Enfermedad metastásica

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Con la colaboración de:

Bristol Myers Squibb™

Janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Organizado por:

GECP
lung cancer research

DISCLOSURES

- I am working as Medical Oncologist in Hospital Son Llatzer
- Receipt of honoraria and consultation fees: Roche, Novartis, Pfyzer, Celgene, Pharmamar, Lilly, Eisai, Astra Zeneca, Pierre Fabre, Bristol, Merck, Takeda.
- Comments on the presented data reflect my point of view.

ESQUEMA PRESENTACIÓN

- Inmunoterapia +/ quimioterapia
- Inmunoterapia más otras terapias
- Terapias dirigidas

INMUNOTERAPIA +/- QUIMIOTERAPIA

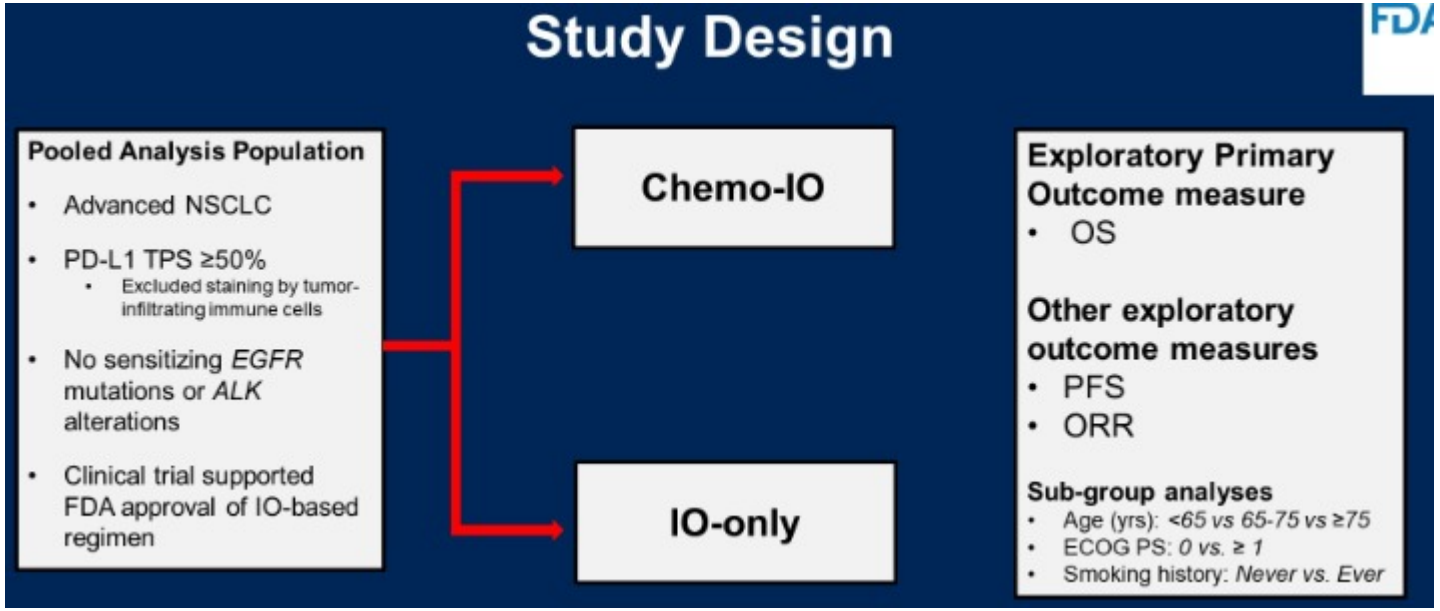
Outcomes of anti-PD-(L)1 therapy with or without chemotherapy (chemo) for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score ≥50%: FDA Pooled Analysis

Oladimeji Akinboro[1], Jonathon Vallejo[1], Erica Nakajima[1], Yi Ren[1], Pallavi Mishra-Kalyani[1], Erin Larkins[1], Paz Vellanki[1], Nicole Drezner[1], Mathieu Luckson[1], Shenghui Tang[1], Martha Donoghue[1,2], Richard Pazdur[1,2], Julia A. Beaver[1,2], Harpreet Singh[1,2]

[1]Center for Drug Evaluation and Research, U.S. Food and Drug Administration

[2]Oncology Center of Excellence, U.S. Food and Drug Administration

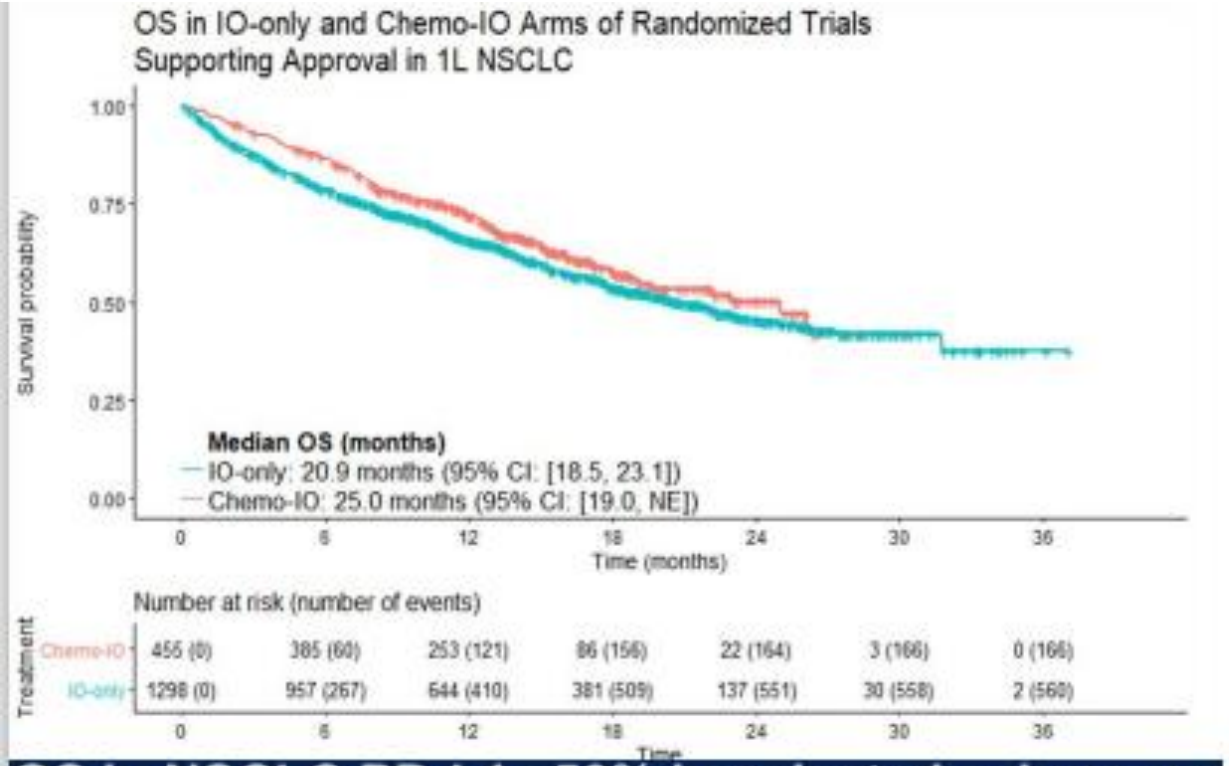
Oladimeji Akinboro, MD, MPH

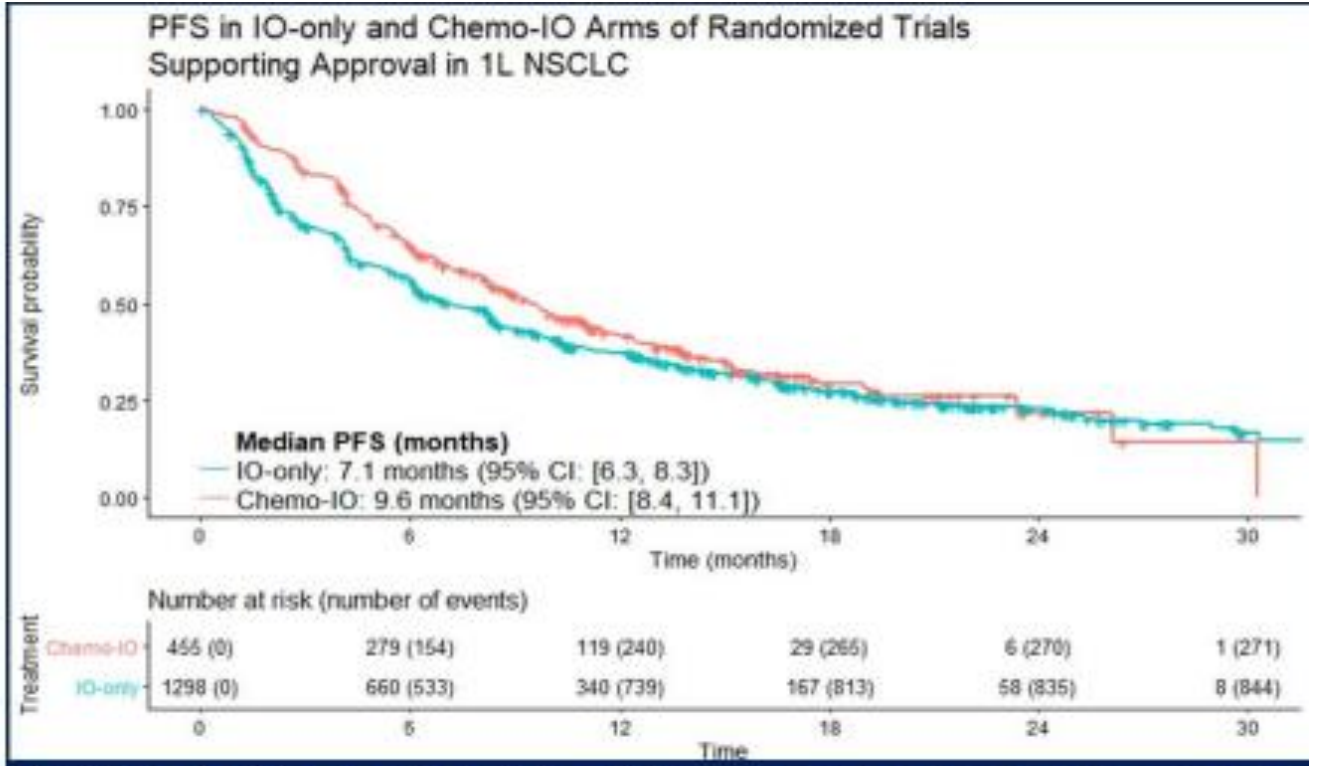


Clinical trials of first-line Chemo-IO and IO regimens included in FDA pooled analysis

Chemo-IO Trials		IO-only Trials	
Trial	Investigational Regimen	Trial	Investigational Regimen
KEYNOTE-021*	**Pembrolizumab** + Chemo**	CheckMate 026	**Nivolumab****
KEYNOTE-189	**Pembrolizumab** + Chemo**	KEYNOTE-024	**Pembrolizumab****
KEYNOTE-407	**Pembrolizumab** + Chemo**	KEYNOTE-042	**Pembrolizumab****
IMpower150	**Atezolizumab** + Bevacizumab + Chemo***	IMpower110	**Atezolizumab****
IMpower130	**Atezolizumab** + Chemo**	CheckMate 227	**Nivolumab** + **Ipilimumab****
CheckMate-9LA	**Nivolumab** + **Ipilimumab** + Chemo**	EMPOWER-Lung 1	**Cemiplimab****

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy immunotherapy; IO=immunotherapy.
* Cohort G
** Control arms: Platinum-based doublet chemotherapy
*** Control arm in IMpower150: Bevacizumab plus platinum-based doublet chemotherapy





OS in NSCLC PD-L1 ≥50% in selected subgroups

Subgroup	N	Hazard Ratio	Median OS (95% CI) Chemo-IO	Median OS (95% CI) IO-Only
Overall	1753		25.0 (19.0, NE)	20.9 (18.5, 23.1)
Age				
<65 years	898		25.0 (19.2, NE)	23.3 (20.0, NE)
65-74 years	642		22.2 (16.5, NE)	18.6 (16.0, 21.9)
>=75 years	185		NE (12.0, NE)	18.9 (15.1, NE)
ECOG				
0	602		NE (23.0, NE)	31.8 (22.4, NE)
1+	1148		17.7 (14.8, NE)	18.0 (15.7, 21.0)
Smoking Status				
Current/former smokers	1549		23.0 (18.2, NE)	22.1 (19.7, 25.1)
Never smokers	197		NE (22.2, NE)	14.4 (12.2, 21.0)

0.25 0.50 1.0 2.0
<---Chemo-IO Better--- ---IO-only Better--->

PFS in NSCLC PD-L1 ≥50% in selected subgroups

Subgroup	N	Hazard Ratio	Median PFS (95% CI) Chemo-IO	Median PFS (95% CI) IO-Only
Overall	1753		9.6 (8.4, 11.1)	7.1 (6.3, 8.3)
Age				
<65 years	898		9.4 (8.2, 13.4)	7.7 (6.2, 8.5)
65-74 years	642		9.7 (8.3, 11.1)	6.8 (6.1, 8.3)
>=75 years	185		11.8 (4.9, NE)	7.2 (6.1, 9.9)
ECOG				
0	602		13.7 (10.2, 17.4)	8.5 (7.7, 11.2)
1+	1148		8.2 (6.8, 9.7)	6.3 (6.1, 7.4)
Smoking Status				
Current/former smokers	1549		9.3 (8.3, 11.1)	8.2 (6.8, 8.4)
Never smokers	197		10.2 (7.7, 23.4)	3.7 (2.6, 5.5)

0.25 1.0 2.0
<---Chemo-IO Better--- ---IO-only Better--->

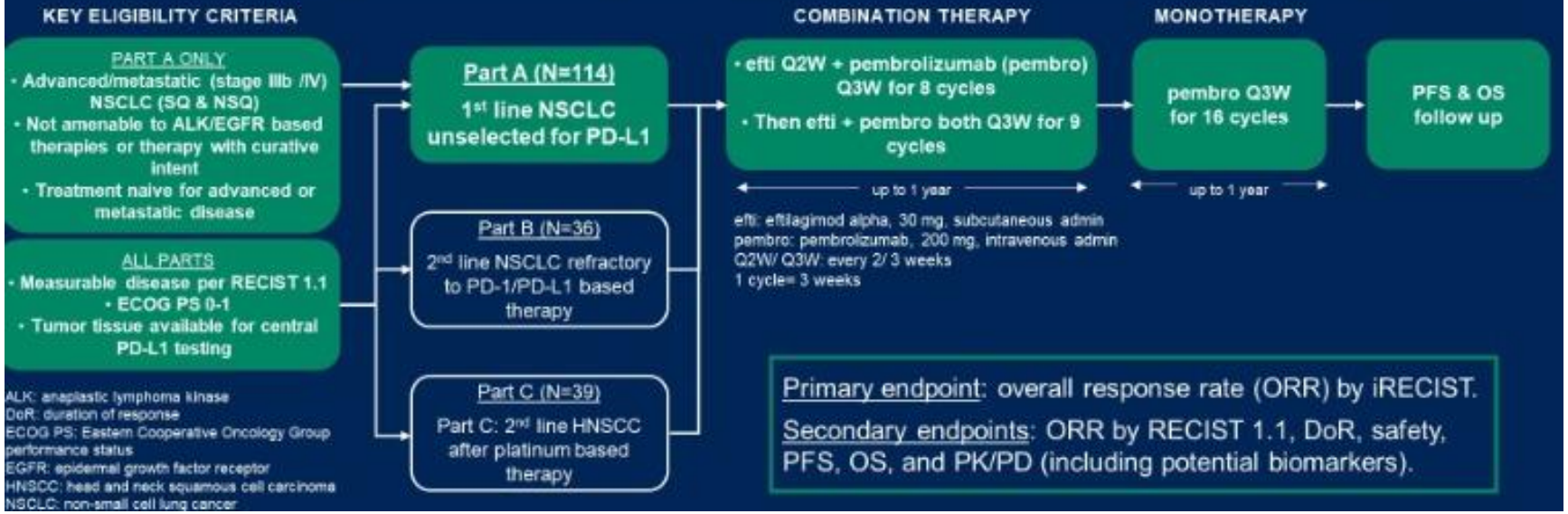
2022 ASCO ANNUAL MEETING

A Phase II study (TACTI-002) in 1st line metastatic non-small cell lung cancer (NSCLC) investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab: updated results from a PD-L1 unselected population

E Felip[1], M Majem[2], B Doger[3], T Clay[4], E Carcereny[5], I Bondarenko[6], J Peguero[7], M Cobo Dols[8], M Forster[9], G Ursol[10], E Kalinka[11], G Garcia Ledo[12], L Vila Martinez[13], MG Krebs[14], W Iams[15], B Campos Balea[16], C Mueller[17], and F Triebel[18]

Trial Design – TACTI-002

TACTI-002 is a Phase II, multinational, open label trial with patients from 3 indications unselected for PD-L1.

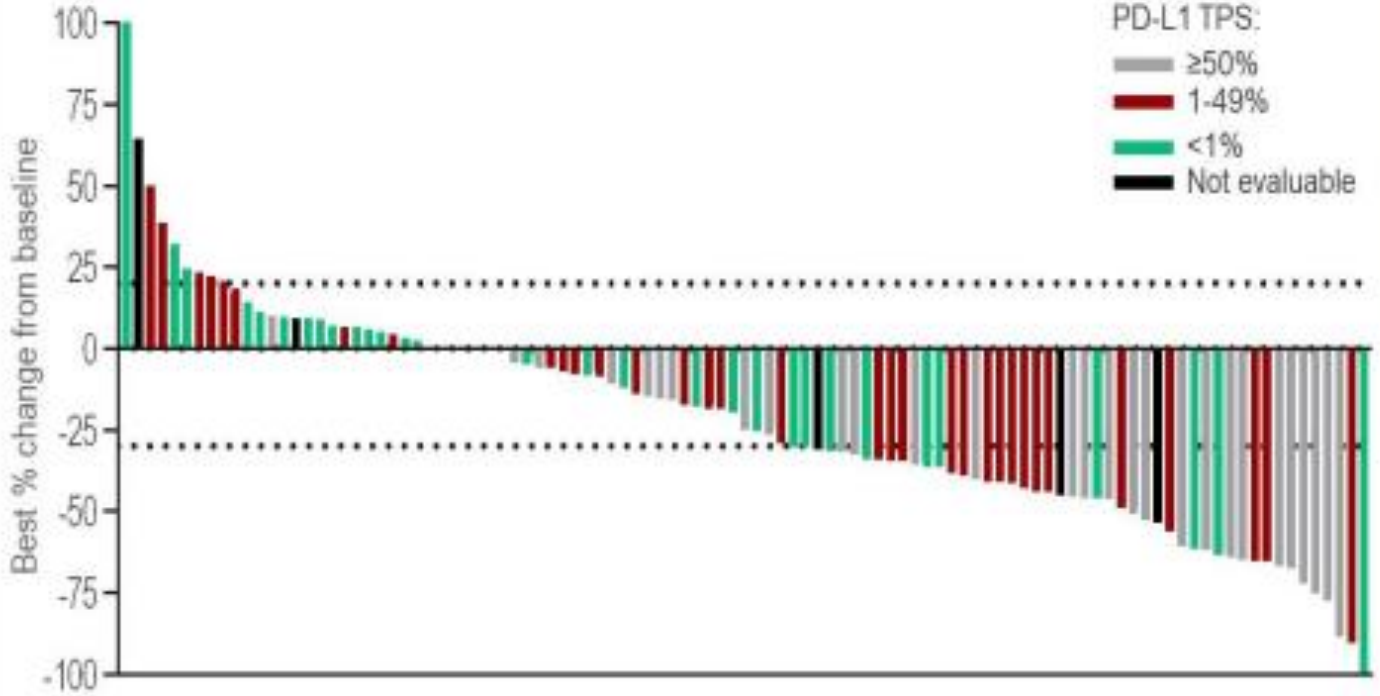


Primary endpoint: overall response rate (ORR) by iRECIST.

Secondary endpoints: ORR by RECIST 1.1, DoR, safety, PFS, OS, and PK/PD (including potential biomarkers).

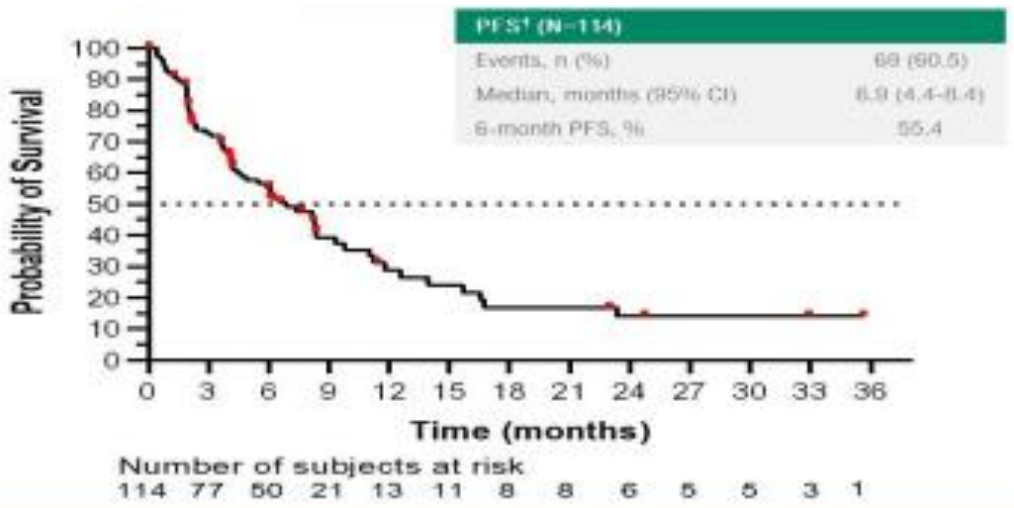
Organizado por:

GECP lung cancer research



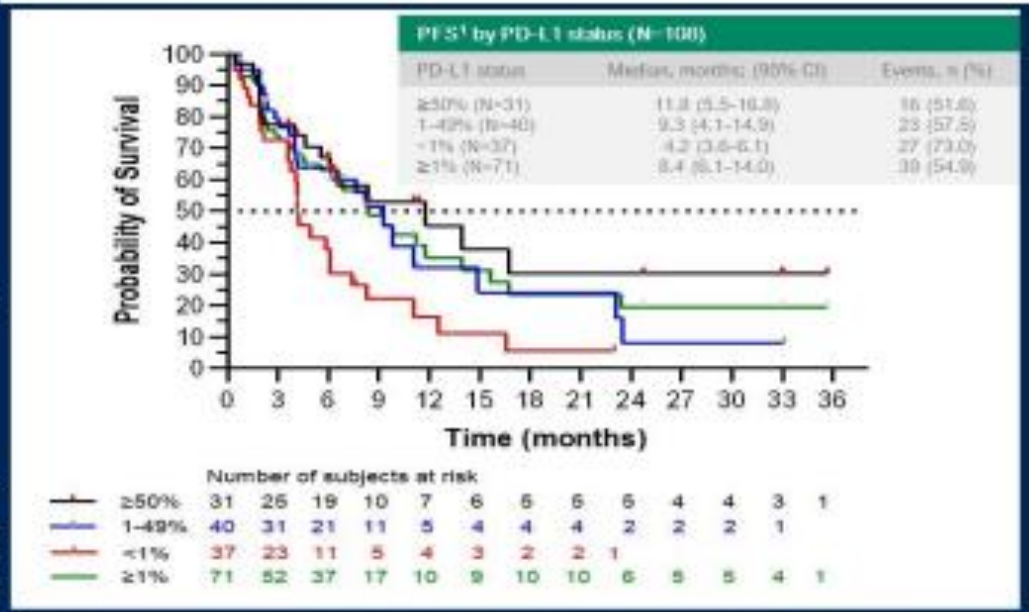
[1] all patients with ≥1 post-baseline CT scan n=103; [2] PD-L1 assessed by central assessment (Dako kit); n=79; [3] local assessment included due to non evaluable central assessment results, n=19; [4] no results available for neither central nor local testing, n=5.

- 2 complete responses and 19.4% of patients with a target lesion decrease ≥50%.
- 68/103 (66.0%) of patients with a post-baseline assessment had a decrease in target lesions.



Interim median PFS[1] in the ITT (unselected for PD-L1) was 6.9 (95% CI: 4.4.-8.4) months.

[1] by IRECIST.
[2] central (N=87) & local (N=21) as previously described on slide 9.



Interim median PFS[1] in PD-L1 ≥1% was 8.4 (95% CI: 6.1 14.0) months and 11.8 (5.5-16.8) months in PD-L1 ≥50%.

Data cut-off date: Ap

#ASCO22

PRESENTED BY:
Enriqueta Felip. A Phase I study (TACTI-002) in 1st line metastatic NSCLC investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab: updated results from a PD-L1 unselected population

Exposure & Safety[1] – TACTI-002

Safety parameter[1]	n (%)
Any TEAE	113 (99.1)
Any Serious TEAE	45 (39.5)
Serious TEAE related to study treatment[3]	*10 (8.8)*
Any Grade ≥3 TEAE	59 (51.8)
Grade ≥3 TEAE related to study treatment[3]	*12 (10.5)*
Any Grade 4 TEAE	5 (4.4)
Any Grade 5 TEAE	12 (10.5)
Grade 5 TEAE related to study treatment[3]	*3 (2.6)*
Any TEAEs leading to discontinuation of study treatment[2]	23 (20.2)
TEAEs leading to discontinuation related to study treatment[3]	*11 (9.6)*

- Median exposure of efti was 23.1 weeks (range 1-52.4) and 21.8 weeks for pembro (range 0.1-103.3).
- 5 patients completed 2 years of treatment until data cut-off.
- 11 patients (9.6%) permanently discontinued treatment due to AEs related to study treatment[2]:
  - *peripheral sensory neuropathy (G2), n=2*
  - *gait disturbance (G2), n=1*
  - *ALT (G3) and AST elevation (G3), n=1*
  - *acute kidney injury (G3), n=1*
  - *drug hypersensitivity (G3), n=1*
  - *bronchospasm (G3), n=1*
  - *immune-related hepatitis (G4), n=1*
  - *pneumonitis (G5), n=1*
  - *sudden death- unknown cause (G5), n=1*
  - *pulmonary embolism (G5), n=1*

AE: adverse event
ALT: alanine aminotransferase
AST: aspartate aminotransferase
G: grade
SAE: serious adverse event
TEAE: treatment emergent adverse event; AEs with onset date on or after the first dose of study drug regardless of causality
[1] AEs rated according to the current National Cancer Institute Common Terminology Criteria for Adverse Events (v4.0).
[2] Study treatment= efti and/or pembrolizumab.

Data cut-off date: April 15, 2022

2022 ASCO ANNUAL MEETING #ASCO22

ASCO KNOWLEDGE CONQUERS CANCER

Frequent TEAEs (incidence ≥15%) by PT regardless of relationship to any study drug

Adverse event by PT	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Dyspnea	39 (34.2)	13 (11.4)	1 (0.9)	1 (0.9)
Asthenia	35 (30.7)	2 (1.8)	-	-
Decreased appetite	27 (23.7)	1 (0.9)	-	-
Cough	27 (23.7)	2 (1.8)	-	-
Anemia	24 (21.1)	3 (2.6)	-	-
Fatigue	23 (20.2)	1 (0.9)	-	-
Pruritus	22 (19.3)	-	-	-
Constipation	20 (17.5)	1 (0.9)	-	-
Diarrhea	18 (15.8)	1 (0.9)	-	-
Nausea	18 (15.8)	2 (1.8)	-	-

- 20.3% of patients had any type of local injection site reactions (any PT contained injection site) any grade and thereof 1.8 % with severity of G2. None ≥G3 were reported.

Frequency of AEs (by PT) with possible immune etiology regardless of relationship to any study drug

Adverse event by PT	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
(Immune related) Hypothyroidism	10 (8.8)	-	-	-
Pneumonitis	4 (3.5)	-	1 (0.9)	1 (0.9)
Hyperthyroidism	6 (5.3)	-	-	-
Diarrhea	18 (15.8)	1 (0.9)	-	-
Thyroiditis	1 (0.9)	-	-	-
(Immune related) Hepatitis	3 (2.6)	-	1 (0.9)	-
Nephritis + Acute kidney injury	1 (0.9)	1 (0.9)	-	-
Adrenal insufficiency	1 (0.9)	-	-	-
Infusion related reaction*	1 (0.9)	1 (0.9)	-	-

* (i.e. drug hypersensitivity, serum sickness, infusion related hypersensitivity reaction, infusion related reaction, CRS, anaphylactic reaction, anaphylactic shock, anaphylactoid reaction, anaphylactoid shock)

- No cytokine release syndrome reported.

IASLC 2022 World Conference on Lung Cancer

AUGUST 6-9, 2022 | VIENNA, AUSTRIA

JAVELIN Lung 100: a multicenter, randomized, phase 3 trial

Key eligibility criteria

- Metastatic or recurrent NSCLC (Stage IV)*
- No *EGFR* mutation or *ALK* rearrangement
- PD-L1 expression in ≥1% of tumor cells
- Measurable disease according to RECIST 1.1
- ECOG PS 0 or 1

Randomized patients: N=1214

Safety run-in: N=10

Before protocol amendment
Randomization 1:1
Stratified by histology

R1

- **Avelumab Q2W** 10 mg/kg IV **n=205**
- **Platinum-based doublet chemotherapy** Q3W **n=205**

Post protocol amendment
Randomization 1:2:2
Stratified by histology and PD-L1 expression

R2

- **Avelumab Q2W** 10 mg/kg IV **n=161**
- **Platinum-based doublet chemotherapy** Q3W **n=321**
- **Avelumab QW** 10 mg/kg IV Safety run-in **N=10**
- **Avelumab QW** first 12 weeks, then Q2W 10 mg/kg IV **n=322**

Primary endpoints

- PFS† and OS‡ in patients with high-expression PD-L1+ tumors§

Key secondary endpoints

- PFS and OS in patients with moderate-to-high-expression PD L1+ tumors¶
- OS in patients with PD L1+ ≥1% tumors
- Best overall response†
- Duration of response†
- Safety

*Patients with pretreated and stable brain metastases were eligible for enrollment. †Per independent review committee. ‡OS was changed to a primary endpoint in the protocol amendment that added the avelumab QW arm. §PD-L1 expression on ≥80% of tumor cells determined by Dako PD-L1 IHC 73-10 pharmDx assay, which is comparable to the TPS ≥50% cutoff for the PD-L1 IHC 22C3 pharmDx (pembrolizumab) assay. ¶PD-L1 expression on ≥50% of tumor cells determined by Dako PD-L1 IHC 73-10 pharmDx assay.

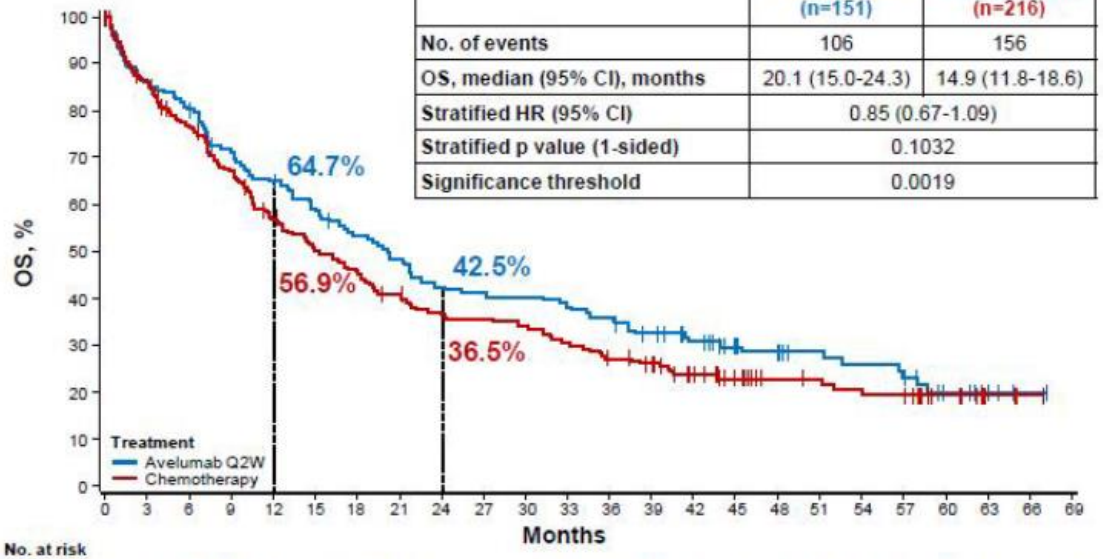
Grote HJ, et al. J Thorac Oncol. 2020;15(8):1306-1316.

ECOG PS, Eastern Cooperative Oncology Group performance status; **IHC**, immunohistochemistry; **IV**, intravenous; **NSCLC**, non-small cell lung cancer; **OS**, overall survival; **PFS**, progression-free survival; **QW**, once weekly; **Q2W**, every 2 weeks; **Q3W**, every 3 weeks; **R1**, randomization before protocol amendment; **R2**, randomization after protocol amendment; **TPS**, tumor proportion score

Primary endpoint: OS in the high PD-L1+ populations*

Avelumab Q2W vs chemotherapy

	Avelumab Q2W (n=151)	Chemotherapy (n=216)
No. of events	106	156
OS, median (95% CI), months	20.1 (15.0-24.3)	14.9 (11.8-18.6)
Stratified HR (95% CI)	0.85 (0.67-1.09)	
Stratified p value (1-sided)	0.1032	
Significance threshold	0.0019	

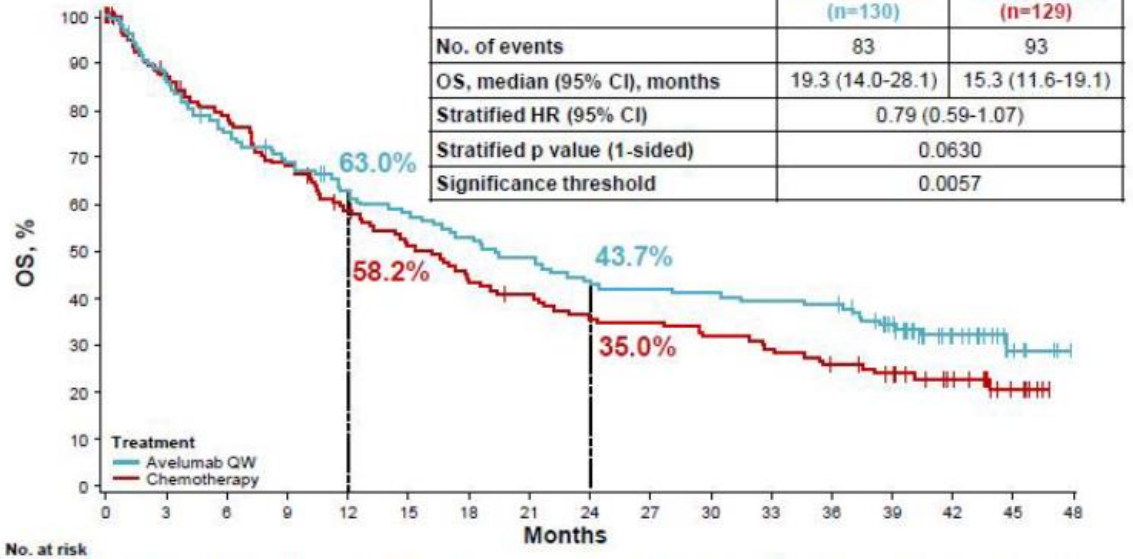


No. at risk

Avelumab Q2W	151	125	116	101	92	83	74	67	59	57	56	53	50	43	37	28	24	21	19	17	10	5	1	0
Chemotherapy	216	178	156	135	113	98	89	79	70	68	65	58	51	47	36	26	20	19	17	16	9	3	1	0

Avelumab QW vs chemotherapy

	Avelumab QW (n=130)	Chemotherapy (n=129)
No. of events	83	93
OS, median (95% CI), months	19.3 (14.0-28.1)	15.3 (11.6-19.1)
Stratified HR (95% CI)	0.79 (0.59-1.07)	
Stratified p value (1-sided)	0.0630	
Significance threshold	0.0057	



No. at risk

Avelumab QW	130	107	93	84	75	69	63	58	52	50	49	47	46	35	20	7	0						
Chemotherapy	129	107	95	82	69	59	51	46	40	39	36	33	28	24	16	6	0						

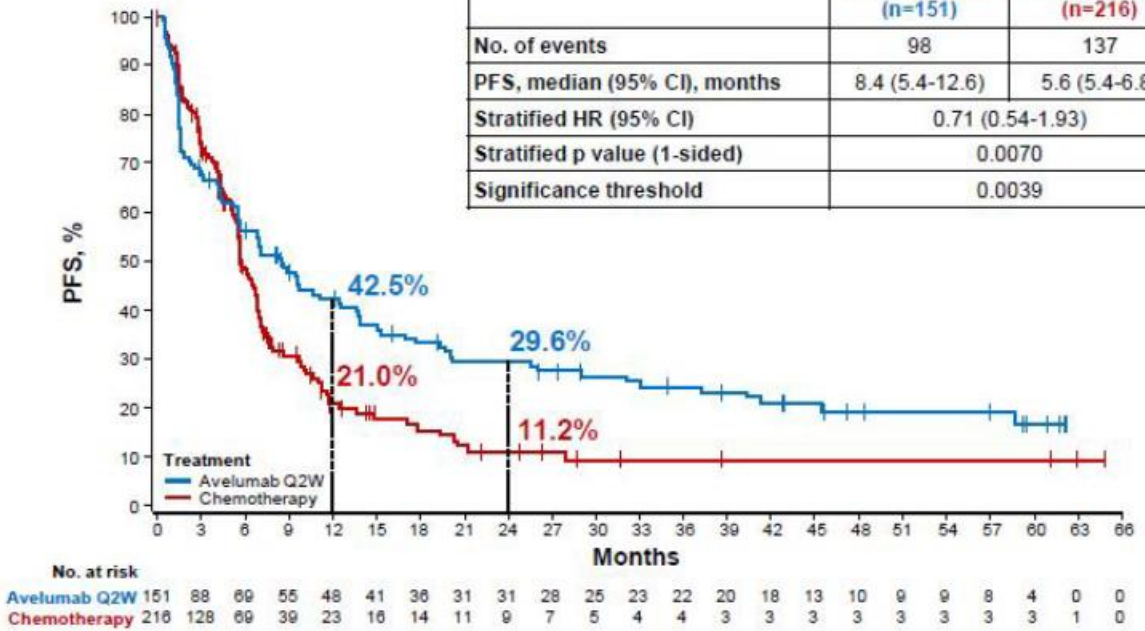
OS analyses favored avelumab vs chemotherapy but differences were not statistically significant

Median follow up in primary analysis populations across all arms was 41.7-48.8 months (data cutoff: October 15, 2021)
*High-expression PD-L1+ (≥80% of tumor cells) determined by Dako PD-L1 IHC 73-10 pharmDx assay (avelumab QW vs chemotherapy: in patients randomized post protocol amendment).

Primary endpoint: PFS by IRC in the high PD-L1+ populations*

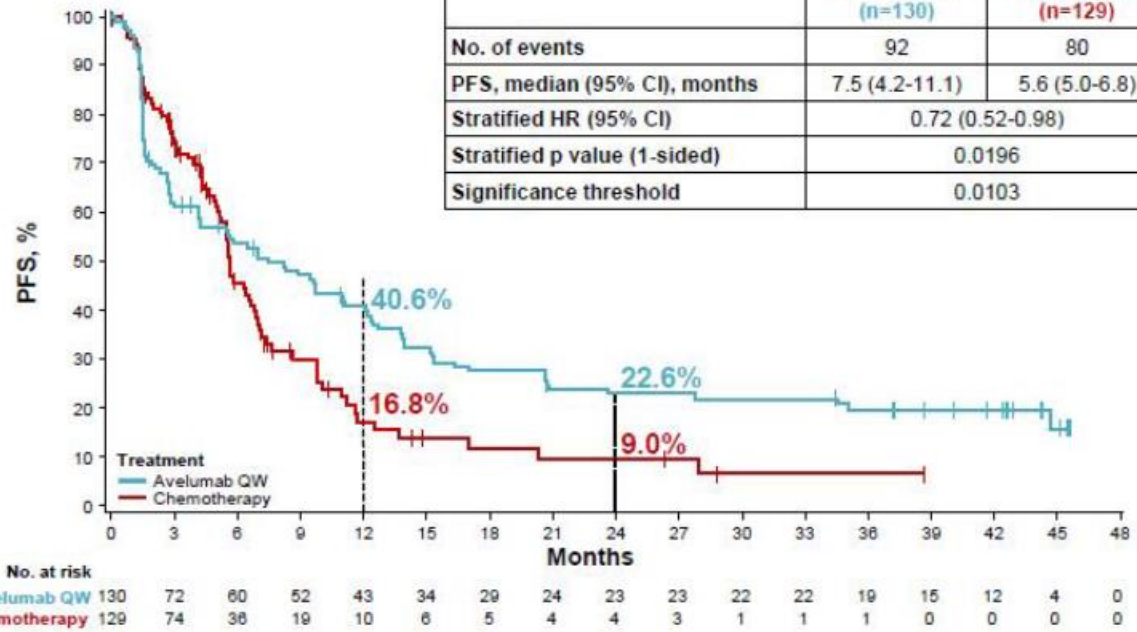
Avelumab Q2W vs chemotherapy

	Avelumab Q2W (n=151)	Chemotherapy (n=216)
No. of events	98	137
PFS, median (95% CI), months	8.4 (5.4-12.6)	5.6 (5.4-6.8)
Stratified HR (95% CI)	0.71 (0.54-1.93)	
Stratified p value (1-sided)	0.0070	
Significance threshold	0.0039	



Avelumab QW vs chemotherapy

	Avelumab QW (n=130)	Chemotherapy (n=129)
No. of events	92	80
PFS, median (95% CI), months	7.5 (4.2-11.1)	5.6 (5.0-6.8)
Stratified HR (95% CI)	0.72 (0.52-0.98)	
Stratified p value (1-sided)	0.0196	
Significance threshold	0.0103	



PFS analyses also favored avelumab vs chemotherapy but differences were not statistically significant

*High-expression PD-L1+ (≥80% of tumor cells) determined by Dako PD-L1 IHC 73-10 pharmDx assay (avelumab QW vs chemotherapy: in patients randomized post protocol amendment).

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AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Association Between *KRAS/STK11/KEAP1* Mutations and Outcomes in POSEIDON: Durvalumab ± Tremelimumab + Chemotherapy in mNSCLC

Solange Peters,[1] Byoung Chul Cho,[2] Alexander Luft,[3] Jorge Alatorre-Alexander,[4] Sarayut Lucien Geater,[5] Sang-We Kim,[6] Grygorii Ursol,[7] Maen Hussein,[8] Farah Louise Lim,[9] Cheng-Ta Yang,[10] Luiz Henrique Araujo,[11] Haruhiro Saito,[12] Niels Reinmuth,[13] Ross Stewart,[14] Zhongwu Lai,[15] Ruth Doake,[14] Lee Krug,[16] Edward B. Garon,[17] Tony Mok,[18] Melissa L. Johnson[19]

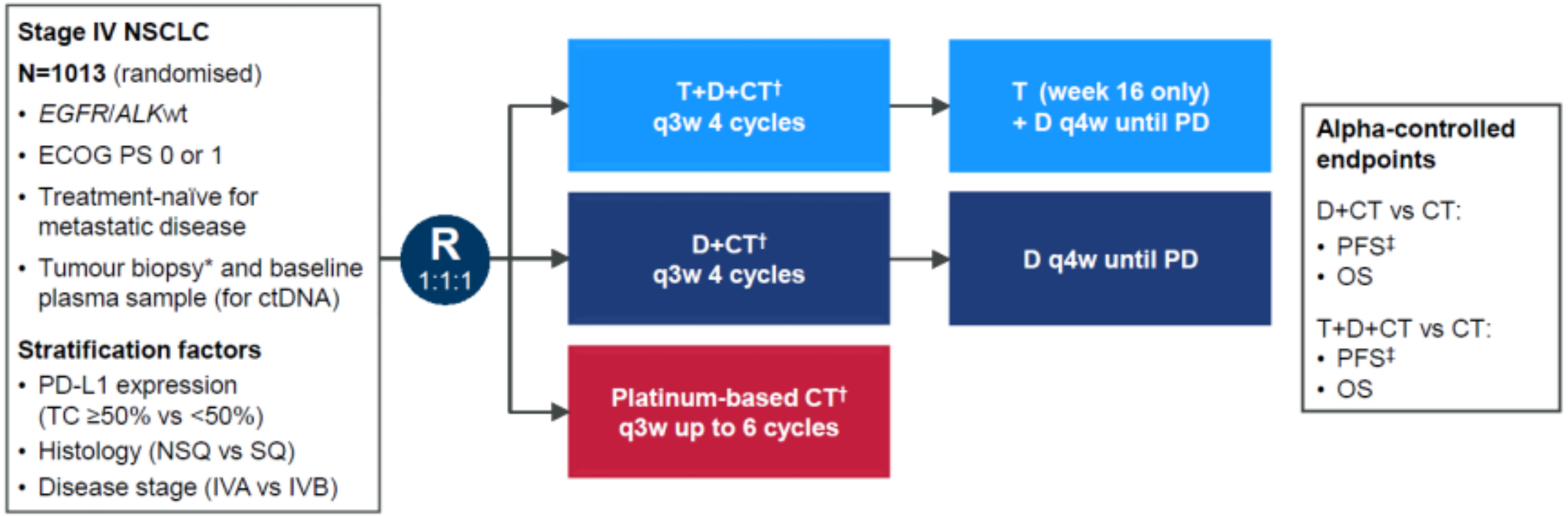
[1]Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland; [2]Yonsei Cancer Center, Seoul, Korea; [3]Leningrad Regional Clinical Hospital, St Petersburg, Russia; [4]Health Pharma Professional Research, Mexico City, Mexico; [5]Prince of Songkla University, Songkhla, Thailand; [6]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [7]Acinus, Kropyvnytskyi, Ukraine; [8]Florida Cancer Specialists – Sarah Cannon Research Institute, Leesburg, FL, USA; [9]Queen Mary University of London, London, United Kingdom; [10]Chang Gung Memorial Hospital, Taoyuan City, Taiwan; [11]Instituto Nacional de Cancer-INCA, Rio de Janeiro, Brazil; [12]Kanagawa Cancer Center, Yokohama, Japan; [13]Asklepios Lung Clinic, Munich-Gauting, Germany; [14]AstraZeneca, Cambridge, UK; [15]AstraZeneca, Waltham, MA, USA; [16]AstraZeneca, Gaithersburg, MD, USA; [17]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [18]Chinese University of Hong Kong, Hong Kong, China; [19]Sarah Cannon Research Institute, Tennessee Oncology, PLLC, Nashville, TN, USA

por:

GECP lung cancer research

POSEIDON Study Design

Phase 3, global, randomised, open-label, multicentre study in 1L mNSCLC



- **Durvalumab** 1500mg **± limited-course tremelimumab** 75mg + **CT** q3w for **4 cycles**
  - One additional dose of tremelimumab post-CT (week 16; 5th dose)
- Followed by **durvalumab q4w maintenance** until PD, and optional pemetrexed q4w§

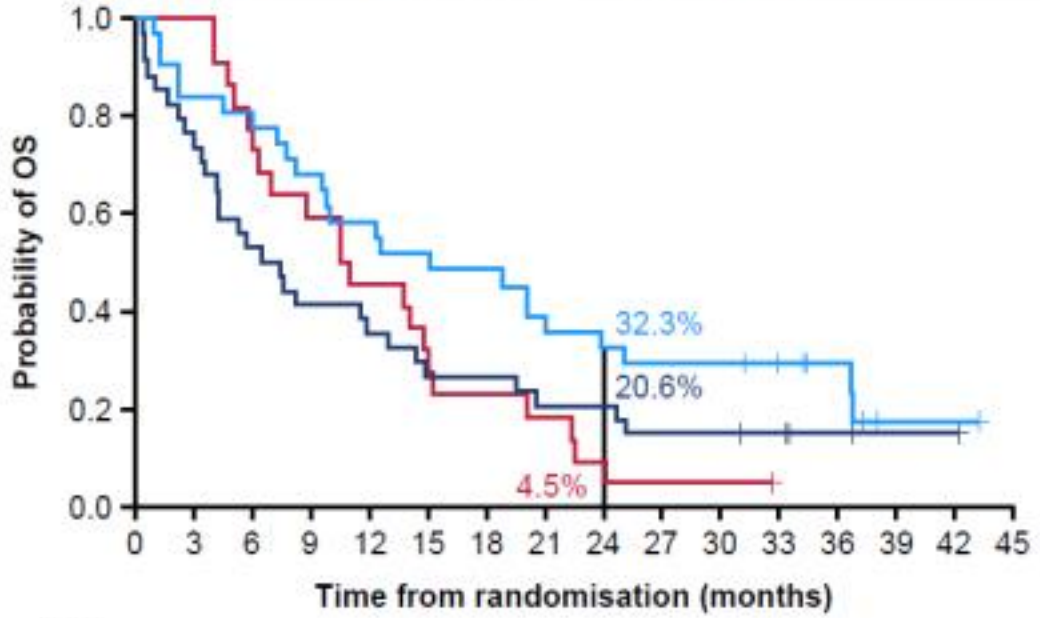
*Newly acquired or archival (<3 months); †CT options: gemcitabine + carboplatin/cisplatin (SQ), pemetrexed + carboplatin/cisplatin (NSQ) or nab-paclitaxel + carboplatin (either histology); ‡By BICR (RECIST v1.1); §Patients with NSQ histology who initially received pemetrexed only (if eligible); pemetrexed q3w also permitted in the CT arm

OS by *STK11* Mutation Status

OS benefit observed for T+D+CT vs CT in STK11m with HR 0.56 and estimated 32.3% alive at 2 yrs vs 4.5%

*STK11*m

	T+D+CT	D+CT	CT
Events, n/N	24/31	29/34	21/22
mOS, mo (95% CI)	**15.0** (8.2–23.8)	**6.9** (3.6–12.9)	**10.7** (6.0–14.9)
HR* (95% CI)	**0.56** (0.30–1.03)	**1.03** (0.59–1.84)	–

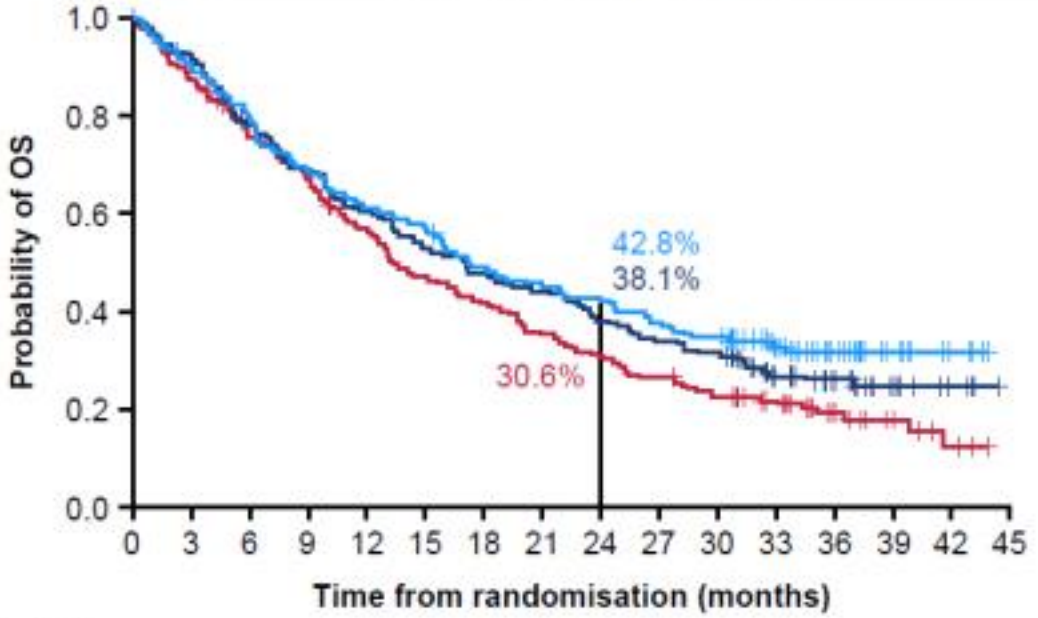


No. at risk

T+D+CT	31	26	24	21	18	15	15	11	10	9	9	7	5	1	1	0
D+CT	34	26	18	14	12	9	9	7	7	5	5	4	2	1	0	0
CT	22	22	16	13	10	6	5	4	1	1	1	0	0	0	0	0

*STK11*wt

	T+D+CT	D+CT	CT
Events, n/N	118/177	123/169	141/179
mOS, mo (95% CI)	**17.2** (14.9–22.1)	**17.1** (13.3–22.3)	**13.4** (11.5–17.5)
HR* (95% CI)	**0.73** (0.57–0.93)	**0.81** (0.64–1.04)	–



No. at risk

T+D+CT	177	159	140	120	107	100	85	79	74	65	60	40	25	11	5	0
D+CT	169	155	130	114	100	87	79	73	63	56	52	33	23	10	4	0
CT	179	154	131	116	97	80	71	60	52	45	37	29	15	8	4	0

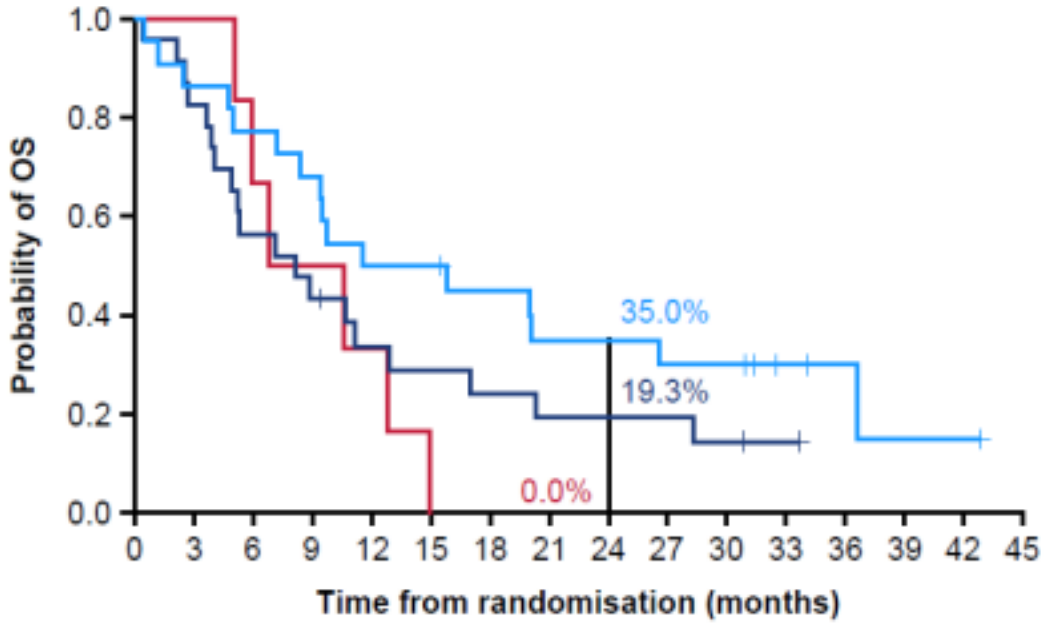
GECP lung cancer research

OS by *KEAP1* Mutation Status

OS benefit observed for T+D+CT vs CT in KEAP1m with HR 0.43 (small sample size)

*KEAP1*m

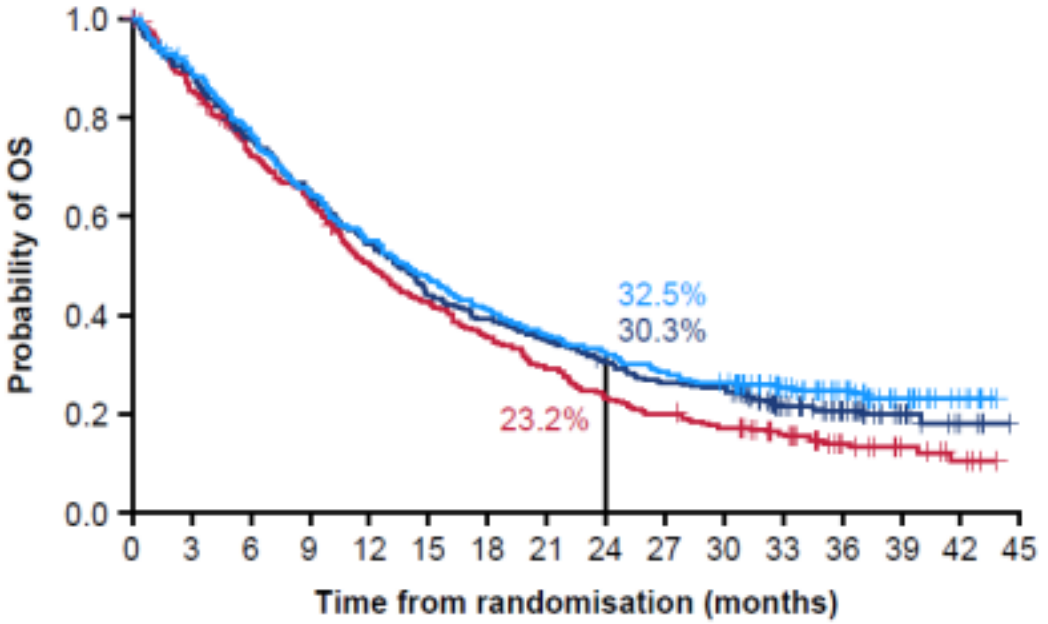
	T+D+CT	D+CT	CT
Events, n/N	16/22	19/23	6/6
mOS, mo (95% CI)	**13.7** (7.2–26.5)	**8.1** (4.0–12.9)	**8.7** (5.1–NE)
HR* (95% CI)	**0.43** (0.16–1.25)	**0.77** (0.31–2.15)	–



No. at risk																
T+D+CT	22	19	17	15	11	11	9	7	7	6	6	3	2	1	1	0
D+CT	23	19	13	10	7	6	5	4	4	4	3	1	0	0	0	0
CT	6	6	4	3	2	0	0	0	0	0	0	0	0	0	0	0

*KEAP1*wt

	T+D+CT	D+CT	CT
Events, n/N	226/303	241/307	262/312
mOS, mo (95% CI)	**14.0** (11.8–16.1)	**13.5** (11.7–14.9)	**12.2** (10.6–13.9)
HR* (95% CI)	**0.79** (0.66–0.94)	**0.85** (0.71–1.01)	–



No. at risk																									
T+D+CT	303	268	230	194	165	142	123	108	97	85	78	57	38	19	8	0
D+CT	307	272	230	198	165	134	119	106	91	79	76	49	33	15	5	0
CT	312	264	221	192	153	129	108	88	70	61	51	38	21	13	6	0

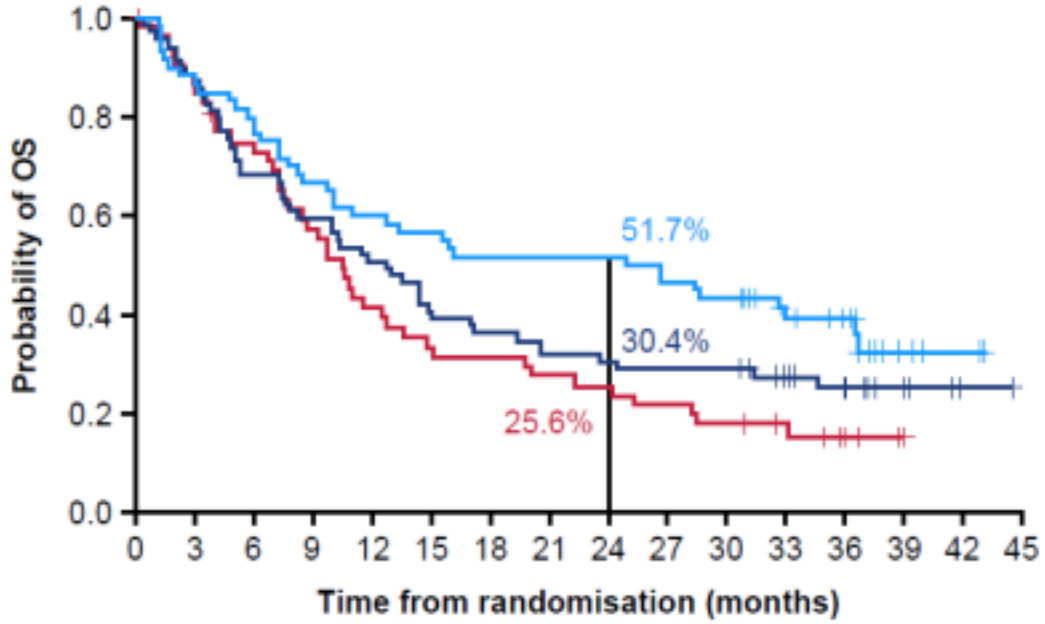
HR (95% CI) vs CT in NSQ *KEAP1*m was 0.33 (0.10–1.15) with T+D+CT and 0.67 (0.23–2.17) with D+CT

OS by *KRAS* Mutation Status

OS benefit observed for T+D+CT vs CT in KRASm with HR 0.56 and estimated 51.7% alive at 2 yrs vs 25.6%

*KRAS*m

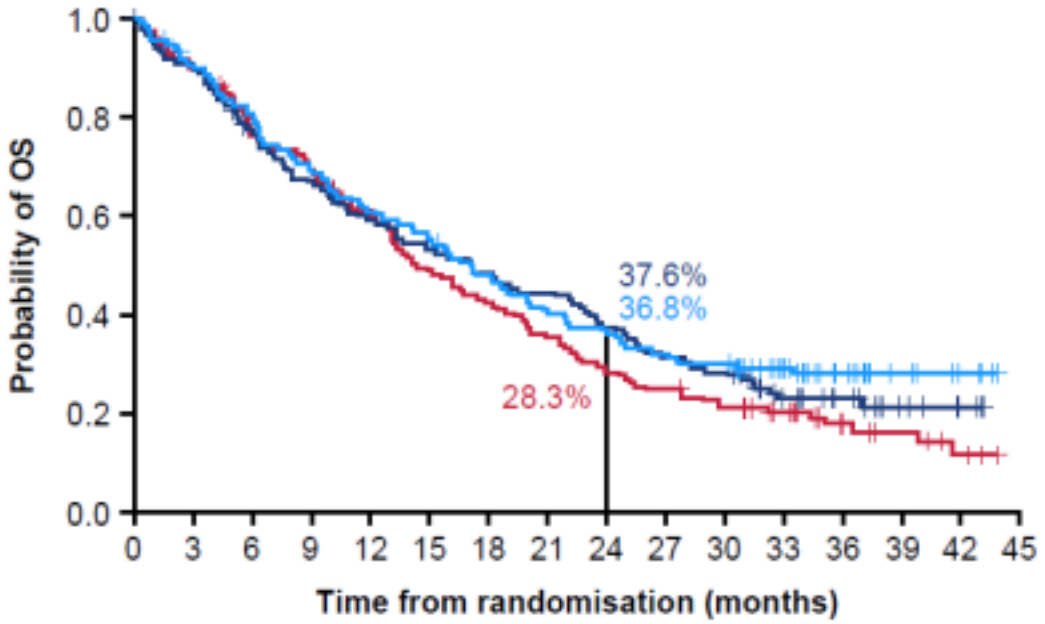
	T+D+CT	D+CT	CT
Events, n/N	38/60	51/69	43/53
mOS, mo (95% CI)	**25.7** (9.9–36.5)	**12.6** (7.5–16.9)	**10.4** (7.5–13.6)
HR* (95% CI)	**0.56** (0.36–0.88)	**0.80** (0.53–1.21)	–



No. at risk																
T+D+CT	60	53	46	40	36	34	31	31	31	28	26	17	14	4	2	0
D+CT	69	61	47	41	35	27	25	22	21	20	20	14	9	4	1	0
CT	53	44	37	29	21	17	16	14	13	11	9	7	3	0	0	0

*KRAS*wt

	T+D+CT	D+CT	CT
Events, n/N	104/148	101/134	119/148
mOS, mo (95% CI)	**17.1** (13.4–20.1)	**17.1** (12.3–22.6)	**14.4** (12.6–18.3)
HR* (95% CI)	**0.80** (0.62–1.04)	**0.86** (0.66–1.12)	–



No. at risk																
T+D+CT	148	132	118	101	89	81	69	59	53	46	43	30	16	8	4	0
D+CT	134	120	101	87	77	69	63	58	49	41	37	23	16	7	3	0
CT	148	132	110	100	86	69	60	50	40	35	29	22	12	8	4	0

GECP lung cancer research

Durvalumab (D) ± tremelimumab (T) + chemotherapy (CT) in 1L metastatic (m) NSCLC: Overall survival (OS) update from POSEIDON after median follow-up (mFU) of approximately 4 years (y)

Study Design

Stage IV NSCLC

N=1013 (randomised)

- *EGFR/ALK*wt
- ECOG PS 0 or 1
- Treatment-naïve for metastatic disease
- Tumour biopsy* and baseline plasma sample (for ctDNA)

Stratification factors

- PD-L1 expression (TC ≥50% vs <50%)
- Disease stage (IVA vs IVB)
- Histology (NSQ vs SQ)

R 1:1:1

- T+D+CT† q3w 4 cycles → T (week 16 only) + D q4w until PD
- D+CT† q3w 4 cycles → D q4w until PD
- Platinum-based CT† q3w up to 6 cycles

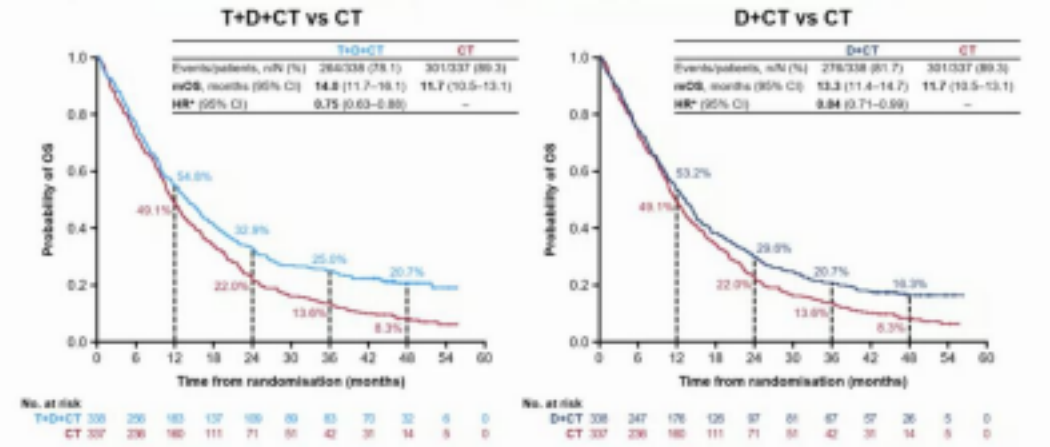
Alpha-controlled endpoints

D+CT vs CT:
- PFS‡
- OS

T+D+CT vs CT:
- PFS‡
- OS

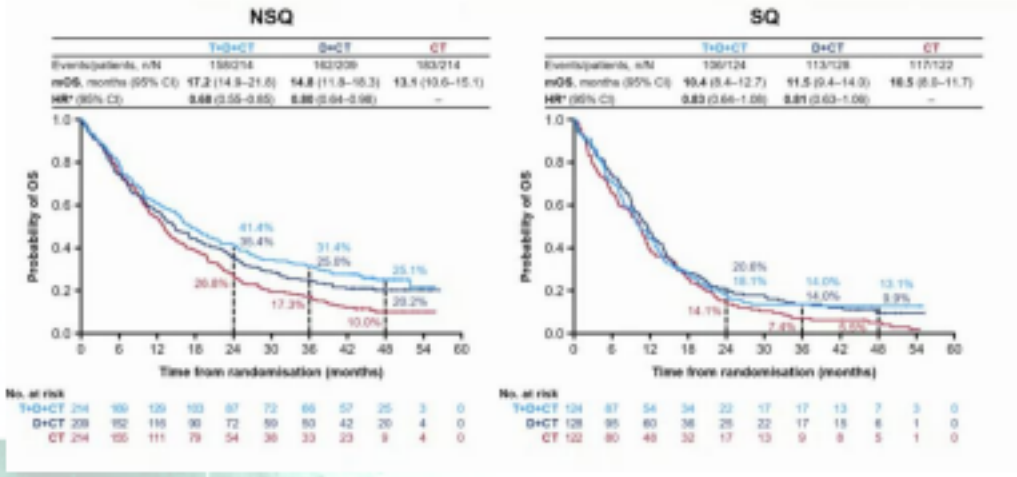
- **Durvalumab** 1500mg ± **limited-course tremelimumab** 75mg + **CT** q3w for **4 cycles**
  - One additional dose of tremelimumab post-CT (week 16; 5th dose)
- Followed by **durvalumab q4w maintenance** until PD, and optional pemetrexed q4w§

Overall Survival



Median follow-up in censored patients at DCO: 46.5 months (range 0.0–56.5)

Overall Survival by histology



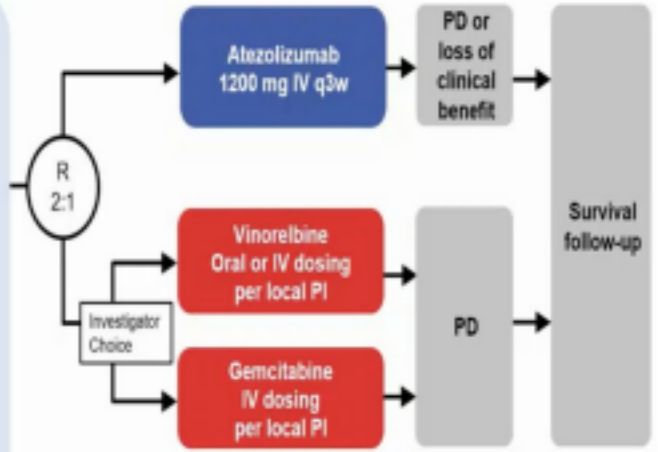
IPSOS: Results from a phase III study of first-line (1L) atezolizumab (atezo) vs single-agent chemotherapy (chemo) in patients (pts) with NSCLC not eligible for a platinum-containing regimen

Study design

Treatment-naive stage IIIB[a]/IV (AJCC 7th edition) NSCLC

- Squamous or non-squamous histology
- Platinum ineligible because of:
  - ECOG PS 2 or 3
  - ECOG PS 0 or 1 permitted if ≥70 years of age with substantial comorbidities or other contraindictions to platinum chemotherapy
- *EGFR*+ (L858R or exon 19 deletion) or *ALK*+ excluded
- Patients with treated asymptomatic brain metastases permitted

n=453



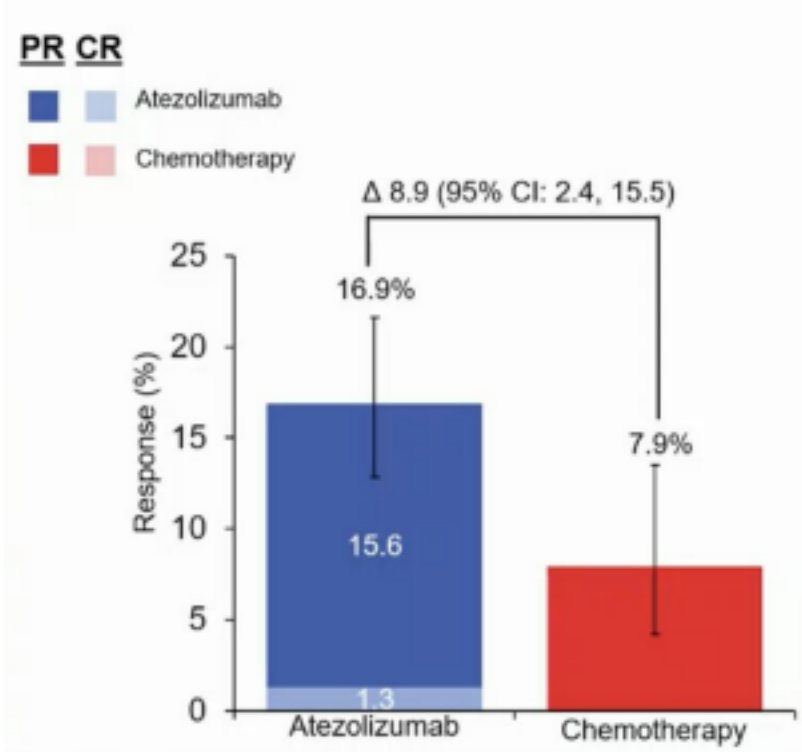
Stratification factors:
- Histology (squamous or non-squamous)
- PD-L1 expression level by SP142 IHC assay (TC3 or IC3 vs TC0/1/2 or IC0/1/2[b] vs unknown)
- Brain metastases (yes/no)

Primary endpoint:
- OS

Secondary endpoints:
- OS rates at 6, 12, 18 and 24 months
- PFS
- Objective response rate
- Duration of response
- OS and PFS in PD-L1 positive subgroup[c]

Other endpoints:
- PROs
- Safety
- Exploratory biomarker analyses

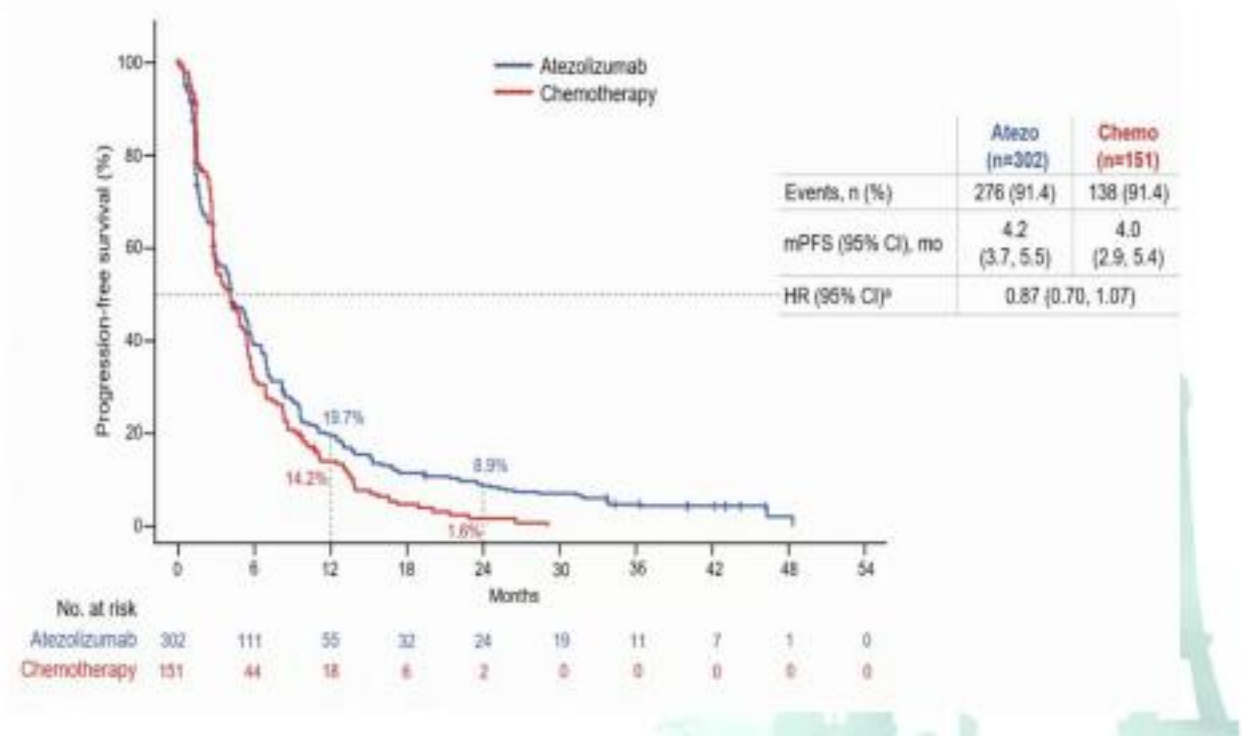
Overall Response Rate



	Atezolizumab	Chemotherapy
Median DOR, months (95% CI)	14.0 (8.1, 20.3)	7.8 (4.8, 9.7)

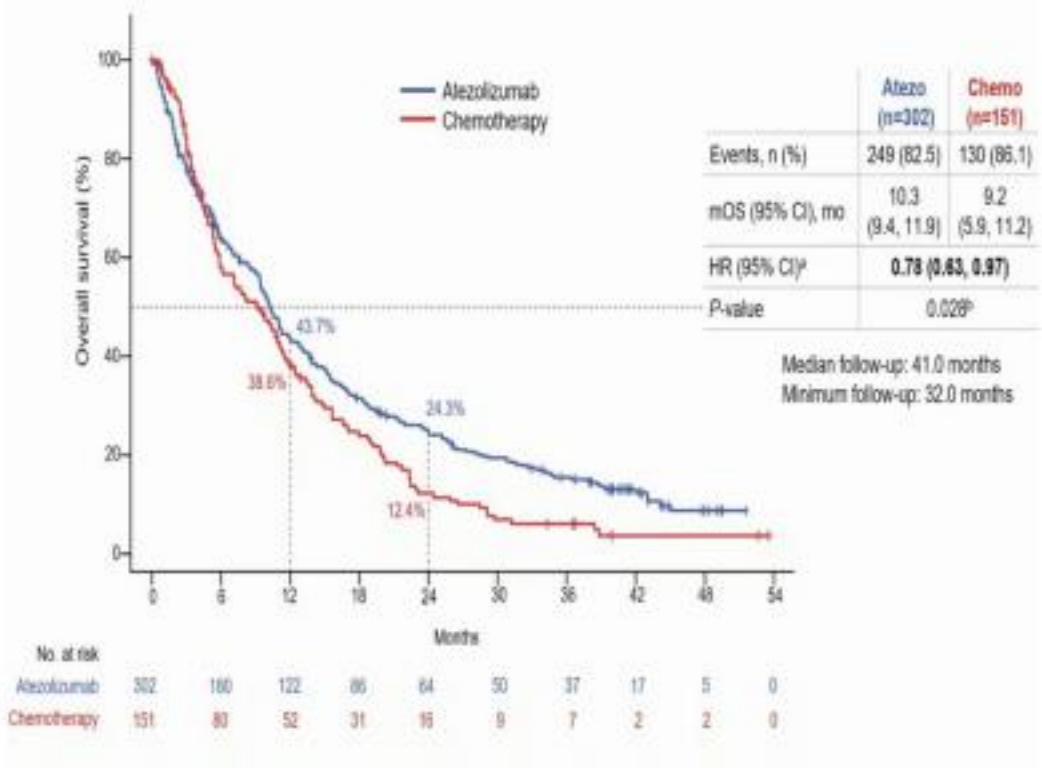
lung cancer research

Progression Free Survival



	Atezo (n=302)	Chemo (n=151)
Events, n (%)	276 (91.4)	138 (91.4)
mPFS (95% CI), mo	4.2 (3.7, 5.5)	4.0 (2.9, 5.4)
HR (95% CI)[a]	0.87 (0.70, 1.07)	

Overall Survival



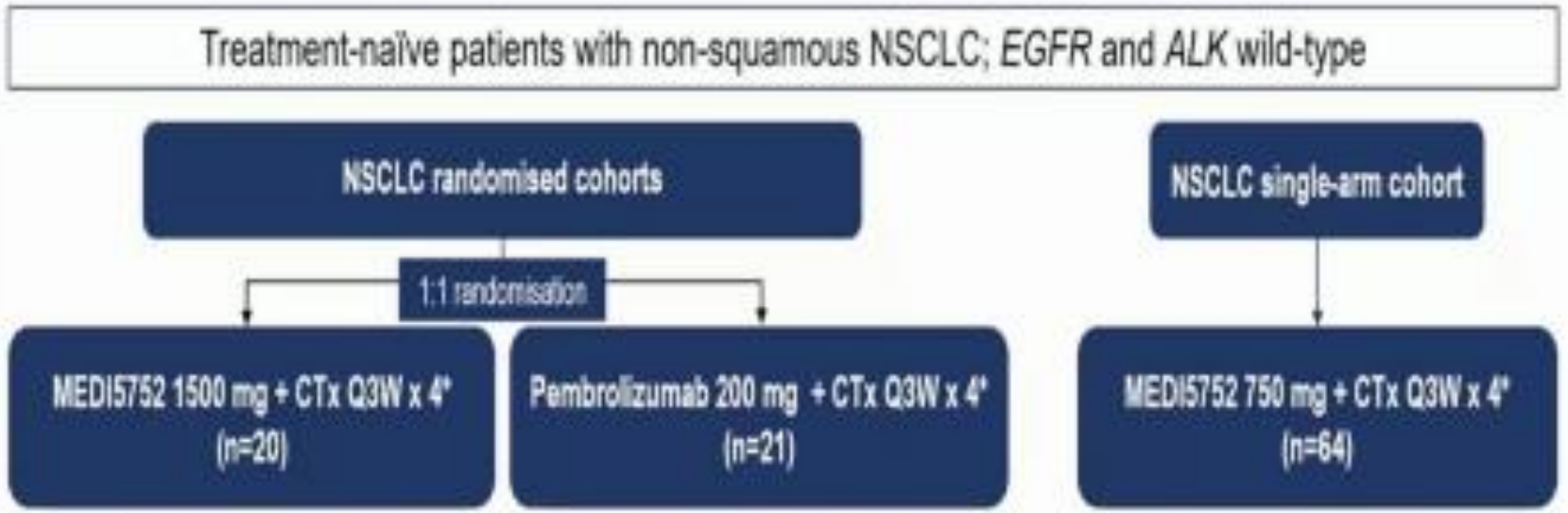
	Atezo (n=302)	Chemo (n=151)
Events, n (%)	249 (82.5)	130 (86.1)
mOS (95% CI), mo	10.3 (9.4, 11.9)	9.2 (5.9, 11.2)
HR (95% CI)[a]	**0.78 (0.63, 0.97)**	
P-value	0.028[b]	

Median follow-up: 41.0 months
Minimum follow-up: 32.0 months

Organizado por:

GECP lung cancer research

MEDI5752 or pembrolizumab (P) plus carboplatin/pemetrexed (CP) in treatment-naïve (1L) non-small cell lung cancer (NSCLC): A phase Ib/II trial

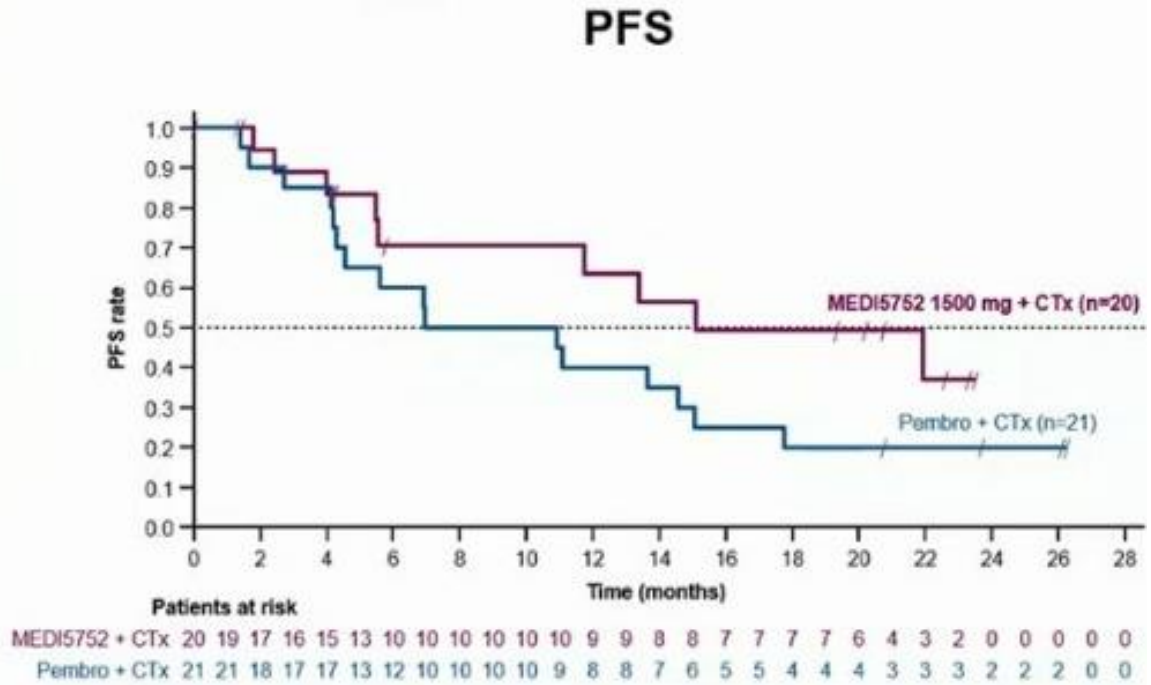


*MEDI5752 or pembrolizumab + carboplatin AUC 5 + pemetrexed 500 mg/m² as initial treatment IV Q3W x 4 cycles, followed by maintenance with MEDI5752 or pembrolizumab + pemetrexed IV Q3W until unacceptable toxicity, disease progression, or withdrawal of consent.

- As of 12 July 2022, 105 patients were enrolled in two 1L non-squamous NSCLC dose expansion cohorts
- Results from 91 patients are presented:
  - 41 patients in the randomised cohorts (MEDI5752 1500 mg + CTx, n=20; pembrolizumab 200 mg + CTx, n=21)
  - First 50 patients in the single-arm cohort (MEDI5752 750 mg + CTx) who had at least 8 weeks of follow-up

MEDI5752 1500 mg + CTx improved DOR, PFS and OS over pembrolizumab + CTx in first-line non-squamous NSCLC

1L Non-squamous NSCLC	Randomised cohort (N=41)	
	MEDI5752 1500 mg + CTx (n=20)	Pembrolizumab + CTx (n=21)
Median follow-up, months (range)	22.8 (0.8–26.9)	14.5 (1.6–27.9)
ORR, n (%)	10 (50.0)	10 (47.6)
Disease control rate, n (%)	17 (85.0)	20 (95.2)
Median DOR, months (95% CI)	20.5 (4.1–NE)	9.9 (2.8–NE)
Median PFS, months	15.1	8.9
Median OS, months	NR	16.5
ORR, PD-L1 <1%, n/N (%) (95% CI)	5/9 (55.6) (21.2–86.3)	3/10 (30.0) (6.7–65.2)
Median PFS, PD-L1 <1%, months	13.4	9



PARIS 2022 ESMO congress

CTx, chemotherapy; CR, complete response; DOR, duration of response; ITT, intent-to-treat; PFS, median progression-free survival; NR, not reached; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand-1; PFS, progression-free survival; PR, partial response; uPR, unconfirmed partial response
Data cut-off 12 July 2022.

lung cancer research

MEDI5752 + CTx – Safety and tolerability

	Randomised cohort (N=41)				Single-arm cohort	
	MEDI5752 1500 mg + CTx (n=20)		Pembrolizumab + CTx (n=21)		MEDI5752 750 mg + CTx (n=50)	
Median duration of exposure to MEDI5752, cycles (range)	4.5 (1–32)		NA		4.0 (1–12)	
Any TEAE, n (%)	20 (100.0)		21 (100.0)		49 (98.0)	
TEAE leading to treatment discontinuation	14 (70.0)		6 (28.6)		10 (20.0)	
Any TRAE*, n (%)	20 (100.0)		21 (100.0)		46 (92.0)	
Grade 3/4 TRAE	16 (80.0)		13 (61.9)		25 (50.0)	
TRAE leading to death	0		1 (4.8)†		1 (2.0)‡	
Select AEs (preferred term), %	**All Grade**	**Grade 3/4**	**All Grade**	**Grade 3/4**	**All Grade**	**Grade 3/4**
Rash	55	10	9.5	0	24	2
ALT increase	55	30	14.3	0	10	2
AST increase	55	20	9.5	0	8	2
Hyperthyroidism	40	0	0	0	12	0
Pneumonitis	20	5	9.5	4.8	0	0
Diarrhea	10	5	4.8	0	4	2

AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTx, chemotherapy; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
*TRAE may be related to MEDI5752, pembrolizumab, carboplatin or pemetrexed.
†One patient treated with pembrolizumab + CTx died due to febrile neutropenia.
‡One patient treated with MEDI5752 750mg + CTx died due to febrile neutropenia.
Data cut-off 12 July 2022.

INMUNOTERAPIA MÁS OTRAS TERAPIAS

2022 ASCO ANNUAL MEETING

Cabozantinib Plus Atezolizumab or Cabozantinib Alone in Patients With Advanced Non-Small Cell Lung Cancer Previously Treated With an Immune Checkpoint Inhibitor: COSMIC-021 Study Cohorts 7 and 20

Joel W. Neal,[1] Armando Santoro,[2] Santiago Viteri,[3] Santiago Ponce Aix,[4] Bruno Fang,[5] Farah Louise Lim,[6] Ryan Gentzler,[7] Jerome Goldschmidt,[8] Polina Khrizman,[9] Erminia Massarelli,[10] Shiven Patel,[11] Sonam Puri,[11] Ramu Sudhagoni,[12] Christian Scheffold,[12] Dominic Curran,[12] Enriqueta Felip[13]

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Abstract 9005

COSMIC-021 Study Design for NSCLC Cohorts

Key Eligibility Criteria

- Stage IV non-squamous NSCLC with radiographic progression on or after one prior ICI for metastatic disease
- ≤2 prior lines of systemic anticancer therapy*
- Patients with known *EGFR*, *ALK*, *ROS1*, or *BRAF* V600E tumor mutations excluded

→ **Cohort 7**† Cabozantinib 40 mg QD PO + Atezolizumab 1200 mg Q3W IV (N=80)

→ **Cohort 20**† Cabozantinib 60 mg QD PO (N=30)

→ Tumor assessment per RECIST v1.1 by investigator every 6 weeks for the first year and every 12 weeks thereafter

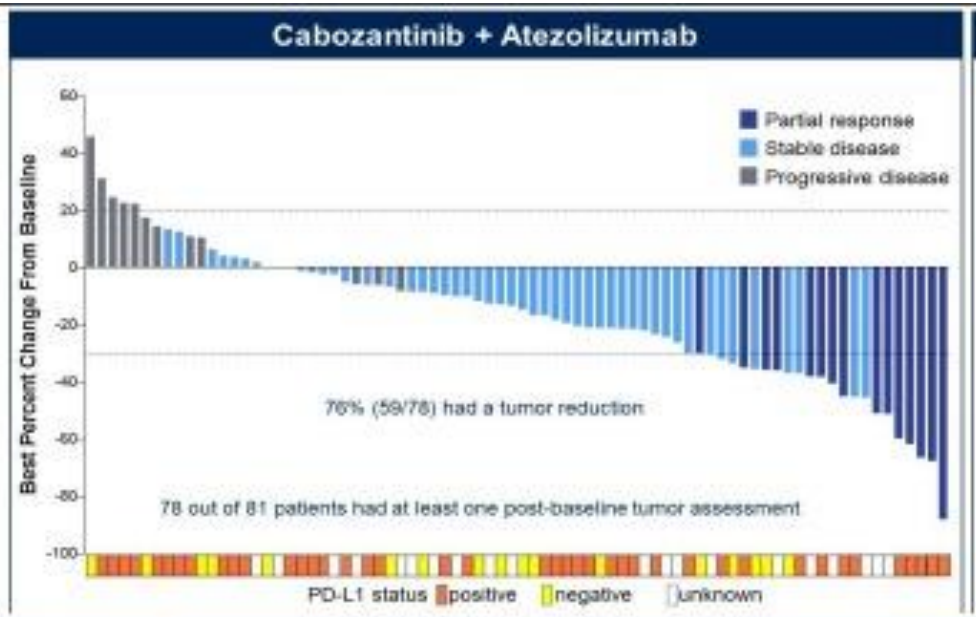
Primary endpoint:	ORR per RECIST v1.1 by investigator
Secondary endpoint:	Safety (AEs, SAEs, AESIs)
Exploratory endpoints:	DOR, PFS per RECIST v1.1 by investigator, OS

*Prior treatment with platinum-based chemotherapy was not required. †Patients were initially enrolled to cohort 7 (n=35). Following an initial assessment of clinical activity, subsequent patients were randomized between cohorts 7 and 20. ‡Patients in cohort 20 may receive combination therapy after radiographic disease progression per RECIST v1.1 by the investigator.
SAEs, serious adverse events; AESIs, adverse events of special interest

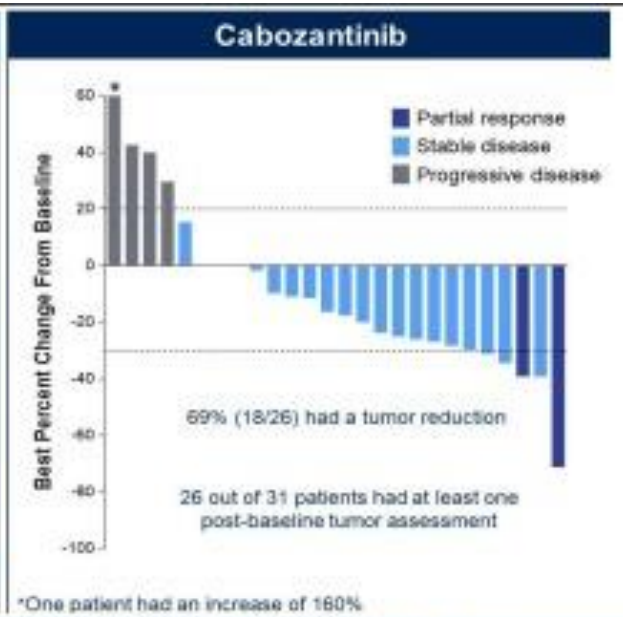
2022 ASCO ANNUAL MEETING #ASCO22 Presented by: Joel W. Neal, MD, PhD

	Cabozantinib + Atezolizumab (N=81)				Cabozantinib (N=31)*
	All patients (N=81)	PD-L1 <1% (n=19)	PD-L1 ≥1% (n=41)	PD-L1 unknown (n=21)	
ORR, n (%)	**15 (19)**	2 (11)	8 (20)	5 (24)	**2 (6)**
Best overall response, n (%)					
Complete response	**0**	0	0	0	**0**
Partial response	**15 (19)**	2 (11)	8 (20)	5 (24)	**2 (6)**
Stable disease	**50 (62)**	12 (63)	25 (61)	13 (62)	**18 (58)**
Progressive disease	**13 (16)**	3 (16)	8 (20)	2 (10)	**6 (19)**
Missing / not evaluable	**3 (4)**	2 (11)	0	1 (5)	**5 (16)**
Disease control rate, n (%)	**65 (80)**	14 (74)	33 (80)	18 (86)	**20 (65)**
PFS, mo (95% CI)	**4.5 (3.5–5.6)**	4.0 (2.6–5.6)	4.7 (2.7–5.6)	5.4 (2.9–10.9)	**3.4 (1.4–5.6)**
Median DOR, mo (95% CI)	**5.8 (4.2–6.9)**	3.4 (2.6–NE)	6.5 (3.5–NE)	6.2 (4.2–NE)	**10.6 (6.3–NE)†**
OS, mo (95% CI)	**13.8 (7.2–15.7)**	6.8 (5.1–15.4)	10.4 (5.9–17.1)	17.4 (9.4–NE)	**9.4 (4.5–11.7)**

Cabozantinib + Atezolizumab



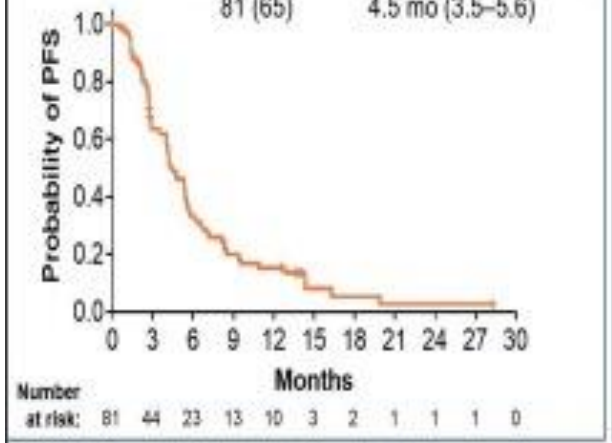
Cabozantinib



*One patient had an increase of 160%

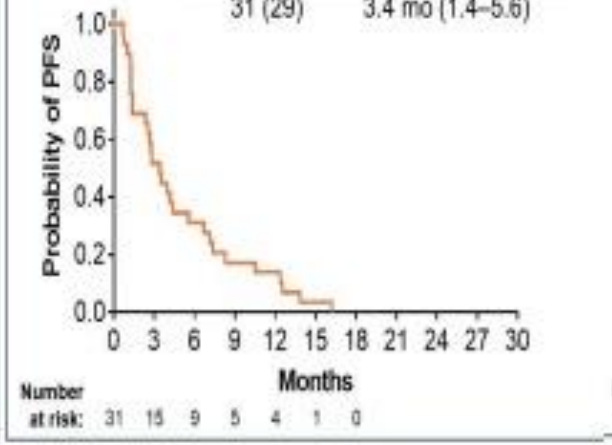
Cabozantinib + Atezolizumab

N (events)	Median (95% CI), mo
81 (65)	4.5 mo (3.5–5.6)



Cabozantinib

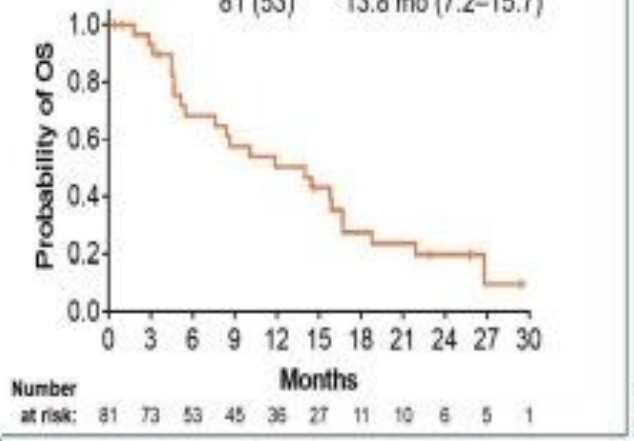
N (events)	Median (95% CI), mo
31 (29)	3.4 mo (1.4–5.6)



Median PFS (95% CI):
- 4.0 mo (2.6–5.6) for PD-L1 negative
- 4.7 mo (2.7–5.6) for PD-L1 positive
- 5.4 mo (2.9–10.9) for PD-L1 unknown

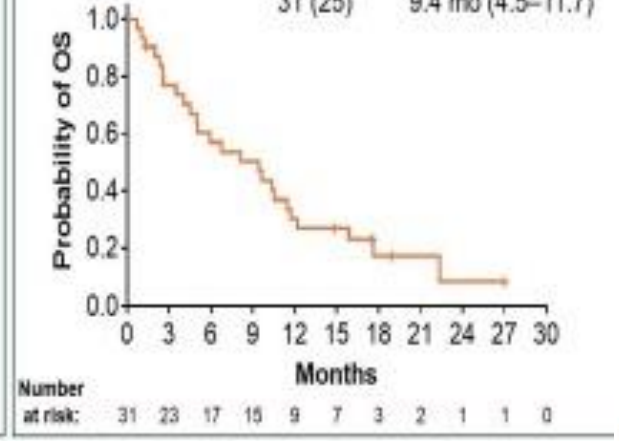
Cabozantinib + Atezolizumab

N (events)	Median (95% CI), mo
81 (53)	13.8 mo (7.2–15.7)



Cabozantinib

N (events)	Median (95% CI), mo
31 (25)	9.4 mo (4.5–11.7)



Median OS (95% CI):
- 6.8 mo (5.1–15.4) for PD-L1 negative
- 10.4 mo (5.9–17.1) for PD-L1 positive
- 17.4 mo (9.4–NE) for PD-L1 unknown

Seguridad

	Cabozantinib + Atezolizumab (N=81)	Cabozantinib* (N=31)
Patients on study treatment at data cut-off, n (%)	6 (7)	2 (6)
Duration of exposure, median (range), months		
Cabozantinib + Atezolizumab†	5.2 (0.3–28.8)	4.8 (0.7–19.4)
Cabozantinib	5.2 (0.3–28.8)	4.8 (0.7–19.4)
Atezolizumab	4.6 (0–28.0)	1.6 (0–11.8)
AEs leading to cabozantinib dose reductions, n (%)	32 (40)	18 (58)
AEs leading to cabozantinib dose hold, n (%)	60 (74)	25 (81)
AEs leading to atezolizumab dose delay, n (%)	41 (51)	2 (6)
Discontinuation due to TRAEs, n (%)		
Cabozantinib	11 (14)	3 (10)
Atezolizumab	8 (10)	1 (3)
Either	13 (16)	3 (10)
Both	5 (6)	1 (3)

	Cabozantinib + Atezolizumab (N=81)		Cabozantinib (N=31)†	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE, n (%)	81 (100)	43 (53)	31 (100)	22 (71)
Diarrhea	36 (44)	1 (1)	16 (52)	3 (10)
Decreased appetite	30 (37)	1 (1)	11 (35)	1 (3)
Fatigue	29 (36)	4 (5)	11 (35)	2 (6)
Nausea	28 (35)	2 (2)	15 (48)	2 (6)
Asthenia	24 (30)	5 (6)	12 (39)	3 (10)
Constipation	21 (26)	0	5 (16)	0
Pyrexia	20 (25)	0	2 (6)	0
AST increased	19 (23)	2 (2)	9 (29)	0
Hypertension	19 (23)	5 (6)	10 (32)	7 (23)
Vomiting	19 (23)	0	9 (29)	1 (3)
ALT increased	17 (21)	3 (4)	10 (32)	1 (3)
PPE	17 (21)	3 (4)	6 (19)	0
Hypomagnesemia	16 (20)	1 (1)	5 (16)	0
Weight decreased	16 (20)	3 (4)	4 (13)	2 (6)
Pneumonitis	3 (4)‡	0	0	0
Gastric ulcer hemorrhage	0	0	1 (3)¶	0

	Cabozantinib + Atezolizumab† (N=81)		Cabozantinib‡ (N=31)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any adverse events of special interest (AESI), n (%)	59 (73)	21 (26)	23 (74)	4 (13)
Rash	34 (42)	7 (9)	12 (39)	2 (6)
Hepatitis (lab abnormalities)	28 (35)	5 (6)	14 (45)	1 (3)
Pancreatitis	14 (17)	5 (6)	2 (6)	0
Hypothyroidism	13 (16)	0	8 (26)	0
Colitis	3 (4)	1 (1)	2 (6)	1 (3)
Hyperthyroidism	3 (4)	0	0	0
Pneumonitis	3 (4)	0	0	0
Hepatitis (diagnosis)	2 (2)	1 (1)	2 (6)	0
Infusion-related reactions	2 (2)	1 (1)	0	0

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HUDSON: Phase II multi-arm umbrella study

- Locally advanced or metastatic NSCLC
- Previous platinum-based chemotherapy
- Failure of prior anti-PD-(L)1 immunotherapy
- Suitable for new tumor biopsy / biopsy post-progression on anti-PD-(L)1 therapy
- No targetable alterations in *EGFR*, *ALK*, *ROS1*, *BRAF*, *MET*, or *RET*

Central molecular screen,‡ ***n* = 255** (Jan 26, 2018–Apr 14, 2021)

Primary endpoint: ORR
Secondary endpoints: DCR, PFS, OS, safety and tolerability

Group A: biomarker-matched, *n* = 86

HRRm	Durvalumab + olaparib (PARPi), *n* = 21
LKB1	Durvalumab + olaparib (PARPi), *n* = 21
ATM	**Durvalumab + ceralasertib (ATRi), *n* = 21***
ATM	Single-agent ceralasertib (ATRi)*
CD73h	Durvalumab + oleclumab (CD73 mAb), *n* = 23
HER2e	Durvalumab plus trastuzumab deruxtecan (HER2i)†
HER2m	

Group B: biomarker-non-matched, *n* = 169

Primary resistance (disease progression ≤24 weeks)§	Acquired resistance (disease progression >24 weeks)#
Durvalumab + olaparib (PARPi), *n* = 22	Durvalumab + olaparib (PARPi) , *n* = 23
Durvalumab + danvatirsen (STAT3i), *n* = 23	Durvalumab + danvatirsen (STAT3i), *n* = 22
Durvalumab + ceralasertib (ATRi), *n* = 20	**Durvalumab + ceralasertib (ATRi), *n* = 25**
Durvalumab + oleclumab (CD73 mAb), *n* = 9	Durvalumab + oleclumab (CD73 mAb), *n* = 25
	Durvalumab + cediranib (VEGFi)†

*Ongoing. †Data not mature. ‡Immunohistochemistry was also performed. §/# Progression on prior anti-PD-(L)1 therapy within 24 weeks / after > 24 weeks.
ATM, ataxia telangiectasia mutated; ATRi, ataxia telangiectasia receptor inhibitor; CD73(h), (high expression of) cluster of differentiation 73; DCR, disease control rate; HER2e/i/m, human epidermal growth factor receptor 2 expression/inhibitor/mutated; HRRm, homologous recombination repair mutated; LKB1, LKB1/STK11 aberration; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PARPi, poly ADP

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Baseline characteristics by regimen (Group A + Group B)

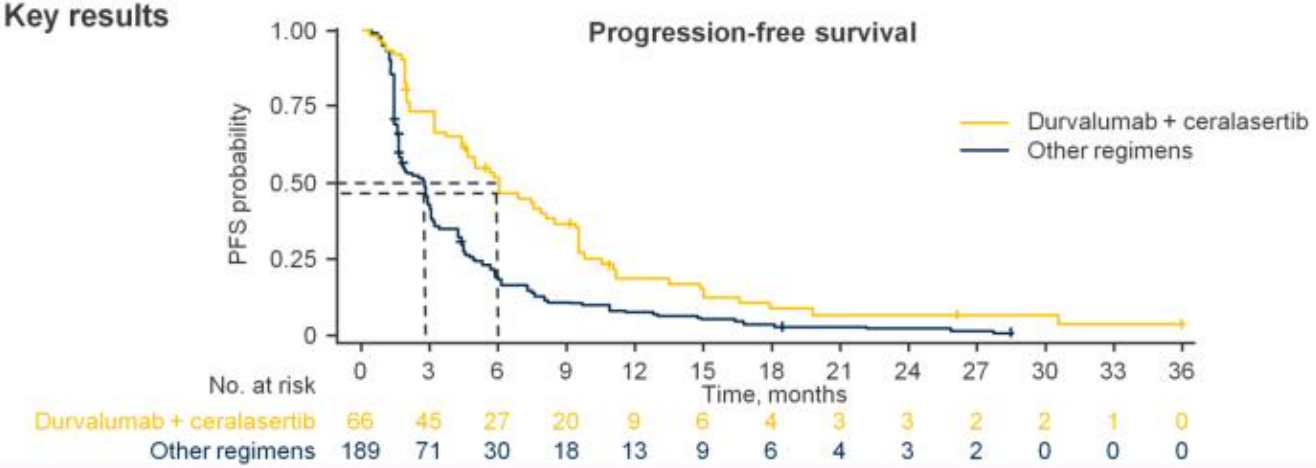
	Durvalumab + ceralasertib n=66	Durvalumab + olaparib n=87	Durvalumab + danvatirsen n=45	Durvalumab + oleclumab n=57
Median age (range), years	64.0 (45–80)	63.0 (35–85)	65.0 (39–80)	64.0 (37–79)
Male, n (%)	43 (65.2)	50 (57.5)	23 (51.1)	30 (52.6)
Histology, n (%)				
Adenocarcinoma	44 (66.7)	62 (71.3)	31 (68.9)	38 (66.7)
Squamous cell carcinoma	17 (25.8)	18 (20.7)	12 (26.7)	13 (22.8)
Other	5 (7.5)	7 (8.0)	2 (4.4)	6 (10.5)
Metastatic sites, n (%)				
0	2 (3.0)	1 (1.1)	2 (4.4)	3 (5.3)
1–2	28 (42.4)	40 (46.0)	37 (82.2)	31 (54.4)
≥3	36 (54.5)	46 (52.9)	6 (13.3)	23 (40.4)
PD-L1 status, n (%)				
Positive (TC ≥1%)	26 (39.4)	22 (25.3)	21 (46.7)	31 (54.4)
Negative	22 (33.3)	27 (31.0)	11 (24.4)	13 (22.8)
Unknown	18 (27.3)	38 (43.7)	13 (28.9)	13 (22.8)
Prior regimens, n (%)				
1–2	33 (50.0)	51 (58.6)	25 (55.6)	32 (56.1)
≥3	33 (50.0)	36 (41.4)	20 (44.4)	25 (43.9)
Current/former smoker, n (%)	58 (87.9)	69 (79.3)	40 (88.9)	52 (91.2)

Treatment efficacy by regimen

	Durvalumab + ceralasertib n=66	Durvalumab + olaparib n=87	Durvalumab + danvatirsen n=45	Durvalumab + oleclumab n=57
Median treatment duration, months				
Durvalumab*	7.3	3.7	2.8	2.9
Other agent†	6.3	3.2	2.8	2.9
12-week disease control rate, %	60.6	36.8	26.7	29.8
24-week disease control rate, %	42.4	17.2	13.3	15.8
ORR, %	16.7%	4.6%	0%	1.8%

PFS

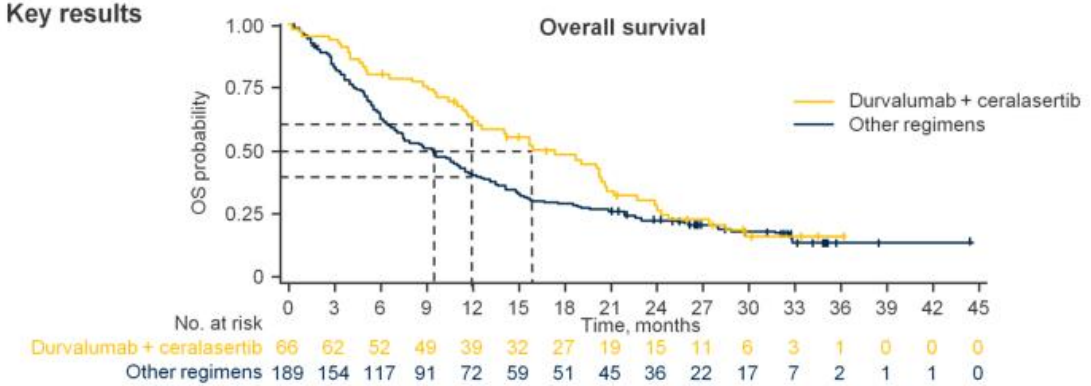
Key results



	Durvalumab + ceralasertib (n=66)	Other regimens (n=189)	Durvalumab + olaparib (n=87)	Durvalumab + danvatirsen (n=45)	Durvalumab + oleclumab (n=57)
mPFS, mo (80%CI)	6.0 (4.6, 7.5)	2.7 (1.8, 2.8)	2.7 (1.6, 3.0)	2.9 (1.7, 3.1)	1.8 (1.6, 2.7)
6-mo PFS, % (80%CI)	46.3 (37.9, 54.2)	18.0 (14.5, 21.9)	18.7 (13.5, 24.5)	18.8 (11.5, 27.6)	16.6 (10.8, 23.6)

OS

Key results



	Durvalumab + ceralasertib (n=66)	Other regimens (n=189)	Durvalumab + olaparib (n=87)	Durvalumab + danvatirsen (n=45)	Durvalumab + oleclumab (n=57)
mOS, mo (80%CI)	15.9 (14.1, 20.3)	9.4 (7.5, 10.6)	9.4 (6.9, 10.8)	7.9 (6.0, 10.6)	11.0 (7.6, 13.5)
6-mo OS, % (80%CI)	61.6 (53.4, 68.8)	39.7 (35.1, 44.3)	40.8 (34.0, 47.5)	28.8 (20.2, 38.0)	46.2 (37.5, 54.5)

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Sintilimab Plus Anlotinib Versus Platinum-based Chemotherapy as First-line Therapy in Metastatic NSCLC (SUNRISE): An Open Label, Multi-center, Randomized, Phase 2 Study

Baohui Han[1], Tianqing Chu[1], Zhuang Yu[2], Jing Wang[2], Ya
Xinmin Yu[4], Xun Shi[4], Qqingming Shi[5], Maojing Guan[5], C

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Cancer Hospital of Zhengzhou University, Zhengzhou, China, [4]Department of Thoracic Me
Affiliated to the University of Chinese Academy of Sciences, Hangzhou, China, [5]Medical C
Hospital, Hefei, China, [6]Department of Respiratory Medicine, The Fourth Hospital of Hebe

SUNRISE STUDY DESIGN

An Open Label, Multi-center, Randomized, Phase 2 Study

Key Eligibility Criteria

- Metastatic NSCLC* (Stage IV)
- EGFR/ALK/ROS1 negative
- No prior systemic treatment for metastatic disease
- ECOG PS 0 or 1
- 18 to 75 years

R 1:1

N=98

- Sintilimab (Sint) 200mg iv D1 + Anlotinib (Anlo) 12mg PO D1-14 Q3W
- Platinum-Doublet Chemotherapy Q3W，4-6 Cycle† pemetrexed maintenance (NSQ)

Crossover permitted after PD → Sintilimab 200mg iv D1 Q3W

Treatment until PD, intolerable toxicity, patient withdrawal, or death

Stratification Factors

- Histology (Squamous vs non-Squamous)
- PD-L1 expression(≥1% vs < 1%) §

Endpoints

- Primary: ORR
- Secondary: DCR、PFS、OS、Safety

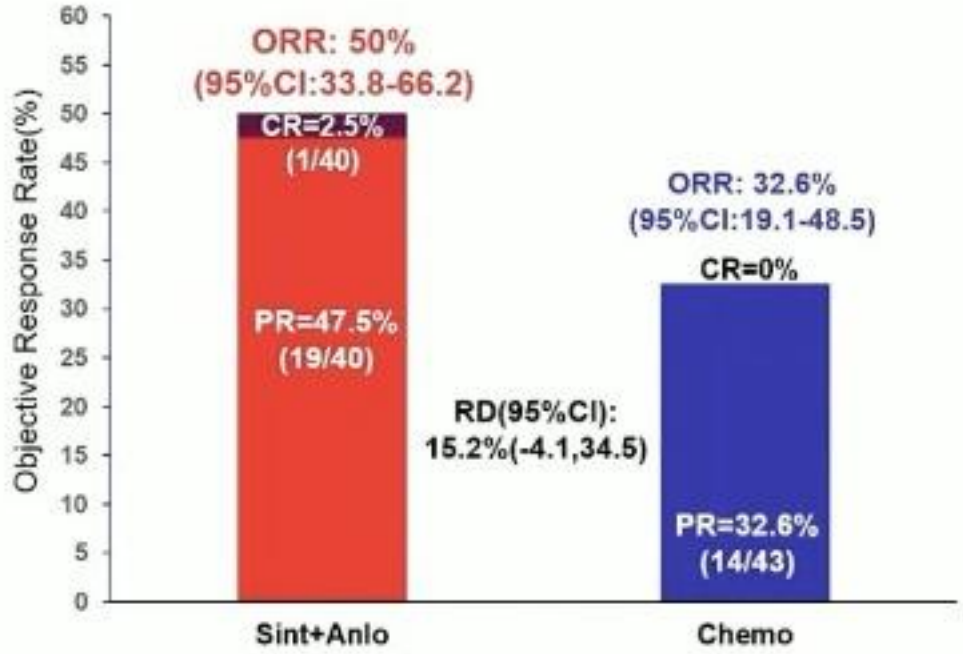
* Patients with asymptomatic brain metastases are eligible
† NSQ: pemetrexed + carboplatin; SQ: gemcitabine + carboplatin;
§ Assessed using the PD-L1 IHC 22C3 pharmDx assay

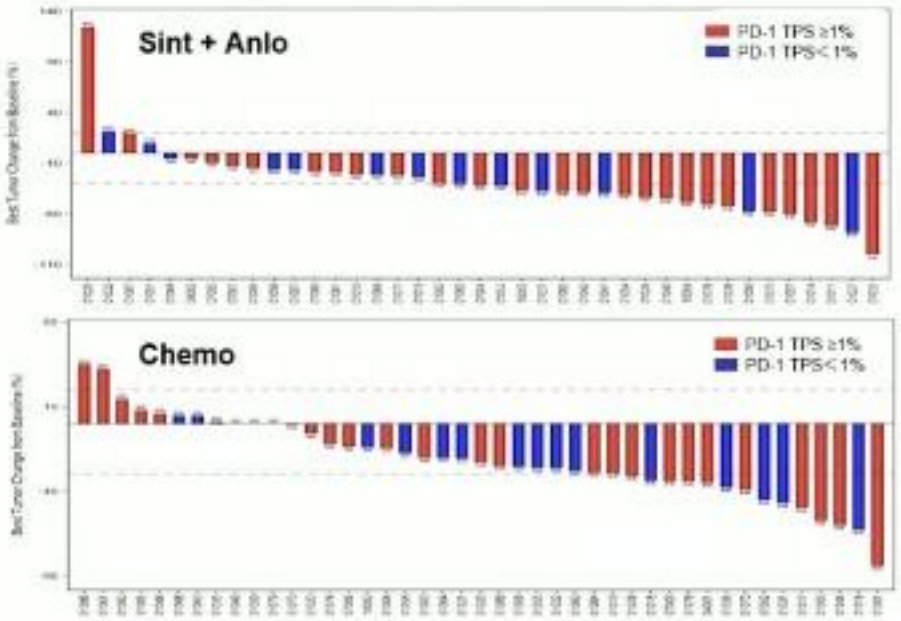
Statistical Consideration

- A sample size of 87 patients was required under the assumption of an ORR improved from 25% (Platinum-Doublet Chemotherapy) to 50% (Sintilimab+Anlotinib) with a power of 80% and one-sided α=0.05. With an expected drop-out rate of 10%, a total of 98 patients to be enrolled for 49 participants in each arm.
- A preliminary interim analysis was conducted when 89 participants were enrolled. (Data cut off: Jul. 15th, 2022)

PRIMARY ENDPOINT : ORR

Tumor Response by RECIST 1.1 (investigators assessment)





*83 patients received at least one tumor assessment at data cutoff (Jul. 15th, 2022) .

ORR/DCR were calculated with binomial distribution method, RD were calculated using stratified Miettinen-Nurminen method; RD, rate difference

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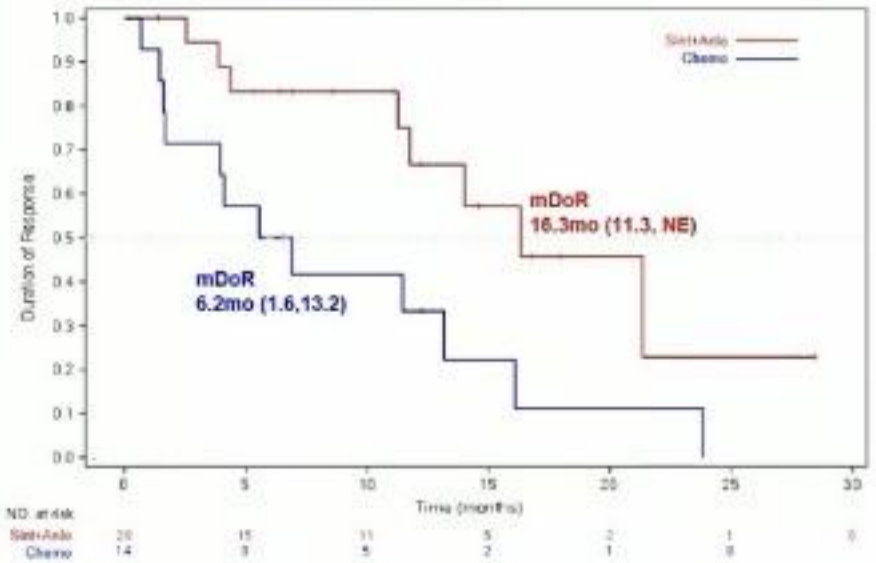
SECONDARY ENDPOITS

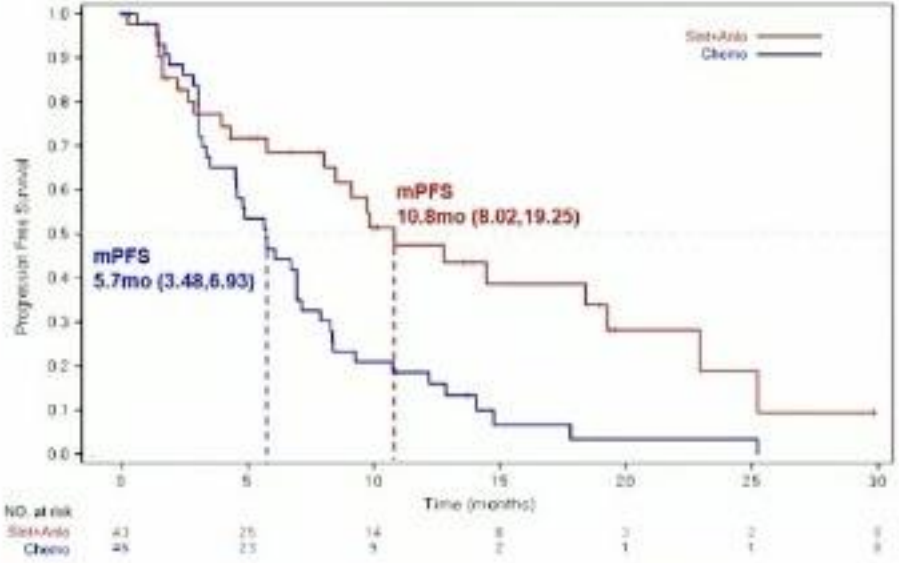
Duration of Response and Progression-Free Survival

DOR



	Patients	Events	median DOR (95%CI)
Sint+Anlo	20	8 (40.0)	16.3 (11.3, NE)
Chemo	14	12 (85.7)	6.2 (1.6,13.2)

PFS



	Patients	Events	HR (95%CI)	P
Sint+Anlo	43	24 (55.8)	0.4 (0.25,0.74)	0.002
Chemo	46	41 (89.1)		

HR was calculated with stratified Cox model, and was stratified by Histology(Squamous vs non-Squamous) PD-L1 expression(≥1% vs <1%)
P value was calculated with stratified log rank test); Data cutoff : Jul. 15th 2022 ; Median follow-up 13.1 months

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SAFETY SUMMARY

	Sint+Anlo (N=43)		Chemo (N=46)	
Treatment-related AEs, n (%)	Any Grade	Grade 3-4	Any Grade	Grade 3-4
Any TRAE	32 (74.4)	5 (11.6)	40 (87.0)	20 (43.5)
Immune-related TRAE	20 (46.5)	2 (4.7)	2 (4.3)	0
TRAE leading to any treatment discontinuation	0	0	2 (4.3)	0
TRAE leading to any treatment interruption	9 (20.9)	4 (9.3)	13 (28.3)	7 (15.2)
TRAE leading to death	0	0	1 (2.3)	0
Serious TRAE	6 (14.0)	3 (7.0)	9 (19.6)	7 (15.2)

- Hypothyroidism, hyponatremia and AST increased were most frequently observed in Sint+Anlo Arm. 2 pts experienced treatment discontinuation and 1 died due to TRAE in Chemo Arm, while none were observed in Sint+Anlo Arm.
- No unexpected toxicities was observed in either of Arm.

TERAPIAS DIRIGIDAS

- EGFR
- MET exon 14
- KRAS G12C
- ROS-1

EGFR

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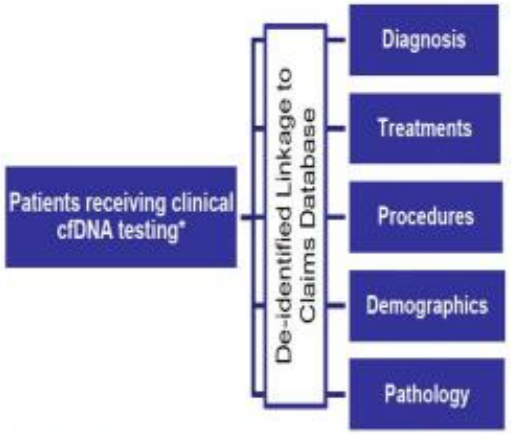
Real-World Landscape of EGFR C797X Mutation as a Resistance Mechanism to Osimertinib in NSCLC

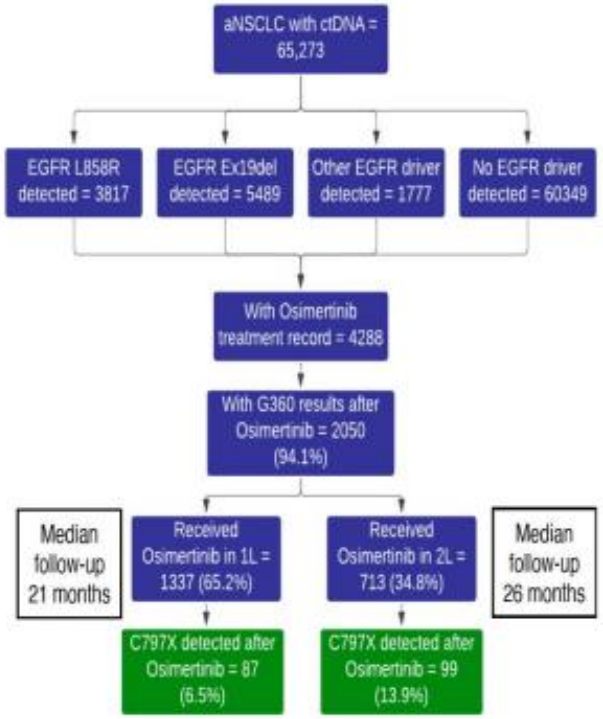
Suresh S. Ramalingam[1], Nicole Zhang[2], Junhua Yu[2], Carin Espenschied[2], Teresa Green[3], Joshua Infantine[3], Brenton G. Mar[3]

[1]Emory University, Atlanta, GA, United States, [2]Guardant Health, Redwood City, CA, United States, [3]Blueprint Medicines Corporation, Cambridge, MA, United States

Real world data integrating Guardant360 cfDNA and INFORM data

- INFORM is an aggregated commercial payer claims database with de-identified records of over 174,000 U.S.-based advanced cancer patients with clinical cfDNA* results.





Ramalingam S, et al. MA 07.03

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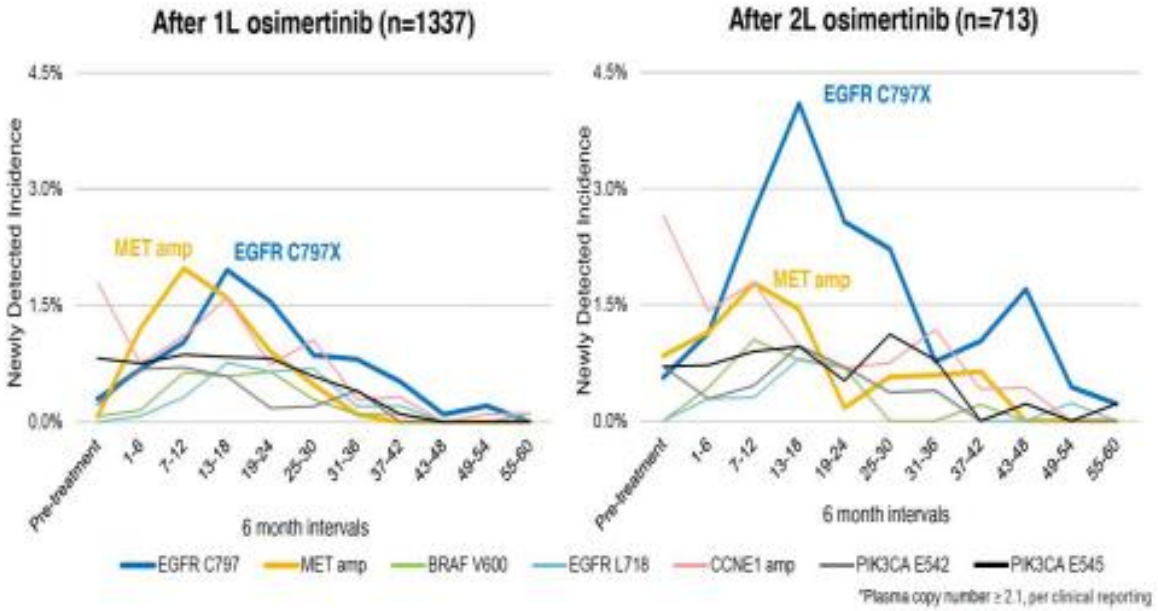
Early vs late resistance

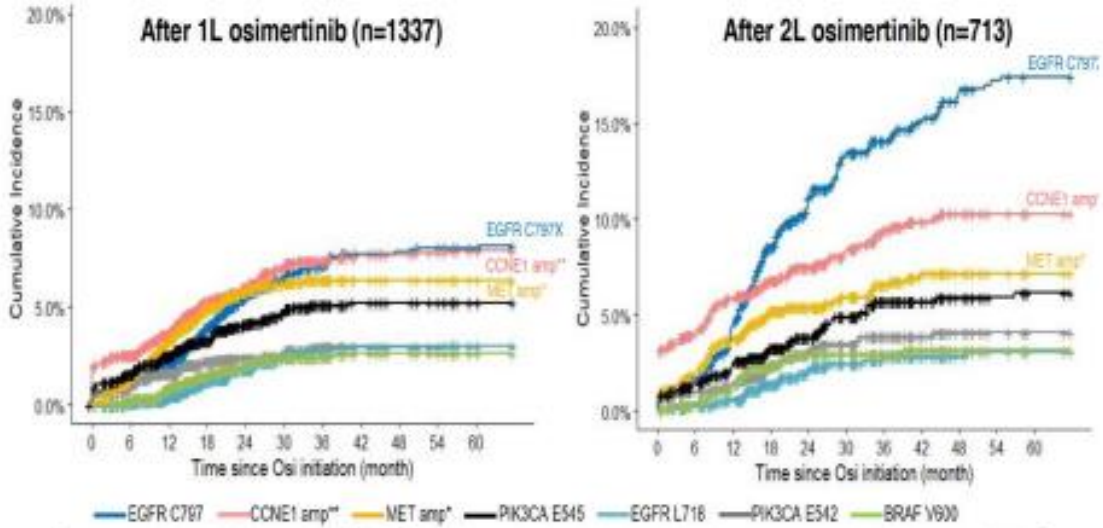
MET amp is most common acquired resistance mechanism in 1st year of 1L osimertinib, while EGFR C797X is most common after the 1st year

6-month Incidence of Common Acquired Resistance Mutations after osimertinib



EGFR C797X is the most common on-target or off-target resistance mutation, cumulatively, after osimertinib treatment

Cumulative incidence of common resistance mutations after osimertinib initiation#



- The cumulative incidence of EGFR C797X in a subset of likely 1L osi progressors (n=600) was 12.5%[δ]

*Including pts who were sequenced anytime after osimertinib. [δ]When analysis limited to those who discontinued osimertinib within 60 days of G360 (likely progressors). *Including focal MET amp, per clinical reporting. **Including both focal and aneuploidy of CCNE1 amplification, per clinical reporting.

- MET amplification is the most common initial resistance mutation in the first year of 1L osimertinib, but EGFR C797X mutations subsequently emerge and are the most common resistance after the first year
- Cumulatively, EGFR C797X mutations were 1.25 times more common than MET amplification after 1L osimertinib and 2.4 times more common after 2L osimertinib
- In patients likely progressing after 1L osimertinib, the cumulative incidence of EGFR C797X was 12.5%

lung cancer research

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JIN-A02, a Highly Effective 4th Generation EGFR-TKI, Targeting EGFR C797S Triple Mutation in NSCLC

Byoung Chul Cho
Yonsei Cancer Center
Korea

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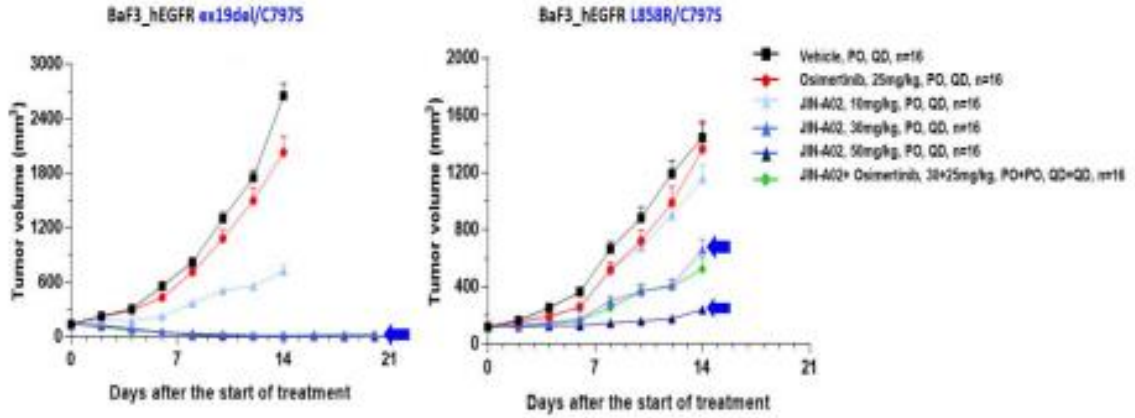
▶ The antitumor efficacy of JIN-A02 in xenograft mouse model



▶ **Conclusions:** JIN-A02 showed robust activities against EGFR resistant mutations including C797S and T790M and sensitizing mutations. JIN-A02 is a potential best-in-class fourth-generation EGFR TKI with high potency and selectivity.

JIN-A02 showed robust activities against EGFR resistant mutations including C797S and T790M and sensitizing mutations.

Cho et al. MA 07.08

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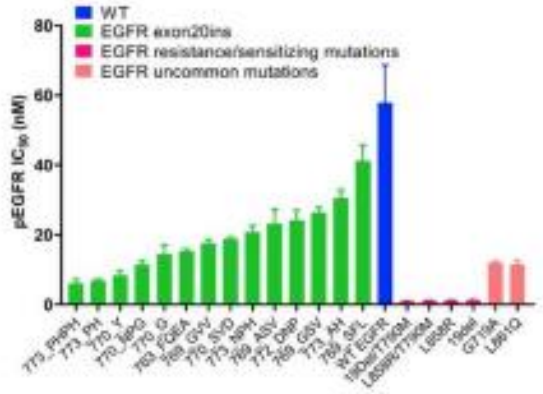
Sunvocertinib in NSCLC pts with *EGFR* ex20ins

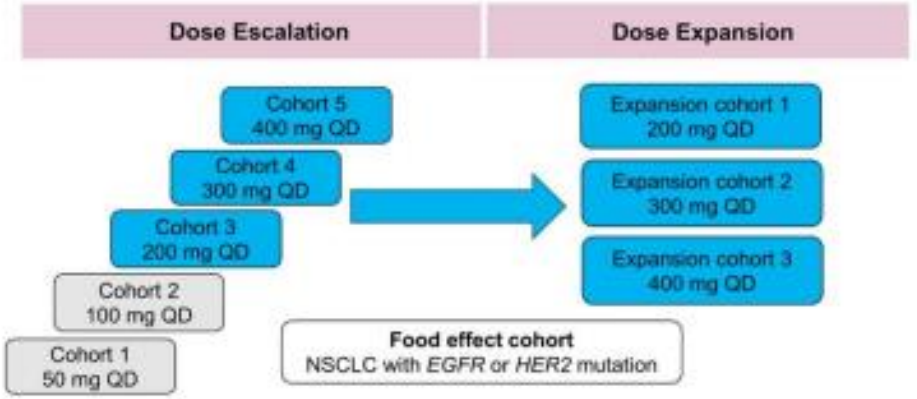
Passi Jänne, et al

Sunvozertinib is an oral, irreversible, selective EGFR TKI:

- Exon 19 deletions/L858R
- T790M
- EGFR exon 20 insertions



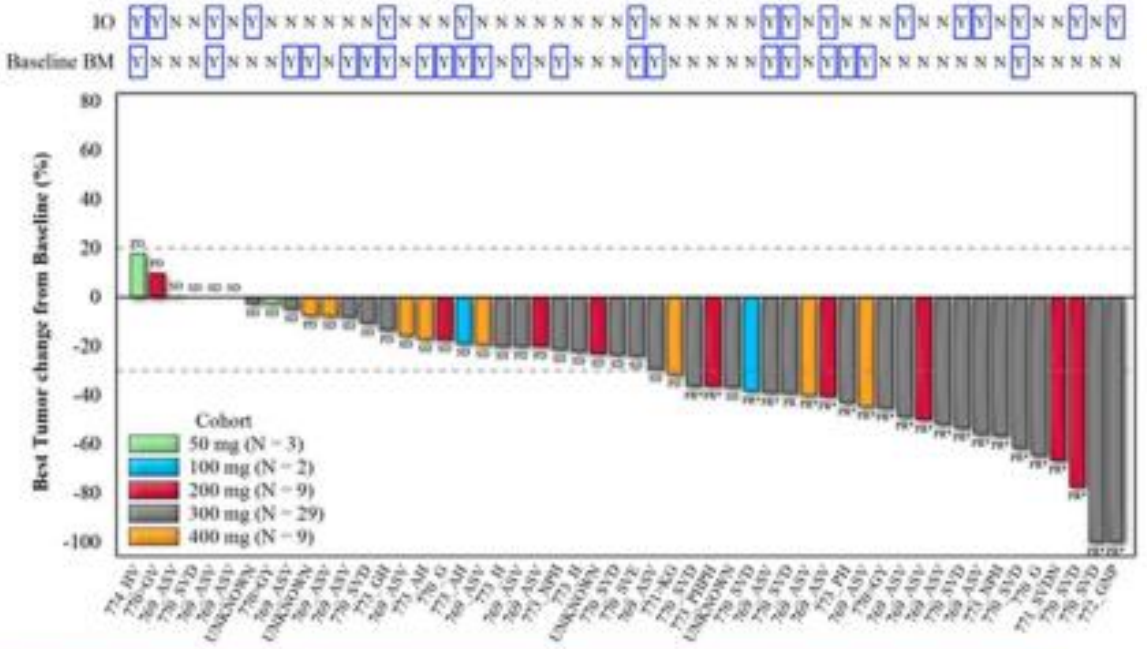
Phase 1 study design (WU-KONG1 and WU-KONG2 trials)



Characteristics	50 mg (N = 3)	100 mg (N = 2)	200 mg (N = 9)	300 mg (N = 29)	400 mg (N = 9)	Total (N = 52)
Median age, y (range)	48 (36-72)	58 (55-61)	61 (36-83)	59 (32-82)	54 (47-85)	59 (32-85)
Female, n (%)	3 (100.0)	1 (50.0)	7 (77.8)	15 (51.7)	5 (55.6)	31 (59.6)
Race, n (%),						
White	0 (0.0)	0 (0.0)	0 (0.0)	7 (24.1)	1 (11.1)	8 (15.4)
Asian	3 (100.0)	2 (100.0)	9 (100.0)	22 (75.9)	8 (88.9)	44 (84.6)
Previous cancer therapy						
Lines, Median (range)	5 (2-5)	4 (3-5)	3 (1-4)	2 (1-10)	1 (1-3)	3 (1-10)
Baseline BM, n (%)	1 (33.3)	1 (50.0)	2 (22.2)	13 (44.8)	4 (44.4)	21 (40.4)
Post radiotherapy, n(%)	1 (33.3)	0 (0.0)	0 (0.0)	4 (13.8)	0 (0.0)	5 (9.6)

BM: brain metastasis. Data cut-off date: 30 July, 2021.

Results	N = 52
Previous therapies median (range)	3 (1-10)
Brain Mets	21 (40%)
Prior Immunotherapy	15 (29%)
ORR (%)	40.4%
DCR. (%)	84.6%
mDOR (months)	5.9



Tumor Response	50 mg (N = 3)	100 mg (N = 2)	200 mg (N = 9)	300 mg (N = 29)	400 mg (N = 9)	Total (N = 52)
Confirmed ORR, n (%)	0 (0.0)	1 (50.0)	5 (55.6)	13 (44.8)	2 (22.2)	21 (40.4)
Confirmed DCR, n (%)	2 (66.7)	2 (100.0)	7 (77.8)	26 (89.7)	7 (77.8)	44 (84.6)
Median DoR, months	NA	5.9	Not reached*	5.5	9.7	5.9

Group	PR n (%)	SD n (%)	PD n (%)	DCR n (%)
With prior anti-PD(L)1 treatment (N = 15)	8 (53.3)	4 (26.7)	3 (20.0)	12 (80.0)
Without prior anti-PD(L)1 treatment (N = 34)	13 (38.2)	17 (50.0)	4 (11.8)	30 (88.2)
Total (N = 49)	21 (42.9)	21 (42.9)	7 (14.3)	42 (85.7)

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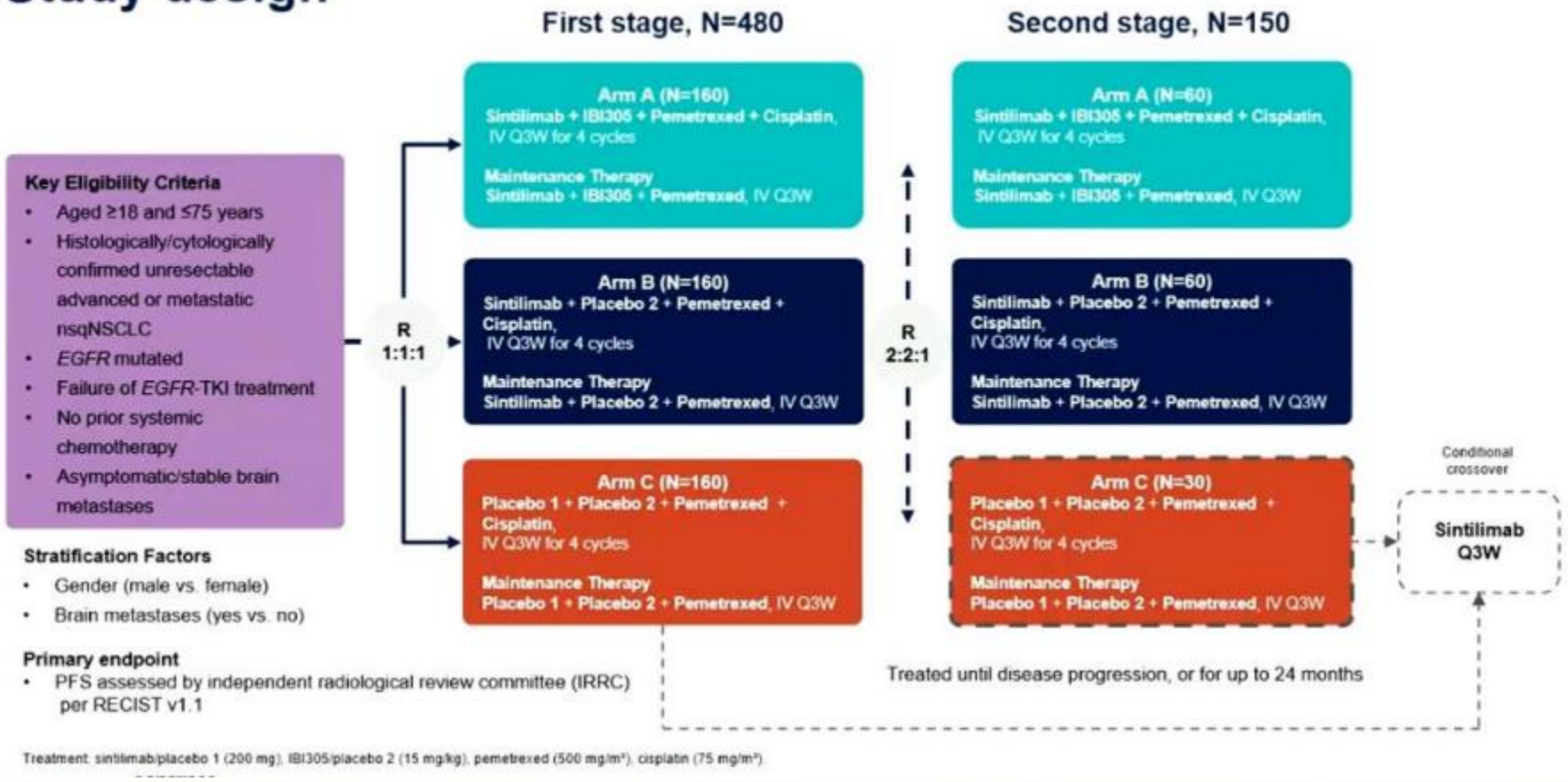
Sintilimab with or without IBI305 plus chemotherapy in patients with EGFR mutated non-squamous non-small-cell lung cancer (EGFRm nsqNSCLC) who progressed on EGFR tyrosine-kinase inhibitors (TKIs) therapy: second interim analysis of phase 3 ORIENT-31 study

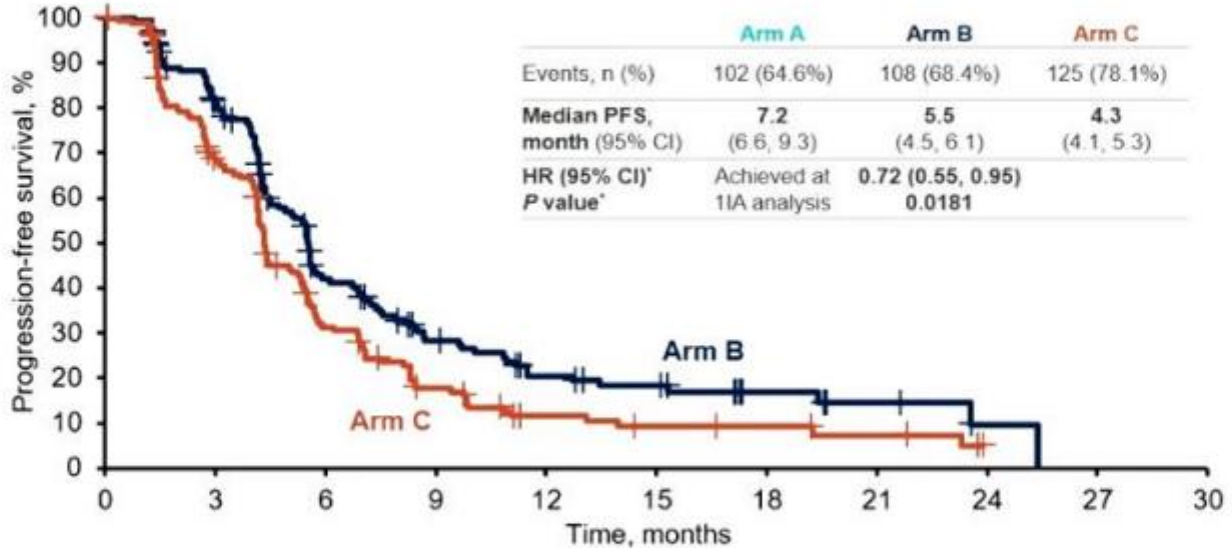
Shun Lu, MD
Department of Medical Oncology, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

September 11, 2022

Study design



Study met primary endpoint of PFS (by IRRC) in Arm B vs Arm C



	Arm A	Arm B	Arm C
Events, n (%)	102 (64.6%)	108 (68.4%)	125 (78.1%)
Median PFS, month (95% CI)	**7.2** (6.6, 9.3)	**5.5** (4.5, 6.1)	**4.3** (4.1, 5.3)
HR (95% CI)*	Achieved at	**0.72 (0.55, 0.95)**	
P* value	1IA analysis	**0.0181**	

Number at risk										
Arm B	158	111	52	31	19	15	7	4	1	0
Arm C	160	97	41	21	10	7	6	3	0	

* Compared with Arm C. HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by gender (male vs. female), presence of brain metastases (yes vs. no) and prior EGFR-TKI treatment (1 line vs. 2 lines). The two-sided α boundary is 0.0444 as calculated using Lan-Demets spending function with O'Brien-Fleming approximation. Data cutoff, 31 Mar 2022; median follow up, 13.1 months. IA, interim analysis; HR, hazard ratio; CI, confidence interval

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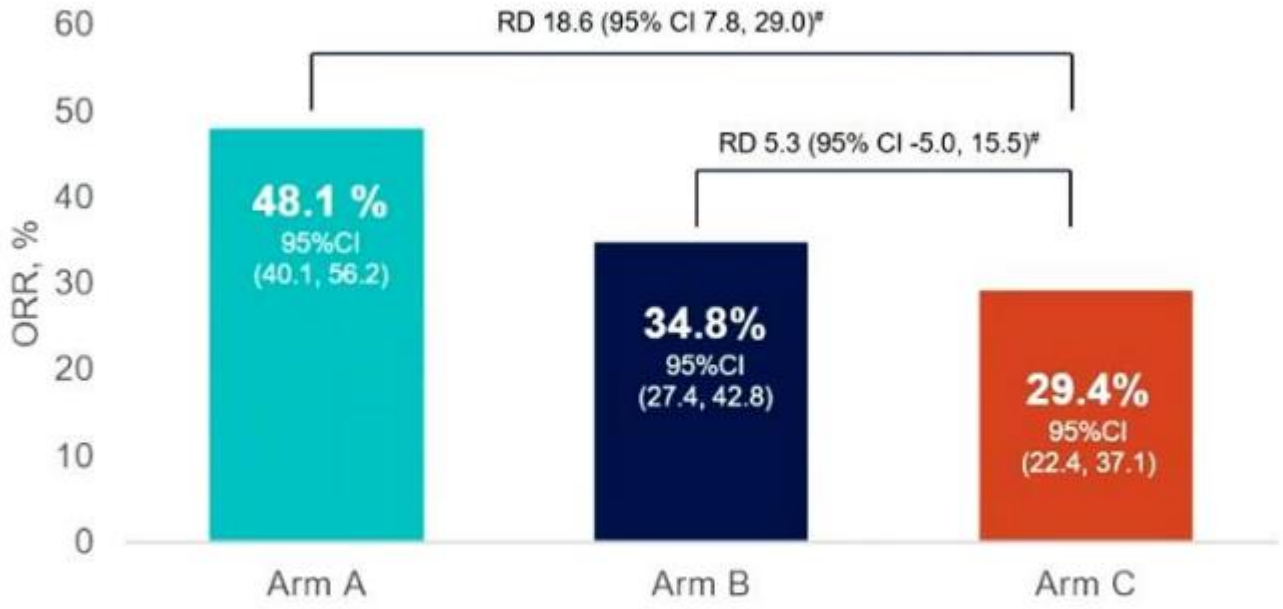
Secondary endpoint: ORR, DCR and DOR (by IRRC)



	Arm A	Arm B	Arm C
DCR (95% CI)	86.1% (79.7%, 91.1%)	81.6% (74.7%, 87.3%)	75.6% (68.2%, 82.1%)
Median DOR, month (95% CI)	8.5 (5.6, 11.7)	7.4 (4.7, 12.0)	5.7 (4.1, 7.1)

ORR, objective response rate; DCR, disease control rate; DOR, duration of response; RD, rate difference; CI confidence interval.
*RD and CI was calculated using Miettinen & Nurminen method stratified by gender (male vs. female), presence of brain metastases (yes vs. no) and prior EGFR-TKI treatment (1 line vs. 2 lines).

Organizado por:

GECP lung cancer research

Amivantamab and lazertinib in patients with *EGFR*-mutant NSCLC after progression on osimertinib and platinum-based CT: updated results from CHRYSALIS-2

Catherine Shu, et al

Dose Expansion Cohorts

RP2CD: Lazertinib 240 mg PO +
Amivantamab 1050 mg (1400 mg for ≥80 kg) IV

- **Cohort A:** EGFR ex19del or L858R
  Post-osimertinib and platinum-based chemotherapy (n=162)
- **Cohort B:** EGFR ex20ins
  Post-standard of care and platinum-based chemotherapy
- **Cohort C:** Uncommon EGFR mutations
  Treatment naïve or post-1st or 2nd generation EGFR TKI
- **Cohort D:** EGFR ex19del or L858R
  Post-osimertinib, chemotherapy naïve, biomarker validation

Endpoints

- Overall response rate (primary)
- Duration of response
- Clinical benefit rate[a]
- Progression-free survival
- Overall survival
- Adverse events

Characteristic, n (%)	n=162
Median age, years (range)	61.5 (31–83)
Male / female	57 (35) / 105 (65)
Race	
White	42 (26)
Asian	99 (61)
Black	1 (0.6)
Not reported	20 (12)
ECOG PS 0 /1	49 (30) / 113 (70)
Brain metastases at baseline[a]	66 (41)
Untreated	30 (19)
Treated	36 (22)

Characteristic, n (%)	n=162
Smoking history	
Non-smoker	111 (69)
Smoker	49 (30)
Unknown	2 (1)
Median number of prior therapy lines (range)	3 (2–14)
2–3	117 (72)
≥4	45 (28)
Prior therapy regimens	
Frontline osimertinib → platinum-based chemo	39 (23)
1st/2nd-gen EGFR TKI → osimertinib → platinum-based chemo	67 (42)
Heavily pretreated or out of sequence	56 (35)

Amivantamab and lazertinib in patients with *EGFR*-mutant NSCLC after progression on osimertinib and platinum-based CT: updated results from CHRYSALIS-2

Catherine Shu, et al

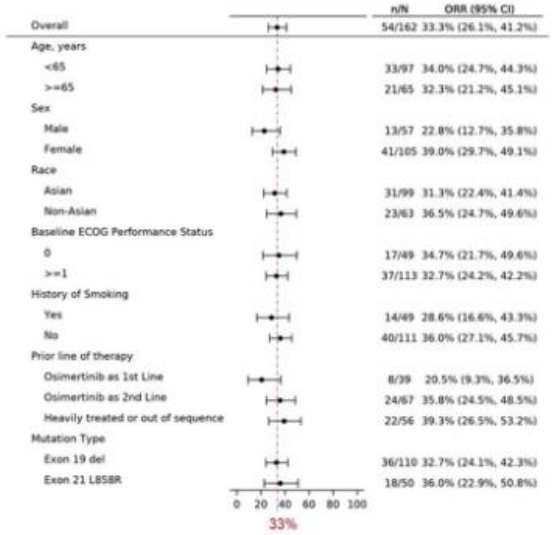
Antitumor Activity of Amivantamab + Lazertinib

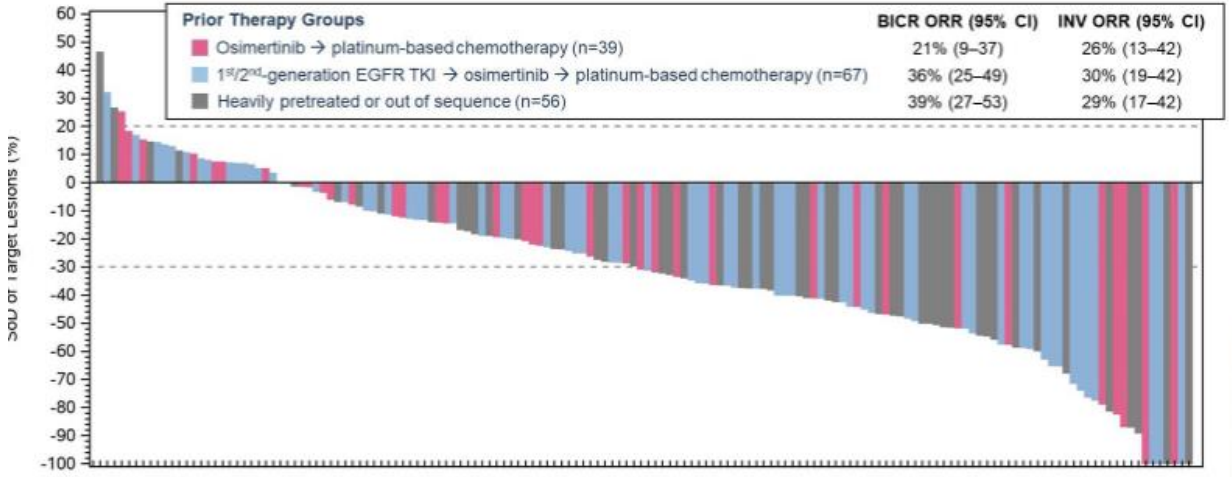
BICR-assessed Response	n=162
ORR	33% (95% CI, 26–41)
Median DOR	9.6 mo (95% CI, 7.0–NE)
Best response, n (%)	
Complete response	2 (1)
Partial response	52 (32)
Unconfirmed partial response	1 (0.6)
Stable disease	69 (43)
Progressive disease	28 (17)
NE	10 (6)
Clinical benefit rate[a]	57% (95% CI, 49–65)

Investigator-assessed ORR=28% (95% CI, 22–36)
Investigator-assessed median DOR=8.4 mo (95% CI, 5.6–NE)

Median follow-up=10.0 mo (range, 0.3–20.2)
Median progression free survival=5.1 mo (95% CI, 4.2–6.9)
Median overall survival=14.8 mo (95% CI, 12.1–NE)

[a]Percentage of patients with confirmed response or durable stable disease (duration of ≥11 weeks).
BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; mo, months; NE, not evaluable; ORR, overall response rate.





10 efficacy-evaluable patients did not have any evaluable post-baseline target lesion measurements

TEAEs (≥15%) by Preferred Term, n (%)	n=162	
	All grade	Grade ≥3
EGFR-related		
Rash	71 (44)	4 (2)
Dermatitis acneiform	55 (34)	8 (5)
Paronychia	84 (52)	6 (4)
Stomatitis	63 (39)	2 (1)
Diarrhea	36 (22)	1 (1)
Pruritus	30 (19)	1 (1)
MET-related		
Hypoalbuminemia	70 (43)	11 (7)
Peripheral edema	43 (27)	2 (1)
Other		
Infusion related reaction	108 (67)	13 (8)
Increased ALT	46 (28)	5 (3)
Nausea	40 (25)	3 (2)
Decreased appetite	39 (24)	1 (1)
Constipation	38 (23)	0
Asthenia	37 (23)	7 (4)
Dry skin	37 (23)	0
Vomiting	36 (22)	1 (1)
Increased AST	35 (22)	3 (2)
Dyspnea	33 (20)	13 (8)
Thrombocytopenia	33 (20)	2 (1)
Fatigue	32 (20)	4 (2)
Headache	29 (18)	2 (1)
Anemia	27 (17)	4 (2)
Hypocalcemia	26 (16)	1 (1)

Tepotinib + osimertinib for *EGFR*m NSCLC with *MET* amplification (*MET*amp) after progression on first-line (1L) osimertinib:

Initial results from the INSIGHT 2 study

Julien Mazieres, Tae Min Kim, Boon Khaw Lim, Marie Wislez, Christophe Dooms, Giovanna Finocchiaro, Hidetoshi Hayashi, Chong Kin Liam, Jo Raskin, Lye Mun Tho, Filippo de Marinis, Ernest Nadal, Egbert F. Smit, Xiuning Le, Sabine Brutlach, Aurora O'Brate, Svenja Adrian, Barbara Ellers-Lenz, Niki Karachaliou, Yi-Long Wu

Toulouse, France

Study Design of INSIGHT 2

An open-label, two-arm Phase II study of advanced *EGFR*m NSCLC with *MET*amp after progression on 1L osimertinib (N=~120)

Key inclusion criteria

- Locally advanced or metastatic NSCLC with activating *EGFR* mutation
- Acquired resistance to 1L osimertinib
- *MET*amp detected by either central or local* FISH testing (TBx) or central NGS testing (LBx)†
- ECOG PS of 0 or 1
- Stable, treated brain metastases allowed

Tepotinib 500 mg QD
+
Osimertinib 80 mg QD‡

Tepotinib monotherapy arm#

Primary objective

- ORR by IRC for patients with *MET*amp centrally confirmed by TBx FISH treated with tepotinib plus osimertinib

Secondary objectives include:

- ORR by IRC in patients with:
  - *MET*amp by LBx NGS treated with tepotinib plus osimertinib
  - *MET*amp centrally confirmed by TBx FISH treated with tepotinib monotherapy

Initial results are presented; global enrollment is complete, primary analysis is planned when all patients have ≥9 months' follow-up

Objective Response Rate of Tepotinib plus Osimertinib

Tepotinib plus osimertinib (IRC)

	*MET*amp by central TBx FISH		*MET*amp by central LBx NGS	
Follow-up	≥9 months (N=22)	≥3 months (N=48)	≥9 months (N=16)	≥3 months (N=23)
ORR (95% CI)	**54.5%** (32.2, 75.6)	**45.8%** (31.4, 60.8)	**50.0%** (24.7, 75.3)	**56.5%** (34.5, 76.8)
BOR, n (%)				
PR	12 (54.5)	22 (45.8)	8 (50.0)	13 (56.5)
SD	2 (9.1)	5 (10.4)	1 (6.3)	1 (4.3)
PD	4 (18.2)	10 (20.8)	5 (31.3)	5 (21.7)
NE	4 (18.2)	11 (22.9)*	2 (12.5)	4 (17.4)

Similar ORRs were reported according to *MET*amp GCN (TBx FISH):

Patients with ≥3 months' follow-up (N=48): **≥10 GCN:** 51.9% (95% CI: 31.9, 71.3) (N=27);
5–<10 GCN: 40.0% (95% CI: 19.1, 63.9) (N=20)†

Tepotinib monotherapy (IRC)

	*MET*amp by central TBx FISH
Follow-up	≥6 months (N=12)
ORR (95% CI)	**8.3%** (0.2, 38.5)
BOR, n (%)	
PR	1 (8.3)
SD	2 (16.7)
PD	8 (66.7)
NE	1 (8.3)

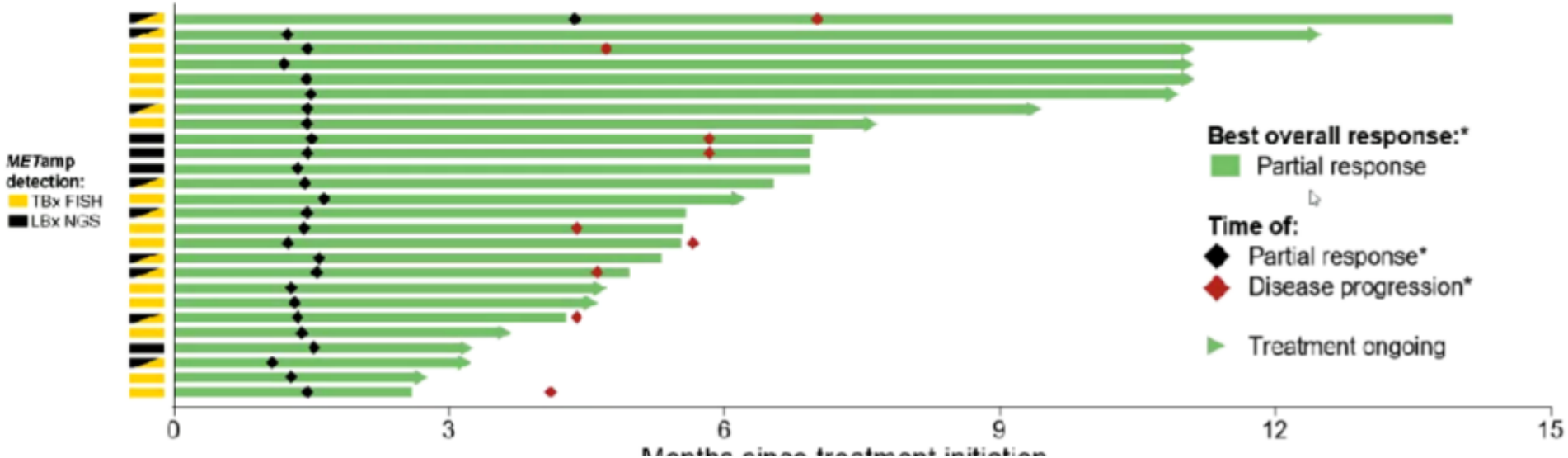
Seven patients switched to tepotinib plus osimertinib and five of them are still on combination treatment

Confirmed ORR was 54.5% in patients with *MET*amp detected by TBx FISH with ≥9 months' follow-up

*Incomplete post-baseline assessments (n=2), SD <12 weeks (n=3), COVID-19-related early discontinuation (n=1), and PD/AE-related early discontinuations (n=5). †One patient had GCN 4.96 and enrolled through a *MET*/CEP7 ratio ≥2.

Responses to Tepotinib Plus Osimertinib were Rapid and Long-lasting

Time on treatment in responders (IRC) with *MET*amp detected by central TBx FISH and/or LBx NGS treated with tepotinib plus osimertinib (N=26)



Safety Profile of Tepotinib plus Osimertinib

TRAEs of any grade in >10% all patients, n (%)	Tepotinib + osimertinib N=88	
	Any grade	Grade ≥3
Any	**65 (73.9)**	**21 (23.9)**
Diarrhea	36 (40.9)	0
Peripheral edema	21 (23.9)	4 (4.5)
Paronychia	15 (17.0)	1 (1.1)
Nausea	12 (13.6)	0
Decreased appetite	10 (11.4)	2 (2.3)
Vomiting	10 (11.4)	1 (1.1)

- AEs led to a dose reduction in 16 patients (18.2%)
  - Tepotinib dose was reduced in 14 patients (15.9%)
  - Osimertinib dose was reduced in four patients (4.5%)
  - Two patients had a dose reduction in both drugs
- Primary reason for treatment discontinuation was AEs in six patients (6.8%)
- Two patients had AEs leading to death that were considered potentially related to either trial drug by the investigator
  - One patient had pneumonia/pneumonitis
  - One patient had pleural effusion

Osimertinib+Necituzumab+Trastuzumab in refractory EGFR mut NSCLC

IASLC 2022 World Conference on Lung Cancer
AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Phase 1b/2 study of combined HER inhibition in refractory EGFR-mutated metastatic non-small cell lung cancer (NSCLC)

J. Goldman[1], H.K.T. Huang[1], A. Cummings[1], Z. Noor[1], S. Slomowitz[1], E. Kirimis[1], O. Olevsky[1], K. Arzoo[1], S. Ashouri[1], B. DiCarlo[1], E.H-L. Hu[1], D.J. Wong[1], J. Chauv[1], E.B. Garon[1], Y. Yarden[2], D. Slamon[1]

[1]David Geffen School of Medicine at UCLA, Los Angeles/CA/USA
[2]Weizmann Institute of Science, Rehovot/IL

University of California, Los Angeles (UCLA), USA

IASLC 2022 World Conference on Lung Cancer
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Trial Introduction, Objectives and Design

Trial Background:

- Preclinical models (A, western blot; B, orthotopic murine model) show that osimertinib, cetuximab, and trastuzumab overcome osimertinib resistance. Necitumumab was substituted for cetuximab due to higher binding affinity and lower hypersensitivity reactions. (Romaniello, Yarden, et al. Clin Can Res, 2018)

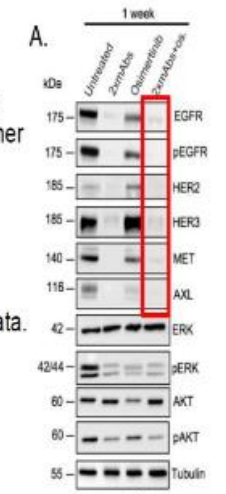
Key Objectives:

- Determine the recommended phase 2 dose (RP2D), safety, tolerability, and preliminary efficacy of the combination of osimertinib, necitumumab and trastuzumab (ONT).
- Exploratory endpoints include patient reported outcomes (PRO-CTCAE) and quality of life (FACT-L) data.

Study Design:

- In phase 1b, we utilized an accelerated dose-escalation to determine the RP2D.
- In phase 2, a Simon's two-stage optimum design will be used to treat up to 20 patients at the RP2D.

Dose Level	Osimertinib (mg)	Necitumumab (mg)	Trastuzumab (mg/kg)
-1	40 qd	400 q2w	6, followed by 4 q2w
1	40 qd	600 q2w	6, followed by 4 q2w
2	80 qd	600 q2w	6, followed by 4 q2w
3	80 qd	800 q2w	6, followed by 4 q2w

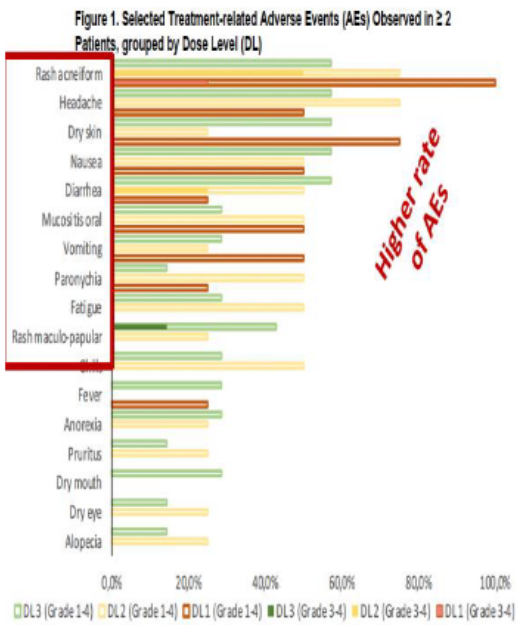


Patient Demographics

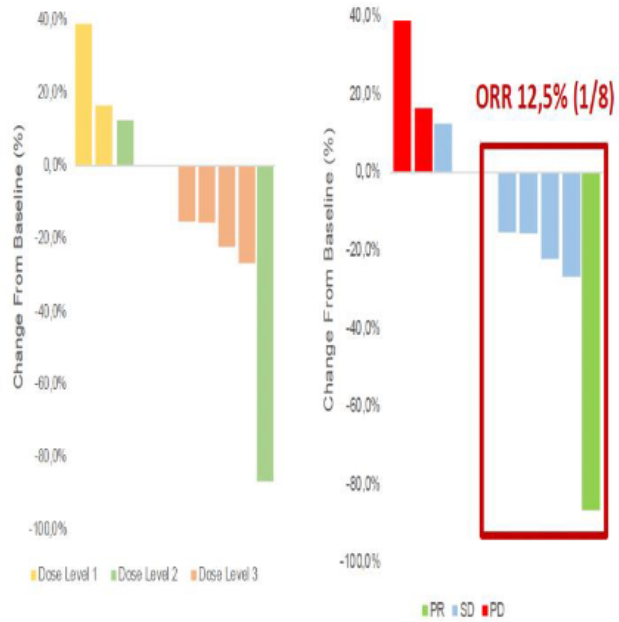
- Number of patients: 15
- Median Age: 61, Range: 54 – 82

Gender	Total = 15	%
Male	3	20.0%
Female	12	80.0%
Age Group	**Total = 15**	**%**
> 50 & ≤ 60	7	46.7%
> 60 & ≤ 70	3	20.0%
> 70 & ≤ 80	4	26.7%
> 80 & ≤ 90	1	6.7%
Race	**Total = 15**	**%**
Asian	5	33.3%
Decline to Answer	1	6.7%
Other	1	6.7%
White	7	46.7%
Unknown	1	6.7%
Ethnicity	**Total = 15**	**%**
Hispanic or Latino	1	6.7%
Not Hispanic or Latino	14	93.3%
Smoking History	**Total = 15**	**%**
Former Smoker	3	26.7%
Current Smoker	1	6.7%
Never Smoker	11	73.3%

Treatment-related AEs



Objective responses



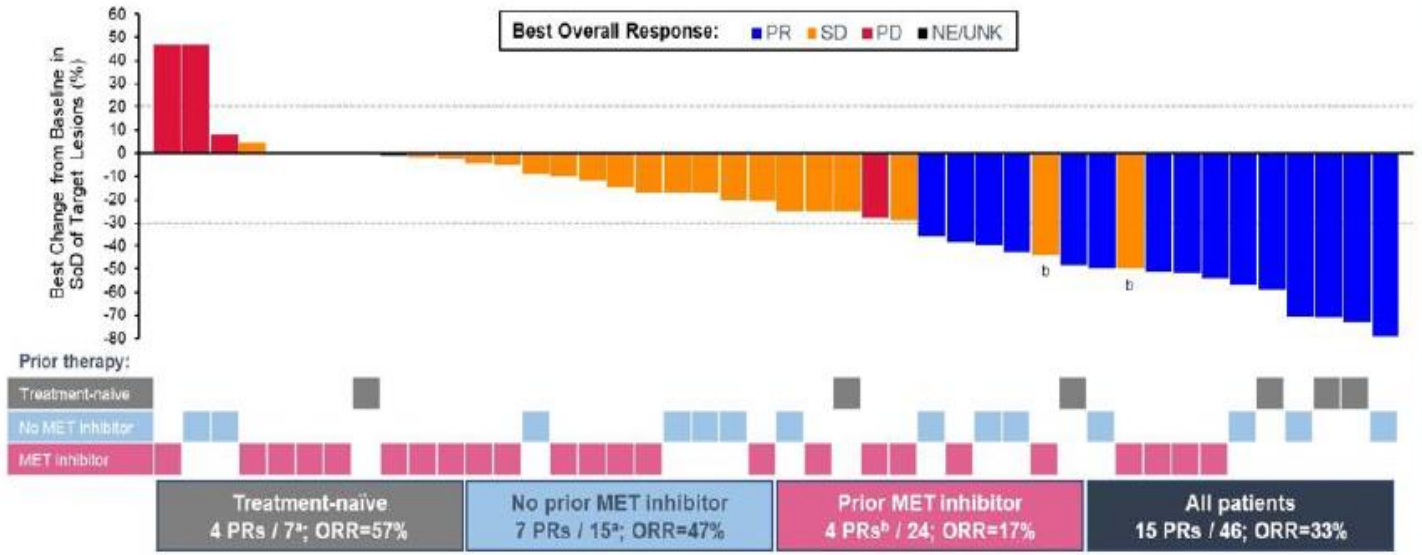
Goldman J, et al. MA 07.05

MET exon 14

Amivantamab in NSCLC patients with MET exon 14 skipping mutation: Updated results from the CHRYSALIS study

- Median duration of response is not estimable
  - 11/15 patients who responded are ongoing
  - 10 patients (67% of responders) with response duration ≥6 months
- Clinical benefit rate=59%[a]
  - Treatment-naïve: 71%
  - No prior MET: 53%
  - Prior MET: 58%
- Median PFS=6.7 mo (95% CI 2.9–15.3)
  - Treatment-naïve: NE (95% CI 2.6–NE)
  - No prior MET: 8.3 mo (95% CI 1.5–15.3)
  - Prior MET: 4.2 mo (95% CI 2.9–NE)
- Median time to response=1.6 mo (range, 1.2–9.9)

- A total of 46 patients were efficacy evaluable



Krebs, ASCO, 2022

IASLC 2022 World Conference on Lung Cancer

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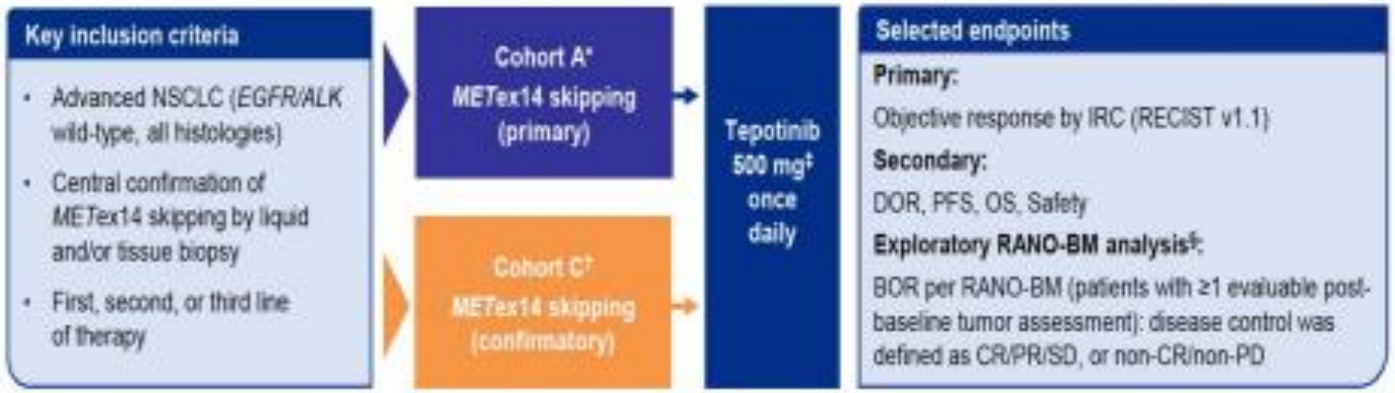
Tepotinib in patients with *MET* exon 14 skipping NSCLC: Primary analysis of the confirmatory VISION Cohort C

Michael Thomas,[1] Marina C. Garassino,[2,3] Enriqueta Felip,[4] Hiroshi Sakai,[5] Xiuning Le,[6] Remi Veillon,[7] Egbert F. Smit,[8] Julien Mazieres,[9] Alexis B. Cortot,[10] Jo Raskin,[11] Santiago Viteri,[12] James CH Yang,[13] Myung-Ju Ahn,[14] Yi-Long Wu,[15] Rui Ma,[16] Jun Zhao,[17] Aurora O'Brate,[18] Karin Berghoff,[19] Rolf Bruns,[20] Gordon Otto,[21] Paul K. Paik[22,23]

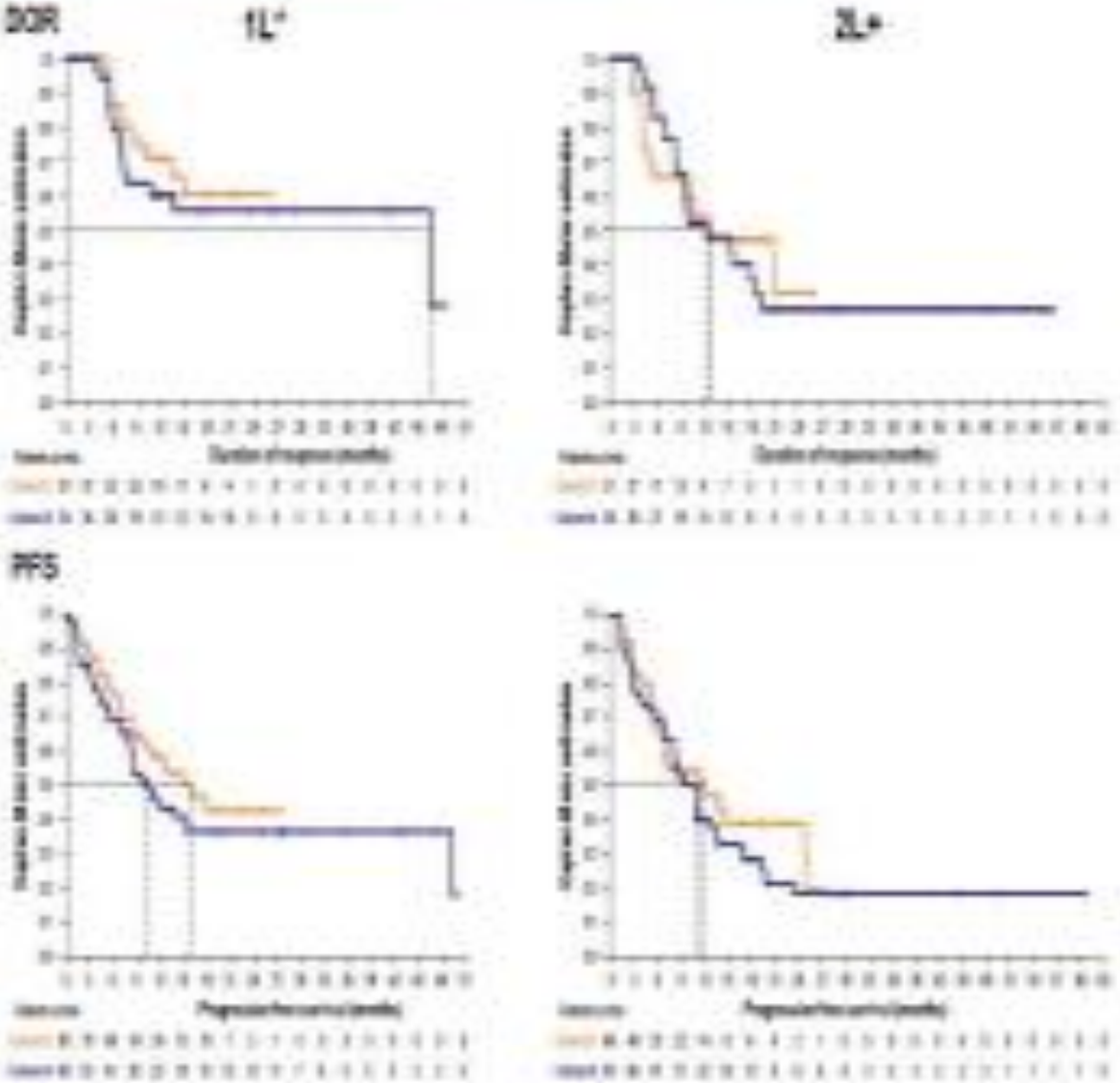
Tepotinib is a once daily and highly selective MET TKI approved for *MET*ex14 skipping NSCLC based mainly on Cohort A of the multi-cohort Phase II VISION study[1]



Here, we report the primary analysis (>9-months' follow-up) of the independent confirmatory Cohort C; data cut-off February 20, 2022‡

Overall efficacy in Cohort C and Cohort A was robust and durable across therapy lines

	1L+ (T+ and/or L+)	2L+ (T+ and/or L+)
	Cohort C	Cohort C
ORR, % (95% CI)	60.8 (49.4, 69.9)	47.3 (34.5, 59.7)
Median DOR, months (95% CI)	ne (13.4, ne)	12.9 (5.1, ne)
Median PFS, months (95% CI)	15.8 (10.4, ne)	12.1 (6.9, ne)
Median OS, months (95% CI)	21.1 (12.7, ne)	18.8 (13.5, ne)

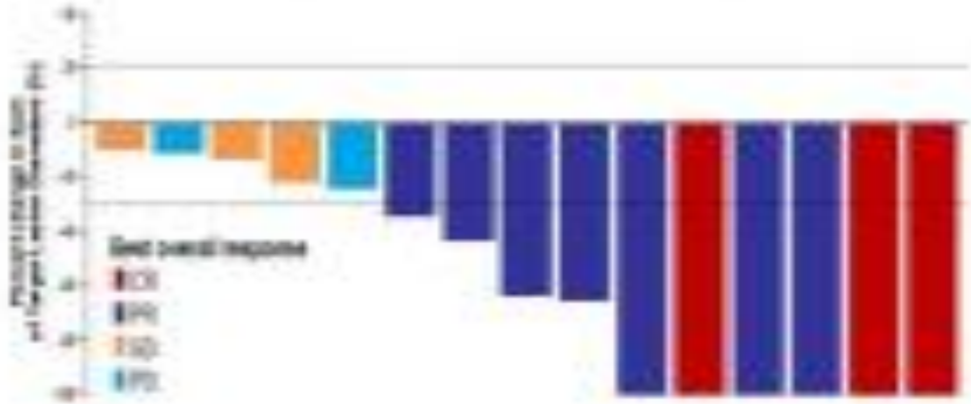


1L, first line; 2L+, second-or later-line; CI, confidence interval; DOR, duration of response; ctDNA, circulating tumor DNA; mBICR, modified Blinded Independent Central Review; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T+, ctDNA detected in tissue biopsy.

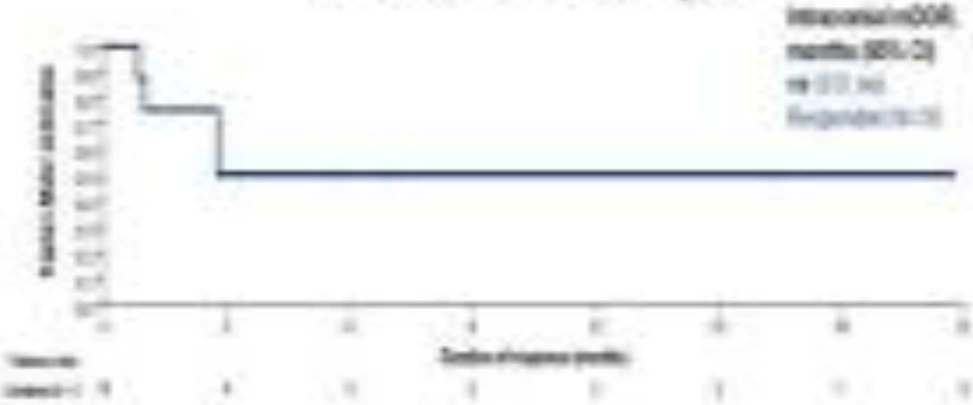
Tepotinib showed promising intracranial activity in patients with brain metastases (RANO-BM analysis)

- Tepotinib crosses the blood brain barrier to a significant extent, leading to concentrations of unbound tepotinib in the brain of 25% compared to plasma (Kp_{uu}=0.25), within a similar range to other CNS–penetrant TKIs[1]
- Across Cohorts A+C, 43 patients with brain metastases were evaluable by RANO-BM (1L, n=23; 2L+, n=20)
- 30 patients (69.8%) received prior brain radiotherapy or surgery
- <u>In patients with target or non-target lesions (n=43)</u>, **intracranial disease control rate was 88.4%** (95% CI: 74.9, 96.1) with **intracranial mPFS of 20.9 months** (95% CI: 5.7, ne)
- <u>In patients with target lesions (n=15)</u>, **intracranial ORR was 66.7%** (95% CI: 38.4, 88.2) with **intracranial mDOR ne** (95% CI: 0.9, ne)

Intracranial response in patients with target lesions (n=15)



Intracranial duration of response



Organizado por:

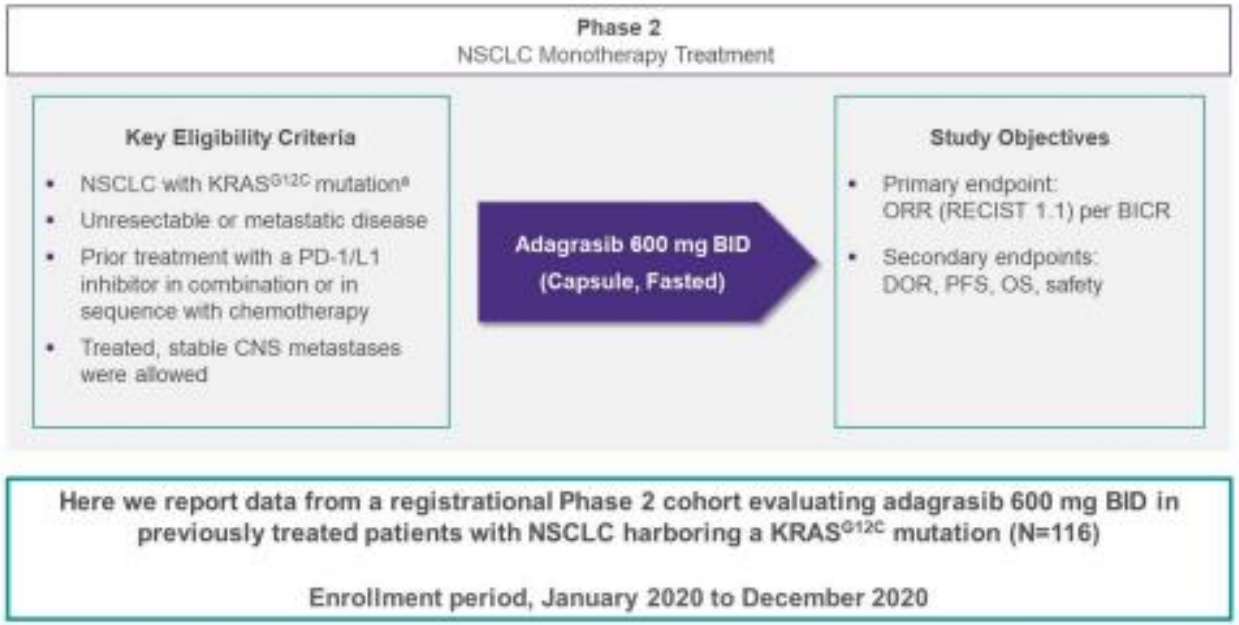
GECP lung cancer research

KRAS G12C

KRYSTAL-1: activity and safety of adagrasib in pts with a/mNSCLC harboring a *KRAS*^{G12C} mutation

#9002

Alexander Spira, et al



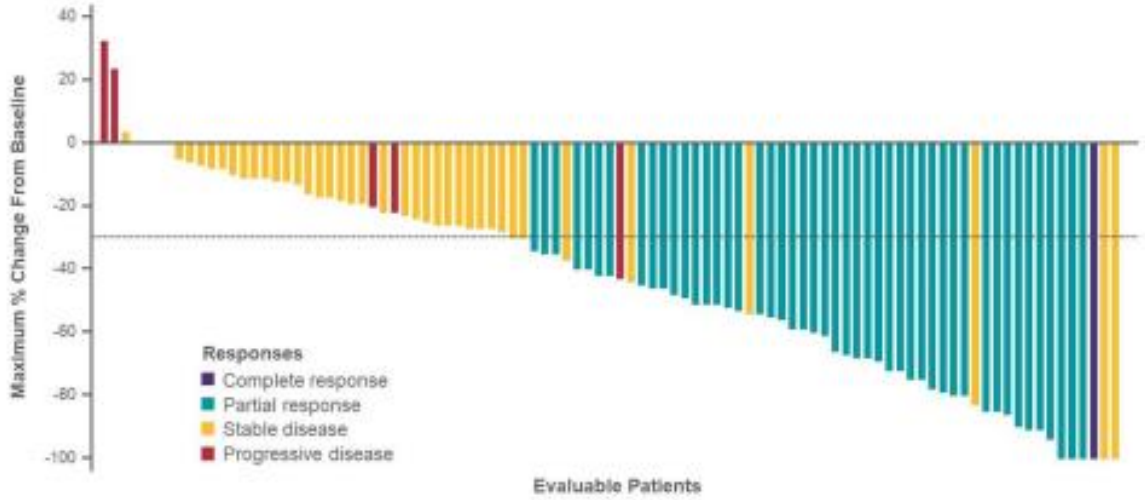
Here we report data from a registrational Phase 2 cohort evaluating adagrasib 600 mg BID in previously treated patients with NSCLC harboring a KRAS^{G12C} mutation (N=116)

Enrollment period, January 2020 to December 2020

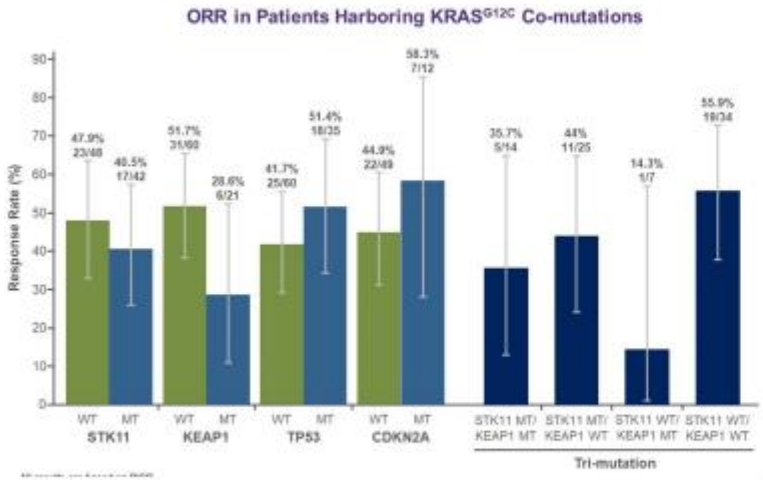
	Adagrasib Monotherapy (N=116)[a]
Median age (range), years	64 (25–89)
Female sex, n (%)	65 (56%)
Race, n (%)	
White	97 (84%)
Black or African American	9 (8%)
Asian / Other	5 (4%) / 5 (4%)
ECOG PS, n (%)[b]	
0 / 1	18 (16%) / 97 (84%)
Smoking history, n (%)	
Never smoker	5 (4%)
Current smoker / former smoker	11 (10%) / 100 (86%)
Prior lines of systemic therapy, n (%)	
1	50 (43%)
2	40 (35%)
3+	26 (22%)
Prior platinum-based therapy and/or checkpoint inhibitor therapy, n (%)[c]	
Received prior platinum-based therapy only	2 (2%)
Received both	114 (98%)
Baseline metastases, n (%)	
Bone	46 (40%)
CNS	24 (21%)
Adrenal	22 (19%)
Liver	19 (16%)

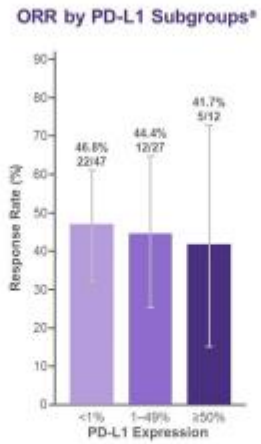
GECP lung cancer research

Efficacy Outcome	Adagrasib Monotherapy (n=112)[a]
Objective response rate, n (%)	48 (43%)
Best overall response, n (%)	
Complete response	1 (1%)
Partial response	47 (42%)
Stable disease	41 (37%)
Progressive disease	6 (5%)
Not evaluable	17 (15%)
Disease control rate, n (%)	89 (80%)



- Objective responses were observed in 43% (95% CI, 33.5–52.6); DCR was 80% (95% CI, 70.8–86.5)
- Responses were deep with 75% of responders achieving >50% tumor reduction



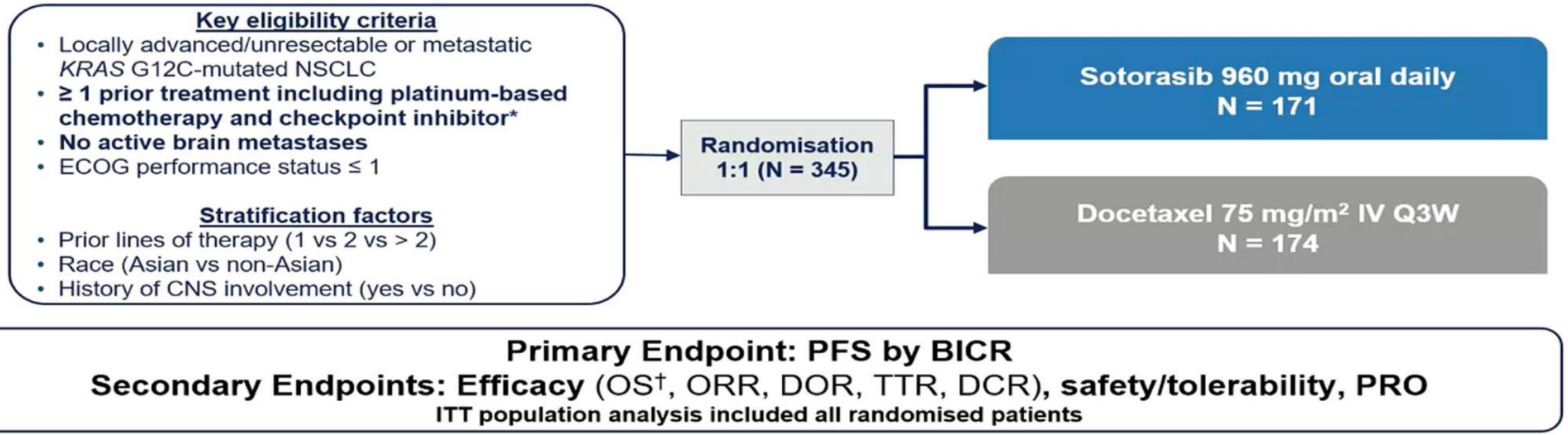


Treatment-Related Adverse Events

	Adagrasib Monotherapy (N=116) Capsule, Fasted	
TRAEs, n (%)	**Any Grade**	**Grades 3–4**
Any TRAEs	113 (97%)	50 (43%)
Most frequent TRAEs[a], n (%)		
Diarrhea	73 (63%)	1 (<1%)
Nausea	72 (62%)	5 (4%)
Vomiting	55 (47%)	1 (<1%)
Fatigue	47 (41%)	5 (4%)
ALT increase	32 (28%)	5 (4%)
Blood creatinine increase	30 (26%)	1 (<1%)
AST increase	29 (25%)	4 (3%)
Decreased appetite	28 (24%)	4 (3%)

- Grade 1–2 TRAEs occurred in 53% of patients
- There were 2 grade 5 TRAEs (cardiac failure [n=1] and pulmonary hemorrhage [n=1])
- TRAEs led to dose reduction in 60/116 (52%) patients[b] and to dose interruption in 71/116 (61%) patients
- TRAEs led to discontinuation of study drug in 8/116 (7%) patients

SOTORASIB: CODE BREAK 200



Primary Endpoint: PFS by BICR

Secondary Endpoints: Efficacy (OS†, ORR, DOR, TTR, DCR), **safety/tolerability, PRO**

ITT population analysis included all randomised patients

Per regulatory guidance, protocol was amended to reduce planned enrolment from 650 to ~330 patients, and crossover from docetaxel to sotorasib was permitted.

Enrollment period: June 4, 2020 to April 26, 2021; protocol amendment: February 15, 2021; data cutoff: August 2, 2022.

NCT04303780; EudraCT: 2019-003582-18.
*Treatment with chemotherapy and checkpoint inhibitor could be concurrent or sequential; patients with medical contraindication to these therapies could be included with approval.
†Analysis of OS planned if PFS was found to be statistically significant and when at least 198 OS events have been reached.

Johnson et al, ESMO 2022

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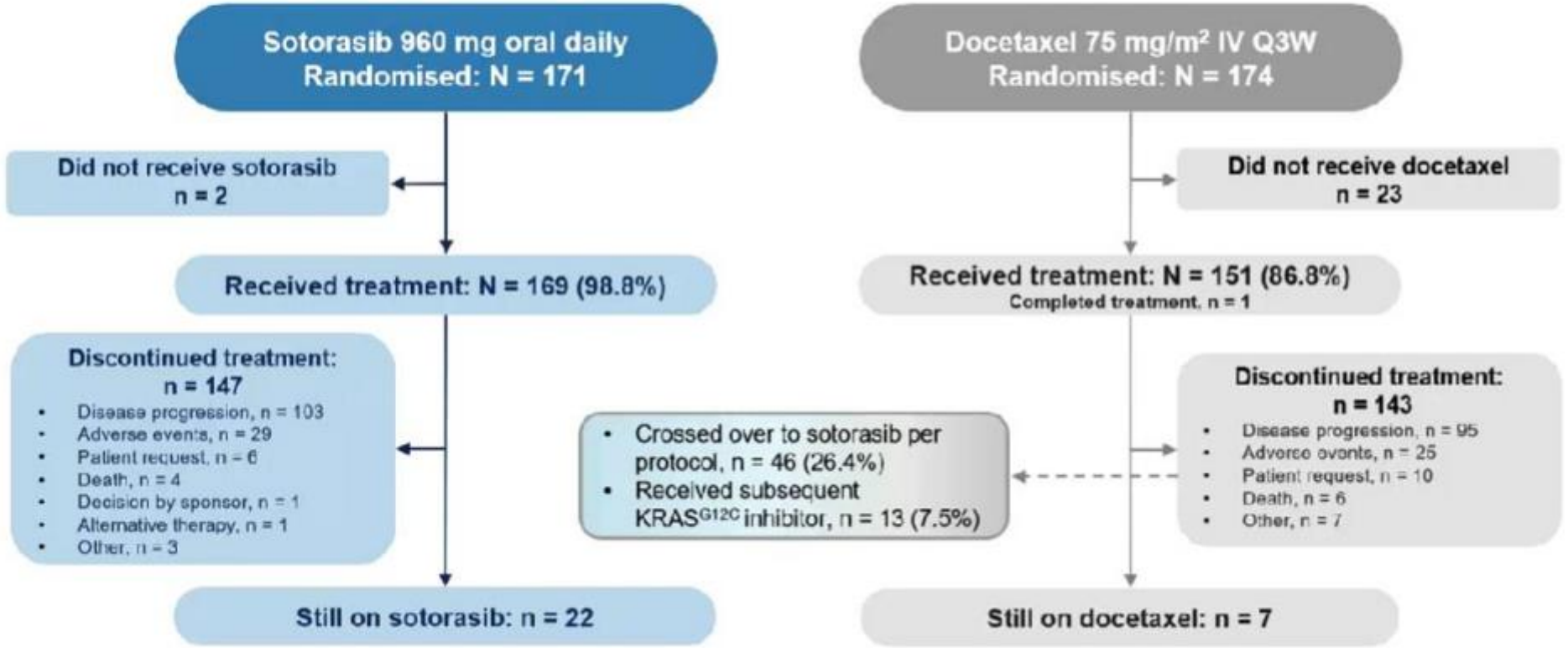
Patient Disposition



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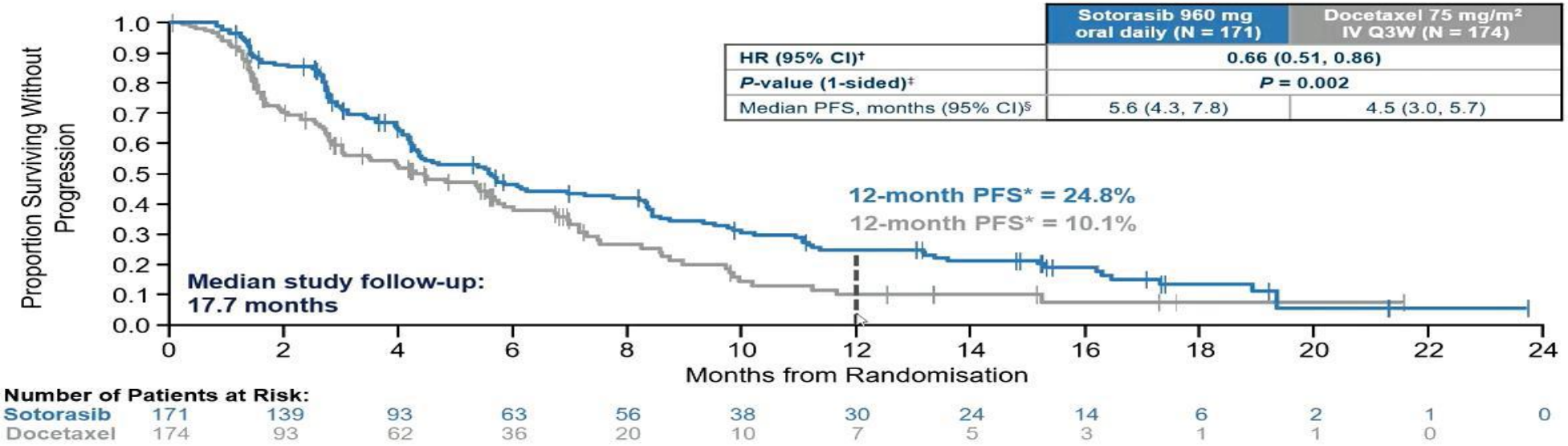
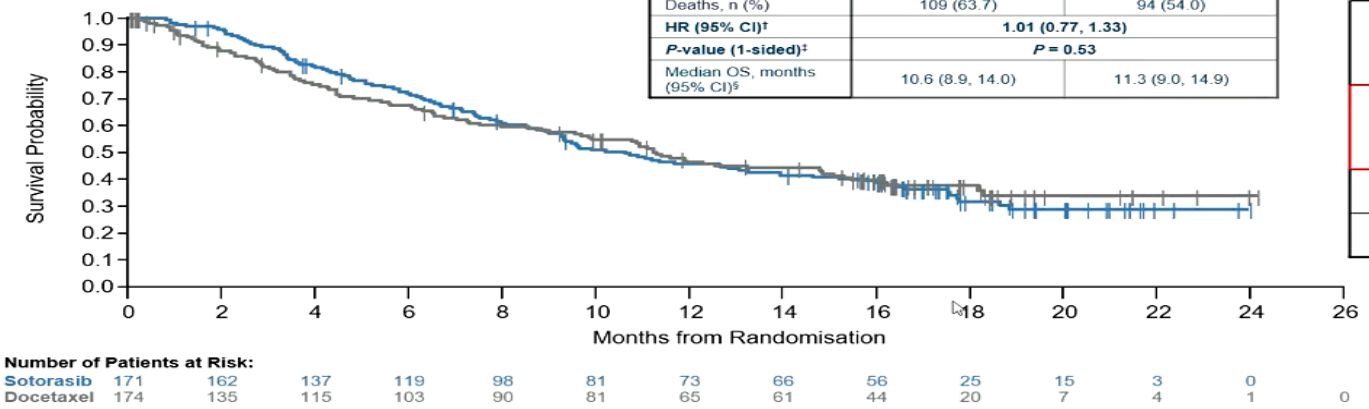


	Sotorasib 960 mg oral daily (N = 171)	Docetaxel 75 mg/m² IV Q3W (N = 174)
HR (95% CI)†	0.66 (0.51, 0.86)	
P-value (1-sided)‡	*P* = 0.002	
Median PFS, months (95% CI)§	5.6 (4.3, 7.8)	4.5 (3.0, 5.7)

CodeBreaK 200 met its primary endpoint with sotorasib demonstrating superior PFS over docetaxel (HR 0.66, *P* = 0.002); 12-month PFS rate was 24.8% for sotorasib and 10.1% for docetaxel



	Sotorasib 960 mg oral daily (N = 171)	Docetaxel 75 mg/m² IV Q3W (N = 174)
Deaths, n (%)	109 (63.7)	94 (54.0)
HR (95% CI)†	1.01 (0.77, 1.33)	
P-value (1-sided)‡	*P* = 0.53	
Median OS, months (95% CI)§	10.6 (8.9, 14.0)	11.3 (9.0, 14.9)

	Sotorasib	Docetaxel
Any subsequent treatment, including crossover**	36%	42%
Subsequent $KRAS^{G12C}$ inhibitor, including crossover	4%	34%
Subsequent chemo	21%	12%
Subsequent IO	9%	6%

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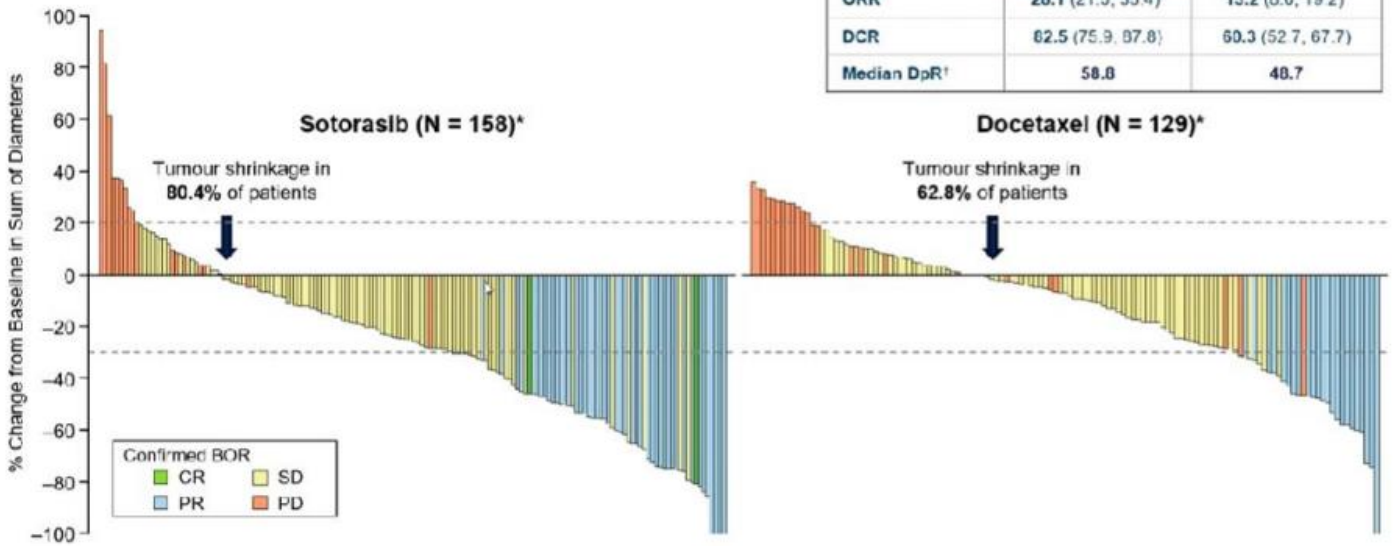
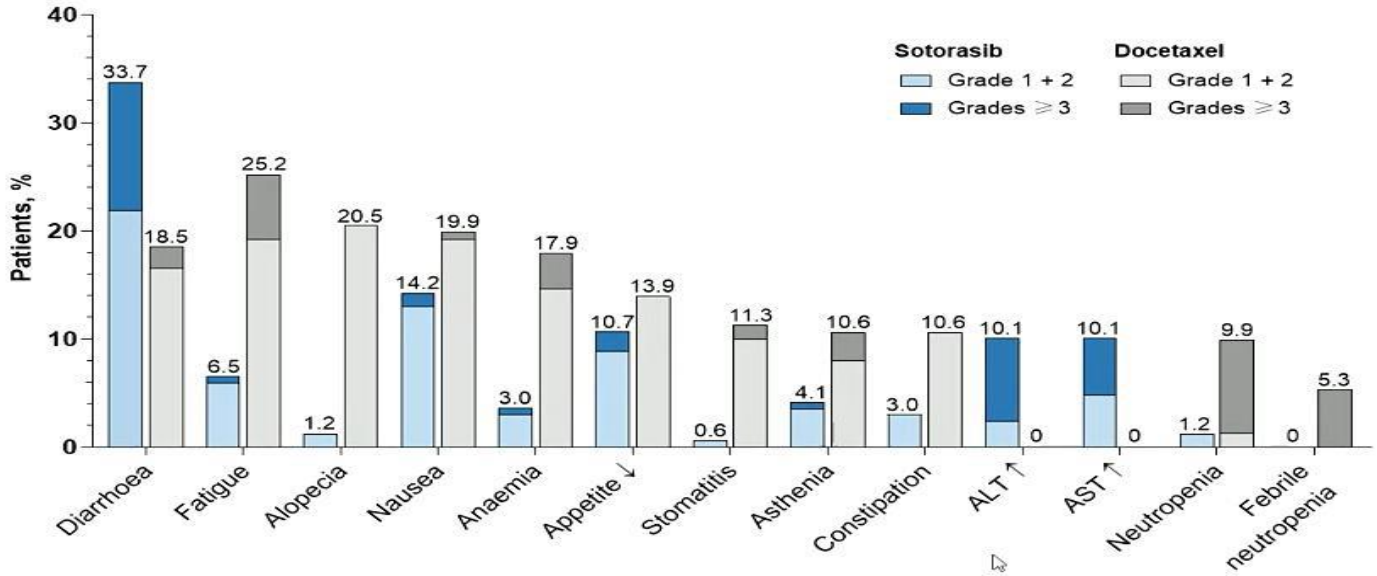
Tumour Response by BICR

% (95% CI)	Sotorasib	Docetaxel
ORR	28.1 (21.5, 35.4)	13.2 (8.6, 19.2)
DCR	82.5 (75.9, 87.8)	60.3 (52.7, 67.7)
Median DpR†	58.8	48.7





Most common Grade 3+ TRAEs with sotorasib were diarrhoea and elevated liver enzymes, and with docetaxel were neutropenia, fatigue, and febrile neutropenia

ROS-1

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Entrectinib in Patients with *ROS1* Fusion-Positive NSCLC: Updated Efficacy and Safety Analysis

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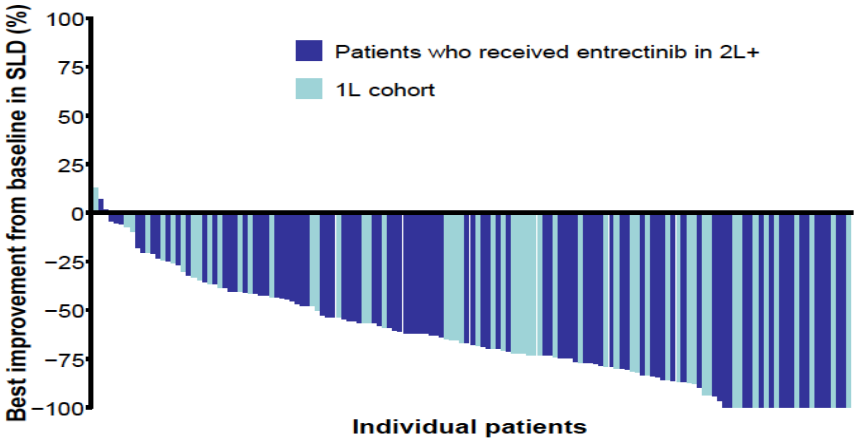
**Currently at Taipei Cancer Center and Taipei Medical University Hospital, Taipei, Taiwan*

Patient demographics and baseline characteristics

	Overall efficacy population N=172	First-line population* n=67
Median age, years (range)	54.5 (20–86)	55.0 (33–86)
Female, n (%)	113 (65.7)	41 (61.2)
ECOG PS, n (%) 0 / 1 / 2	66 (38.4) / 90 (52.3) / 16 (9.3)	25 (37.3) / 37 (55.2) / 5 (7.5)
Smoking status, n (%) Never smoker / Previous or current smoker	111 (64.5) / 61 (35.5)	42 (62.7) / 25 (37.3)
Prior lines of systemic therapy in metastatic setting, n (%) 0 / 1 / ≥2	67 (39.0) / 65 (37.8) / 40 (23.3)	NA
CNS metastases at baseline by investigator, n (%) Yes / No	60 (34.9) / 112 (65.1)	26 (38.8) / 41 (61.2)

Data cut-off: 02 Aug 2021. *Patients who had not received any prior lines of systemic therapy in the metastatic setting
CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology group performance status; NA, not applicable

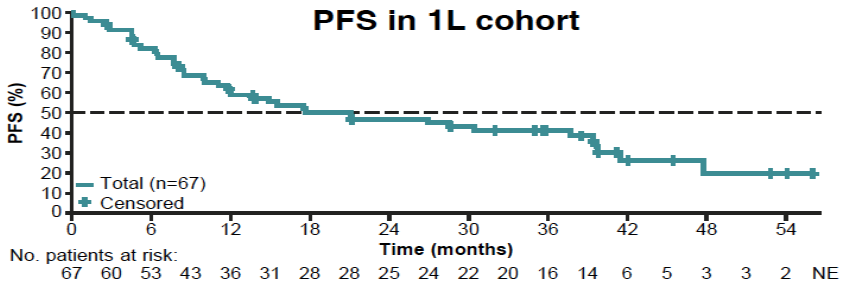
Entrectinib demonstrated robust and durable responses regardless of baseline CNS status

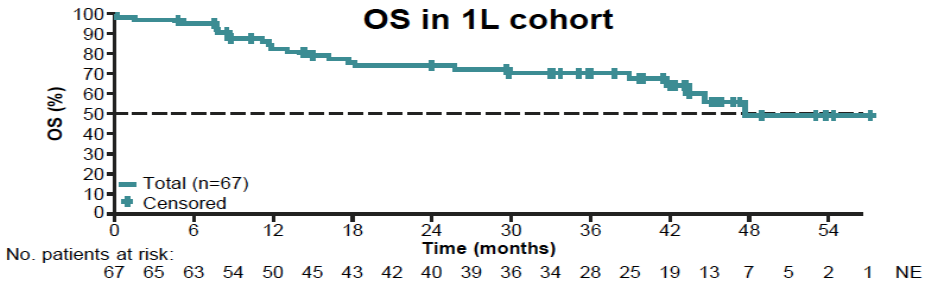


	Overall efficacy population (N=172)	Baseline CNS metastases* (n=60)	No baseline CNS metastases* (n=112)	First-line population† (n=67)
ORR, n (%) [95% CI]	**116 (67.4)** [59.9–74.4]	**38 (63.3)** [49.9–75.4]	**78 (69.6)** [60.2–78.0]	**46 (68.7)** [56.2–79.4]
CR	23 (13.4)	4 (6.7)	19 (17.0)	10 (14.9)
PR	93 (54.1)	34 (56.7)	59 (52.7)	36 (53.7)
SD	16 (9.3)	6 (10.0)	10 (8.9)	7 (10.4)
PD	16 (9.3)	8 (13.3)	8 (7.1)	5 (7.5)
Non CR / PD	10 (5.8)	2 (3.3)	8 (7.1)	6 (9.0)
Missing / unevaluable	14 (8.1)	6 (10.0)	8 (7.1)	3 (4.5)
Median DoR, months [95% CI]	**20.4** [14.8–34.8]	**14.6** [11.0–20.4]	**28.6** [14.9–38.6]	**35.6** [13.9–38.8]

Data cut-off: 02 Aug 2021. *Investigator-assessed CNS metastases; †Exploratory analysis. 1L, first line; 2L, second line; CI, confidence interval; CR, complete response; DoR, duration of response; ORR, objective response rate, PD, progressive disease; PR, partial response; SD, stable disease; SLD, sum of longest diameters

	Overall efficacy population (N=172)	Baseline CNS metastases* (n=60)	No baseline CNS metastases* (n=112)	First-line population† (n=67)
Median PFS, months [95% CI]	**16.8** [12.2–22.4]	**11.8** [7.2–15.7]	**25.2** [15.7–36.6]	**17.7** [11.8–39.4]
Median OS, months [95% CI]	**44.1** [40.1–NE]	**28.3** [17.0–44.6]	**NE** [41.8–NE]	**47.7** [43.2–NE]





Data cut-off: 02 Aug 2021. *Investigator-assessed CNS metastases; †Exploratory analysis.
OS, overall survival; PFS, progression-free survival

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CONCLUSIONES

- Futuro de la inmunoterapia combinación de anti PD-PDL1 con nuevos fármacos inmunocheckpoints.

- Prometedores estudios con combinaciones inhibidores tirosin-quinasa con inmunoterapia.

- Múltiples avances en terapias dirigidas con nuevos fármacos en
  - Progresión a fármacos en dianas conocidas (EGFR)
  - Nuevas dianas terapéuticas (MET, KRAS).


GRACIAS