XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Lung Cancer. Best of ASCO 2023

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Spain

23 de junio de 2023

Disclosure Information

- Personal fees/honoraria for consultancy/Advisory role and lectures from Roche/Genentech, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Merck Sharp and Dohme, Merck Serono, Eli Lilly, Gilead, Sanofi, Regeneron, Incyte, Pfizer, Takeda and Novartis
- Travel expenses from Roche, Bristol-Myers Squibb, Merck Sharp and Dohme, Sanofi, Regeneron and Novartis
- Study funding to the institution from BMS, MSD, ROCHE to support studies conduct.

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

2023 ASCO ANNUAL MEETING

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)

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Terufumi Kato[4], Margarita Majem[5], Christian Grohé[6], Jie Wang[7], Jonathan Goldman[8], Shun Lu[9], Wu-Chou Su[10], Filippo de Marinis[11], Frances A. Shepherd[12], Ki Hyeong Lee[13], Nhieu Thi Le[14], Arunee Dechaphunkul[15], Dariusz Kowalski[16], Lynne Poole[17], Marta Stachowiak[18], Yuri Rukazenkov[19], Yi-Long Wu[20]

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Maximum interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization 1:1 (N=682)

- **Osimertinib 80 mg, once daily**
- **Placebo, once daily**

Planned treatment duration:
3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

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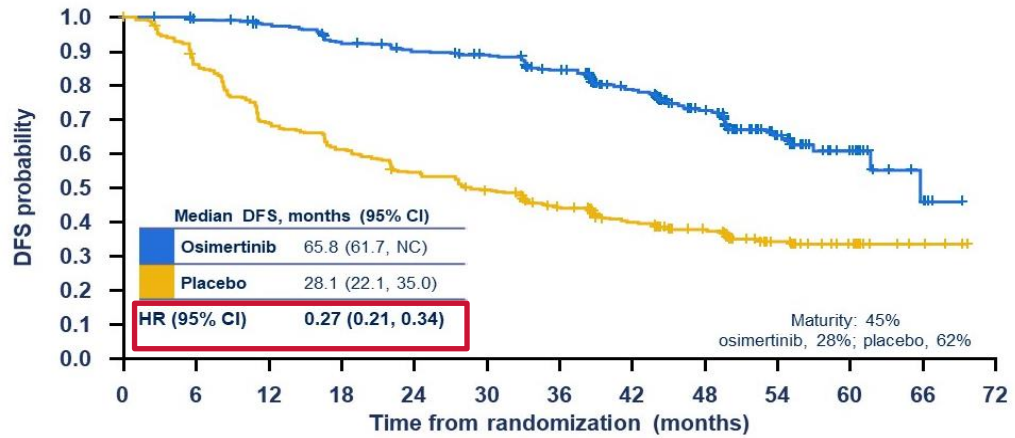
Significantly improved DFS

ADAURA updated DFS analysis[3,4] (stage IB–IIIA)†

JCO January 2023



No. at risk													
Osimertinib	339	316	307	289	278	270	249	201	139	73	33	5	0
Placebo	343	288	230	205	181	162	137	115	84	48	25	4	0

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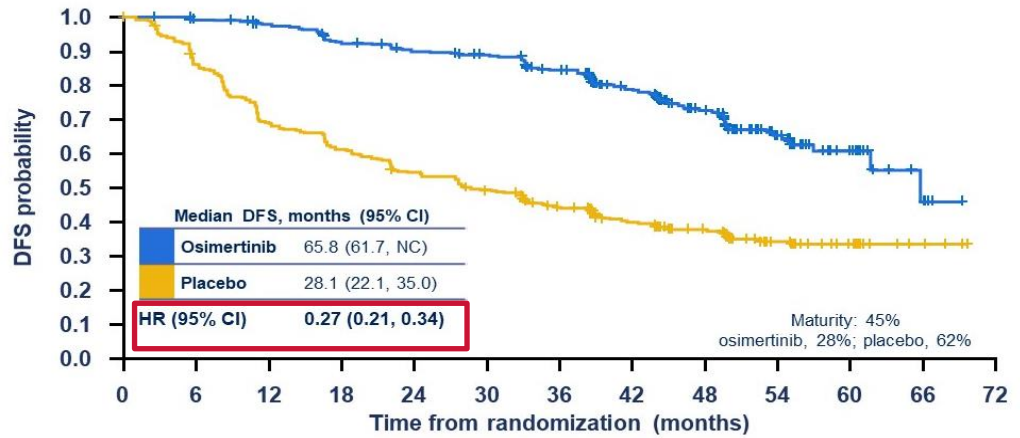

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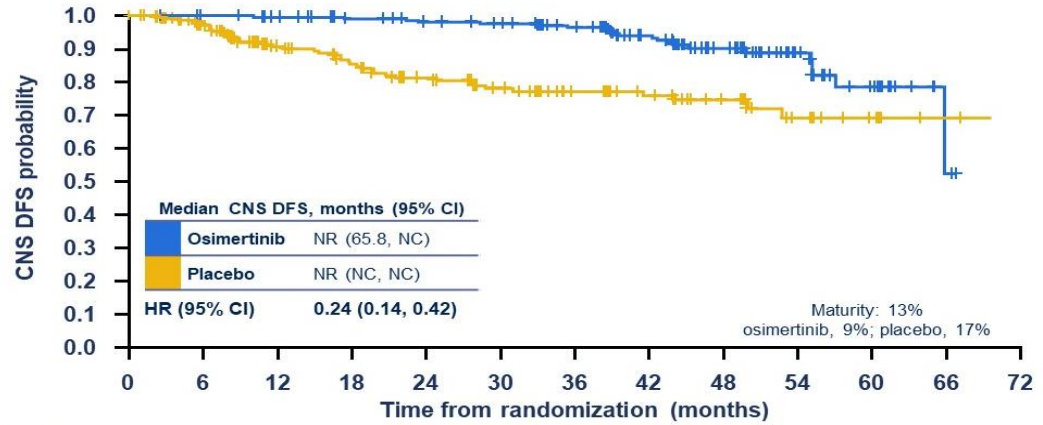

No. at risk

Osimertinib	233	222	216	202	196	192	175	138	90	45	20	2	0
Placebo	237	192	142	126	107	91	74	61	41	23	11	1	0

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18 Dec 2020 | 26 Apr 2021 | 1 Dec 2022

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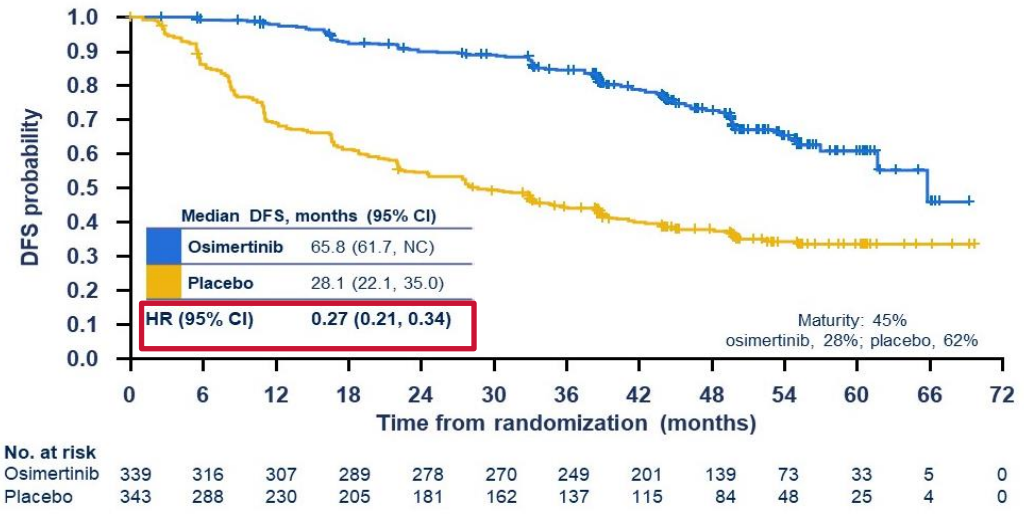

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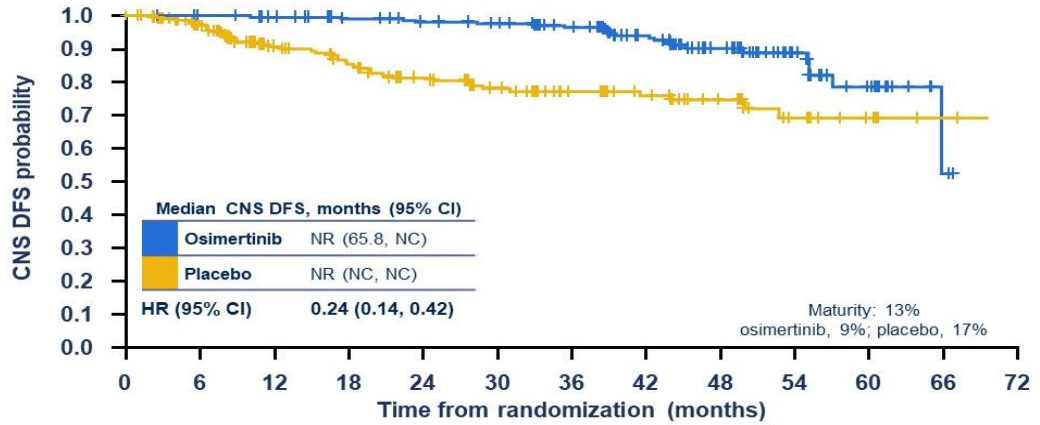

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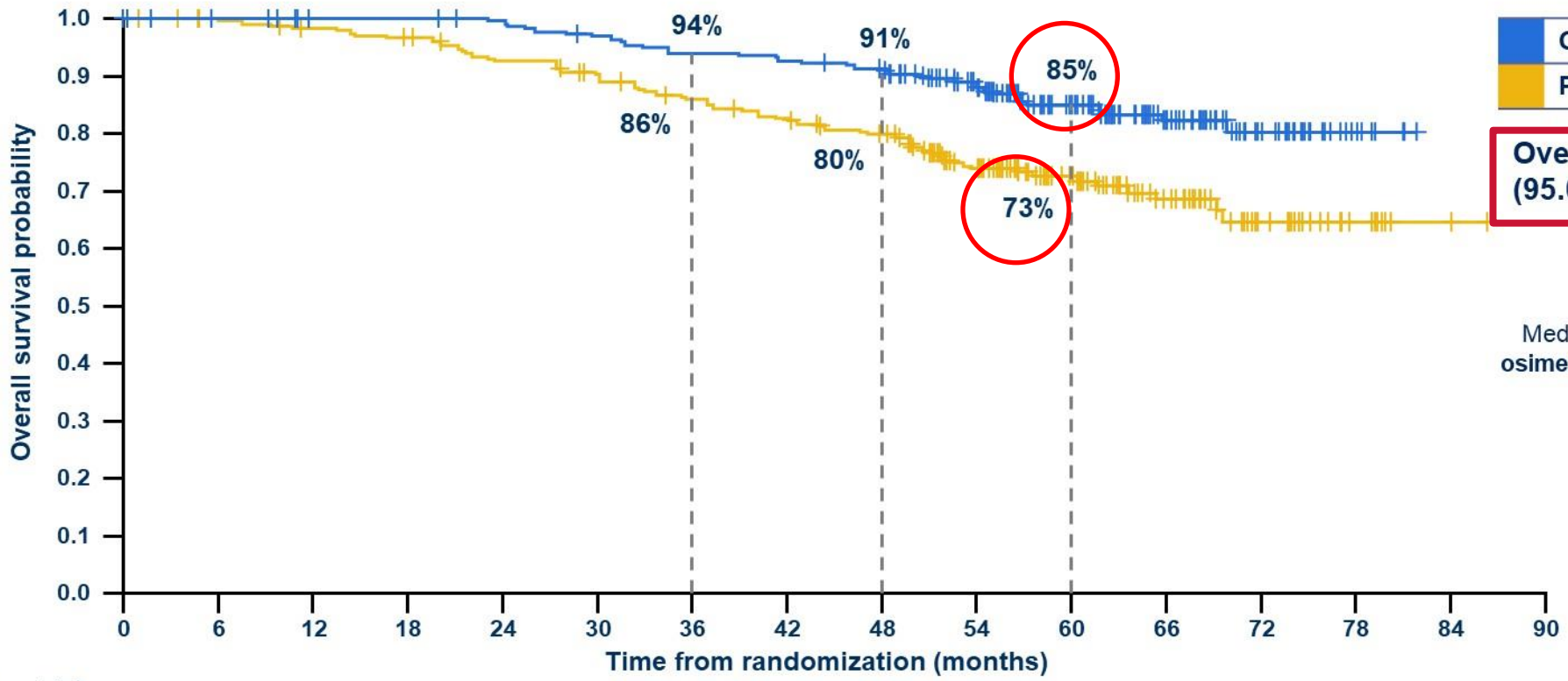
Overall survival: patients with stage II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the primary population of stage II–IIIA disease



5-year OS rate, % (95% CI)	
Osimertinib (n=233)	85 (79, 89)
Placebo (n=237)	73 (66, 78)

Overall OS HR (95.03% CI)	**0.49 (0.33, 0.73); p=0.0004**

Maturity: 21%
osimertinib 15%, placebo 27%

Median follow-up for OS* (censored patients):
osimertinib 61.7 months, placebo 60.4 months

No. at risk

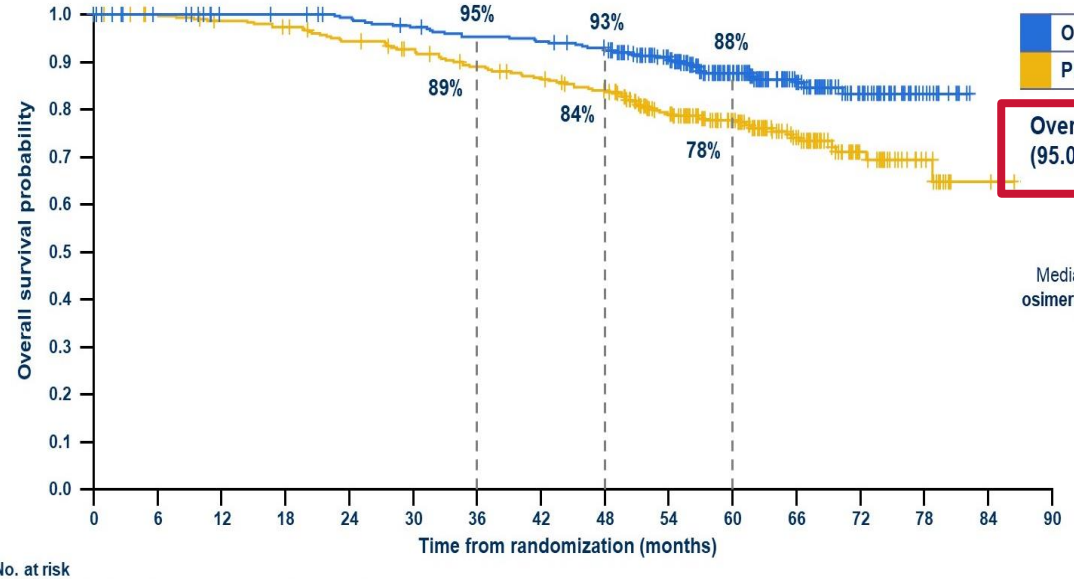
Osimertinib	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0	-
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0

Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 59.9 months, placebo 56.2 months.

CI, confidence interval; HR, hazard ratio; OS, overall survival

Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB–IIIA disease



No. at risk															
Osimertinib	339	332	325	324	319	311	304	301	294	252	176	108	50	15	0	-
Placebo	343	338	332	326	314	304	290	281	267	223	164	97	44	17	3	0

5-year OS rate, % (95% CI)	
Osimertinib (n=339)	88 (83, 91)
Placebo (n=343)	78 (73, 82)

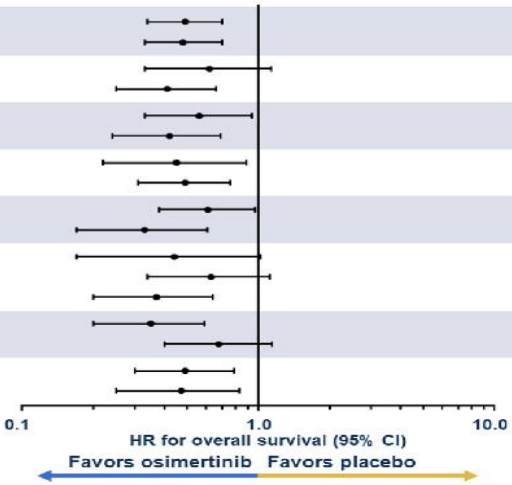
Overall OS HR (95.03% CI)	0.49 (0.34, 0.70); p<0.0001

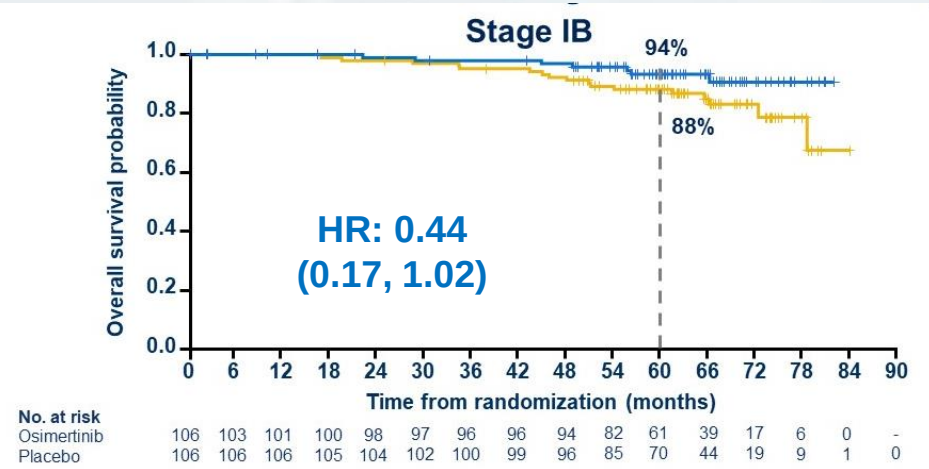
Maturity: 18%
osimertinib 12%, placebo 24%

Median follow-up for OS* (censored patients):
osimertinib 61.5 months, placebo 61.5 months

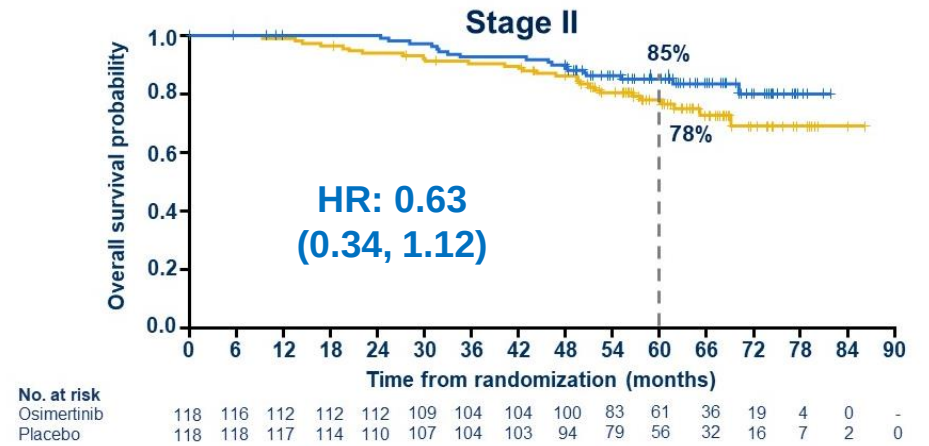
Data cut-off: January 27, 2023.

Subgroup		No. of events / patients	HR	95% CI
Overall (N=682)	Stratified log-rank	124 / 682	0.49	0.34, 0.70
	Unadjusted Cox PH	124 / 682	0.48	0.33, 0.70
Sex	Male	42 / 204	0.62	0.33, 1.13
	Female	82 / 478	0.41	0.25, 0.66
Age	<65 years	60 / 380	0.56	0.33, 0.94
	≥65 years	64 / 302	0.42	0.24, 0.69
Smoking history	Yes	34 / 194	0.45	0.22, 0.89
	No	90 / 488	0.49	0.31, 0.76
Race	Asian	73 / 434	0.61	0.38, 0.97
	Non-Asian	51 / 248	0.33	0.17, 0.61
Stage*	IB	24 / 212	0.44	0.17, 1.02
	II	46 / 236	0.63	0.34, 1.12
	IIIA	54 / 234	0.37	0.20, 0.64
EGFR mutation	Ex19del	65 / 378	0.35	0.20, 0.59
	L858R	59 / 304	0.68	0.40, 1.14
Adjuvant chemotherapy	Yes	74 / 410	0.49	0.30, 0.79
	No	50 / 272	0.47	0.25, 0.83

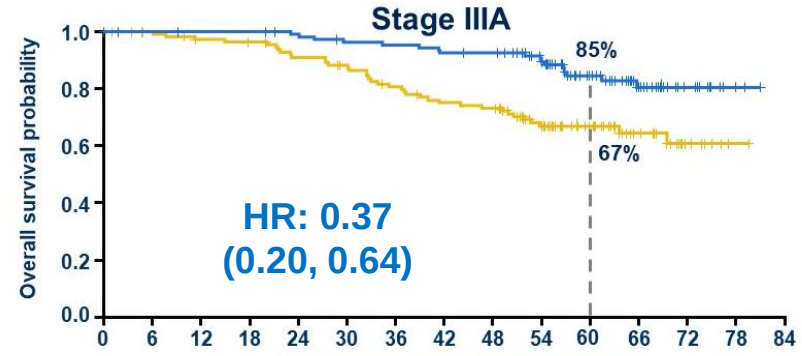




No. at risk															
Osimertinib	106	103	101	100	98	97	96	96	94	82	61	39	17	6	0	-
Placebo	106	106	106	105	104	102	100	99	96	85	70	44	19	9	1	0

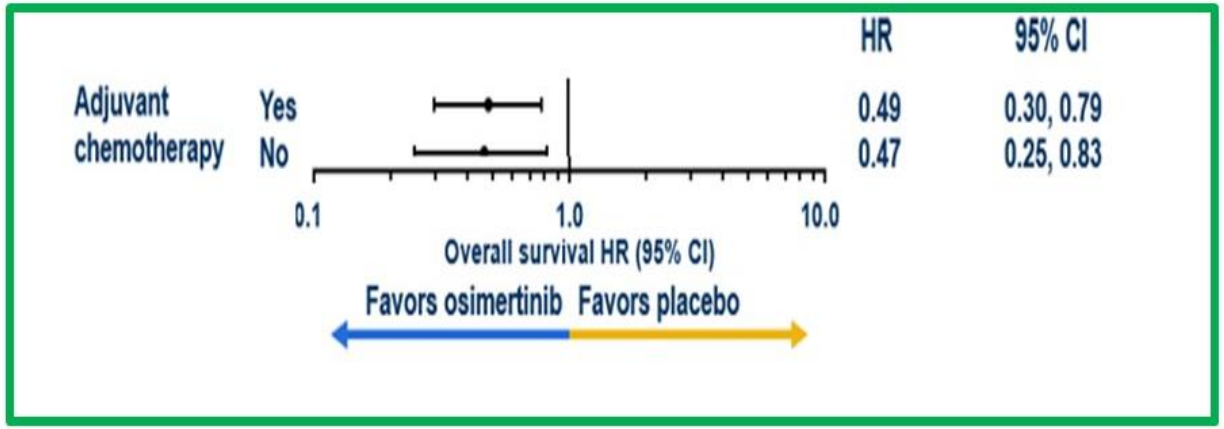


No. at risk															
Osimertinib	118	116	112	112	112	109	104	104	100	83	61	36	19	4	0	-
Placebo	118	118	117	114	110	107	104	103	94	79	56	32	16	7	2	0



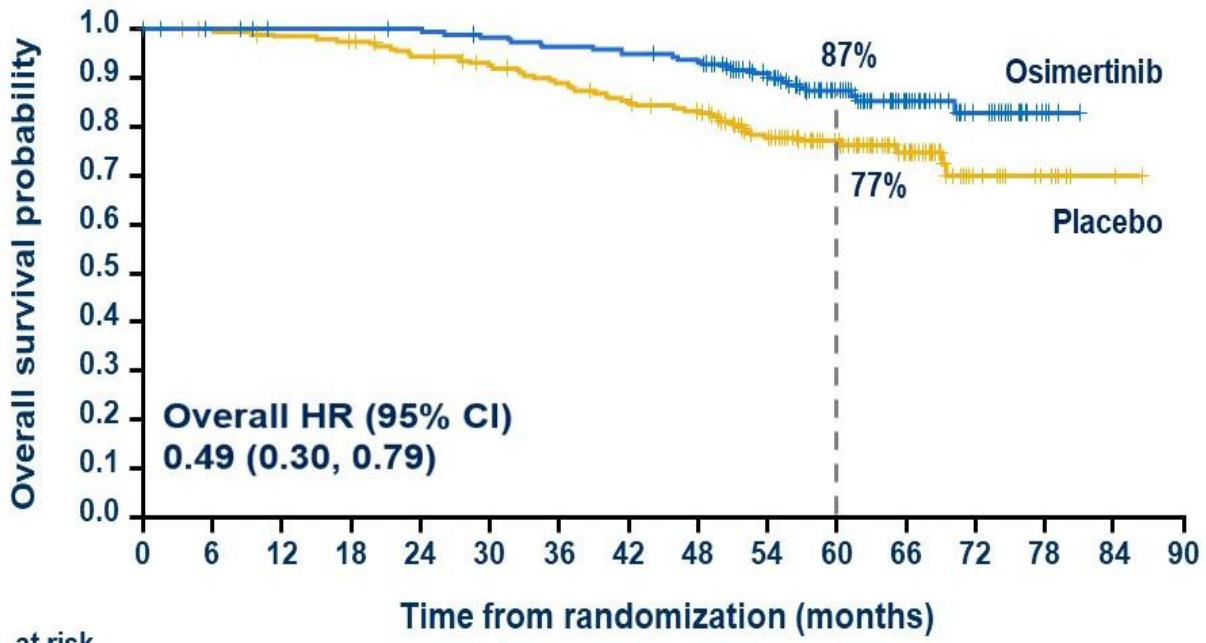
No. at risk															
Osimertinib	115	113	112	112	109	105	104	101	100	87	54	33	14	5	0
Placebo	119	114	109	107	100	95	86	79	77	59	38	21	9	1	0

Benefit regardless of adjuvant chemotherapy



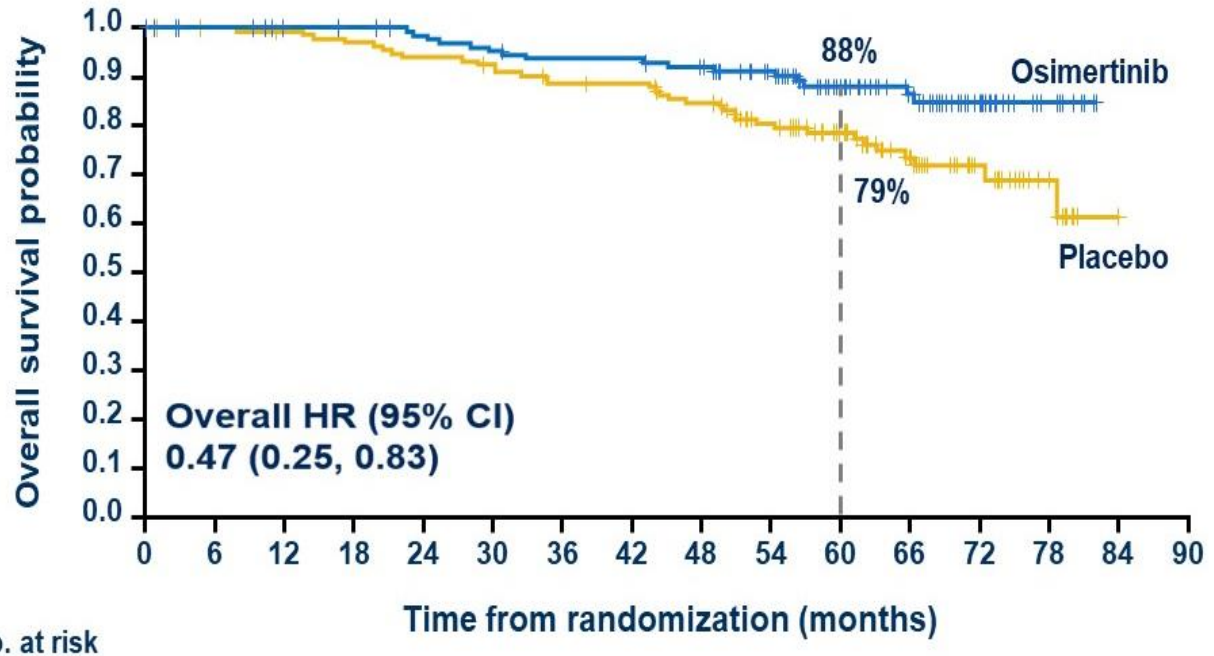
Subsequent treatment: More patients in placebo arm received EGFR TKIs (88% vs 76%)

With adjuvant chemotherapy



No. at risk

Without adjuvant chemotherapy



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Questions following ADAURA

How can therapy be optimized:

What is the optimal duration of osimertinib therapy?
Is chemotherapy necessary for all patients?
What about neoadjuvant osimertinib?

Who may benefit:

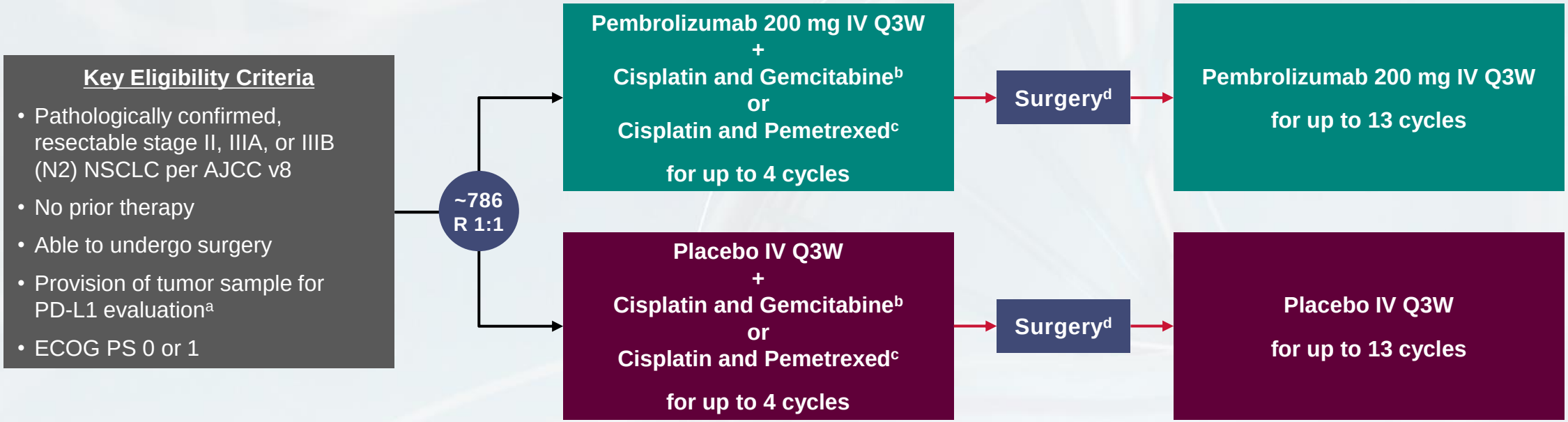
Will pts with Stage IA disease or locally advanced disease benefit?
What about *EGFR* mutations other than Exon19del/L858R?
Role of ctDNA?

What happens after relapse?

Do tumors retain sensitivity to EGFR TKIs?

What are mechanisms of resistance?

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



Stratification Factors

- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

Key secondary end points: mPR and pCR per blinded, independent pathology review, and safety

[a] Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b] Cisplatin 75 mg/m^2 IV Q3W + gemcitabine 1000 mg/m^2 IV on days 1 and 8 Q3W was permitted for squamous histology only. [c] Cisplatin 75 mg/m^2 IV Q3W + pemetrexed 500 mg/m^2 IV Q3W was permitted for nonsquamous histology only. [d] Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Dr. Heather Wakelee

Baseline Characteristics

	Pembro Arm (N = 397)	Placebo Arm (N = 400)
Histology		
Nonsquamous	226 (56.9%)	227 (56.8%)
Squamous	171 (43.1%)	173 (43.3%)
Smoking status		
Current	96 (24.2%)	103 (25.8%)
Former	247 (62.2%)	250 (62.5%)
Never	54 (13.6%)	47 (11.8%)
Disease stage at baseline (per AJCC v8)		
II	118 (29.7%)	121 (30.3%)
IIIA	217 (54.7%)	225 (56.3%)
IIIB	62 (15.6%)	54 (13.5%)
pN status		
N0	148 (37.3%)	142 (35.5%)
N1	81 (20.4%)	71 (17.8%)
N2	168 (42.3%)	187 (46.8%)
PD-L1 TPS		
≥50%	132 (33.2%)	134 (33.5%)
1-49%	127 (32.0%)	115 (28.8%)
<1%	138 (34.8%)	151 (37.8%)
Known *EGFR* mutation[a]	14 (3.5%)	19 (4.8%)
Known *ALK* translocation[a]	12 (3.0%)	9 (2.3%)

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

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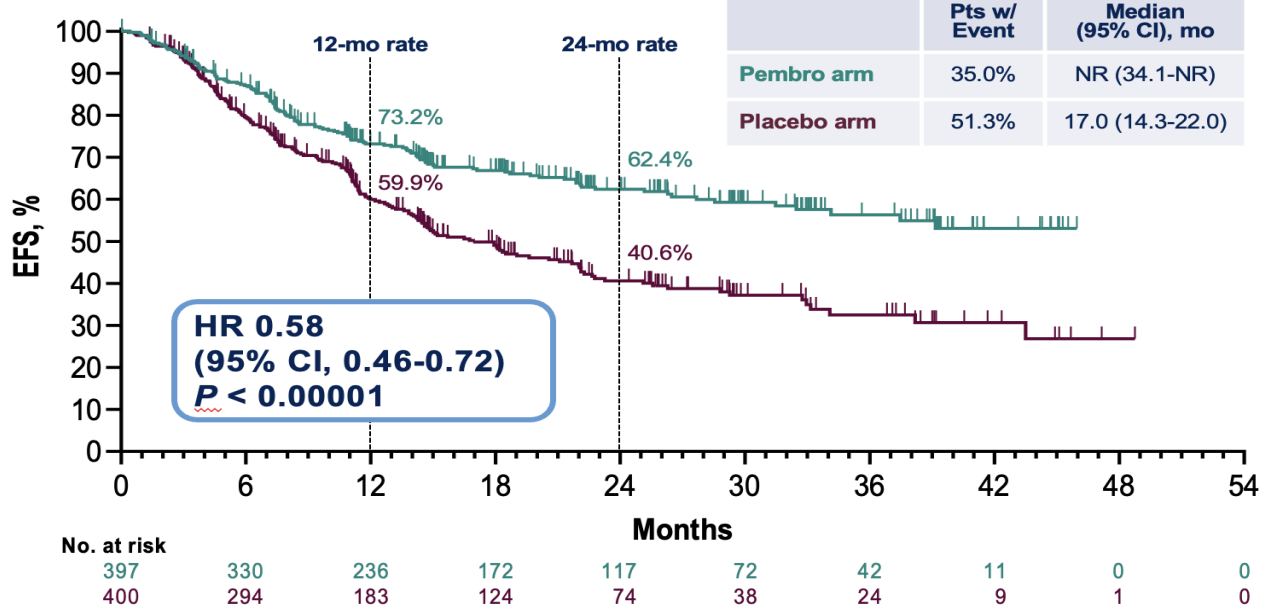
Event-Free Survival



	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

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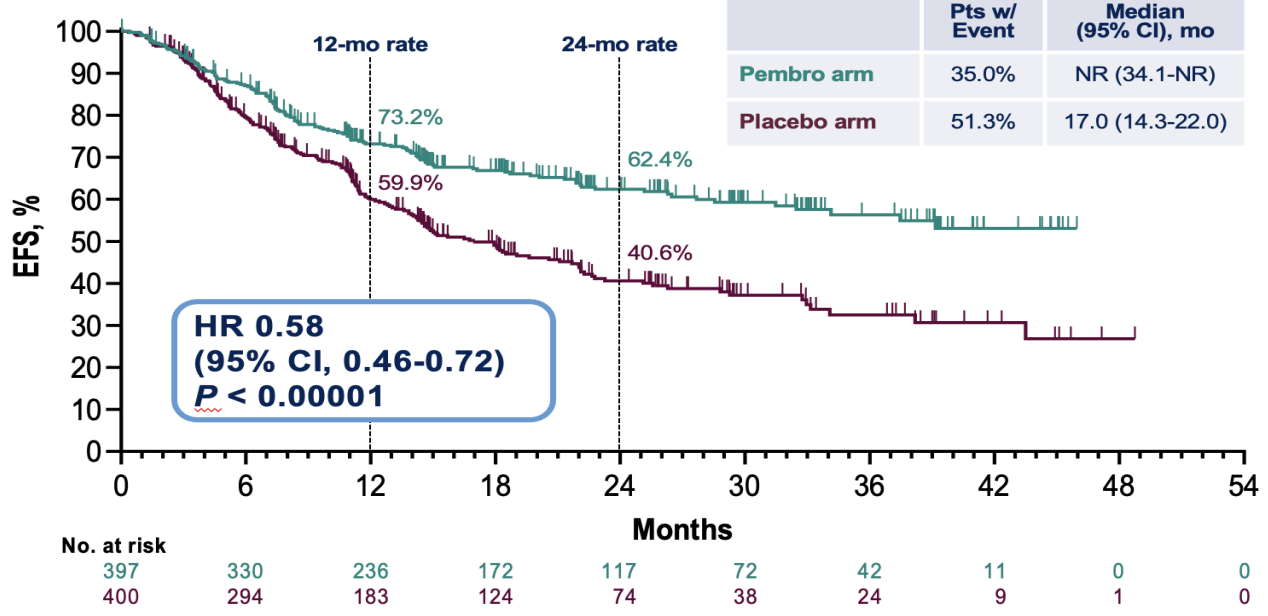
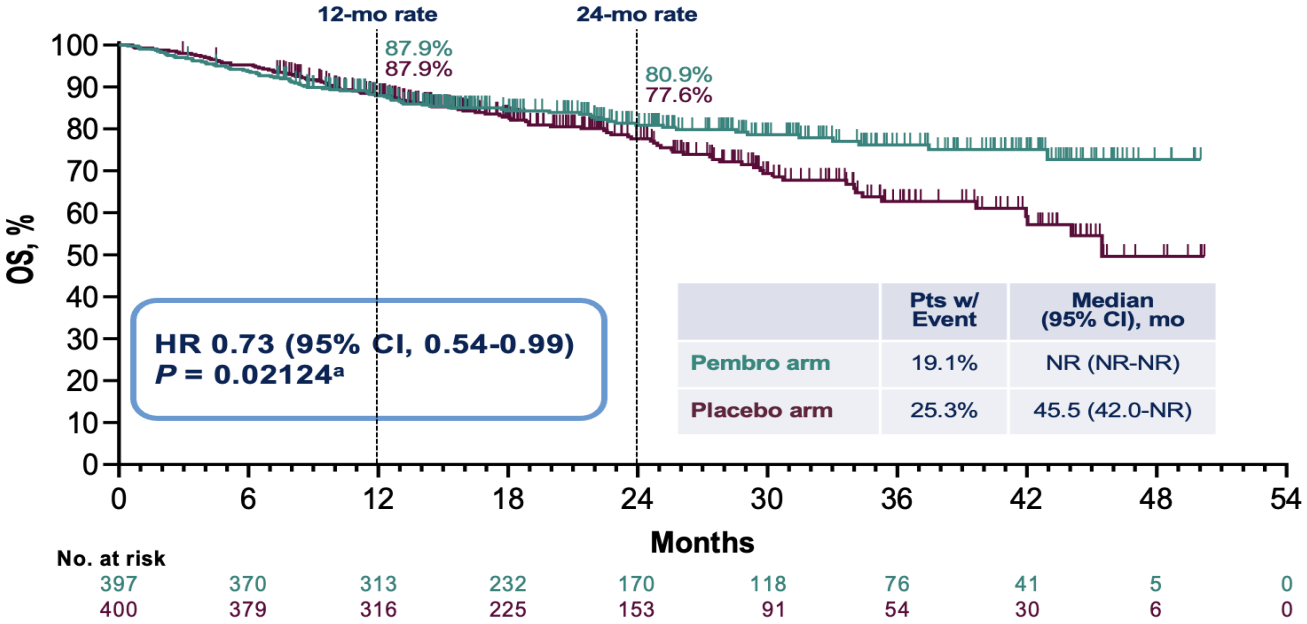
Event-Free Survival



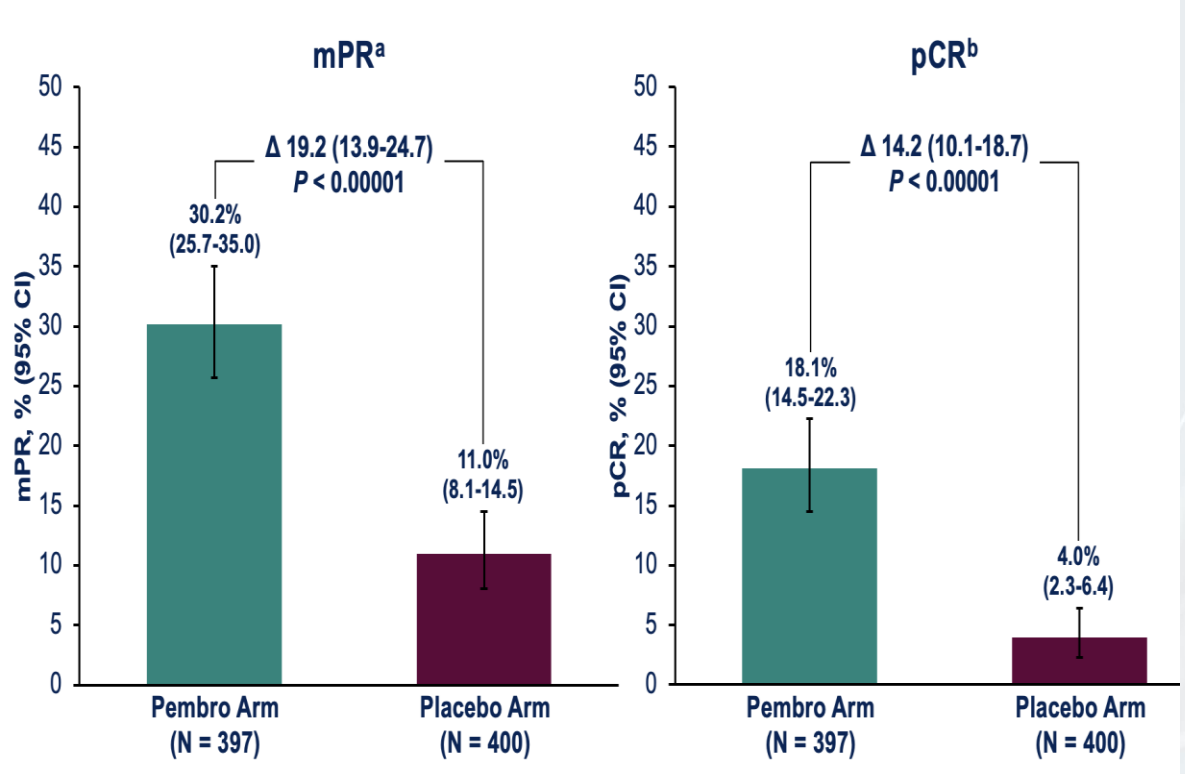
	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

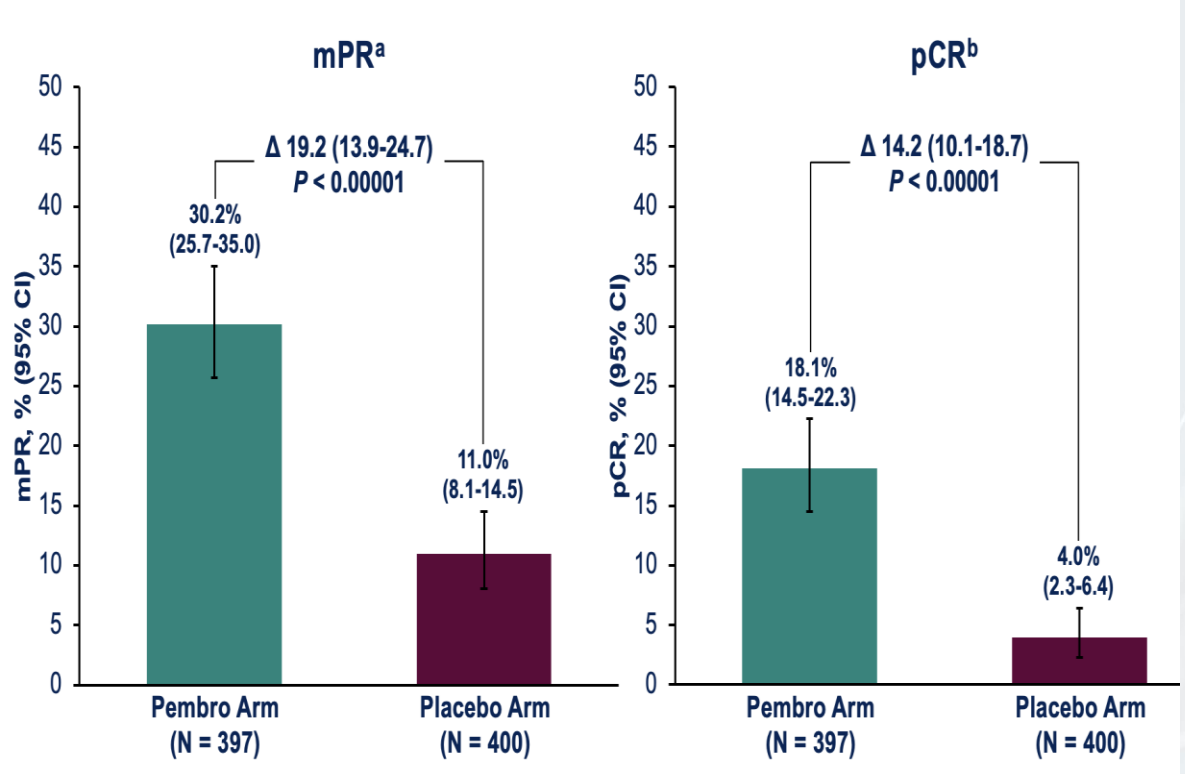
Overall Survival



	Pts w/ Event	Median (95% CI), mo
Pembro arm	19.1%	NR (NR-NR)
Placebo arm	25.3%	45.5 (42.0-NR)

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


mPR[a]
mPR, % (95% CI)
50
45
40
35
30
25
20
15
10
5
0
Δ 19.2 (13.9-24.7)
P < 0.00001
30.2%
(25.7-35.0)
11.0%
(8.1-14.5)
Pembro Arm
(N = 397)
Placebo Arm
(N = 400)
pCR[b]
pCR, % (95% CI)
Δ 14.2 (10.1-18.7)
P < 0.00001
18.1%
(14.5-22.3)
4.0%
(2.3-6.4)
Pembro Arm
(N = 397)
Placebo Arm
(N = 400)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P < 0.00001
30.2%
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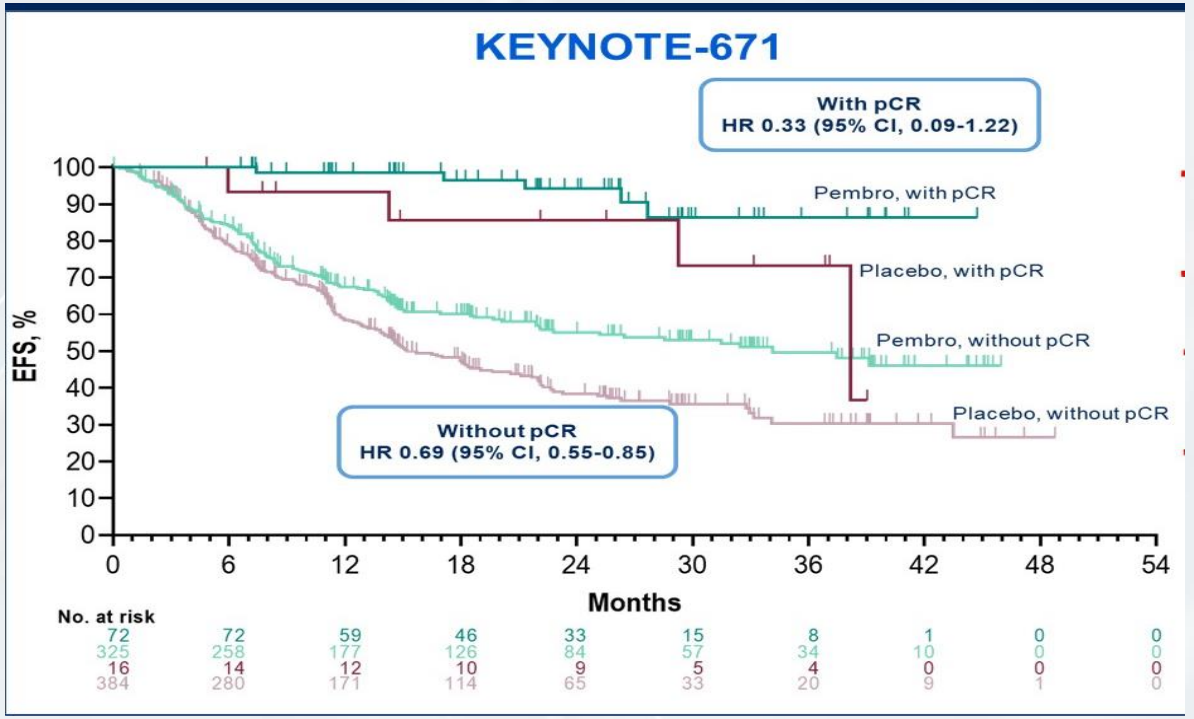
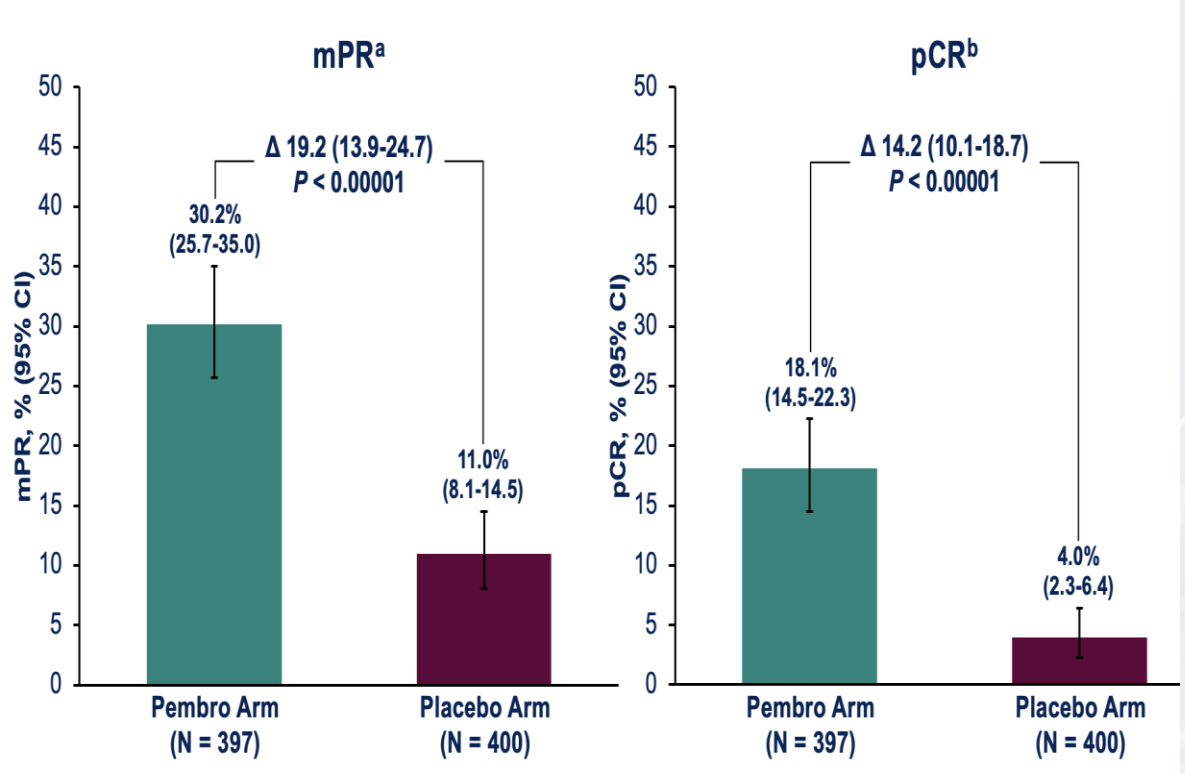
(2.3-6.4)
Pembro Arm
(N = 397)
Placebo Arm
(N = 400)


KEYNOTE-671
With pCR
HR 0.33 (95% CI, 0.09-1.22)
Pembro, with pCR
Placebo, with pCR
Pembro, without pCR
Placebo, without pCR
Without pCR
HR 0.69 (95% CI, 0.55-0.85)
EFS, %
Months
No. at risk
72 72 59 46 33 15 8 1 0 0
325 258 177 126 84 57 34 10 0 0
16 14 12 10 9 5 4 0 0 0
384 280 171 114 65 33 20 9 1 0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Δ 19.2 (13.9-24.7)
P < 0.00001
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Pembro Arm
(N = 397)
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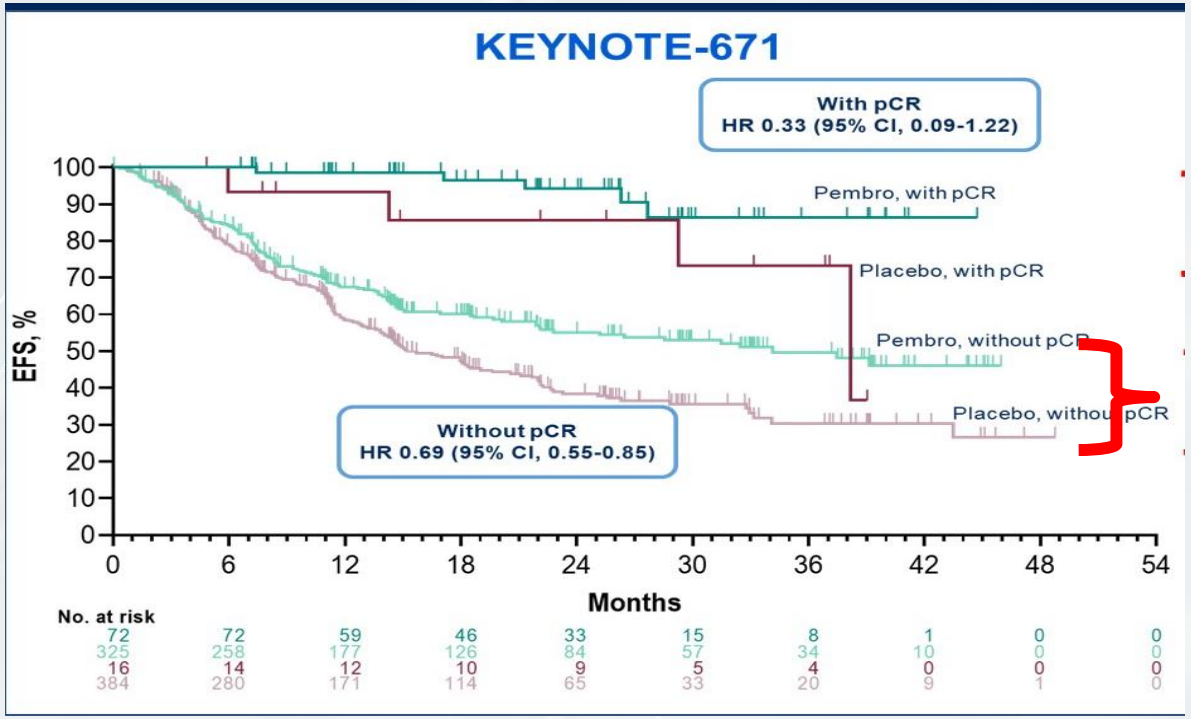
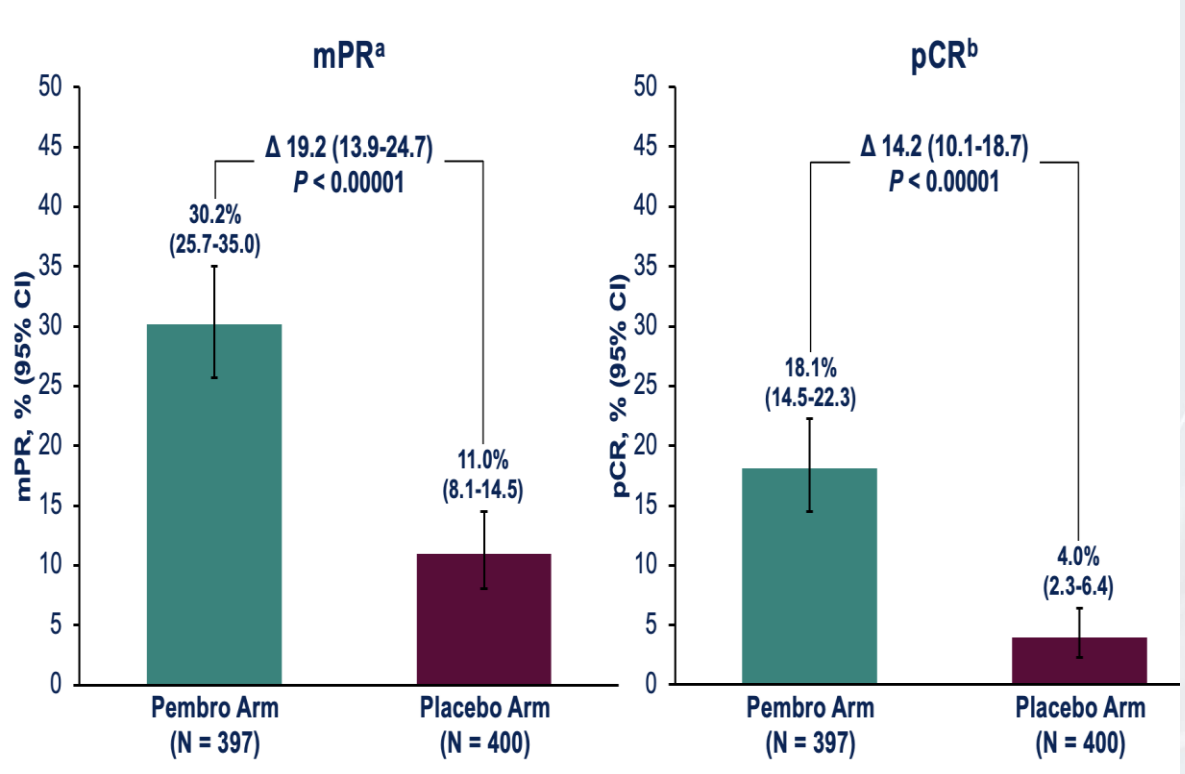
Pembro Arm
(N = 397)
Placebo Arm
(N = 400)


KEYNOTE-671
With pCR
HR 0.33 (95% CI, 0.09-1.22)
Pembro, with pCR
Placebo, with pCR
Pembro, without pCR
Placebo, without pCR
Without pCR
HR 0.69 (95% CI, 0.55-0.85)
EFS, %
Months
No. at risk
72 72 59 46 33 15 8 1 0 0
325 258 177 126 84 57 34 10 0 0
16 14 12 10 9 5 4 0 0 0
384 280 171 114 65 33 20 9 1 0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mPR, % (95% CI)
Δ 19.2 (13.9-24.7)
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30.2%
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Pembro Arm
(N = 397)
Placebo Arm
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pCR[b]
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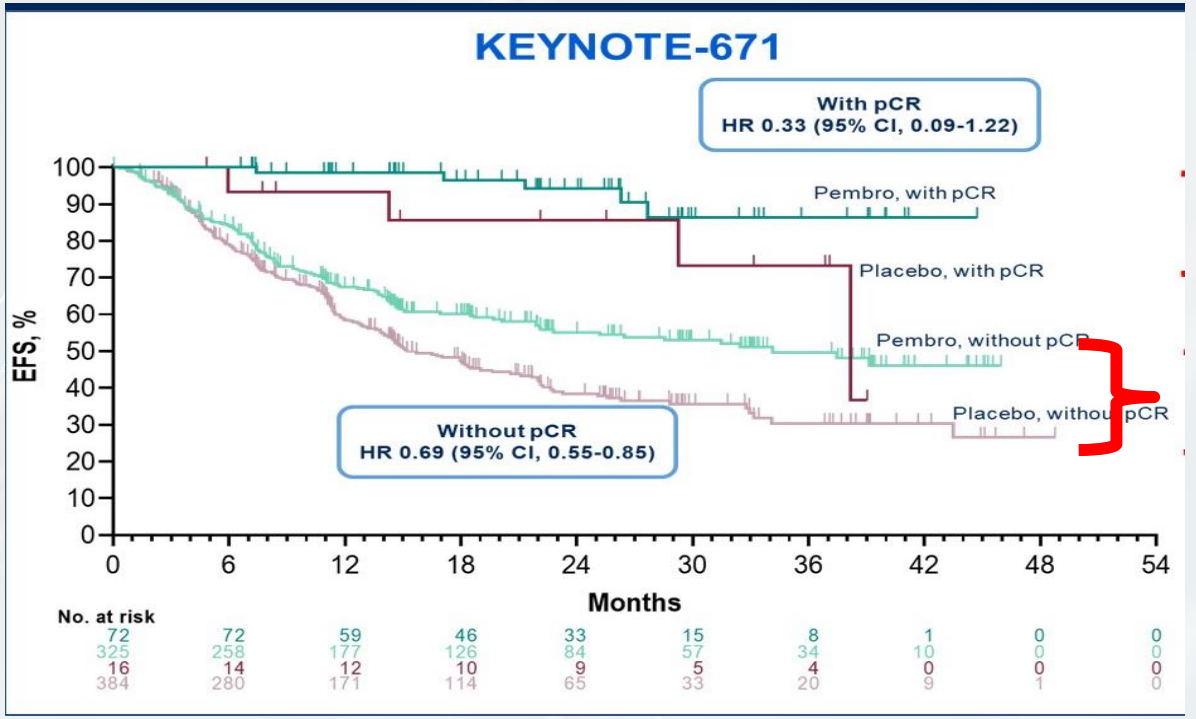
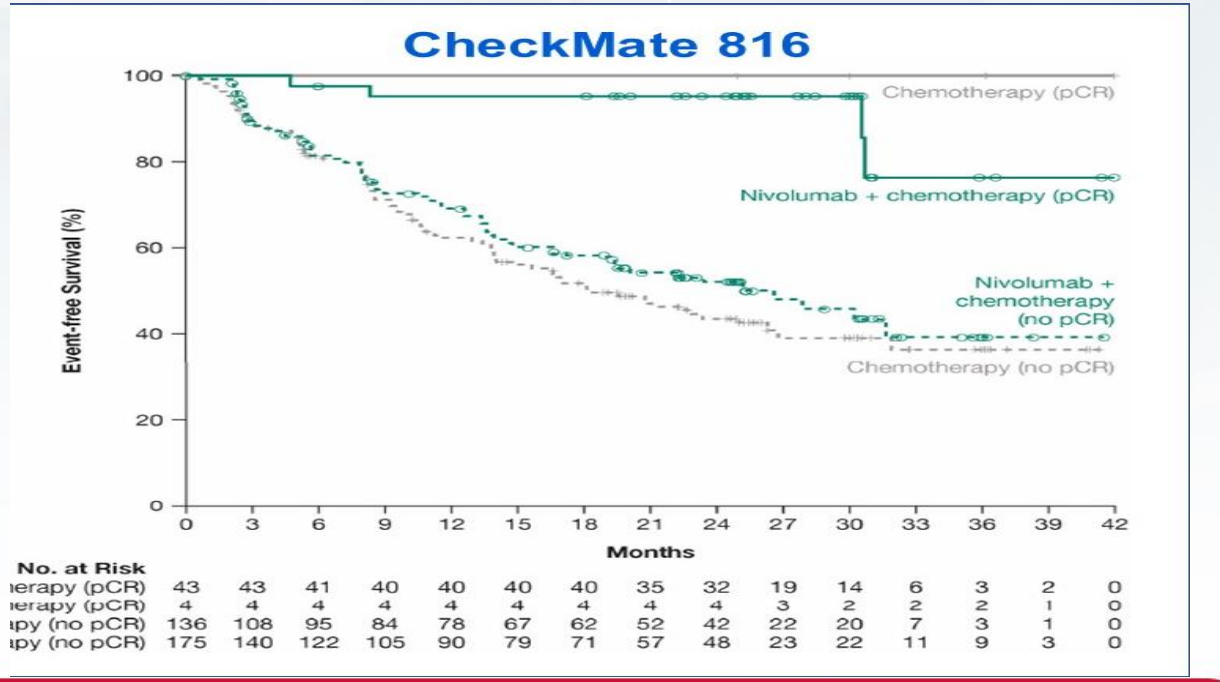
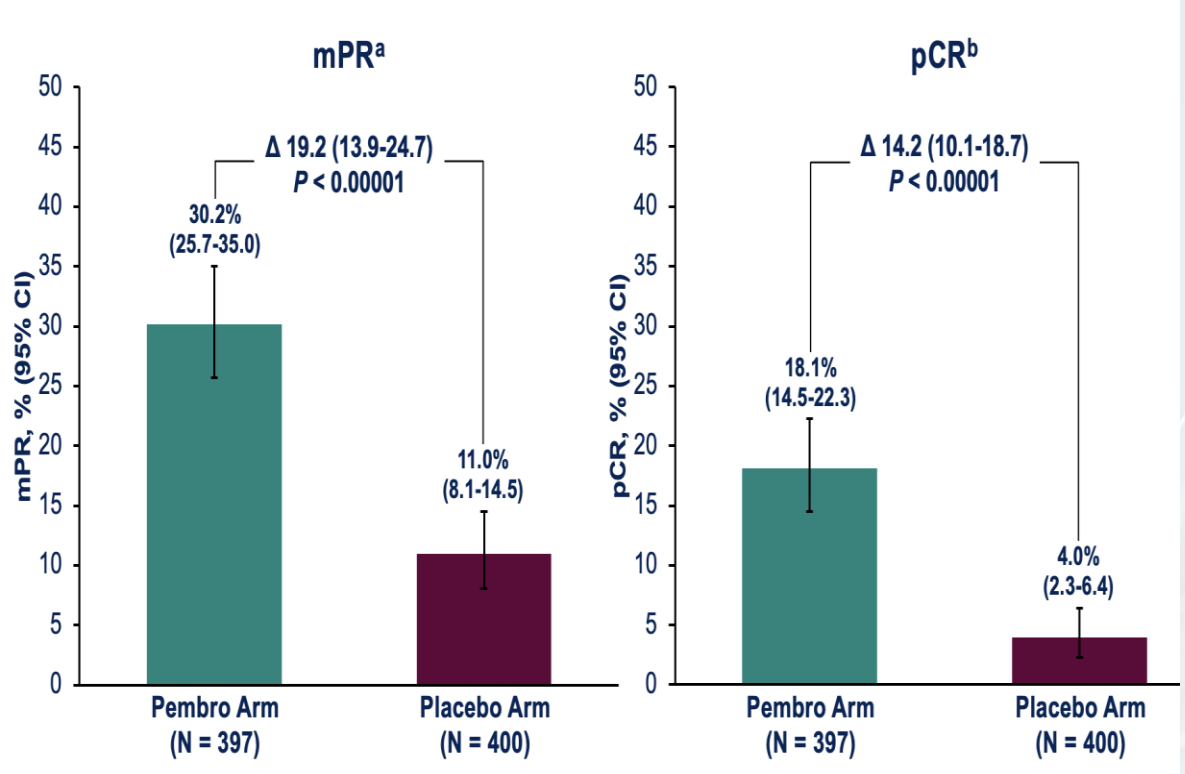
Δ 14.2 (10.1-18.7)
P < 0.00001
18.1%
(14.5-22.3)
4.0%
(2.3-6.4)
Pembro Arm
(N = 397)
Placebo Arm
(N = 400)


KEYNOTE-671
With pCR
HR 0.33 (95% CI, 0.09-1.22)
Pembro, with pCR
Placebo, with pCR
Pembro, without pCR
Placebo, without pCR
Without pCR
HR 0.69 (95% CI, 0.55-0.85)
EFS, %
Months
No. at risk
72 72 59 46 33 15 8 1 0 0
325 258 177 126 84 57 34 10 0 0
16 14 12 10 9 5 4 0 0 0
384 280 171 114 65 33 20 9 1 0


CheckMate 816
Chemotherapy (pCR)
Nivolumab + chemotherapy (pCR)
Nivolumab + chemotherapy (no pCR)
Chemotherapy (no pCR)
Event-free Survival (%)
Months
No. at Risk
erapy (pCR) 43 43 41 40 40 40 40 35 32 19 14 6 3 2 0
erapy (pCR) 4 4 4 4 4 4 4 4 4 3 2 2 2 1 0
py (no pCR) 136 108 95 84 78 67 62 52 42 22 20 7 3 1 0
py (no pCR) 175 140 122 105 90 79 71 57 48 23 22 11 9 3 0


mPR[a]
mPR, % (95% CI)
Δ 19.2 (13.9-24.7)
P < 0.00001
30.2%
(25.7-35.0)
11.0%
(8.1-14.5)
Pembro Arm
(N = 397)
Placebo Arm
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pCR[b]
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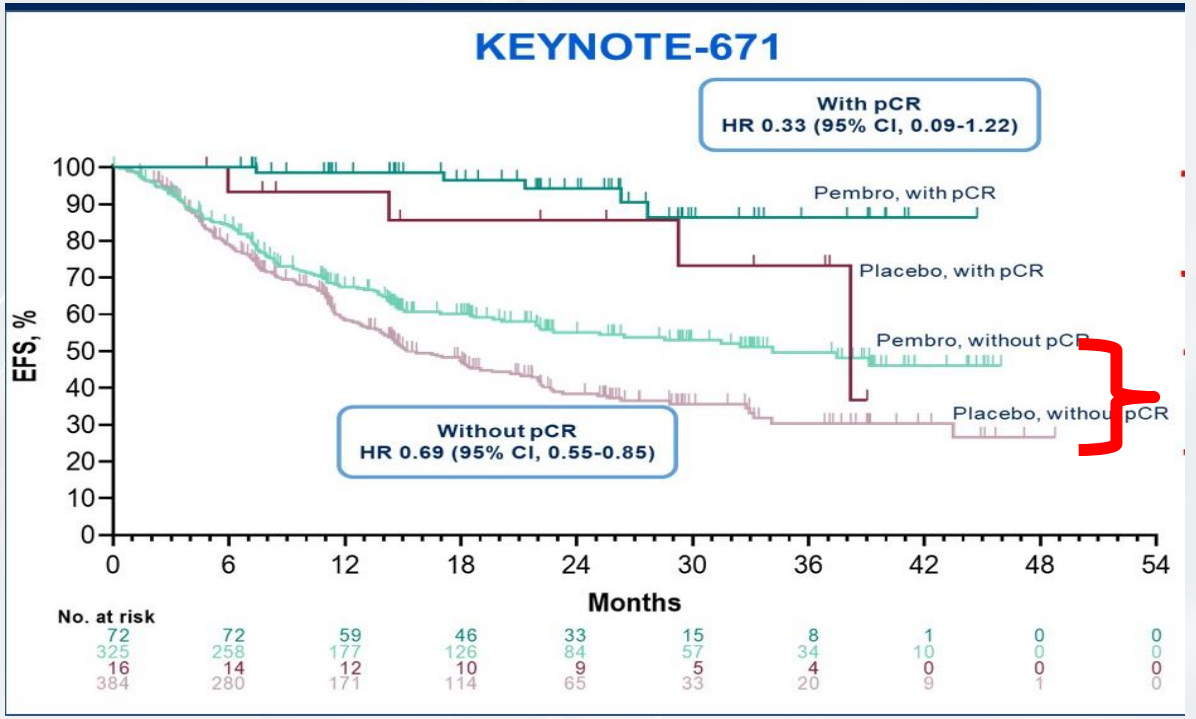
(N = 397)
Placebo Arm
(N = 400)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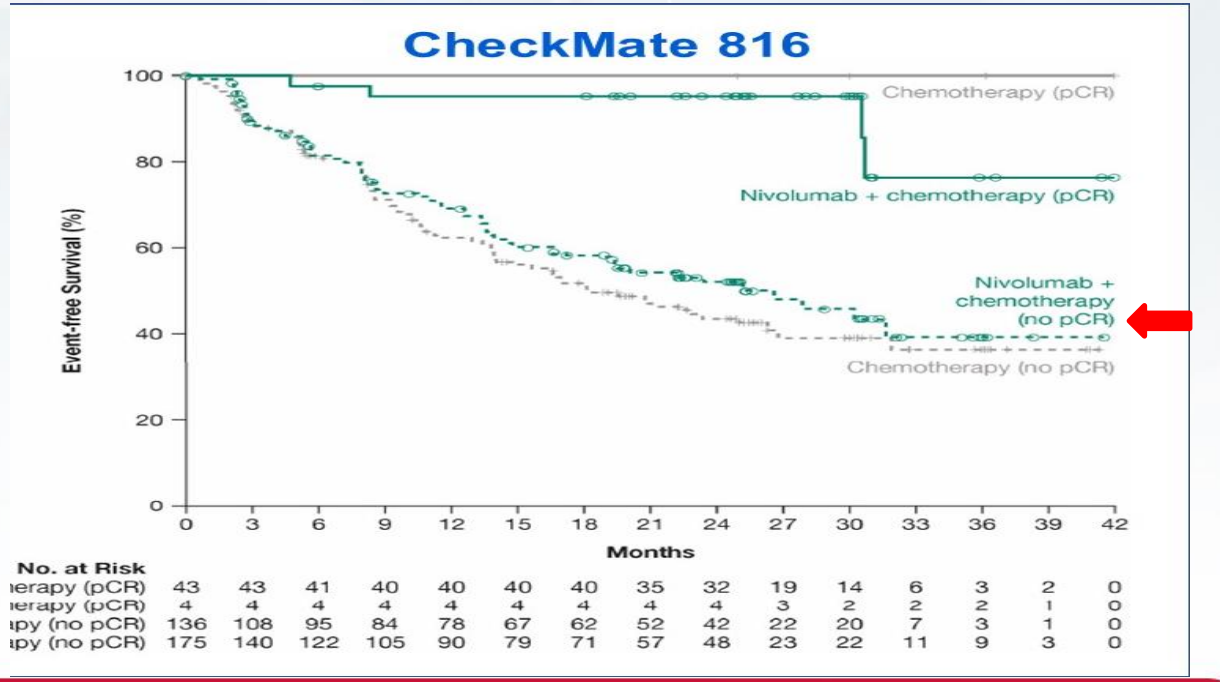
With pCR
HR 0.33 (95% CI, 0.09-1.22)
Pembro, with pCR
Placebo, with pCR
Pembro, without pCR
Placebo, without pCR
Without pCR
HR 0.69 (95% CI, 0.55-0.85)
EFS, %
Months
No. at risk
72 72 59 46 33 15 8 1 0 0
325 258 177 126 84 57 34 10 0 0
16 14 12 10 9 5 4 0 0 0
384 280 171 114 65 33 20 9 1 0


CheckMate 816
Chemotherapy (pCR)
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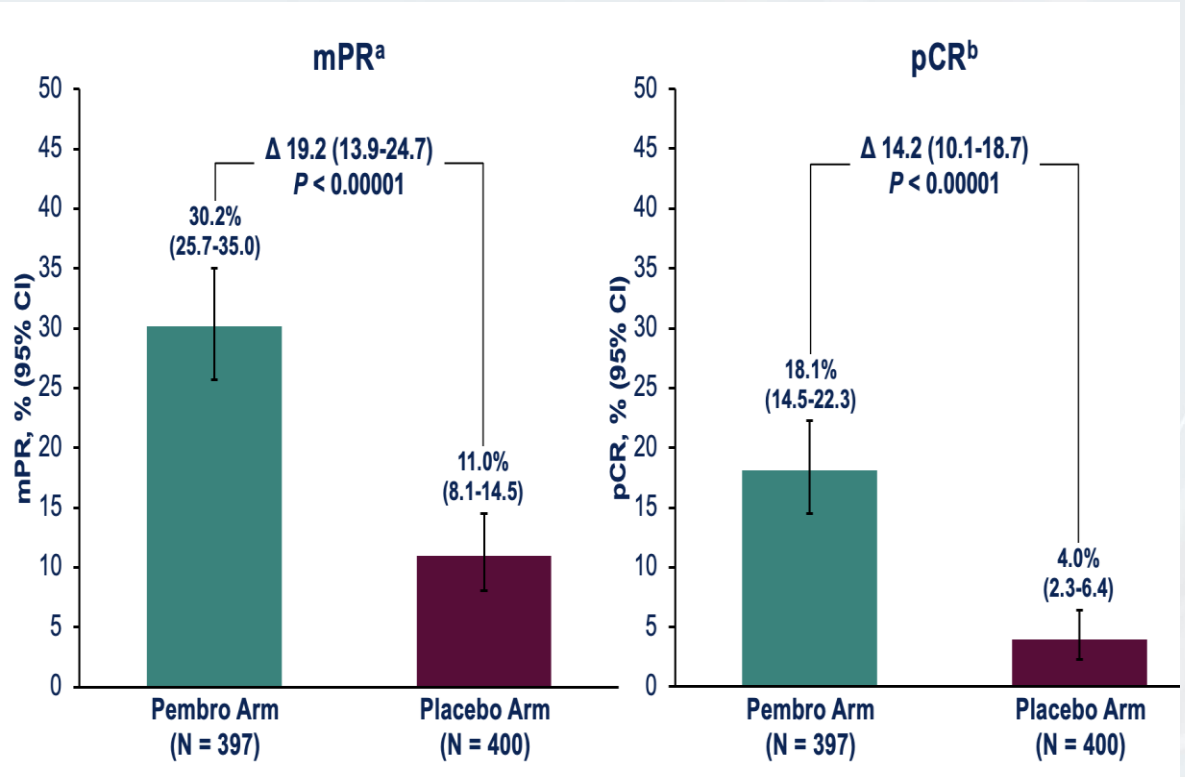
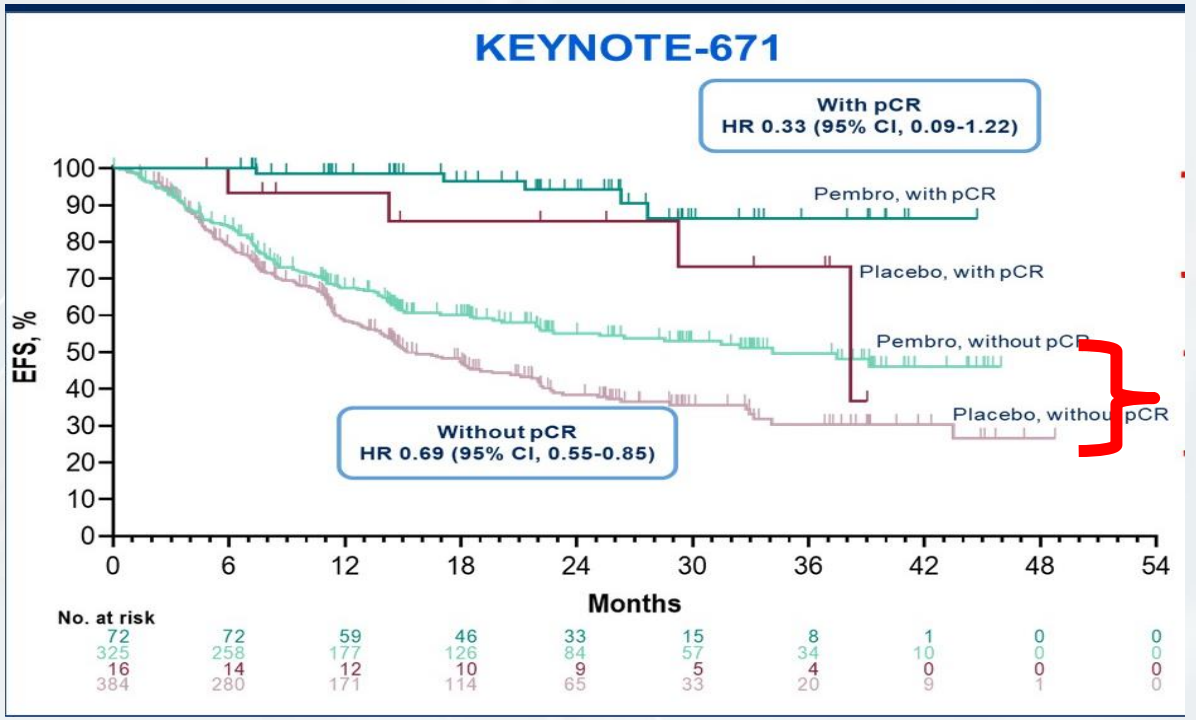
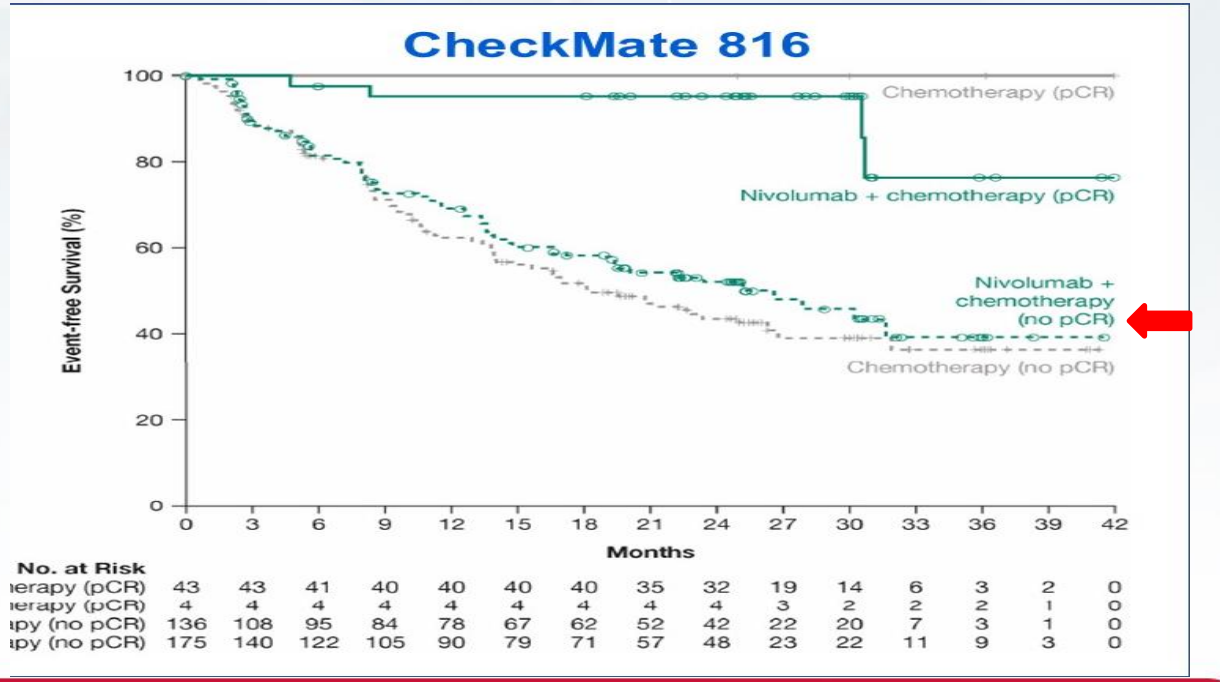
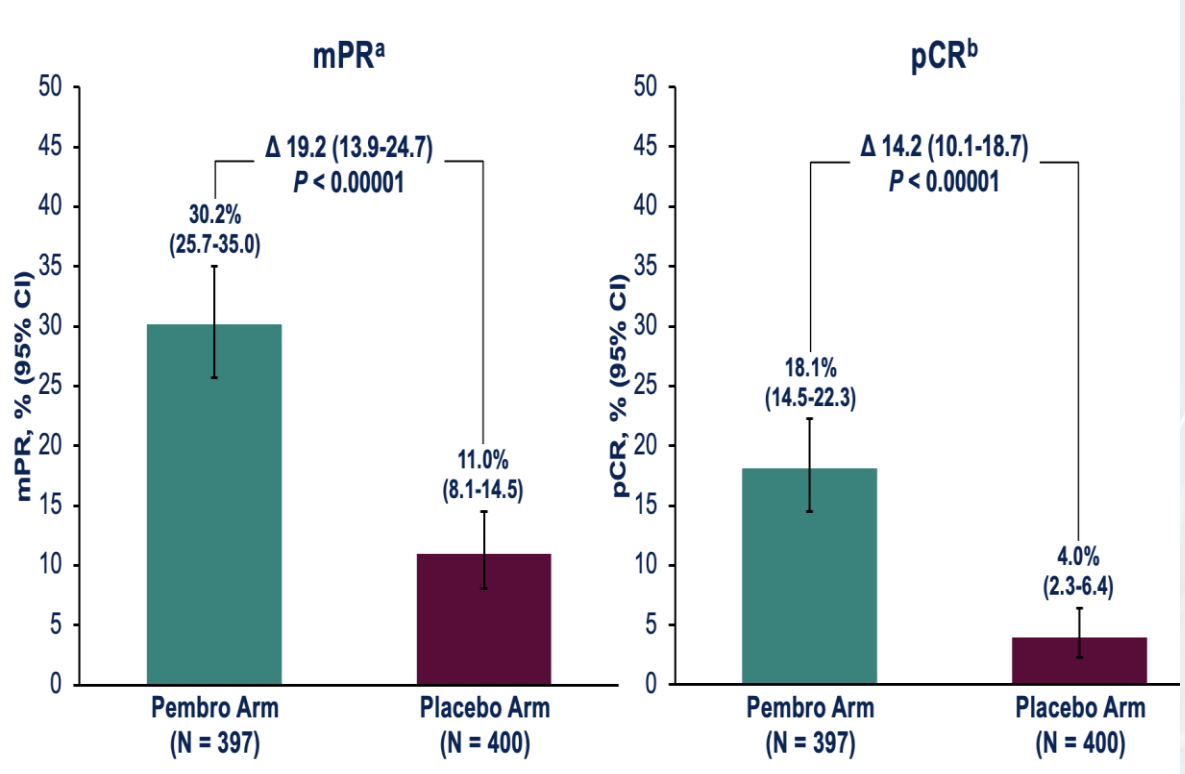
Nivolumab + chemotherapy (no pCR)
Chemotherapy (no pCR)
Event-free Survival (%)
Months
No. at Risk
erapy (pCR) 43 43 41 40 40 40 40 35 32 19 14 6 3 2 0
erapy (pCR) 4 4 4 4 4 4 4 4 4 3 2 2 2 1 0
py (no pCR) 136 108 95 84 78 67 62 52 42 22 20 7 3 1 0
py (no pCR) 175 140 122 105 90 79 71 57 48 23 22 11 9 3 0

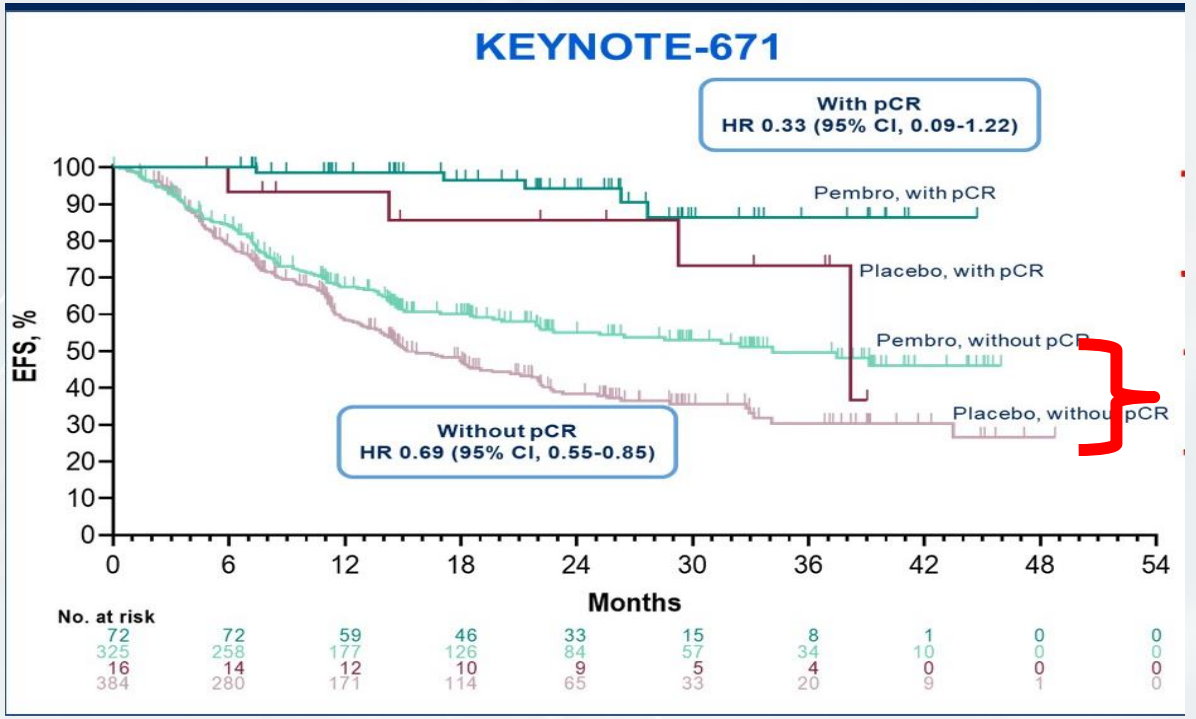


AEs, n (%)	Pembrolizumab (n=396)	Placebo (n=399)
TRAEs	383 (96.7)	379 (95.0)
Grade 3–5	178 (44.9)	149 (37.3)
Serious	70 (17.7)	57 (14.3)
Led to death	4 (1.0)	3 (0.8)
Led to treatment discontinuation	50 (12.6)	21 (5.3)
irAEs and infusion reactions	**100 (25.3)**	**42 (10.5)**
Grade 3–5	23 (5.8)	6 (1.5)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









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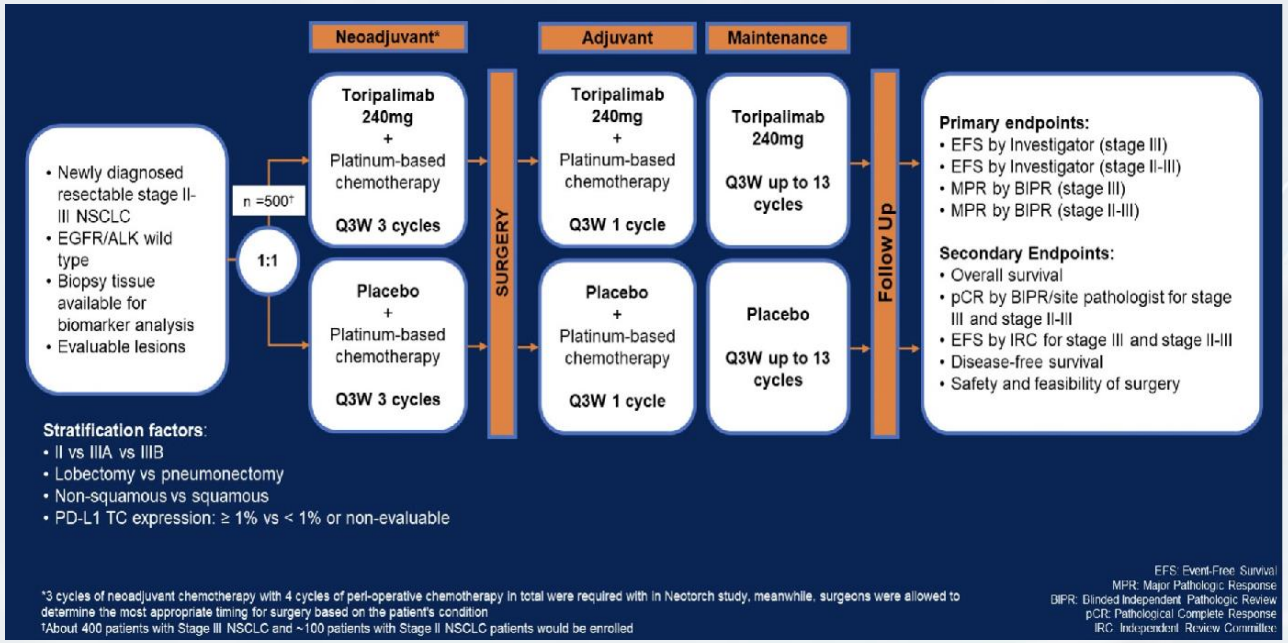
TRAEs	383 (96.7)	379 (95.0)
Grade 3–5	178 (44.9)	149 (37.3)
Led to death	1 (0.3)	0
Led to treatment discontinuation	20 (5.1)	3 (0.8)

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



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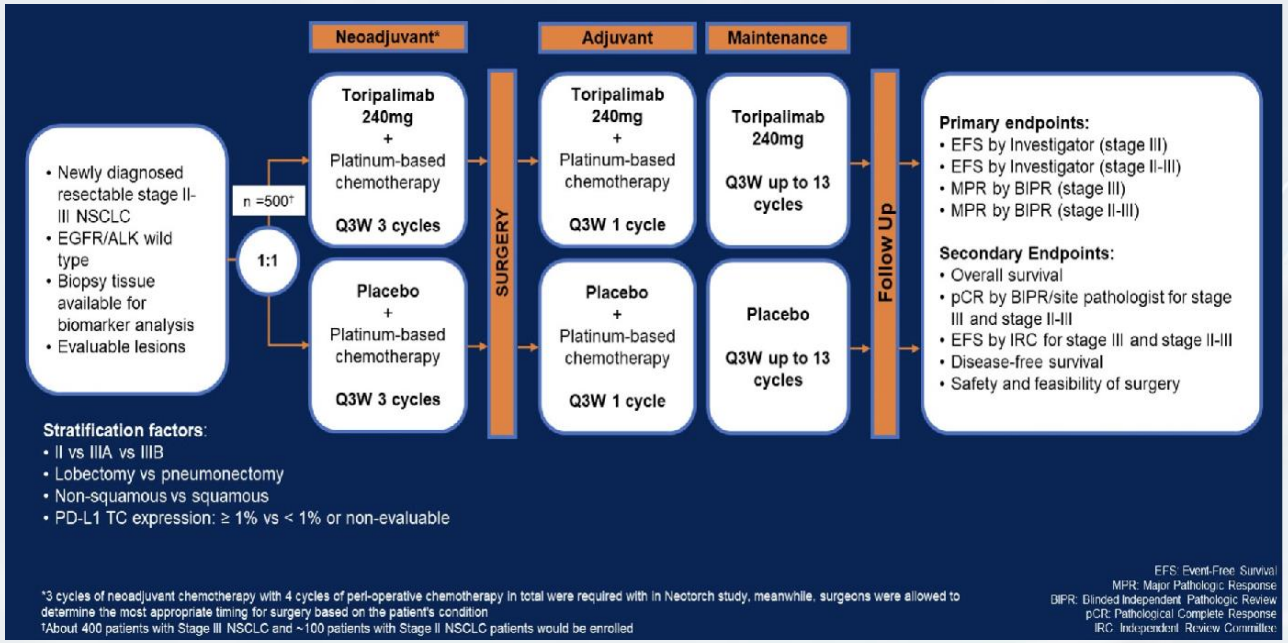

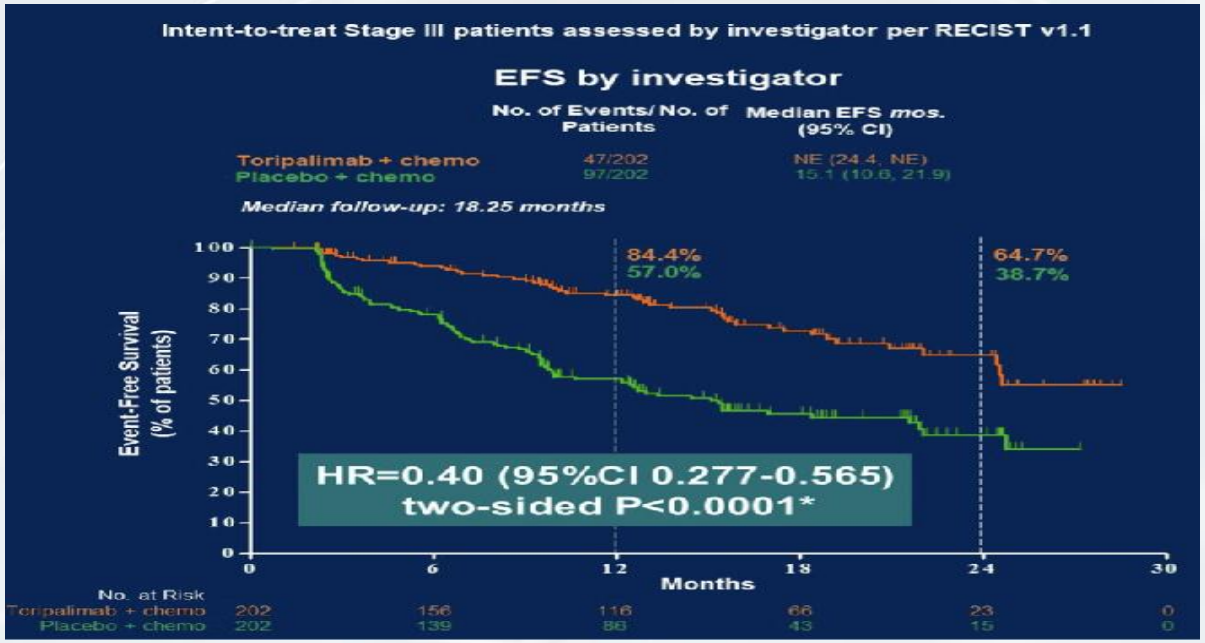

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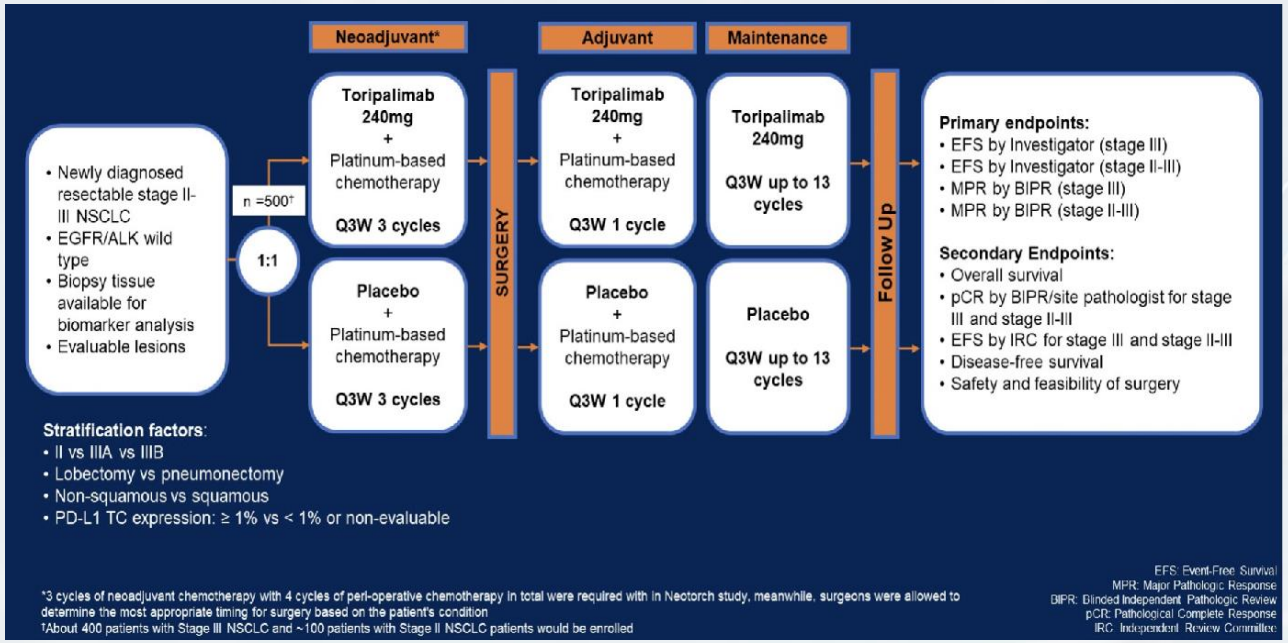

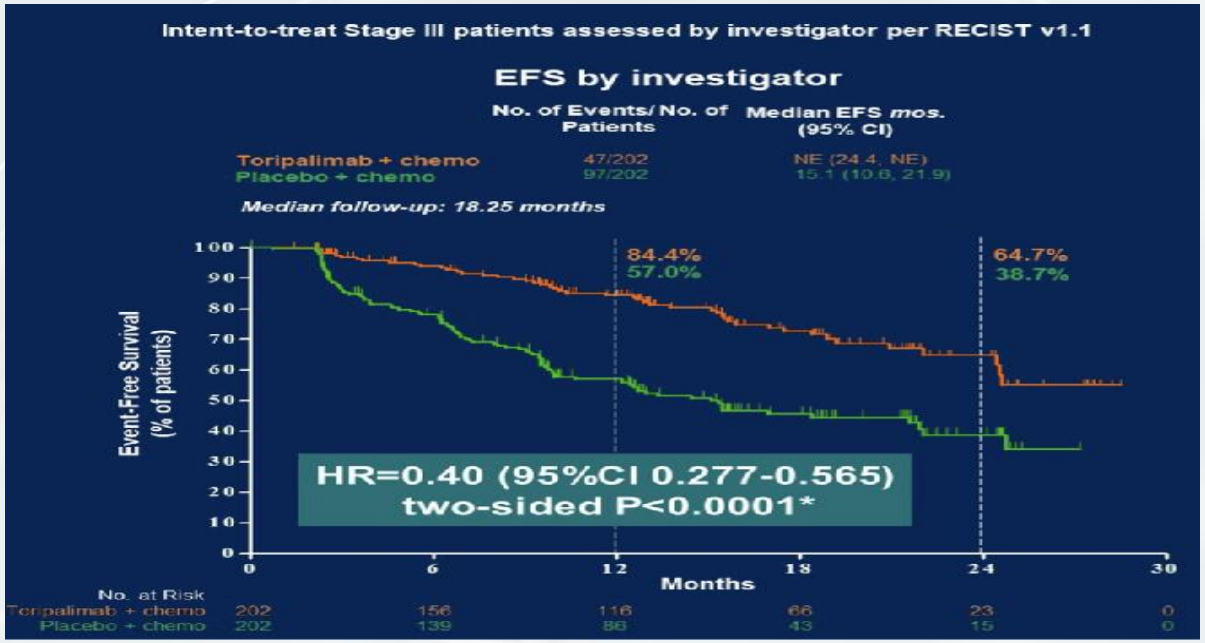

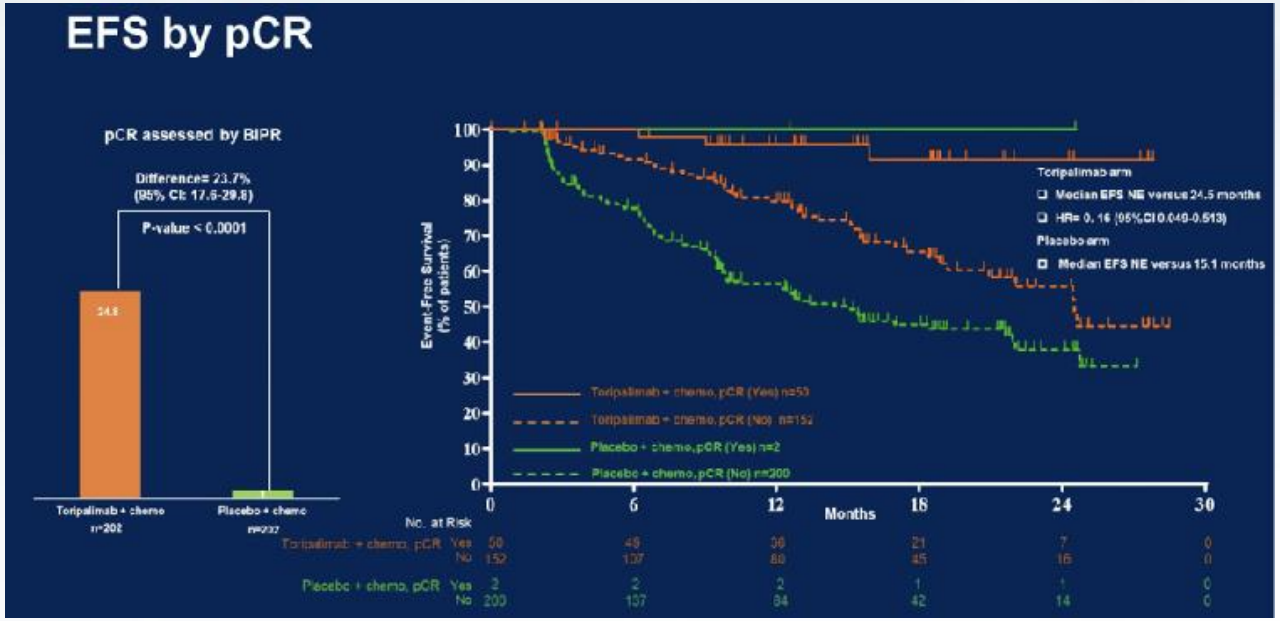

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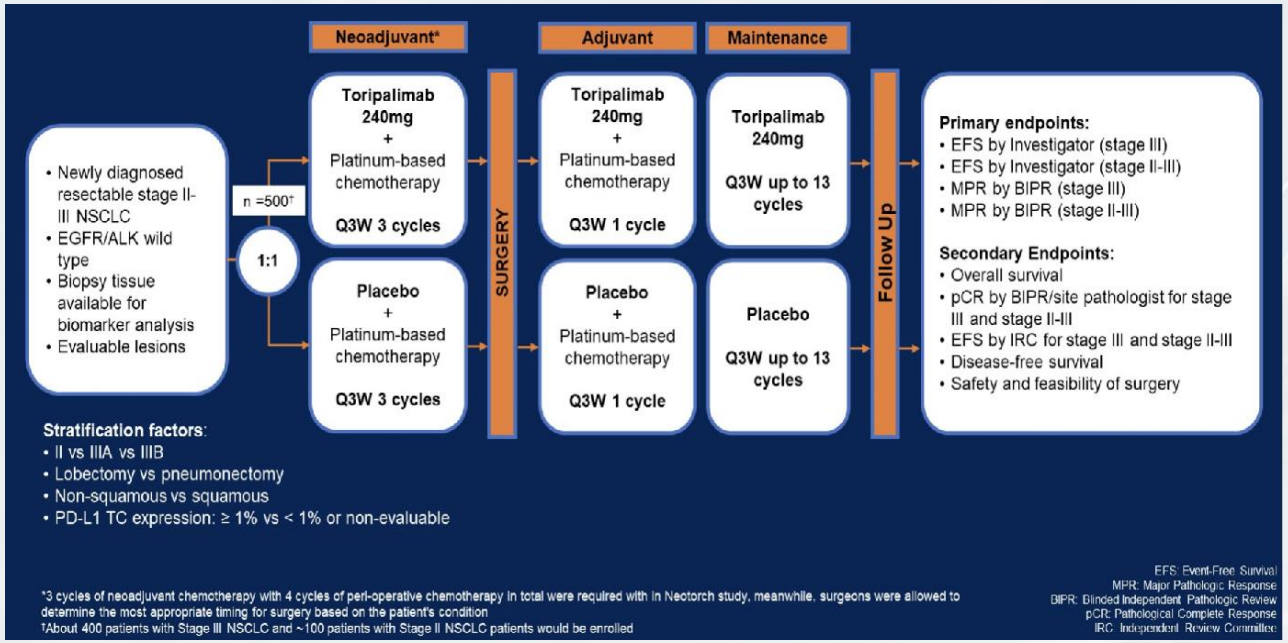
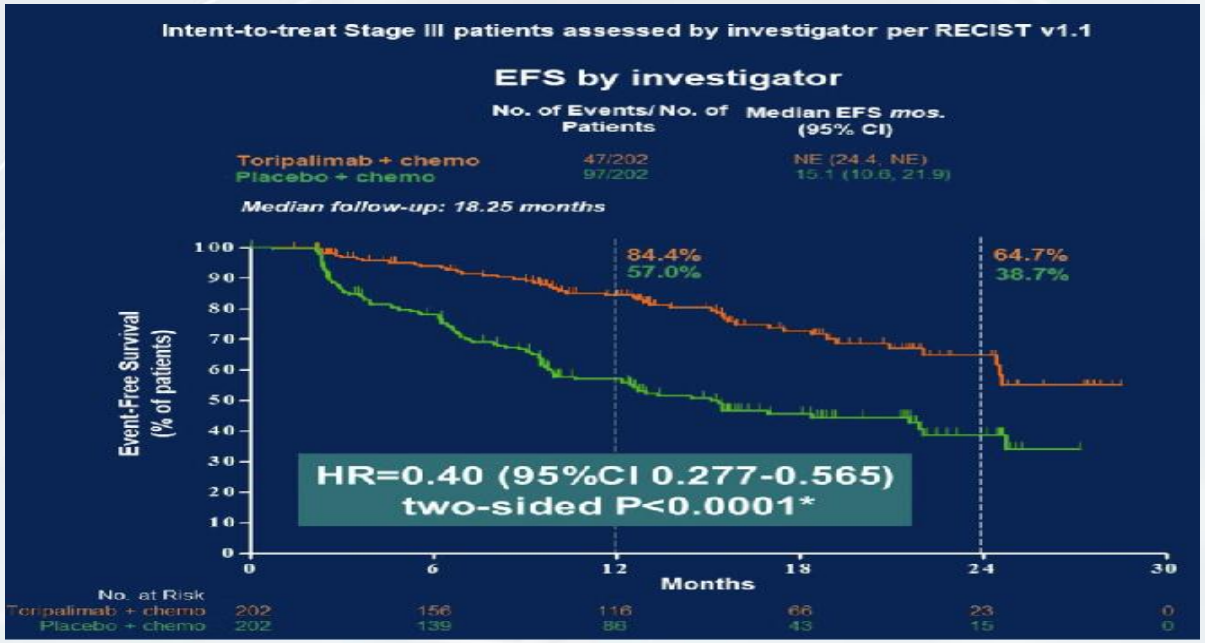
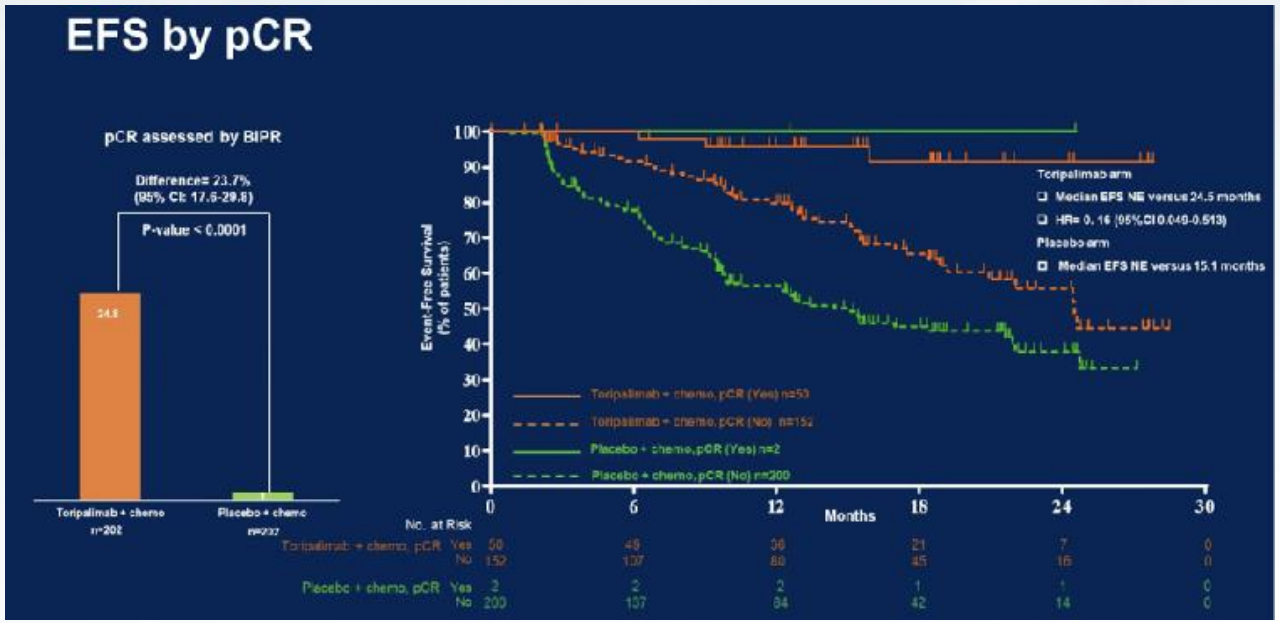
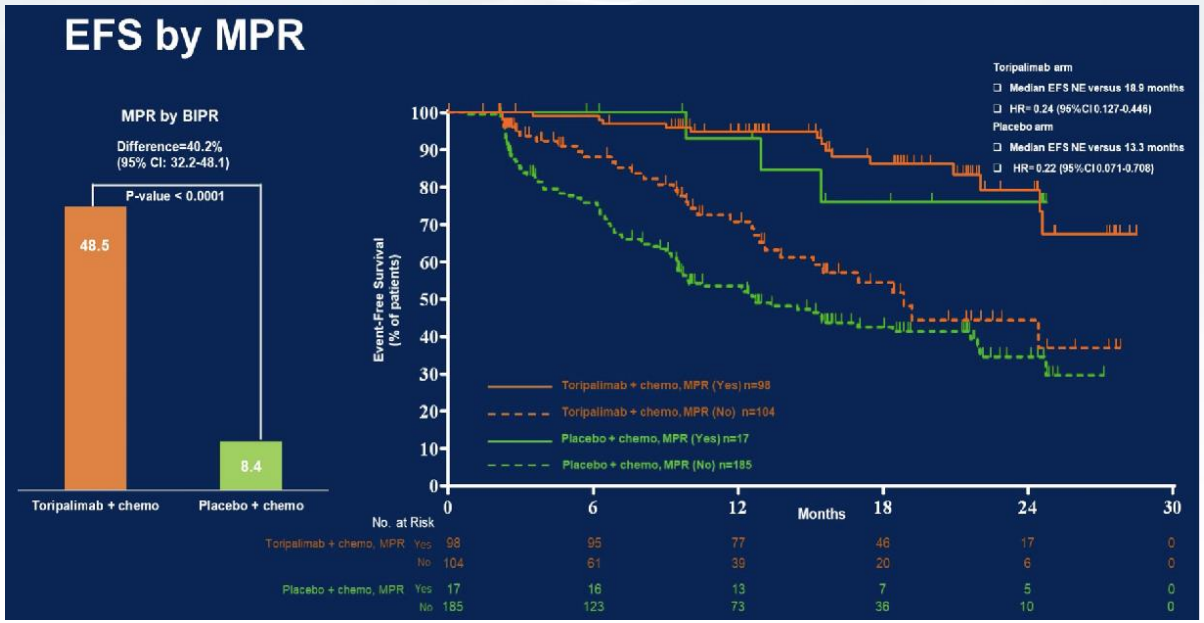








8522: IMpower010: Exploratory analysis of disease-free survival by KRAS status in patients with stage II-IIIA NSCLC treated with adjuvant atezolizumab vs best supportive care – Reck M, et al

- **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

Key patient inclusion criteria
- Stage IB (≥4 cm)–IIIA NSCLC
- Completely resected
- ECOG PS 0–1

(n=1005)

Cisplatin + pemetrexed, docetaxel, gemcitabine or vinorelbine (1–4 cycles)

R 1:1

Atezolizumab 1200 mg q3w (16 cycles) (n=507)

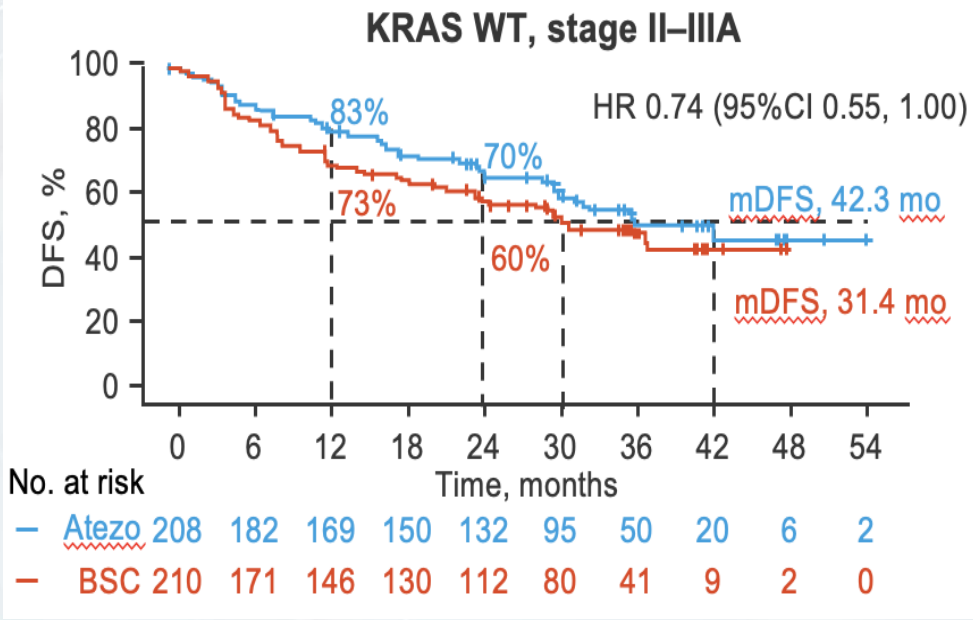
Best supportive care (n=498)

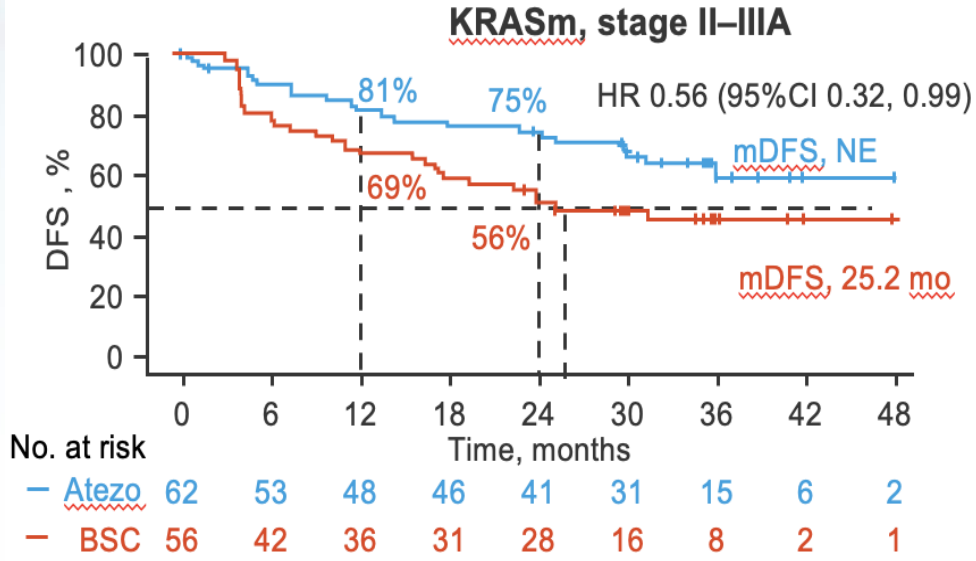
Stratification
- Sex
- Stage (IB vs. II vs. IIIA)
- Histology
- PD-L1 status[b] (TC <1% vs. ≥1%)

Primary endpoint
- DFS (investigator assessed)

Exploratory endpoint
- DFS according to KRAS mutational status[a]

- **Key results**



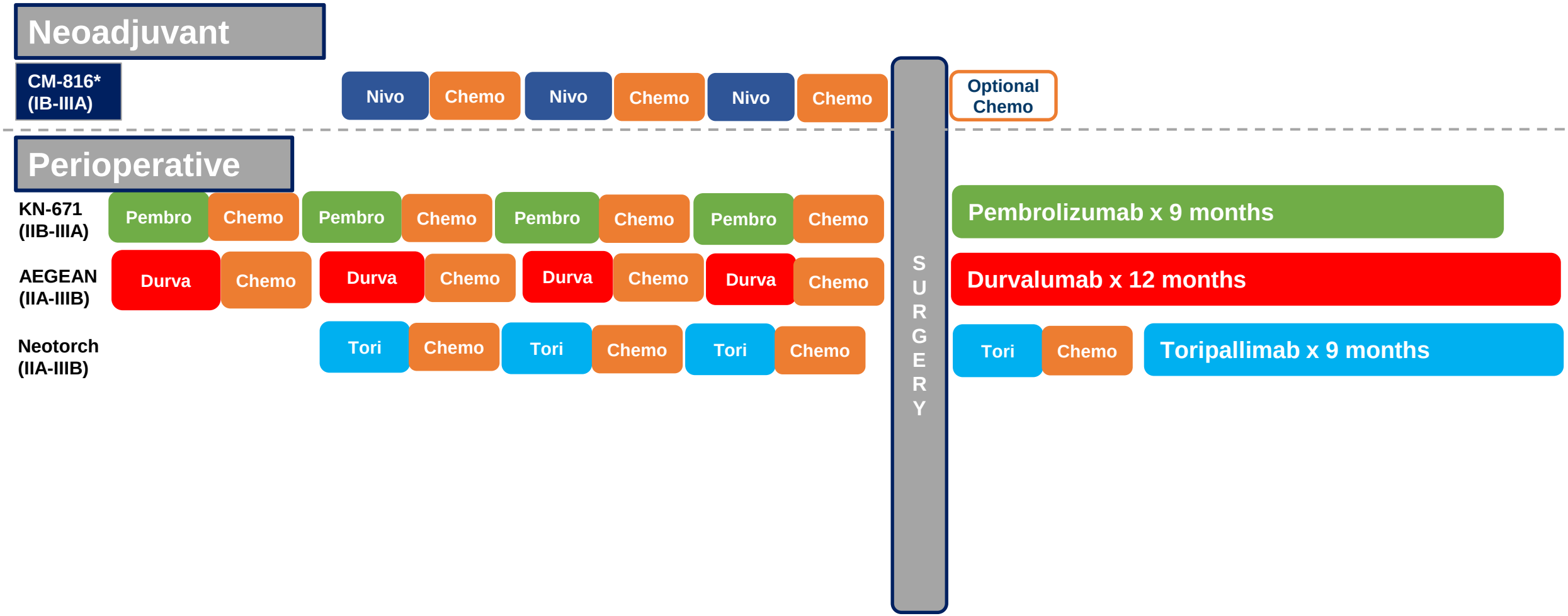


- **Conclusions**
  - In patients with stage II–IIIA NSCLC, atezolizumab showed improvement in DFS regardless of KRAS mutation status and PD-L1 expression compared with BSC in this exploratory analysis

Many evolving approaches:
Neoadjuvant vs. adjuvant vs. perioperative ICIs

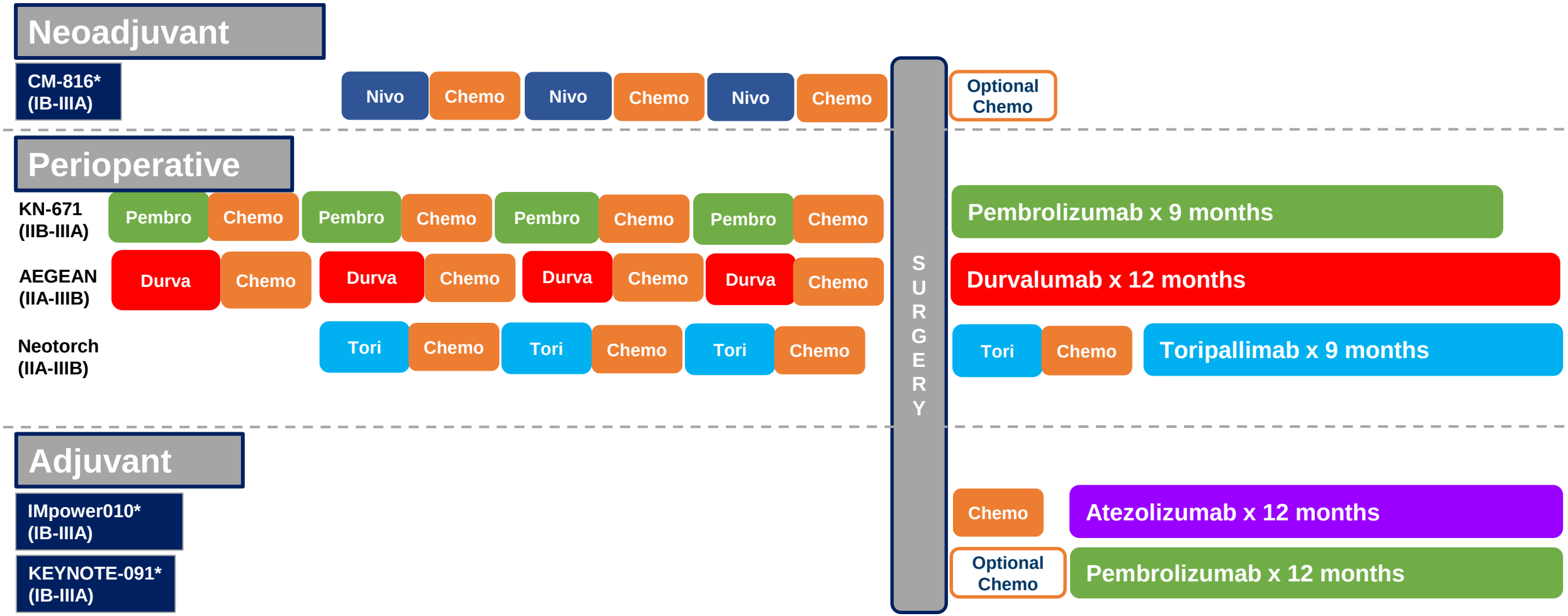
*FDA-Approved Regimens

Many evolving approaches:
Neoadjuvant vs. adjuvant vs. perioperative ICIs



*FDA-Approved Regimens

Many evolving approaches:
Neoadjuvant vs. adjuvant vs. perioperative ICIs



Neoadjuvant vs. perioperative Chemo-ICI : Outcomes to date

	Trial	Primary Endpoint	S-III (%)	Treatment	pCR (%)	MPR (%)	Definitive Surgery Rate (%)	EFS, median (HR)	OS, median (HR)	Median FU
Neoadjuvant	**CheckMate-816** (358 patients) IB-IIIA (7th TNM)	pCR EFS	63/64	Cis/ Carbo doublet x 3 cycles **Nivolumab**+CT x 3 cycles	2.2 vs 24	8.9 vs 36.9	75.4 vs 83.2	21.1 vs NR (HR=0.68)	NR vs NR (HR=0.62)	41.8 months
Perioperative	**AEGEAN** (740 patients) IIA-IIIB(T3N2) (8th TNM)	pCR EFS	71,3/70,3	Cis/Carbo doublet x 4+ placebo 12 cycles **Durvalumab**+CT x 4 + **Durvalumab** 12 cycles	4.3 vs 17.2	12.3 vs 33.3	76.7 vs 77.6	25. vs NR (HR=0.68)	NE	11.7 months
	Neo-TORCH (404 patients) IIIA/B (8th TNM)	EFS MPR	100	Cis/Carbo doublet x 3 + 1 CT placebo 13 cycles **Toripalimab**+CT x 3 + 1 CT-**Toripalimab** 13 cycles	1 vs 24.8	8 vs 48	73 vs 82	15.5 vs NR (HR=0.40)	30.4 vs NR (HR=0.62)	18.25 months
	KeyNote-671 (797patients) II-IIIA (8th TNM)	EFS OS	70	Cisplatinum doublet x 4 + placebo 13 cycles **Pembrolizumab**+CT x 4 + **Pembrolizumab**13 cycles	**4 vs 18.1**	**11 vs 30.2**	**75 vs 80**	**17vs NR**	**45.5 vs NR**	**25.2 months**

Forde PM et al (ELCC 2023). Heymach J et al (AACR 2023). Lu S et al (ASCO Plen Ses 2023). Heather Wakelee. (ASCO 2023)

Advanced NSCLC
Not radically treatable stage III and stage IV

- Immunotherapy

KEYNOTE-789: Phase 3 Randomized Study (NCT03515837)

Study Population

- Histologically/cytologically confirmed stage IV nonsquamous NSCLC
- *EGFR DEL19* or *L858R* mutation
- ECOG PS 0 or 1
- PD per RECIST v1.1:
  - After 1st- or 2nd-generation *EGFR* TKI without *T790M* mutation
  - After 1st or 2nd *EGFR* TKI with *T790M* mutation and osimertinib failure
  - Osimertinib failure as 1st-line therapy, regardless of *T790M* status

Stratification Factors

- PD-L1 TPS[a]: <50% vs ≥50%
- Treatment history: with vs without osimertinib
- Geographic region: East Asia vs not East Asia

R (1:1)
N = 492

Pembrolizumab 200 mg[b]
+
Pemetrexed 500 mg/m²
+
Carboplatin AUC 5 or Cisplatin 75 mg/m²[c]
Q3W × 4 cycles

Pembrolizumab 200 mg Q3W × 31 cycles[b]
+
Pemetrexed 500 mg/m² Q3W[d]

Placebo
+
Pemetrexed 500 mg/m²
+
Carboplatin AUC 5 or Cisplatin 75 mg/m²[c]
Q3W × 4 cycles

Placebo Q3W × 31 cycles[b]
+
Pemetrexed 500 mg/m² Q3W[d]

PD[e]

Optional crossover:
Pembrolizumab 200 mg Q3W × 35 cycles

End Points

- **Dual Primary:** PFS per RECIST v1.1 by BICR and OS
- **Secondary:** ORR and DOR per RECIST v1.1 by BICR, safety, and patient-reported outcomes

Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000

KEYNOTE-789: Phase 3 Randomized Study (NCT03515837)

Study Population

- Histologically/cytologically confirmed stage IV nonsquamous NSCLC
- *EGFR DEL19* or *L858R* mutation
- ECOG PS 0 or 1
- PD per RECIST v1.1:
  - After 1st- or 2nd-generation *EGFR* TKI without *T790M* mutation
  - After 1st or 2nd *EGFR* TKI with *T790M* mutation and osimertinib failure
  - Osimertinib failure as 1st-line therapy, regardless of *T790M* status

Stratification Factors

- PD-L1 TPS[a]: <50% vs ≥50%
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N = 492

- Pembrolizumab 200 mg[b] + Pemetrexed 500 mg/m^2 + Carboplatin AUC 5 or Cisplatin 75 mg/m^2[c] Q3W × 4 cycles → Pembrolizumab 200 mg Q3W × 31 cycles[b] + Pemetrexed 500 mg/m^2 Q3W[d]
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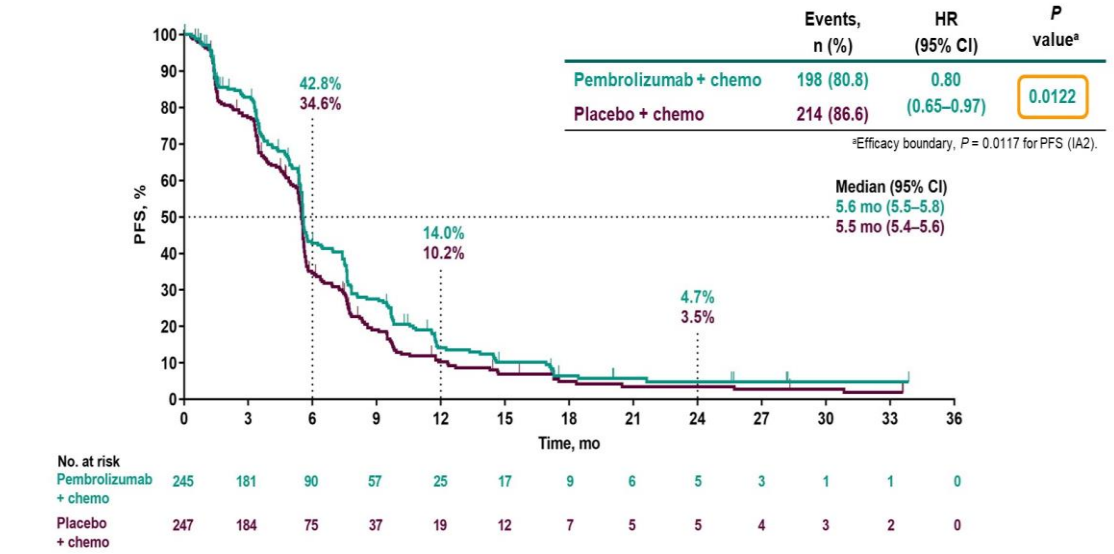
- **Secondary:** ORR and DOR per RECIST v1.1 by BICR, safety, and patient-reported outcomes

Progression-Free Survival at IA2
(RECIST v1.1, BICR)



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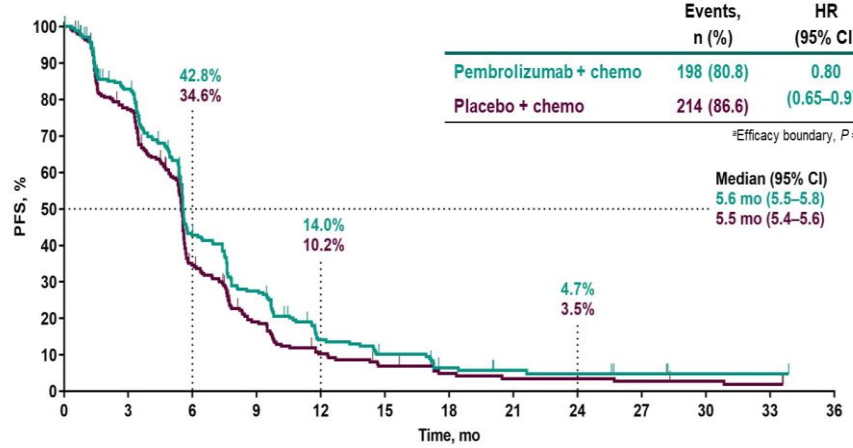
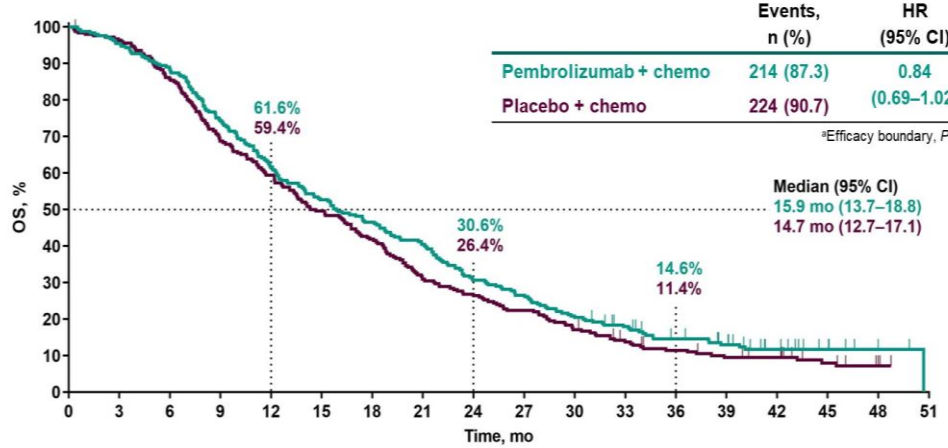


	Events, n (%)	HR (95% CI)	P value[a]
Pembrolizumab + chemo	198 (80.8)	0.80 (0.65–0.97)	0.0122
Placebo + chemo	214 (86.6)		

[a]Efficacy boundary, $P = 0.0117$ for PFS (IA2).

No. at risk													
Pembrolizumab + chemo	245	181	90	57	25	17	9	6	5	3	1	1	0
Placebo + chemo	247	184	75	37	19	12	7	5	5	4	3	2	0

Overall Survival at FA



	Events, n (%)	HR (95% CI)	P value[a]
Pembrolizumab + chemo	214 (87.3)	0.84 (0.69–1.02)	0.0362
Placebo + chemo	224 (90.7)		

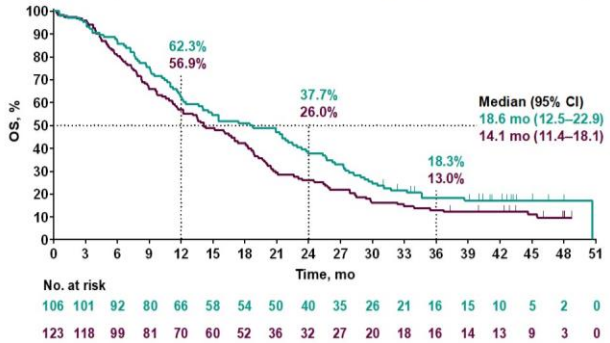
[a]Efficacy boundary, $P = 0.0117$ for OS (FA).

No. at risk																	
Pembrolizumab + chemo	245	234	217	182	151	129	114	99	75	65	50	40	29	23	13	7	3	0
Placebo + chemo	247	237	211	169	146	122	103	76	65	55	42	31	24	19	17	10	3	0

Overall Survival in PD-L1 TPS ≥1% and <1% at FA

PD-L1 TPS ≥1%

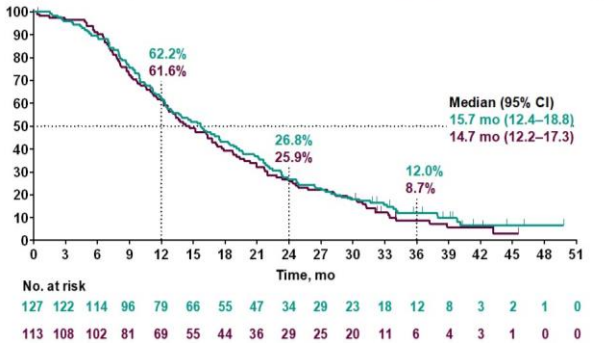
	Events, n (%)	HR (95% CI)
Pembrolizumab + chemo	88 (83.0)	0.77 (0.58–1.02)
Placebo + chemo	110 (89.4)	



No. at risk																	
Pembrolizumab + chemo	106	101	92	80	66	58	54	50	40	35	26	21	16	15	10	5	2	0
Placebo + chemo	123	118	99	81	70	60	52	36	32	27	20	18	16	14	13	9	3	0

PD-L1 TPS <1%

	Events, n (%)	HR (95% CI)
Pembrolizumab + chemo	115 (90.6)	0.91 (0.70–1.19)
Placebo + chemo	104 (92.0)	



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Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000

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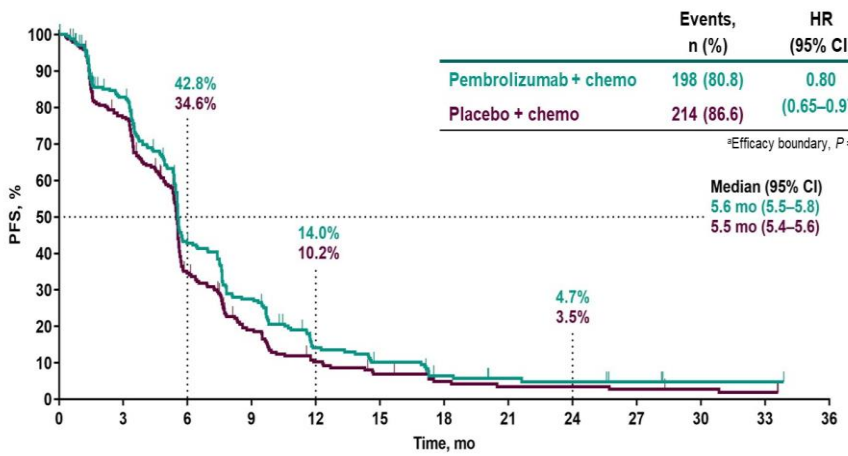
- **Secondary:** ORR and DOR p

Progression-Free Survival at IA2
(RECIST v1.1, BICR)



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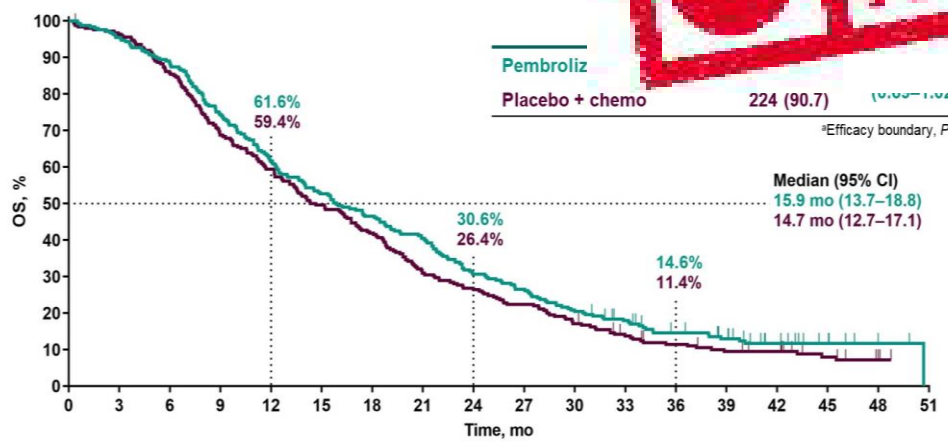
NEGATIVE

Overall Survival at FA



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al in PD-L1 TPS ≥1% and <1% at FA

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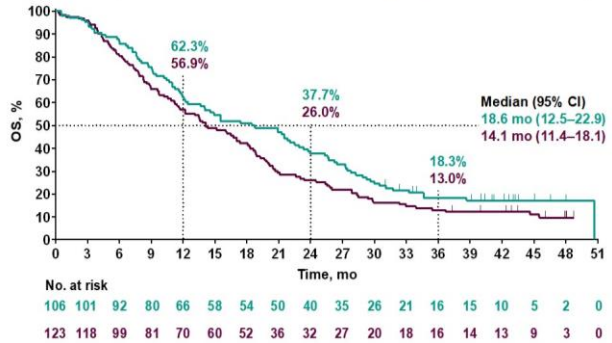

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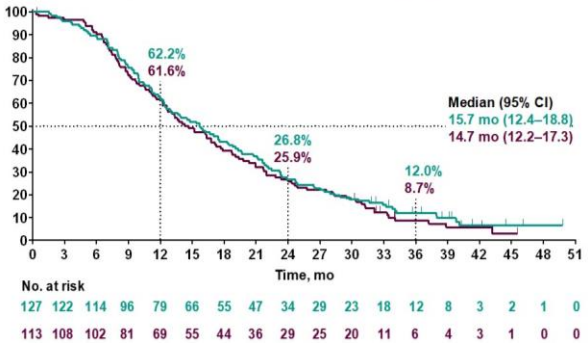

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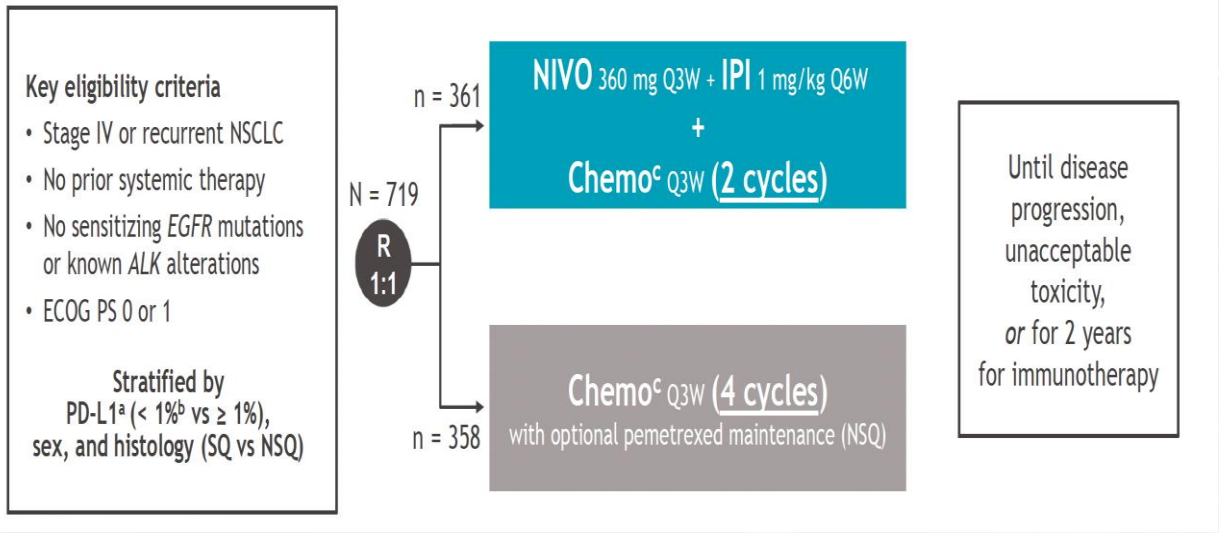
Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000

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. J Clin Oncol 2023;41(suppl 16):Abstr LBA9023

Figure 1. CheckMate 9LA study design[7]



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Carbone DP, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9023

Figure 1. CheckMate 9LA study design[7]

Key eligibility criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0 or 1

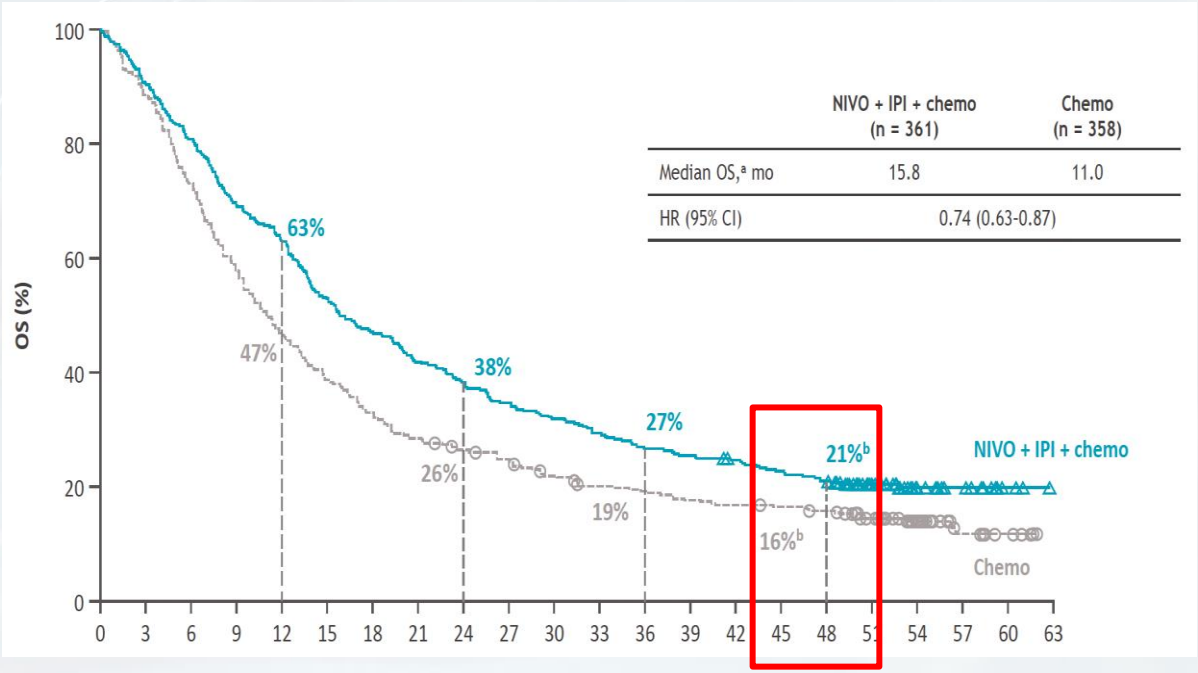
Stratified by PD-L1[a] (< 1%[b] vs ≥ 1%), sex, and histology (SQ vs NSQ)

N = 719
R 1:1

n = 361: NIVO 360 mg Q3W + IPI 1 mg/kg Q6W + Chemo[c] Q3W (2 cycles)

n = 358: Chemo[c] Q3W (4 cycles) with optional pemetrexed maintenance (NSQ)

Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy



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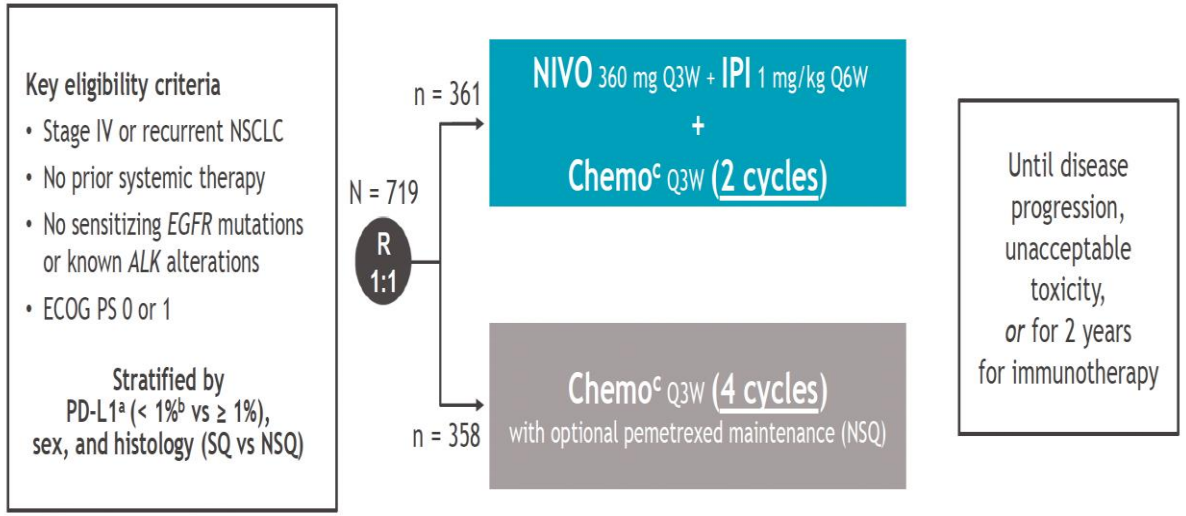
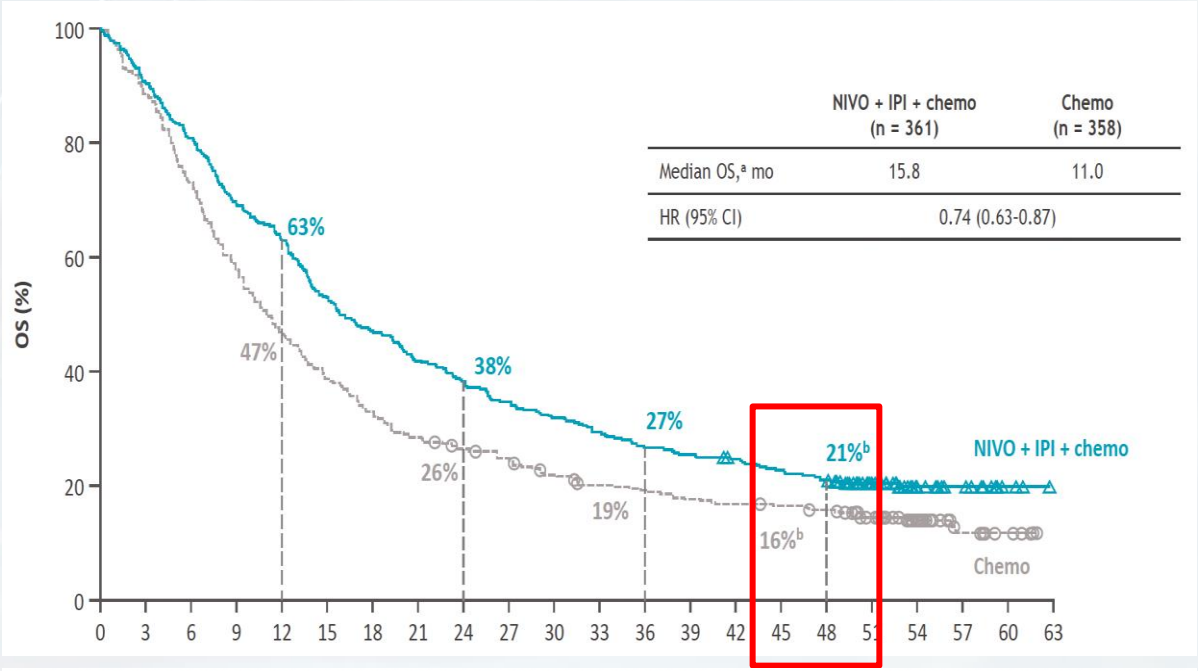
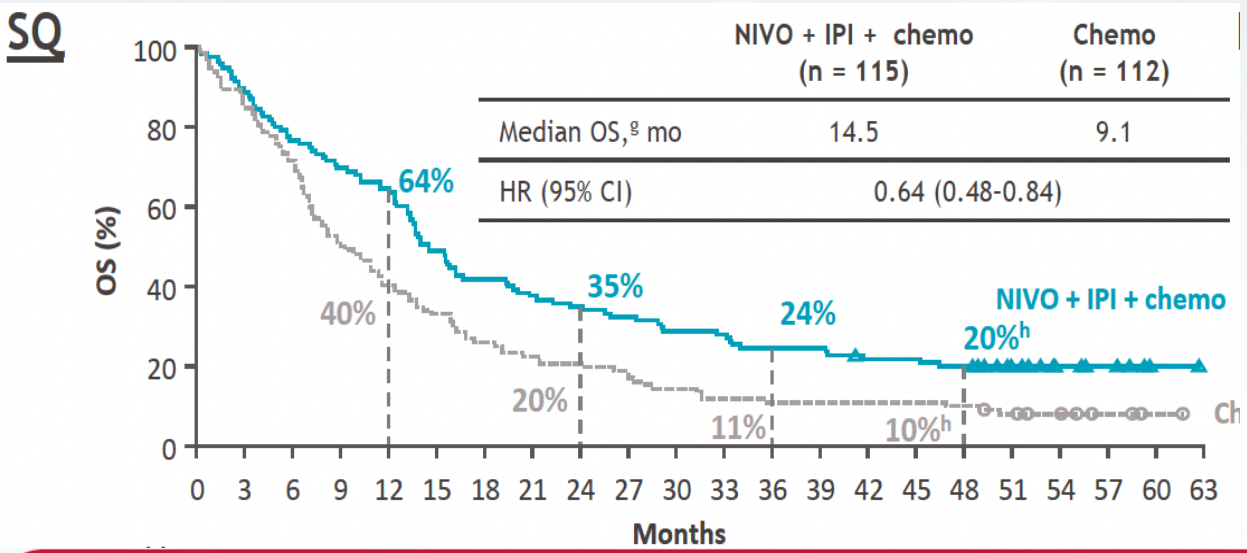
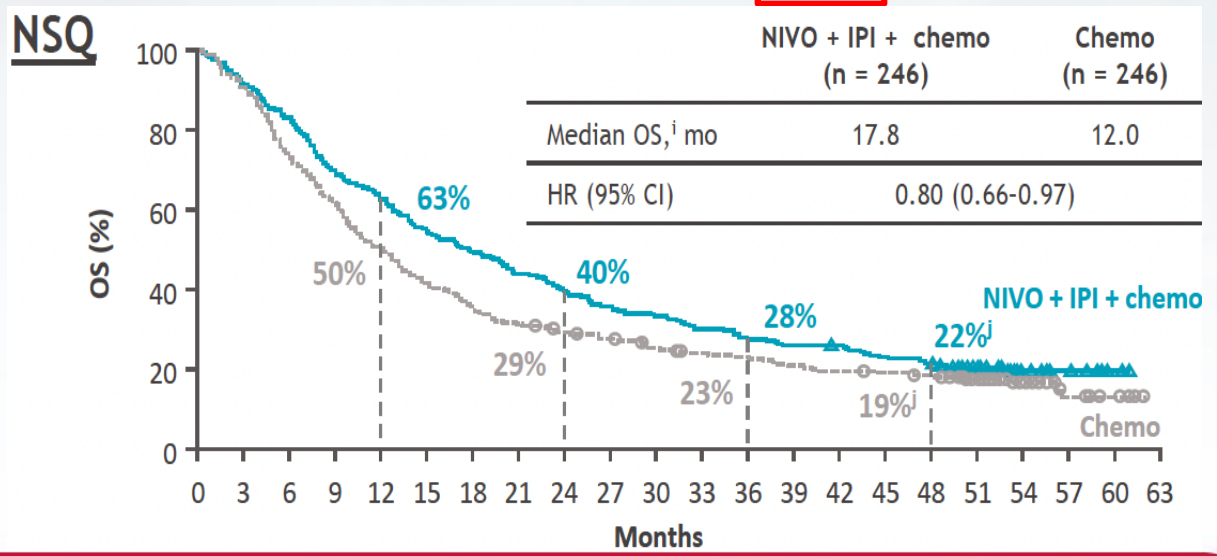






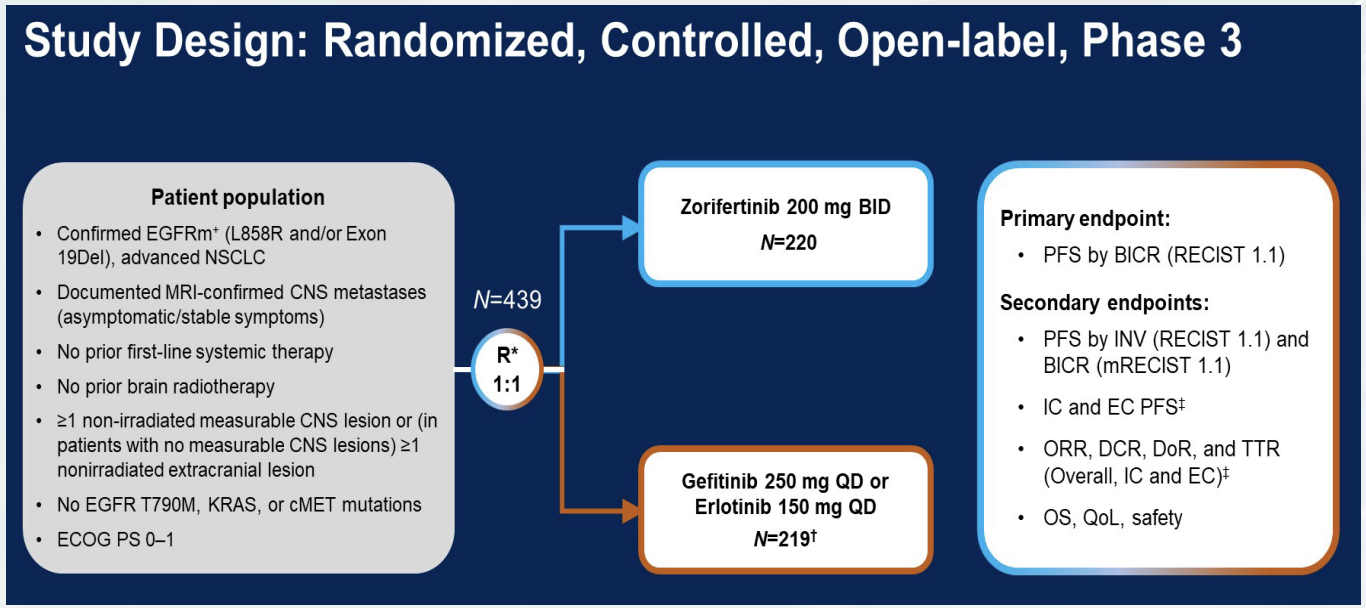


Advanced NSCLC
Not radically treatable stage III and stage IV

- Targeted therapies

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. J Clin Oncol 2023;41(suppl 16):Abstr 9001



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Wu Y, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9001

Study Design: Randomized, Controlled, Open-label, Phase 3

Patient population

- Confirmed EGFRm+ (L858R and/or Exon 19Del), advanced NSCLC
- Documented MRI-confirmed CNS metastases (asymptomatic/stable symptoms)
- No prior first-line systemic therapy
- No prior brain radiotherapy
- ≥1 non-irradiated measurable CNS lesion or (in patients with no measurable CNS lesions) ≥1 nonirradiated extracranial lesion
- No EGFR T790M, KRAS, or cMET mutations
- ECOG PS 0–1

N=439

R* 1:1

Zorifertinib 200 mg BID
N=220

Gefitinib 250 mg QD or Erlotinib 150 mg QD
N=219†

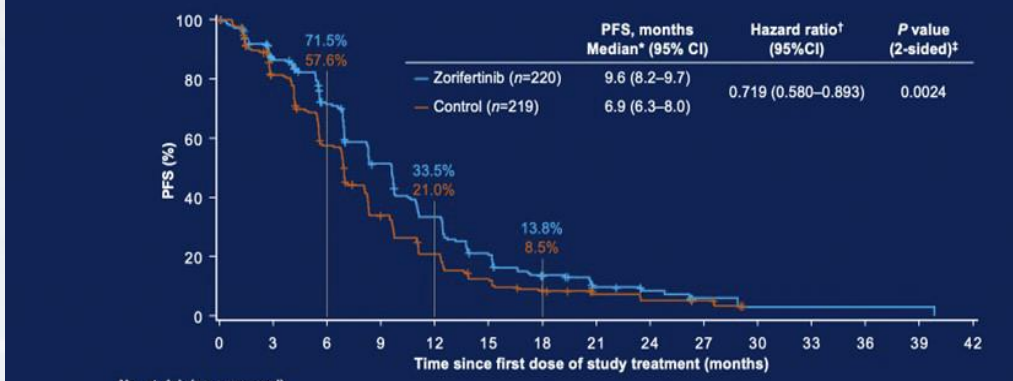
Primary endpoint:

- PFS by BICR (RECIST 1.1)

Secondary endpoints:

- PFS by INV (RECIST 1.1) and BICR (mRECIST 1.1)
- IC and EC PFS‡
- ORR, DCR, DoR, and TTR (Overall, IC and EC)‡
- OS, QoL, safety

Primary Endpoint: PFS Assessed by BICR per RECIST 1.1 (ITT)



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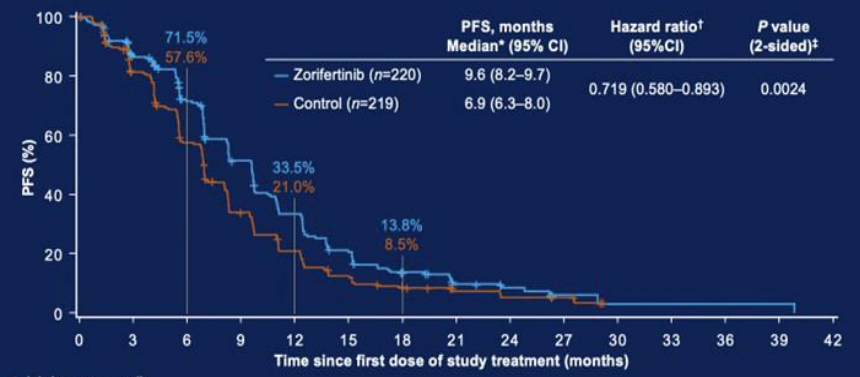
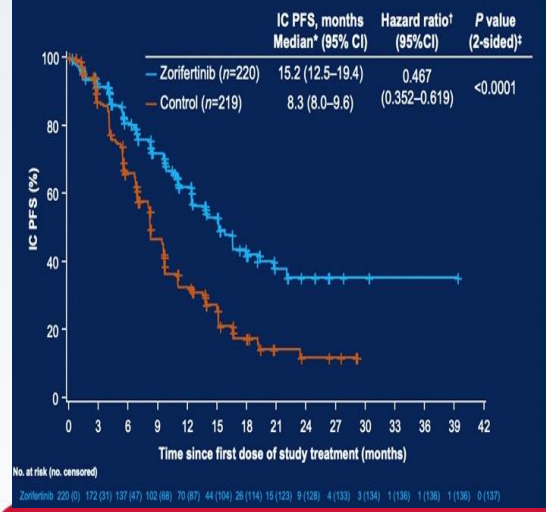
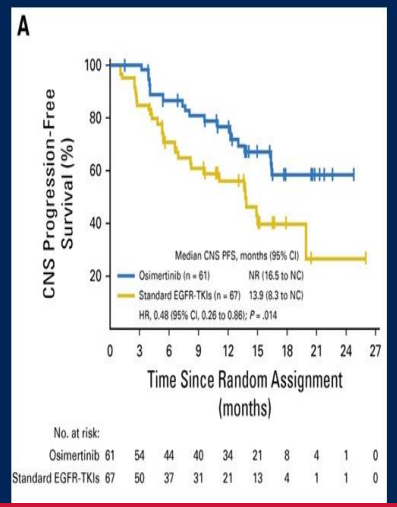


Zorifertinib (AZD3759) IC PFS BICR



Osimertinib BICR-assessed CNS PFS in FLAURA*



* 25% of pts in osi arm and 24% of pts in control arm had prior brain RT

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N=439 → R* 1:1

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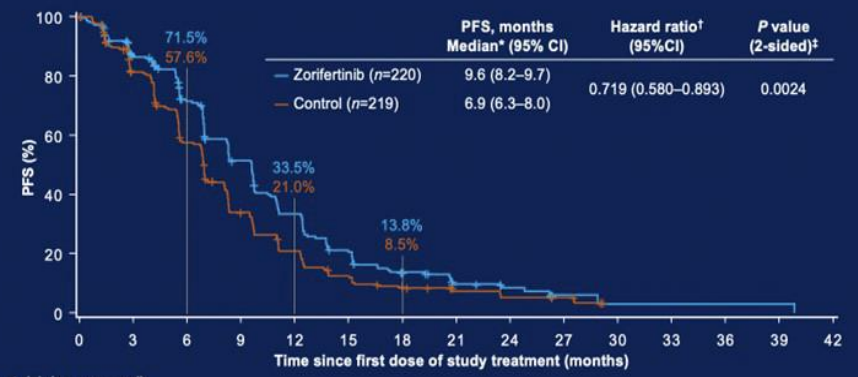
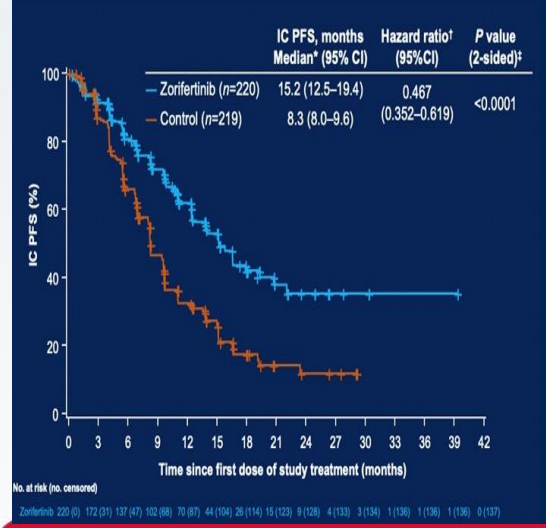


Zorifertinib (AZD3759) IC PFS BICR



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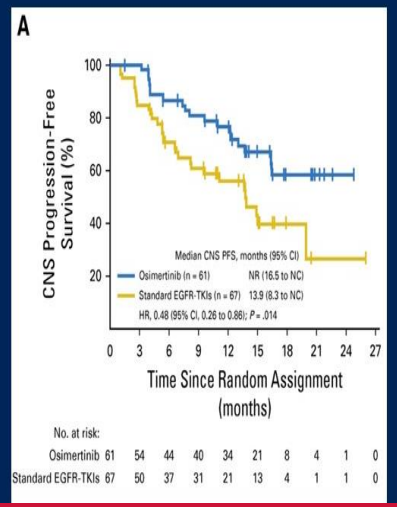
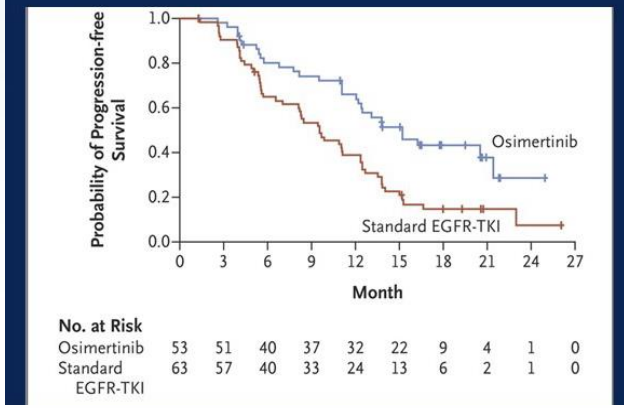


* 25% of pts in osi arm and 24% of pts in control arm had prior brain RT

Osimertinib PFS Pts with CNS Disease in FLAURA (Inv)

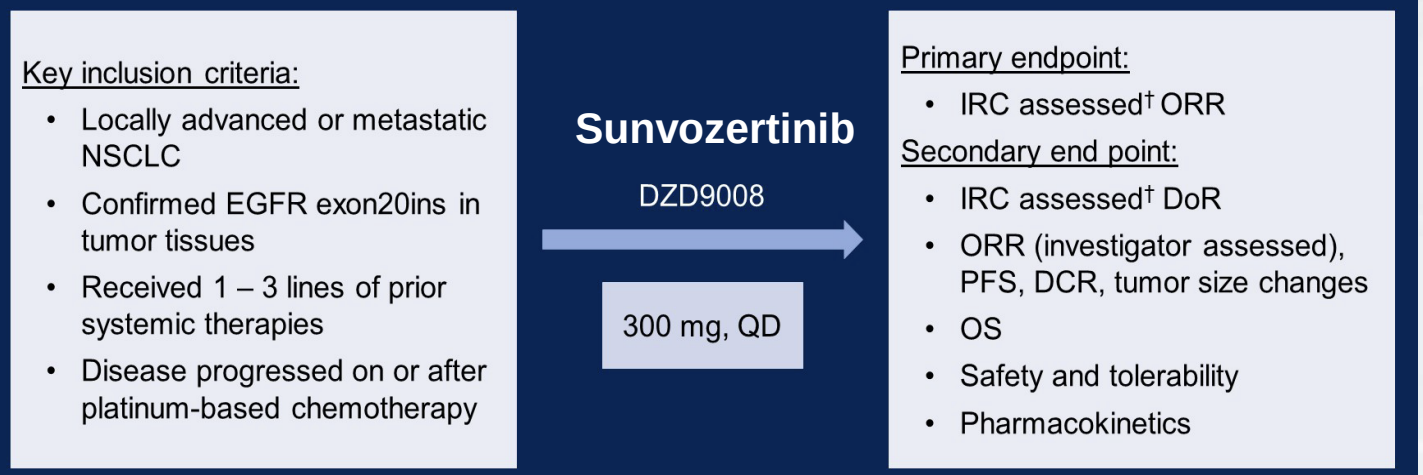


mPFS 15.2 mo. (12.1-21.4) vs 9.6 mo. (7-12.4) (95% CI)

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

Wang M, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9002

WU-KONG6 Study Design



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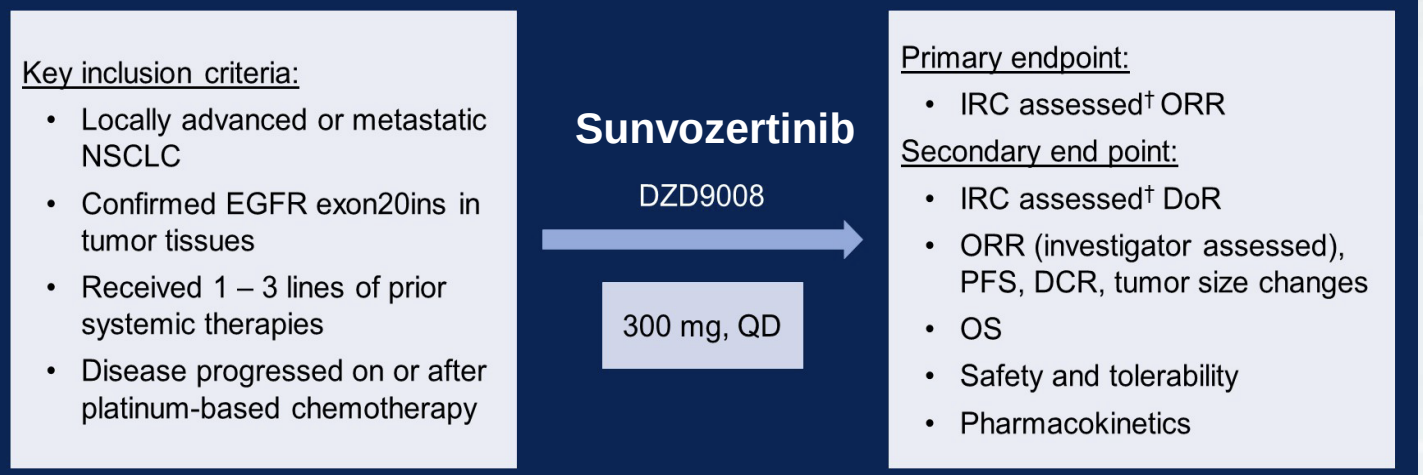

Response	Sunvozertinib (n=97)
ORR, n (%) [95%CI]; p-value	**59 (60.8) [50.4, 70.6]; <0.0001**
BOR, n (%)	
PR (confirmed)	59 (60.8)
SD	26 (26.8)
PD	6 (6.2)
NR	6 (6.2)
DCR, n (%) [95%CI]	85 (87.6) [79.4, 93.4]

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Key inclusion criteria:

- Locally advanced or metastatic NSCLC
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- Disease progressed on or after platinum-based chemotherapy

Sunvozertinib

DZD9008

300 mg, QD

Primary endpoint:

- IRC assessed† ORR

Secondary end point:

- IRC assessed† DoR
- ORR (investigator assessed), PFS, DCR, tumor size changes
- OS
- Safety and tolerability
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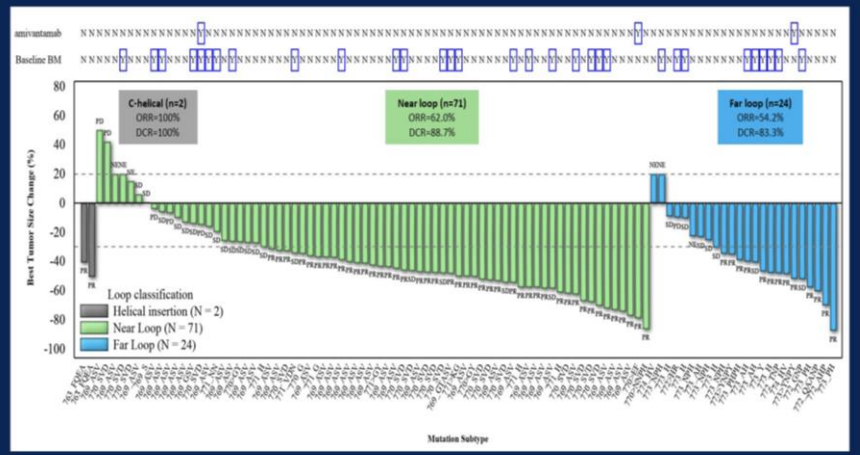
Anti-tumor Efficacy in Different EGFR Exon20ins Subtypes



- A total of 30 different subtypes of EGFR exon20ins were enrolled. Anti-tumor efficacy was observed regardless of mutation subtypes and insertion locations.

Efficacy

	Mobocertinib[1] (N=114)	Amivantamab[2] (N=81)	Sunvozertinib (DZD9008) (N=97) WUKONG6[3]
Investigator assessed			
ORR, %	35%	36%	46.4%
Disease control rate, %	78%	73%	
Duration of response, mos	11.2 mo	-	
IRC assessed (95% CI)			
ORR, % (95% CI)	28% (20-37%)	40% (29-51%)	60.8% (50.4-70.6%)
Disease control rate, %	78%	74%	87.6%
Duration of response, months	17.5 mo	11.1 mo	64.4% responding at median fup of 5.6 mo.
PFS, months	7.3 mo	8.3 mo	-
Brain Mets, ORR (N=)	-	-	44% (N=25)[4]

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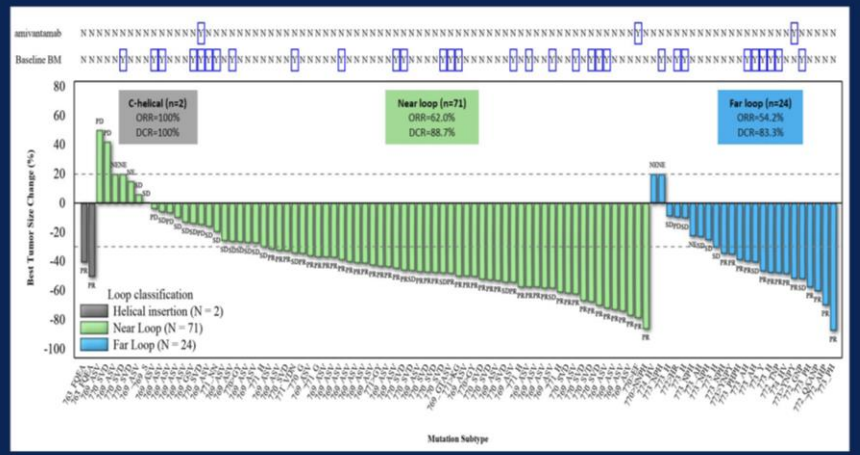

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TEAEs, n (%)	Sunvozertinib (n=104) All grade	Grade ≥3
Diarrhea	**70 (67.3)**	**8 (7.7)**
Blood CPK increased	60 (57.7)	18 (17.3)
Rash	**56 (53.8)**	1 (1.0)
Anemia	51 (49.0)	6 (5.8)
Blood creatine increased	39 (37.5)	0
Paronychia	34 (32.7)	2 (1.9)
Body 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

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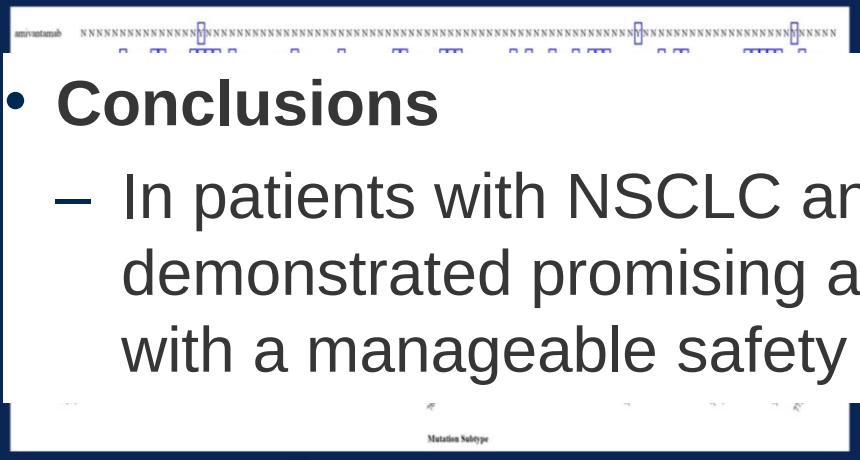

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Mouth ulceration	24 (23.1)	0

- **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

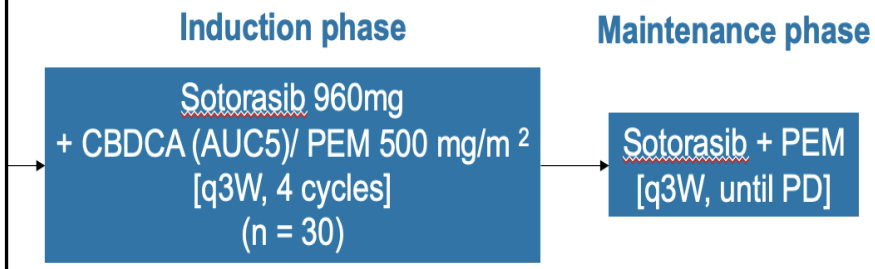
9006: The primary endpoint analysis of SCARLET study: A single-arm, phase II study of sotorasib plus carboplatin-pemetrexed in patients with advanced non-squamous, non-small cell lung cancer with KRAS G12C mutation (WJOG14821L)

Akamatsu H, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9006

SCARLET: study schema

Key inclusion criteria

- Advanced non-Sq, NSCLC
- With KRAS G12C
- Naïve for Cytotoxic chemotherapy and KRAS inhibitor
- With measurable lesion
- ECOG PS 0-1
- Asymptomatic CNS mets allowed



- Primary endpoint; ORR by blinded independent central review (BICR)
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- Translational research; NGS analysis (tissue and plasma [at baseline, 3 wks, and PD])

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Induction phase

Sotorasib 960mg
+ CBDCA (AUC5)/ PEM 500 mg/m ^{2}
[q3W, 4 cycles]
(n = 30)

Maintenance phase

Sotorasib + PEM
[q3W, until PD]

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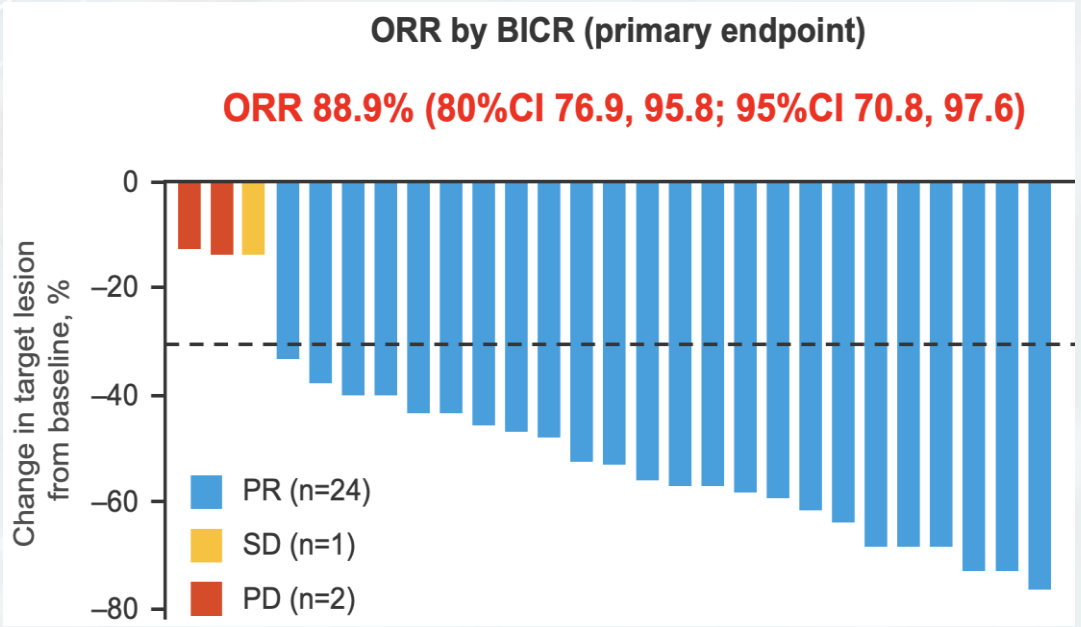

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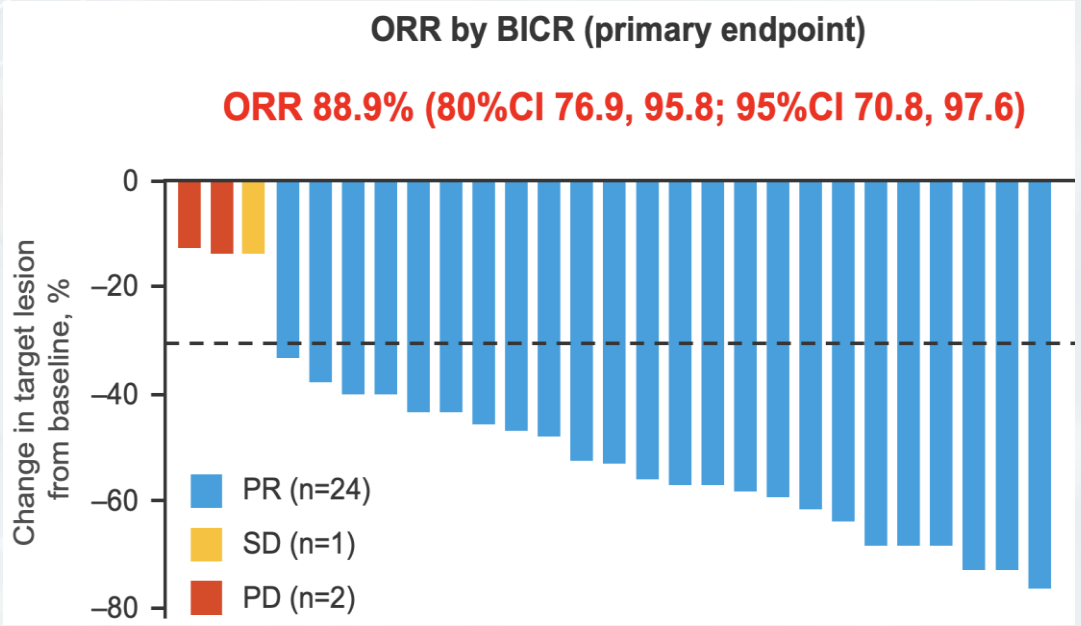

	Sotorasib + carboplatin-pemetrexed (n=27)
mPFS, mo*	5.7
6-mo PFS rate, %	49.6
mOS, mo	NR
6-mo OS rate, %	87.3

	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

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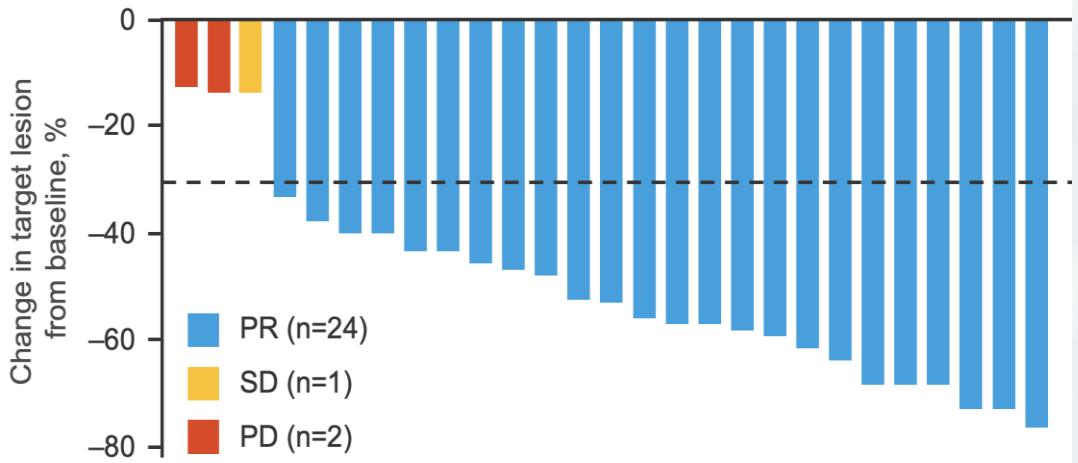
ORR by BICR (primary endpoint)

ORR 88.9% (80%CI 76.9, 95.8; 95%CI 70.8, 97.6)



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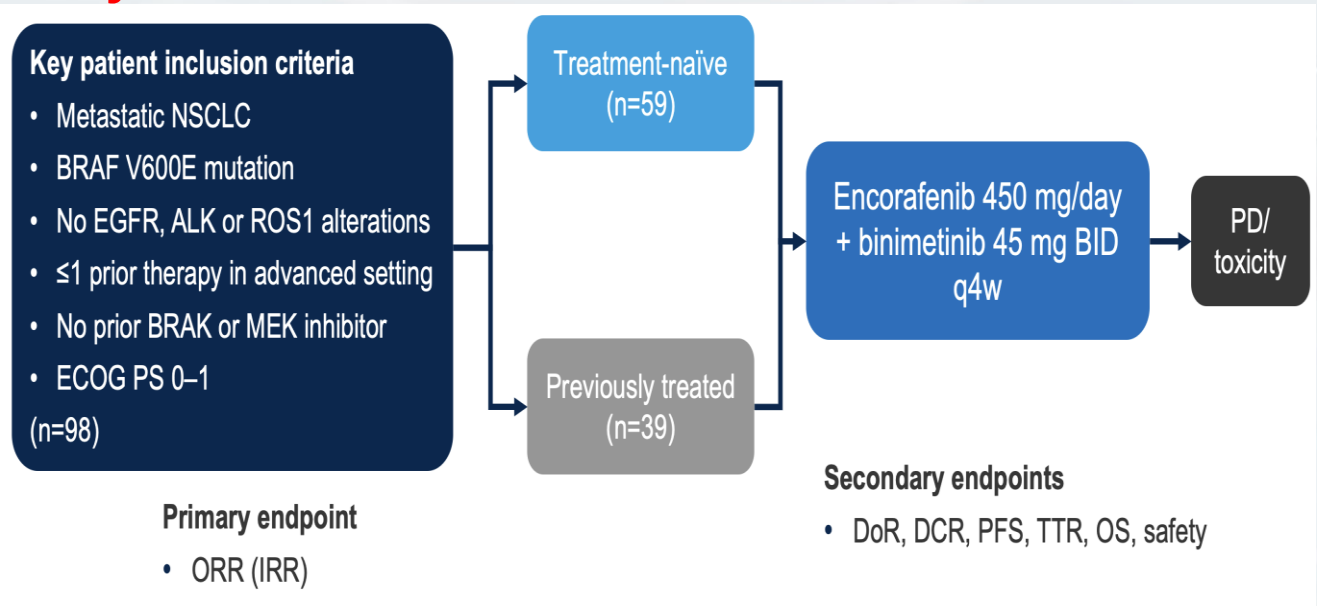
mPFS, mo	7.5	5.7	NR

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)

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. J Clin Oncol 2023;41(suppl 16):Abstr 9018



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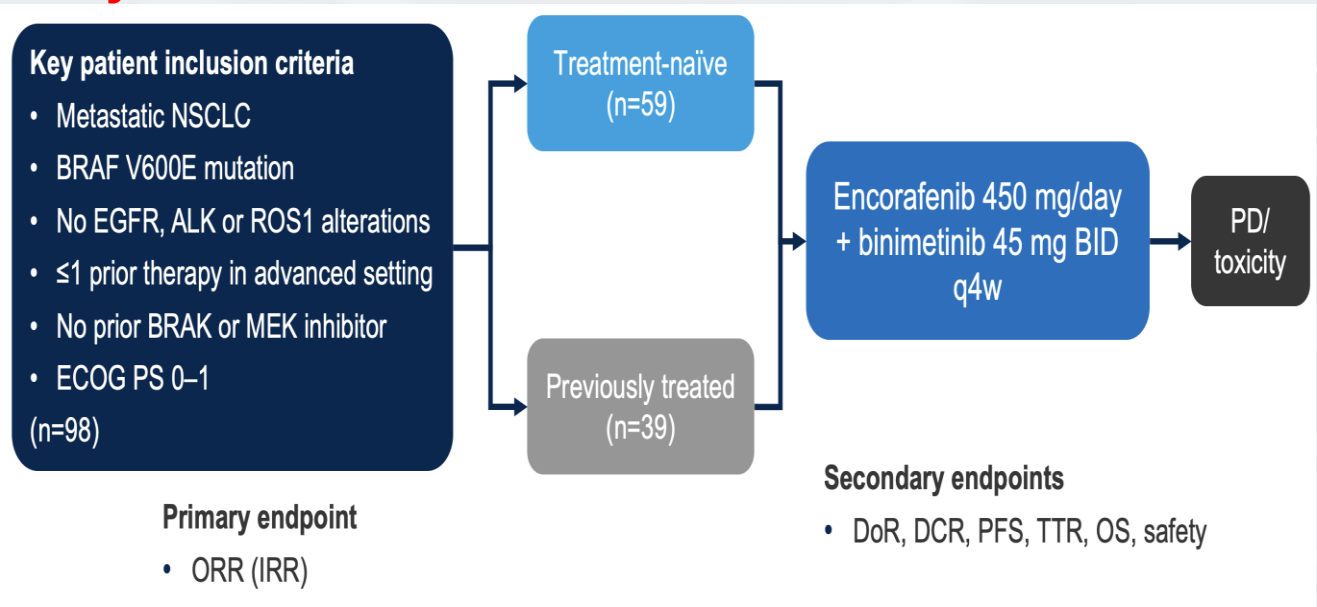

Response	Treatment-naïve (n=59)	Previously treated (n=39)
ORR,[a] % (95%CI)	**75 (62, 85)**	**46 (30, 63)**
BOR, n (%)		
CR	**9 (15)**	**4 (10)**
PR	35 (59)	14 (36)
SD	10 (17)	13 (33)
PD	2 (3)	3 (8)
DCR at 24 weeks, % (95%CI)	64 (51, 76)	41 (26, 58)
mDoR, mo (95%CI)	NE (23.1, NE)	16.7 (7.4, NE)
Duration 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)
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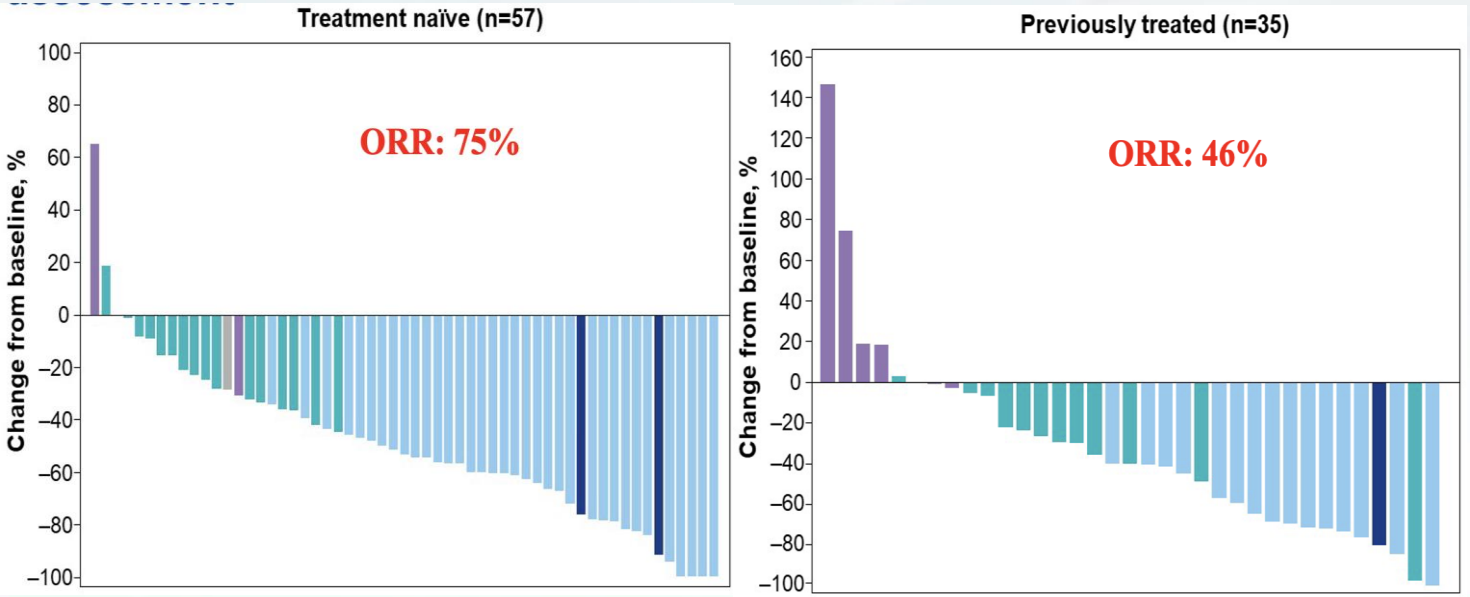

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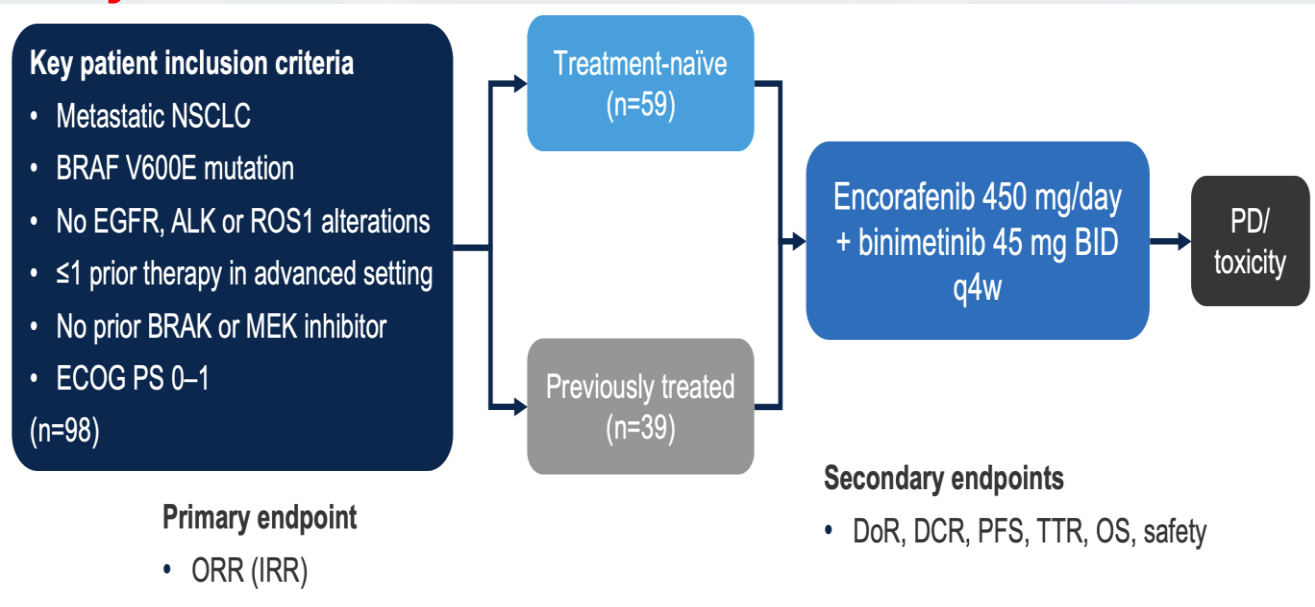

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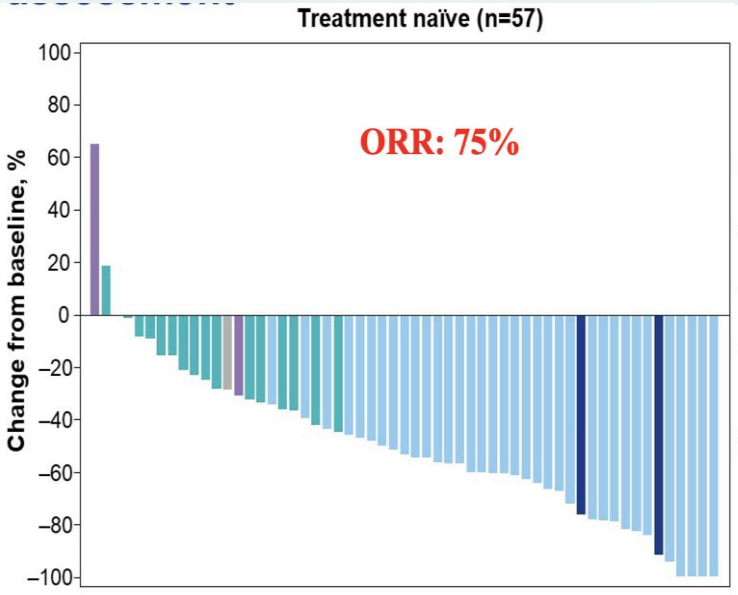

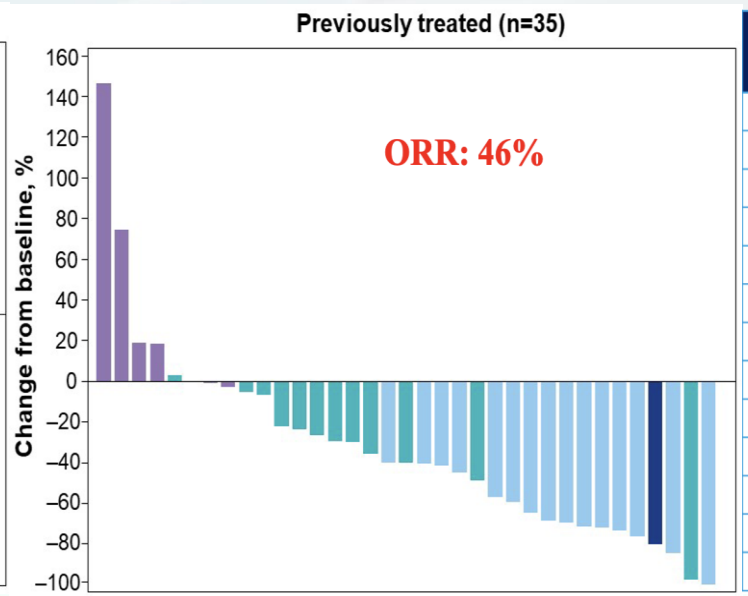

TRAEs occurring in ≥10% of patients, n (%)	Overall (n=98)		
	Any grade	Grade 3	Grade 4
Any TRAEs[a]	**92 (94)**	**37 (38)**	**3 (3)**
Nausea	49 (50)	3 (3)	0
Diarrhea	42 (43)	4 (4)	0
Fatigue	31 (32)	2 (2)	0
Vomiting	28 (29)	1 (1)	0
Anemia	18 (18)	3 (3)	0
Vision blurred	17 (17)	1 (1)	0
Constipation	13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

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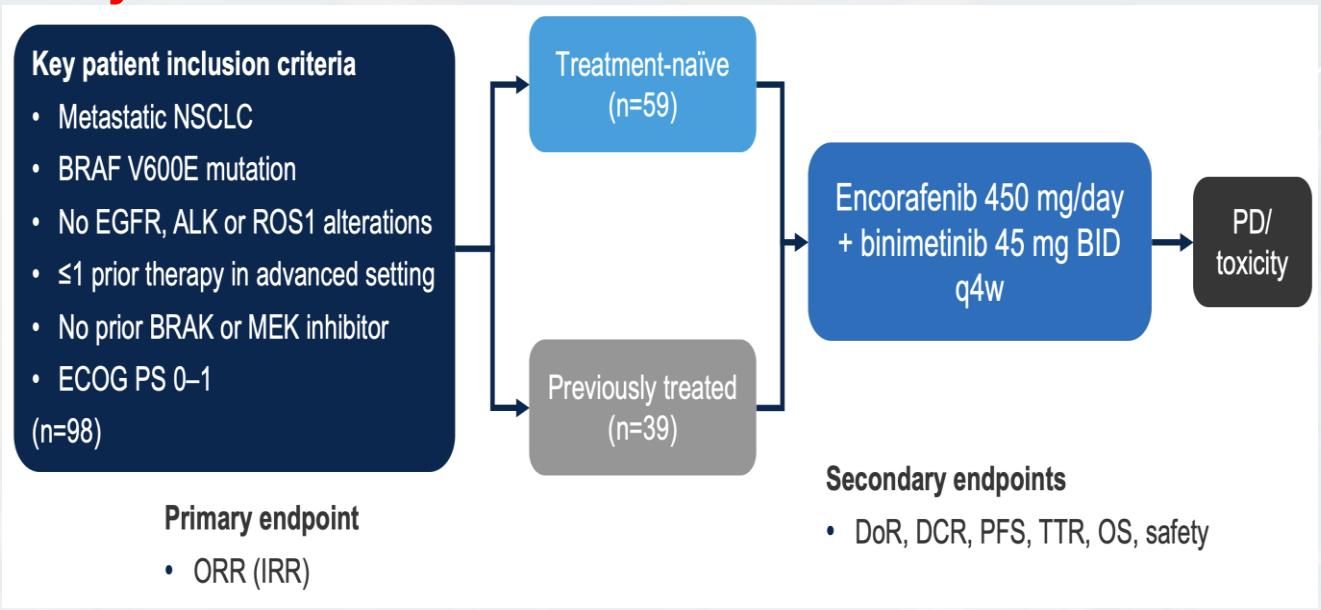

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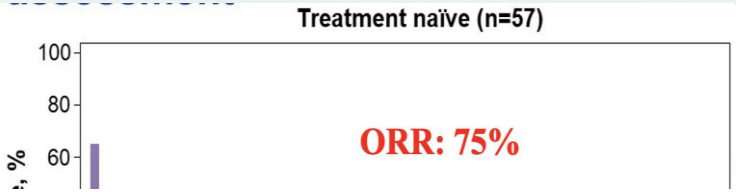
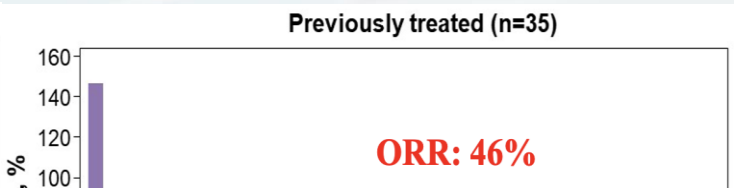
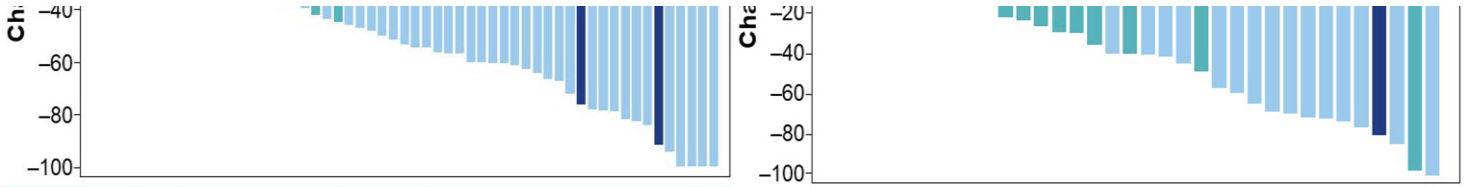




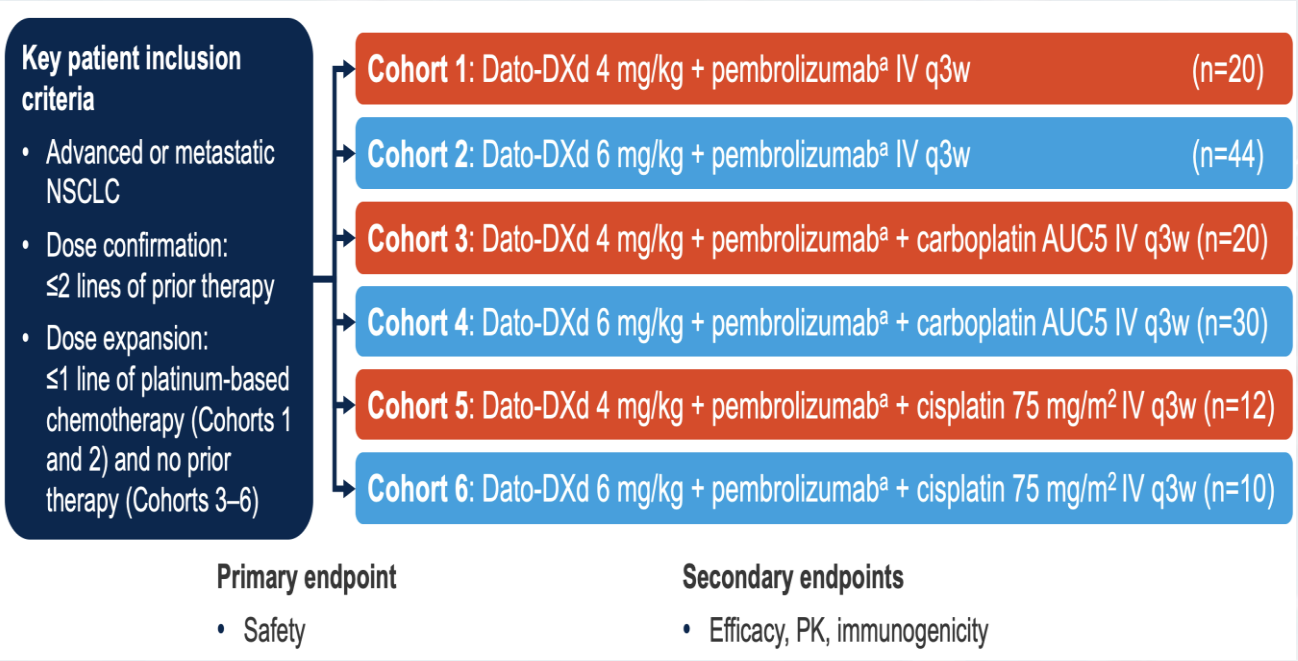
TRAEs occurring in ≥10% of patients, n (%)	Overall (n=98) Any grade	Grade 3	Grade 4
Any TRAEs[a]	**92 (94)**	**37 (38)**	**3 (3)**
Nausea	49 (50)	3 (3)	0
Diarrhea	42 (43)	4 (4)	0
ALT increased	12 (12)	5 (5)	0
AST increased	12 (12)	7 (7)	0
Pruritus	12 (12)	0	0
Blood creatine phosphokinase increased	11 (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**



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) –



Antitumor Activity

	All patients		Patients in 1L	
Response[a]	**Doublet (n=61)[b]**	**Triplet (n=71)[b]**	**Doublet (n=34)[b]**	**Triplet (n=53)[b]**
Confirmed + pending ORR, n (%)[c,d] [95% CI]	23 (38) [26-51]	35 (49) [37-61]	17 (50) [32-68]	30 (57) [42-70]
Confirmed + pending BOR, n (%)[d,e]				
Confirmed CR	0	1 (1)	0	1 (2)
Pending CR[d]	0	0	0	0
Confirmed PR	21 (34)	34 (48)	15 (44)	29 (55)
Pending PR[d]	2 (3)	0	2 (6)	0
SD, n (%)[f]	30 (49)	27 (38)	16 (47)	18 (34)
DCR, n (%)[g]	51 (84)	62 (87)	31 (91)	48 (91)
Median DOR, months [95% CI]	NE [8.8-NE]	NE [5.8-NE]	NE [5.5-NE]	NE [5.7-NE]

- Goto Y, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9004

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) –

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)

- **Cohort 1**: Dato-DXd 4 mg/kg + pembrolizumab[a] IV q3w (n=20)
- **Cohort 2**: Dato-DXd 6 mg/kg + pembrolizumab[a] IV q3w (n=44)
- **Cohort 3**: Dato-DXd 4 mg/kg + pembrolizumab[a] + carboplatin AUC5 IV q3w (n=20)
- **Cohort 4**: Dato-DXd 6 mg/kg + pembrolizumab[a] + carboplatin AUC5 IV q3w (n=30)
- **Cohort 5**: Dato-DXd 4 mg/kg + pembrolizumab[a] + cisplatin 75 mg/m^2 IV q3w (n=12)
- **Cohort 6**: Dato-DXd 6 mg/kg + pembrolizumab[a] + cisplatin 75 mg/m^2 IV q3w (n=10)

Primary endpoint

- Safety

Secondary endpoints

- Efficacy, PK, immunogenicity

Antitumor Activity

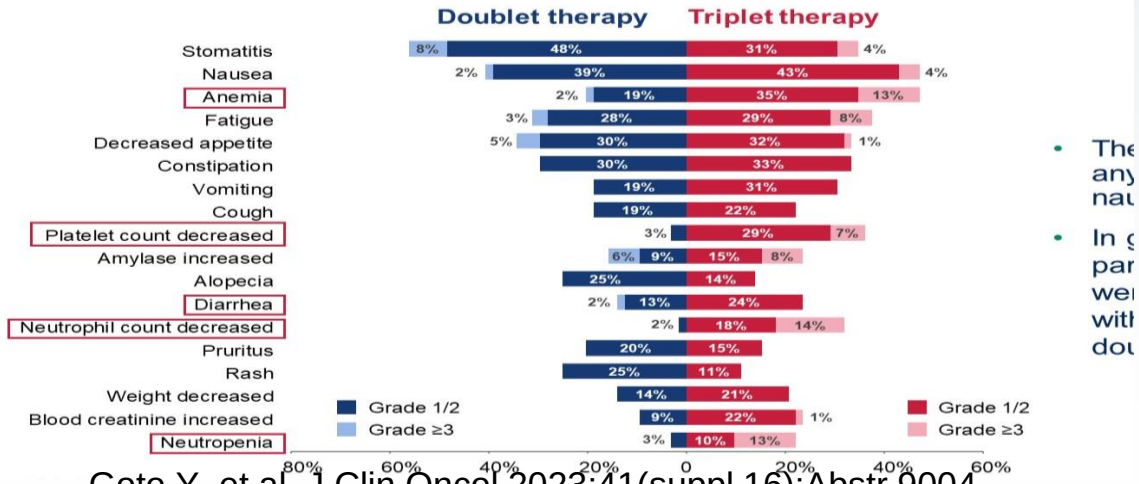
	All patients		Patients in 1L	
Response[a]	**Doublet (n=61)[b]**	**Triplet (n=71)[b]**	**Doublet (n=34)[b]**	**Triplet (n=53)[b]**
Confirmed + pending ORR, n (%)[c,d] [95% CI]	23 (38) [26-51]	35 (49) [37-61]	17 (50) [32-68]	30 (57) [42-70]
Confirmed + pending BOR, n (%)[d,e]				
Confirmed CR	0	1 (1)	0	1 (2)
Pending CR[d]	0	0	0	0
Confirmed PR	21 (34)	34 (48)	15 (44)	29 (55)
Pending PR[d]	2 (3)	0	2 (6)	0
SD, n (%)[f]	30 (49)	27 (38)	16 (47)	18 (34)
DCR, n (%)[g]	51 (84)	62 (87)	31 (91)	48 (91)
Median DOR, months [95% CI]	NE [8.8-NE]	NE [5.8-NE]	NE [5.5-NE]	NE [5.7-NE]

Safety Summary

Event, n (%)	Doublet (n=64)	Triplet (n=72)
TEAEs[a]	62 (97)	72 (100)
Study treatment related[b]	58 (91)	72 (100)
Grade ≥3 TEAEs	34 (53)	55 (76)
Study treatment related[b]	20 (31)	42 (58)
Serious TEAEs	20 (31)	29 (40)
Study treatment related	6 (9)	16 (22)
TEAEs associated with:		
Death[f]	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[g]	15 (23)	20 (28)

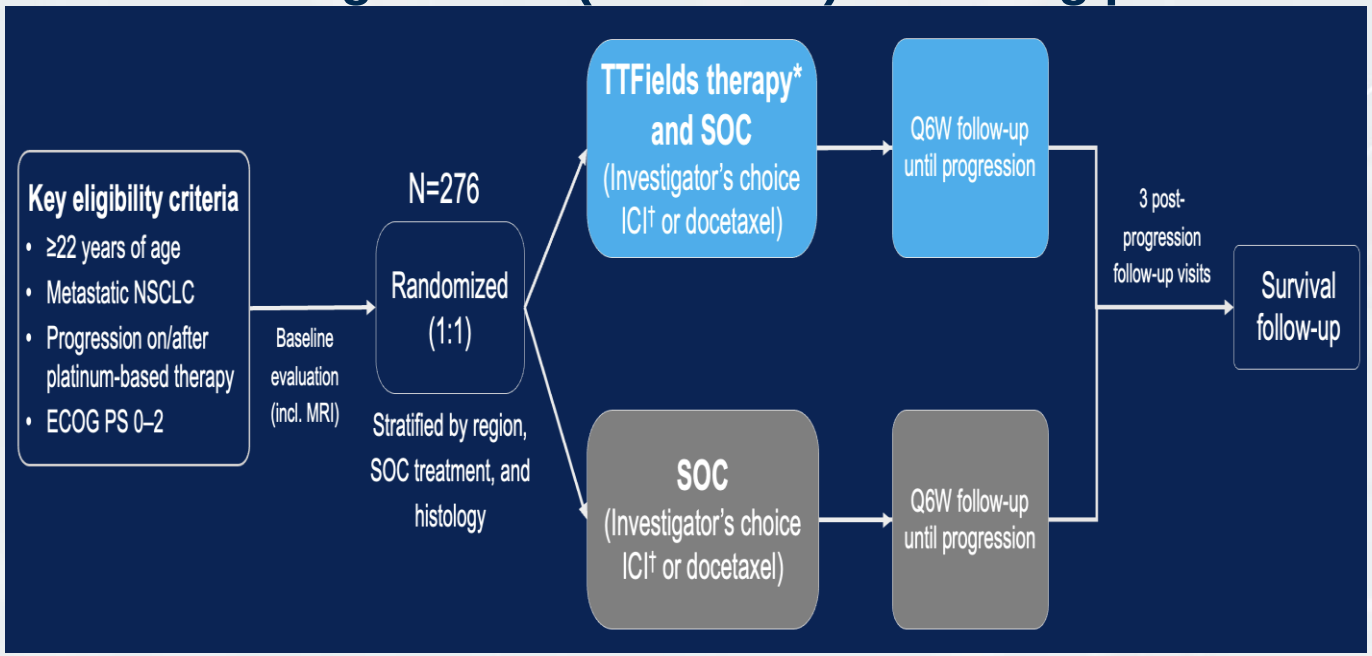
Data cutoff: April 7, 2023

TEAEs Occurring in ≥20% of Patients



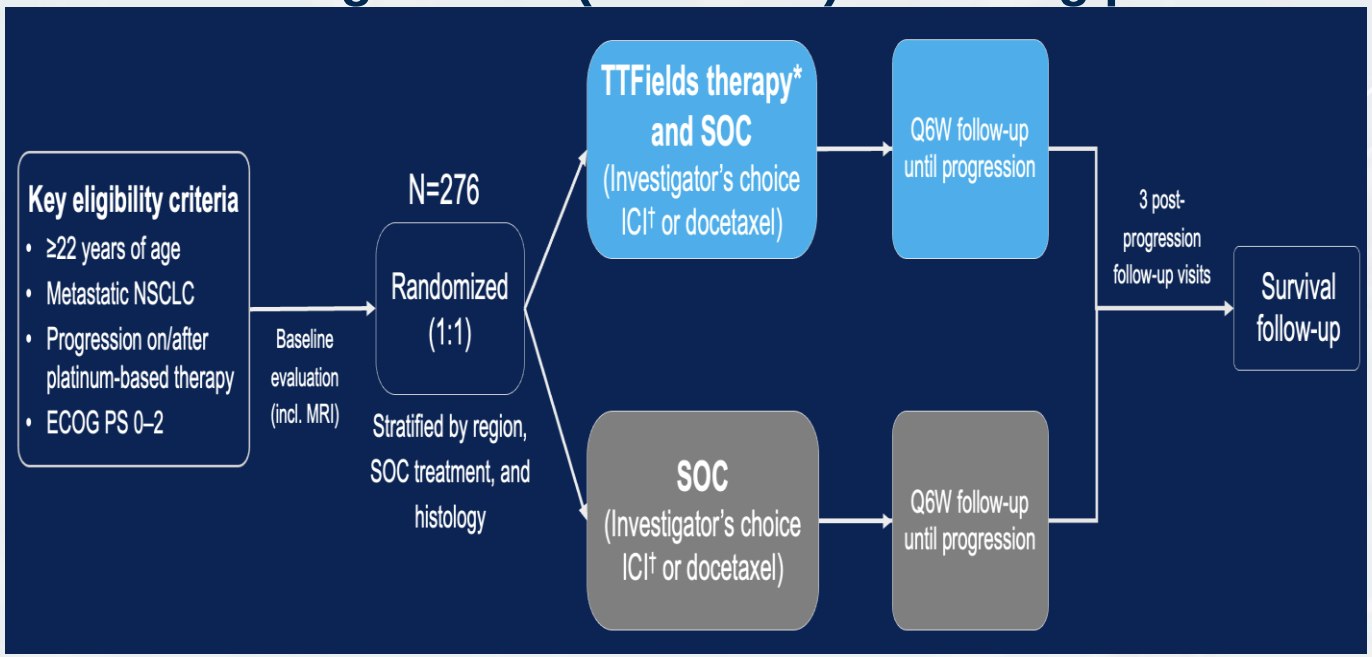
- Goto Y, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9004

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

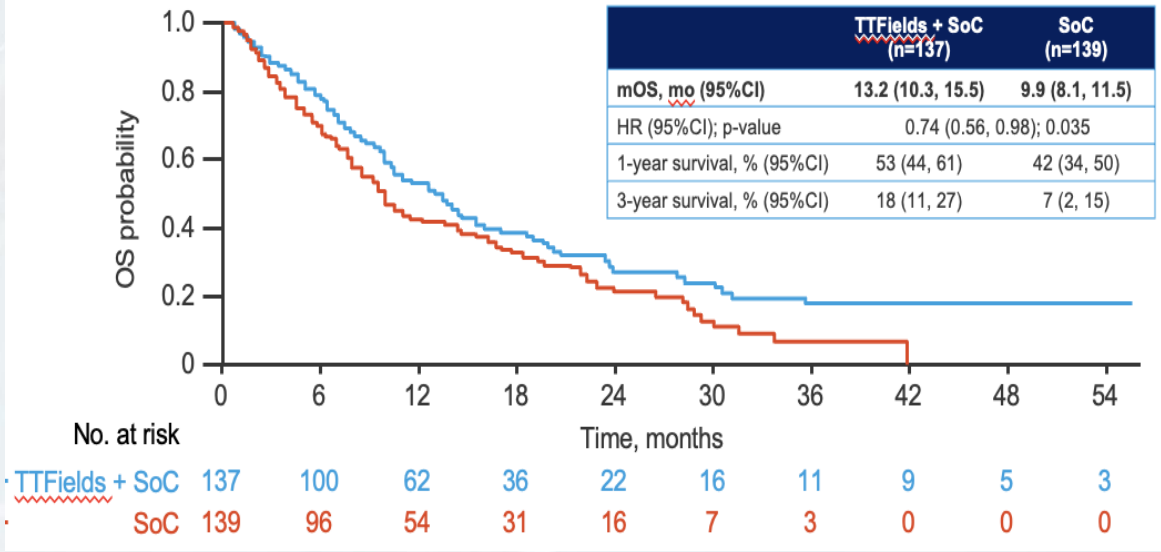


Leal T, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9005

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



Overall survival in the ITT population



	TTFields + SoC (n=137)	SoC (n=139)
mOS, mo (95%CI)	13.2 (10.3, 15.5)	9.9 (8.1, 11.5)
HR (95%CI); p-value	0.74 (0.56, 0.98); 0.035	
1-year survival, % (95%CI)	53 (44, 61)	42 (34, 50)
3-year survival, % (95%CI)	18 (11, 27)	7 (2, 15)

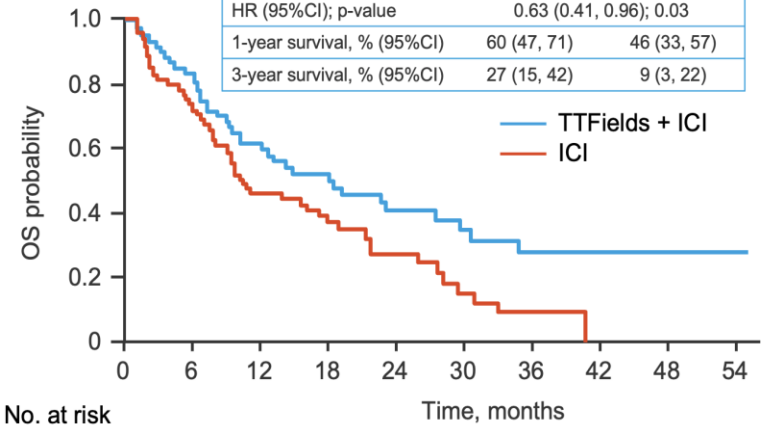
No. at risk

TTFields + SoC	137	100	62	36	22	16	11	9	5	3
SoC	139	96	54	31	16	7	3	0	0	0

Overall survival

ICI

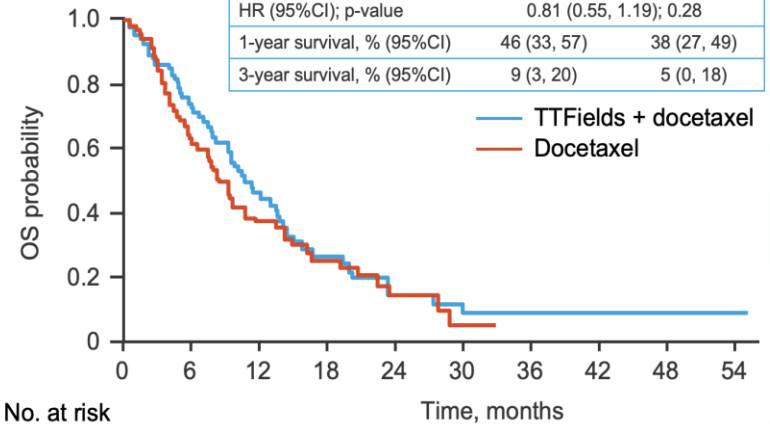
	TTFields + ICI (n=66)	ICI (n=68)
mOS, mo (95%CI)	18.5 (10.6, 30.3)	10.8 (8.2, 18.4)
HR (95%CI); p-value	0.63 (0.41, 0.96); 0.03	
1-year survival, % (95%CI)	60 (47, 71)	46 (33, 57)
3-year survival, % (95%CI)	27 (15, 42)	9 (3, 22)



No. at risk

Docetaxel

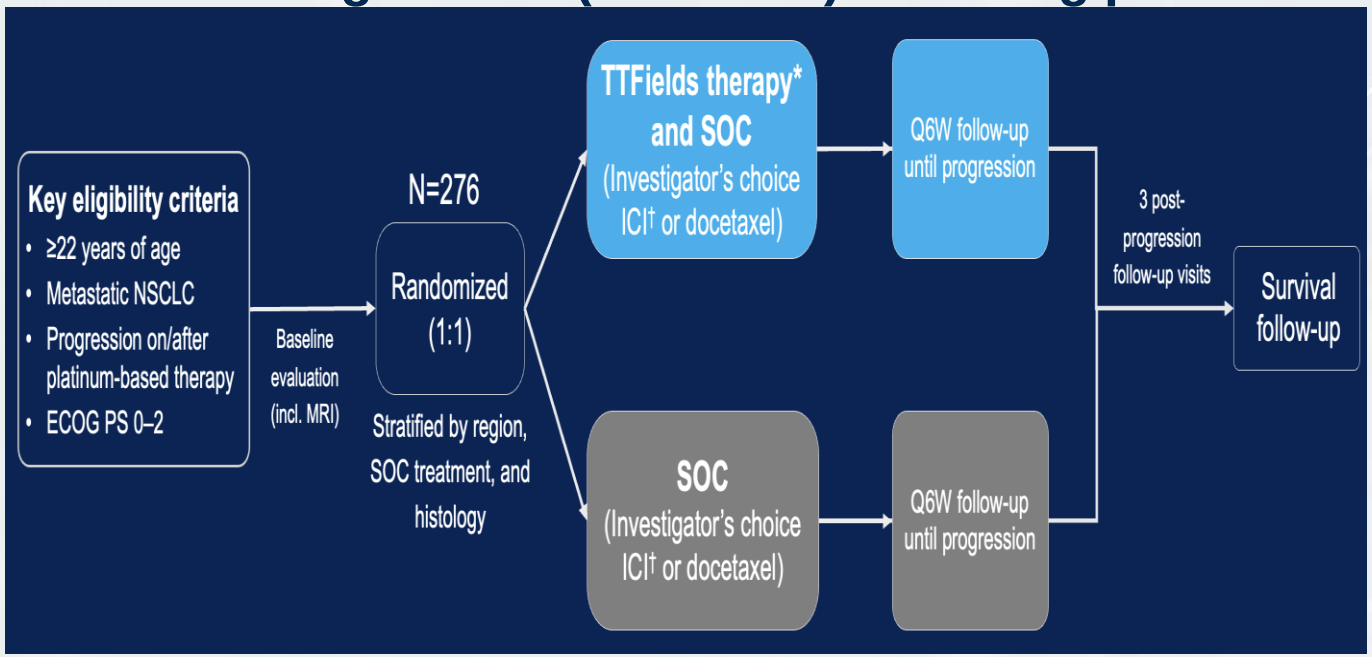
	TTFields + DTX (n=71)	DTX (n=71)
mOS, mo (95%CI)	11.1 (8.2, 14.1)	8.7 (6.3, 11.3)
HR (95%CI); p-value	0.81 (0.55, 1.19); 0.28	
1-year survival, % (95%CI)	46 (33, 57)	38 (27, 49)
3-year survival, % (95%CI)	9 (3, 20)	5 (0, 18)



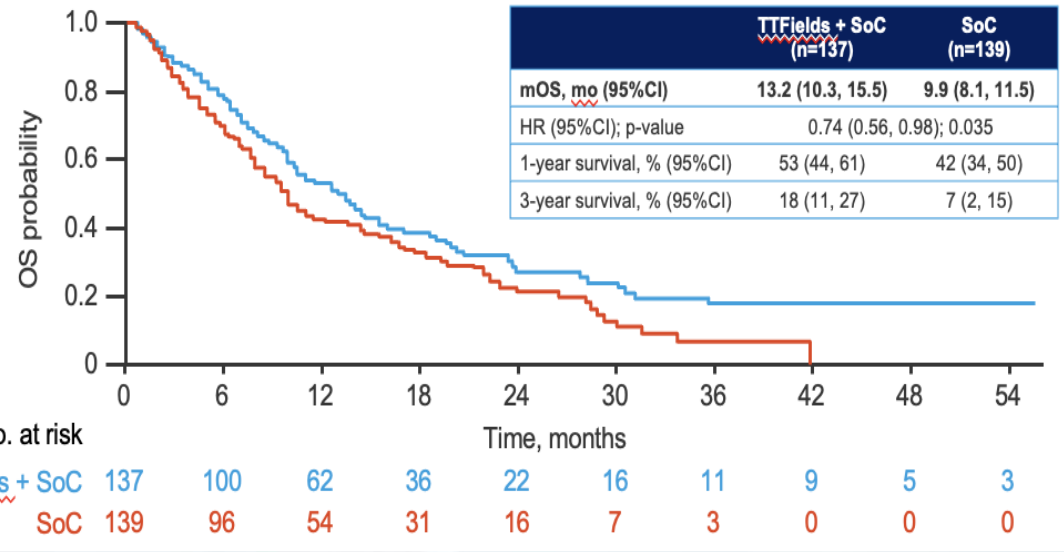
No. at risk

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

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



Overall survival in the ITT population



	TTFields + SoC (n=137)	SoC (n=139)
mOS, mo (95%CI)	13.2 (10.3, 15.5)	9.9 (8.1, 11.5)
HR (95%CI); p-value	0.74 (0.56, 0.98); 0.035	
1-year survival, % (95%CI)	53 (44, 61)	42 (34, 50)
3-year survival, % (95%CI)	18 (11, 27)	7 (2, 15)

No. at risk

TTFields + SoC	137	100	62	36	22	16	11	9	5	3
SoC	139	96	54	31	16	7	3	0	0	0

Overall survival

ICI

	TTFields + ICI (n=66)	ICI (n=68)
mOS, mo (95%CI)	18.5 (10.6, 30.3)	10.8 (8.2, 18.4)
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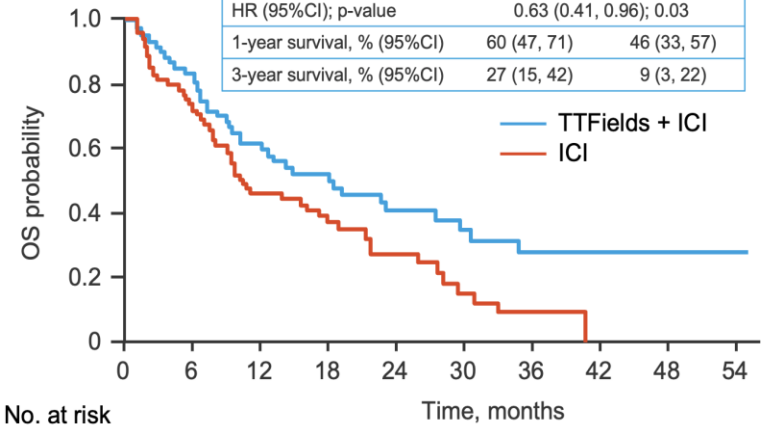
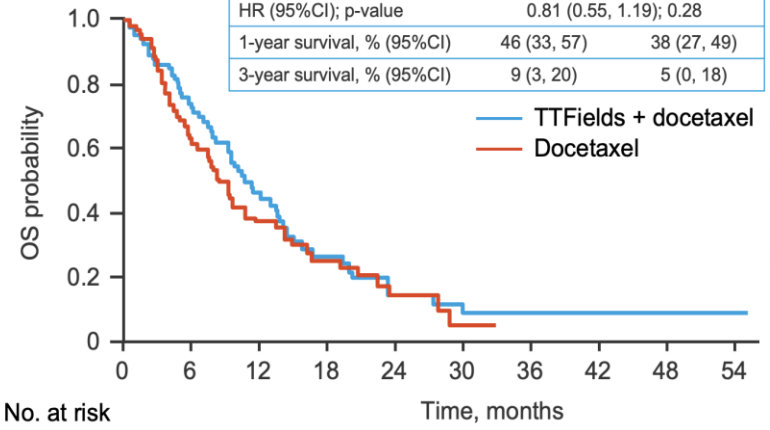


No. at risk

Docetaxel

	TTFields + DTX (n=71)	DTX (n=71)
mOS, mo (95%CI)	11.1 (8.2, 14.1)	8.7 (6.3, 11.3)
HR (95%CI); p-value	0.81 (0.55, 1.19); 0.28	
1-year survival, % (95%CI)	46 (33, 57)	38 (27, 49)
3-year survival, % (95%CI)	9 (3, 20)	5 (0, 18)

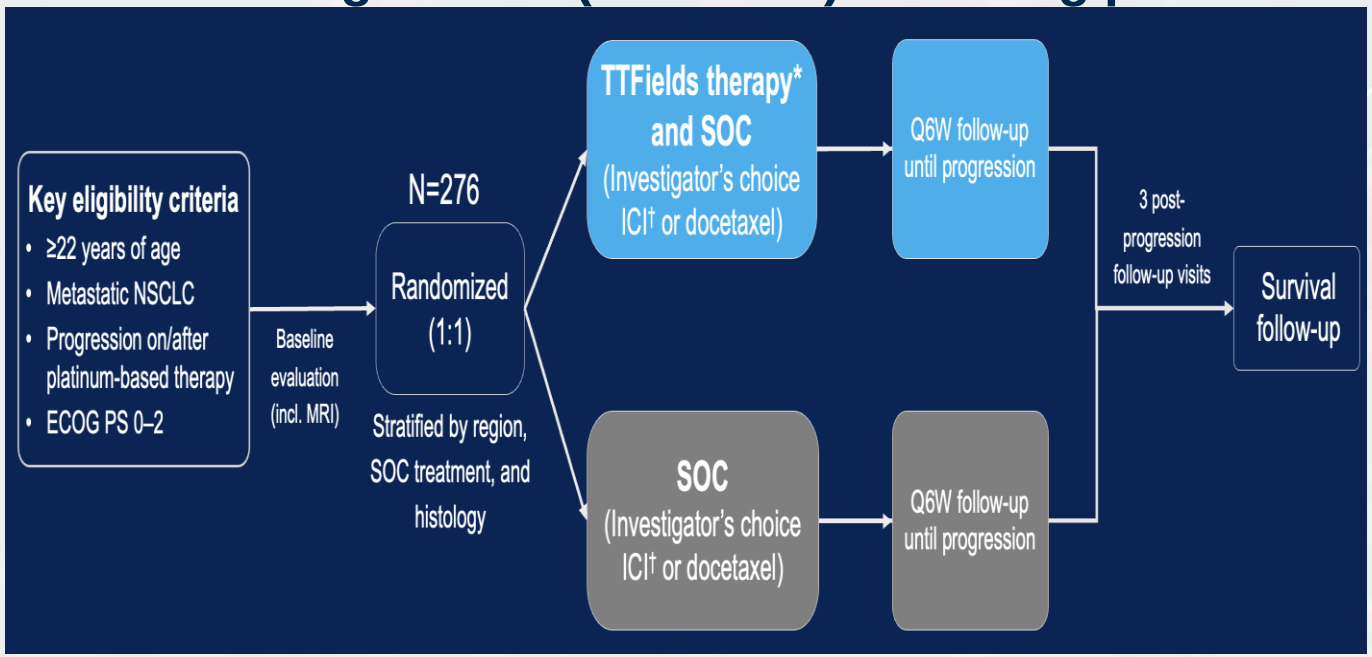


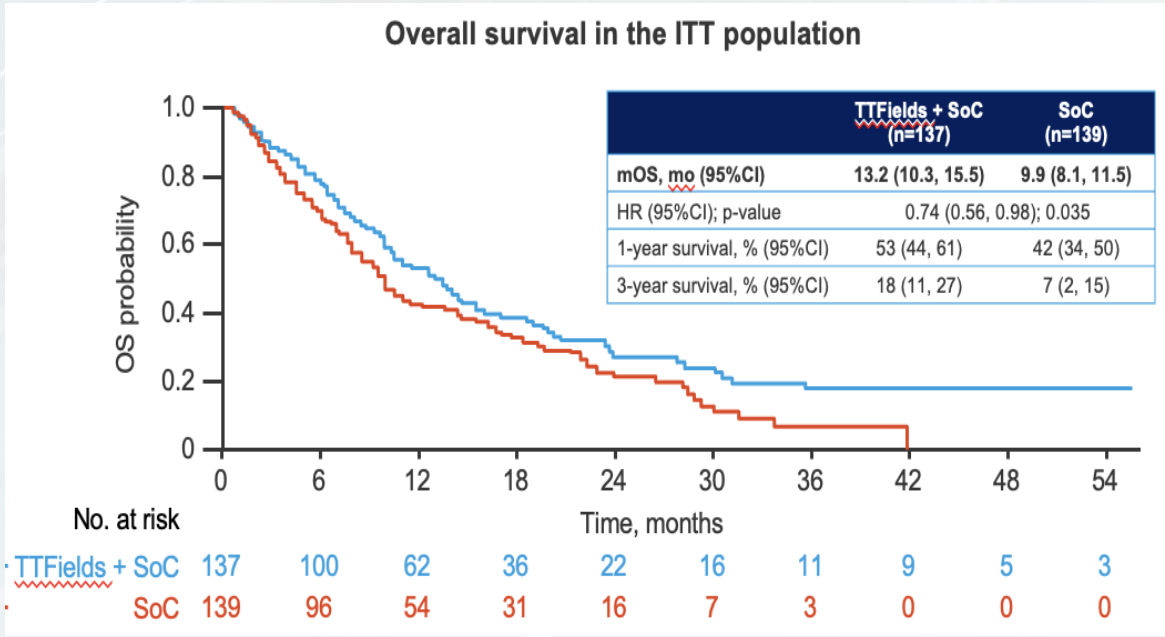
No. at risk

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

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

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





	TTFields + SoC (n=137)	SoC (n=139)
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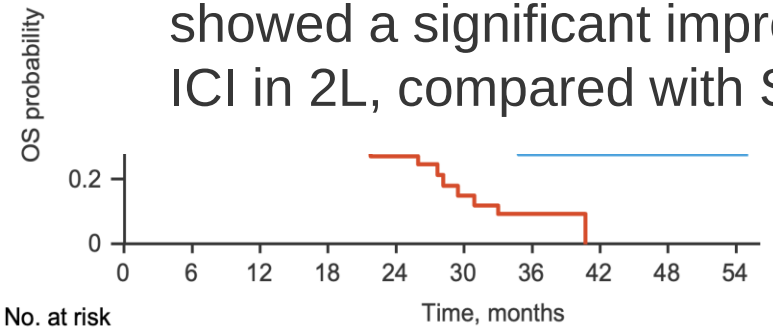
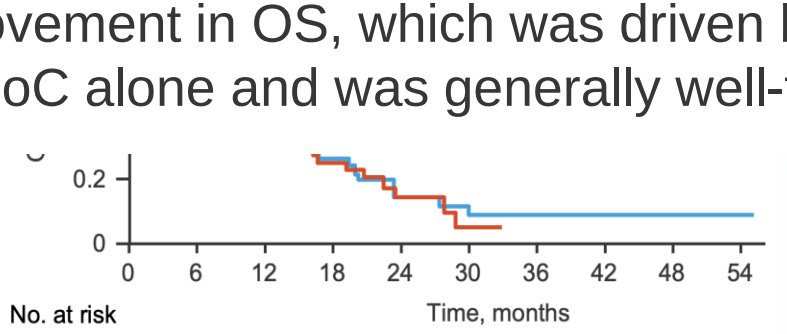
1-year survival, % (95%CI)	53 (44, 61)	42 (34, 50)
3-year survival, % (95%CI)	18 (11, 27)	7 (2, 15)

- **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





	TTFields + SoC	SoC
Led to discontinuation	36	20
Led to death	10	8

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

Other malignancies

SCLC, mesothelioma

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 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)

→ Regimen A: BI 764532 fixed IV dose q3w → Regimen B1: BI 764532 fixed IV dose qw → Regimen B2: BI 764532 step-in dose then fixed dose → 36 months of treatment/PD/toxicity/other

Primary endpoint

- MTD, DLTs

Secondary endpoints

- ORR, PK

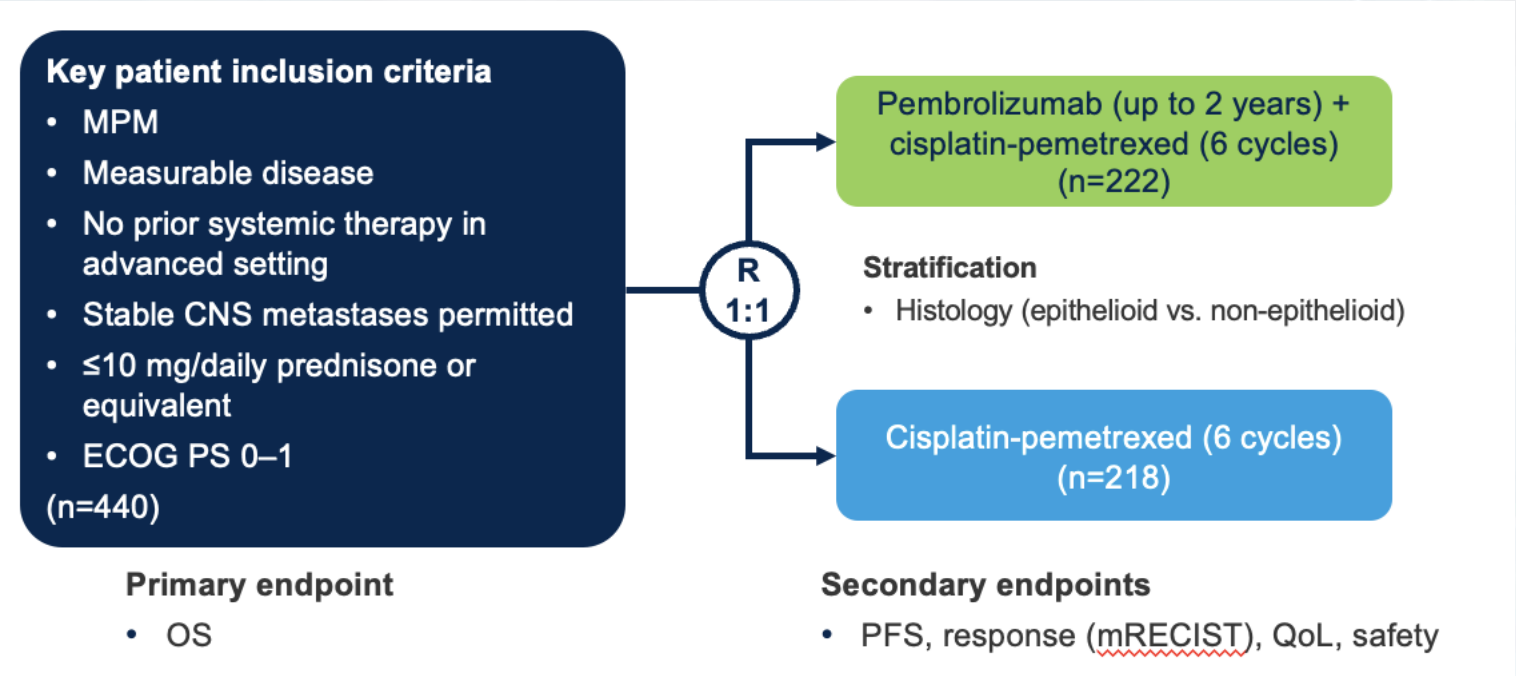
Response, n (%)	All dose levels (n=99)	<90 µg/kg (n=28)	≥90 µg/kg (n=28)
PR	18 (18)	0	18 (25)
SD	23 (23)	4 (14)	19 (27)
PD	45 (45)	20 (71)	25 (35)
NE	13 (13)	4 (14)	9 (13)
DCR	41 (41)	4 (14)	37 (52)

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

Wermke M, et al. J Clin Oncol 2023;41(suppl 16):Abstr 8502

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

Chu QS, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA8505



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

Chu QS, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA8505

Key patient inclusion criteria

- MPM
- Measurable disease
- No prior systemic therapy in advanced setting
- Stable CNS metastases permitted
- ≤10 mg/daily prednisone or equivalent
- ECOG PS 0–1

(n=440)

R 1:1

- Pembrolizumab (up to 2 years) + cisplatin-pemetrexed (6 cycles) (n=222)
- Cisplatin-pemetrexed (6 cycles) (n=218)

Stratification

- Histology (epithelioid vs. non-epithelioid)

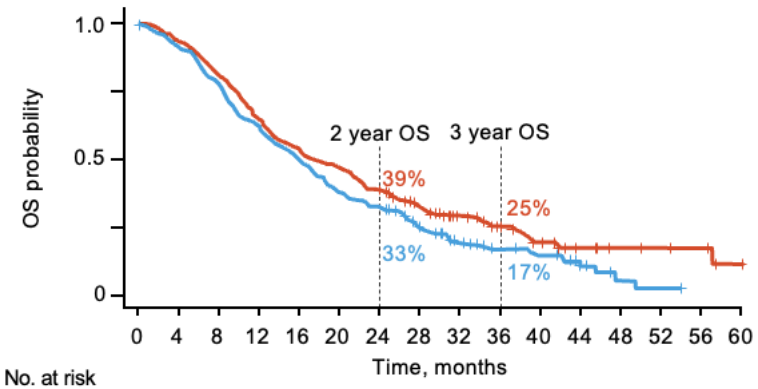
Primary endpoint

- OS

Secondary endpoints

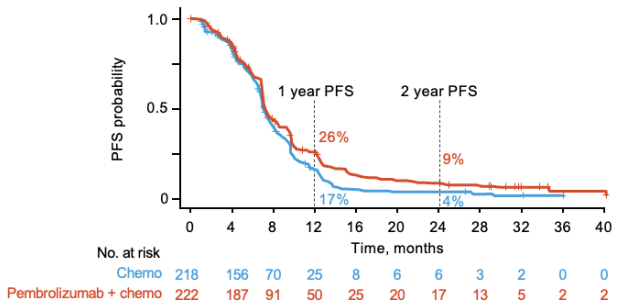
- PFS, response (mRECIST), QoL, safety

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

Chu QS, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA8505

Key patient inclusion criteria

- MPM
- Measurable disease
- No prior systemic therapy in advanced setting
- Stable CNS metastases permitted
- ≤10 mg/daily prednisone or equivalent
- ECOG PS 0–1

(n=440)

R 1:1

- Pembrolizumab (up to 2 years) + cisplatin-pemetrexed (6 cycles) (n=222)
- Cisplatin-pemetrexed (6 cycles) (n=218)

Stratification

- Histology (epithelioid vs. non-epithelioid)

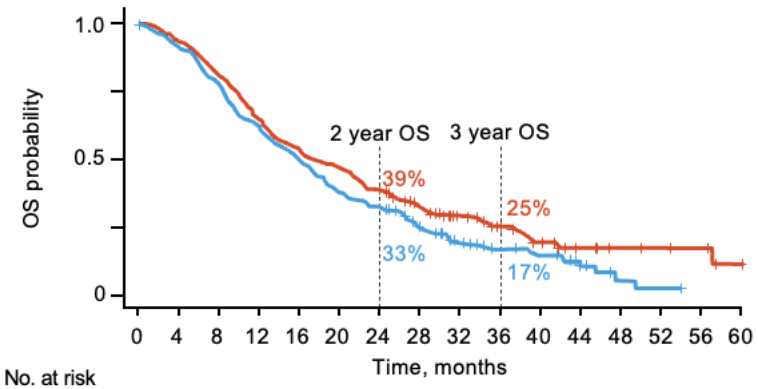
Primary endpoint

- OS

Secondary endpoints

- PFS, response (mRECIST), QoL, safety

Overall survival



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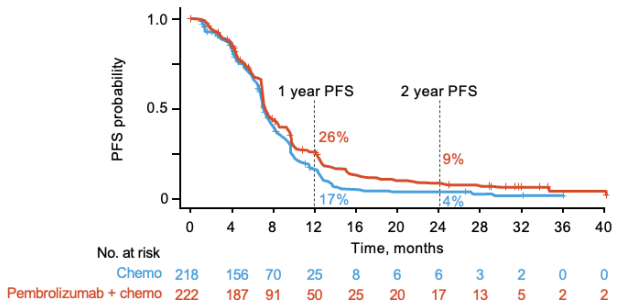
Progression-free survival



	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	

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)	

XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Muchas gracias