IASLC 2023 World Conference on Lung Cancer

SEPTEMBER 9-12, 2023 | SINGAPORE

Adjuvant/Neo-adjuvant Systemic Therapy

Heather Wakelee, MD, FASCO
Stanford University Cancer Institute

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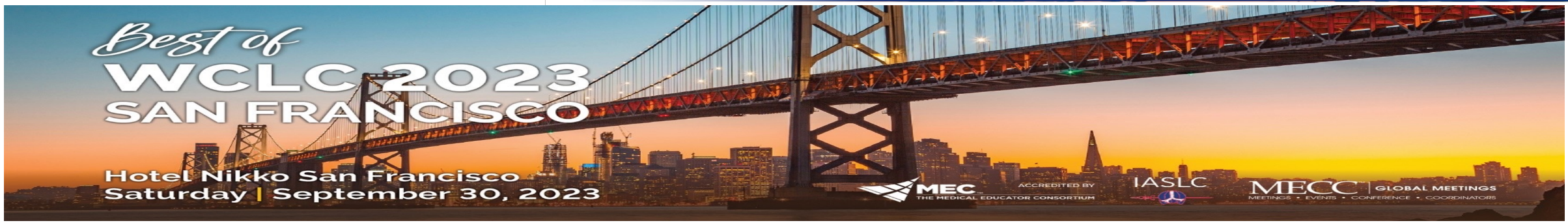


OA12.05: *Surgical outcomes with neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in resectable NSCLC (AEGEAN) – Dr. Kratz*

OA12.06: Neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in resectable EGFR-mutated NSCLC (AEGEAN)

MA11.08: IMpower010: Exploratory analysis of tumour mutational burden and disease-free survival with adjuvant atezolizumab in NSCLC

MA11.09: SAKK 16/18: Neoadjuvant chemotherapy, durvalumab and immune-modulatory RT in Stage III(N2) NSCLC. Surgical interim analysis

MA 11.11: Drug tolerant persister (DTP) to neoadjuvant osimertinib in resectable NSCLC harbouring *EGFR* mutations (NORA)

Peri-Operative IO

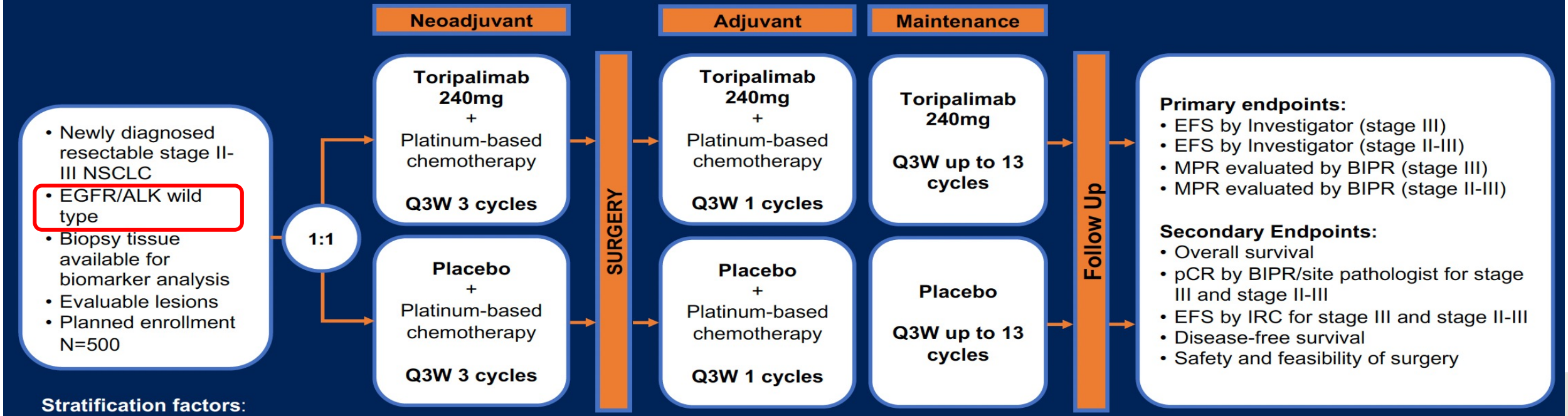
NEOCOAST

KN671

AEGEAN

Neotorch Study Design

- Neotorch is a randomized, double-blind, placebo-controlled, Phase III trial evaluating the efficacy and safety of perioperative toripalimab plus chemotherapy, followed by toripalimab maintenance vs perioperative chemotherapy alone in resectable stage II/III non-small cell lung cancer (NSCLC)



Stratification factors:
- II vs IIIA vs IIIB
- Lobectomy vs pneumonectomy
- Non-squamous vs squamous
- PD-L1 TC expression: ≥ 1% vs < 1% or non-evaluable

66% PD-L1 >1; 78% squamous

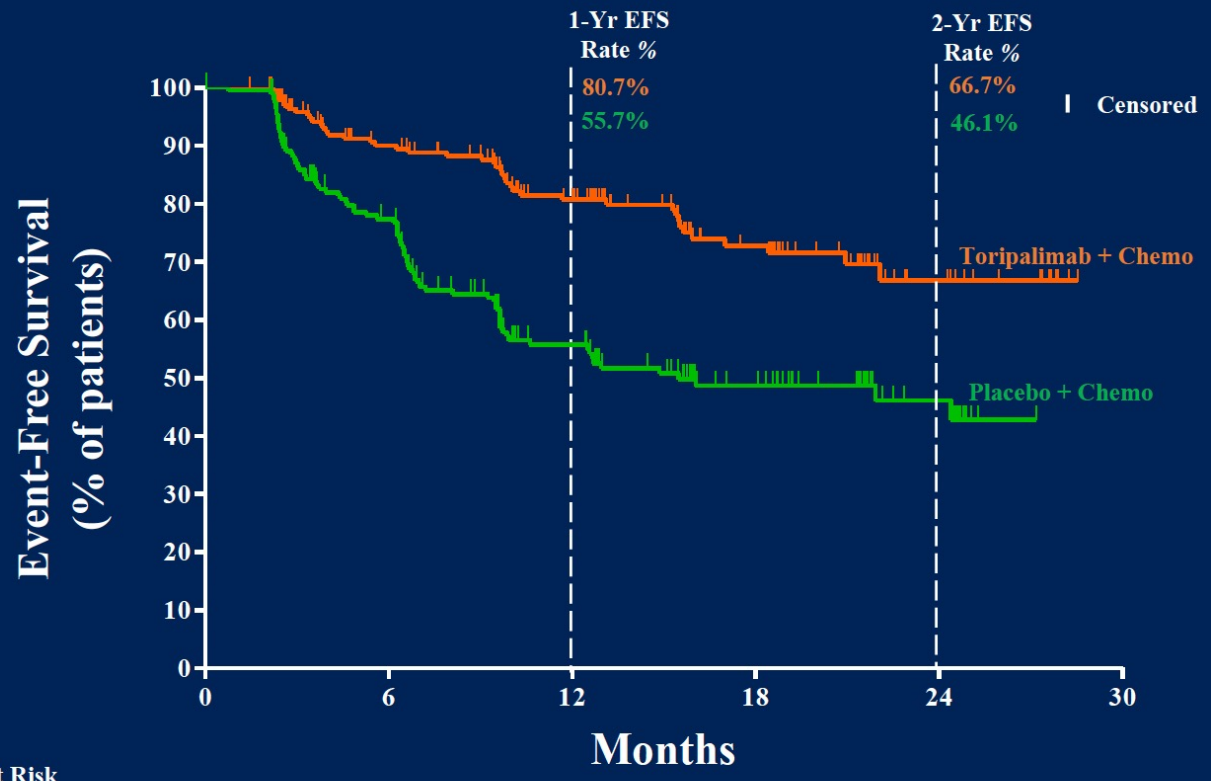
EFS: Event-Free Survival
MPR: Major Pathologic Response
BIPR: Blinded Independent Pathologic Review
pCR: Pathological Complete Response
IRC: Independent Review Committee

Lu, S ASCO Virtual Plenary April 20, 2023, ASCO 2023

NEOTORCH ~25% pCR

Event-Free Survival Analysis by IRC

Intent-to-treat Stage III patients assessed by IRC per RECIST v1.1



No. at Risk						
Toripalimab + Chemo	202	150	107	60	17	0
Placebo + Chemo	202	134	74	38	14	0

	No. of Events/ No. of Patients	Median EFS *mo* (95% CI)
Toripalimab + Chemo	43/202	NE (NE, NE)
Placebo + Chemo	87/202	15.5 (9.9, NE)

Median follow-up: 18.25 months

HR 0.40 (95%CI 0.271, 0.572)

nominal P<0.0001

Data cutoff date: Nov. 30, 2022
NE: not evaluable
HR; Hazard ratio
CI: confidence interval

KEYNOTE-671 Study Randomized, Double-Blind, Phase 3 Trial

Key Eligibility Criteria

- Pathologically confirmed, resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC v8
- No prior therapy
- Able to undergo surgery
- Provision of tumor sample for PD-L1 evaluation[a]
- ECOG PS 0 or 1

~786
R 1:1

Pembrolizumab 200 mg IV Q3W
+
Cisplatin and Gemcitabine[b]
or
Cisplatin and Pemetrexed[c]
for up to 4 cycles

→ **Surgery[d]** → **Pembrolizumab 200 mg IV Q3W for up to 13 cycles**

Placebo IV Q3W
+
Cisplatin and Gemcitabine[b]
or
Cisplatin and Pemetrexed[c]
for up to 4 cycles

→ **Surgery[d]** → **Placebo IV Q3W for up to 13 cycles**

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)

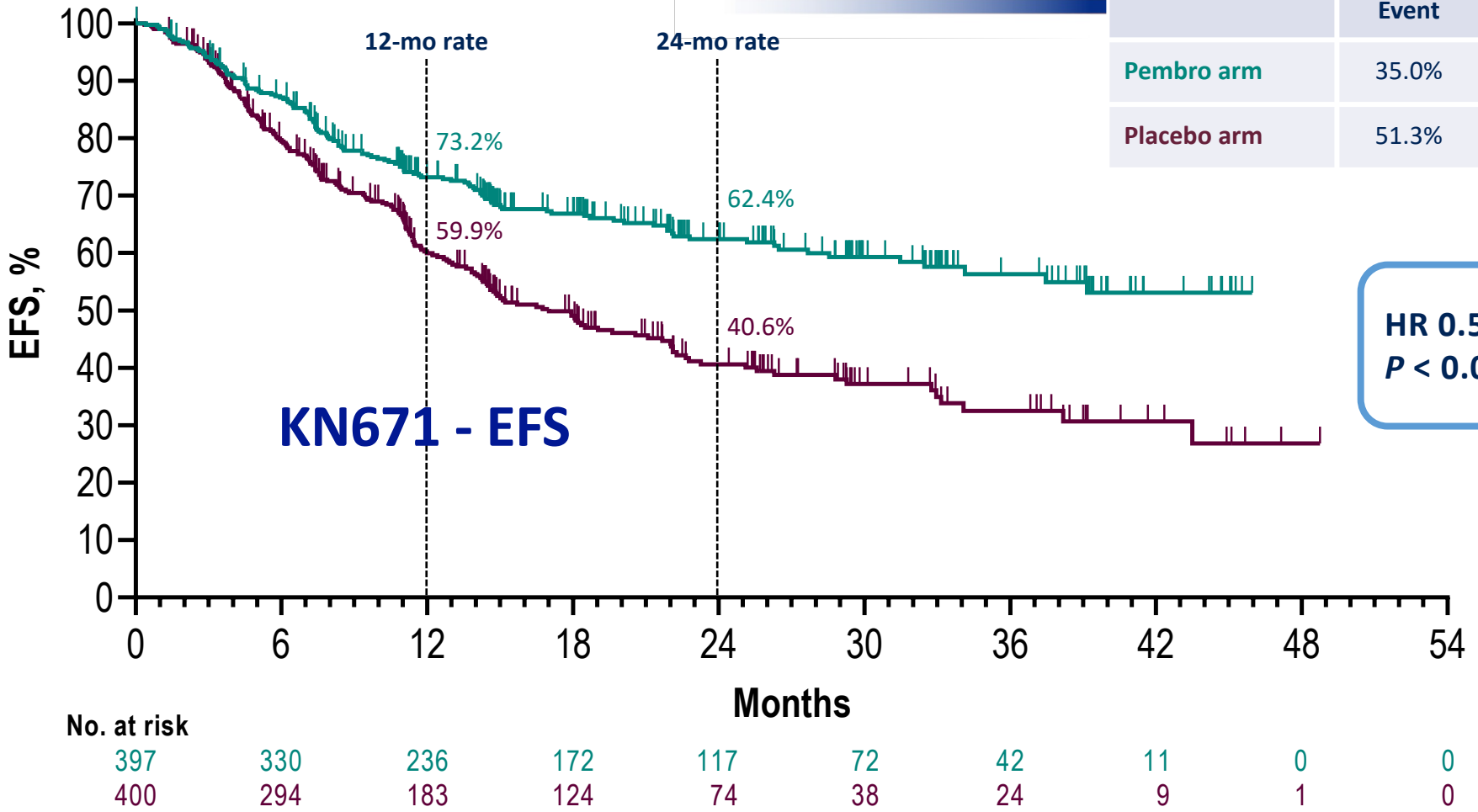
Dual primary end points: EFS per investigator review and OS

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.

~30% stage II; ~1/3 each PD-L1 group (<1, 1-49, 50+)

	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)



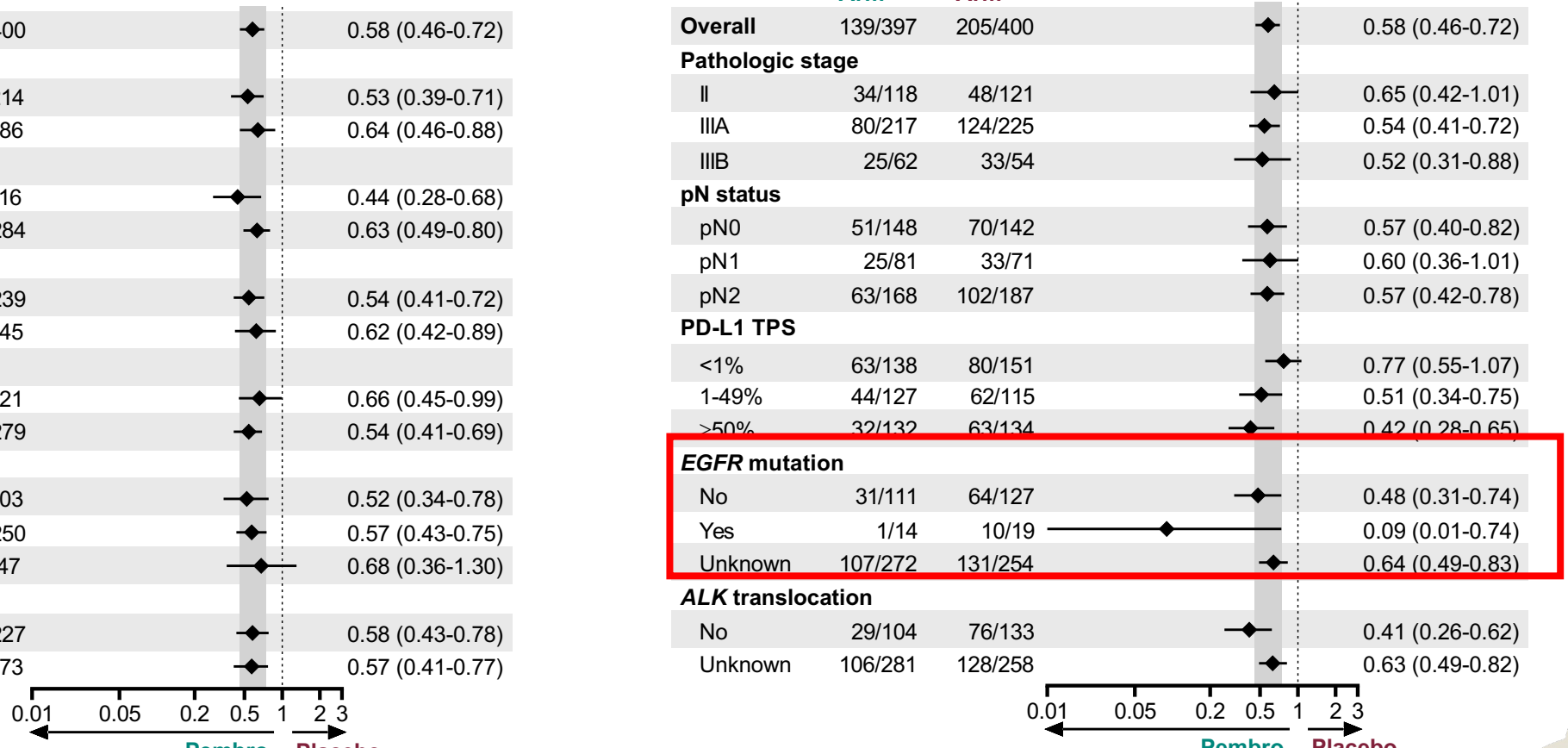
HR 0.58 (95% CI, 0.46-0.72)
***P* < 0.00001**

18% pCR
30% mPR

EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

KN671: Event-Free Survival in Subgroups

Subgroup	Events/participants Pembro Arm	Placebo Arm	Hazard ratio (95% CI)
Overall	139/397	205/400	0.58 (0.46-0.72)
Age			
<65 y	74/221	113/214	0.53 (0.39-0.71)
≥65 y	65/176	92/186	0.64 (0.46-0.88)
Sex			
Female	31/118	55/116	0.44 (0.28-0.68)
Male	108/279	150/284	0.63 (0.49-0.80)
Race			
White	85/250	123/239	0.54 (0.41-0.72)
All others	46/134	70/145	0.62 (0.42-0.89)
Geographic region			
East Asia	43/123	57/121	0.66 (0.45-0.99)
Not east Asia	96/274	148/279	0.54 (0.41-0.69)
Smoking status			
Current	37/96	57/103	0.52 (0.34-0.78)
Former	84/247	128/250	0.57 (0.43-0.75)
Never	18/54	20/47	0.68 (0.36-1.30)
Histology			
Nonsquamous	73/226	107/227	0.58 (0.43-0.78)
Squamous	66/171	98/173	0.57 (0.41-0.77)
Pathologic stage			
II	34/118	48/121	0.65 (0.42-1.01)
IIIA	80/217	124/225	0.54 (0.41-0.72)
IIIB	25/62	33/54	0.52 (0.31-0.88)
pN status			
pN0	51/148	70/142	0.57 (0.40-0.82)
pN1	25/81	33/71	0.60 (0.36-1.01)
pN2	63/168	102/187	0.57 (0.42-0.78)
PD-L1 TPS			
<1%	63/138	80/151	0.77 (0.55-1.07)
1-49%	44/127	62/115	0.51 (0.34-0.75)
≥50%	32/132	63/134	0.42 (0.28-0.65)
***EGFR* mutation**			
No	31/111	64/127	0.48 (0.31-0.74)
Yes	1/14	10/19	0.09 (0.01-0.74)
Unknown	107/272	131/254	0.64 (0.49-0.83)
***ALK* translocation**			
No	29/104	76/133	0.41 (0.26-0.62)
Unknown	106/281	128/258	0.63 (0.49-0.82)



Per the prespecified analysis plan, subgroups with <30 participants were excluded from the forest plot. Subgroups for stage IIIA and IIIB and pN status were post hoc; all other subgroups were prespecified. Data cutoff date for IA1: July 29, 2022.

Study population

- Treatment-naïve
- ECOG PS 0 or 1
- Resectable NSCLC* (stage IIA–IIIB[N2]; AJCC 8th ed)
- Lobectomy, sleeve resection, or bilobectomy as planned surgery*
- Confirmed PD-L1 status†
- No documented *EGFR/ALK* aberrations*

R 1:1

N=802 randomized

Randomization stratified by:

- Disease stage (II vs III)
- PD-L1 expression (≥1% vs <1%)

Durvalumab 1500 mg IV + platinum-based CT‡ Q3W for 4 cycles → Surgery§ → **Durvalumab 1500 mg IV** Q4W for 12 cycles

Placebo IV + platinum-based CT‡ Q3W for 4 cycles → Surgery§ → **Placebo IV** Q4W for 12 cycles

AEGEAN: A Phase 3 Trial of Neoadjuvant Durvalumab + Chemotherapy Followed by Adjuvant Durvalumab in Patients with Resectable NSCLC

~30% stage II; ~ 1/3 each PD-L1 group (0, 1-49, 50+%)

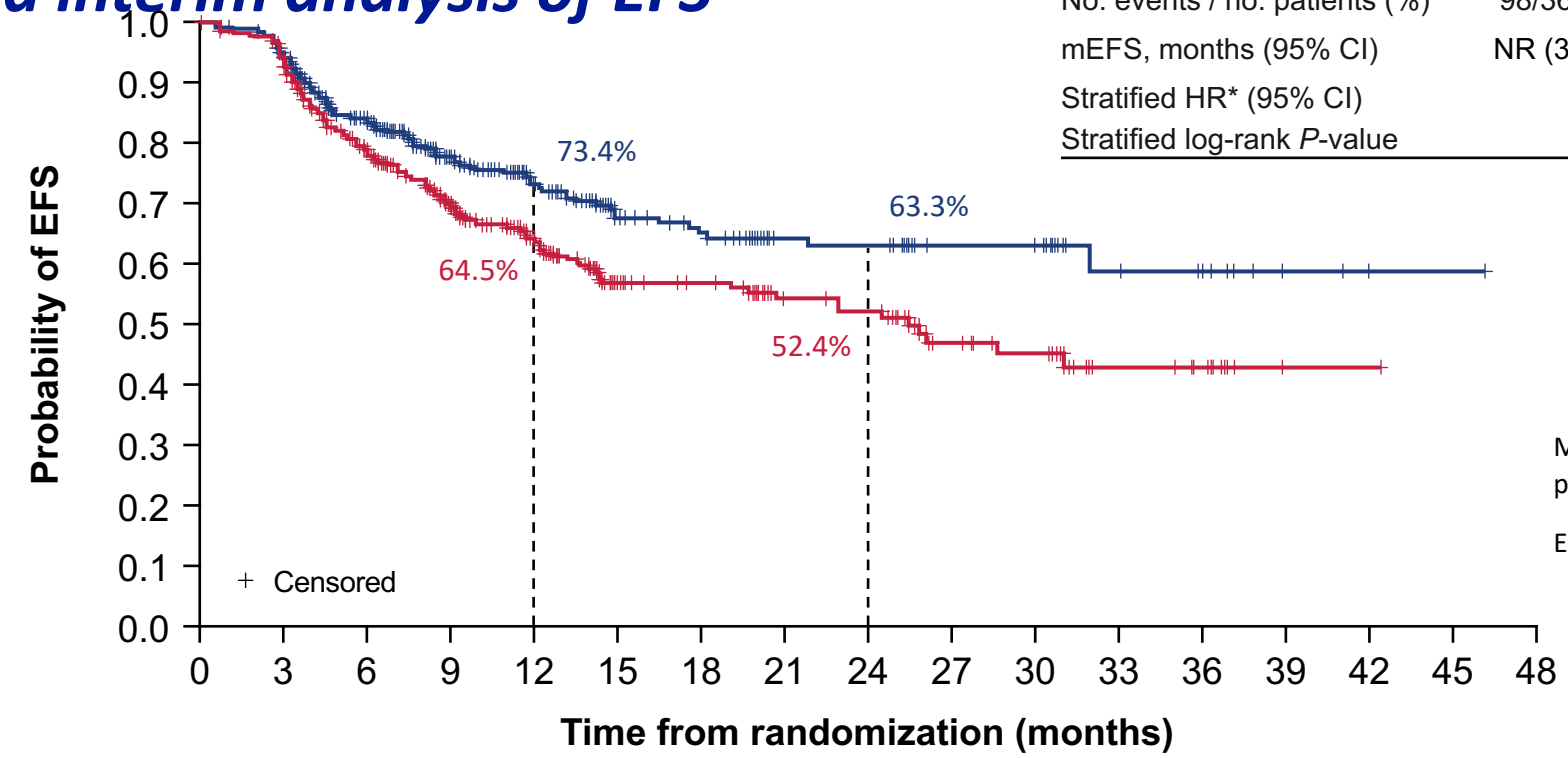
*The protocol was amended while enrollment was ongoing to exclude (1) patients with tumors classified as T4 for any reason other than size; (2) patients with planned pneumonectomies; and (3) patients with documented *EGFR/ALK* aberrations. †Ventana SP263 immunohistochemistry assay. ‡Choice of CT regimen determined by histology and at the investigator's discretion. For non-squamous: cisplatin + pemetrexed or carboplatin + pemetrexed. For squamous: carboplatin + paclitaxel or cisplatin + gemcitabine (or carboplatin + gemcitabine for patients who have comorbidities or who are unable to tolerate cisplatin per the investigator's judgment). §Post-operative radiotherapy (PORT) was permitted where indicated per local guidance. ¶All efficacy analyses reported in this presentation were performed on the mITT population, which includes all randomized patients who did not have documented *EGFR/ALK* aberrations.

[1]Travis WD, et al. *J Thorac Oncol* 2020;15:709-40.

AEGEAN: EFS using RECIST v1.1 (BICR) (mITT)

First planned interim analysis of EFS

	D arm	PBO arm
No. events / no. patients (%)	98/366 (26.8)	138/374 (36.9)
mEFS, months (95% CI)	NR (31.9–NR)	25.9 (18.9–NR)
Stratified HR* (95% CI)	0.68 (0.53–0.88)	
Stratified log-rank *P*-value	0.003902	



Median follow-up (range) in censored patients: 11.7 months (0.0–46.1)

EFS maturity: 31.9%

17% pCR
33% mPR

No. at risk:

D arm	366	336	271	194	140	90	78	50	49	31	30	14	11	3	1	1	0
PBO arm	374	339	257	184	136	82	74	53	50	30	25	16	13	1	1	0	0

DCO = Nov 10, 2022. EFS is defined as time from randomization to the earliest of: (A) progressive disease (PD) that precludes surgery; (B) PD discovered and reported by the investigator upon attempting surgery that prevents completion of surgery; (C) local/distant recurrence using BICR per RECIST v1.1; or (D) death from any cause. *HR <1 favors the D arm versus the PBO arm. Median and landmark estimates calculated using the Kaplan–Meier method; HR calculated using a stratified Cox proportional hazards model; and *P*-value calculated using a stratified log rank test. Stratification factors: disease stage (II vs III) and PD-L1 expression status (<1% vs ≥1%). Significance boundary = 0.009899 (based on total 5% alpha), calculated using a Lan-DeMets alpha spending function with O'Brien Fleming boundary. mEFS, median EFS; NR, not reached.

New Data at WCLC:

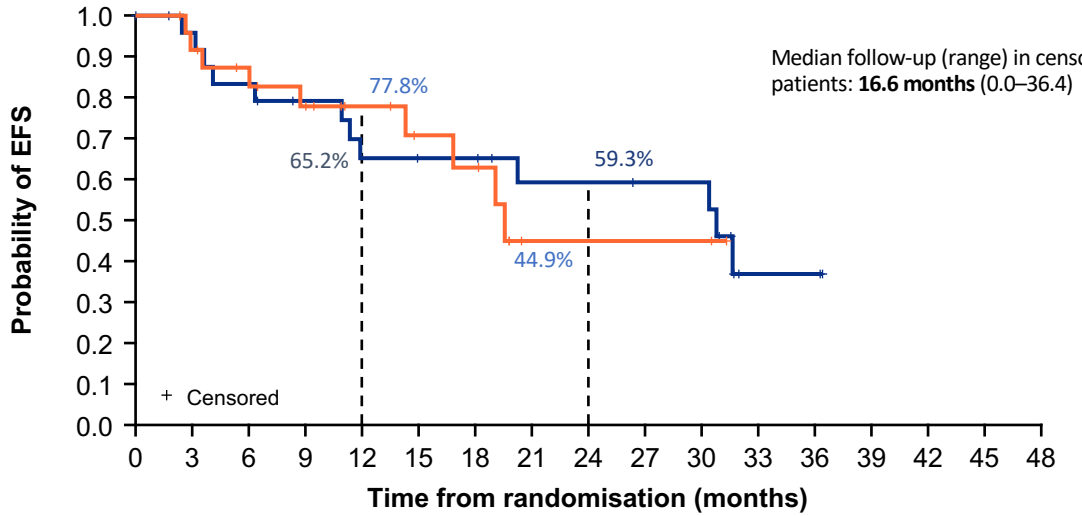
AEGEAN

OA12.05 Surgical Outcomes – Dr. Kratz

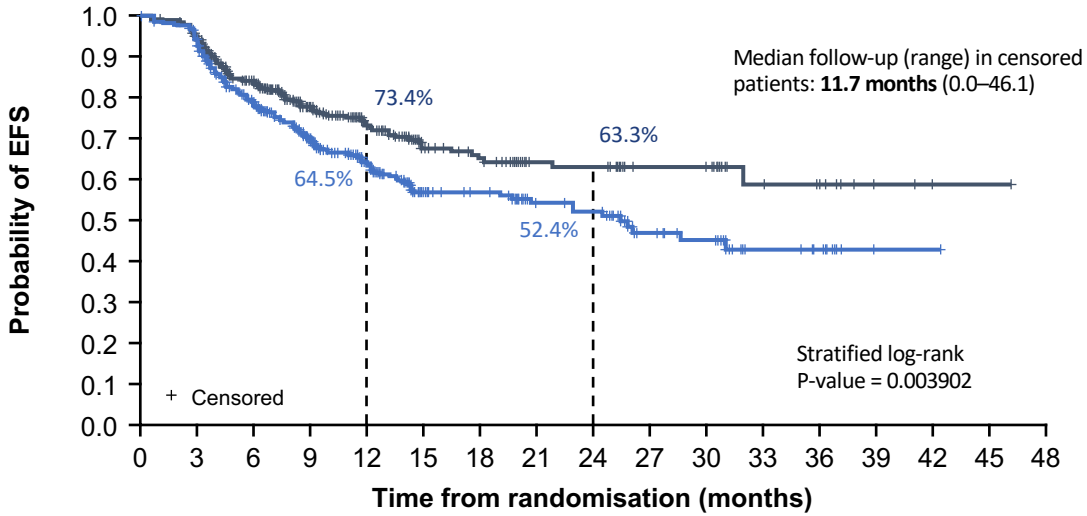
OA12.06 EGFR outcomes

*EGFR*m subgroup	Durvalumab arm	Placebo arm
No. events / no. patients (%)	12/26 (46.2)	9/25 (36.0)
mEFS, months (95% CI)	30.8 (11.4, NR)	19.6 (14.3, NR)
Unstratified HR† (95% CI)	**0.86 (0.35, 2.19)**	

mITT population[1]	Durvalumab arm	Placebo arm
No. events / no. patients (%)	98/366 (26.8)	138/374 (36.9)
mEFS, months (95% CI)	NR (31.9, NR)	25.9 (18.9, NR)
Stratified HR† (95% CI)	**0.68 (0.53, 0.88)**	



No. at risk:																	
D arm	26	23	20	17	14	13	13	10	10	9	9	2	2	0	0	0	0
PBO arm	25	22	19	16	12	9	8	2	2	2	2	0	0	0	0	0	0

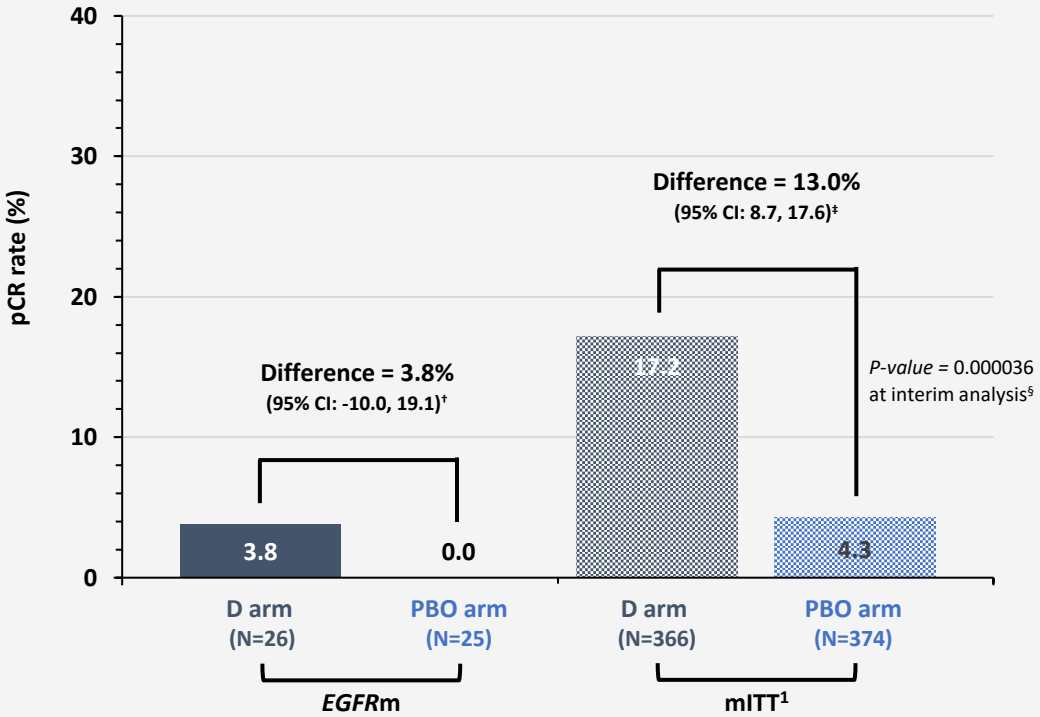


No. at risk:																	
D arm	366	336	271	194	140	90	78	50	49	31	30	14	11	3	1	1	0
PBO arm	374	339	257	184	136	82	74	53	50	30	25	16	13	1	1	0	0

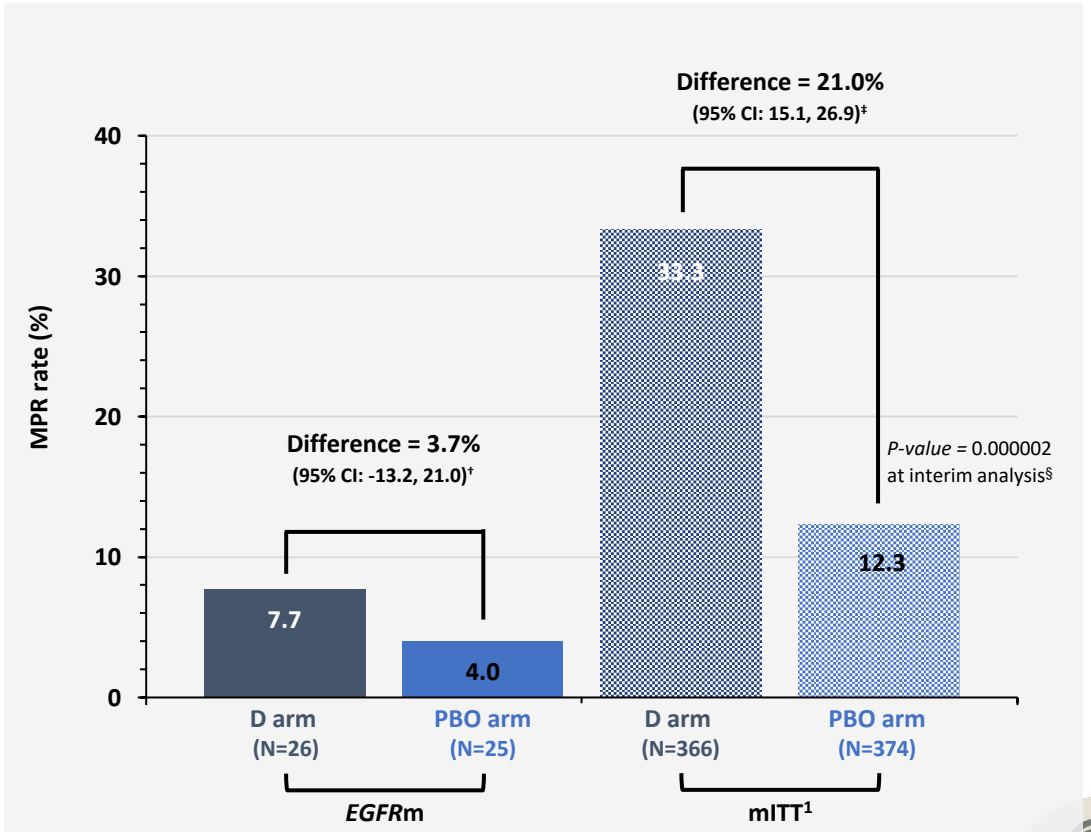
AEGEAN: EFS using RECIST v1.1 (BICR) (*EGFR*m and mITT)*

[1]Heymach JV, et al. *Cancer Res* 2023;83(8_Supplement):CT005

pCR (central lab)



MPR (central lab)



AEGEAN: Pathologic response per IASLC 2020 methodology (*EGFR*m and mITT)*

[1]Heymach JV, et al. *Cancer Res* 2023;83 (8_Supplement):CT005;
[2]Travis WD, et al. J Thorac Oncol 2020;15:709-40

David Harpole, Department of Surgery, Duke University Medical Center, Durham, North Carolina, USA

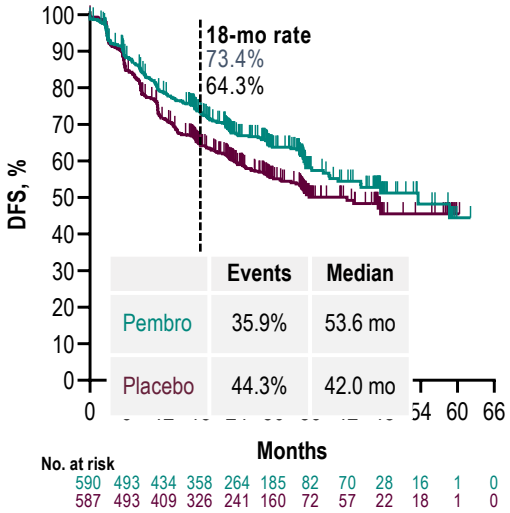
Adjuvant

KN091 (Pearls)

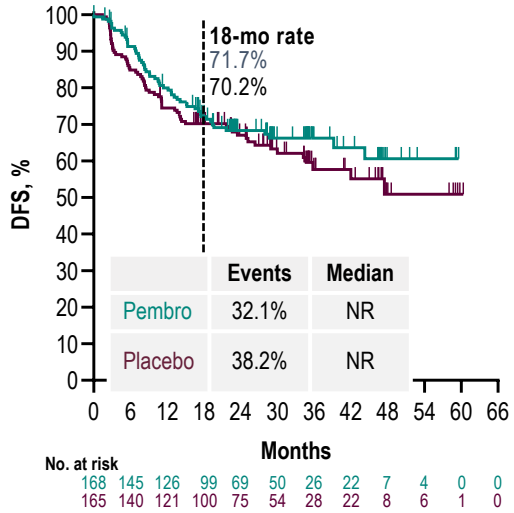
Impower010

PEARLS/KN-091: Results Second Interim Analysis

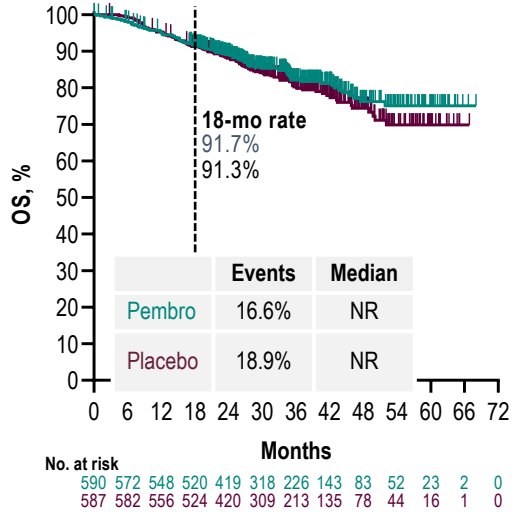
DFS, Overall Population
HR 0.76 (95% CI 0.63-0.91)
***P* = 0.0014**



DFS, PD-L1 TPS ≥50% Population
HR 0.82 (95% CI 0.57-1.18)
***P* = 0.14**



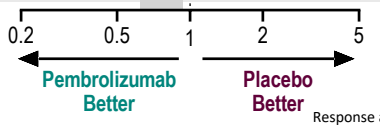
OS, Overall Population
HR 0.87 (95% CI 0.67-1.15)
***P* = 0.170**



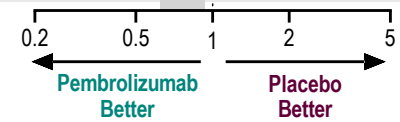
Adjuvant Pembrolizumab
EGFR mut+ in ~6%; *EGFR* mutation status was unknown for 670 (63.5%) in the overall population

US FDA approval Jan 26, 2023

Subgroup	No. Events/ No. Participants	Hazard Ratio (95% CI)
Overall	472/1177	0.76 (0.63-0.91)
Age		
<65 years	213/558	0.73 (0.56-0.96)
≥65 years	259/619	0.84 (0.66-1.07)
Sex		
Female	158/373	0.73 (0.54-1.00)
Male	314/804	0.81 (0.65-1.01)
Geographic region		
Asia	96/211	0.74 (0.49-1.10)
Eastern Europe	90/229	0.84 (0.56-1.27)
Western Europe	245/604	0.77 (0.60-1.00)
Rest of world	41/133	0.74 (0.40-1.39)
ECOG performance status		
0	288/723	0.78 (0.62-0.99)
1	184/454	0.79 (0.59-1.06)
Smoking status		
Current	53/165	0.42 (0.23-0.77)
Former	340/859	0.84 (0.68-1.04)
Never	79/153	0.72 (0.47-1.13)



Subgroup	No. Events/ No. Participants	Hazard Ratio (95% CI)
Overall	472/1177	0.76 (0.63-0.91)
Pathologic stage		
IB	46/169	0.76 (0.43-1.37)
II	246/667	0.70 (0.55-0.91)
IIIA	178/339	0.92 (0.69-1.24)
Received adjuvant chemotherapy		
No	64/167	1.25 (0.76-2.05)
Yes	408/1010	0.73 (0.60-0.89)
Histology		
Nonsquamous	330/761	0.67 (0.54-0.83)
Squamous	142/416	1.04 (0.75-1.45)
PD-L1 TPS		
<1%	195/465	0.78 (0.58-1.03)
1-49%	160/379	0.67 (0.48-0.92)
≥50%	117/333	0.82 (0.57-1.18)
***EGFR* mutation**		
No	186/434	0.78 (0.59-1.05)
Yes	40/73	0.44 (0.23-0.84)
Unknown	246/670	0.82 (0.63-1.05)



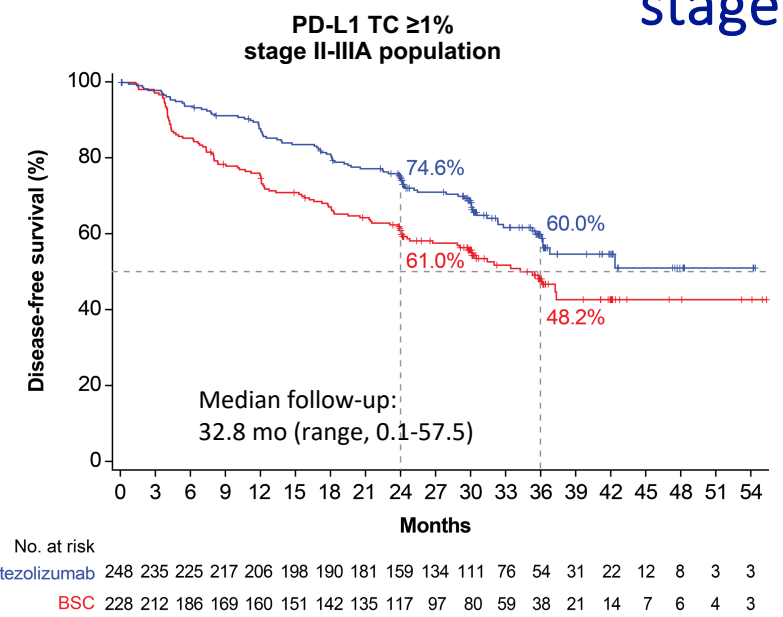
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

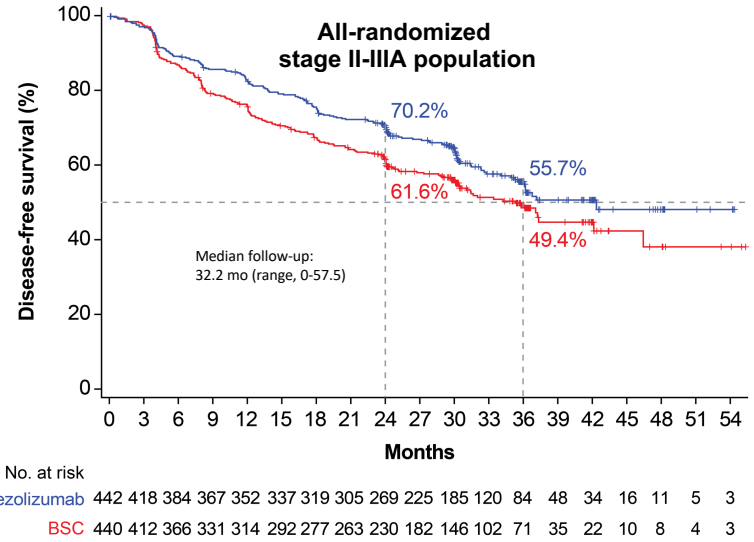
KN-091 Results: DFS in Subgroups

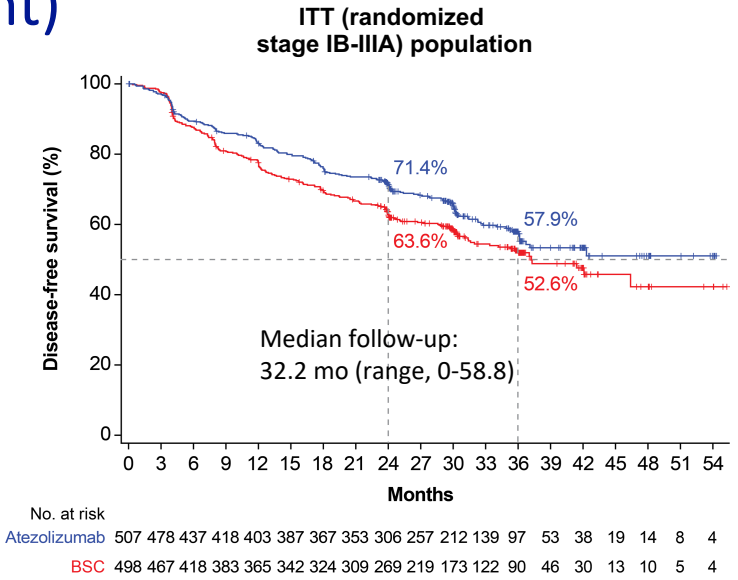
Paz Ares VirtualESMO2022, O'Brien ASCO 2022, Peters ESMO 2022

Adjuvant Atezolizumab

IMpower010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA, all-randomized stage II-IIIA and ITT pop (primary endpoint)







	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[b]	0.02[c]	

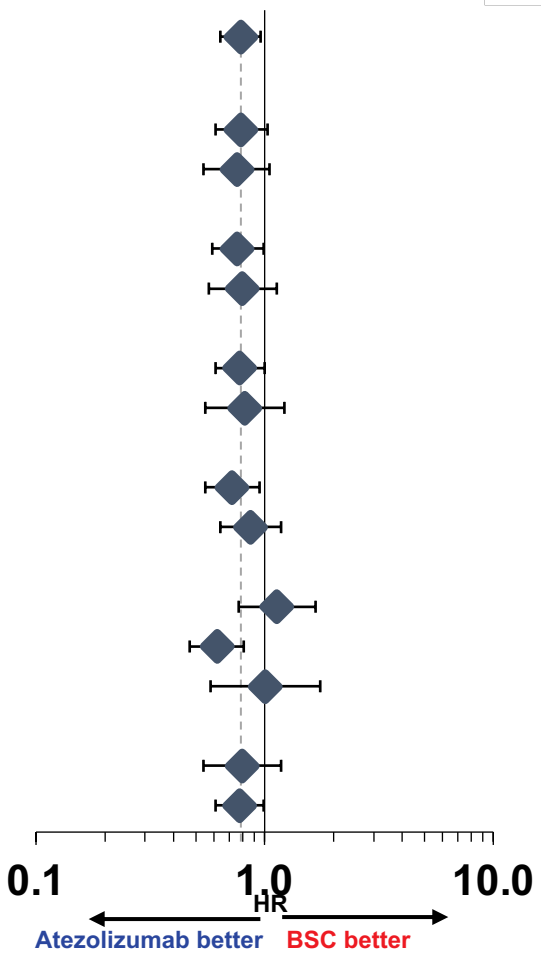
	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[b]	0.04[d]	

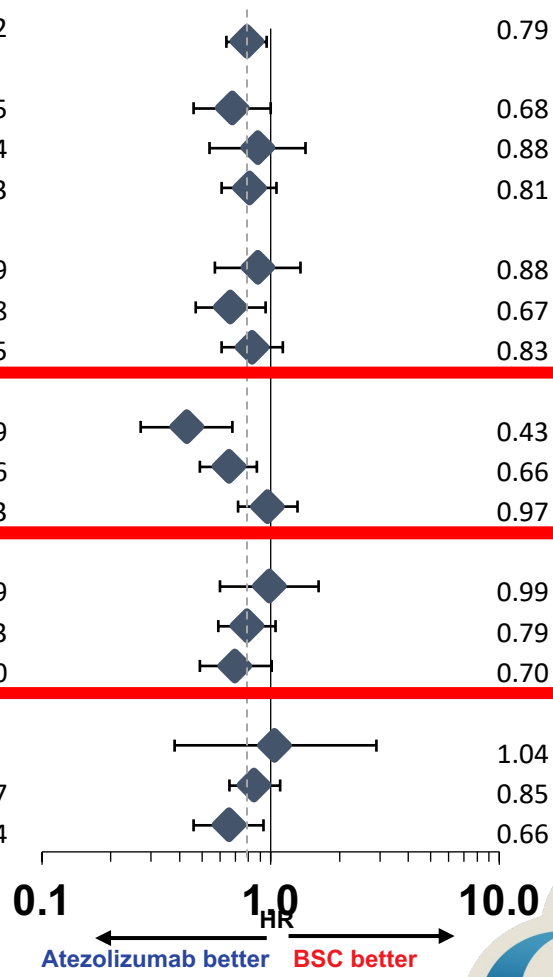
Clinical cutoff: January 21, 2021. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS. [d] The statistical significance boundary for DFS was not crossed.

US FDA approval Oct 15, 2021

Wakelee ASCO 2021 abstr 8500; Felip Lancet 2021

Subgroup	N	HR (95% CI)[a]
All patients	882	0.79 (0.64, 0.96)
Age		
<65 y	544	0.79 (0.61, 1.03)
≥65 y	338	0.76 (0.54, 1.05)
Sex		
Male	589	0.76 (0.59, 0.99)
Female	293	0.80 (0.57, 1.13)
Race		
White	631	0.78 (0.61, 1.00)
Asian	227	0.82 (0.55, 1.22)
ECOG PS		
0	491	0.72 (0.55, 0.95)
1	388	0.87 (0.64, 1.18)
Tobacco use history		
Never	196	1.13 (0.77, 1.67)
Previous	547	0.62 (0.47, 0.81)
Current	139	1.01 (0.58, 1.75)
Histology		
Squamous	294	0.80 (0.54, 1.18)
Non-squamous	588	0.78 (0.61, 0.99)
All patients	882	0.79 (0.64, 0.96)
Stage		
IIA	295	0.68 (0.46, 1.00)
IIB	174	0.88 (0.54, 1.42)
IIIA	413	0.81 (0.61, 1.06)
Regional lymph node stage (pN)		
N0	229	0.88 (0.57, 1.35)
N1	348	0.67 (0.47, 0.95)
N2	305	0.83 (0.61, 1.13)
SP263 PD-L1 status		
TC≥50%	229	0.43 (0.27, 0.68)
TC≥1%	476	0.66 (0.49, 0.87)
TC<1%	383	0.97 (0.72, 1.31)
***EGFR* mutation status**		
Yes	109	0.99 (0.60, 1.62)
No	463	0.79 (0.59, 1.05)
Unknown	310	0.70 (0.49, 1.01)
***ALK* rearrangement status**		
Yes	31	1.04 (0.38, 2.90)
No	507	0.85 (0.66, 1.10)
Unknown	344	0.66 (0.46, 0.93)





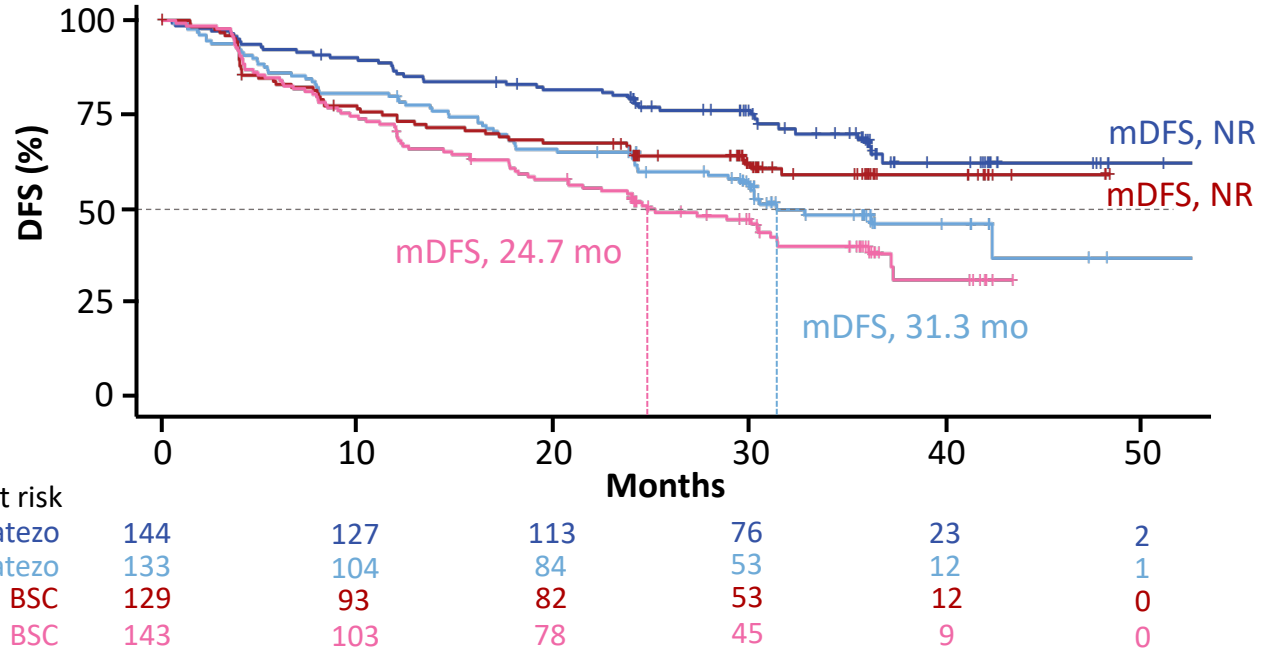
Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups.

IMpower010: DFS in key subgroups of all-rand stage II-IIIA population

New Data at WCLC
Adjuvant
MA: 11.08 Impower010 TMB

DFS by TMB status in the stage II-IIIA TMB-evaluable population

- Baseline characteristics of the stage II-IIIA TMB-evaluable population (n=549) were similar between treatment arms and consistent with those of the stage II-IIIA population[1] (not shown)



No. at risk						
TMB-H: atezo	144	127	113	76	23	2
TMB-L: atezo	133	104	84	53	12	1
TMB-H: BSC	129	93	82	53	12	0
TMB-L: BSC	143	103	78	45	9	0

TMB-H vs TMB-L	DFS HR (95% CI)
TMB-H: atezo vs TMB-L: atezo	0.52 (0.36, 0.78)
TMB-H: BSC vs TMB-L: BSC	0.62 (0.44, 0.89)

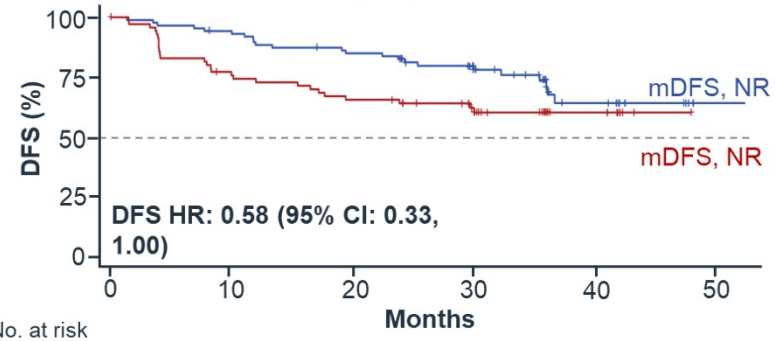
Atezolizumab vs BSC	DFS HR (95% CI)
TMB-H: atezo vs TMB-H: BSC	0.67 (0.44, 1.01)
TMB-L: atezo vs TMB-L: BSC	0.76 (0.54, 1.05)

- In both treatment arms, improved DFS was observed in the TMB-H vs TMB-L populations
- DFS improvement with atezolizumab vs BSC was similar for the TMB-H and TMB-L populations

HR, hazard ratio; mDFS, median disease-free survival; NR, not reached; TMB-H, high tumour mutation burden; TMB-L, low tumour mutation burden. TMB-H (n=273) and TMB-L (n=276) were defined as TMB levels above or below the median (6.23 mutations/Mb), respectively. 1. Felip, E et al Lancet 2021; 938:1344-57.

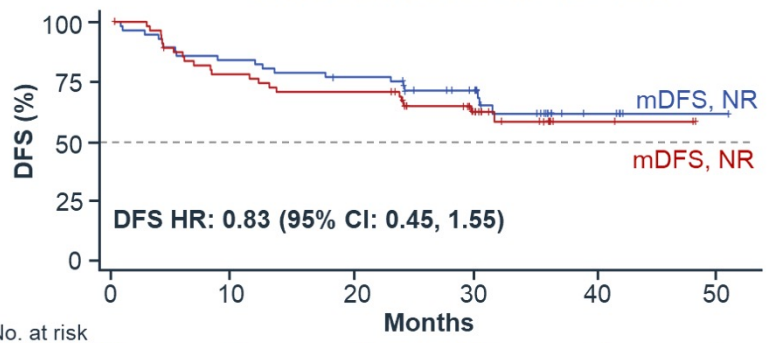
IMpower010: TMB irrelevant regardless of PD-L1

TMB-H and PD-L1 TC ≥1%



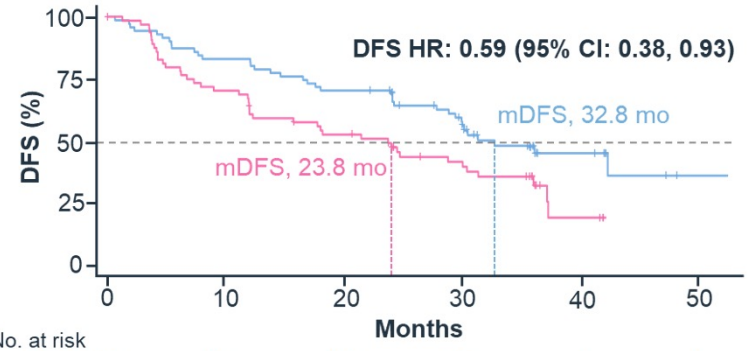
No. at risk						
Atezo	88	80	71	47	17	1
BSC	72	51	44	31	9	0

TMB-H and PD-L1 TC <1%



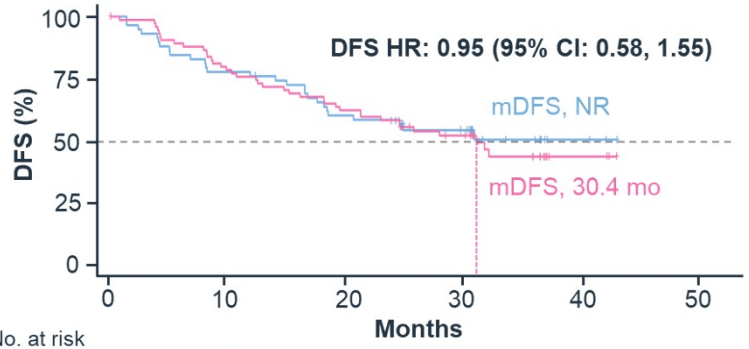
No. at risk						
Atezo	56	47	42	29	6	1
BSC	57	42	38	22	3	0

TMB-L and PD-L1 TC ≥1%



No. at risk						
Atezo	73	59	50	35	9	1
BSC	67	45	32	21	3	0

TMB-L and PD-L1 TC <1%



No. at risk						
Atezo	60	45	34	18	3	
BSC	76	58	46	24	6	

TMB, tumor mutation burden; DFS, disease-free survival. Felip E, et al. WCLC 2023. Abstract MA11.08.

Novel Approach: Neo-adjuvant XRT
MA 11:08. SAKK 16/18

SAKK 16/18: Neoadjuvant chemo, durvalumab + immune-modulatory radiotherapy for Stage III(N2) NSCLC – surgical interim

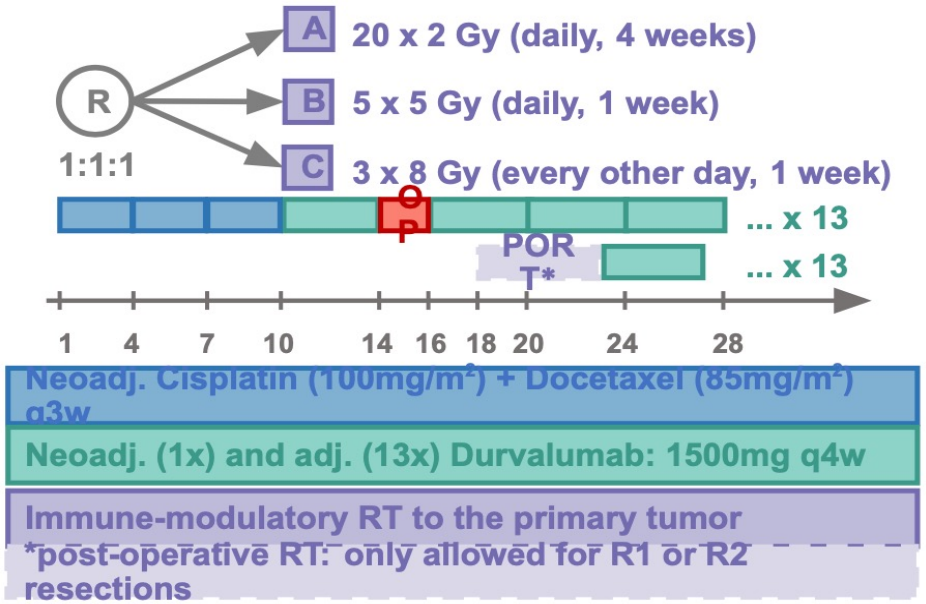
Background and study design

- Neo-adjuvant and peri-operative chemo-IO is a new standard of care (SOC) for resectable NSCLC [1,2,3,4]
- SAKK 16/14 trial: sequential neo-adjuvant cisplatin-docetaxel □ durvalumab significantly increased pCR and 1-yr-EFS rates in stage III(N2) NSCLC [5]
- Radiotherapy (RT) can act synergistically with PD-(L)1 blockade to improve systemic immune response
- Optimal RT regimen unknown

[1] Forde PM et al, NEJM 2022; [2] Wakelee H et al, NEJM 2023; [3] Heymach J V, AACR Meeting 2023; [4] Lu S, ASCO Meeting 2023; [5] Rothschild S. I. et al, JCO 2021

Inclusion criteria:
- NSCLC, cT1-4$_{>7}$ N2 M0 (8th ed.)
- Primarily resectable and operable
- ECOG 0-1
- Adequate organ function (incl. eGFR ≥ 60 mL/min)

Exclusion criteria:
- Any previous treatment for NSCLC
- Previous checkpoint inhibitor or thoracic RT
- Active auto-immune disease, ≥ 10 mg/day of prednisone

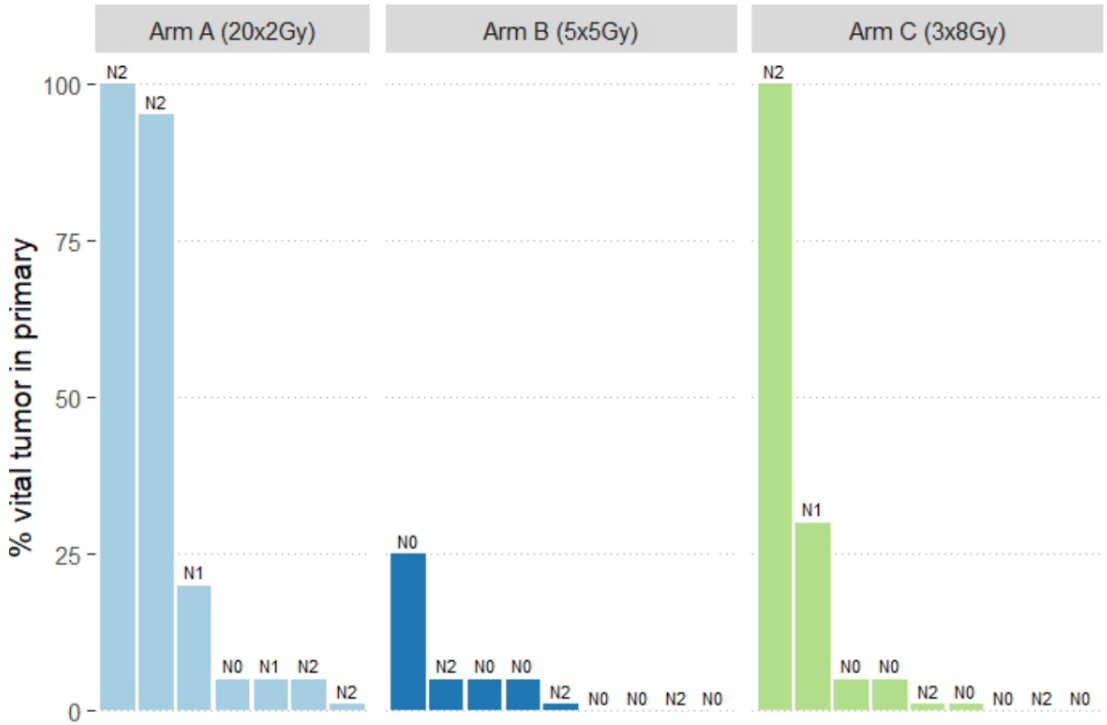


- Primary endpoint: 1-yr EFS
- Interim safety analysis after 25 resections
- Unresected patients: safety F/U ≥ 90 days

SAKK 16/18: Neoadjuvant chemo, durvalumab + immune-modulatory radiotherapy for Stage III(N2) NSCLC – surgical interim

Efficacy and Conclusion

- N= 31 Cis/Doce
  - 1PD/1Covid
- N= 29 Durva
  - 2PD/2NR
- N= 25 Surgery



Variable	Arm A N = 7	Arm B N = 9	Arm C N = 9	Total N = 25
MPR	4	8	7	19
pCR	0	3	2	5
<ypN2	3	6	6	15

Conclusions:

Surgical feasibility as in other neo-adjuvant / perioperative IO trials

No clear difference in safety / surgical outcomes between the 3 arms

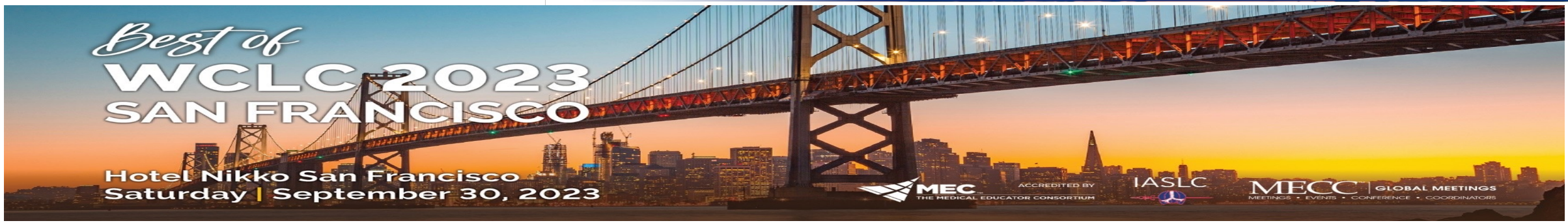
Based on interim safety analysis trial continues as planned to N = 90

No conclusion can be drawn yet as to differential efficacy between the 3 RT regimen

Drug tolerant persister (DTP) to neoadjuvant osimertinib in resectable NSCLC harbouring *EGFR* mutations (NORA)

Take Home Points

- Neoadjuvant osimertinib is a feasible option that was not associated with surgical delays and induced an **MPR rate of 24%** of resected tumors.
- **Single-cell RNA-seq analysis** reveal post-osimertinib samples with AT1-like features with **Hippo-YAP/TAZ, Wnt and TGF-β pathway**. Compared to MPR, **AT1-like cells** and **apCAF** were enriched in the nMPR subset.
- Using **Natera assay, 6/20 (30%)** positive patients at baseline timepoint (N=2/2/2 for stage I/II/III) were identified. **All 6 patients showed ctDNA clearance after 1 cycle of osimertinib.**
- Further analysis:
  - Identification of molecular mechanisms of DTP using genomics and transcriptomics
  - Longitudinal time points, incumbent upon data collection



OA12.05 + OA 12.06: AEGEAN and other + peri-operative trials rapidly changing landscape – the surgical outcomes were expected (Dr. Kratz to discuss) and the EGFR results are not unexpected, but conflict with data from other trials (KN091, KN671, IMpower010)

MA11.08: IMpower010: TMB not a useful biomarker in this trial

MA11.09: SAKK 16/18: Neoadjuvant immune-modulatory RT in Stage III(N2) NSCLC showed increased MPR but actual impact unclear

MA 11.11: Drug tolerant persister (DTP) to neoadjuvant osimertinib in resectable NSCLC harbouring *EGFR* mutations (NORA) – very exploratory