AIGOM
ASSOCIAZIONE ITALIANA
GRUPPI ONCOLOGICI MULTIDISCIPLINARI

19 GIUGNO 2023
ore 15.00 - 18.00

LE NOVITA' DA CHICAGO 2023:
l'evoluzione delle conoscenze in oncologia...

Con il contributo non condizionante

GOLD: Eisai, hre Hanse Renal Health Care

SILVER: AMGEN

Si ringrazia: ROPI

SEGRETERIA ORGANIZZATIVA
ETRUSCA CONVENTIONS
Via M. Bonciario 6/8 - 06123 Perugia
tel./fax 075.8089485 - info@etruscaconventions.com
www.etruscaconventions.com

Con il Patrocinio
ALLEANZA CONTRO IL CANCRO
SICO

NEOPLASIE POLMONARI

Stadi precoci e malattia metastatica

Ettore D'Argento
UOC Oncologia Medica

Gemelli
Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

Comprehensive Cancer Center


WELCOME

Chicago

CHINATOWN

CHINATOWN

POSTCARD

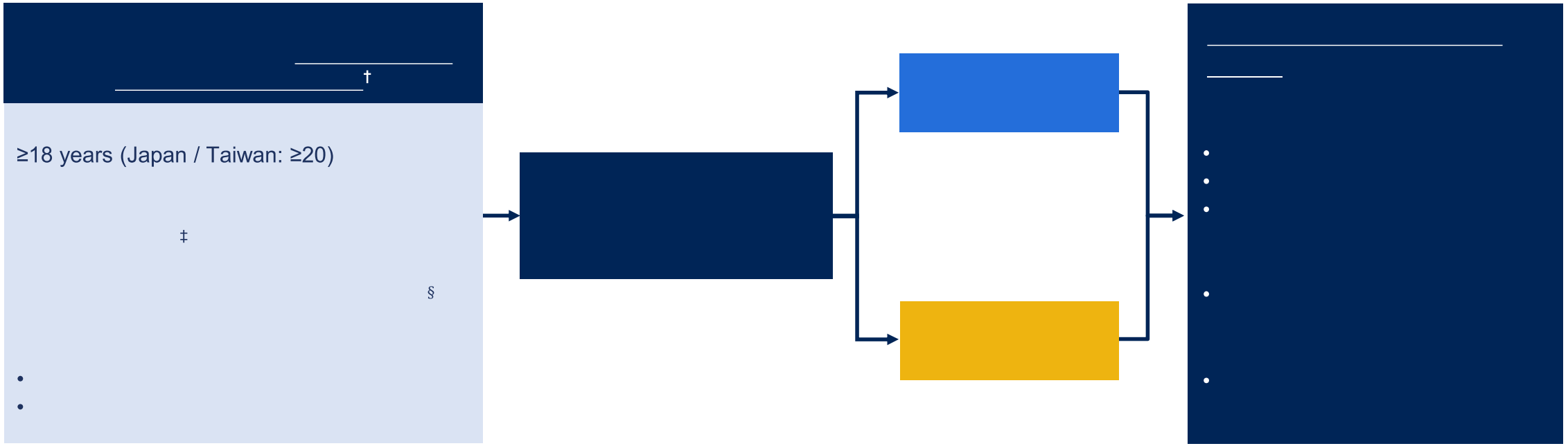
PERI-OPERATIVE NSCLC
ONCOGENE ADDICTED

ADAURA

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]

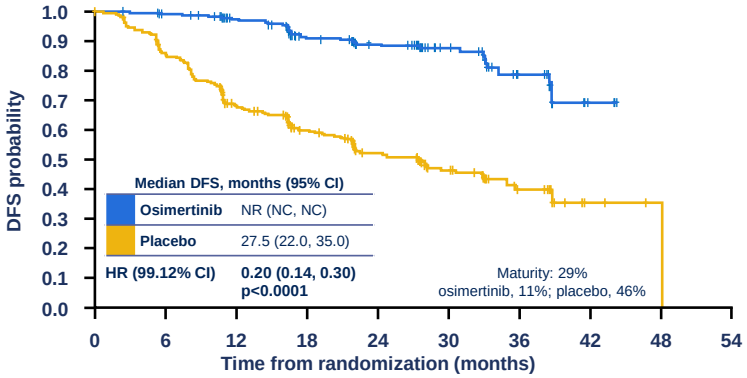
[1]Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2]Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia; [4]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; [5]Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [7]Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; [8]David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [9]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [10]Department of Oncology, National Cheng Kung University, Tainan, Taiwan; [11]Thoracic Oncology Division, European Institute of Oncology (IEO), IRCCS, Milan, Italy; [12]Department of Medical Oncology and Hematology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [13]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Republic of Korea; [14]Ho Chi Minh City Oncology Hospital, Binh Thanh District, Ho Chi Minh City, Vietnam; [15]Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [16]Department of Lung Cancer and Thoracic Tumours, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [17]Oncology Biometrics, AstraZeneca, Cambridge, UK; [18]Late Oncology Research & Development, AstraZeneca, Warsaw, Poland; [19]Oncology Research & Development, AstraZeneca, Cambridge, UK; [20]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China


†
≥18 years (Japan / Taiwan: ≥20)
‡
§

Adjuvant osimertinib has significantly improved DFS

ADAURA primary DFS analysis[1,2] (stage IB–IIIA)*

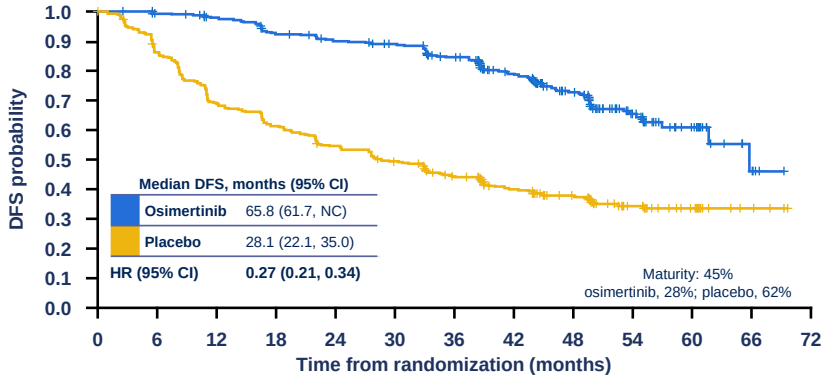
NEJM October 2020



No. at risk										
Osimertinib	339	313	272	208	138	74	27	5	0	-
Placebo	343	287	207	148	88	53	20	3	1	0

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

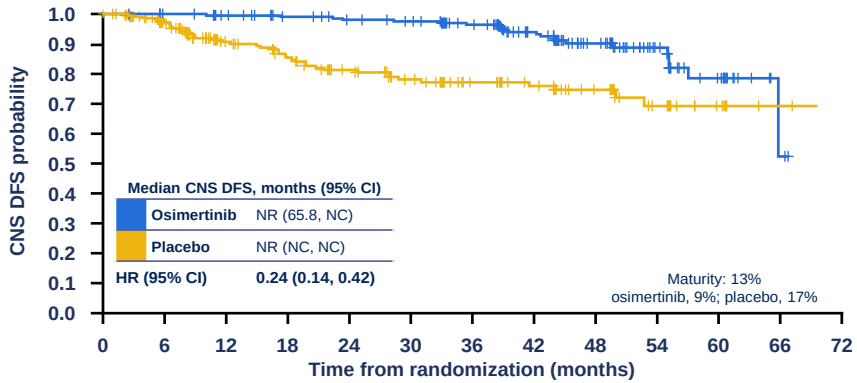
JCO January 2023



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

ADAURA updated CNS DFS analysis[5,6] (stage II–IIIA)

JCO January 2023



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

The NEW ENGLAND JOURNAL of MEDICINE

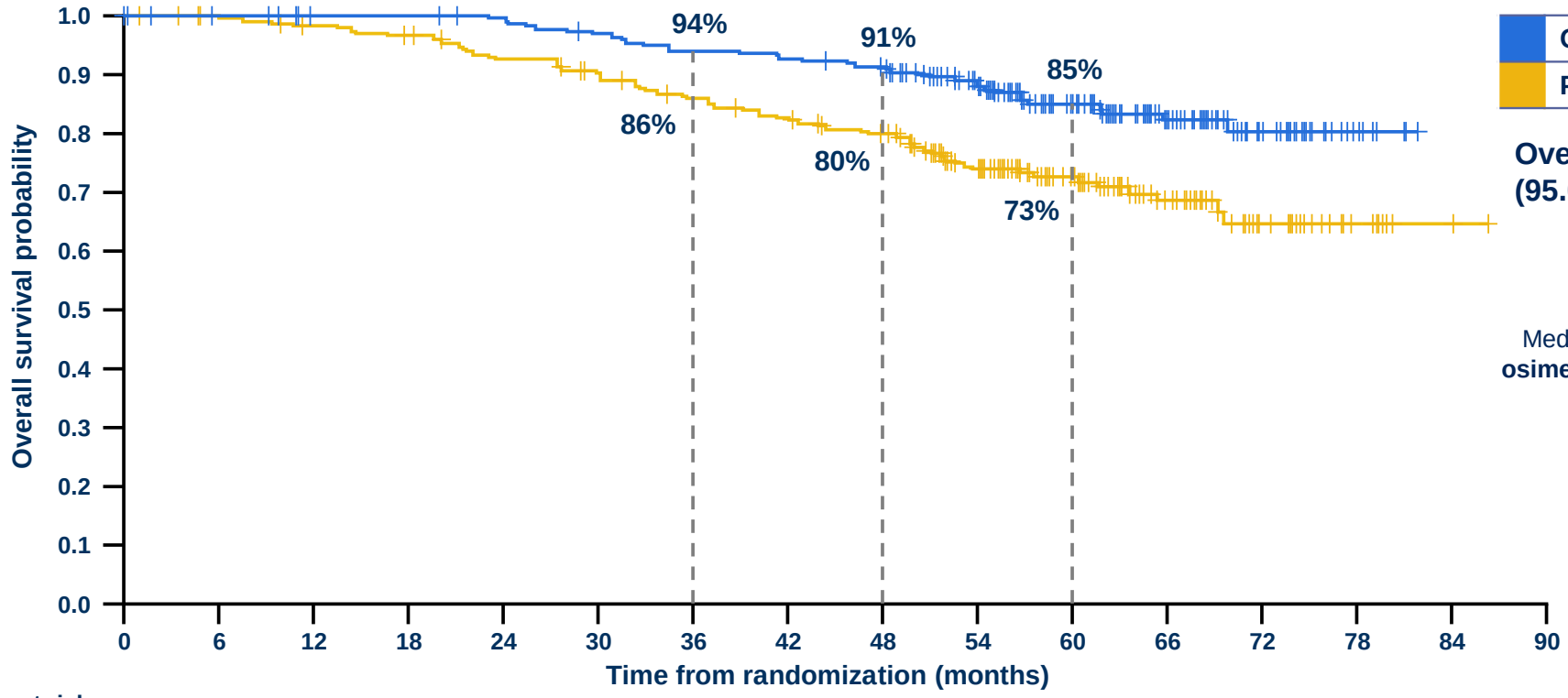
ORIGINAL ARTICLE

Overall Survival with Osimertinib in Resected *EGFR*-Mutated NSCLC

Masahiro Tsuboi, M.D., Roy S. Herbst, M.D., Ph.D., Thomas John, M.B., B.S., Ph.D., Terufumi Kato, M.D., Margarita Majem, M.D., Ph.D., Christian Grohé, M.D., Jie Wang, M.D., Ph.D., Jonathan W. Goldman, M.D., Shun Lu, M.D., Wu-Chou Su, M.D., Filippo de Marinis, M.D., Frances A. Shepherd, M.D., Ki Hyeong Lee, M.D., Ph.D., Nhieu Thi Le, M.D., Arunee Dechaphunkul, M.D., Dariusz Kowalski, M.D., Ph.D., Lynne Poole, M.Sc., Ana Bolanos, M.D., Yuri Rukazenkov, M.D., Ph.D., and Yi-Long Wu, M.D., for the ADAURA Investigators*

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)

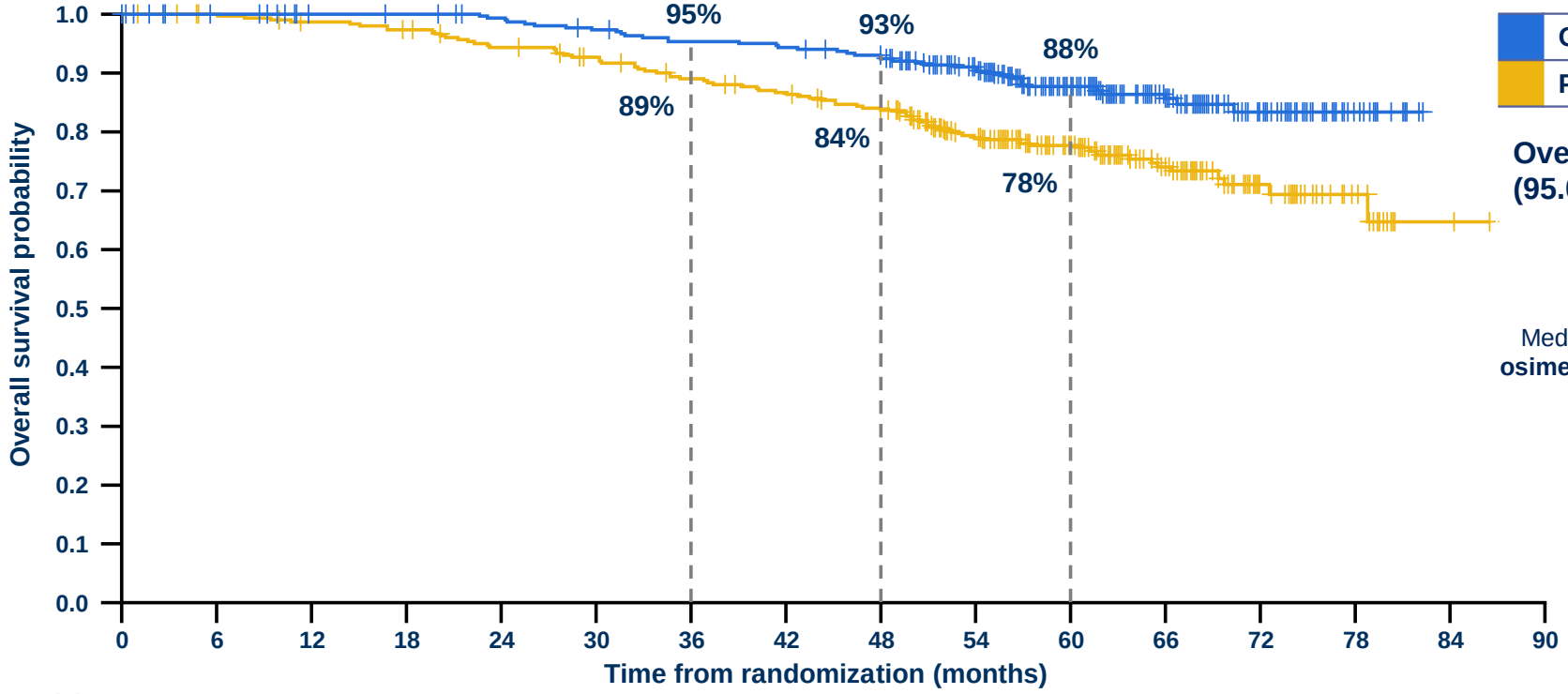
Overall OS HR (95.03% CI) **0.49 (0.33, 0.73); p=0.0004**

Maturity: 21%
osimertinib 15%, placebo 27%

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

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**

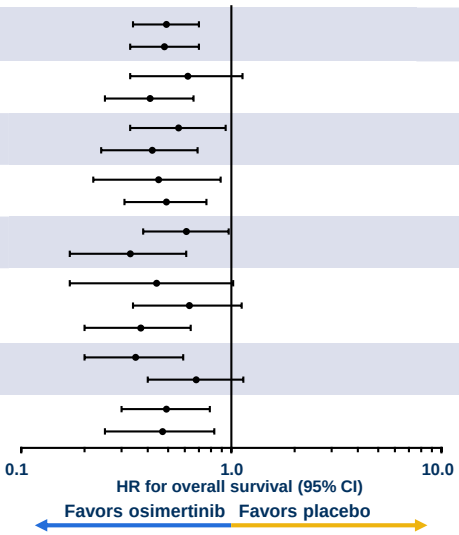
Maturity: 18%
osimertinib 12%, placebo 24%

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

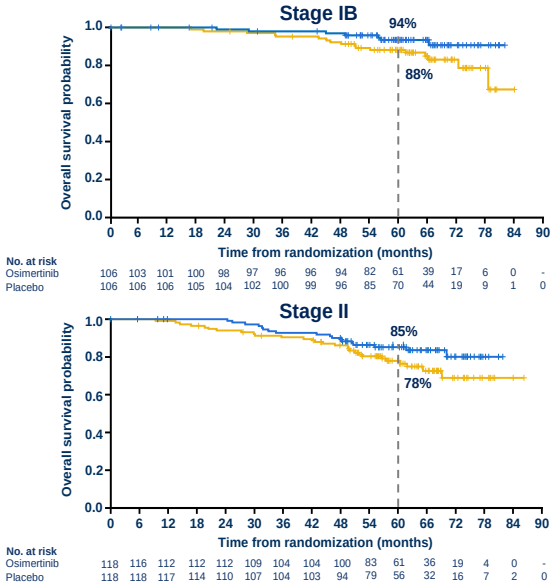
Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 60.4 months, placebo 59.4 months.

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

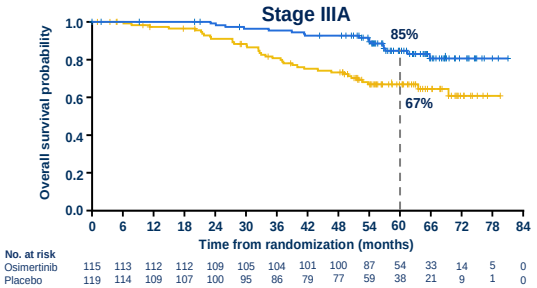
Subgroup		No. of events / patients	HR	95% CI
Overall (N=682)	Stratified log-rank	124 / 682	0.49	0.34, 0.70
	Unadjusted Cox PH	124 / 682	0.48	0.33, 0.70
Sex	Male	42 / 204	0.62	0.33, 1.13
	Female	82 / 478	0.41	0.25, 0.66
Age	<65 years	60 / 380	0.56	0.33, 0.94
	≥65 years	64 / 302	0.42	0.24, 0.69
Smoking 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



Data cut-off: January 27, 2023.
*AJCC / UICC 7th edition.

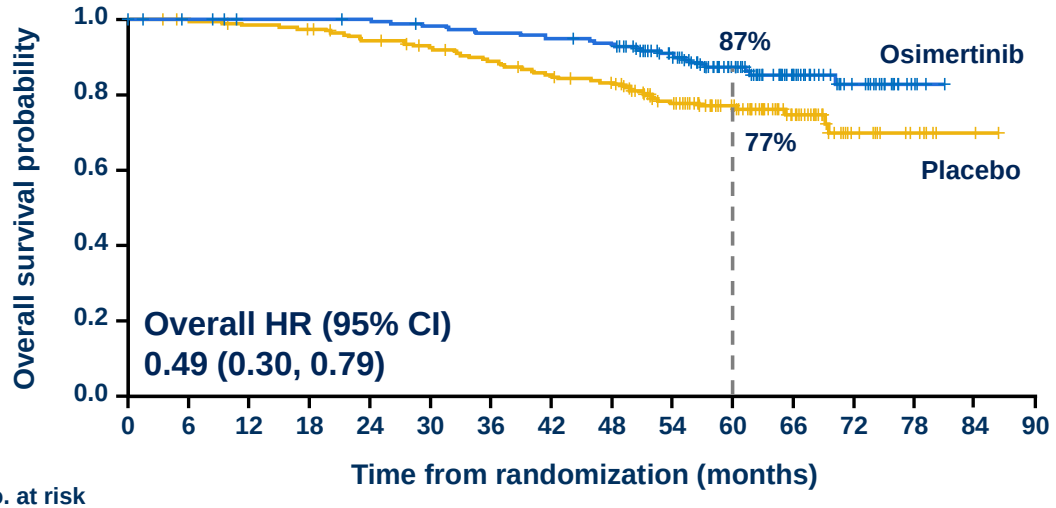


	Stage IB	Stage II	Stage IIIA
5 year OS rate, % (95% CI)			
Osimertinib	94 (86, 97)	85 (77, 91)	85 (76, 91)
Placebo	88 (80, 93)	78 (69, 85)	67 (57, 75)
Overall HR (95% CI)	0.44 (0.17, 1.02)	0.63 (0.34, 1.12)	0.37 (0.20, 0.64)



OS in patients with and without adjuvant chemotherapy: patients with stage IB / II / IIIA disease

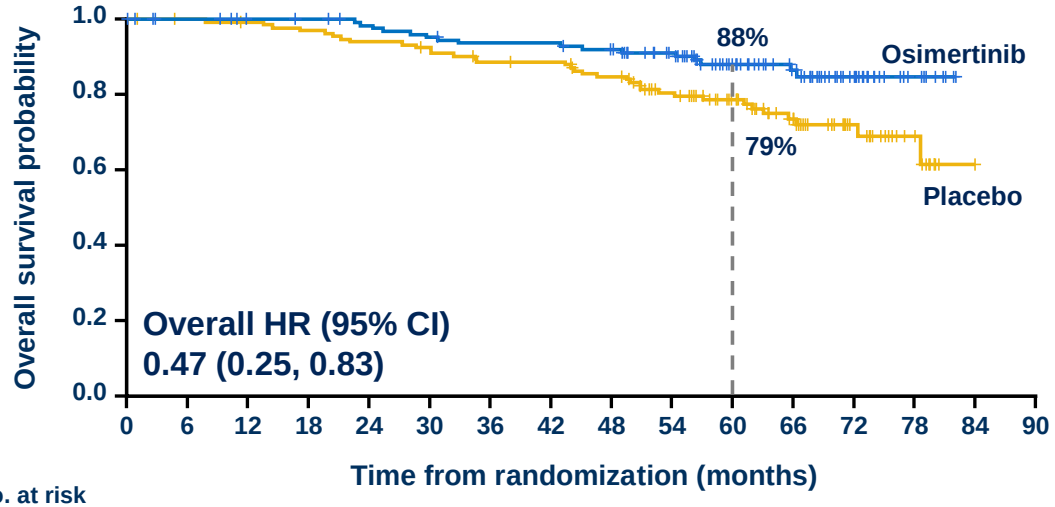
With adjuvant chemotherapy



No. at risk

Osimertinib	203	200	197	197	196	192	188	185	182	155	104	58	25	7	0	-
Placebo	207	204	200	197	189	182	174	166	159	133	92	48	19	7	2	0

Without adjuvant chemotherapy



No. at risk

Osimertinib	136	132	128	127	123	119	116	116	112	97	72	50	25	8	0	-
Placebo	136	134	132	129	125	122	116	115	108	90	72	49	25	10	1	0

Data cut-off: January 27, 2023.
Overall population: stage IB / II / IIIA. Tick marks indicate censored data.
Use of adjuvant chemotherapy before randomization was allowed but not mandatory; decided by the physician and patient before enrollment.

Safety summary

- At the final DFS analysis (data cut-off: April 11, 2022), all patients had completed or discontinued study treatment; the safety profile of adjuvant osimertinib with extended follow-up[1,2] was consistent with the ADAURA primary analysis[3]

AE, any cause*, n (%)	**Osimertinib (n=337)**	**Placebo (n=343)**
Any AE	330 (98)	309 (90)
Any AE Grade ≥3	79 (23)	48 (14)
Any AE leading to death	1 (<1)	2 (1)
Any serious AE	68 (20)	47 (14)
Any AE leading to discontinuation	43 (13)	9 (3)
Any AE leading to dose reduction	42 (12)	3 (1)
Any AE leading to dose interruption	91 (27)	43 (13)
AE, possibly causally related*†, n (%)		
Any AE	308 (91)	199 (58)
Any AE Grade ≥3	36 (11)	7 (2)
Any AE leading to death	0	0
Any serious AE	10 (3)	2 (1)

- At the time of the current data cut-off for OS (January 27, 2023), one additional serious AE (COVID-19 pneumonia) had been reported, which occurred >28 days after treatment discontinuation; the investigator determined that this was not treatment related and the patient made a full recovery

*Data cut-off: April 11, 2022. Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category counted once in each of those categories. Includes AEs with an onset date on or after the date of first dose and up to and including 28 days following the discontinuation of study treatment and before starting subsequent cancer therapy. †As assessed by the investigator.

1. Herbst et al. J Clin Oncol 2023;41:1830–1840; 2. John et al. J Thorac Oncol 2023; online ahead of print; 3. Wu et al. N Engl J Med 2020;383:1711–1723.

Subsequent treatments

- At data cut-off for this final OS analysis, 76 patients (22%) in the osimertinib arm and 184 patients (54%) in the placebo arm had received any subsequent anti-cancer treatment
- EGFR-TKIs were the most common subsequent anti-cancer treatment received across both arms; most frequently osimertinib

Subsequent treatments, n (%)	Osimertinib (n=339)	Placebo (n=343)
Patients who received subsequent anti-cancer treatment*	76 (22)	184 (54)
EGFR-TKIs	58 (76)	162 (88)
Osimertinib	31 (41)	79 (43)
Other EGFR-TKIs	28 (37)	114 (62)
Chemotherapy	20 (26)	46 (25)
Radiotherapy	30 (39)	53 (29)
Other anti-cancer treatments	12 (16)	29 (16)

Osimertinib is the first EGFR-TKI to show significant OS benefit in a Phase III adjuvant study

Reinforces osimertinib as standard of care

EGFR mutation testing

Best treatments early

New era for targeted treatment in early-stage disease

Conclusions

- In the ADAURA primary analysis, adjuvant osimertinib demonstrated a statistically significant[1] and clinically meaningful DFS benefit vs placebo in resected EGFRm stage IB–IIIA NSCLC, along with improved CNS DFS and a tolerable safety profile[1,2]
- **DFS benefit in ADAURA has translated into a statistically significant OS benefit with adjuvant osimertinib vs placebo**
  - **Primary (stage II–IIIA) population, OS HR 0.49; 95.03% CI 0.33, 0.73; p=0.0004**
  - **Overall (stage IB–IIIA) population, OS HR 0.49; 95.03% CI 0.34, 0.70; p<0.0001**
- OS benefit with adjuvant osimertinib vs placebo was generally consistent across subgroups, including by disease stage (IB / II / IIIA) and prior adjuvant chemotherapy use (yes / no)

ADAURA is the first global Phase III study to demonstrate statistically significant and clinically meaningful OS benefit with targeted treatment in this patient population, reinforcing adjuvant osimertinib as the standard of care for patients with resected EGFRm stage IB–IIIA NSCLC

Data cut-off: January 27, 2023.

1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2023;41:1830–1840.

POSTCARD

PERI-OPERATIVE NSCLC
NON ONCOGENE ADDICTED

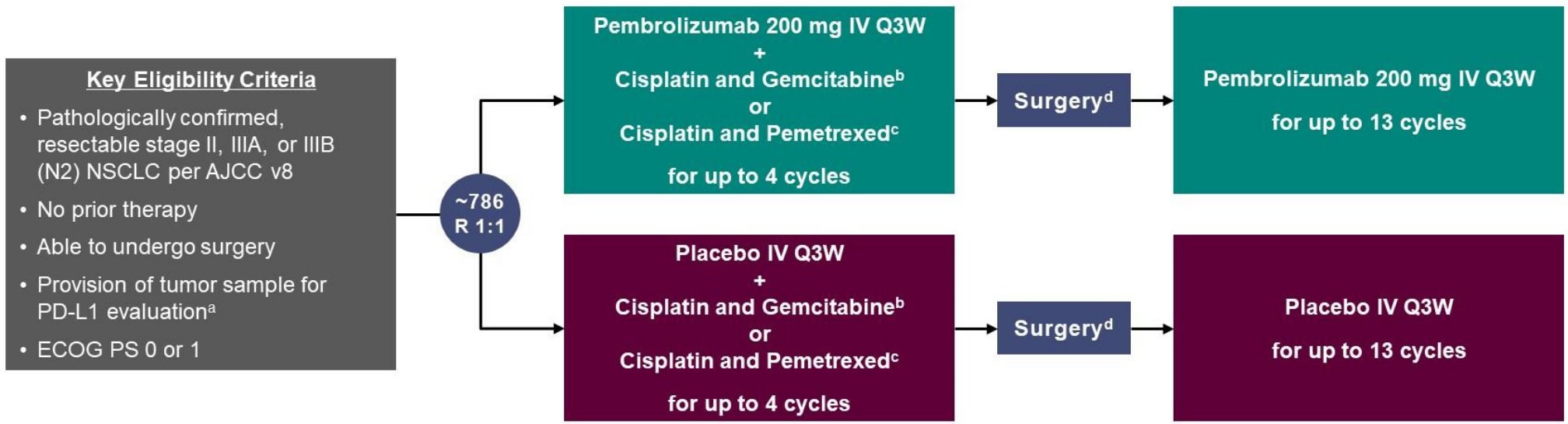
KEYNOTE-671

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

Heather Wakelee,[1] Moishe Liberman,[2] Terufumi Kato,[3] Masahiro Tsuboi,[4] Se-Hoon Lee,[5] Jie He,[6] Shugeng Gao,[6] Ke-Neng Chen,[7] Christophe Dooms,[8] Margarita Majem,[9] Ekkehard Eigendorff,[10] Gastón L Martinengo,[11] Olivier Bylicki,[12] Delvys Rodríguez-Abreu,[13] Jamie Chaft,[14] Silvia Novello,[15] Jing Yang,[16] Steven M Keller,[16] Ayman Samkari,[16] Jonathan D Spicer,[17] on behalf the KEYNOTE-671 Investigators

[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]Centre Hospitalier de Universite to Montréal (CHUM), Montréal, QC, Canada; [3]Kanagawa Cancer Center, Yokohama, Japan; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [7]Beijing Cancer Hospital, Peking University, Beijing, China; [8]University Hospitals Leuven, Leuven, Belgium; [9]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [10]Zentralklinik Bad Berka, Bad Berka, Germany; [11]Sanatorio Parque, Córdoba, Argentina; [12]HIA Sainte-Anne, Toulon, France; [13]Hospital Universitario Insular de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [14]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA; [15]Department of Oncology, University of Turin, A.O.U. San Luigi Gonzaga di Orbassano, Turin, Italy; [16]Merck & Co. Inc., Rahway, NJ, USA; [17]McGill University Health Centre, Montréal, QC, Canada

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



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.

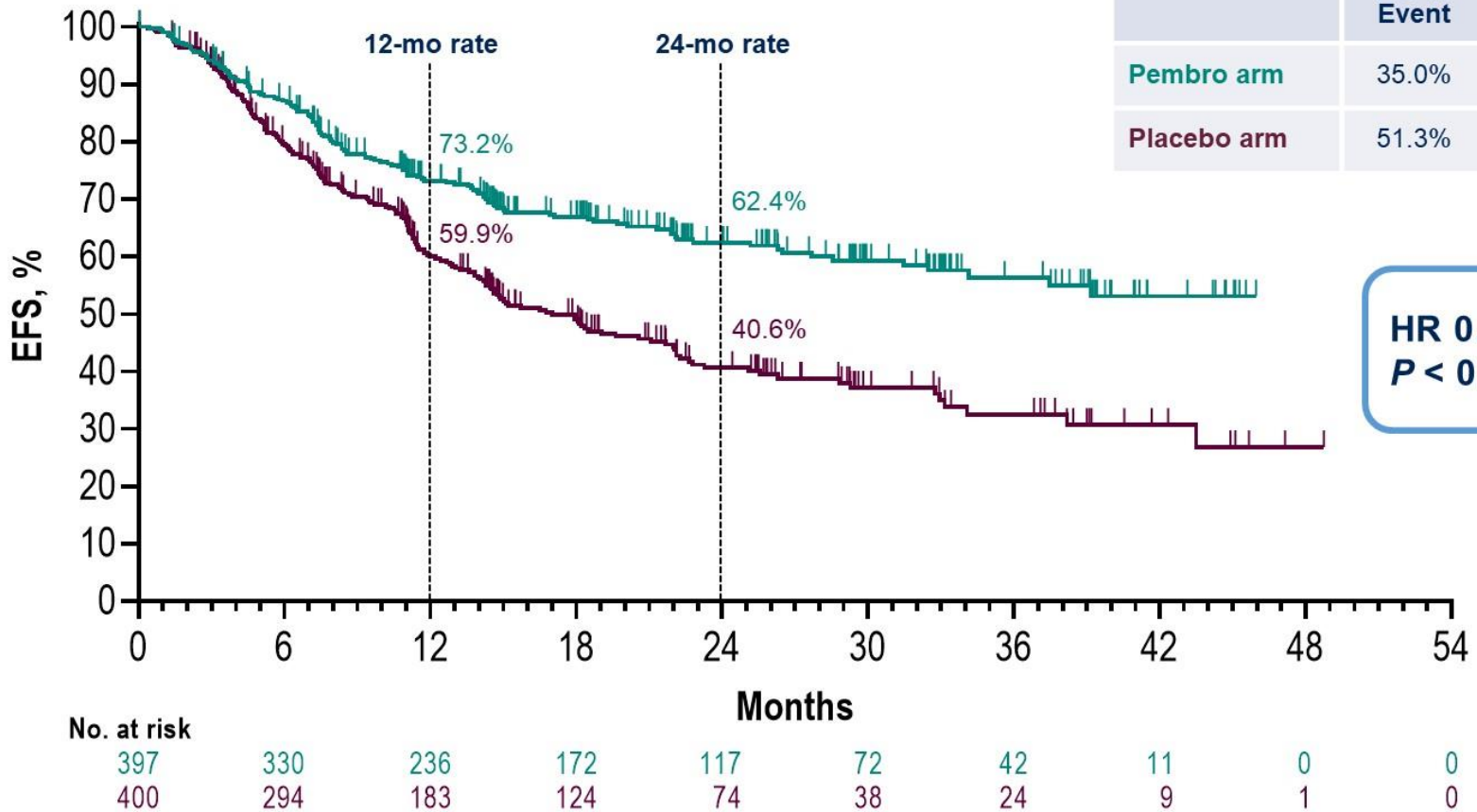
Baseline Characteristics

	Pembro Arm (N = 397)	Placebo Arm (N = 400)
Median age (range), years	63 (26-83)	64 (35-81)
Male	279 (70.3%)	284 (71.0%)
Race		
American Indian or Alaska Native	1 (0.3%)	0
Asian	124 (31.2%)	125 (31.3%)
Black or African American	6 (1.5%)	10 (2.5%)
Multiple	3 (0.8%)	10 (2.5%)
White	250 (63.0%)	239 (59.8%)
Missing data	13 (3.3%)	16 (4.0%)
Geographic region		
East Asia	123 (31.0%)	121 (30.3%)
Not east Asia	274 (69.0%)	279 (69.8%)
ECOG PS		
0	253 (63.7%)	246 (61.5%)
1	144 (36.3%)	154 (38.5%)
Histology		
Nonsquamous	226 (56.9%)	227 (56.8%)
Squamous	171 (43.1%)	173 (43.3%)

	Pembro Arm (N = 397)	Placebo Arm (N = 400)
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%)

[a] *EGFR* mutation and *ALK* translocation status were tested locally per investigator discretion. *EGFR* status was unknown in 272 (68.5%) participants in the pembro arm and 254 (63.5%) in the placebo arm; *ALK* status was unknown in 281 (70.8%) and 258 (64.5%), respectively. Data cutoff date for IA1: July 29, 2022.

Event-Free Survival



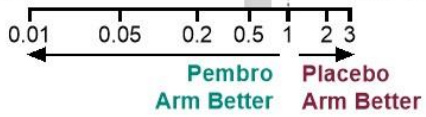
	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

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

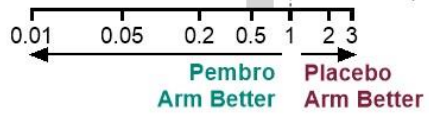
EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause.
Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

Event-Free Survival in Subgroups

Subgroup	Events/participants Pembro Arm	Events/participants 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)



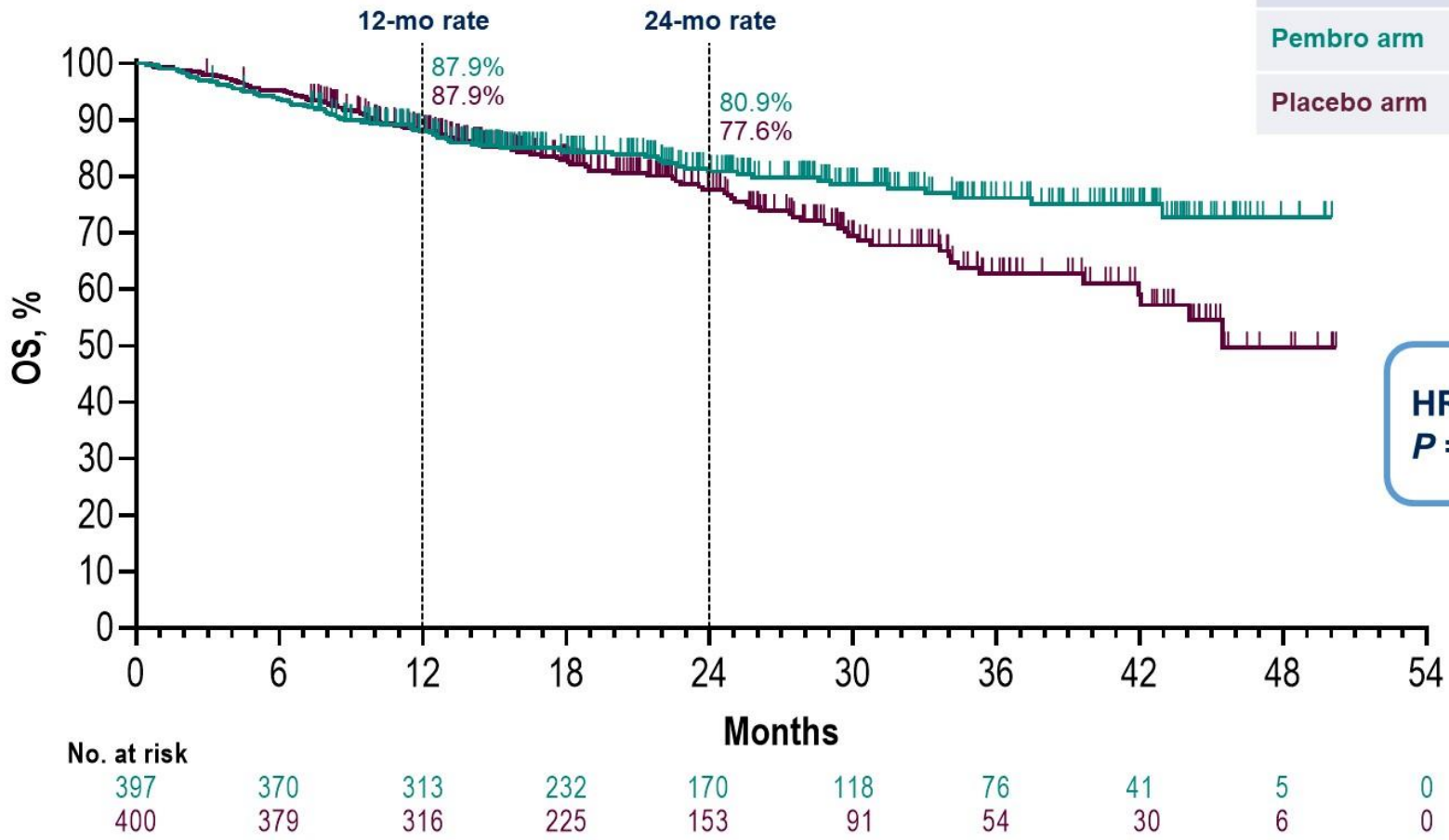
Subgroup	Events/participants Pembro Arm	Events/participants Placebo Arm	Hazard ratio (95% CI)
Overall	139/397	205/400	0.58 (0.46-0.72)
Pathologic stage			
II	34/118	48/121	0.65 (0.42-1.01)
IIIA	80/217	124/225	0.54 (0.41-0.72)
IIIB	25/62	33/54	0.52 (0.31-0.88)
pN status			
pN0	51/148	70/142	0.57 (0.40-0.82)
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)



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. Per the prespecified analysis plan, subgroups with <30 participants are 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.

Overall Survival

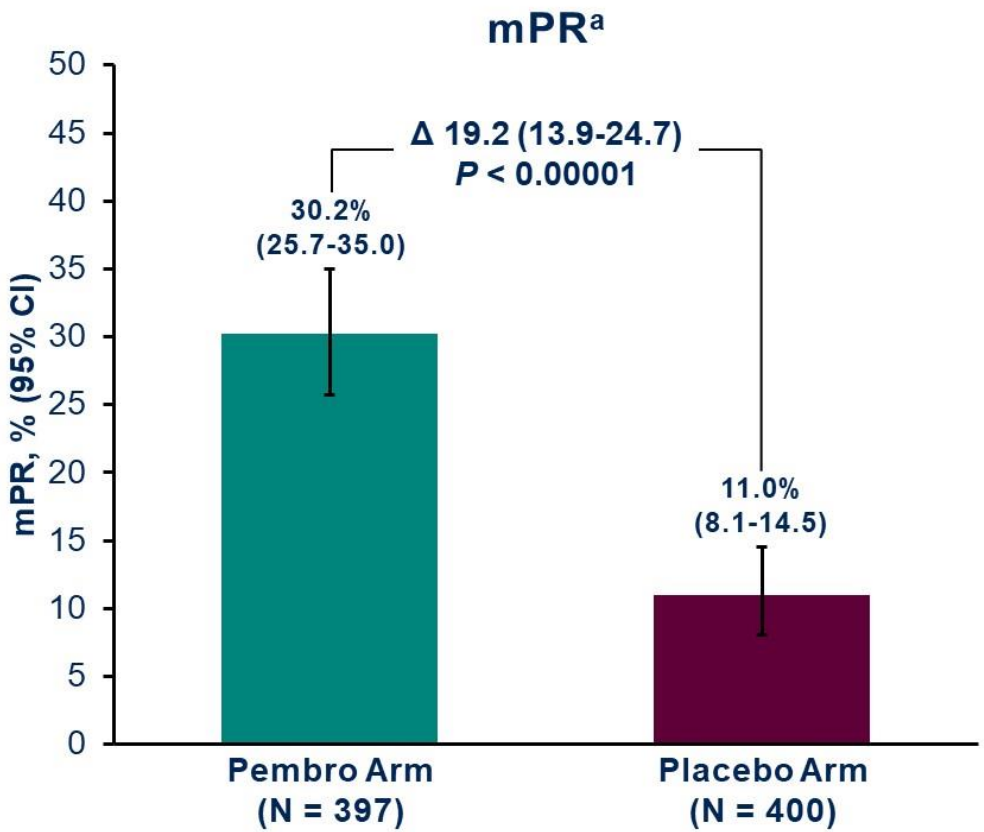
	Pts w/ Event	Median (95% CI), mo
Pembro arm	19.1%	NR (NR-NR)
Placebo arm	25.3%	45.5 (42.0-NR)

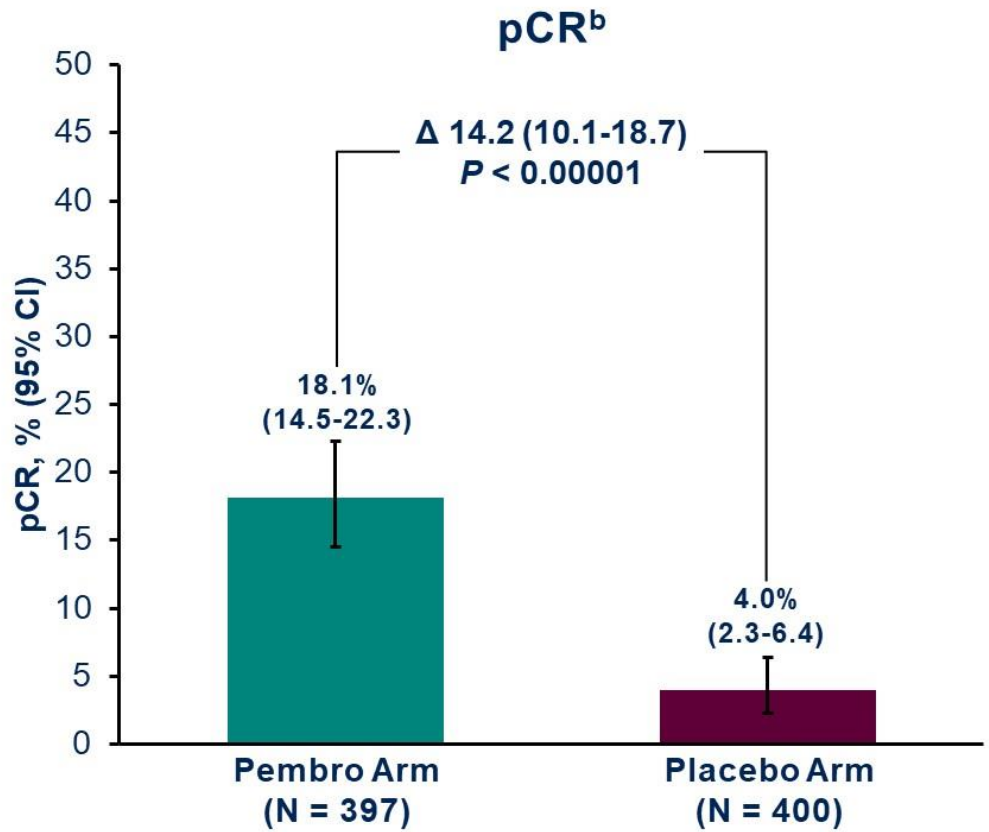


HR 0.73 (95% CI, 0.54-0.99)
***P* = 0.02124[a]**

OS defined as time from randomization to death from any cause. [a] Significance boundary not met at IA1; OS will continue to be tested according to the analysis plan. Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

Pathologic Response
Assessed per Blinded, Independent Pathologist Review

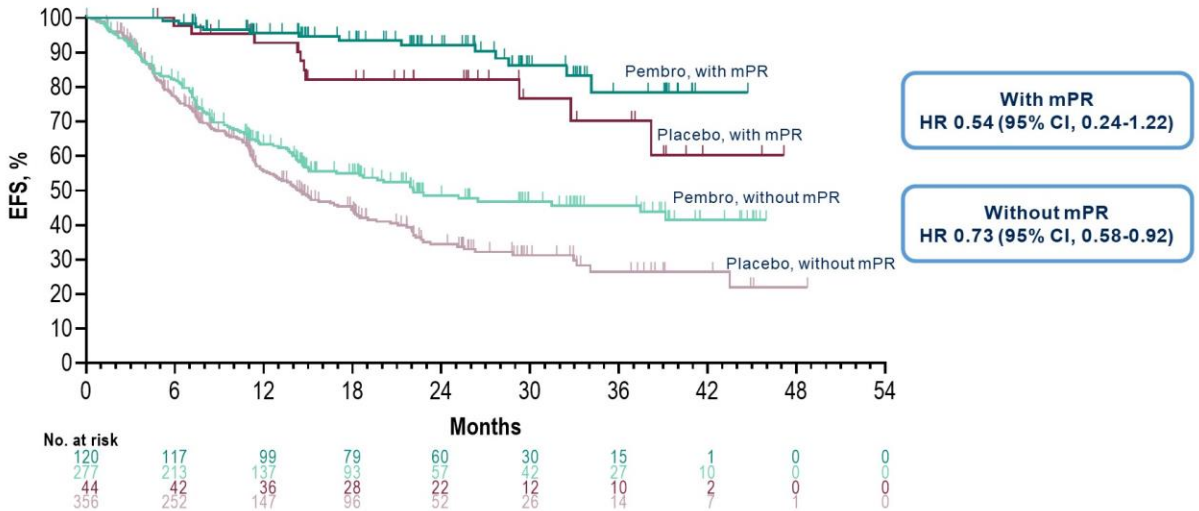




[a] Defined as ≤10% viable tumor cells in resected primary tumor and lymph nodes. [b] Defined as absence of residual invasive cancer in resected primary tumor and lymph nodes (ypT0/Tis ypN0). Data cutoff date for IA1: July 29, 2022.

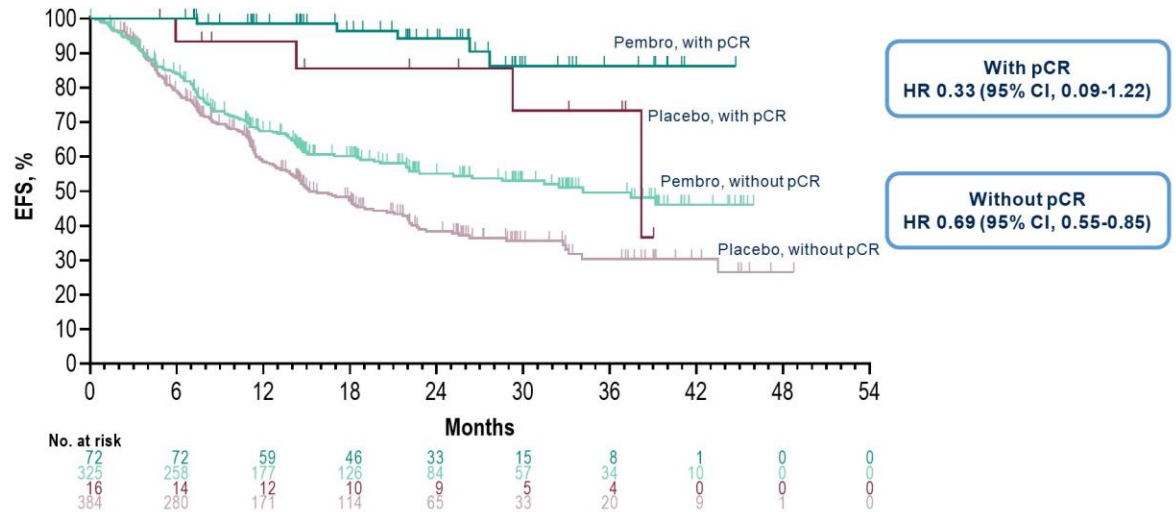
Exploratory Analysis of EFS by mPR Status

Exploratory Analysis of EFS by mPR Status



mPR defined as ≤10% viable tumor cells in resected primary tumor and lymph nodes. 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]).

Exploratory Analysis of EFS by pCR Status



pCR defined as absence of residual invasive cancer in resected primary tumor and lymph nodes (ypT0/Tis ypN0). 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]).

Exposure and Adverse Event Summary Across Treatment Phases

	Pembro Arm (n = 396)	Placebo Arm (n = 399)
Exposure		
Days on pembro or placebo, median (range)	332 days (1-567)	315 days (1-596)
No. pembro or placebo administrations, median (range)	12 (1-17)	10 (1-17)
Treatment-related AEs	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%)[a]	3 (0.8%)[b]
Led to discontinuation of all study treatment	50 (12.6%)	21 (5.3%)
Immune-mediated AEs 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%)[c]	0
Led to discontinuation of all study treatment	20 (5.1%)	3 (0.8%)

[a] AEs leading to death (n = 1 each): atrial fibrillation, immune-mediated lung disease, pneumonia, and sudden cardiac death. [b] AEs leading to death (n = 1 each): acute coronary syndrome, pneumonia, and pulmonary hemorrhage.
[c] AE leading to death: pneumonitis (recorded in the database as immune-mediated lung disease). Data cutoff date for IA1: July 29, 2022.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

H. Wakelee, M. Liberman, T. Kato, M. Tsuboi, S.-H. Lee, S. Gao, K.-N. Chen, C. Dooms, M. Majem, E. Eigendorff, G.L. Martinengo, O. Bylicki, D. Rodríguez-Abreu, J.E. Chaft, S. Novello, J. Yang, S.M. Keller, A. Samkari, and J.D. Spicer, for the KEYNOTE-671 Investigators*

Summary and Conclusion

- Neoadjuvant pembrolizumab plus chemotherapy followed by surgery and adjuvant pembrolizumab provided statistically significant, clinically meaningful improvement in EFS compared with neoadjuvant chemotherapy and surgery alone
  - Median EFS was not reached in the pembrolizumab arm vs 17.0 months in the placebo arm; 24-month EFS estimates were 62.4% vs 40.6%
  - EFS benefit was generally consistent across all subgroups analyzed
- Pathological response rates were significantly higher in the pembrolizumab arm versus the placebo arm
  - mPR rates were 30.2% vs 11.0%; pCR rates were 18.1% vs 4.0%
- Exploratory analysis showed an EFS benefit for perioperative pembrolizumab regardless of whether patients achieved pCR or mPR
- OS benefit of perioperative pembrolizumab had not reached statistical significance at IA1
  - OS will continue to be tested according to the statistical analysis plan
- AE profile was as expected based on the known profiles of the individual treatment components
- **Data support neoadjuvant pembrolizumab plus chemotherapy followed by surgery and adjuvant pembrolizumab as a promising new treatment option for patients with resectable stage II, IIIA, or IIIB (N2) NSCLC**

POSTCARD

METASTATIC NSCLC
ONCOGENE ADDICTED

WU-KONG6

PHAROS

2023 ASCO ANNUAL MEETING

Sunvozertinib for the Treatment of NSCLC with *EGFR* Exon20 Insertion Mutations: the First Pivotal Study Results

Mengzhao Wang[1], Yun Fan[2], Meili Sun[3], Yongsheng Wang[4], Yanqiu Zhao[5], Bo Jin[6] Ying Hu[7], Zhigang Han[8], Xia Song[9], Anwen Liu[10], Kejing Tang[11], Cuimin Ding[12], Li Liang[13], Lin Wu[14], Junzhen Gao[15], Jianghong Wang[16], Ying Cheng[17], Jianying Zhou[18] Yong He[19], Li Zheng[20]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, CN; [2]Zhejiang Cancer Hospital, Hangzhou, CN; [3]Central Hospital Affiliated to Shandong First Medical University, Jinan, CN; [4]Clinical Trial Center, National Medical Products Administration Key Laboratory for Clinical Research and Evaluation of Innovative Drugs, West China Hospital, Sichuan University, Chengdu, CN; [5]Respiratory Department of Internal Medicine, The Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, CN; [6]The First Hospital of China Medical University, Shenyang, CN; [7]Beijing Chest Hospital, Capital Medical University, Beijing, CN; [8]The Affiliated Cancer Hospital of Xinjiang Medical University, Wulumuqi, CN; [9]Shanxi Cancer Hospital, Taiyuan, CN; [10]Second Affiliated Hospital of Nanchang University, Nanchang, CN; [11]The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, CN; [12]The Fourth Hospital of Hebei Medical University, Shijiazhuang, CN; [13]Peking University Third Hospital, Beijing, CN; [14]Hunan Cancer Hospital, Changsha, CN; [15]The Affiliated Hospital of Inner Mongolia Medical University, Huhehaote, CN; [16]Chongqing Cancer Hospital, Chongqing, CN; [17]Jilin Cancer Hospital, Changchun, CN; [18]The First Affiliated Hospital, Zhejiang University School of Medicine, Zhejiang University, Hang Zhou, CN; [19]Army Medical Center of PLA, Chongqing, China; [20]Dizal Pharmaceutical, Shanghai, CN.

PRESENTED BY: Mengzhao Wang, MD, Ph.D

WU-KONG6 Study Design

Key inclusion criteria:

- Locally advanced or metastatic NSCLC
- Confirmed EGFR exon20ins in tumor tissues
- Received 1 – 3 lines of prior systemic therapies
- Disease progressed on or after platinum-based chemotherapy

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
- Pharmacokinetics

† According to RECIST 1.1. Tumor assessment every 6 weeks

IRC, independent review committee; ORR, objective response rate; DoR, duration of response; PFS, progression free survival; DCR, disease control rate; OS, overall survival.

Data cut-off for analysis: October 17, 2022

PRESENTED BY: Mengzhao Wang, MD, Ph.D

Patient Demographics and Treatment History

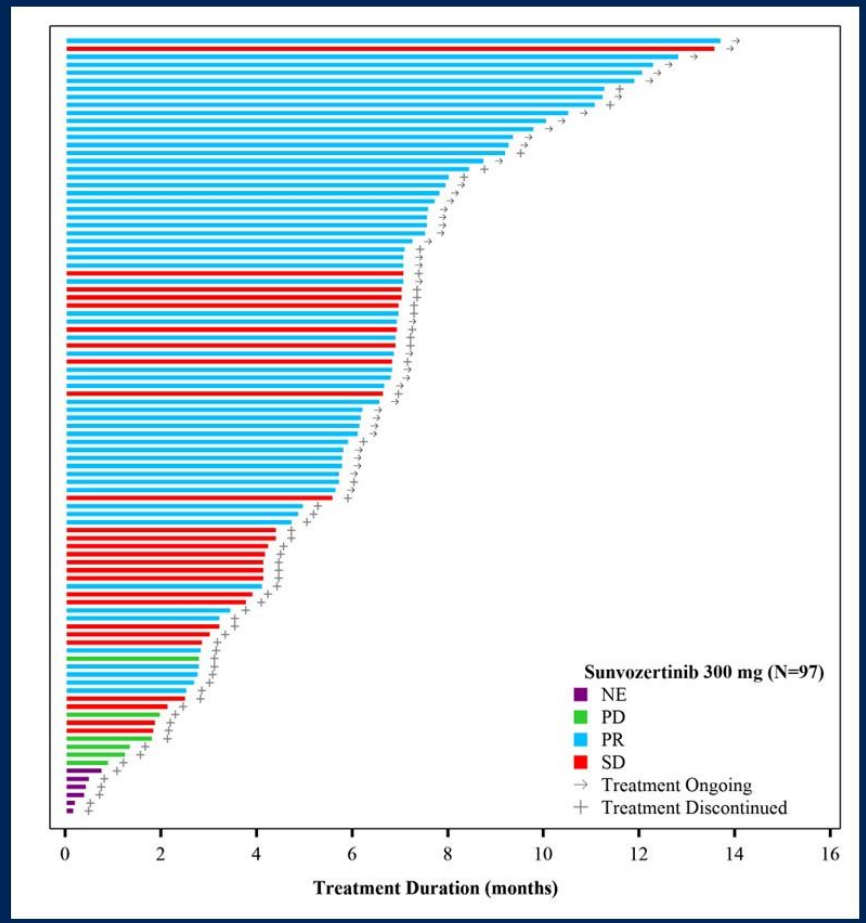
Demographics and Baseline Characteristics	N = 97
Median age, years (range)	58 (29, 79)
Male/Female, n (%)	39 (40.2)/58 (59.8)
History of smoking, Yes(%)/No(%)	32 (33)/65 (67)
Baseline brain metastasis, n (%)	31 (32.0)
Mutation subtypes, n (%)	
769_ASV	38 (39.2)
770_SVD	17 (17.5)
Others	42 (43.3)

Patient Treatment History	N = 97
Median prior anti-cancer therapy, n (range)	2 (1, 3)
Prior anti-cancer therapy type, n (%)	
Chemotherapy	97 (100)
Platinum-based chemotherapy	97 (100)
EGFR TKI	26 (26.8)
PD-1/PD-L1	34 (35.1)
Anti-VEGF	58 (59.8)
Others	16 (16.5)

- As of October 17, 2022, a total of 104 subjects with over 30 EGFR Exon20ins subtypes were enrolled and the last subject has been followed up for 6 months. A total of 97 patients were included in the efficacy analysis set.

Duration on Treatment

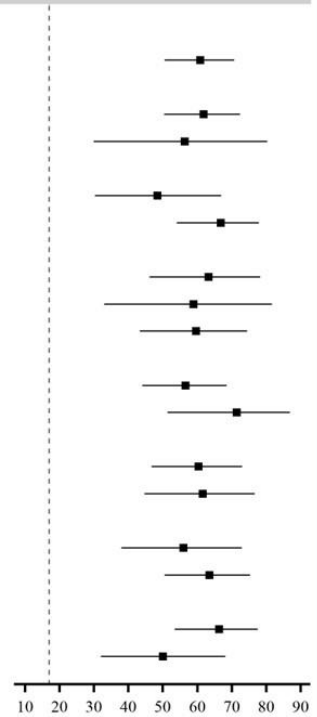
- At the data cut-off date, median duration on treatment (DoT) was 7.0 months, and the longest DoT was 19.2 months.
- With median follow-up of 5.6 months after documented response, 38 of 59 responders (64.4%) were still responding. Median DoR was not reached. The longest DoR was > 11.2 months and the patient was still responding.



Tumor response was assessed by IRC
Data cut-off: Oct 17, 2022

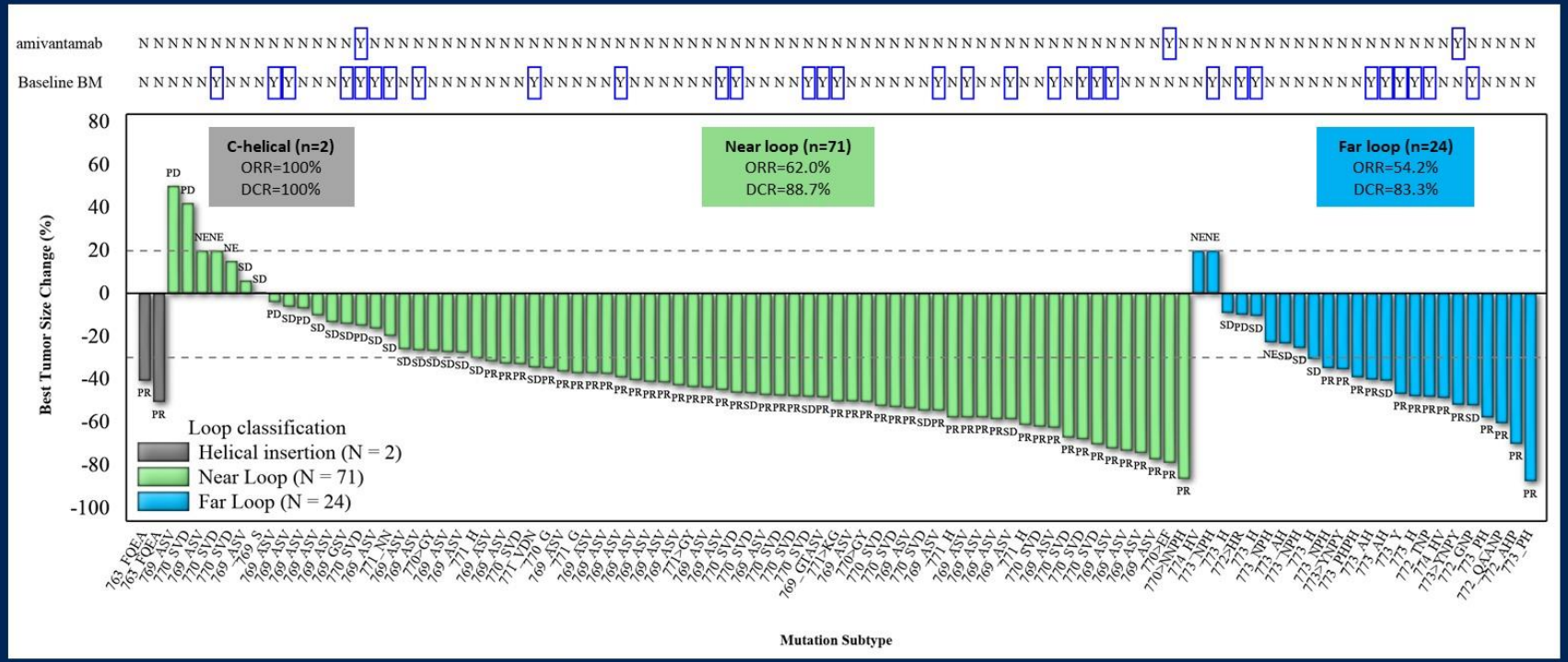
Subgroup Analysis of Anti-tumor Efficacy

Subgroup	Total Number of Participants	No. of Responders (%)
Overall	97	59 (60.8)
Number of Previous Regimens		
< 3	81	50 (61.7)
3	16	9 (56.3)
Baseline Brain Metastasis		
Yes	31	15 (48.4)
No	66	44 (66.7)
Mutation Subtype		
769_ASV	38	24 (63.2)
770_SVD	17	10 (58.8)
Other	42	25 (59.5)
Age Group		
<65 years old	69	39 (56.5)
≥65 years old	28	20 (71.4)
Sex		
Female	58	35 (60.3)
Male	39	24 (61.5)
PD-1 or PD-L1		
Yes	34	19 (55.9)
No	63	40 (63.5)
Smoking Status		
Never	65	43 (66.2)
Smoke	32	16 (50.0)



- Anti-tumor efficacy (ORR) of sunvozertinib was observed irrespective of age, sex, smoking status, baseline brain metastasis, lines of prior therapies, mutation subtypes and prior PD-1/PD-L1 treatment status.

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.

Safety Profile of Sunvozertinib

Common TEAE by PT	N = 104 All Grade	N = 104 ≥ Grade 3
Diarrhea	70（67.3）	8（7.7）
Blood CPK increase	60（57.7）	18（17.3）
Rash	56（53.8）	1（1.0）
Anemia	51（49.0）	6（5.8）
Blood creatinine increase	39（37.5）	0（0.0）
Paronychia	34（32.7）	2（1.9）
Body weight decrease	30（28.8）	1（1.0）
White blood cell decrease	27（26.0）	0（0.0）
Lipase increase	27（26.0）	2（1.9）
Vomiting	25（24.0）	1（1.0）
Decreased appetite	25（24.0）	2（1.9）
Mouth ulceration	24（23.1）	0（0.0）

- Safety profile of sunvozertinib was similar to other EGFR TKIs. Majorities of the AEs were grade 1 or 2.

Conclusion

- In WU-KONG6 pivotal study, sunvozertinib demonstrated significant anti-tumor efficacy and well-tolerated safety profile in platinum-based chemotherapy pretreated NSCLC with EGFR exon20ins.
  - The confirmed ORR at 300 mg QD was 60.8% assessed by IRC.
  - Anti-tumor efficacy was observed across a variety of EGFR exon20ins subtypes and regardless of insertion locations.
  - Anti-tumor efficacy was observed in patients with baseline brain metastasis and who failed amivantamab treatment.
  - Sunvozertinib demonstrated comparable safety profile to other EGFR TKIs.
- Sunvozertinib can be a potential treatment option for NSCLC with EGFR exon20ins.
- A phase III, randomized, multinational study (WU-KONG28, NCT05668988) is ongoing to assess sunvozertinib versus platinum-based chemotherapy in the 1st line EGFR exon20ins NSCLC.

Abstract 9018

Efficacy and safety of encorafenib plus binimetinib in patients with metastatic *BRAF* V600E-mutant (*BRAF*^{V600E}) non-small cell lung cancer (NSCLC) from the phase 2 PHAROS study

Gregory J. Riely,[1] Egbert F. Smit,[2] Myung-Ju Ahn,[3] Enriqueta Felip,[4] Suresh S. Ramalingam,[5] Anne Tsao,[6] Melissa Johnson,[7] Francesco Gelsomino,[8] Raymond Esper,[9] Ernest Nadal,[10] Michael Offin,[1] Mariano Provencio,[11] Gregory A. Otterson,[12] Ibiayi Dagogo-Jack,[13] Ann Alcasid,[14] Tiziana Usari,[15] Keith Wilner,[16] Nuzhat Pathan,[16] Bruce E. Johnson[17]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]Department of Pulmonary Diseases, Leiden University Medical Center, Leiden, Netherlands; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [5]Winship Cancer Institute of Emory University, Atlanta, GA; [6]MD Anderson Cancer Center, Houston, TX; [7]Tennessee Oncology, Sarah Cannon Research Institute, Nashville, TN; [8]Medical Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [9]Florida Cancer Specialists, Fort Myers, FL; [10]Medical Oncology, Catalan Institute of Oncology, Barcelona, Spain; [11]Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain; [12]Ohio State University Comprehensive Cancer Center, Columbus, OH; [13]Massachusetts General Hospital, Boston, MA; [14]Pfizer, Collegeville, PA; [15]Pfizer, Milan, Italy; [16]Pfizer, La Jolla, CA; [17]Dana-Farber Cancer Institute, Boston, MA

Presented at the 2023 ASCO Annual Meeting, June 2-6, 2023; Chicago, IL, and Online
Correspondence: Gregory Riely, rielyg@MSKCC.ORG

Encorafenib plus binimetinib in patients with metastatic BRAF V600E NSCLC

- The combination of encorafenib (BRAF inhibitor) plus binimetinib (MEK inhibitor) has demonstrated clinical efficacy with an acceptable safety profile in patients with metastatic BRAF V600E/K–mutant melanoma[1]
- For patients with metastatic BRAF V600E–mutant NSCLC the combination of dabrafenib and trametinib was approved by the US FDA and is a current standard of care [2]
  - This approval was based on the results of a single-arm, phase 2 study that showed meaningful antitumor activity and a manageable safety profile[3,4]
    - In treatment-naïve and previously treated patients, the ORR by IRR was 64% and 63%, respectively
    - The median DOR by IRR was 15.2 months and 9.0 months, respectively
- Given the observed efficacy and safety profile of encorafenib plus binimetinib in patients with BRAF V600E/K–mutant metastatic melanoma, this combination therapy was assessed in patients with metastatic BRAF V600E–mutant NSCLC

PHAROS (NCT03915951):
A single-arm, open-label, multicenter, phase 2 study

Key eligibility criteria

- Metastatic BRAF V600E–mutant NSCLC
- ECOG performance status 0 or 1
- No *EGFR* mutation, *ALK* fusion, or *ROS1* rearrangement
- No more than 1 prior line of treatment in the advanced setting
- No prior treatment with BRAF or MEK inhibitor
- No symptomatic brain metastases

***BRAF* mutation testing**

- Determined locally by PCR- or NGS-based assay; sent to central laboratory[a]
- Pleural fluid, fresh and archived tissue, and fine needle aspiration were acceptable

Patients enrolled

- Treatment naïve n=59
- Previously treated n=39

Encorafenib: 450 mg QD
Binimetinib: 45 mg BID
28-day cycles
Treat until progression or unacceptable toxicity

Primary endpoint

- ORR[b] by IRR

Secondary endpoints

- ORR by investigator
- DOR, DCR, PFS, and TTR (all by IRR and investigator)
- OS
- Safety

Exploratory endpoints

- Biomarker and pharmacokinetic analyses

BID, twice daily; **DCR**, disease control rate; **DOR**, duration of response; **ECOG**, Eastern Cooperative Oncology Group; **IRR**, independent radiology review; **ORR**, objective response rate; **NGS**, next-generation sequencing; **OS**, overall survival; **PCR**, polymerase chain reaction; **PFS**, progression-free survival; **QD**, once daily; **TTR**, time to response.

[a]BRAF V600 mutations were retrospectively confirmed by FoundationOne CDx (Foundation Medicine, Cambridge, MA). [b]According to RECIST 1.1.

1. Dummer R, et al. *Lancet Oncol*. 2018;19(5):603-615. 2. Dabrafenib prescribing information. June 2022. 3. Planchard D, et al. *Lancet Oncol*. 2016;17(7):984-993. 4. Planchard D, et al. *Lancet Oncol*. 2017;18(10):1307-1316.

Encorafenib plus binimetinib in metastatic BRAF-V600E mutant NSCLC

Antitumor activity endpoints by IRR

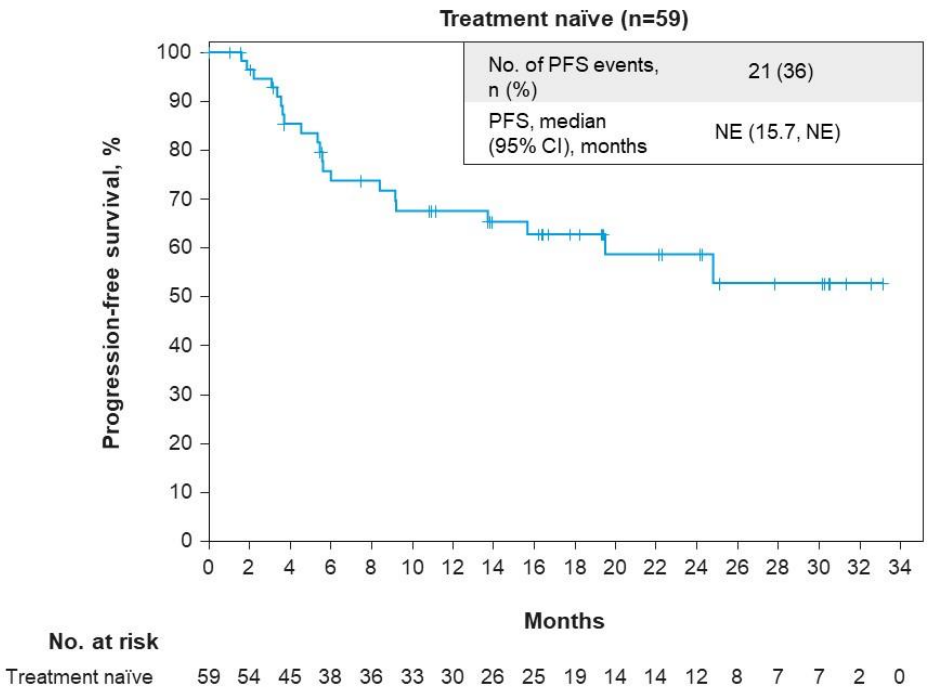
	Treatment naïve (n=59)	Previously treated (n=39)
Objective response rate (95% CI), %[a]	75 (62, 85)	46 (30, 63)
Complete response	9 (15)	4 (10)
Partial response	35 (59)	14 (36)
Stable disease	10 (17)	13 (33)
Progressive disease	2 (3)	3 (8)
Disease control rate at 24 weeks (95% CI), %	64 (51, 76)	41 (26, 58)
Duration of response, median (95% CI), months	NE (23.1, NE)	16.7 (7.4, NE)
Duration of response ≥12 months, n/N (%)	26/44 (59)	6/18 (33)
Time to response, median (range), months	1.9 (1.1-19.1)	1.7 (1.2-7.3)

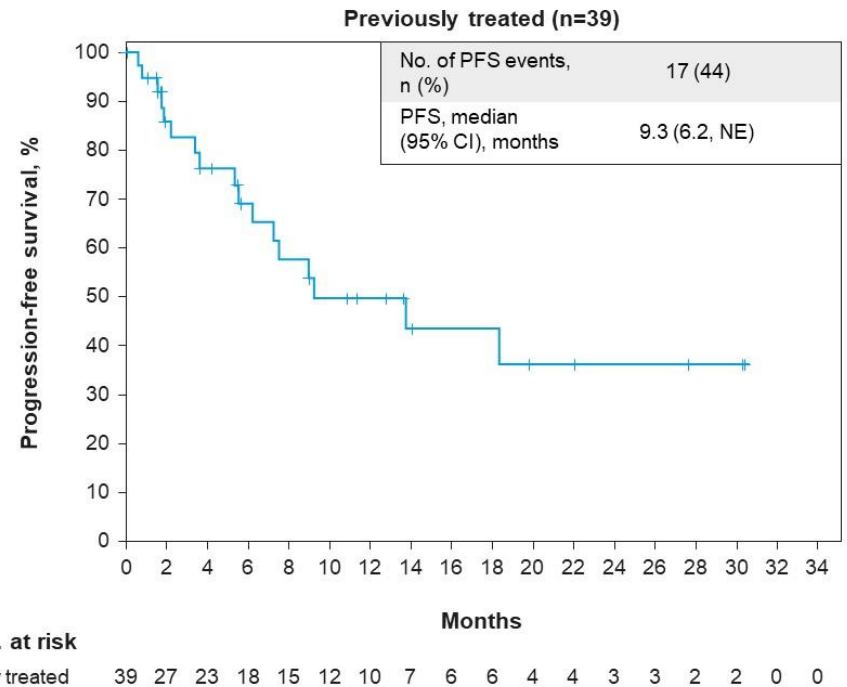
IRR, independent radiology review; **NE**, not estimable.

[a]Response of 3 patients were not evaluable in the treatment-naïve group, and 5 were not evaluable in the previously treated group.

Encorafenib plus binimetinib in metastatic BRAF-V600E mutant NSCLC

Progression-free survival by IRR





- The median duration of follow-up for PFS by IRR was 18.2 months (95% CI, 16.4, 22.3 months) in treatment-naïve patients and 12.8 months (95% CI, 9.0, 19.8 months) in previously treated patients

IRR, independent radiology review; **NE**, not estimable; **PFS**, progression-free survival.

Encorafenib plus binimetinib in metastatic BRAF-V600E mutant NSCLC
Incidence of TRAEs of any grade >10% in all patients

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

Note: Any-grade abdominal pain, alopecia, asthenia, and dry skin occurred in 10% of patients; any-grade pyrexia occurred in 8% of patients.
ALT, alanine aminotransferase; **AST**, aspartate aminotransferase; **TRAE**, treatment-related adverse event.
[a]One patient died due to intracranial hemorrhage, which was assessed as treatment related by the investigator. [b]Grade 4 TRAEs were colitis, disseminated intravascular coagulation, increased γ-glutamyl transferase, and hyponatremia.

Encorafenib plus binimetinib in metastatic BRAF-V600E mutant NSCLC
Conclusions

- The combination of encorafenib plus binimetinib showed a meaningful clinical benefit with an acceptable safety profile in patients with BRAF V600E–mutant metastatic NSCLC in the phase 2 PHAROS study
  - Efficacy was observed in both cohorts:
    - ORRs by IRR were 75% (95% CI: 62-85%) in treatment –naïve patients and 46% (95% CI: 30-63%), in previously treated patients
    - Median DORs by IRR were NE (95% CI, 23.1 months, NE) and 16.7 months (95% CI, 7.4 months, NE), respectively
  - The safety profile was consistent with that observed in the approved indication in melanoma
- Encorafenib plus binimetinib represents a potential new treatment option for patients with BRAF V600E–mutant metastatic NSCLC

IRR, independent radiology review; **NE**, not estimable; **ORR**, objective response rate.

POSTCARD

METASTATIC NSCLC
NON ONCOGENE ADDICTED

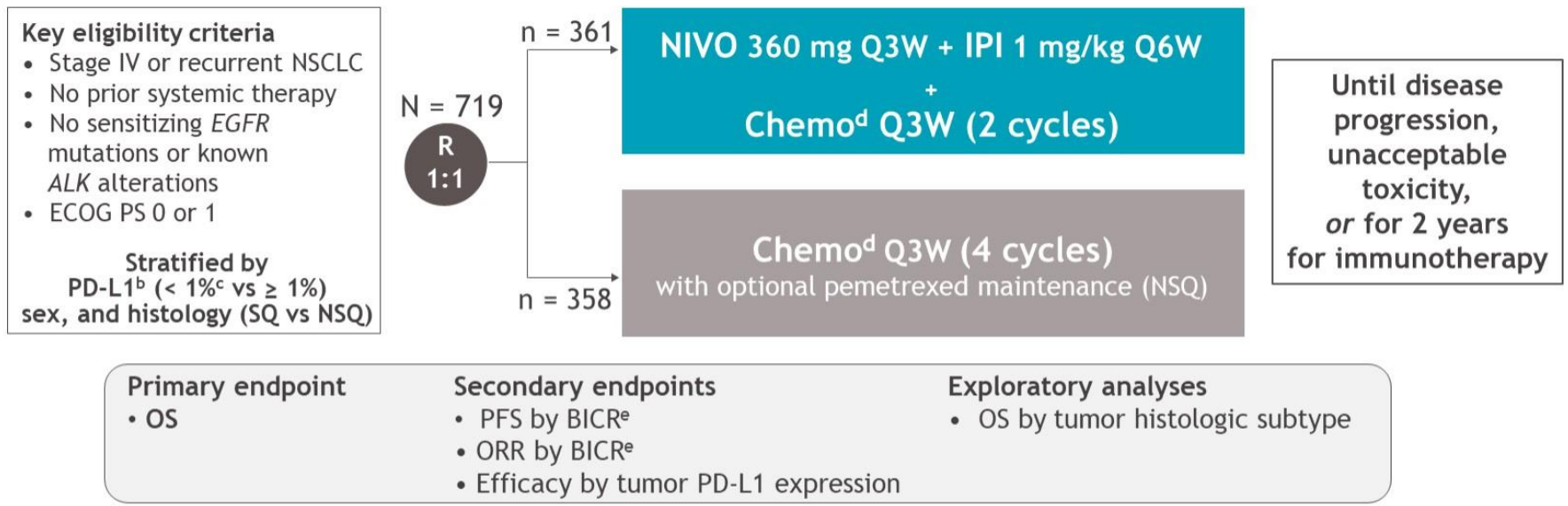
CHECKMATE 9-LA

TROPION-Lung 02

First-line nivolumab + ipilimumab + chemotherapy vs chemotherapy alone in patients with mNSCLC from CheckMate 9LA: 4-year clinical update and outcomes by tumor histologic subtype

David P. Carbone, et al. Poster LBA9023

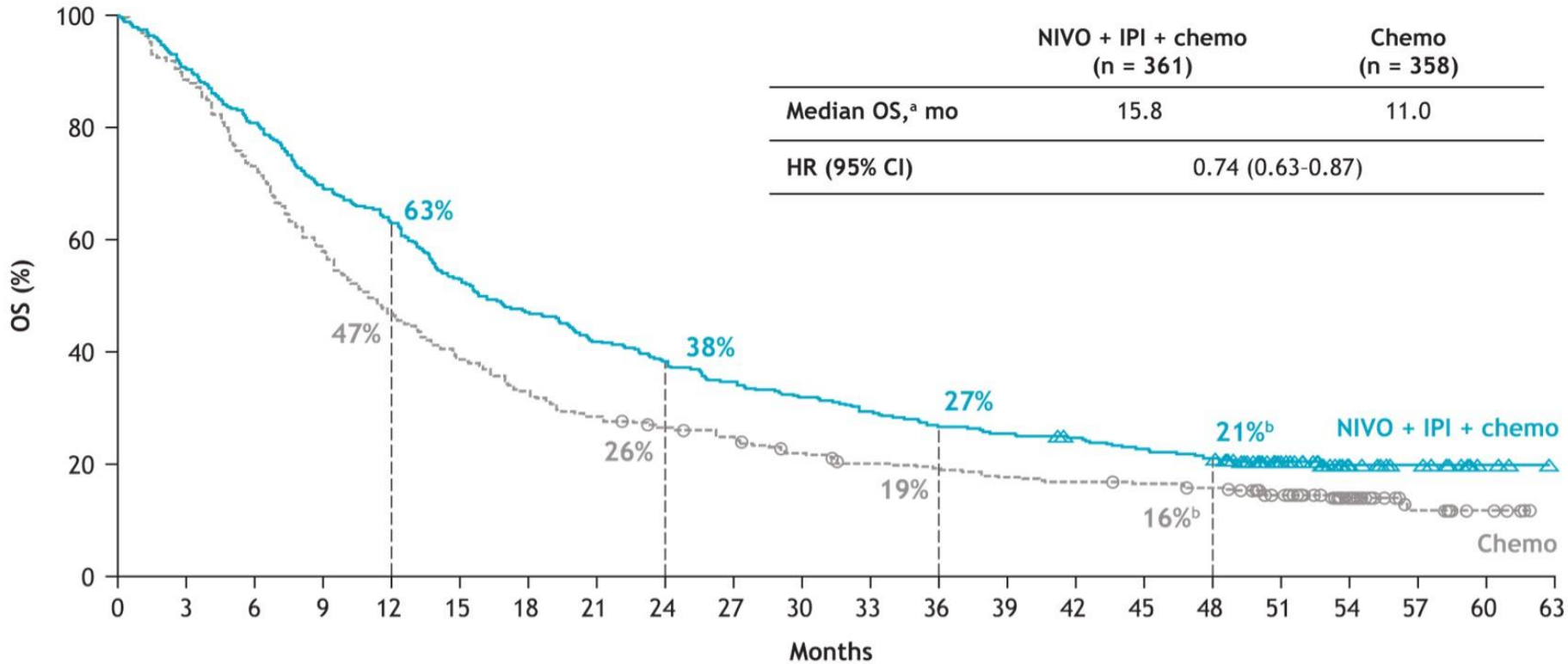
- In the randomized phase 3 CheckMate 9LA study,[a] 1L NIVO + IPI plus 2 cycles of chemo significantly improved OS vs chemo alone (4 cycles) in patients with metastatic NSCLC[1,2]
- Here, we present the updated efficacy and safety results of CheckMate 9LA, with a minimum follow-up of 4 years, as well as exploratory biomarker analyses of OS by tumor histologic subtype



Database lock: February 13, 2023; minimum/median follow-up for OS: 47.9/54.5 months.
Figure reproduced from Paz-Ares L, et al. *Lancet Oncol* 2021;22:198-211, with permission from Elsevier.
[a]NCT03215706. [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako). [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients. [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin. [e]Hierarchically statistically tested.
1. Paz-Ares L, et al. *Lancet Oncol* 2021;22:198-211. 2. Paz-Ares LG, et al. *J Thorac Oncol* 2023;18:204-222.

4-year update: OS in all randomized patients

	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS,[a] mo	15.8	11.0
HR (95% CI)	0.74 (0.63-0.87)	



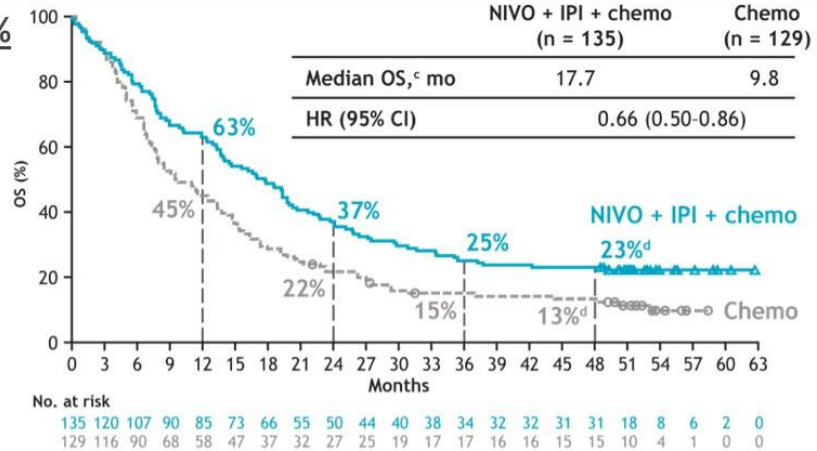
No. at risk

NIVO + IPI + chemo	361	326	292	250	227	191	170	151	138	125	115	106	96	92	87	80	74	47	21	14	4	0
Chemo	358	319	260	208	168	139	115	102	93	86	74	66	63	58	55	53	50	38	22	10	5	0

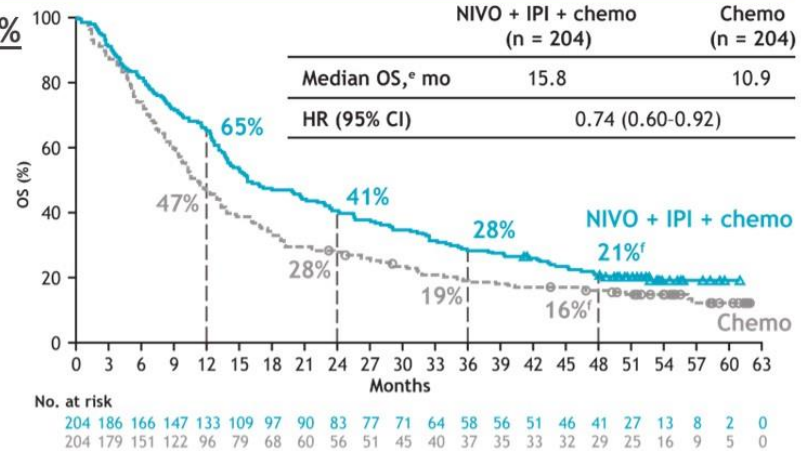
Database lock: February 13, 2023; minimum/median follow-up for OS: 47.9/54.5 months.
In the all-randomized population, subsequent systemic therapy was received by 37% (NIVO + IPI + chemo) and 49% (chemo) of patients, subsequent immunotherapy by 7% and 36%, and subsequent platinum-doublet chemo by 20% and 6%, respectively. 95% CIs for NIVO + IPI + chemo and chemo, respectively: [a]13.9-19.7 and 9.5-12.7; [b]17-25 and 12-20.

OS by tumor PD-L1 expression or histology

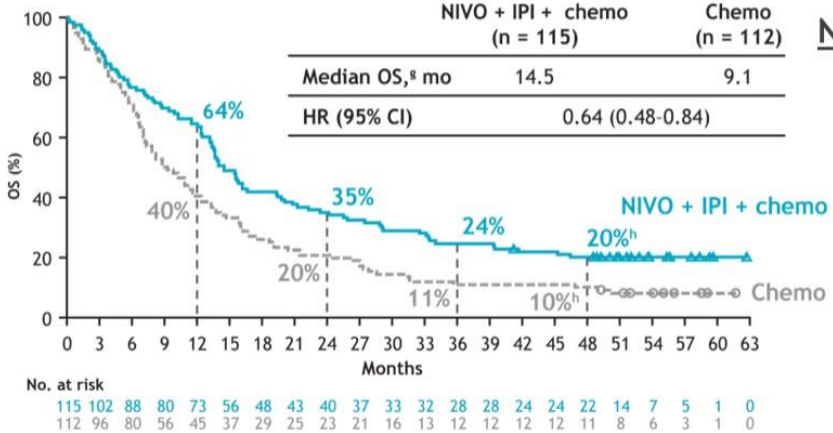
PD-L1 < 1%



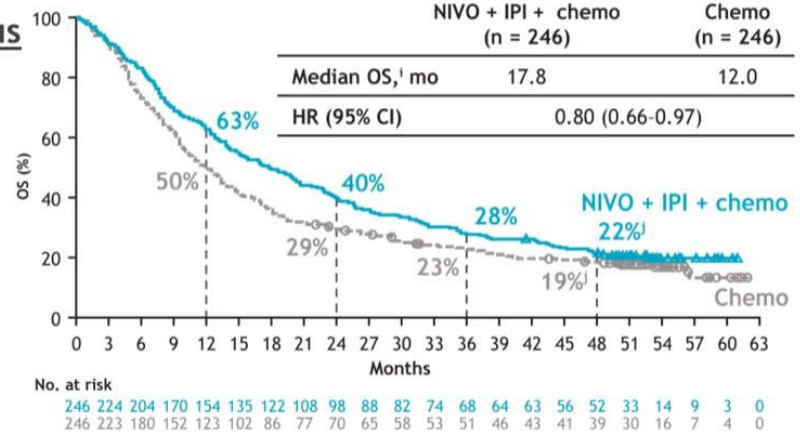
PD-L1 ≥ 1%



Squamous



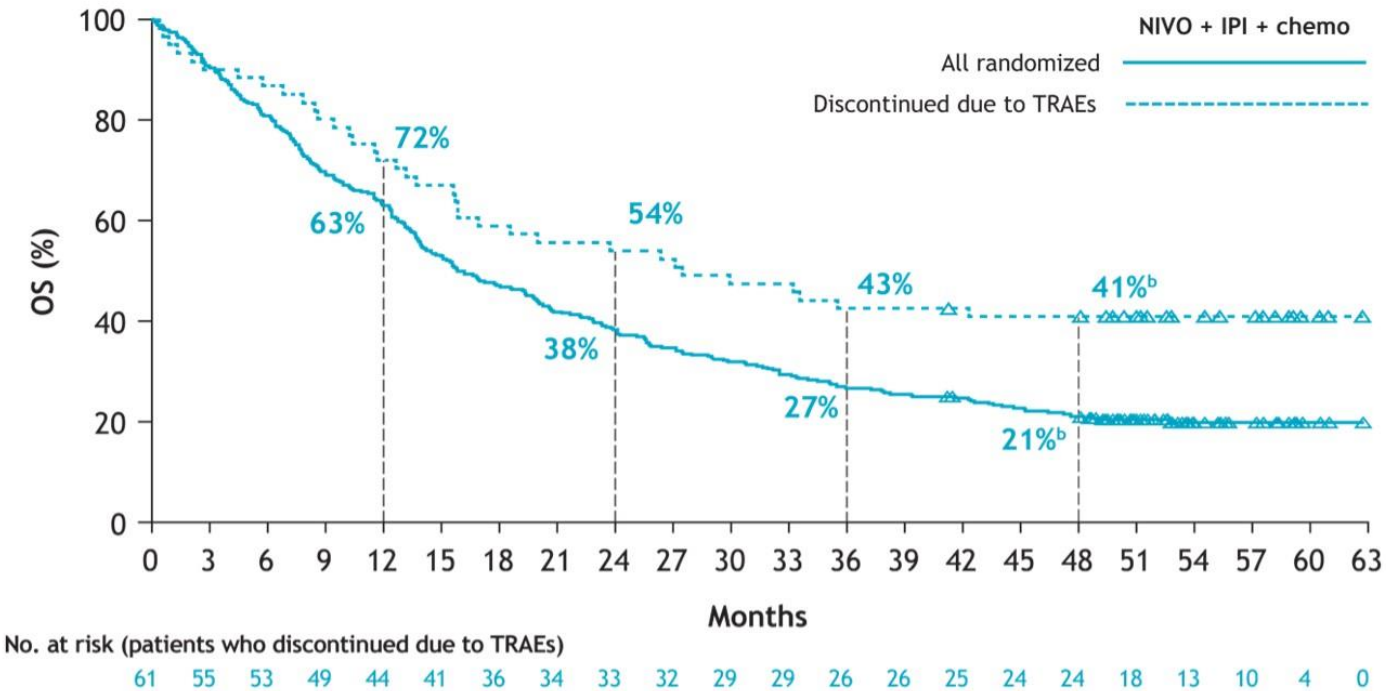
Non-squamous



Database lock: February 13, 2023; minimum/median follow-up for OS: 47.9/54.5 months.

95% CIs for NIVO + IPI + chemo and chemo, respectively: [c]13.7-20.3 and 7.7-13.5; [d]16-30 and 8-20; [e]13.8-22.2 and 9.5-13.2; [f]16-27 and 11-22; [g]13.1-19.3 and 7.2-11.6; [h]13-28 and 5-16; [i]14.1-20.7 and 9.9-13.9; [j]17-27 and 14-24.

Efficacy in patients who discontinued NIVO + IPI + chemo due to treatment-related adverse events (TRAEs)[a]



- Among patients who discontinued all components of NIVO + IPI + chemo due to TRAEs (n = 61), median OS was 27.5 months, and ORR was 51%
- Median treatment-free interval (TFI) in all patients treated with NIVO + IPI + chemo was 2.2 months, with 11% of patients alive and treatment-free 4 years after treatment cessation
  - In those who discontinued due to TRAEs, median TFI was 10.6 months, with 27% of patients alive and treatment-free 4 years after discontinuing study therapy

Database lock: February 13, 2023; minimum/median follow-up for OS: 47.9/54.5 months.
TFI was defined as the time from last study dose to the start of first subsequent systemic treatment or death. [a]Post hoc analysis includes patients with TRAEs (reported between first dose and 30 days after last dose of study treatment) leading to discontinuation of all components of study treatment. [b]95% CIs for discontinued due to TRAEs and all randomized, respectively: 29-53 and 17-25.

Conclusions

- With a 4-year minimum follow-up, patients treated with NIVO + IPI + chemo continued to derive long-term, durable OS benefit vs chemo alone regardless of tumor PD-L1 expression or histology
- Magnitude of OS benefit with NIVO + IPI + chemo vs chemo was greater in patients with tumor PD-L1 < 1% or SQ NSCLC; 4-year OS rates were 23% vs 13% and 20% vs 10%, respectively
  - PFS and DOR benefit were also maintained in patients with tumor PD-L1 < 1% or SQ NSCLC
- Discontinuation of NIVO + IPI + chemo due to TRAEs did not negatively impact the long-term clinical or efficacy benefit, with a 4-year OS rate of 41%
  - 27% of these patients were alive and treatment-free 4 years after discontinuing study therapy
- Exploratory analyses suggested an OS benefit with NIVO + IPI + chemo vs chemo alone in both acinar and solid (a subtype associated with poor prognosis) tumor histologic subtypes
- No new safety signals were reported across tumor histologic subtypes
- These data further support the use of NIVO + IPI + chemo as an efficacious 1L treatment option for patients with metastatic NSCLC, particularly for those with tumor PD-L1 < 1% or SQ histology, populations with high unmet needs

TROPION-Lung02: Datopotamab Deruxtecan (Dato-DXd) Plus Pembrolizumab With or Without Platinum Chemotherapy in Advanced Non-Small Cell Lung Cancer

Yasushi Goto, MD, PhD,[1] Wu Chou Su, MD,[2] Benjamin Levy, MD,[3] Olivier Rixe, MD, PhD,[4,5] Tsung Ying Yang, MD, PhD,[6] Anthony Tolcher, MD,[7] Yanyan Lou, MD, PhD,[8] Yoshitaka Zenke, MD, PhD,[9] Panayiotis Savvides, MD,[10] Enriqueta Felip, MD, PhD,[11] Manuel Domine, MD, PhD,[12] Konstantinos Leventakos, MD, PhD,[13] Mariano Provencio Pulla, MD, PhD,[14] Atsushi Horiike, MD, PhD,[15] Edward Pan, MD,[5] Daisy Lin, PhD,[5] Jessie Gu, PhD, MS,[5] Priyanka Basak, MD, MBE,[5] Michael Chisamore, PhD,[16] Luis Paz-Ares, MD, PhD[17]

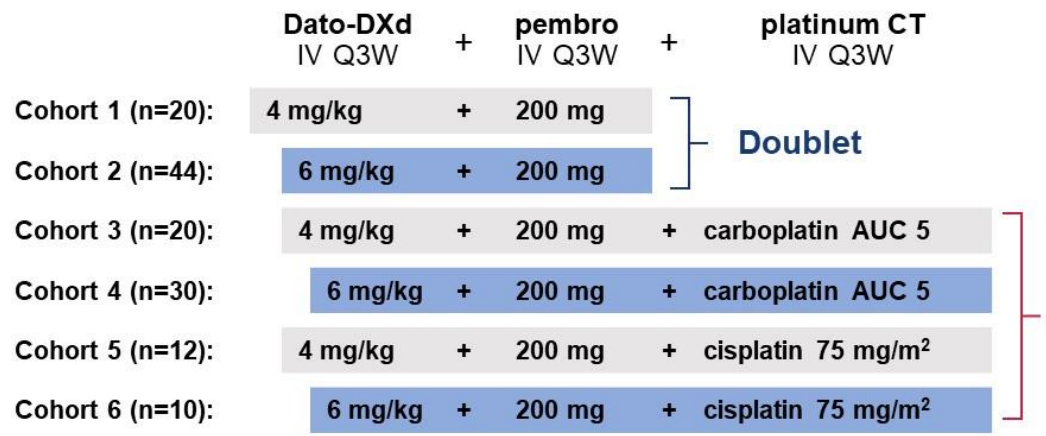
[1]National Cancer Center Hospital, Tokyo, Japan; [2]Department of Oncology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; [4]Quantum Santa Fe, Santa Fe, NM; [5]Daiichi Sankyo, Inc, Basking Ridge, NJ; [6]Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [7]NEXT Oncology, San Antonio, TX; [8]Mayo Clinic, Jacksonville, FL; [9]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [10]Mayo Clinic, Phoenix, AZ; [11]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [12]Department of Oncology, Hospital Universitario Fundación Jiménez Díaz (IIS-FJD), Madrid, Spain; [13]Mayo Clinic, Rochester, MN; [14]Department of Medical Oncology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain; [15]Division of Medical Oncology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan; [16]Merck & Co, Inc, Rahway, NJ; [17]Hospital Universitario 12 de Octubre, CNIO-H12O Lung Cancer Unit, Universidad Complutense and CIBERONC, Madrid, Spain

TROPION-Lung02: Phase 1b Study

- TROPION-Lung02 is the first study evaluating Dato-DXd + pembrolizumab ± platinum CT[a] in advanced NSCLC without actionable genomic alterations[b] (NCT04526691)
  - The safety of the Dato-DXd + pembrolizumab doublet was established prior to evaluation of the platinum-containing triplet
  - The safety of Dato-DXd 4-mg/kg combinations was established prior to evaluation of 6-mg/kg combinations

Key eligibility criteria

- **Advanced/metastatic NSCLC**
- **Dose escalation**[c]: ≤2 lines of prior therapy[d]
- **Dose expansion**
  - ≤1 line of platinum-based CT (cohorts 1 and 2)[d]
  - Treatment naive (cohort 2; enrollment after Jun 30, 2022)[d]
  - Treatment naive (cohorts 3-6)[d]



- **Primary objectives:** safety and tolerability
- **Secondary objectives:** efficacy, pharmacokinetics, and antidrug antibodies

Data cutoff: April 7, 2023.

AUC, area under the curve; CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DLT, dose-limiting toxicity; IV, intravenous; NSCLC, non-small cell lung cancer; pembro, pembrolizumab; Q3W, every 3 weeks.

[a] Administered sequentially at the same visit. [b] Patients with known actionable *EGFR, ALK, ROS1, NTRK, BRAF, RET,* or *MET* mutations or alterations in other actionable oncogenic driver kinases were not eligible for this study. Testing for *EGFR* and *ALK* alterations was not required for patients with squamous histology who were smokers or ≥40 years of age. [c] The first 3 to 6 patients in each cohort were enrolled to confirm acceptable safety/DLT rate; the remaining patients are considered part of dose expansion (for which enrollment was ongoing at the time of data cutoff). [d] Prior therapy requirements are for treatment in the advanced/metastatic setting.

Antitumor Activity

Response[a]	All patients: Doublet (n=61)[b]	All patients: Triplet (n=71)[b]	Patients in 1L: Doublet (n=34)[b]	Patients in 1L: Triplet (n=53)[b]
Confirmed + pending ORR, n (%)[c,d]	23 (38)	35 (49)	17 (50)	30 (57)
[95% CI]	[26-51]	[37-61]	[32-68]	[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	NE	NE	NE	NE
[95% CI]	[8.8-NE]	[5.8-NE]	[5.5-NE]	[5.7-NE]

- In the 1L setting, the ORR (confirmed and pending)[d] was 50% in patients receiving doublet therapy and 57% in those receiving triplet therapy
- Among all patients, the DCR was 84% (doublet) and 87% (triplet); in the 1L setting, the DCR was 91% in both therapy subgroups

Preliminary PFS in all patients, median (95% CI), months: doublet, 8.3 (6.8-11.8); triplet 7.8 (5.6-11.1)[h]

Data cutoff: April 7, 2023.

1L, first line; 2L+, second line and later; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not estimable; ORR, objective response rate; PFS, progression-free survival; PR, partial response; SD, stable disease.

[a] By investigator. [b] Response-evaluable patients, which includes patients with ≥1 postbaseline overall response and those who discontinued without a postbaseline overall response. [c] ORR defined as BOR of CR + PR. [d] Responses pending confirmation. [e] BOR was determined using tumor assessments at different evaluation time points from the date of the first dose of study treatment until documented disease progression or the start of the next line of nonpalliative anticancer therapy (inclusive), whichever was earlier. [f] SD defined as ≥1 SD assessment (or better) ≥5 weeks after starting treatment and before progression without qualification for CR or PR (includes pending responses). [g] DCR defined as BOR of confirmed CR + confirmed PR + SD. [h] Preliminary PFS is limited by immature duration of follow-up.

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)

- During the dose-finding phase, 2 patients receiving Dato-DXd + pembrolizumab + platinum CT had DLTs[c,d,e]
- TEAEs (treatment-emergent adverse events) associated with discontinuation of Dato-DXd occurred in 23% of patients receiving the doublet regimen and in 28% of patients receiving the triplet regimen

Data cutoff: April 7, 2023.

CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DLT, dose-limiting toxicity; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent adverse event; TMG, toxicity management guideline.

[a] TEAEs were defined as AEs with a start or worsening date on or after the start of study treatment until 37 days after the end date of study treatment. [b] Drug-related TEAEs may be associated with any component of the study treatment: Dato-DXd, pembrolizumab, cisplatin, or carboplatin. [c] DLT defined as any TEAE not attributable to disease or any disease-related process that occurs during the DLT evaluation period (days 1-21 in cycle 1) and is grade ≥3 according to NCI CTCAE version 5.0, with certain exceptions. [d] Two grade 4 platelet count decreased, and 1 grade 4 neutrophil count decreased. [e] One additional patient was incorrectly reported as having a DLT and is not included here. [f] All TEAEs associated with death were considered by the investigator to be unrelated to study treatment, except for 1 case of grade 5 pneumonitis, which was ultimately adjudicated as not ILD.

[g] Twenty of these 35 events (11 in doublet cohorts and 9 in triplet cohorts) were due to ILD/pneumonitis events, and TMGs necessitate drug discontinuation for grade 2 events and grade 1 events lasting >49 days.

Adverse Events of Special Interest

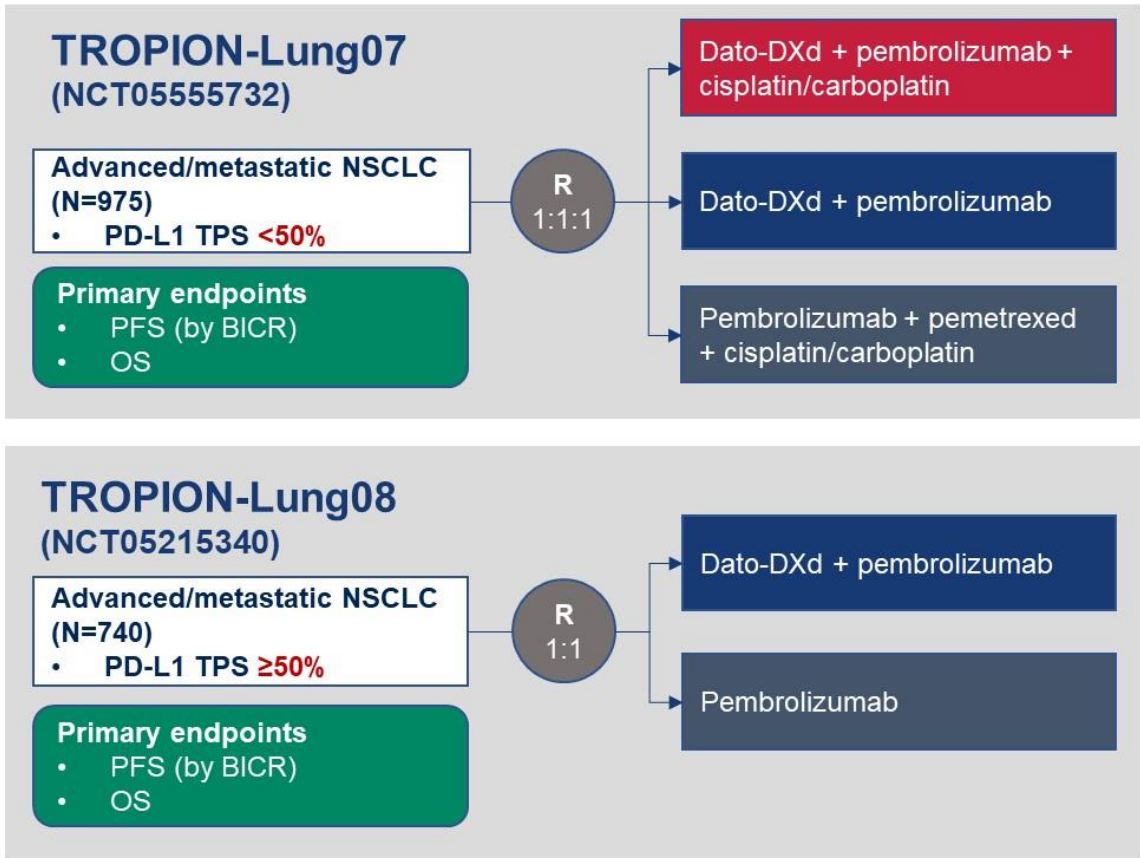
AESI, n (%)[a,b]	Doublet (n=64)		Triplet (n=72)	
	All grades	Grade ≥3	All grades	Grade ≥3
Oral mucositis/stomatitis	37 (58)	5 (8)	31 (43)	4 (6)
ILD/pneumonitis adjudicated as drug related[c]	11 (17)	2 (3)	16 (22)	2 (3)
Ocular surface toxicity[d]	10 (16)	1 (2)	17 (24)	2 (3)
IRR[e]	15 (23)	0	10 (14)	0

- Oral mucositis/stomatitis was the most common AESI and was predominantly grade 1/2
- No grade 5 AESIs have occurred
- There were no grade 4 or 5 adjudicated ILD/pneumonitis events[f]

Data cutoff: April 7, 2023.
AESI, adverse event of special interest; ILD, interstitial lung disease; IRR, infusion-related reaction.
[a] AESIs listed in this slide include all preferred terms that define the medical concept. [b] No cases of mucosal inflammation occurred in patients receiving doublet or triplet therapy. [c] Five ILD cases are pending adjudication.
[d] The majority of these events were cases of dry eye (n=12 patients) and lacrimation increased (n=8 patients); grade ≥3 events were keratitis (n=2 patients) and dry eye (n=1 patient). [e] IRR refers to all IRR events that occurred in a patient who experienced any of the preselected preferred terms within the same day of Dato-DXd infusion. [f] There was 1 grade 5 event initially adjudicated as drug-related ILD in a patient receiving triplet therapy; this event was ultimately readjudicated to be grade 2.

Conclusions and Ongoing Studies With Pembrolizumab

- In this study, Dato-DXd + pembrolizumab ± platinum chemotherapy demonstrated encouraging antitumor activity in patients with NSCLC in the 1L and 2L+ settings
- No new safety signals were observed
  - The most frequent TEAEs of any grade were stomatitis, nausea, anemia, and fatigue
- Dato-DXd + pembrolizumab ± chemotherapy is being compared with SOC therapies in the 1L setting in the pivotal phase 3 TROPION-Lung07 and TROPION-Lung08 studies



1L, first line; 2L+, second line and later; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; R, randomized; SOC, standard of care; TEAE, treatment-emergent adverse event; TPS, tumor proportion score.

AIGOM

ASSOCIAZIONE ITALIANA
GRUPPI ONCOLOGICI MULTIDISCIPLINARI

19 GIUGNO 2023
ore 15.00 - 18.00

LE NOVITA' DA CHICAGO 2023:

l'evoluzione delle conoscenze in oncologia.

Con il contributo non condizionante

GOLD

Eisai

SILVER

AMGEN

Si ringrazia

ROPI

SEGRETERIA ORGANIZZATIV
ETRUSCA
CONVENTIONS
Via M. Bonciario 6/8 - 06123 Perugia
tel. / fax 075.8089485 - info@etruscaconventions.com
www.etruscaconventions.com

Con il Patrocinio