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

Expert: **Prof Andrea Riccardo Filippi**, Policlinico S. Matteo IRCCS Foundation, Pavia, Italy

Discussant: **Prof Nicolas Girard**, Institut Curie, Paris, France

Discussant: **Dr Giulia Veronesi**, IRCCS San Raffaele Hospital, Milan, Italy

Disclosures

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- Speaker's bureau: Astra Zeneca, Roche, Ipsen
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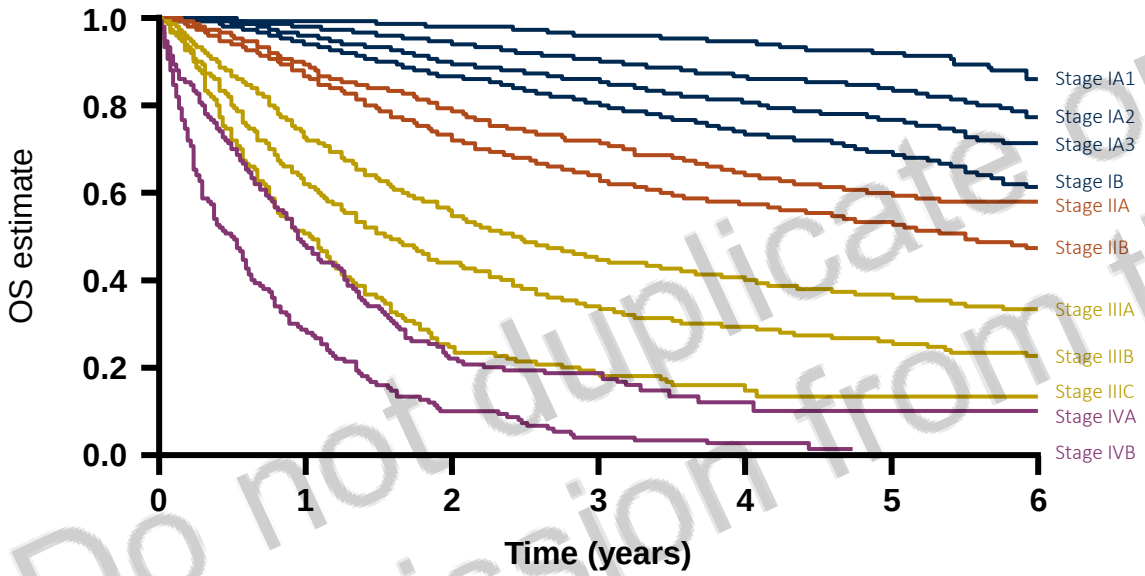
- Institutional grant: Astra Zeneca

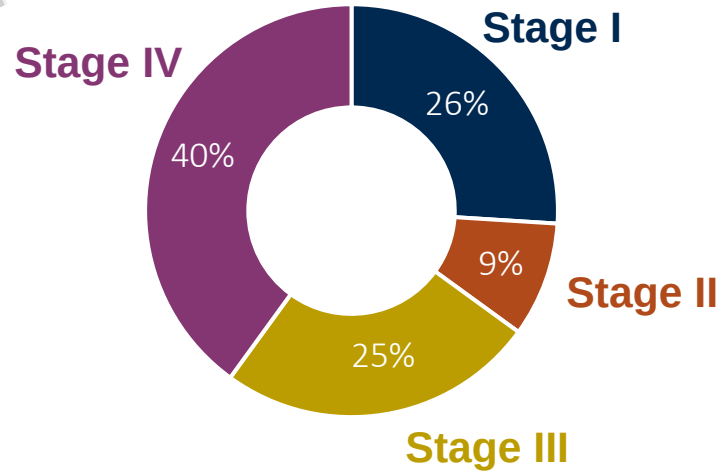
Over half of all patients with NSCLC are initially diagnosed with stage I–III disease



5-year survival[1]

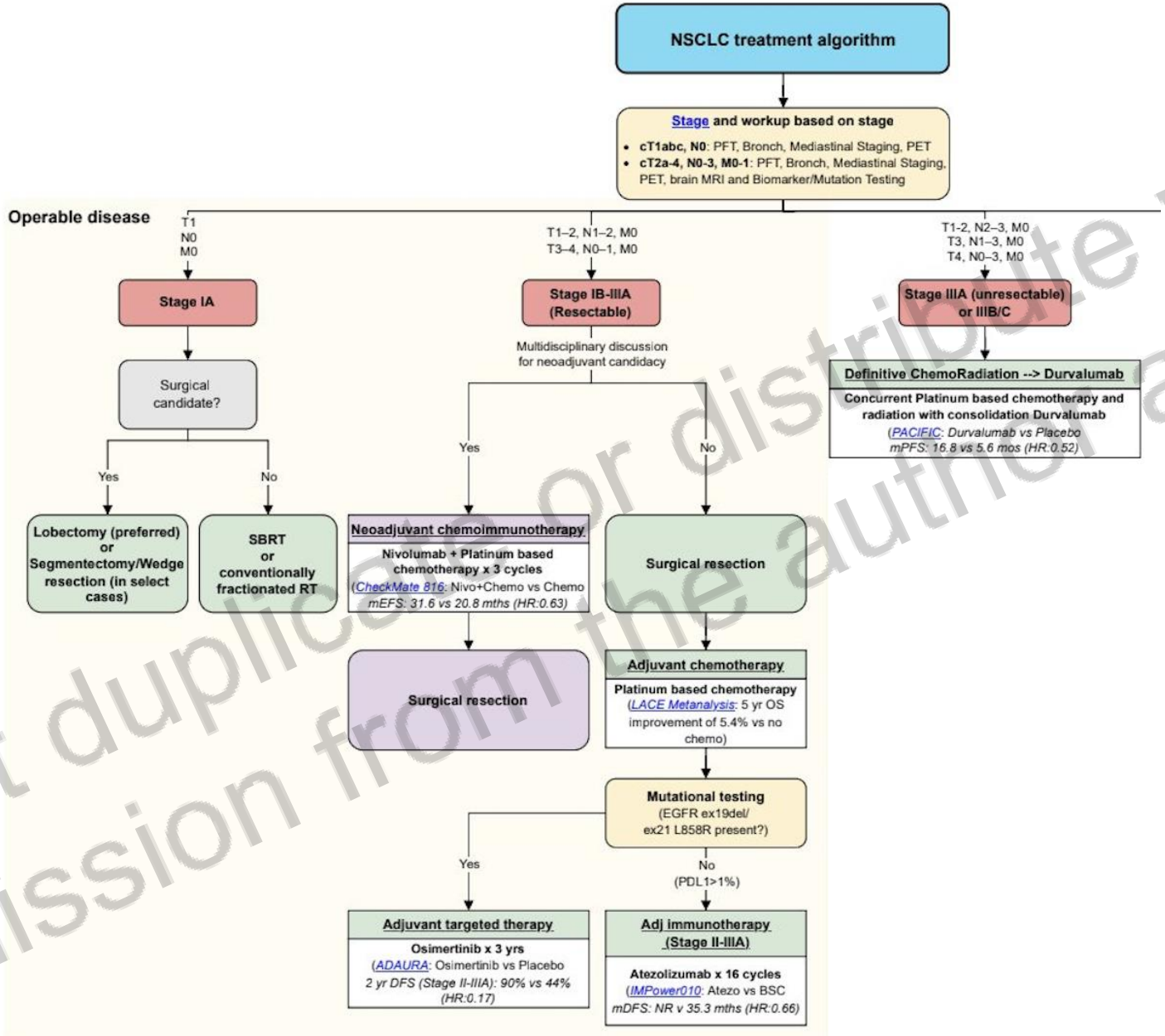
Stage I	**68–92%**
Stage II	**53–60%**
Stage III	**13–36%**
Stage IV	**0–10%**

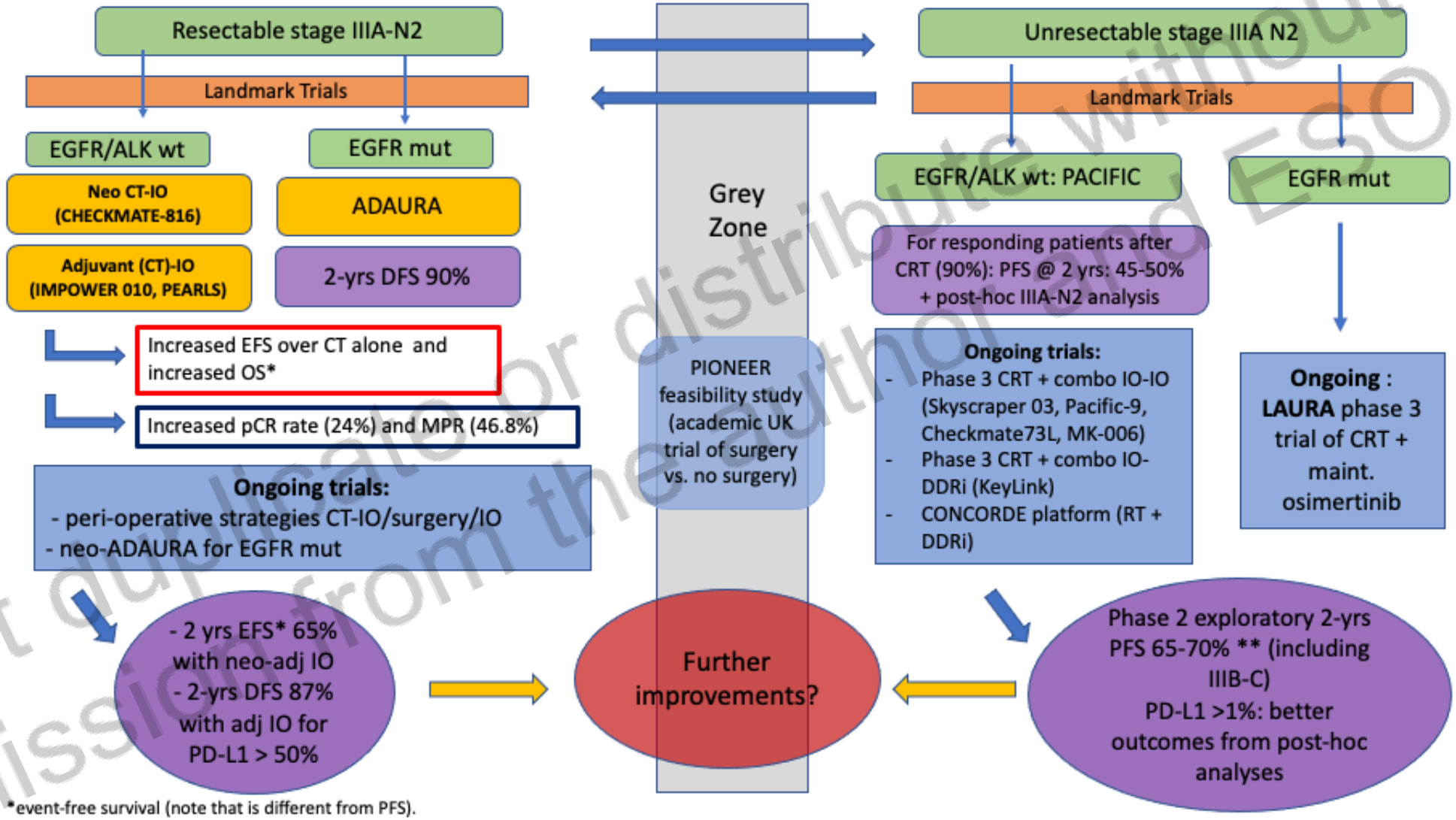
% at diagnosis[2]*



*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



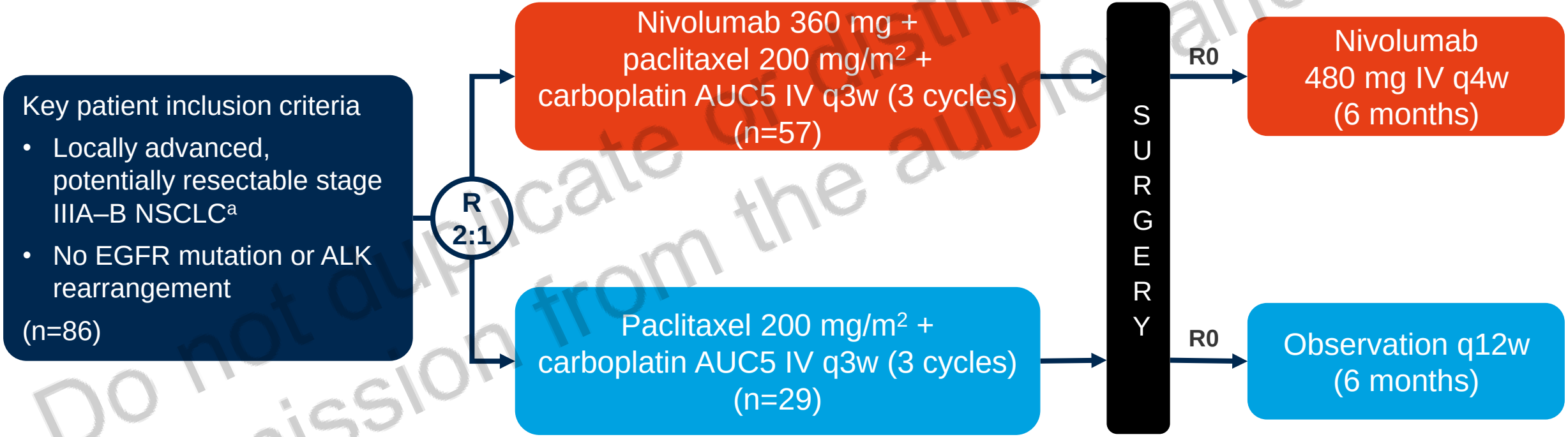


*event-free survival (note that is different from PFS).

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

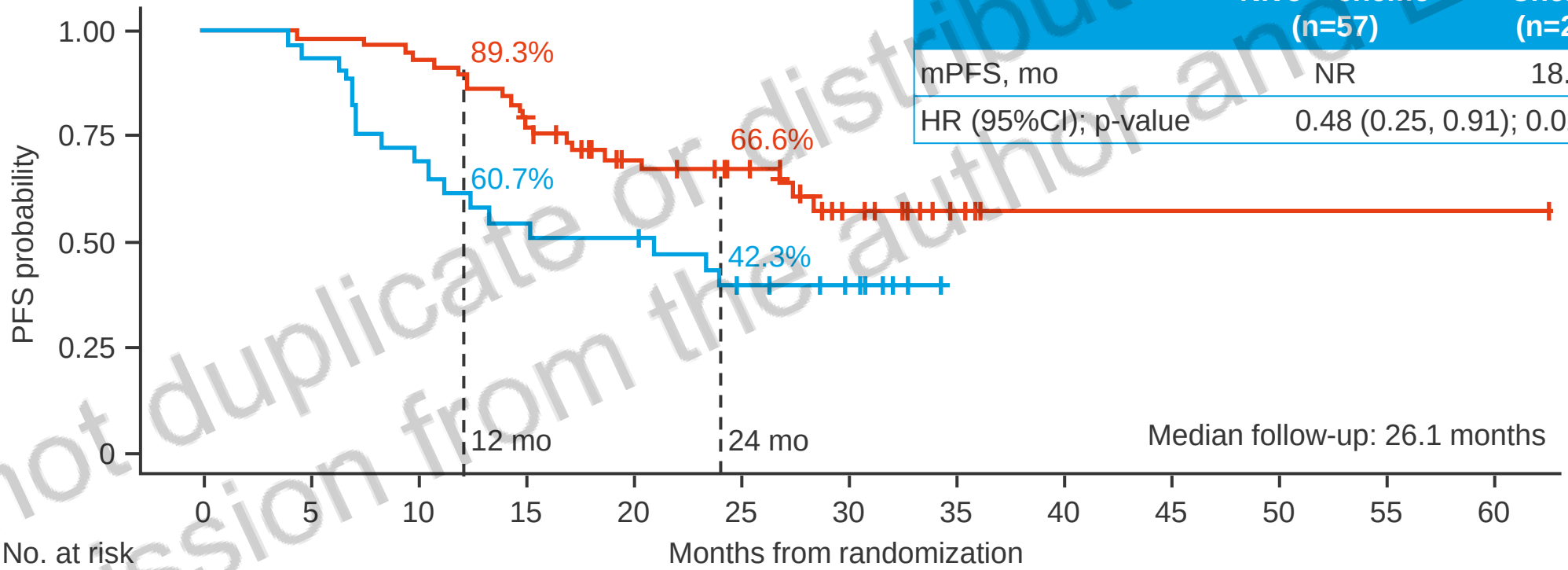
- MPR, surgical outcomes, OS, PFS, safety

[a]Per American Joint Committee on Cancer (AJCC) cancer staging manual, 8th edition

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

- **Key results**

Progression-free survival (ITT)

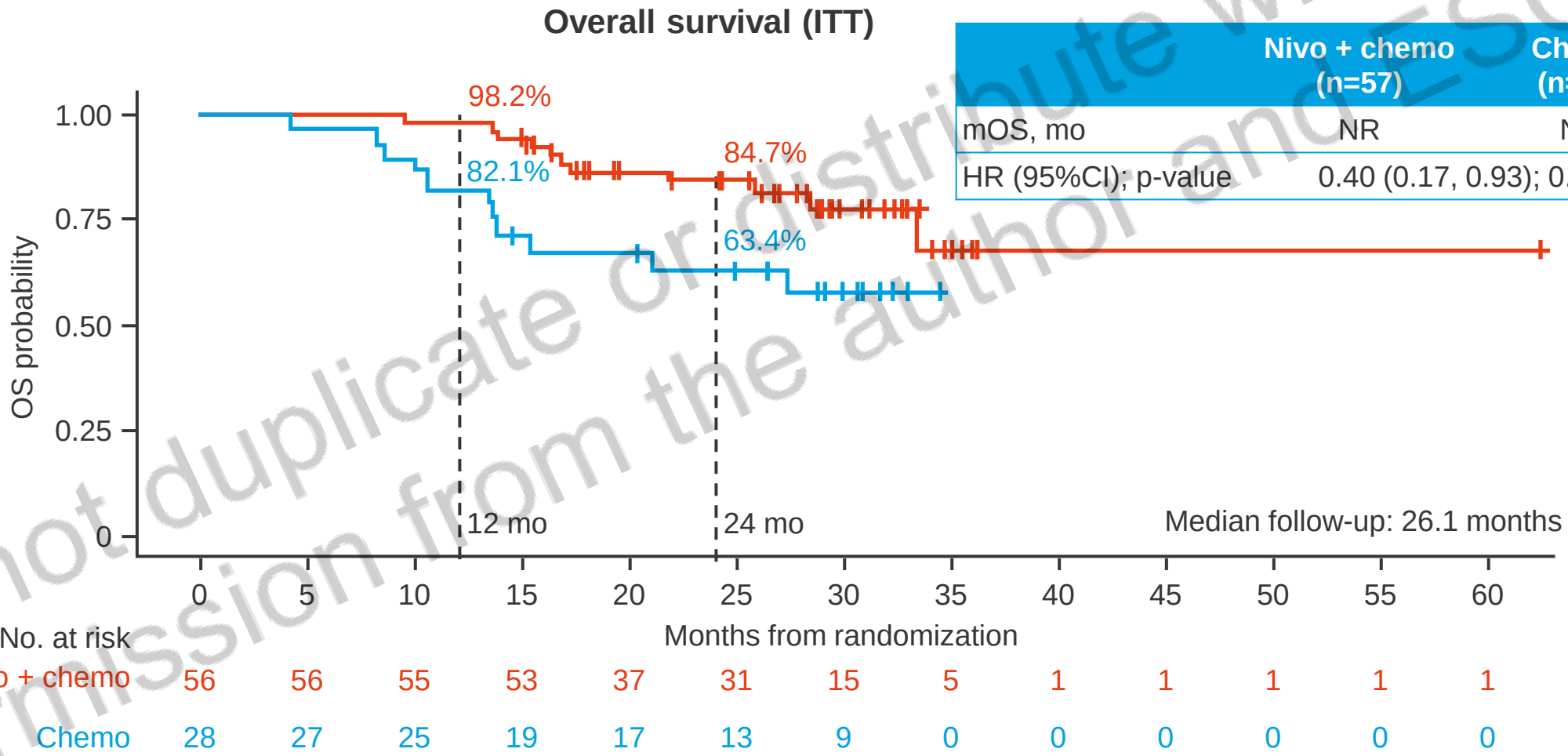


	Nivo + chemo (n=57)	Chemo (n=29)
mPFS, mo	NR	18.3
HR (95%CI); p-value	0.48 (0.25, 0.91); 0.025	

No. at risk													
Nivo + chemo	56	55	52	44	30	24	11	4	1	1	1	1	1
Chemo	28	26	20	15	14	9	7	0	0	0	0	0	0

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

- **Key results**



	Nivo + chemo (n=57)	Chemo (n=29)
mOS, mo	NR	NR
HR (95%CI); p-value	0.40 (0.17, 0.93); 0.034	

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

- **Key results (cont.)**

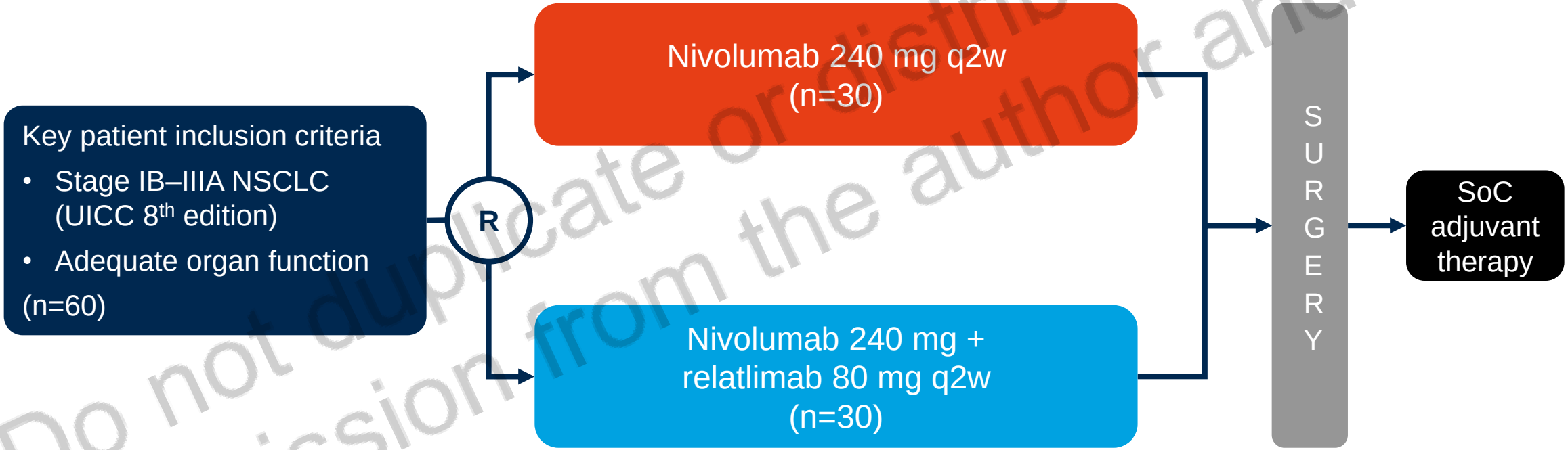
Surgical outcomes	Nivo + chemo (n=57)	Chemotherapy (n=29)
R0, n (%)	49 (92.5)	13 (65.0)
OR (95%CI); p-value	6.60 (1.67, 26.02); 0.007	
Definitive surgery[a], %	93.0	69.0
OR (95%CI); p-value	5.96 (1.65, 21.56); 0.008	
Downstaging, n (%) Yes No	 37 (69.8) 16 (30.2)	 8 (40.0) 12 (60.0)
Downstaging rate,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

[a]Defined 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 ≤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

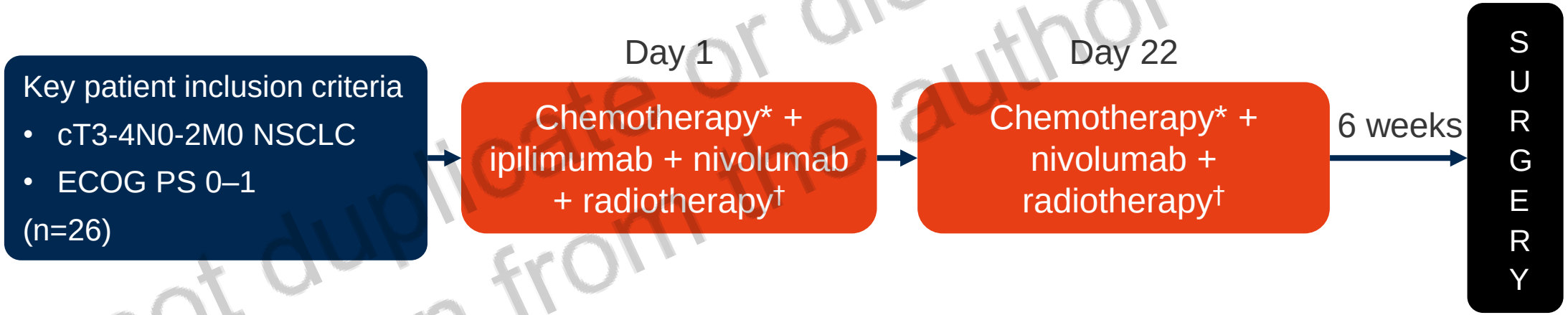
- **Key results (cont.)**

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

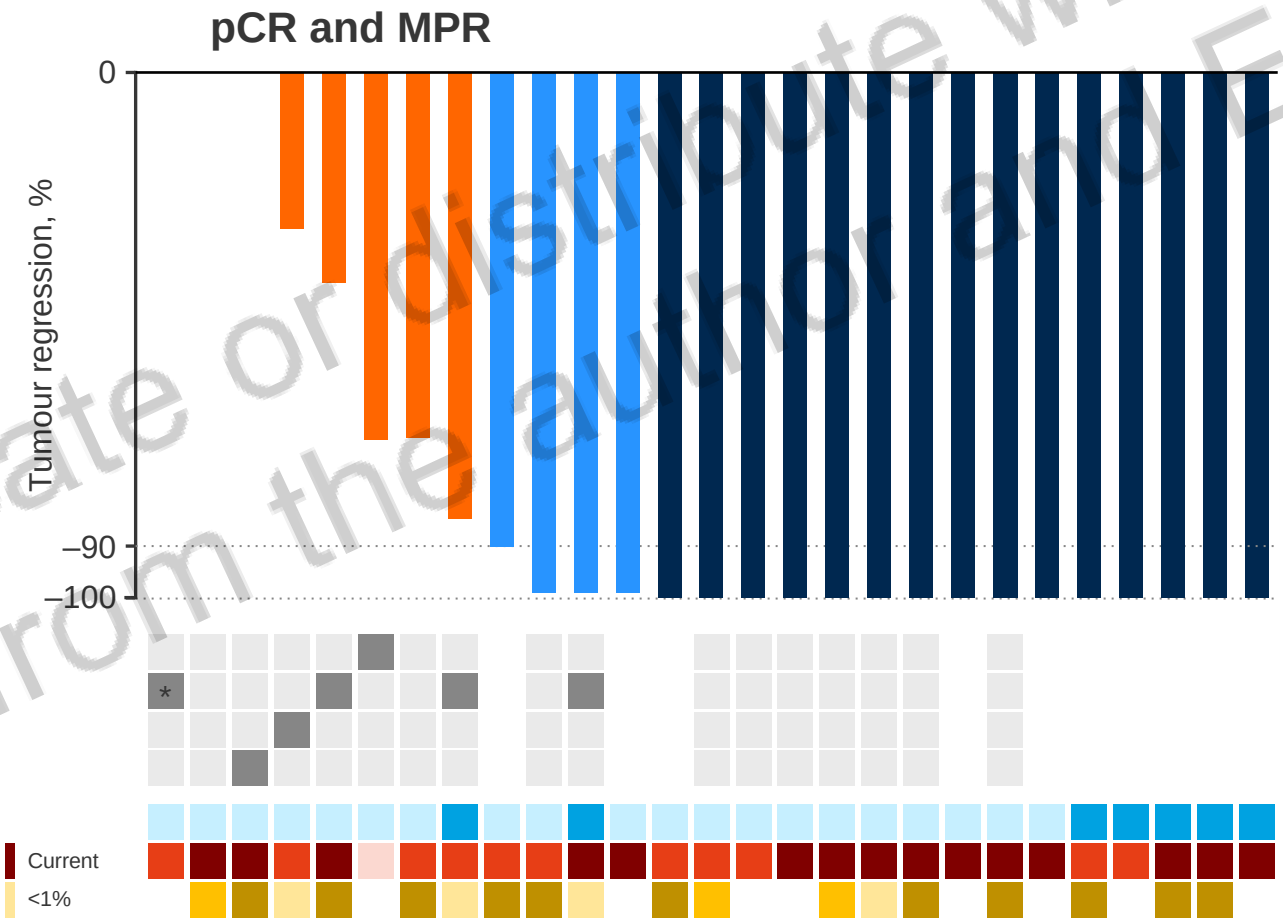
*Platinum-doublet chemotherapy; †once daily dose of 2 Gy;
‡defined as a residual viable tumour cells percentage of ≤10%

Bahce I, et al. Ann Oncol 2022;33(suppl):Abstr 950O

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)



[a]Binomial probability using 30% pCR as historical reference; [b]excluding patients on treatment.
*This patient developed pleural metastases during induction therapy and did not receive surgery

Bahce I, et al. Ann Oncol 2022;33(suppl):Abstr 950O

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.)**

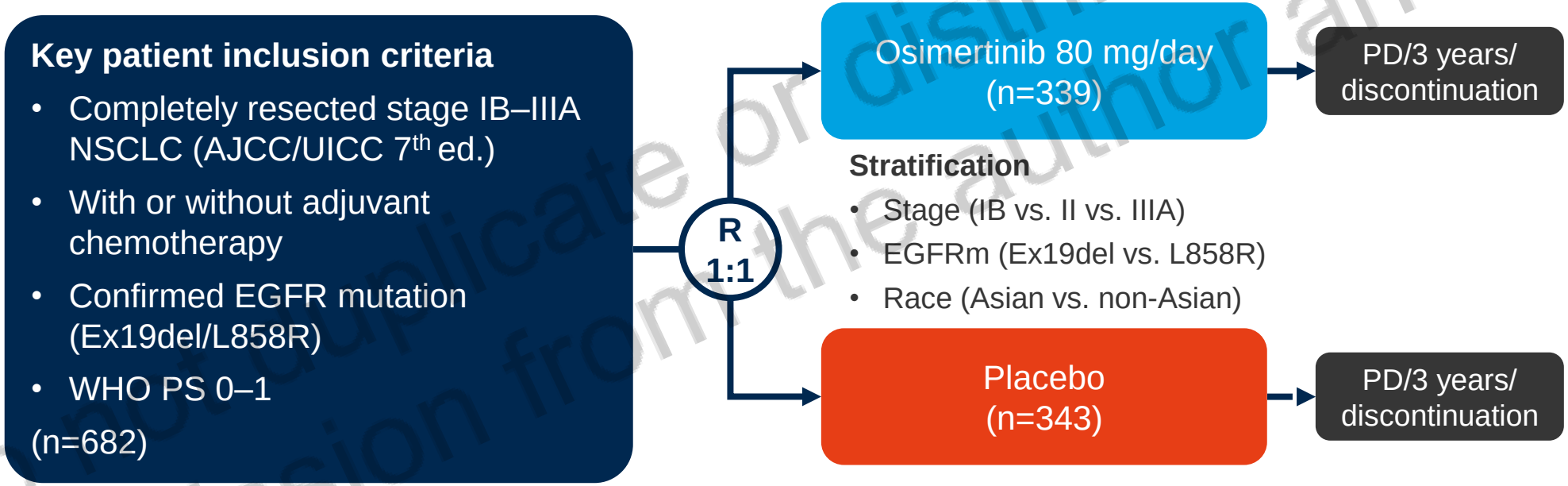
	n (%)
Any TEAE	27 (100)
Grade 3–4	22 (81)
Serious AE	10 (37)
Grade 5	1 (4)
Any TRAE	21 (78)
Grade 3-4	18 (67)
Ir-AE grade 3–4	5 (19)
Grade 5	0
Led to IO discontinuation	2 (7)

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



Primary endpoint

- DFS (in stage II/IIIA)

Secondary endpoints

- DFS (overall population[a]), OS, HRQoL, safety

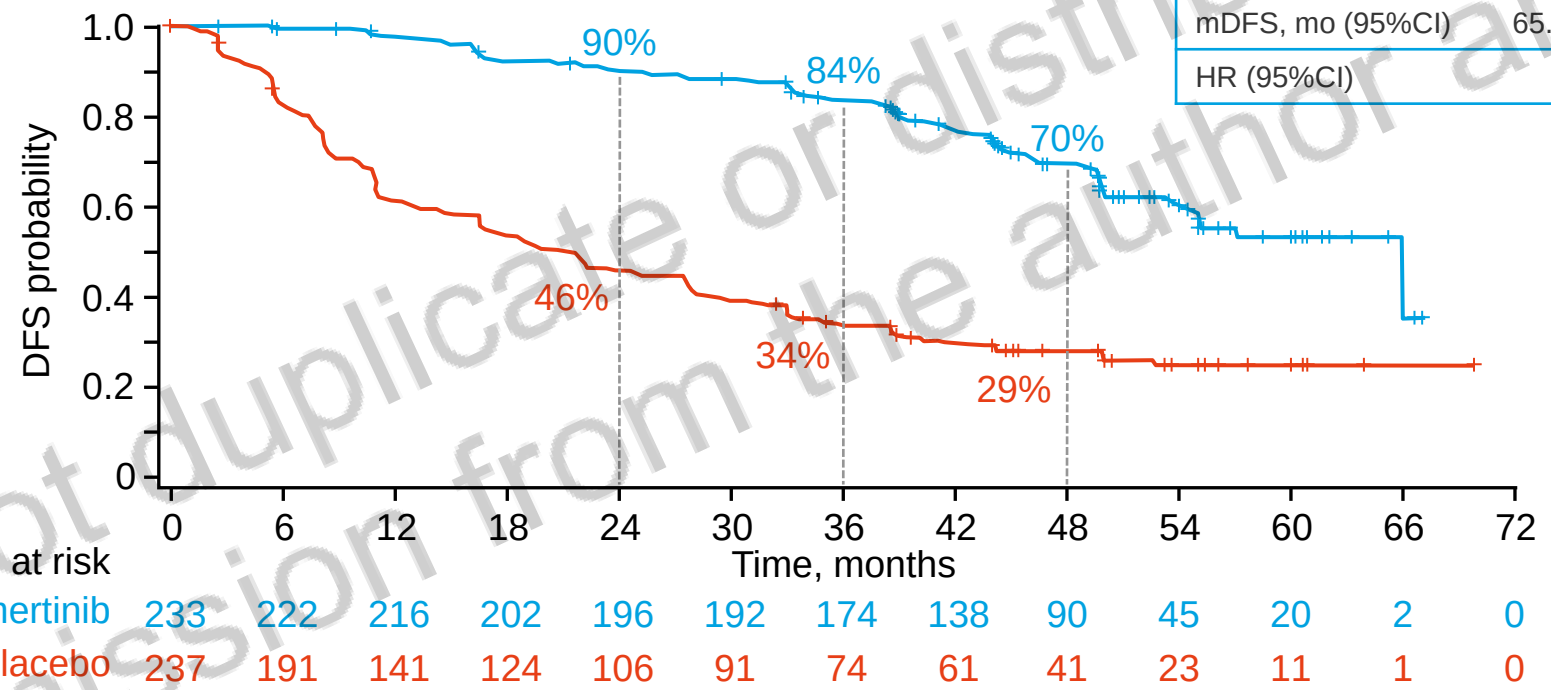
[a]Stage IB, II and IIIA

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

	Osimertinib (n=233)	Placebo (n=237)
mDFS, mo (95%CI)	65.8 (54.4, NC)	21.9 (16.6, 27.5)
HR (95%CI)	0.23 (0.18, 0.30)	



– 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])

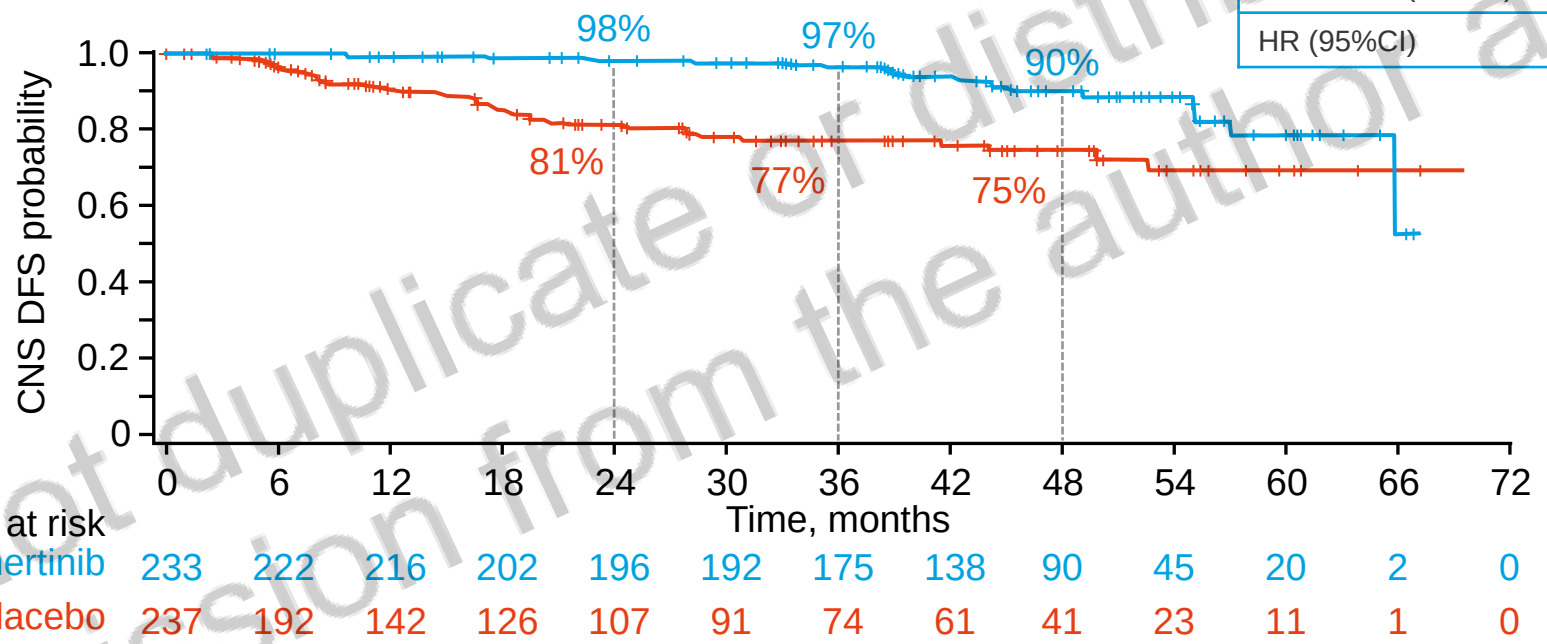
Tsuboi M, et al. Ann Oncol 2022;33(suppl):Abstr LBA47

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

	Osimertinib (n=22)	Placebo (n=41)
mDFS, mo (95%CI)	NR (65.8, NC)	NR (NC, NC)
HR (95%CI)	0.24 (0.14, 0.42)	



– 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.)**

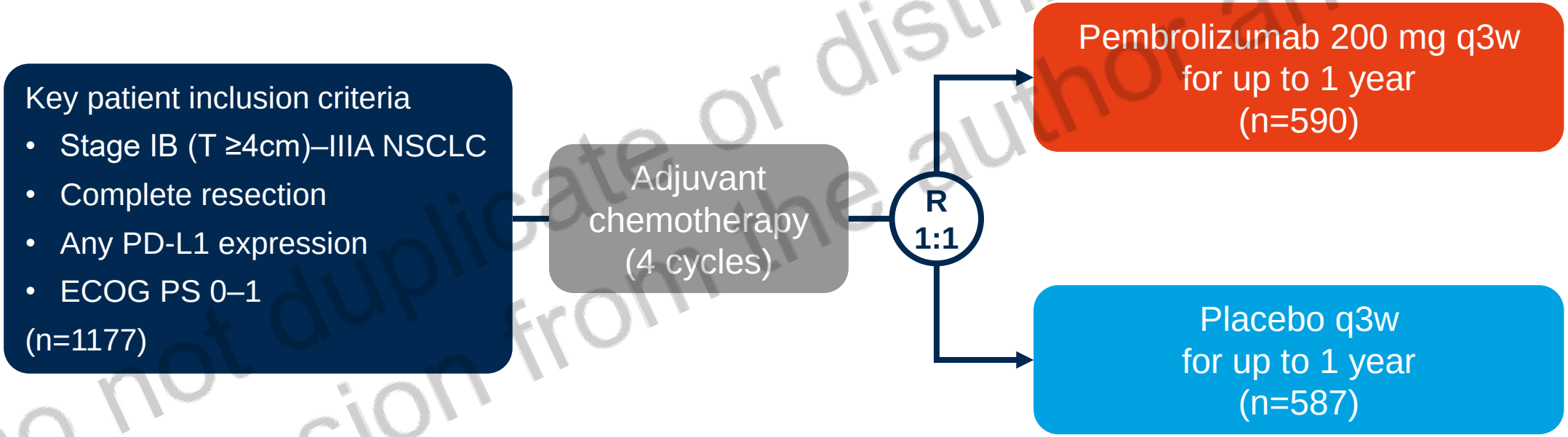
TEAEs, n (%)	Osimertinib (n=337)	Placebo (n=343)
Any	330 (98)	309 (90)
Grade ≥3	79 (23)	48 (14)
Serious	68 (20)	47 (14)
Led to discontinuation	43 (13)	9 (3)
Led to dose reduction	42 (12)	3 (1)
Led to dose interruption	91 (27)	43 (13)
Led to death	1 (<1)	2 (1)

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

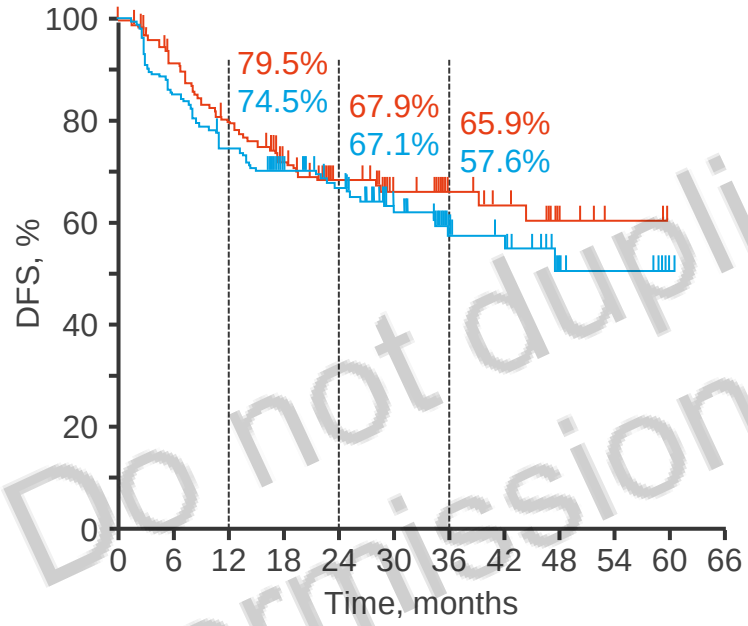
930MO: PD-L1 expression and outcomes of pembrolizumab and placebo in completely resected stage IB-IIIA NSCLC: subgroup analysis of PEARLS/KEYNOTE-091 – Peters S, et al

- **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	

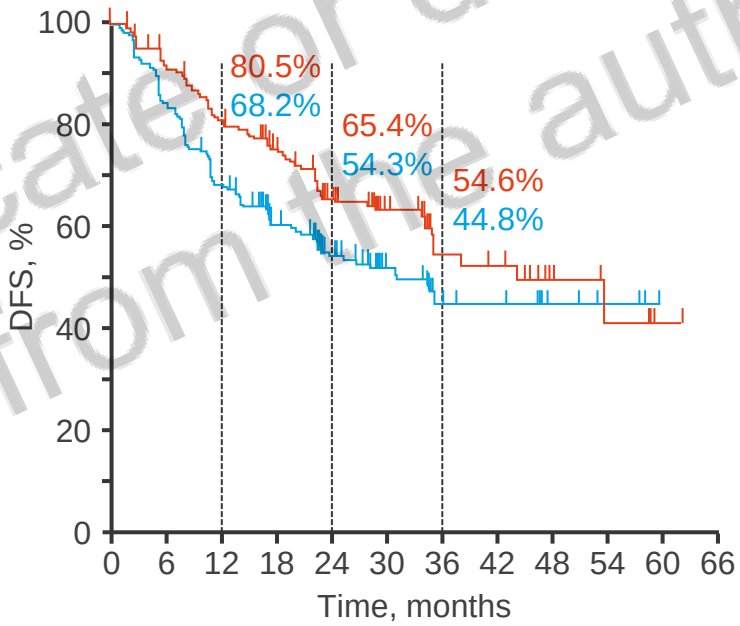


No. at risk

Pembrolizumab	168	145	126	99	69	50	26	22	7	4	0	0
Placebo	165	140	121	100	75	54	28	22	8	6	1	0

TPS 1–49%

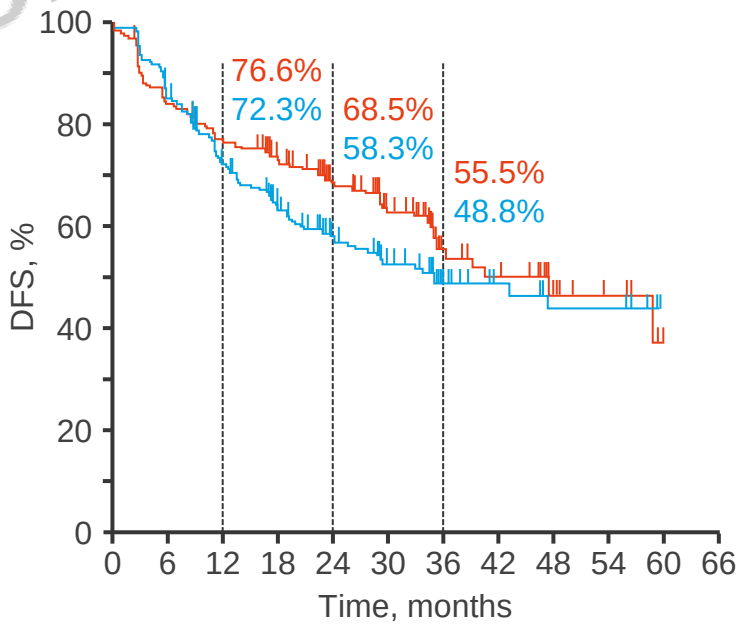
	Pembrolizumab (n=189)	Placebo (n=190)
mDFS, mo (95%CI)	44.2 (34.9, NR)	31.3 (22.5, NR)
HR (95%CI)	0.67 (0.48, 0.92)	



	189	158	137	113	84	61	22	20	9	5	1	0
	190	159	128	97	75	45	15	12	5	3	0	0

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)	



	233	190	171	146	111	74	34	28	12	7	0	0
	232	194	160	129	91	61	29	23	9	9	0	0

Peters S, et al. Ann Oncol 2022;33(suppl):Abstr 930MO

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.)**

	Pembrolizumab		Placebo	
AEs, %	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

	Pembrolizumab		Placebo	
irAEs, %	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

Peters S, et al. Ann Oncol 2022;33(suppl):Abstr 930MO

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

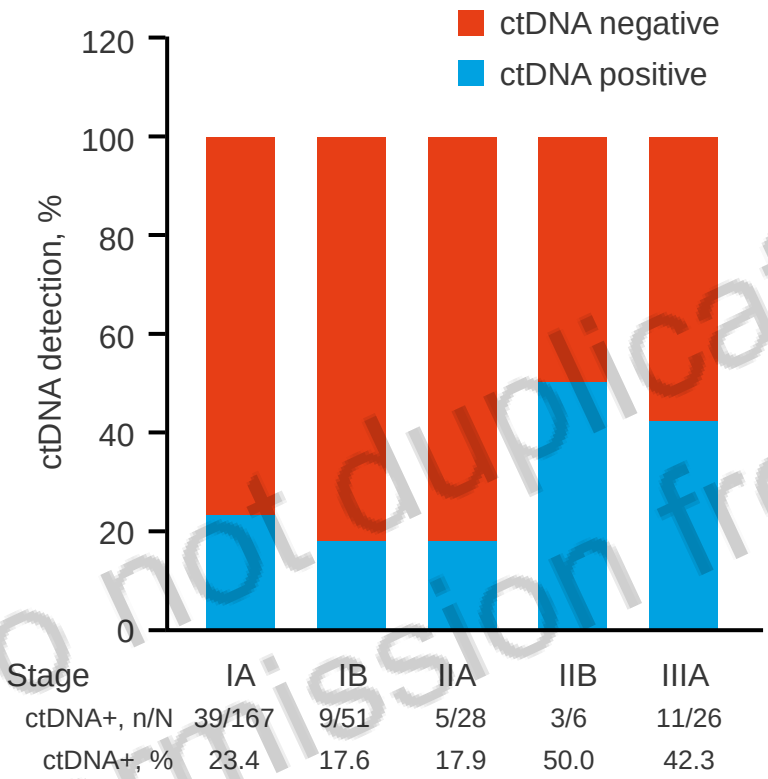
- **Study objective**
  - To assess the role of longitudinal monitoring of ctDNA in patients with resected stage IA–IIIA EGFR-mutant NSCLC

- **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)

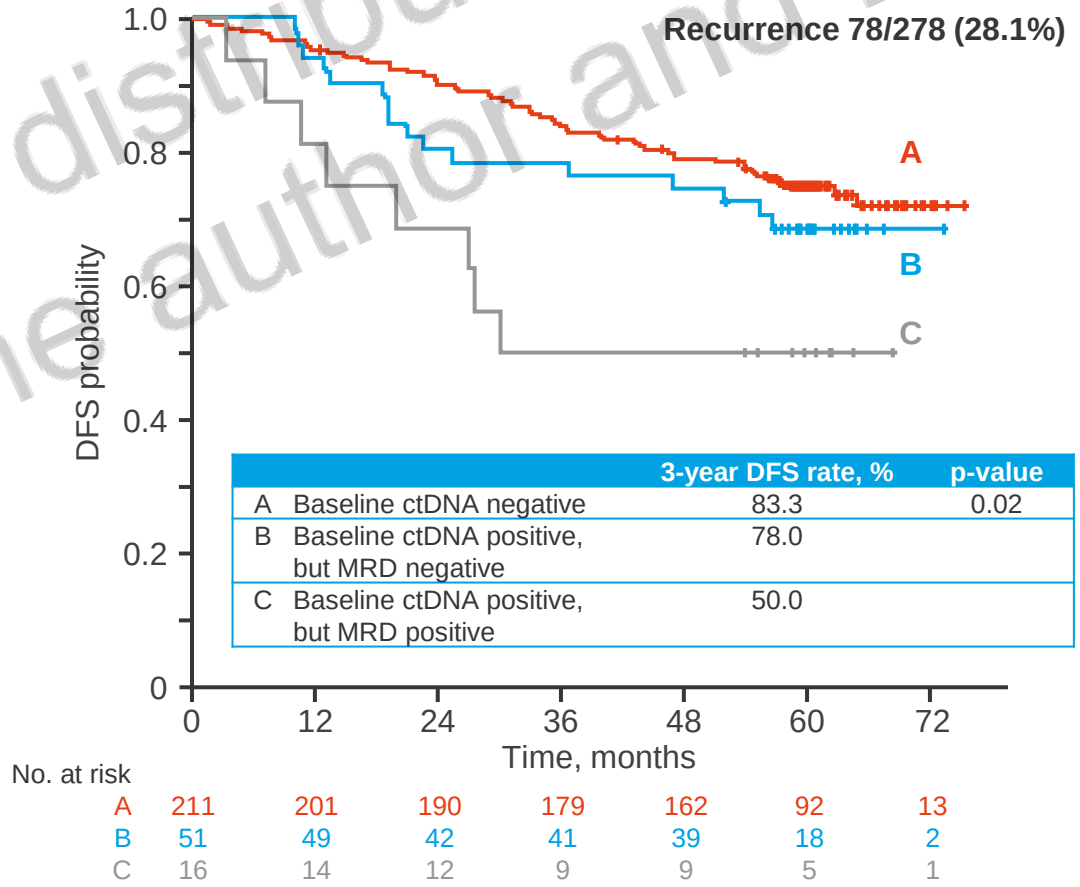
933MO: Longitudinal monitoring of circulating tumor DNA from plasma in patients with curative resected stage IA-IIIA EGFR mutant non-small cell lung cancer – Ahn M-J, et al

- **Key results**

Baseline ctDNA detection rate



DFS by ctDNA status



		3-year DFS rate, %	p-value
A	Baseline ctDNA negative	83.3	0.02
B	Baseline ctDNA positive, but MRD negative	78.0	
C	Baseline ctDNA positive, but MRD positive	50.0	

Ahn M-J, et al. Ann Oncol 2022;33(suppl):Abstr 933MO

Unresectable stage 3 NSCLC

Treatment Landscape in Unresectable Stage III

Current SOC

- Durvalumab

Potential treatment options

- SKYSCRAPER-03 (cCRT →atezo + tiragolumab)
- PACIFIC-8 (cCRT →durva + domvanalimab)
- PACIFIC-9 (cCRT →durva + oleclumab or monalizumab)
- PACIFIC-2 (durva + cCRT →durva)
- CheckMate 73L (nivo + cCRT →nivo ± ipi)
- KEYLYNK-012 (pembro + cCRT →pembro ± olaparib)
- AdvanTIG-301 (tisle + oci + cCRT →tisle ± oci)
- KEYVIBE-006 (pembro + vibo + cCRT →pembro + vibo)

Slide not intended to provide comprehensive list of trials.

ESMO IMMUNO-ONCOLOGY
Annual Congress

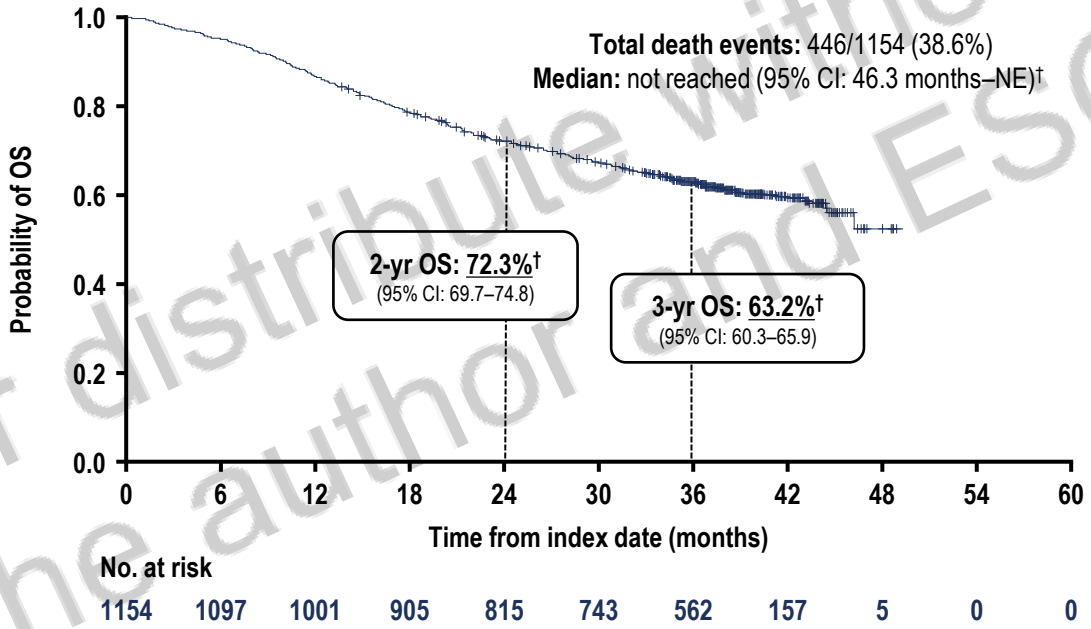
58O – REAL-WORLD OVERALL SURVIVAL WITH DURVALUMAB AFTER CHEMORADIOTHERAPY IN PATIENTS WITH UNRESECTABLE STAGE III NON-SMALL-CELL LUNG CANCER (NSCLC): INTERIM ANALYSIS FROM THE PACIFIC-R STUDY

Nicolas Girard,[1] Daniel C. Christoph,[2] Marina C. Garassino,[3] Fiona McDonald,[4] Françoise Mornex,[5] John K. Field,[6] Rainer Fietkau,[7] Pilar Garrido,[8] Vilde D. Haakensen,[9] Shankar Siva,[10] Michel van den Heuvel,[11] Jair Bar,[12, 13] Christos Chouaid,[14] Piet Vercauter,[15] Pratibha Chander,[16] Muriel Licour,[17] Shawn Anand,[16] Ana Rita Lima,[16] Andrea R. Filippi[18]

[1]Institut du Thorax Curie Montsouris, Institut Curie, Paris, France and UVSQ, Paris Saclay, Versailles, France; [2]Department of Medical Oncology, Evang. Kliniken Essen-Mitte, Evang. Huyssens-Stiftung Essen-Huttrop, Essen, Germany; [3]Department of Hematology/Oncology, The University of Chicago, Chicago, Illinois, USA; [4]Lung Unit, The Royal Marsden NHS Foundation Trust, London, UK; [5]Department of Radiation Oncology, Centre Hospitalier Universitaire de Lyon, Lyon, France; [6]Roy Castle Lung Cancer Research Programme, Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, UK; [7]Department of Radiation Oncology, Universitätsklinikum Erlangen, Erlangen, Germany; [8]Medical Oncology Department, Hospital Ramón y Cajal, Universidad de Alcalá, Madrid, Spain; [9]Department of Oncology and Institute for Cancer Research, Oslo University Hospital, Oslo, Norway; [10]Peter MacCallum Cancer Centre and The University of Melbourne, Melbourne, Victoria, Australia; [11]Department of Pulmonary Diseases, Radboud University Medical Center, Nijmegen, The Netherlands; [12]Institute of Oncology, Sheba Medical Centre, Ramat Gan, Israel; [13]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [14]Service de Pneumologie, Centre Hospitalier Intercommunal de Créteil, Créteil, France; [15]Department of Pneumology, OLV Hospital Aalst, Aalst, Belgium; [16]AstraZeneca, Gaithersburg, Maryland, USA; [17]AstraZeneca, Courbevoie, France; [18]Radiation Oncology Department, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Policlinico San Matteo and University of Pavia, Pavia, Italy

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



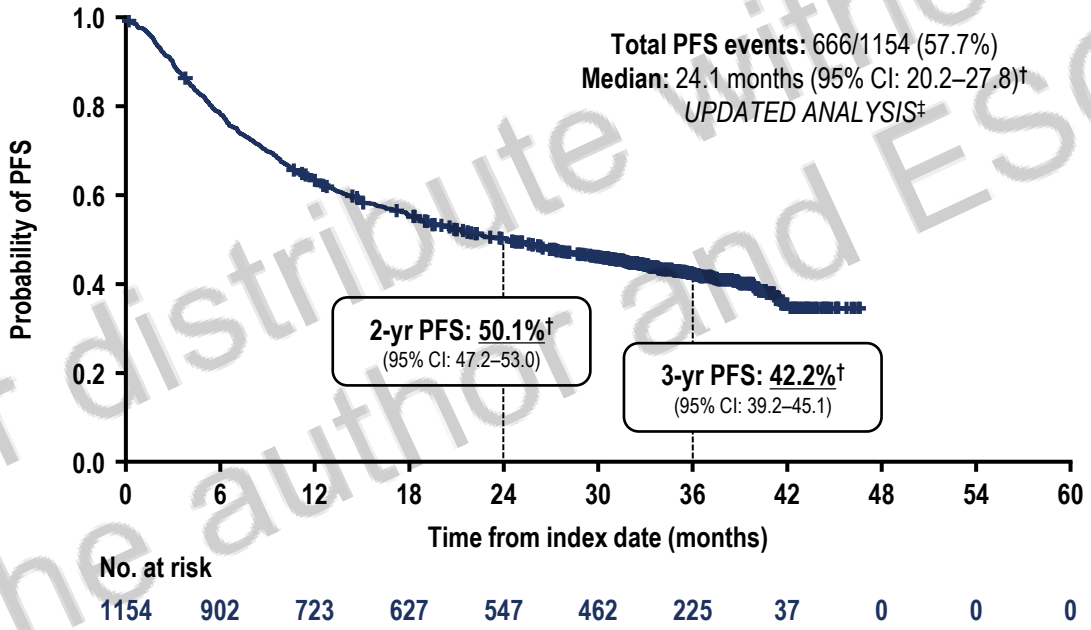
Outcome	Time from end of RT to durva. initiation ≤42 days (N=398)	>42 days (N=732)
2-yr OS rate, % (95% CI)†	***74.8*** (70.2–78.8)	***71.2*** (67.8–74.4)
3-yr OS rate, % (95% CI)†	***66.0*** (61.1–70.5)	***61.8*** (58.1–65.2)

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



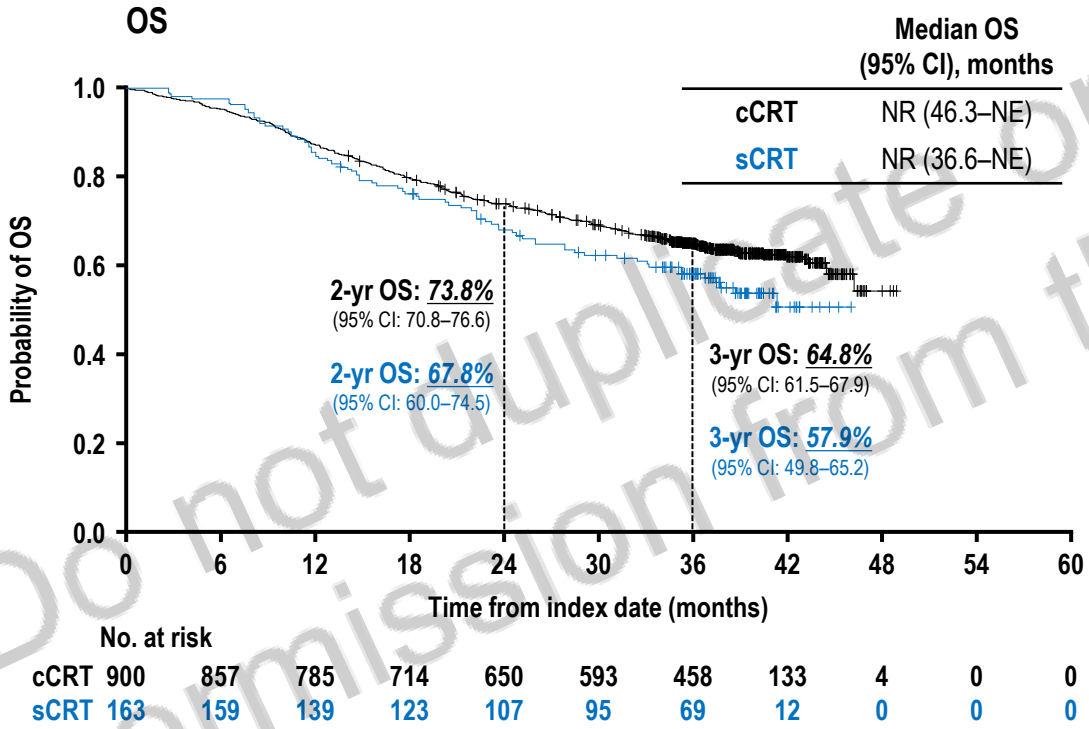
Outcome	Time from end of RT to durva. initiation	
	≤42 days (N=398)	>42 days (N=732)
2-yr PFS rate, % (95% CI)†	***52.3*** (47.3–57.1)	***48.9*** (45.3–52.5)
3-yr PFS rate, % (95% CI)†	***45.5*** (40.4–50.4)	***40.3*** (36.5–44.0)

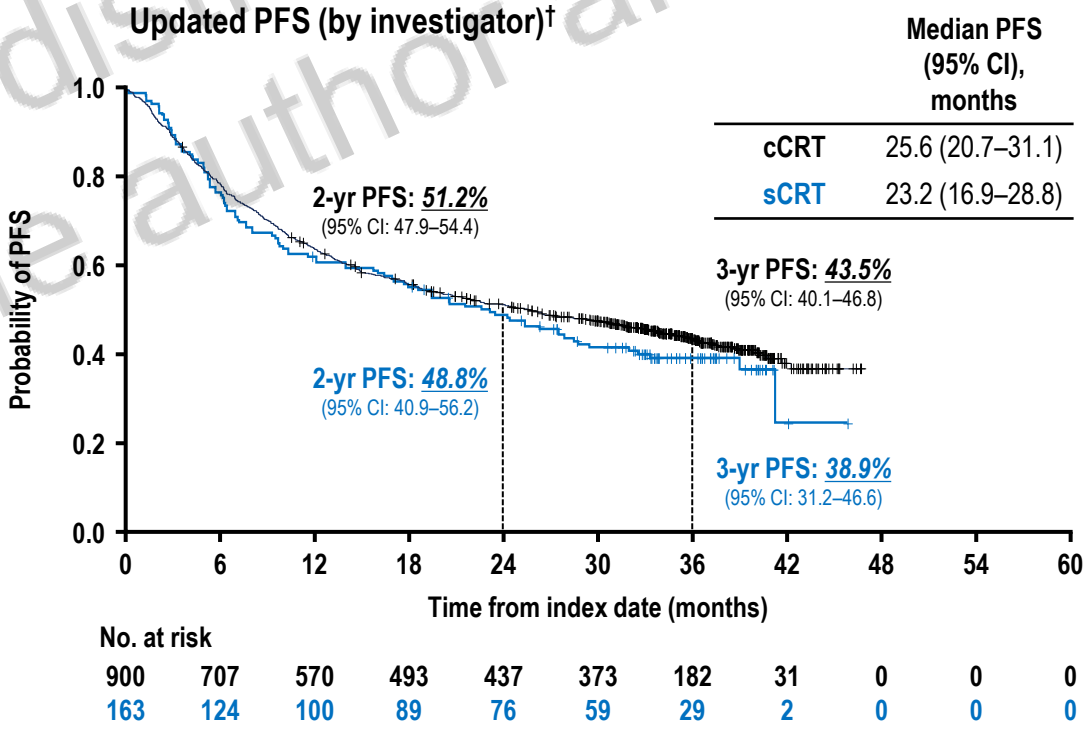
CI, confidence interval; PFS, progression-free survival; RT, radiotherapy; yr, year

*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] [1]Girard N et al,. Ann Oncol 2021;32(suppl_5):S939–48; [2]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*

- 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



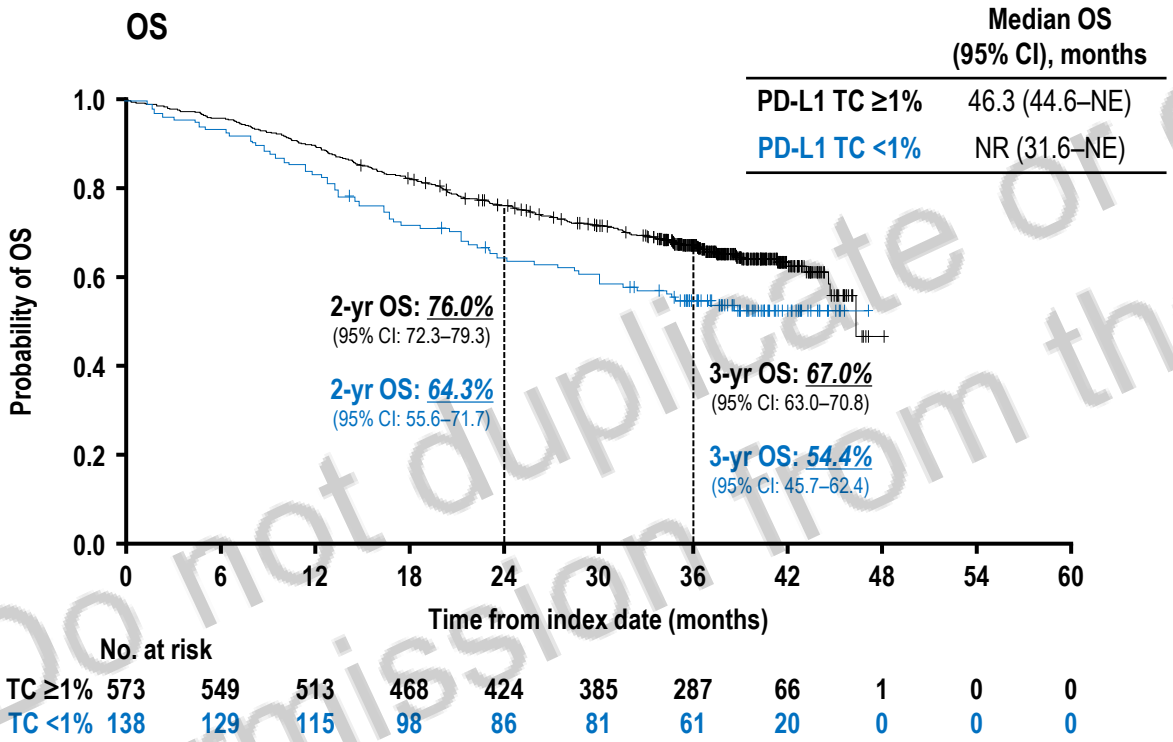


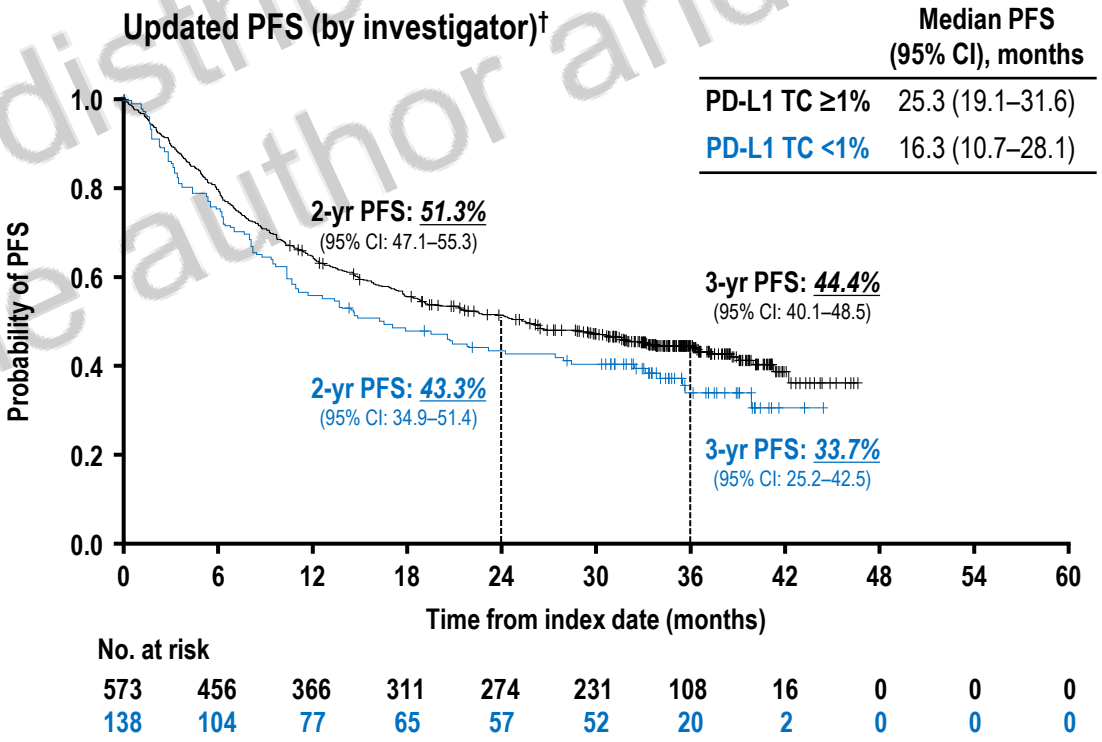
CI, confidence interval; c/sCRT, concurrent/sequential chemoradiotherapy; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; yr, year

*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] [1]Girard N et al,. Ann Oncol 2021;32(suppl_5): S939–48; [2]Girard 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*

- 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] [1]Girard N et al,. Ann Oncol 2021;32(suppl_5): S939–48; [2]Girard N et al,. J Thorac Oncol; doi: https://doi.org/10.1016/j.jtho.2022.10.003 (ePub ahead of print)

8508

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

M. Reck[1]; K.H. Lee[2]; N. Frost[3]; V. Breder[4]; D.M. Kowalski[5]; E. Levchenko[6]; N. Reguart[7]; A. Martinez-Marti[8]; B. Houghton[9]; J.-B. Paoli[10]; S. Safina[11]; T. Komiya[12]; A. Sanford[13]; H. Liu[14]; A.J. Song[14]; S.M. Keller[14]; S.K. Jabbour[15]

[1]LungenClinic, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; [2]Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, South Korea; [3]Department of Infectious Diseases and Respiratory Medicine, Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; [4]N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [5]The Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [6]N.N. Petrov National Medical Research Center of Oncology, St. Petersburg, Russia; [7]Thoracic Oncology Unit, Department of Medical Oncology, IDIBAPS, Hospital Clínic, Barcelona, Spain; [8]Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Barcelona, Spain; [9]Mid North Coast Cancer Institute, Port Macquarie Base Hospital, Port Macquarie, NSW, Australia; [10]Radiotherapie, Clinique Clairval, Marseille, France; [11]Medical Oncology, Republican Dispensary of Tatarstan MoH, Kazan, Russia; [12]Division of Hematology Oncology, University at Buffalo, Buffalo, NY, USA; [13]Sanford Health, Sioux Falls, SD, USA; [14]Merck & Co., Inc., Rahway, NJ, USA; [15]Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, Rutgers Robert Wood Johnson Medical School, Rutgers University, New Brunswick, NJ, USA

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, global, phase 2 KEYNOTE-799 study[2]

Table 1. Outcomes from the primary analysis[a] of KEYNOTE-799[2]

Primary endpoint	Cohort A (squamous and nonsquamous) n = 112	Cohort B (nonsquamous only) n = 102
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)

[a]Database cutoff date: October 28, 2020.

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

Objectives

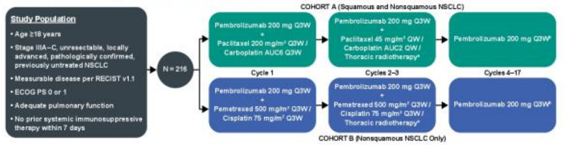
Primary
- ORR per RECIST version 1.1 by blinded independent central review (BICR)
- Proportion of patients with grade ≥3 pneumonitis

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

Methods

Study design, patients, and treatment

Figure 1. KEYNOTE-799 (NCT03631784) study design



AUC, area under the concentration-time curve; ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; QW, once weekly.
[a]60 Gy in 30 daily 2-Gy fractions 5 days per week.
[b]Treatment continued until cycle 17 was completed or until documented disease progression, unacceptable AEs, intercurrent illness that prevented further administration of treatment, or study withdrawal. Pembrolizumab therapy was discontinued permanently in patients who developed grade ≥3 or recurrent grade 2 pneumonitis.

Assessments
- Tumor imaging was performed at baseline, every 9 weeks until week 54, every 12 weeks until week 150, and every 24 weeks thereafter
- Adverse events (AEs), including pneumonitis for assessment of the primary endpoint, were monitored from the time of treatment allocation through 30 days after the end of treatment (90 days for serious AEs) and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0
- PD-L1 expression was assessed centrally using PD-L1 IHC 22C3 pharmDx (Agilent Technologies, Carpinteria, CA, USA)

Statistical analysis
- Efficacy and safety were analyzed in all enrolled patients who received ≥1 dose of study treatment
- The point estimates and 95% CIs for ORR and the percentage of patients with grade ≥3 pneumonitis were estimated using the Clopper-Pearson method
- PFS, OS, and duration of response (DOR) were estimated using the Kaplan-Meier method
- The database cutoff date for this analysis was October 18, 2021

Results

Patients
- Of 216 patients enrolled, 112 in cohort A and 102 in cohort B received study treatment
- Median (range) time from first dose to database cutoff was 30.2 months (25.3–35.5 months) in cohort A and 25.4 months (14.5–35.2 months) in cohort B

Table 2. Demographics and baseline characteristics

	Cohort A[a] (n = 112)	Cohort B[b] (n = 102)
Age, median (range), y	66.0 (46–90)	64.0 (35–81)
Men	76 (67.9)	62 (60.8)
ECOG PS 1	61 (54.5)	45 (44.1)
Former/current smoker	106 (94.6)	97 (95.1)
Squamous histology	75 (67.0)	N/A
Nonsquamous histology	37 (33.0)	102 (100)
PD-L1 status		
TPS <1%	21 (18.8)	28 (27.5)
TPS ≥1%	66 (58.9)	40 (39.2)
Unknown	25 (22.3)	34 (33.3)

N/A, not applicable; TPS, tumor proportion score.
Data are n (%) unless specified otherwise.
[a]Squamous and nonsquamous histology.
[b]Nonsquamous histology only.

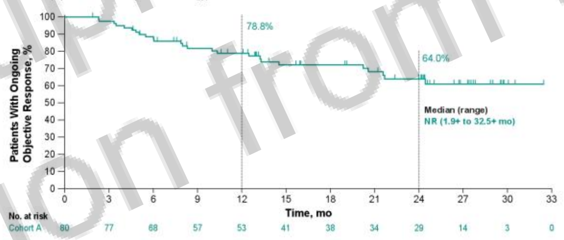
Table 3: ORR (95% CI) in the as-treated population and key patient subgroups

Subgroup	Cohort A[a] (n = 112)	Cohort B[b] (n = 102)
Overall population	71.4 (62.1–79.6)[c]	75.5 (66.0–83.5)[d]
Age		
<65 years	75.5 (61.1–86.7)	74.1 (60.3–85.0)
≥65 years	68.3 (55.3–79.4)	77.1 (62.7–88.0)
Sex		
Female	75.0 (57.8–87.9)	75.0 (58.8–87.3)
Male	69.7 (58.1–79.8)	75.8 (63.3–85.8)
Race		
White	74.2 (63.8–82.9)	79.7 (68.8–88.2)
All others	56.3 (29.9–80.2)	71.4 (41.9–91.6)
Region		
USA	56.5 (34.5–76.8)	81.8 (48.2–97.7)
All others	75.3 (65.0–83.8)	74.7 (64.5–83.3)
Cancer stage		
IIIA	73.2 (57.1–85.8)	76.9 (60.7–88.9)
IIIB	73.0 (60.3–83.4)	73.8 (58.0–86.1)
IIIC	50.0 (15.7–84.3)	76.2 (52.8–91.8)
Histology		
Squamous	72.0 (60.4–81.8)	N/A
Nonsquamous	70.3 (53.0–84.1)	75.5 (66.0–83.5)
ECOG PS		
0	74.5 (60.4–85.7)	73.7 (60.3–84.5)
1	68.9 (55.7–80.1)	77.8 (62.9–88.8)
PD-L1 TPS		
<1%	66.7 (43.0–85.4)	78.6 (59.0–91.7)
≥1%	77.3 (65.3–86.7)	72.5 (56.1–85.4)

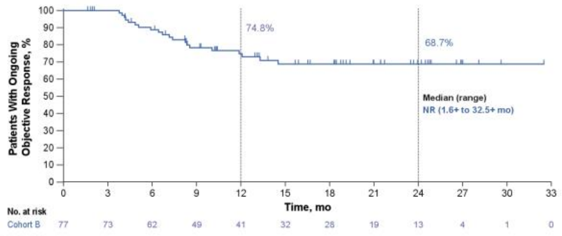
[a]Squamous and nonsquamous histology.
[b]Nonsquamous histology only.
[c]Includes 4 CR and 76 PR.
[d]Includes 5 CR and 72 PR.

Figure 2. Duration of response

A. Cohort A (squamous and nonsquamous histology)



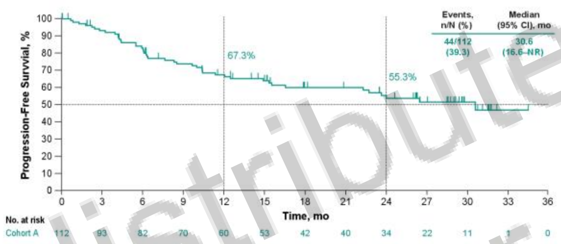
B. Cohort B (nonsquamous histology only)



NR, not reached.

Figure 3. Progression-free survival

A. Cohort A (squamous and nonsquamous histology)



B. Cohort B (nonsquamous histology only)

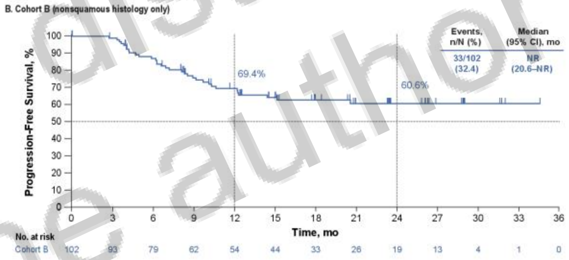
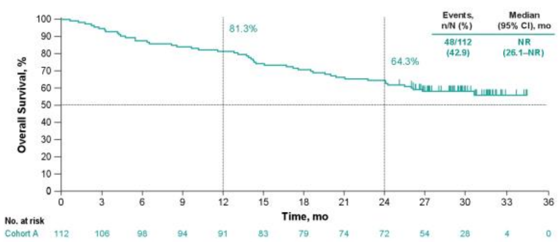
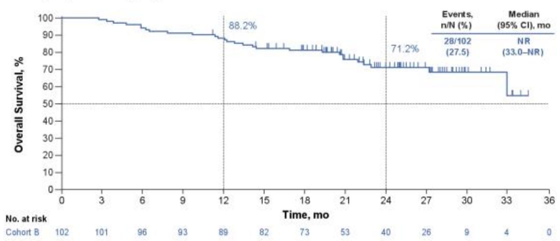


Figure 4. Overall survival

A. Cohort A (squamous and nonsquamous histology)



B. Cohort B (nonsquamous histology only)



Safety

Table 4. Adverse event summary

AE, n (%)	Cohort A[a] (n = 112)	Cohort B[b] (n = 102)
Grade ≥3 pneumonitis[c]	9 (8.0)	7 (6.9)
Treatment-related AEs	105 (93.8)	99 (97.1)
Grade 3–5	72 (64.3)	52 (51.0)
Occurring in >10% of patients in either cohort		
Neutropenia	18 (16.1)	10 (9.8)
Anemia	12 (10.7)	4 (3.9)
Led to death	4 (3.6)[d]	1 (1.0)[e]
Led to discontinuation of any treatment component	38 (33.9)	21 (20.6)
Immune-mediated AEs and infusion reactions[f]	58 (51.8)	46 (45.1)
Grade 3–5	18 (16.1)	9 (8.8)
Occurring in >5% of patients in either cohort		
Pneumonitis	7 (6.3)	6 (5.9)
Led to death	4 (3.6)[d]	1 (1.0)[e]
Led to discontinuation of any treatment component	21 (18.8)	12 (11.8)

[a]Squamous and nonsquamous histology.
[b]Nonsquamous histology only.
[c]Coprimary endpoint; includes immune-mediated AE of "pneumonitis" and the Medical Dictionary for Regulatory Activities (MedDRA) preferred term of "radiation pneumonitis".
[d]4 patients died due to treatment-related pneumonitis.
[e]1 patient died due to treatment-related interstitial lung disease.
[f]Events were considered regardless of attribution to treatment by the investigator.

Conclusions

- After more than 2 years of follow-up, pembrolizumab plus cCRT followed by pembrolizumab continues to demonstrate robust and durable responses in patients with previously untreated, locally advanced, stage III NSCLC
  - Additional responses were observed since the last analysis
  - Antitumor activity was observed regardless of PD-L1 TPS and tumor histology
- Pembrolizumab plus cCRT followed by pembrolizumab also demonstrated promising survival outcomes
  - Median PFS was 30.6 mo in cohort A and NR in cohort B with 2-year PFS rates of 55%–61%
  - Median OS was NR in both cohorts with 2-year OS rates of 64%–71%
- Toxicity was manageable, and the safety profile was as anticipated for pembrolizumab plus cCRT followed by pembrolizumab, with no new safety signals observed
- Pembrolizumab plus cCRT followed by pembrolizumab represents a promising therapy for patients with previously untreated, locally advanced, stage III NSCLC
- Ongoing studies are further investigating pembrolizumab in unresectable, locally advanced, stage III NSCLC:
  - KEYLYNK-012: phase 3 study evaluating pembrolizumab plus cCRT followed by pembrolizumab with or without olaparib (PARP inhibitor) vs cCRT followed by durvalumab[3]
  - KEYVIBE-006: phase 3 study evaluating MK-7684A (co-formulation of vibostolimab plus pembrolizumab) plus cCRT followed by MK-7684A vs cCRT followed by durvalumab[4]

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Contact Information

Contact Martin Reck at m.reck@lungenclinic.de for questions or comments

Poster presented
https://bit.ly/3FtLCB

Poster slides
https://bit.ly/39GMZc5

Presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; Chicago, IL, USA and Online; June 3–7, 2022.

#8510: The Selective Personalized RadioImmunotherapy for Locally Advanced NSCLC Trial (SPRINT)

Nitin Ohri[1], Shruti Jolly[2], Benjamin T. Cooper[3], Rafi Kabarriti[1], William Raymond Bodner[1], Jonathan Klein[1], Shankar Viswanathan[1], Elaine Shum[3], Joshua K. Sabari[3], Haiying Cheng[1], Rasim A. Gucalp[1], Enrico Castellucci[1], Angel Qin[2], Shirish M. Gadgeel[4], Balazs Halmos[1]
[1]Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY; [2]University of Michigan, Ann Arbor, MI; [3]Perlmutter Cancer Center, New York University School of Medicine, New York, NY; [4]Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI

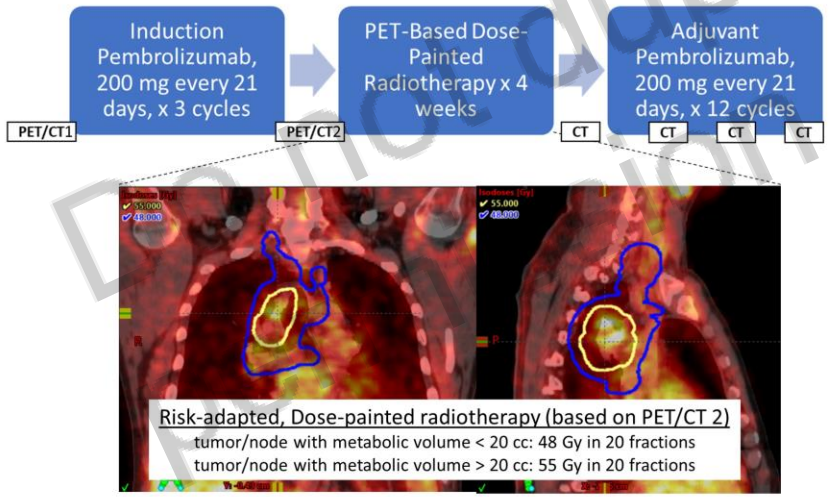
Background/Methods:

- 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) ≥ 50%.

Key eligibility criteria:

- Unresectable AJCC v8 Stage II NSCLC or Stage III NSCLC
- ECOG performance status 0-1
- PD-L1 TPS ≥ 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%)

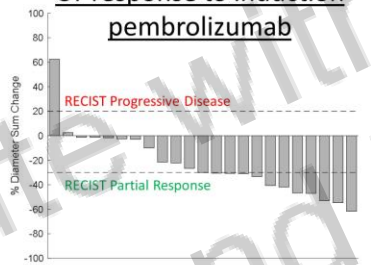
Patient characteristics (left) and adverse events (below). No grade 4-5 toxicities have occurred

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%)

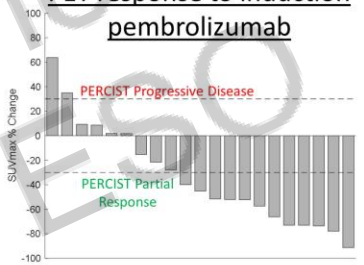
Conclusions:

- This study demonstrates excellent early clinical outcomes for locally advanced NSCLC patients with PD-L1 TPS ≥ 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.

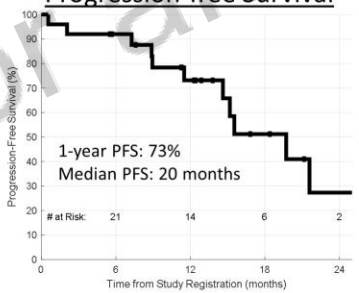
CT response to induction pembrolizumab



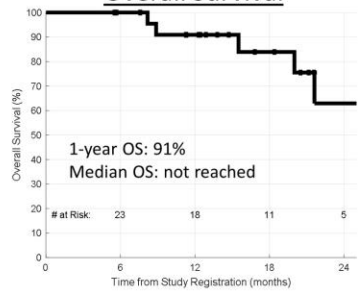
PET response to induction pembrolizumab

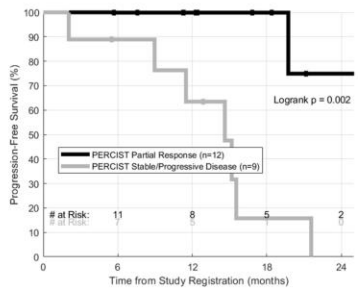


Progression-free Survival



Overall Survival





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

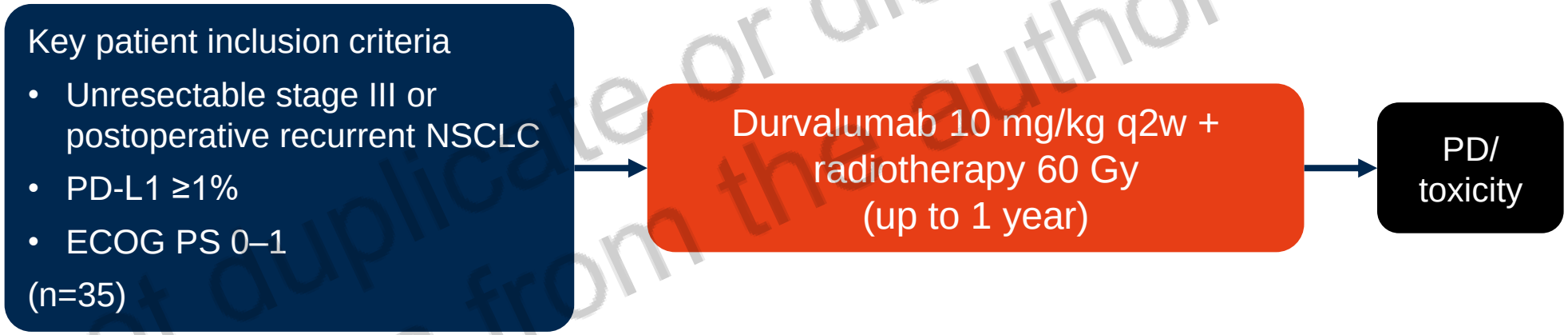
Future Directions:

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

This study was funded through the Merck Investigator Studies Program, Merck Sharp & Dohme Corp and Sanford Research

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



Primary endpoint

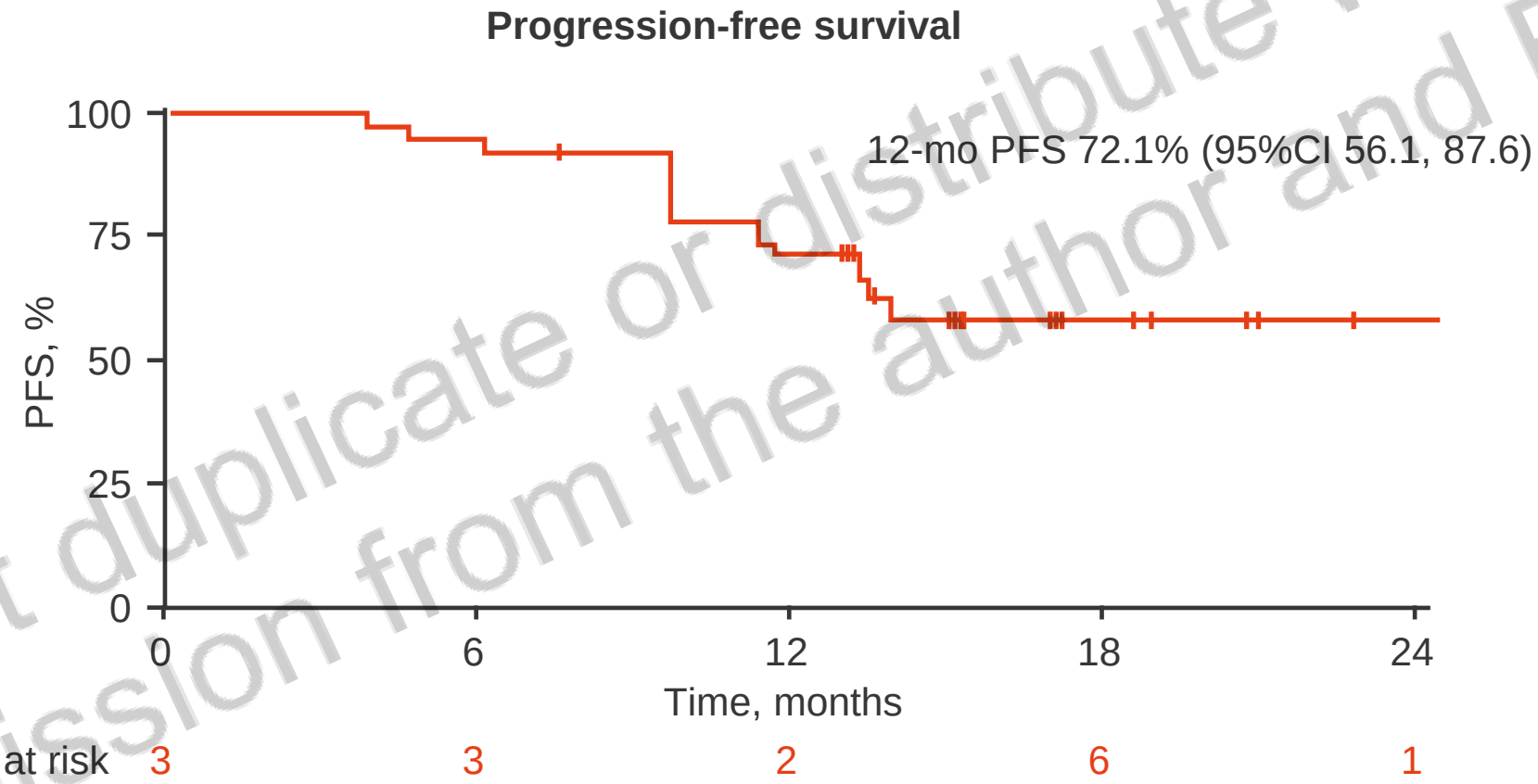
- 12-mo PFS rate

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]

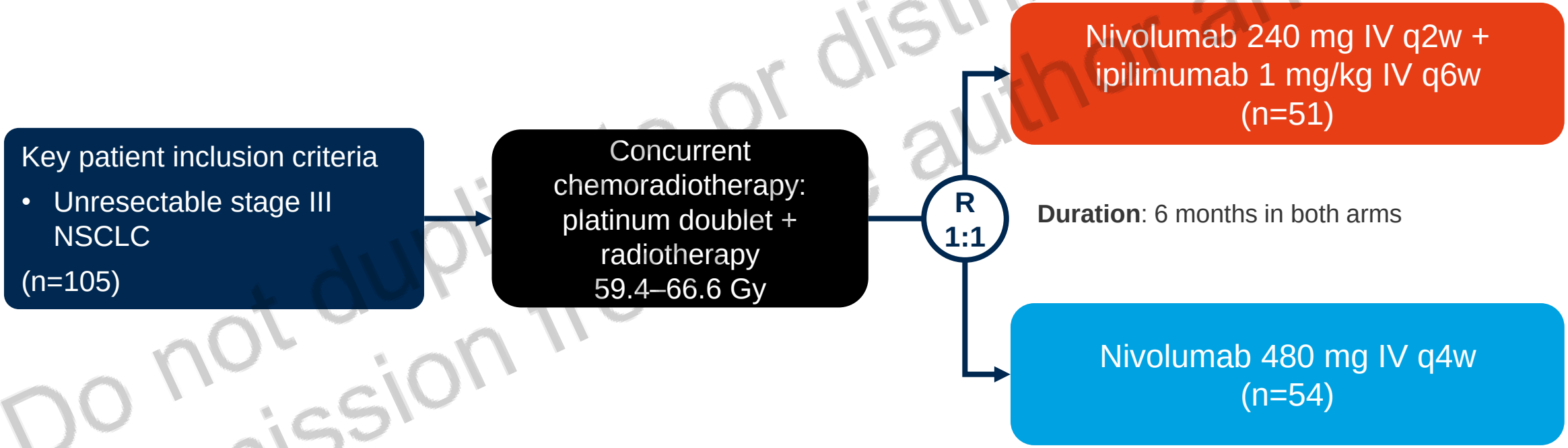
AE, n (%)	
Any grade	34 (100)
Grade 3–4	16 (47.1)
Grade 5	2 (5.9)
Led to discontinuation of durvalumab	6 (17.6)
Led to discontinuation of radiotherapy	0
TRAE	30 (88.2)
SAE	13 (38.2)
Severe immune-mediated AE	10 (29.4)

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



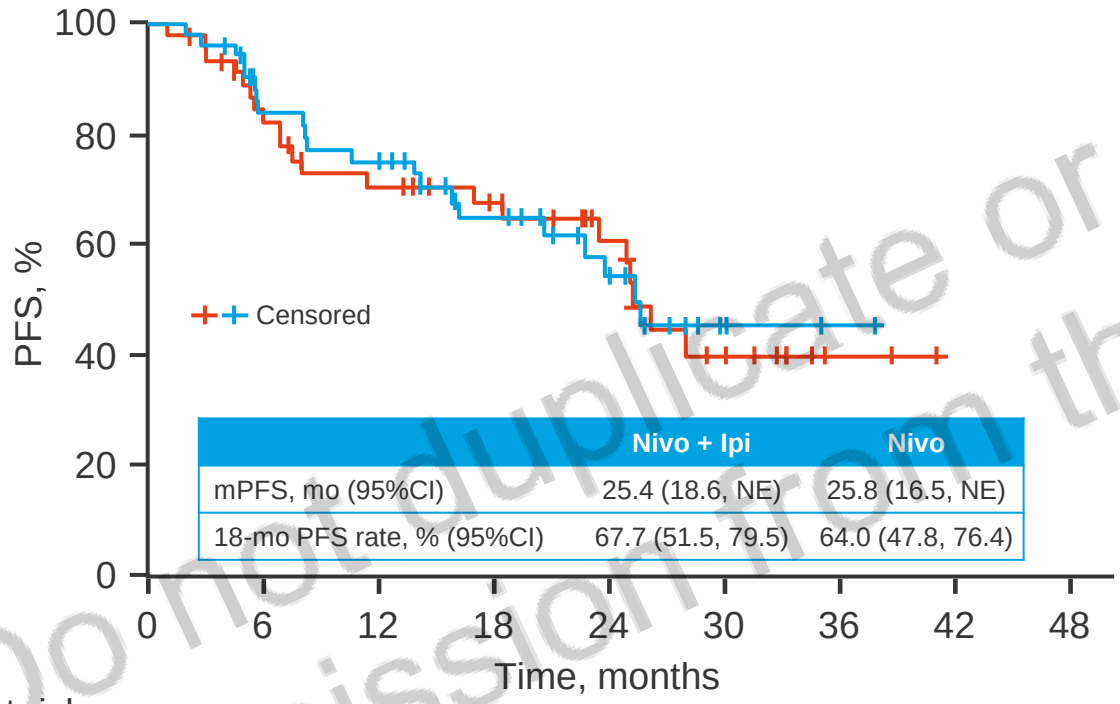
Endpoints

- 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

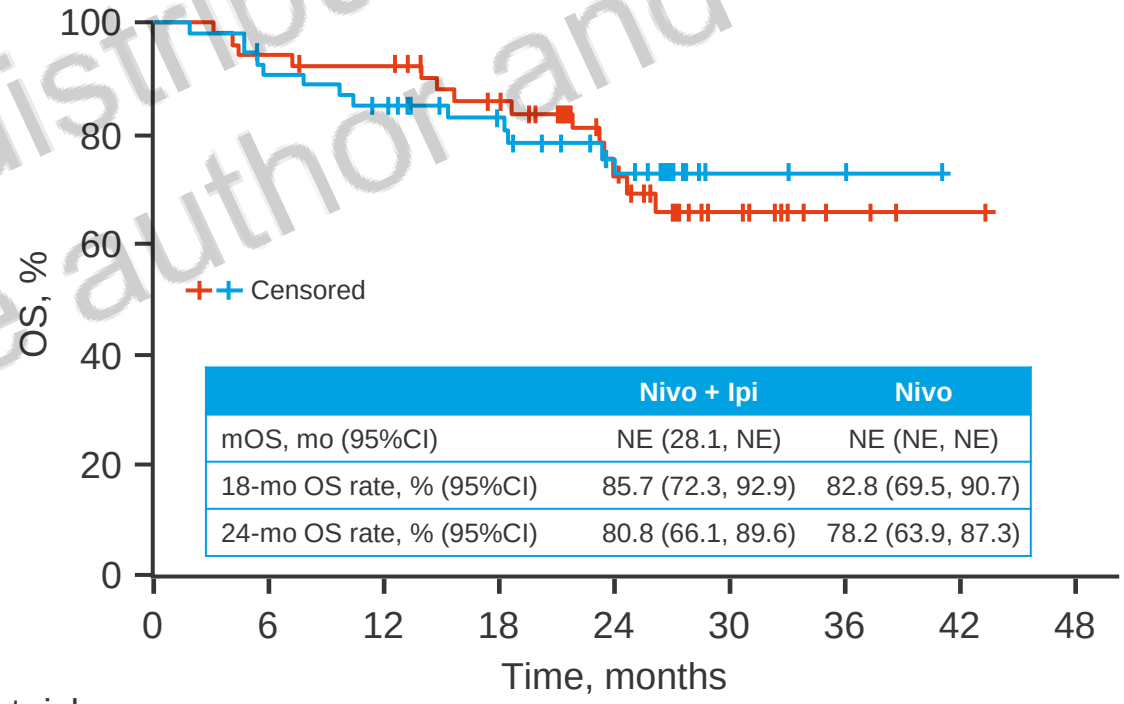


	Nivo + Ipi	Nivo
mPFS, mo (95%CI)	25.4 (18.6, NE)	25.8 (16.5, NE)
18-mo PFS rate, % (95%CI)	67.7 (51.5, 79.5)	64.0 (47.8, 76.4)

No. at risk

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

Overall survival



	Nivo + Ipi	Nivo
mOS, mo (95%CI)	NE (28.1, NE)	NE (NE, NE)
18-mo OS rate, % (95%CI)	85.7 (72.3, 92.9)	82.8 (69.5, 90.7)
24-mo OS rate, % (95%CI)	80.8 (66.1, 89.6)	78.2 (63.9, 87.3)

No. at risk

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

Durm GA, et al. J Thorac Oncol 2022;17(suppl):Abstr MA06.05.

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

*No grade 4 or 5

Durm GA, et al. J Thorac Oncol 2022;17(suppl):Abstr MA06.05.

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