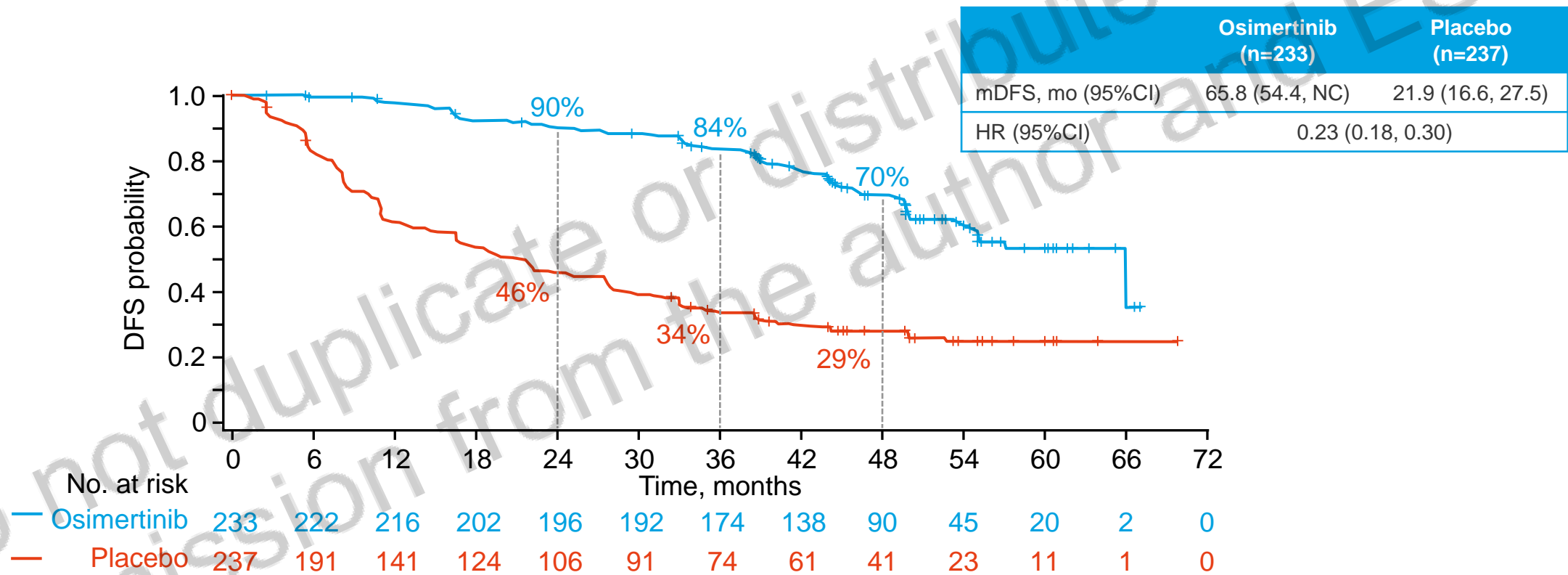
- DFS (overall population^a), OS, HRQoL, safety

^aStage IB, II and IIIA

LBA47: Osimertinib as adjuvant therapy in patients (pts) with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC): updated results from ADAURA – Tsuboi M, et al

- Key results

Disease-free survival in stage II/IIIA patients

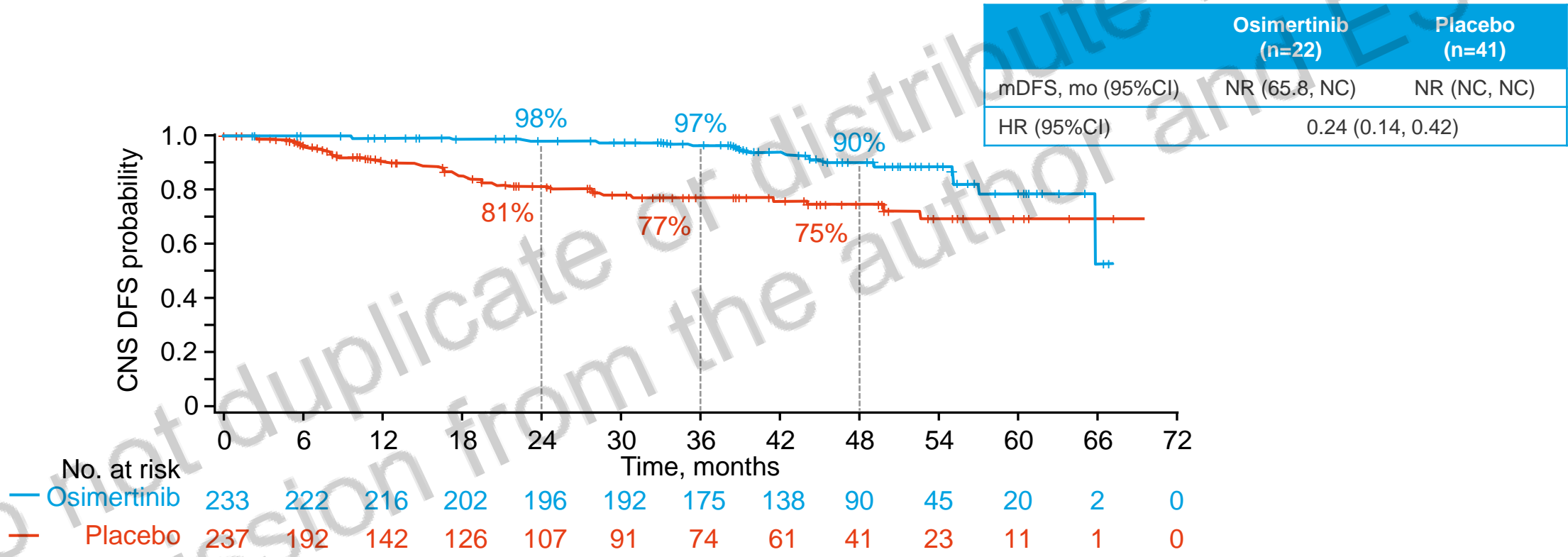


– In the overall population, mDFS was 65.8 mo (95%CI 61.7, NC) and 28.1 mo (95%CI 22.1, 35.0) in the osimertinib and placebo arms, respectively (HR 0.27 [95%CI 0.21, 0.34])

LBA47: Osimertinib as adjuvant therapy in patients (pts) with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC): updated results from ADAURA – Tsuboi M, et al

• Key results (cont.)

CNS disease-free survival in stage II/IIIA patients



– The most common first site of recurrence in the osimertinib and placebo arms were lung (12% vs. 26%), lymph nodes (6% vs. 17%) and CNS (6% vs. 11%), respectively

LBA47: Osimertinib as adjuvant therapy in patients (pts) with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC): updated results from ADAURA – Tsuboi M, et al

- Key results (cont.)

TEAEs, 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 discontinuation	43 (13)	9 (3)
Led to dose reduction	42 (12)	3 (1)
Led to dose interruption	91 (27)	43 (13)
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 (0)

- Conclusions

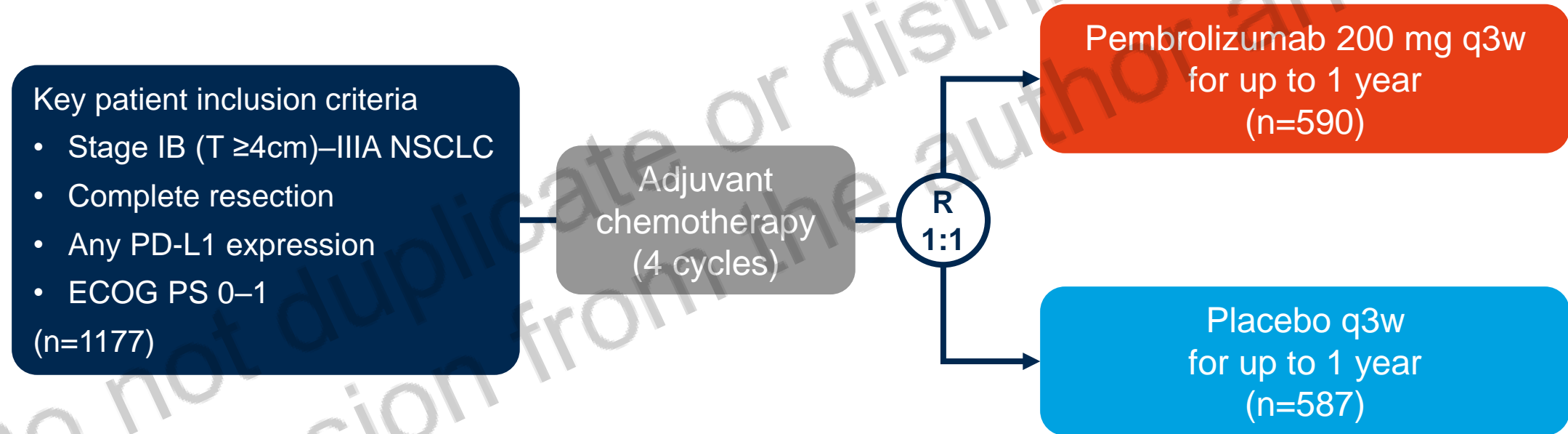
- In patients with stage II–IIIA NSCLC, postoperative osimertinib continued to demonstrate improvements in DFS across all disease stages and regardless of whether patients had received prior adjuvant chemotherapy with a manageable safety profile

930MO: PD-L1 expression and outcomes of pembrolizumab and placebo in completely resected stage IB-IIIa NSCLC: subgroup analysis of PEARLS/KEYNOTE-091

– Peters S, et al

- **Study objective**

- To evaluate the efficacy and safety of adjuvant pembrolizumab in patients with completely resected early stage NSCLC in the PEARLS/KEYNOTE-091 study



Primary endpoint

- DFS (overall population), DFS (PD-L1 TPS ≥50%)

Secondary endpoints

- DFS (PD-L1 TPS ≥1%), OS, safety

930MO: PD-L1 expression and outcomes of pembrolizumab and placebo in completely resected stage IB-IIIa NSCLC: subgroup analysis of PEARLS/KEYNOTE-091 – Peters S, et al

Key results

DFS: Pembrolizumab vs. placebo by PD-L1 TPS

TPS ≥50%

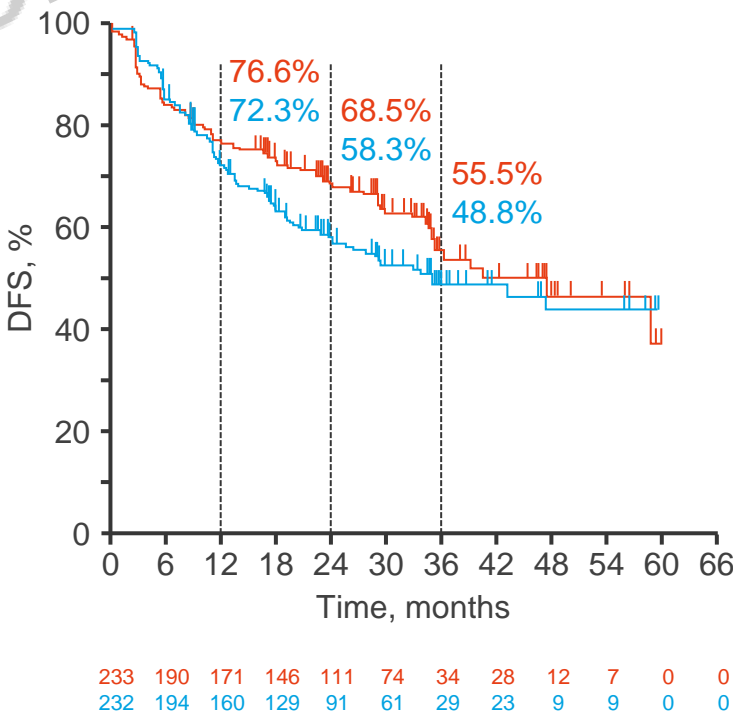
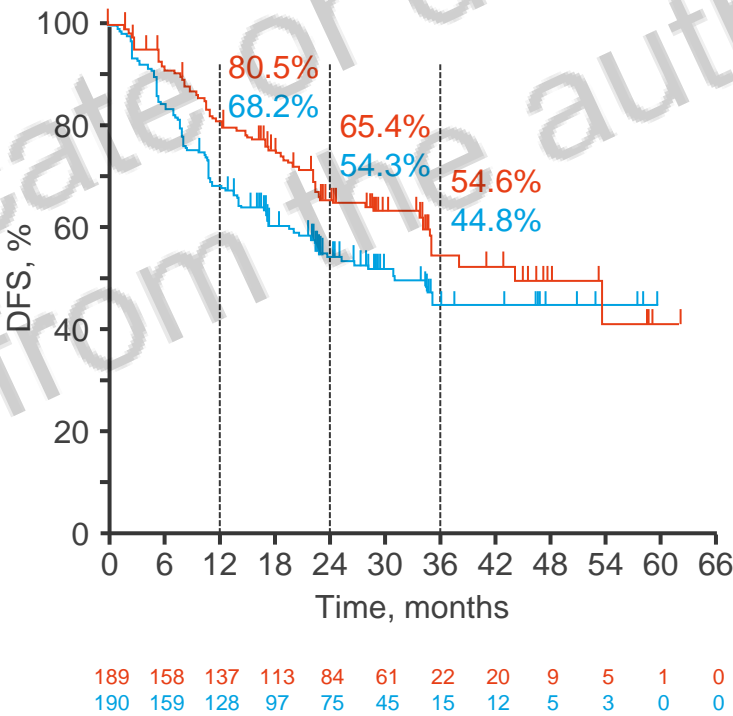
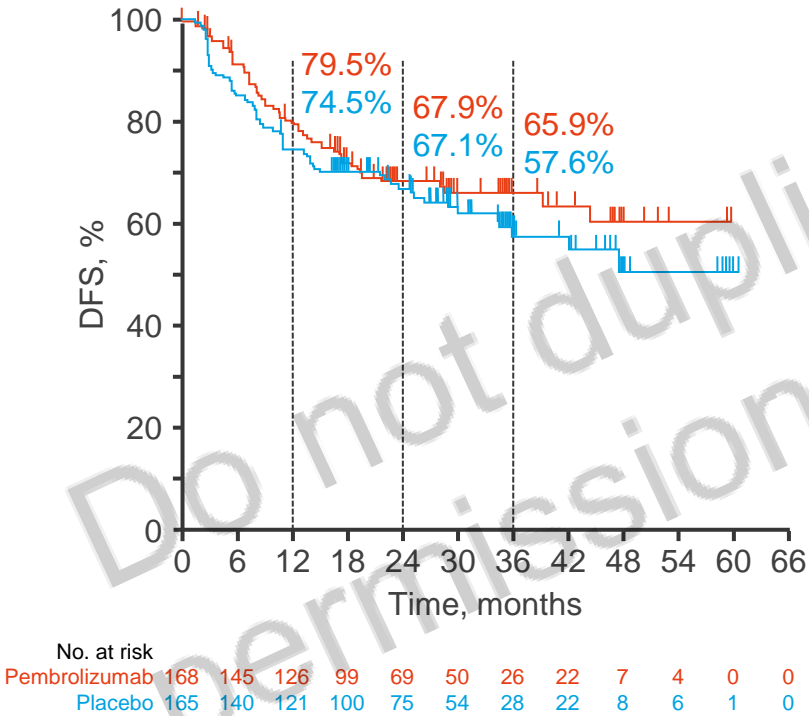
	Pembrolizumab (n=168)	Placebo (n=165)
mDFS, mo (95%CI)	NR (44.3, NR)	NR (35.8, NR)
HR (95%CI); p-value	0.82 (0.57, 1.18); 0.14	

TPS 1–49%

	Pembrolizumab (n=189)	Placebo (n=190)
mDFS, mo (95%CI)	44.2 (34.9, NR)	31.3 (22.5, NR)
HR (95%CI)	0.67 (0.48, 0.92)	

TPS <1%

	Pembrolizumab (n=233)	Placebo (n=232)
mDFS, mo (95%CI)	47.4 (35.0, NR)	34.9 (22.5, NR)
HR (95%CI)	0.78 (0.58, 1.03)	



930MO: PD-L1 expression and outcomes of pembrolizumab and placebo in completely resected stage IB-IIIa NSCLC: subgroup analysis of PEARLS/KEYNOTE-091

– Peters S, et al

- Key results (cont.)

AEs, %	Pembrolizumab		Placebo	
	Overall (n=580)	TPS ≥50% (n=164)	Overall (n=581)	TPS ≥50% (n=164)
Any grade	95.9	97.0	91.0	92.7
Grade 3–5	34.1	37.8	25.8	25.0
Leading to death	1.9	1.8	1.0	0.6
Serious AE	24.5	33.5	15.5	14.0
Led to drug discontinuation	19.8	23.2	5.9	6.7

irAEs, %	Pembrolizumab		Placebo	
	Overall (n=580)	TPS ≥50% (n=164)	Overall (n=581)	TPS ≥50% (n=164)
Any grade	39.0	39.6	12.9	12.2
Grade 3–5	7.9	10.4	1.9	2.4
Leading to death	0.3	0.6	0	0
Serious AE	8.1	11.0	1.5	1.8
Led to drug discontinuation	10.2	12.8	1.5	2.4

- Conclusions

- At this interim analysis, the lack of statistical difference in DFS for the PD-L1 TPS ≥50% population is likely to be a result of over performance in the placebo arm
- In patients with completely resected early stage NSCLC, pembrolizumab demonstrated benefits in DFS regardless of PD-L1 expression and the safety profile was similar across the subgroups

933MO: Longitudinal monitoring of circulating tumor DNA from plasma in patients with curative resected stage IA-IIIa EGFR mutant non-small cell lung cancer

– Ahn M-J, et al

- **Study objective**

- To assess the role of longitudinal monitoring of ctDNA in patients with resected stage IA–IIIa EGFR-mutant NSCLC

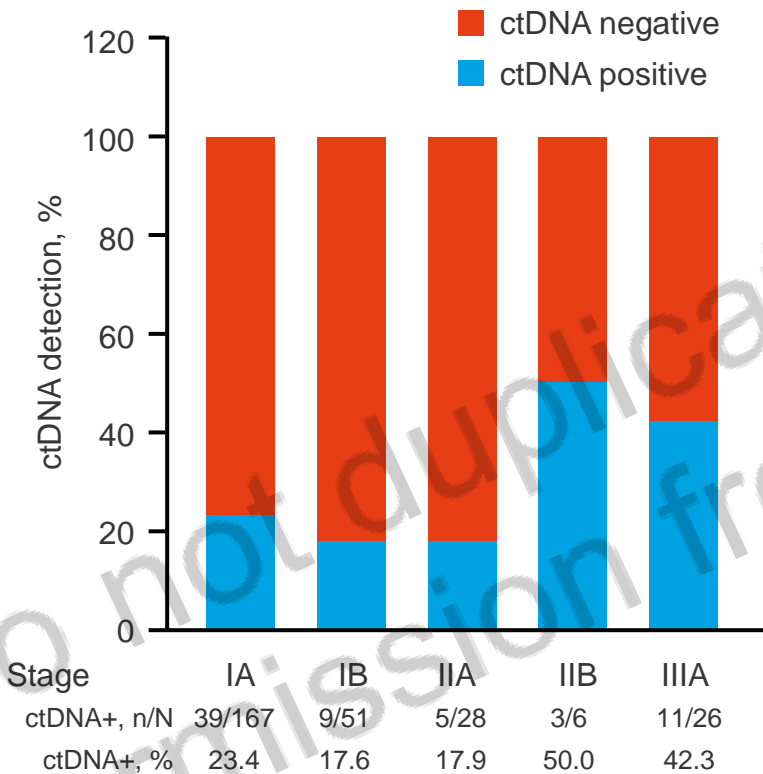
- **Methods**

- Between August 2015 and October 2017, ctDNA samples (droplet digital PCR; BioRad) were collected from eligible patients with stage IA–IIIa NSCLC and Del19 or L859R alternations
- ctDNA samples were analysed before surgery, 4 weeks after surgery, and at regular intervals for the next 5 years or until radiological recurrence (first year: every 3 months; second year: every 4 months; third year: every 6 months; year 4 and 5: once a year)

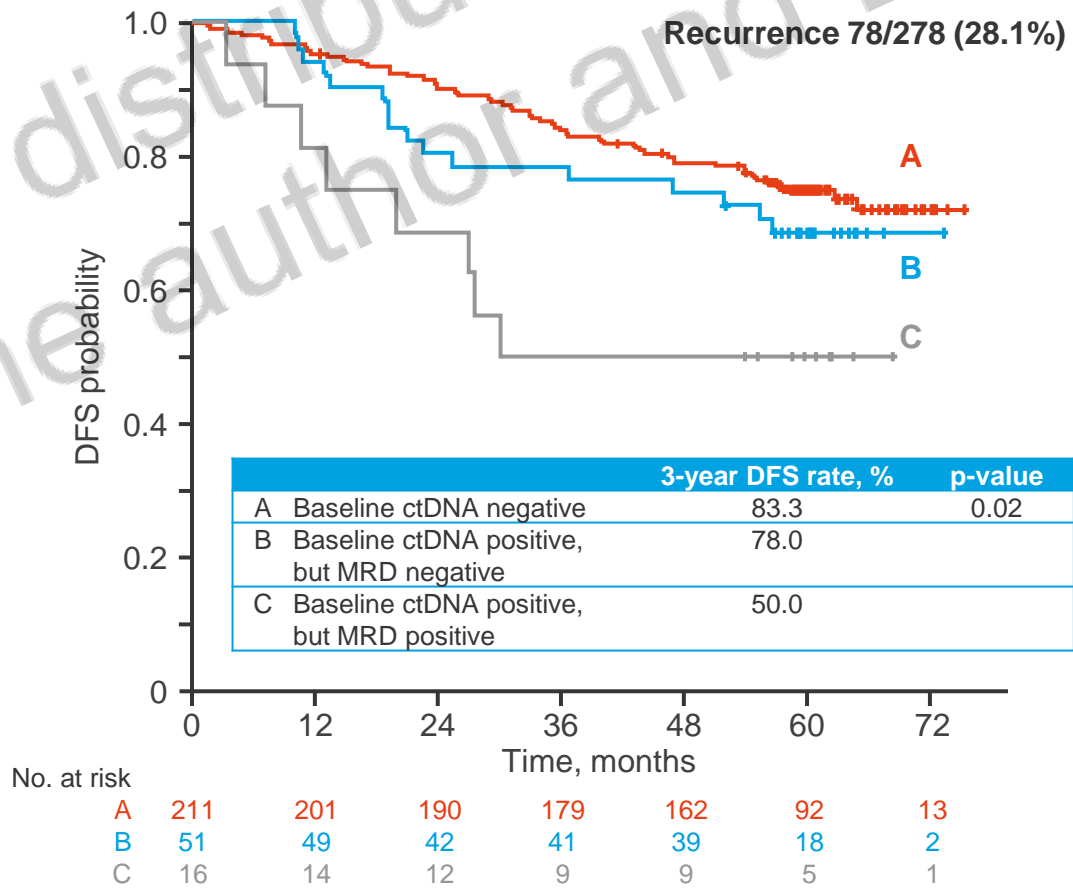
933MO: Longitudinal monitoring of circulating tumor DNA from plasma in patients with curative resected stage IA-IIIA EGFR mutant non-small cell lung cancer – Ahn M-J, et al

- Key results

Baseline ctDNA detection rate

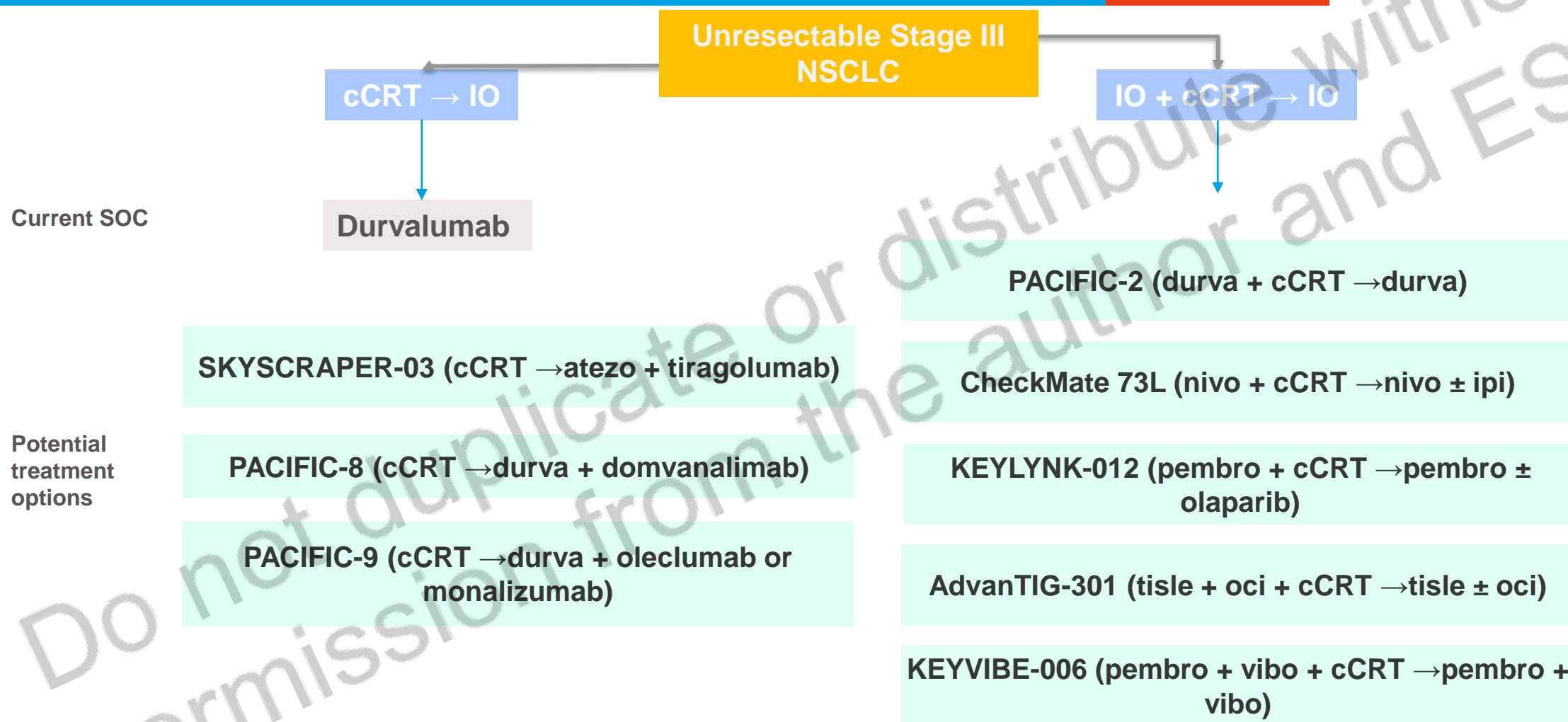


DFS by ctDNA status



Unresectable stage 3 NSCLC

Treatment Landscape in Unresectable Stage III



Slide not intended to provide comprehensive list of trials.

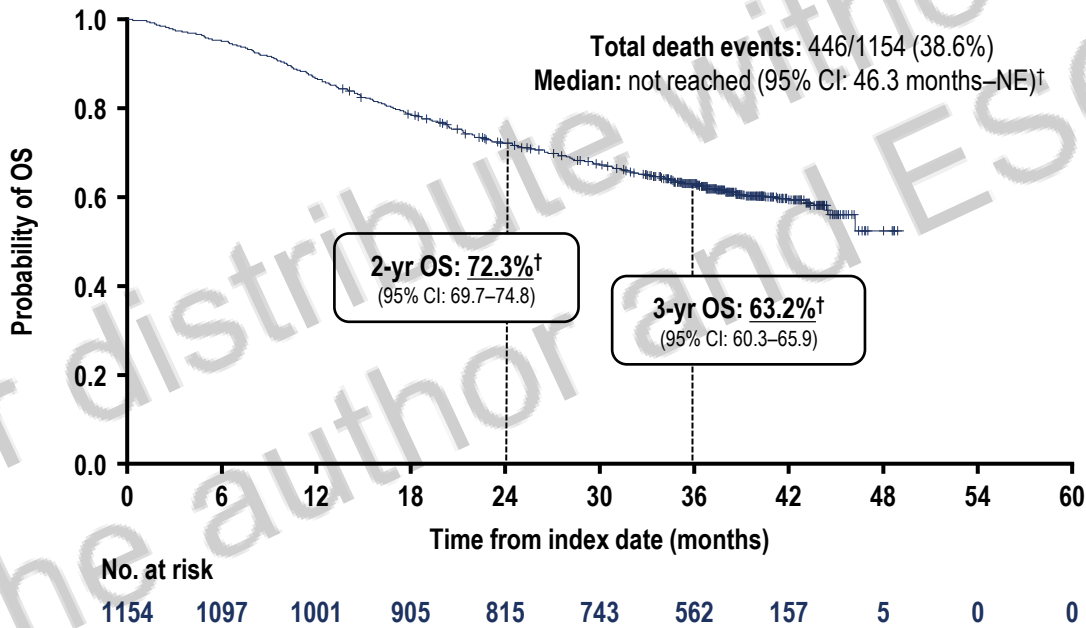
580 – REAL-WORLD OVERALL SURVIVAL WITH DURVALUMAB AFTER CHEMORADIOOTHERAPY IN PATIENTS WITH UNRESECTABLE STAGE III NON-SMALL-CELL LUNG CANCER (NSCLC): INTERIM ANALYSIS FROM THE PACIFIC-R STUDY

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OVERALL SURVIVAL*

- Median OS had not matured at the time of this analysis
 - More than 60% of patients were estimated to be alive at 3 years
- OS outcomes were numerically better among patients who received durvalumab within 42 days of finishing RT



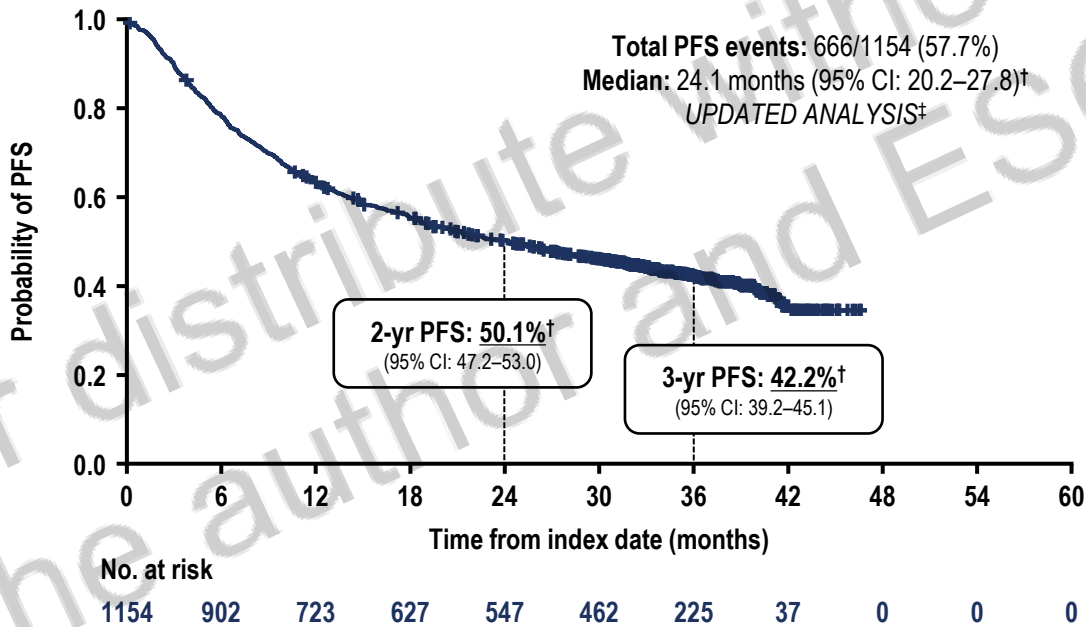
Outcome	Time from end of RT to durva. initiation	
	≤42 days (N=398)	>42 days (N=732)
2-yr OS rate, % (95% CI)†	74.8 (70.2–78.8)	71.2 (67.8–74.4)
3-yr OS rate, % (95% CI)†	66.0 (61.1–70.5)	61.8 (58.1–65.2)

CI, confidence interval; NE, not estimable;
OS, overall survival; RT, radiotherapy; yr, year

*Analyses are based on the 3rd chart extraction from PACIFIC-R (end date: 30 Nov 2021). †Calculated using the Kaplan–Meier method.

PROGRESSION-FREE SURVIVAL*

- Median PFS was 24.1 months (95% CI: 20.2–27.8)
 - More than 40% of patients were estimated to be alive and free of progression at 3 years
- PFS outcomes were numerically better among patients who received durvalumab within 42 days of finishing RT



Outcome	Time from end of RT to durva. initiation	
	≤42 days (N=398)	>42 days (N=732)
2-yr PFS rate, % (95% CI)†	52.3 (47.3–57.1)	48.9 (45.3–52.5)
3-yr PFS rate, % (95% CI)†	45.5 (40.4–50.4)	40.3 (36.5–44.0)

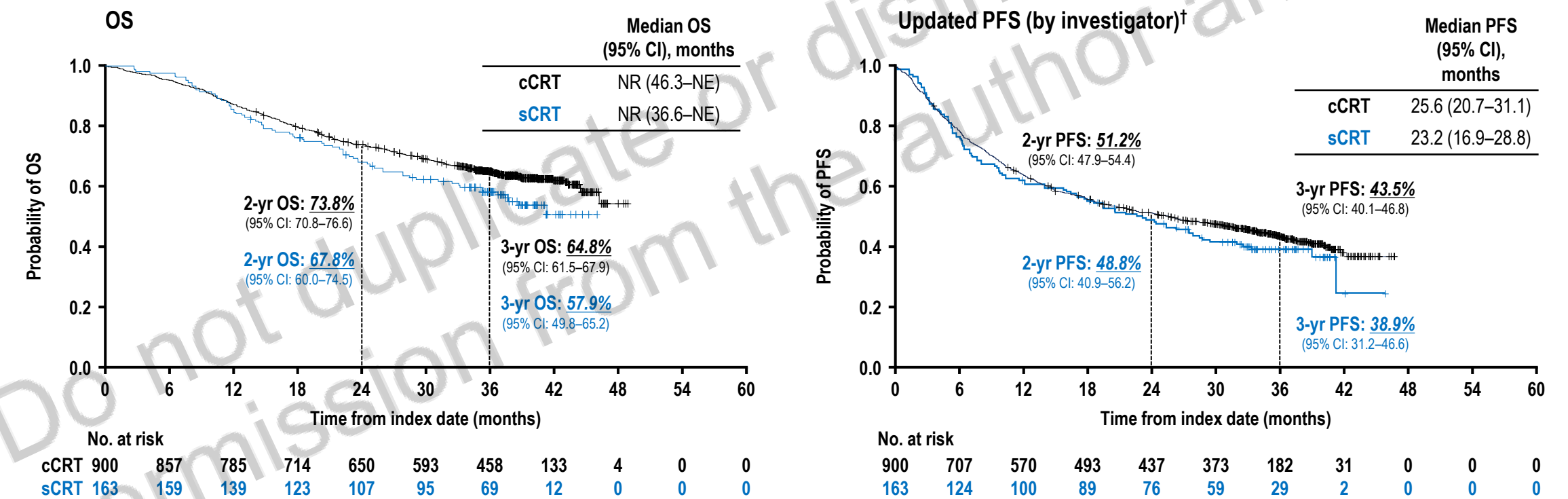
CI, confidence interval; PFS, progression-free survival; RT, radiotherapy; yr, year

*Analyses are based on the 3rd chart extraction from PACIFIC-R (end date: 30 Nov 2021). †Calculated using the Kaplan–Meier method.
‡The original PFS analysis was based on the 2nd chart extraction (end date: 30 Nov 2020) and is published elsewhere.^{1,2} †Girard N et al., Ann Oncol 2021;32(suppl_5):S939–48; ‡Girard N et al., J Thorac Oncol; doi: <https://doi.org/10.1016/j.jtho.2022.10.003> (ePub ahead of print)

OUTCOMES BY CRT TYPE*

ESMO IMMUNO-ONCOLOGY

- Outcomes were numerically better among patients who received cCRT vs sCRT – **3-yr OS rate: 64.8% vs 57.9%**
- Encouraging outcomes were still observed among patients who received sCRT
- The cCRT and sCRT survival curves did not separate until later in the follow-up period



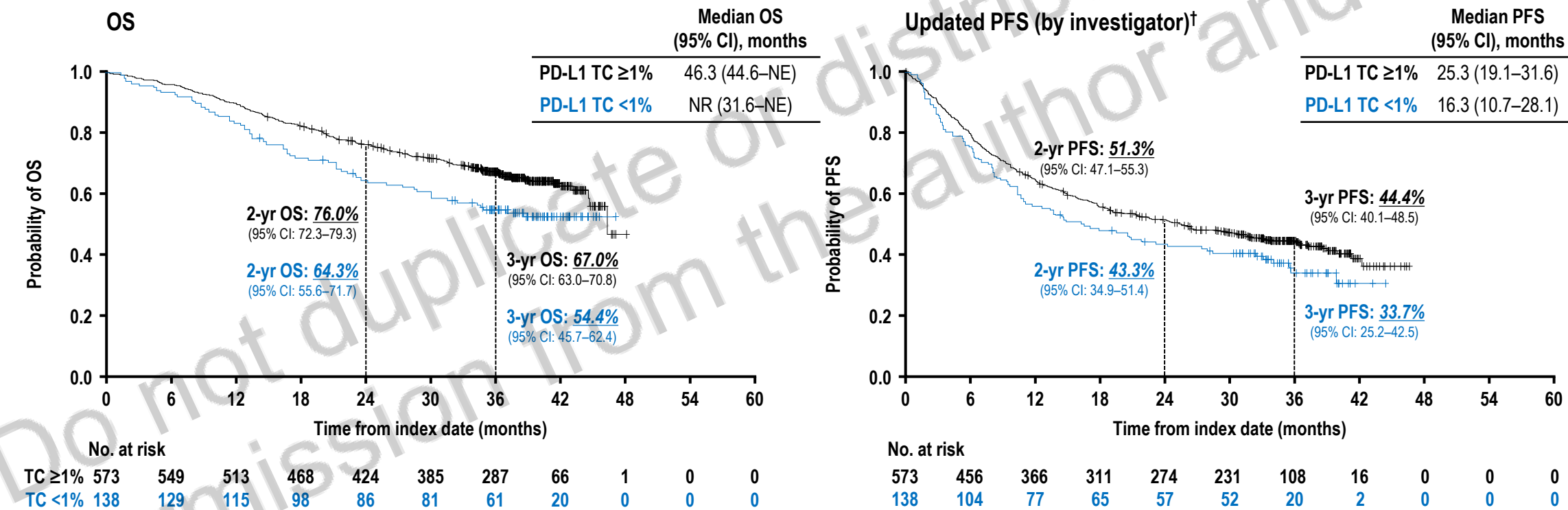
CI, confidence interval; c/sCRT, concurrent/sequential chemoradiotherapy; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; yr, year

*Analyses are based on the 3rd chart extraction (end date: 30 Nov 2021). †The original PFS analysis was based on the 2nd chart extraction (end date: 30 Nov 2020) and is published elsewhere.^{1,2} ¹Girard N et al., Ann Oncol 2021;32(suppl_5): S939–48; ²Girard N et al., J Thorac Oncol; doi: <https://doi.org/10.1016/j.jtho.2022.10.003> (ePub ahead of print)

OUTCOMES BY PD-L1 STATUS*

ESMO IMMUNO-ONCOLOGY

- As expected, outcomes were numerically better among patients with PD-L1 TC ≥1% vs <1% – **3-yr OS rate: 67.0% vs 54.4%**
- Encouraging outcomes were still observed among patients with PD-L1 TC <1%



CI, confidence interval; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; PD-L1, programmed cell death-ligand 1; TC, tumour cell; yr, year

*Analyses are based on the 3rd chart extraction (end date: 30 Nov 2021). †The original PFS analysis was based on the 2nd chart extraction (end date: 30 Nov 2020) and is published elsewhere.^{1,2} 1Girard N et al., Ann Oncol 2021;32(suppl_5): S939–48; 2Girard N et al., J Thorac Oncol; doi: <https://doi.org/10.1016/j.jtho.2022.10.003> (ePub ahead of print)

Two-Year Update From KEYNOTE-799: Pembrolizumab Plus Concurrent Chemoradiation Therapy (cCRT) for Unresectable, Locally Advanced, Stage III NSCLC

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Background

- Standard of care treatment for patients with unresectable, stage III NSCLC includes cCRT followed by consolidation immunotherapy with durvalumab (anti-PD-L1)¹
- Pembrolizumab (anti-PD-1) plus cCRT showed promising antitumor activity and manageable safety in patients with unresectable, locally advanced, stage III NSCLC in the primary analysis of the open-label, nonrandomized, phase 2 KEYNOTE-799 study²

Table 1. Outcomes from the primary analysis^a of KEYNOTE-799²

	Cohort A (squamous and nonsquamous) n = 112	Cohort B (nonsquamous only) n = 102
Primary endpoint		
ORR, % (95% CI)	70.5 (61.2–78.8)	70.6 (60.7–79.2)
Grade ≥3 pneumonitis, n (%)	9 (8.0)	7 (6.9)

^aDatabase cutoff date: October 28, 2021

- We present updated outcomes from KEYNOTE-799 after 1 year of additional follow-up for all enrolled patients

Objectives

Primary

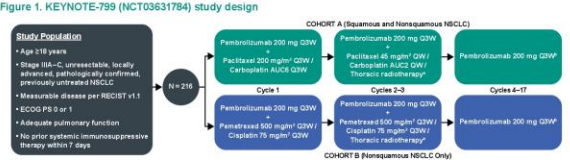
- ORR per RECIST version 1.1 by blinded independent central review (BICR)
- Proportion of patients with grade ≥3 pneumonitis

Secondary

- Progression-free survival (PFS) per RECIST version 1.1 by BICR
- Overall survival (OS)
- Safety

Methods

Study design, patients, and treatment



AE, any adverse event; ORR, overall response rate; PFS, progression-free survival; OS, overall survival; Q3W, every 3 weeks; Q4W, once weekly; Q5W, every 5 weeks; Q6W, every 6 weeks; Q7W, every 7 weeks; Q8W, every 8 weeks; Q9W, every 9 weeks; Q10W, every 10 weeks; Q11W, every 11 weeks; Q12W, every 12 weeks; Q13W, every 13 weeks; Q14W, every 14 weeks; Q15W, every 15 weeks; Q16W, every 16 weeks; Q17W, every 17 weeks; Q18W, every 18 weeks; Q19W, every 19 weeks; Q20W, every 20 weeks; Q21W, every 21 weeks; Q22W, every 22 weeks; Q23W, every 23 weeks; Q24W, every 24 weeks; Q25W, every 25 weeks; Q26W, every 26 weeks; Q27W, every 27 weeks; Q28W, every 28 weeks; Q29W, every 29 weeks; Q30W, every 30 weeks; Q31W, every 31 weeks; Q32W, every 32 weeks; Q33W, every 33 weeks; Q34W, every 34 weeks; Q35W, every 35 weeks; Q36W, every 36 weeks; Q37W, every 37 weeks; Q38W, every 38 weeks; Q39W, every 39 weeks; Q40W, every 40 weeks; Q41W, every 41 weeks; Q42W, every 42 weeks; Q43W, every 43 weeks; Q44W, every 44 weeks; 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#8510: The Selective Personalized RadioImmunotherapy for Locally Advanced NSCLC Trial (SPRINT)

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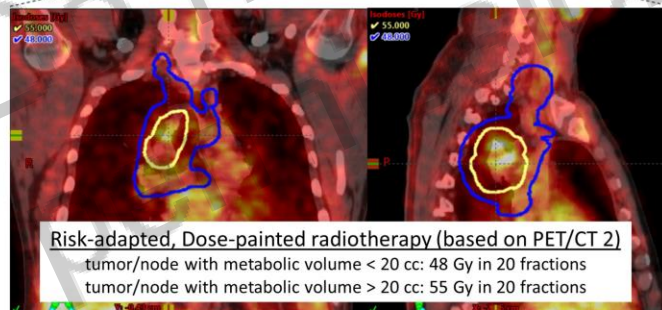
Background/Methods:

- Concurrent chemoradiotherapy with adjuvant immunotherapy is a standard treatment approach for locally advanced non-small cell lung cancer (LA-NSCLC).
- We hypothesized that a combination of pembrolizumab and risk-adapted, dose-painted radiotherapy, without chemotherapy, will improve outcomes and toxicities for LA-NSCLC patients with PD-L1 tumor proportion score (TPS) $\geq 50\%$.

Key eligibility criteria:

- Unresectable AJCC v8 Stage II NSCLC or Stage III NSCLC
- ECOG performance status 0-1
- PD-L1 TPS $\geq 50\%$ using 22C3 immunohistochemistry assay.
 - Subjects with lower TPS could be enrolled to a separate cohort and treated with chemoradiotherapy

Study Design:



Study Design (continued):

Prospective phase II trial, n=25

- Primary endpoint: 1-year progression-free survival (PFS), which we hypothesized would exceed 65%
- Secondary endpoints: adverse events (CTCAE v. 4.03), responses to induction pembrolizumab on CT (RECIST) and PET (PERCIST), overall survival (OS)

Results:

- 25 subjects were enrolled between August 2018 and November 2021.
- Median follow-up duration is 16 months (IQR 11 to 22 months)

Gender	
Male	13 (52%)
Female	12 (48%)
Age, mean (range)	70 (53 to 86)
Clinical stage, n (%)	
II	1 (4%)
IIIA	13 (52%)
IIIB	9 (36%)
IIIC	2 (8%)
ECOG Performance Status, n (%)	
0	8 (32%)
1	17 (68%)
Histology, n (%)	
Adenocarcinoma	12 (48%)
Squamous cell carcinoma	12 (48%)
Other/not specified	2 (8%)
PD-L1 TPS, median (IQR)	75% (70% to 80%)

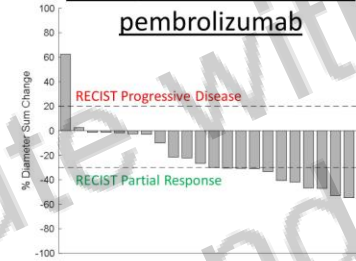
Patient characteristics (left) and adverse events (below). No grade 4-5 toxicities have occurred

Adverse Event	Grade 2+, n (%)	Grade 3+, n (%)
anemia	2 (8%)	1 (4%)
arthritis	1 (4%)	1 (4%)
diarrhea	2 (8%)	1 (4%)
esophagitis	8 (32%)	1 (4%)
pneumonitis	2 (8%)	1 (4%)
weight loss	1 (4%)	1 (4%)

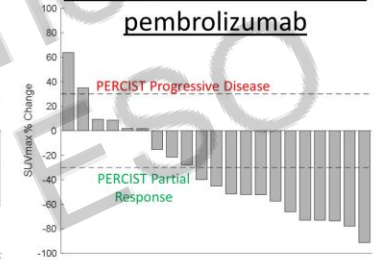
Conclusions:

- This study demonstrates excellent early clinical outcomes for locally advanced NSCLC patients with PD-L1 TPS $\geq 50\%$ who were treated with pembrolizumab and risk-adapted radiotherapy, **without chemotherapy**.
- Response to induction pembrolizumab may serve as a predictor of clinical outcomes and can reduce the extent of thoracic irradiation required to achieve disease control.

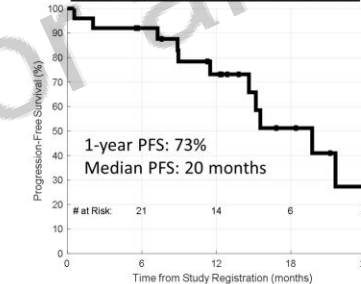
CT response to induction pembrolizumab



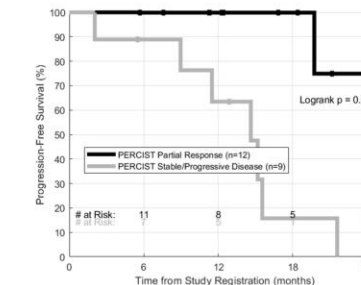
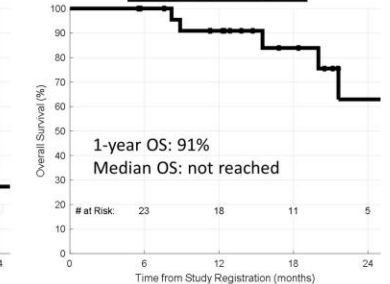
PET response to induction pembrolizumab



Progression-free Survival



Overall Survival



Exploratory analysis demonstrates that PET response to induction pembrolizumab is associated with favorable progression-free survival (left).

Future Directions:

- A follow-up study will further refine our treatment approach by selectively utilizing chemotherapy for patients without response to induction pembrolizumab.

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MA06.04: Phase II Study of Durvalumab Plus Concurrent Radiotherapy in Unresectable Locally Advanced NSCLC: DOLPHIN Study (WJOG11619L) – Tachihara M, et al

- **Study objective**

- To evaluate the efficacy and safety of durvalumab + concurrent radiotherapy in patients with unresectable locally advanced NSCLC in the DOLPHIN study

Key patient inclusion criteria

- Unresectable stage III or postoperative recurrent NSCLC
 - PD-L1 $\geq 1\%$
 - ECOG PS 0–1
- (n=35)

Durvalumab 10 mg/kg q2w +
radiotherapy 60 Gy
(up to 1 year)

PD/
toxicity

Primary endpoint

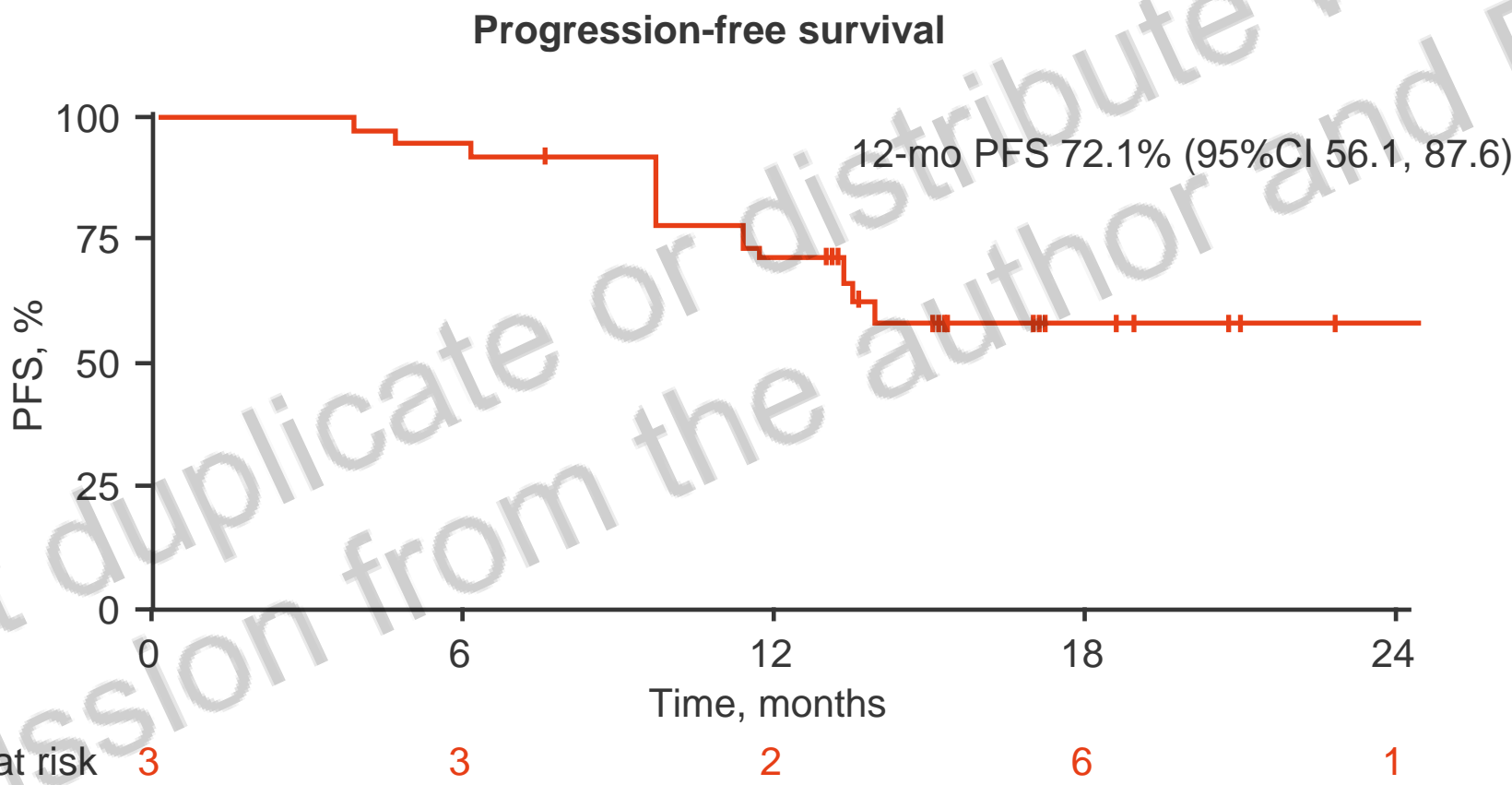
- 12-mo PFS rate

Secondary endpoints

- OS, ORR, DCR, safety

MA06.04: Phase II Study of Durvalumab Plus Concurrent Radiotherapy in Unresectable Locally Advanced NSCLC: DOLPHIN Study (WJOG11619L) – Tachihara M, et al

- Key results



MA06.04: Phase II Study of Durvalumab Plus Concurrent Radiotherapy in Unresectable Locally Advanced NSCLC: DOLPHIN Study (WJOG11619L) – Tachihara M, et al

- Key results (cont.)

Response	n=33
ORR, n (%) [95%CI]	30 (90.9) [75.7, 98.1]
BOR, n (%)	
CR	12 (36.4)
PR	18 (54.5)
SD	3 (9.1)
PD	0
DCR, n (%) [95%CI]	33 (100) [89.4, 100]

AE, n (%)	
Any grade	34 (100)
Grade 3–4	16 (47.1)
Grade 5	2 (5.9)
Led to discontinuation of durvalumab	6 (17.6)
Led to discontinuation of radiotherapy	0
TRAE	30 (88.2)
SAE	13 (38.2)
Severe immune-mediated AE	10 (29.4)

Pneumonitis or radiation pneumonitis, n (%)	
Any grade	21 (61.8)
Grade 3–4	4 (11.8)
Grade 5	0
Led to discontinuation of durvalumab	2 (5.9)
Led to discontinuation of radiotherapy	0

- Conclusions

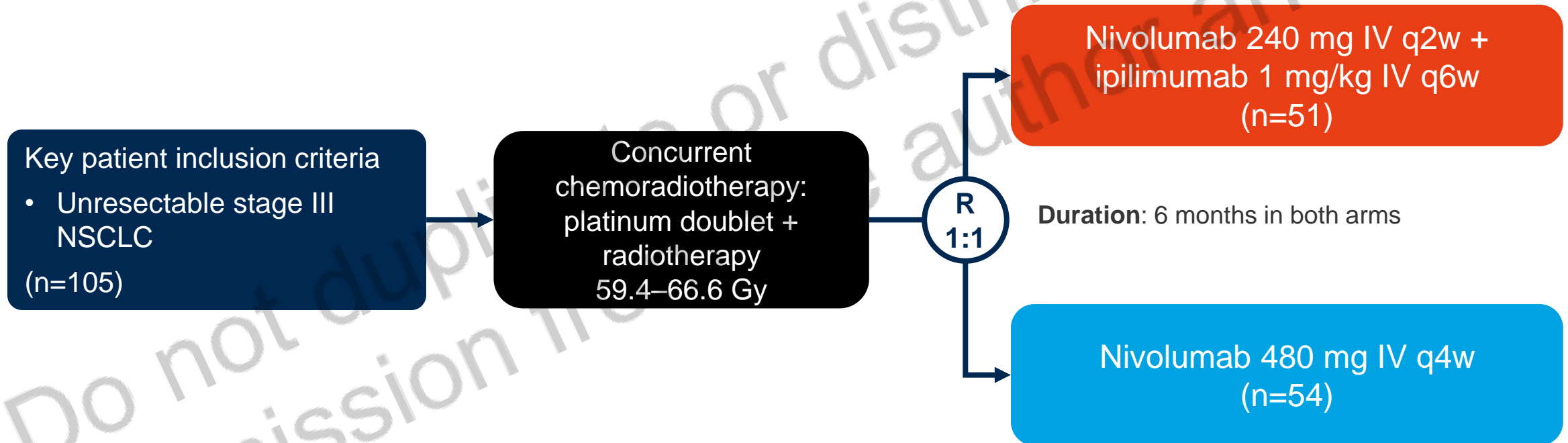
- In patients with unresectable locally advanced PD-L1+ NSCLC, durvalumab + concurrent radiotherapy demonstrated promising PFS benefit and was generally well-tolerated

MA06.05: Consolidation Nivolumab and Ipilimumab or Nivolumab Alone Following Concurrent Chemoradiation for Patients with Unresectable Stage III NSCLC

– Durm GA, et al

- **Study objective**

- To evaluate the efficacy and safety of consolidation nivolumab + ipilimumab compared with nivolumab alone following concurrent chemoradiotherapy in patients with unresectable stage III NSCLC



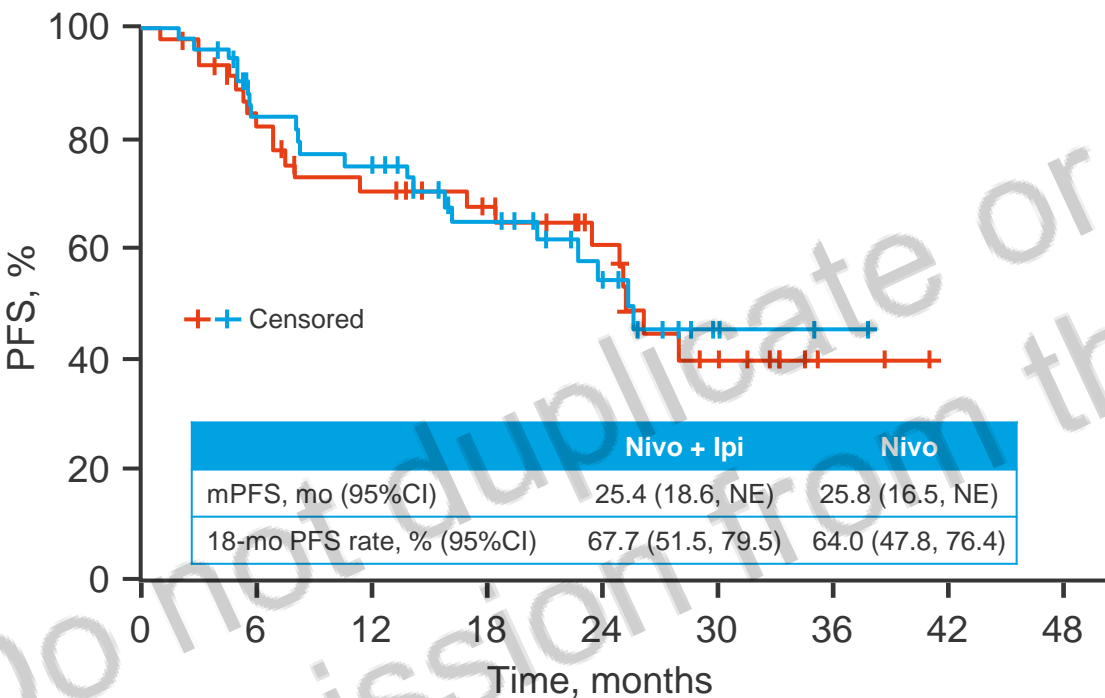
Endpoints

- PFS, OS, safety

MA06.05: Consolidation Nivolumab and Ipilimumab or Nivolumab Alone Following Concurrent Chemoradiation for Patients with Unresectable Stage III NSCLC – Durm GA, et al

- Key results

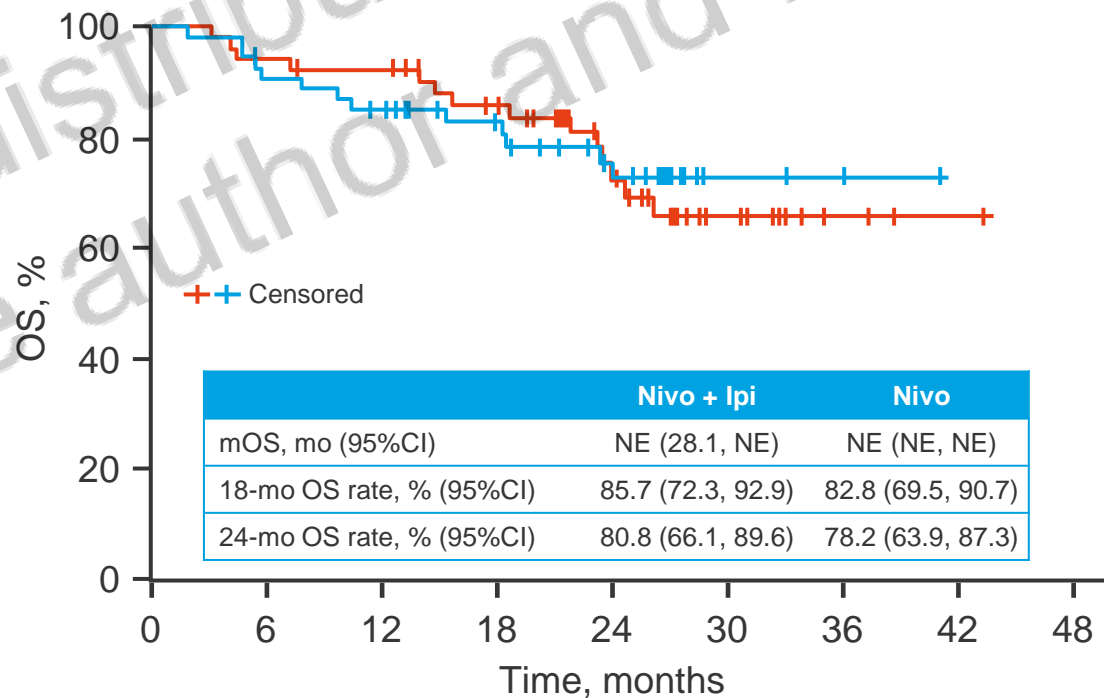
Progression-free survival



No. at risk

Nivo	52	37	33	23	15	4	1	0
Nivo + Ipi	47	36	29	24	16	8	2	0

Overall survival



No. at risk

Nivo	54	49	45	38	30	6	2	1	0
Nivo + Ipi	51	48	46	40	30	15	5	1	0

MA06.05: Consolidation Nivolumab and Ipilimumab or Nivolumab Alone Following Concurrent Chemoradiation for Patients with Unresectable Stage III NSCLC

– Durm GA, et al

- Key results (cont.)

TRAEs, n (%)	Nivo + Ipi (n=51)	Nivo (n=54)
Any	41 (80.4)	39 (72.2)
Grade ≥3	14 (27.5)	10 (18.5)
Most common		
Fatigue	16 (31.4)	17 (31.5)
Dyspnea	10 (19.6)	8 (14.8)
Rash	8 (15.7)	9 (16.7)
Hypothyroidism	8 (15.7)	7 (13.0)
Diarrhea	10 (19.6)	4 (7.4)
Pruritus	9 (17.7)	5 (9.3)
Arthralgia	6 (11.8)	2 (3.7)
Nausea	6 (11.8)	2 (3.7)
Pneumonitis		
Grade ≥2	16 (31.4)	12 (22.2)
Grade 3*	9 (17.6)	5 (9.3)

- Conclusions

- In patients with unresectable stage III NSCLC, consolidation nivolumab ± ipilimumab demonstrated encouraging survival and was generally well-tolerated, although there were higher rates of pneumonitis with the combination therapy

Conclusions

- IO/TKI offers a consistent survival advantage for resectable stage III patients (still waiting for mature OS data)
- Still not enough data to compare neo-adjuvant vs adjuvant vs. perioperative approaches
- IO maintenance after CRT is the standard therapy for unresectable NSCLC and is applicable outside clinical trials
- New data from phase 2 studies indicate possible benefits for various combination and sequences of CT/RT/IO for unresectable stage 3
- New trials will explore intersections on stage 3A(B): res/unresectable?
- New data confirm the prognostic value of MRD, and pave the way for its introduction in phase 3 trials