2022 ASCO ANNUAL MEETING

Lung Cancer

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Disclosure of Conflicts of Interest

Maggie Byrne, MD, MS has no relevant financial relationships to disclose.

Outline

Metastatic NSCLC without targetable genomic alterations

1st line

Abstract 9000, Pooled analysis of 12 randomized studies comparing IO vs Chemo-IO in PD L1 TPS ≥ 50%

Abstract 9003, A phase II study (TACTI-002), investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab

2nd line

Abstract 9004, LUNG MAP 1800 A Randomized phase II study of Ramucirumab and Pembrolizumab vs SoC therapy

Abstract 9005, COSMIC study: Non-randomized study, Cabozantinib and Cabozantinib with Atezolizumab

Metastatic NSCLC with genomic alterations

KRAS

Abstract 9002: KRYSTAL-1: Activity and safety of Adagrasib (MRTX849) in KRAS G12C

EGFR Exon 19 del & L858R

Abstract 9006, Amivantamab and Lazertinib

Abstract 9013, Osimertinib + Teliso-V

EGFR Exon 20 insertion

Abstract 9007, CLN-081

MET Ex14 Skip alteration

Abstract 9008, Amivantamab

Small cell lung cancer

1st line

Abstract LBA8507, SKYSCRAPER-02, A phase III study Atezo + Carbo + VP-16 +/- Tiragolumab (Anti TIGIT)

≥ 2nd line

Abstract 8516, 8517, 8518

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Abstract 9000

FDA

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

PRESENTED BY:
Oladimeji Akinboro, MD, MPH

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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

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Study Design

Pooled Analysis Population

- Advanced NSCLC
- PD-L1 TPS ≥50%
  - Excluded staining by tumor-infiltrating immune cells
- No sensitizing *EGFR* mutations or *ALK* alterations
- Clinical trial supported FDA approval of IO-based regimen

Chemo-IO

IO-only

Exploratory Primary Outcome measure

- OS

Other exploratory outcome measures

- PFS
- ORR

Sub-group analyses

- Age (yrs): *<65 vs 65-75 vs ≥75*
- ECOG PS: *0 vs. ≥ 1*
- Smoking history: *Never vs. Ever*

Abbreviations: *ALK*=anaplastic lymphoma kinase gene; Chemo-IO= platinum-based doublet chemotherapy plus immunotherapy; ECOG PS=Eastern Cooperative Oncology Group Performance Status; *EGFR*=epidermal growth factor receptor gene; FDA=U.S. Food and Drug Administration; IO=immunotherapy; NSCLC=non-small-cell lung cancer; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival; TPS=tumor proportion score; yrs=years.

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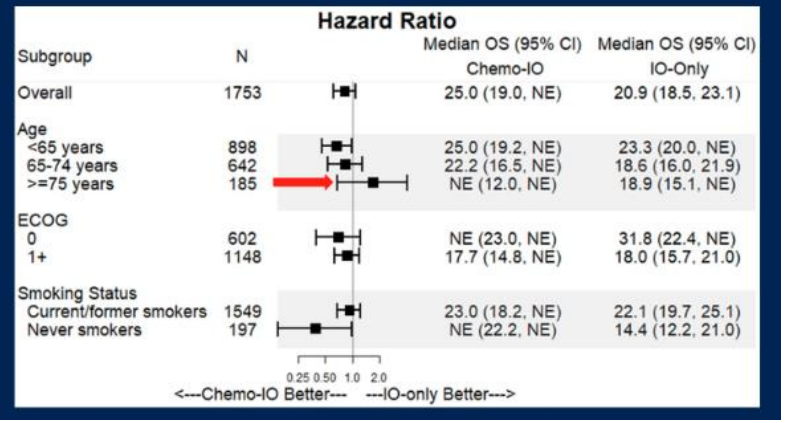
Exploratory OS, PFS, and ORR: NSCLC PD-L1 ≥50%

	Chemo-IO (*N*=455)	IO-alone (*N*=1,298)
OS		
Median, months (95% CI)	25.0 (19.0, NE)	20.9 (18.5, 23.1)
HR (95% CI)	0.82 (0.62, 1.08)	
PFS		
Median, months (95% CI)	9.6 (8.4, 11.1)	7.1 (6.3, 8.3)
HR (95% CI)	0.69 (0.55, 0.87)	
ORR		
% (95% CI)	61 (56, 66)	43 (41, 46)
Odds ratio	1.2 (1.1, 1.3)	

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; CI=confidence interval; HR-hazards ratio; IO=immunotherapy; *N*=number; NSCLC=non-small-cell lung cancer; NE=not estimable; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival.

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



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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]

Affiliates: [1]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [2]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [3]Fundación Jiménez Diaz, Madrid, Spain; [4]St John of God Subiaco Hospital, Perth, Australia; [5]Catalan Institute of Oncology Badalona-Hospital Germans Trias i Pujol, B-ARGO group, Badalona, Spain; [6]City Clinical Hospital № 4" of Dnipro Regional Council, Dnipro, Ukraine; [7]Oncology Consultants, P.A., Houston, USA; [8]Hospital Regional Universitario de Málaga - Hospital General, Malaga, Spain; [9]UCL Cancer Institute/ University College London Hospitals NHS Foundation, London, UK; [10]St. Luke's Hospital- Medical and Diagnostic Center "Acinus", Kropyvnytskyi, Ukraine; [11]Instytut Centrum Zdrowia Matki Polki, Lodz, Poland; [12]HM Universitario Sanchinarro, Madrid, Spain; [13]Parc Tauli Sabadell Hospital Universitari, Barcelona, Spain; [14]Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [15]Vanderbilt Ingram Cancer Center Division of Hematology/Oncology, Tennessee, United States; [16]Hospital Lucus Augusti, Lugo, Spain; [17]Clinical Development, Immutep GmbH, Berlin, Germany; [18]Research & Development, Immutep S.A.S., Orsay, France.

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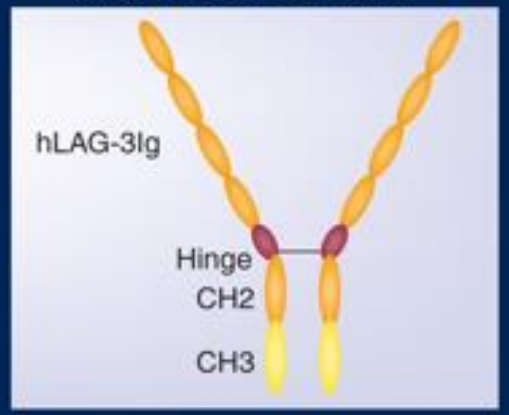
Eftilagimod alpha (efti) – soluble LAG-3

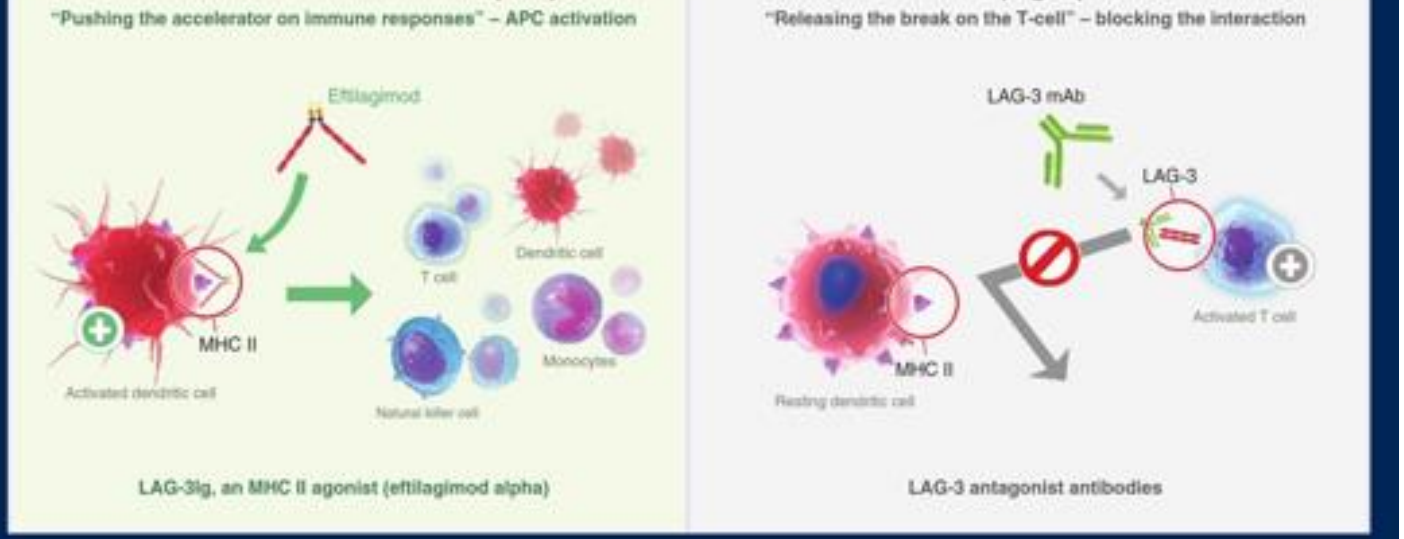
STRUCTURE OF EFTI[4]



- **MoA: efti** (figure, left) is a **soluble LAG-3 protein** (LAG-3 domains fused to human IgG backbone) **targeting** a subset of **MHC class II molecules** to mediate antigen presenting cells (APCs) and CD8 T-cell activation (figure below left).
- **Difference to Anti-LAG-3:** Efti does not bind to the LAG-3 on the T cell (figure, below right).
- **Rationale:** efti activates APCs, leading to an increase in activated T cells, potentially reducing the number of non-responders to PD-1/PD-L1 antagonists.

- In preclinical models, the antitumor activity of PD-1 antagonists was synergistically enhanced when combined with efti[1].
- Recommended phase II dose of 30 mg efti s.c. every two weeks was determined in phase I studies[2,3].

MoA of efti (left) and difference to anti-LAG-3 (right)[4]



MoA: mechanism of action
PD-1/PD-L1: programmed death-(ligand) 1
s.c.: subcutaneous

[1] Internal data, Immutep, not yet published.
[2] Brignone C, Clin Cancer Res. 2009;15: 6225- 6231.
[3] Atkinson V, J Immunoth Cancer. 2020; 8(2):e001681.
[4] Dirix L, Triebel F. Future Oncol. 2019;15(17):1963-1973.

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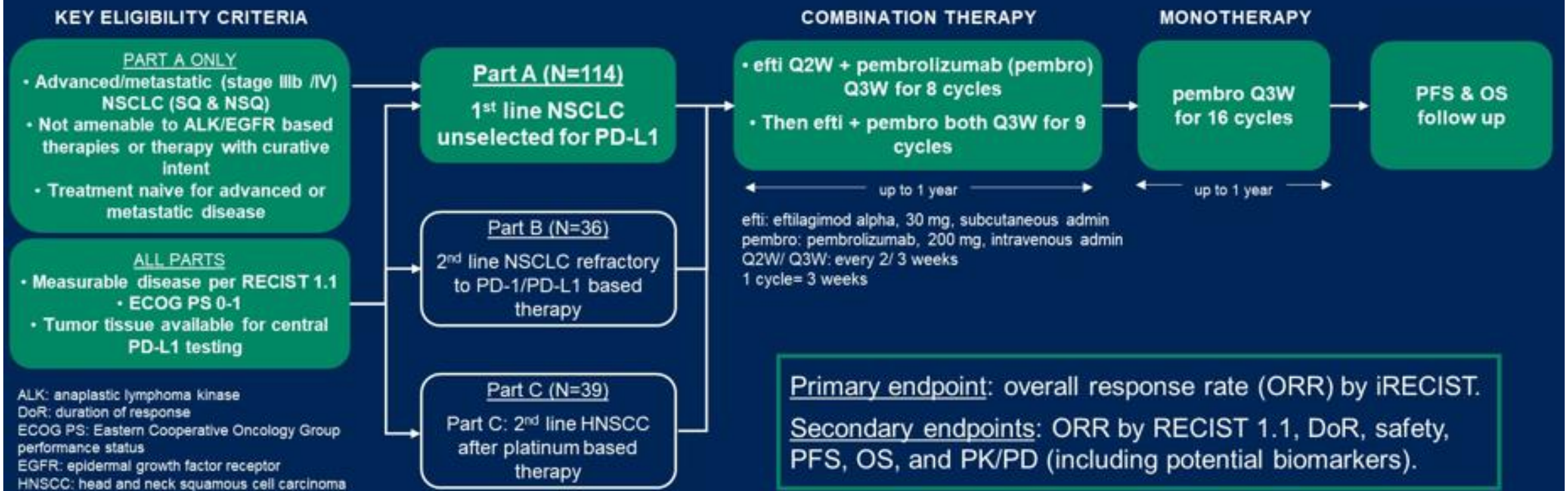
Trial Design – TACTI-002

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).

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Efficacy – ORR[1] by PD-L1 status & tumor type – TACTI-002

Tumor Response by central PD-L1 status (iRECIST, unconfirmed)[2], N=87

Tumor Response, N=87	PD-L1 <1%, n (%), N=32	PD-L1 1-49%, n (%), N=36	PD-L1 ≥50%, n (%), N=19	PD-L1 ≥1% n (%), N=55	PD-L1 <50% n (%), N=68
ORR	9 (28.1)	15 (41.7)	10 (52.6)	25 (45.5)	24 (35.3)
[95% CI][4]	[13.8-46.8]	[25.5-59.2]	[28.9-75.6]	[32.0-59.5]	[24.1-47.8]
DCR	22 (68.8)	28 (77.8)	15 (79.0)	43 (78.2)	50 (73.5)
[95% CI][4]	[50.0-83.9]	[60.9-89.9]	[54.4-94.0]	[65.0-88.2]	[61.4-83.5]

Tumor Response by central & local PD-L1 status (iRECIST, unconfirmed)[3], N=108

Tumor response, N=108	PD-L1 <1%, n (%), N=37	PD-L1 1-49%, n (%), N=40	PD-L1 ≥50%, n (%), N=31	PD-L1 ≥1% n (%), N=71	PD-L1 <50% n (%), N=77
ORR	9 (24.3)	16 (40.0)	16 (51.6)	32 (45.1)	25 (32.5)
[95% CI][4]	[11.8-41.2]	[24.9-56.7]	[33.1-69.9]	[33.2-57.3]	[22.2-44.1]
DCR	26 (70.3)	30 (75.0)	24 (77.4)	54 (76.1)	56 (72.7)
[95% CI][4]	[53.2-84.1]	[58.8-87.3]	[58.9-90.4]	[64.5-85.4]	[61.4-82.3]

- ORR (iRECIST) by PD-L1 (central only):
  - 28.1% in PD-L1 negative
  - 41.7% in PD-L1 1-49%
  - 52.6% in PD-L1 ≥50%
  - 45.5% in PD-L1 ≥1%
- DCR (iRECIST) with a range of 68.8-78.9% across all PD-L1 subgroups.
- ORR (iRECIST) of 35.0% [95% CI: 20.1-51.7] in squamous and 38.9% in non-squamous [95% CI: 27.6-51.1] tumors.

[1] iRECIST, unconfirmed
[2] Central assessment of PD-L1 TPS using Dako PD-L1 IHC 22C3 pharmDx for 87 patients.
[3] Central assessment as per footnote 1 for 87 patients. For 21 patients, local assessment was used due to non evaluable central assessment results.
[4] 95% CIs calculated using Clopper-Pearson method.

Data cut-off date: April 15, 2022

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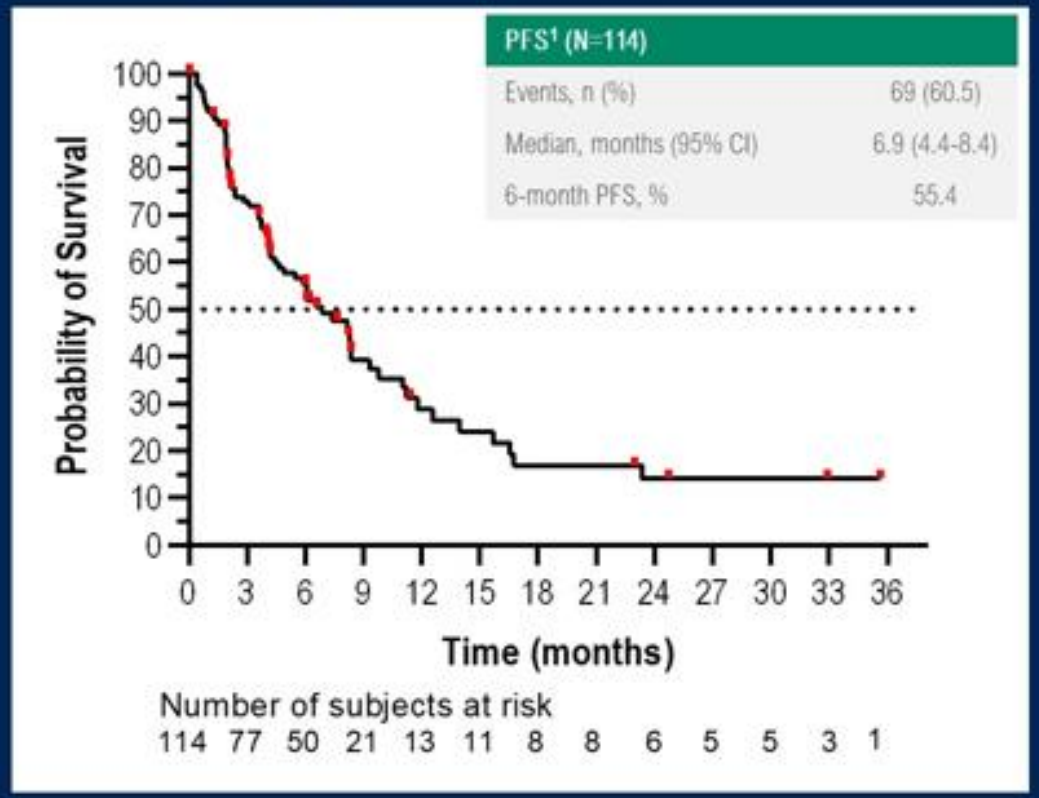
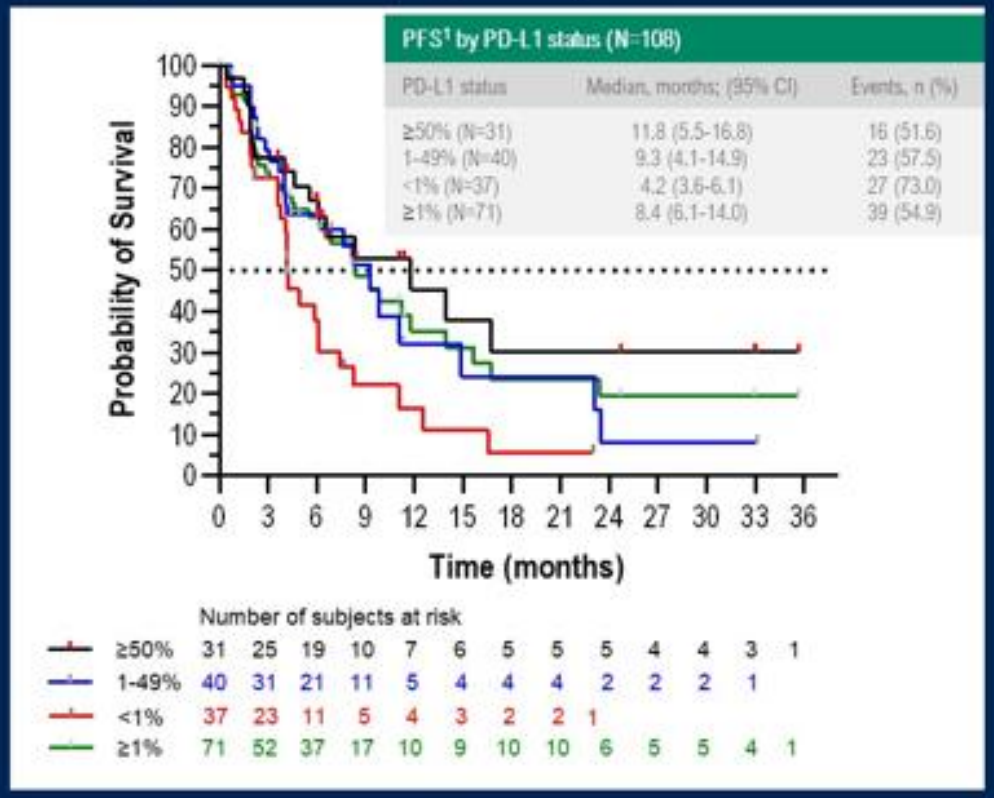
Efficacy – Interim Progression Free Survival[1] (PFS) – TACTI-002

PFS[1] ITT (N=114)



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

PFS[1] by PD-L1 status[2] (N=108)



- 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%.

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

Data cut-off date: April 15, 2022

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Overall survival from a phase II randomized study of ramucirumab plus pembrolizumab versus standard of care for advanced non-small cell lung cancer previously treated with immunotherapy—Lung-MAP non-matched sub-study S1800A

Karen L. Reckamp, M.D.[1], Mary W. Redman, PhD[2], Konstantin H. Dragnev, M.D.[3], Liza Villaruz, M.D.[4], Bryan Faller, MD[5]; Tareq Al Baghdadi, MD[6], Susan Hines, MD[7], Lu Qian, M.S.[2], Katherine Minichiello, M.S.[2], David R. Gandara, M.D.[8], Karen Kelly, MD[8], Roy S. Herbst, M.D., Ph.D.[9]

[1]Cedars-Sinai Medical Center, Los Angeles, CA; [2]SWOG Statistics and Data Management Center & Fred Hutchinson Cancer Research Center, Seattle, WA; [3]Dartmouth-Hitchcock Norris Cotton Cancer Center, Lebanon, NH/Alliance for Clinical Trials in Cancer; [4]University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center; [5]Missouri Baptist Medical Center, St. Louis, MO/Heartland NCORP; [6]IHA Hematology Oncology Consultants-Ann Arbor/Michigan CRC NCORP; [7]Novant Health Cancer Institute - Mount Airy/Southeast Clinical Oncology Research Consortium NCORP); [8]UC Davis Comprehensive Cancer Center, Sacramento, CA; [9]Yale University, New Haven, CT

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S1800A Schema—Randomized Phase II trial

NCT03971474

Stratified by 1) PD-L1 expression, 2) histology, 3) intent to receive ramucirumab in standard of care arm

Primary endpoint: OS

Secondary endpoints: RR, DCR, DoR, PFS, Toxicities

ARM A
Investigator's Choice Standard of Care
docetaxel + ramucirumab;
docetaxel; gemcitabine;
pemetrexed (nonSCC only)

Randomization

R (1:1)
N= 130

ARM B
Pembrolizumab
200 mg Q3W for up to 35 cycles
+
Ramucirumab
10 mg/kg Q3W

Key eligibility: 1) Previously received both PD-1 or PD-L1 inhibitor therapy and platinum-based doublet chemotherapy either sequentially or combined, with PD on at least 84 days after initiation of ICI and platinum-based doublet therapy; 2) ECOG 0-1; 3) all patients met eligibility to receive ramucirumab

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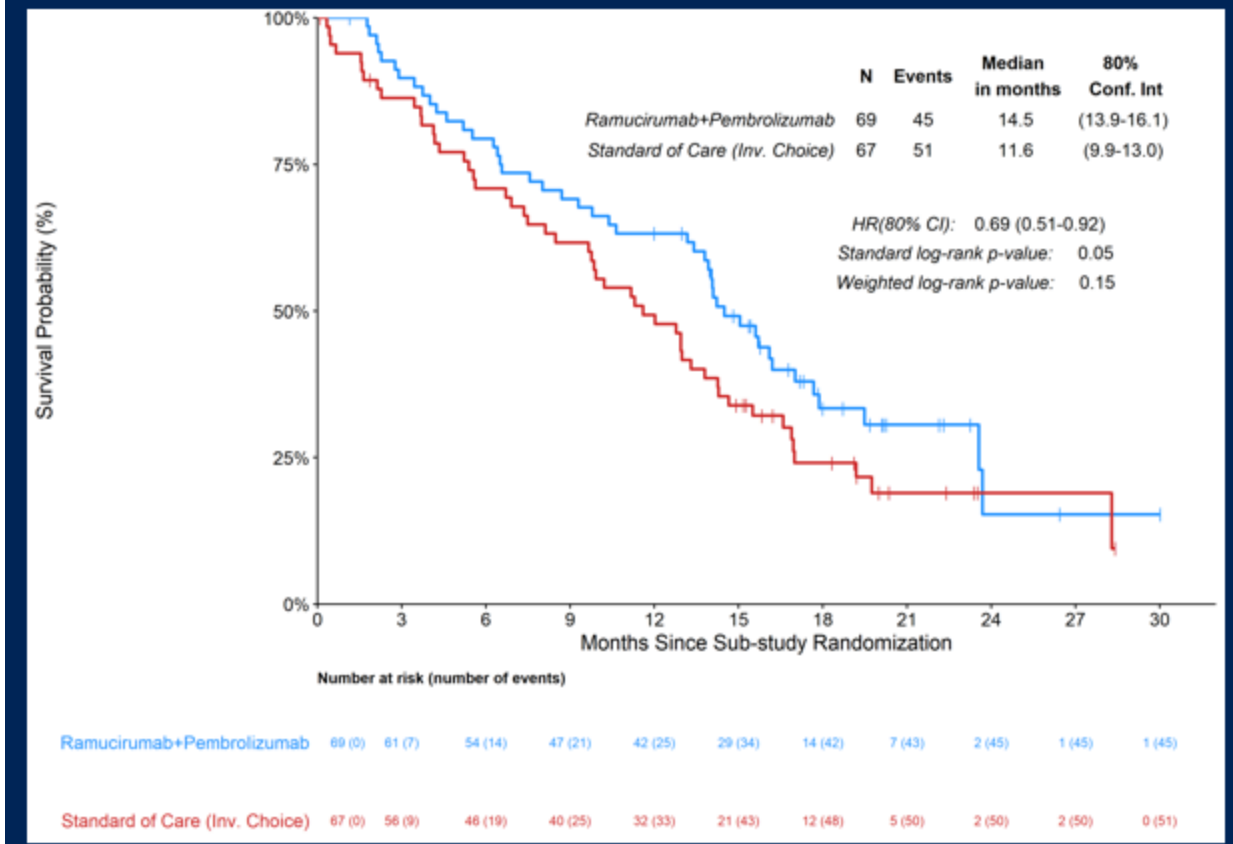
Overall survival



- Median OS for RP 14.5 months v. SOC 11.6 months
- HR= 0.69; SLR p-value 0.05

Standard of care therapy received:
- Docetaxel + Ramucirumab (n = 45)
- Docetaxel (n = 3)
- Gemcitabine (n = 12)
- Pemetrexed (n = 1)
- No treatment (n = 6)

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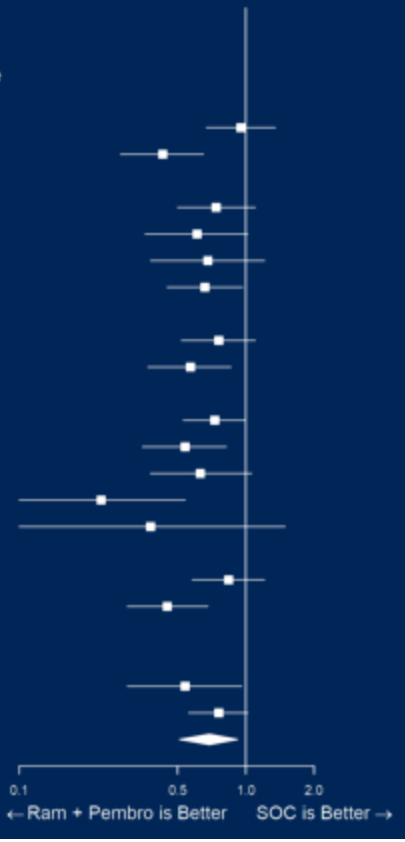
Overall survival—subgroup analysis

	Ram+ Pembro Events/N	SOC Events/N	HR (80% CI)	P-value
HISTOLOGY				
Non-Squamous	27/40	27/39	0.95 (0.67,1.35)	0.43
Squamous/Mixed	18/29	24/28	0.43 (0.28,0.65)	0.005
PD-L1				
PD-L1 0	21/29	21/26	0.74 (0.50,1.10)	0.16
PD-L1 1-49	11/21	15/22	0.61 (0.36,1.02)	0.11
PD-L1 50+	8/12	12/16	0.68 (0.38,1.21)	0.20
PD-L1 1+	19/33	27/38	0.66 (0.45,0.97)	0.08
TMB				
TMB <10	23/32	28/38	0.76 (0.52,1.10)	0.17
TMB 10+	18/33	20/25	0.57 (0.37,0.86)	0.04
BIOMARKER				
TP53	31/48	35/48	0.73 (0.53,1.00)	0.10
CDKN2A	18/27	21/24	0.54 (0.35,0.82)	0.03
KRAS	12/21	13/16	0.63 (0.38,1.06)	0.13
STK11	4/7	10/10	0.23 (0.10,0.54)	0.01
KEAP1	1/3	7/10	0.38 (0.10,1.49)	0.18
PRIOR TREATMENT				
IO+CHEMO COMBO	20/32	32/42	0.84 (0.58,1.21)	0.27
CHEMO->IO	25/36	18/23	0.45 (0.30,0.68)	0.006
PERFORMANCE STATUS				
PS 0	15/23	8/9	0.54 (0.30,0.96)	0.08
PS 1	30/46	43/58	0.76 (0.56,1.02)	0.12
OVERALL	**45/69**	**51/67**	**0.69 (0.51,0.92)**	**0.05**



- All subgroup HRs < 1
- HRs by PD-L1 does not appear to vary
- Pronounced benefit in SCC/mixed histology
- Benefit seen with PS 0 and 1
- Co-mutations did not affect OS improvement

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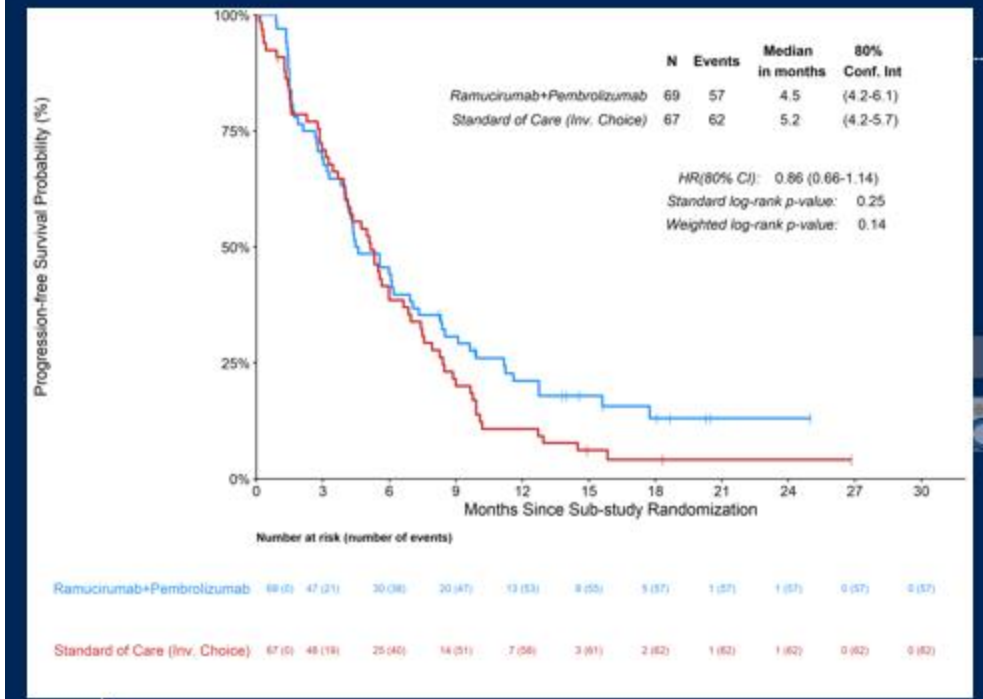
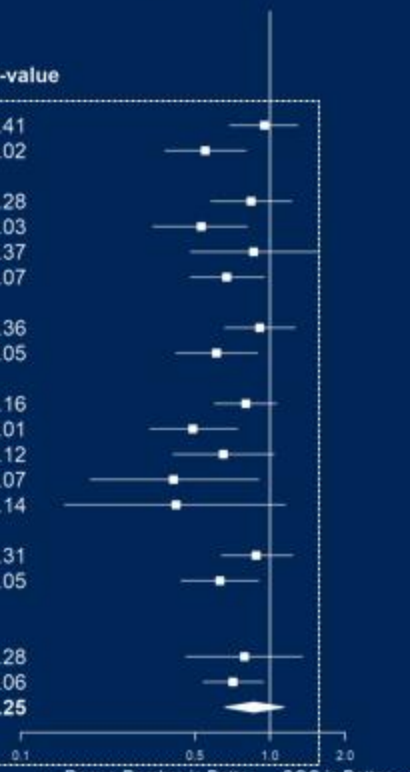
Progression free survival with subgroup analysis



	Ram+ Pembro Events/N	SOC Events/N	HR (80% CI)	P-value
HISTOLOGY				
Non-Squamous	34/40	34/39	0.95 (0.69,1.29)	0.41
Squamous/Mixed	23/29	28/28	0.55 (0.38,0.80)	0.02
PD-L1				
PD-L1 0	27/29	25/26	0.84 (0.58,1.22)	0.28
PD-L1 1-49	16/21	22/22	0.53 (0.34,0.81)	0.03
PD-L1 50+	8/12	12/16	0.86 (0.48,1.55)	0.37
PD-L1 1+	24/33	34/38	0.67 (0.48,0.95)	0.07
TMB				
TMB <10	29/32	36/38	0.91 (0.66,1.26)	0.36
TMB 10+	24/33	23/25	0.61 (0.42,0.89)	0.05
BIOMARKER				
TP53	39/48	43/48	0.80 (0.60,1.06)	0.16
CDKN2A	22/27	24/24	0.49 (0.33,0.74)	0.01
KRAS	16/21	15/16	0.65 (0.41,1.04)	0.12
STK11	5/7	10/10	0.41 (0.19,0.90)	0.07
KEAP1	2/3	10/10	0.42 (0.15,1.15)	0.14
PRIOR TREATMENT				
IO+CHEMO COMBO	26/32	40/42	0.88 (0.64,1.23)	0.31
CHEMO->IO	31/36	21/23	0.63 (0.44,0.90)	0.05
PERFORMANCE STATUS				
PS 0	21/23	8/9	0.79 (0.46,1.35)	0.28
PS 1	36/46	54/58	0.71 (0.54,0.94)	0.06
OVERALL	**57/69**	**62/67**	**0.86 (0.66,1.14)**	**0.25**



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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]

[1]Stanford Cancer Institute, Palo Alto, CA, USA; [2]Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy; [3]Instituto Oncológico Dr Rosell, CM Teknon, Barcelona, Spain; [4]Hospital Universitario 12 de Octubre, Universidad Complutense and Ciberonc, Madrid, Spain; [5]Regional Cancer Care Associates, East Brunswick, NJ, USA; [6]Barts Health NHS Trust, St Bartholomew's Hospital, London, UK; [7]University of Virginia School of Medicine, Charlottesville, VA, USA; [8]Blue Ridge Cancer Care, Blacksburg, VA, USA; [9]MD Anderson Cancer Center at Cooper, Camden, NJ, USA; [10]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [11]University of Utah, Salt Lake City, UT, USA; [12]Exelixis Inc., Alameda, CA, USA; [13]Vall d'Hebron University, Barcelona, Spain.

*Current affiliation: UOMI Cancer Center. Clínica Mi Tres Torres. Barcelona, Spain

Abstract 9005

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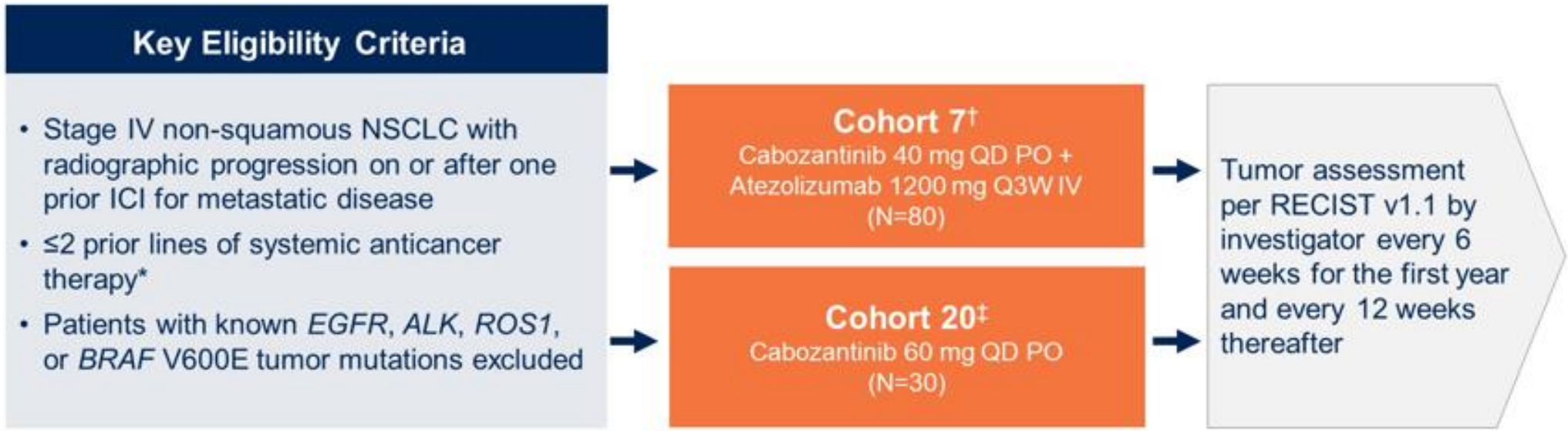
COSMIC-021 Study Design for NSCLC Cohorts



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

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Efficacy Summary

	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)**

*Eight patients in the cabozantinib alone cohort were crossed over to receive cabozantinib plus atezolizumab after experiencing disease progression; the efficacy data of these patients are not reported in this presentation except for OS. †The DOR of the 2 responders was 6.3 and 14.8 months.

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Safety Summary

	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)

*Includes the 8 patients who crossed over to receive cabozantinib + atezolizumab therapy after experiencing disease progression. In patients who were treated with cabozantinib only (n=23), the duration of exposure was 3.5 months (range, 0.7–16.4) and rates of AEs leading to cabozantinib dose reductions and holds, and discontinuation due to TRAEs were similar to all patients.

†The duration between the day of the first dose of any study treatment and the day of discontinuation of the last component of study treatment.

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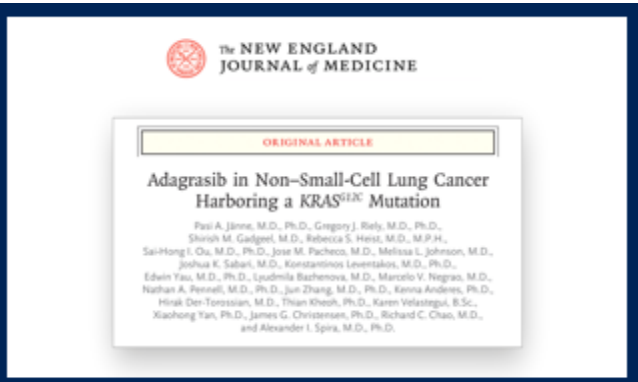
Abstract 9002



KRYSTAL-1: Activity and Safety of Adagrasib (MRTX849) in Patients with Advanced/Metastatic Non-Small Cell Lung Cancer Harboring a $KRAS^{G12C}$ Mutation

Alexander I. Spira[1], Gregory J. Riely[2], Shirish M. Gadgeel[3], Rebecca S. Heist[4], Sai-Hong Ignatius Ou[5], Jose M. Pacheco[6], Melissa L. Johnson[7], Joshua K. Sabari[8], Konstantinos Leventakos[9], Edwin Yau[10], Lyudmila Bazhenova[11], Marcelo V. Negrao[12], Nathan A. Pennell[13], Jun Zhang[14], Karen Velastegui[15], James G. Christensen[15], Xiaohong Yan[15], Kenna Anderes[15], Richard C. Chao[15], Pasi A. Jänne[16]

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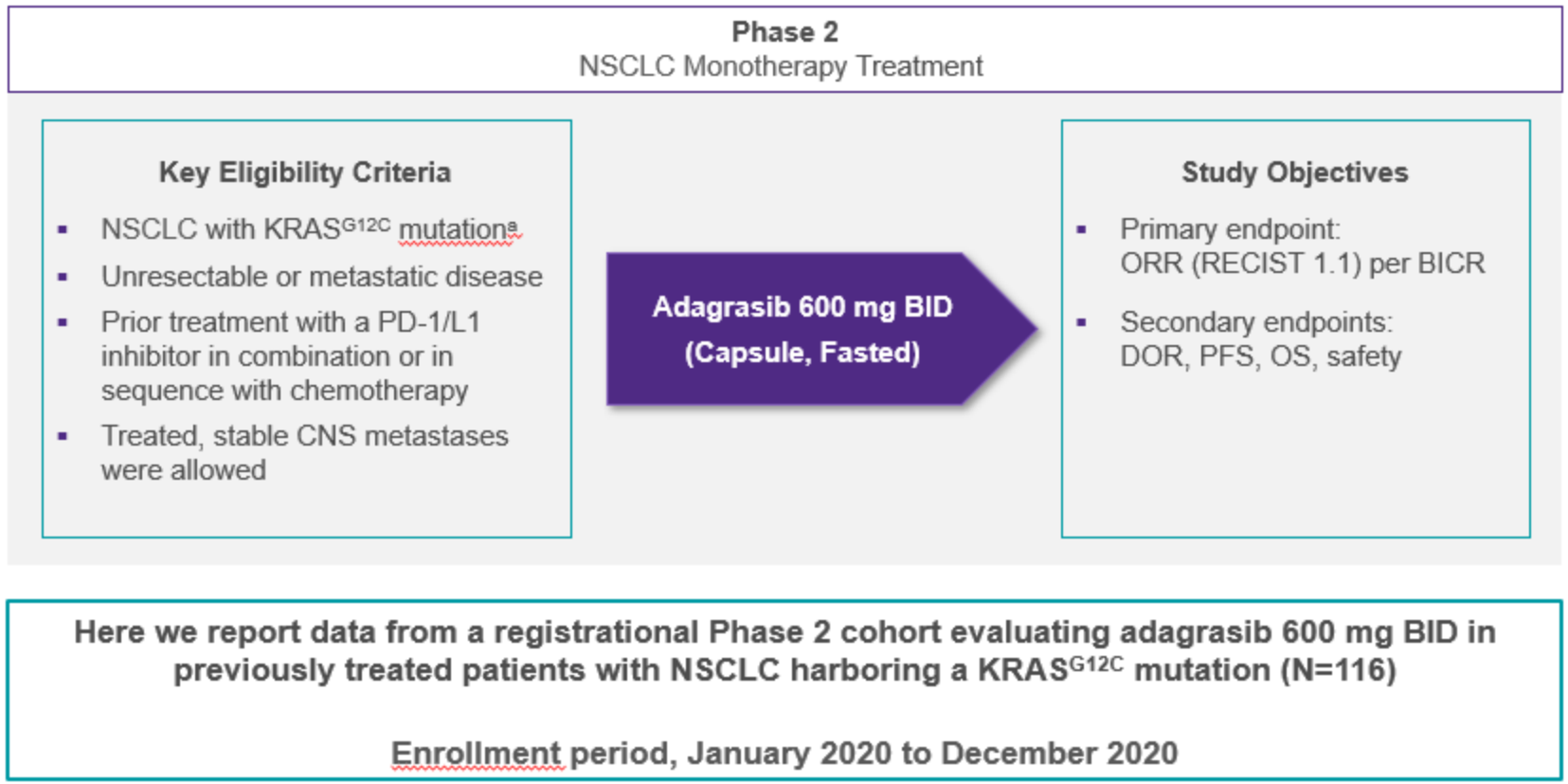
KRYSTAL-1 (849-001) Phase 2 Cohort A Study Design



[a]KRAS^{G12C} mutation detected in tumor tissue by sponsor-approved local laboratory testing
ClinicalTrials.gov. NCT03785249

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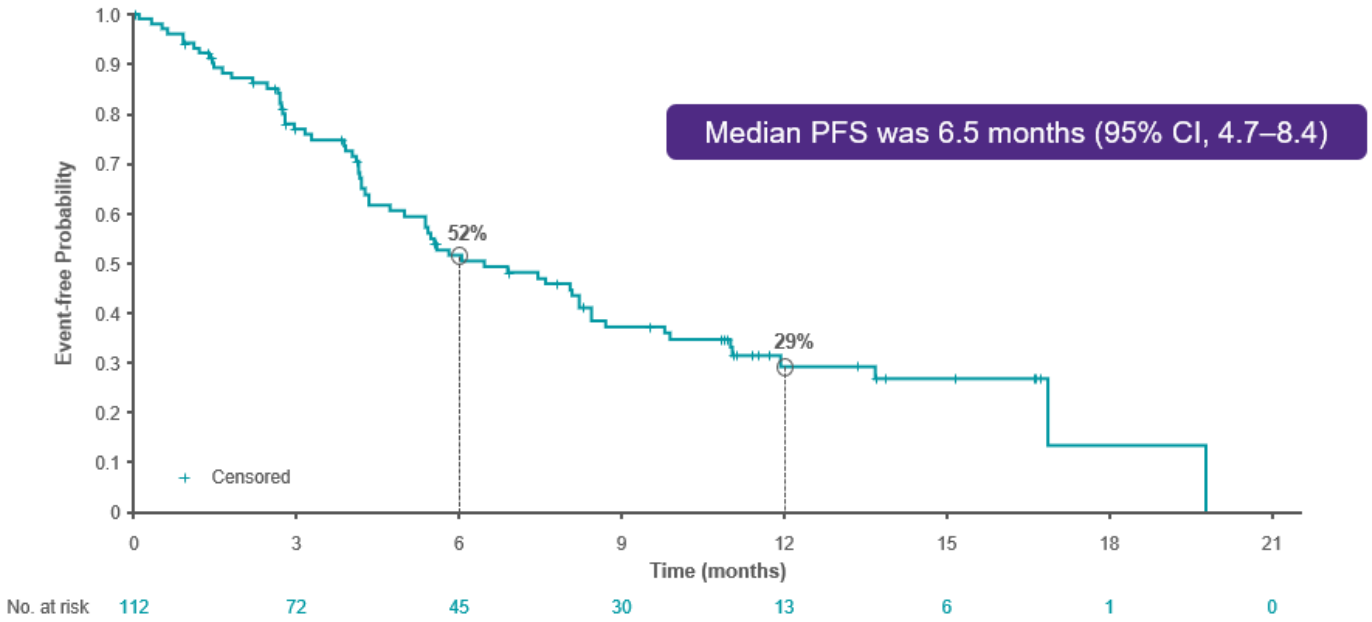
KRYSTAL-1: Efficacy outcomes

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%)



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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

[a]Occurring in >20% of patients (any grade), TRAEs occurring in >15% and <20% of patients were anemia (21 [18%]), amylase increase (20 [17%]) and QT prolongation (19 [16%]);
[b]Percentage of patients who experienced dose reductions: 400 mg BID (33%), 600 mg QD (11%), 200 mg BID/400 mg QD (14%)
Data as of October 15, 2021 (median follow-up: 12.9 months)

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KRYSTAL-1 Trial – activity of adagrasib in patients with active brain metastases

Activity of Adagrasib (MRTX849) in Patients with KRAS^{G12C}-Mutated NSCLC and Active, Untreated CNS Metastases in the KRYSTAL-1 Trial

Joshua K. Sabari,[1] Alexander I. Spira,[2] Rebecca S. Heist,[3] Pasi A. Jänne,[4] Jose M. Pacheco,[5] Jared Weiss,[6] Shirish M. Gadgeel,[7] Hirak Der-Torossian,[8] Karen Velastegui,[8] Thian Kheoh,[8] James G. Christensen,[8] Marcelo V. Negrao[9]

[1]Perlmutter Cancer Center, New York University Langone Health, New York, NY; [2]Virginia Cancer Specialists, Fairfax, VA; US Oncology Research, The Woodlands, TX; NEXT Oncology, VA; [3]Massachusetts General Hospital, Boston, MA; [4]Dana-Farber Cancer Institute, Boston, MA; [5]Division of Medical Oncology, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO; [6]Lineberger Comprehensive Cancer Center, University of North Carolina-Chapel Hill, Chapel Hill, NC; [7]Henry Ford Cancer Institute, Detroit, MI; [8]Mirati Therapeutics, Inc., San Diego, CA; [9]Department of Thoracic/Head & Neck Medical Oncology, MD Anderson Cancer Center, University of Texas, Houston, TX

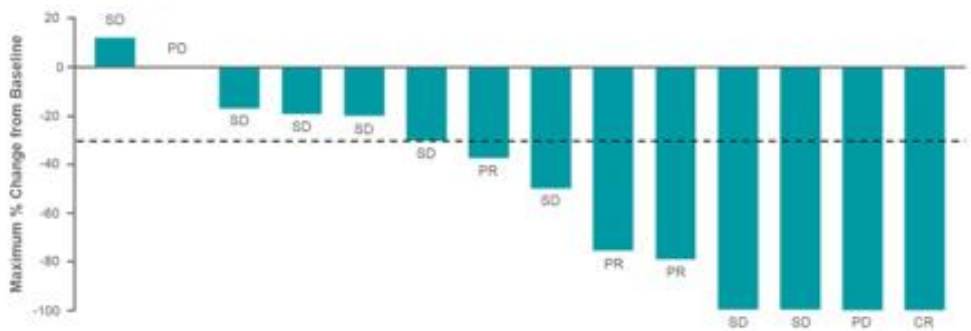
Key Eligibility Criteria

- Solid tumors with KRAS^{G12C} mutation[a]
- Unresectable or metastatic disease
- Active, untreated CNS metastases[b]
  - Asymptomatic, neurologically stable brain lesions, including focal leptomeningeal disease, and cerebellar metastases, but excluding brainstem (midbrain, pons, and medulla) metastases

Adagrasib 600 mg BID (Capsule, Fasted)

Study Objectives

- Safety
- Intracranial and systemic activity via BICR (mRANO-BM,[c] RECIST 1.1)
- Adagrasib concentration in CSF (measured when feasible)



Key Findings:

- Intracranial ORR 32% (6 of 19 patients), DCR 84% (16 of 19 patients)
- Systemic ORR 37%
- Most responses were concordant
- Median intracranial DOR not reached, PFS 4.2 months
- No new safety signals

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Summary:

Efficacy KRAS G12C inhibitor: Adagrasib vs. Sotorasib

Parameter	Adagrasib (KRYSTAL-1)	Sotorasib (CodeBreaK100)[1]
N=	116 (112 for efficacy)	126 (124 for efficacy)
Prior Platinum Chemo + IO	**98%**	**81%**
ORR	**43%** (95% CI 33.5-52.6)	**37.1%** (95% CI 28.6-46.2)
DCR	**80%** (95% CI 70.8-86.5)	**80.6%** (95% CI 72.6-87.2)
TTR, median (range)	**1.4 mo** (0.9-7.2)	**1.4 mo** (1.2-10.1)
DOR, median	**8.5 mo** (95% CI 6.2-13.8)	**11.1 mo** (95% CI 6.9-NE)
PFS, median	**6.5 mo** (95% CI 4.7-8.4)	**6.8 mo** (95% CI 5.1-8.2)
OS, median	**12.6 mo** (95% CI 9.2-19.2)	**12.5 mo**[2] (95% CI 10.0-NE)
Follow-up, median	12.9 mo	15.3 mo[2]

1= Skoulidis et al. N Engl J Med. 2021 Jun 24;384(25):2371-2381; 2=Pooled phase 1/2 of 174 pts with median f/u 24.9 mo, median OS 12.5 mo (95% CI 10.0-17.8), 1-year OS 50.8%, 2-year OS 32.5% (Dy G et al. AACR 2022)

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Amivantamab and lazertinib in patients with EGFR-mutant non-small cell lung cancer (NSCLC) after progression on osimertinib and platinum-based chemotherapy: Updated results from CHRYSALIS-2

Catherine A. Shu,[1] Koichi Goto,[2] Yuichiro Ohe,[3] Benjamin Besse,[4] Se-Hoon Lee,[5] Yongsheng Wang,[6] Frank Griesinger,[7] James Chih-Hsin Yang,[8] Enriqueta Felip,[9] Rachel E. Sanborn,[10] Reyes Bernabe Caro,[11] Joshua C. Curtin,[12] Jun Chen,[12] Janine Mahoney,[12] Leonardo Trani,[12] Joshua M. Bauml,[12] Meena Thayu,[12] Roland E. Knoblauch,[12] Byoung Chul Cho[13]

[1]Columbia University Medical Center, New York, NY, USA; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]National Cancer Center Hospital, Tokyo, Japan; [4]Paris-Sacaly University, Institut Gustave Roussy, Villejuif, France; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]Institute of Clinical Trial Center and Cancer Center, West China Hospital, Sichuan University, Chengdu, China; [7]Pius-Hospital, University of Oldenburg, Oldenburg, Germany; [8]National Taiwan University Cancer Center, Taipei, Taiwan; [9]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [10]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; [11]Hospital Universitario Virgen Del Rocio, Seville, Spain; [12]Janssen R&D, Spring House, PA, USA; [13]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea

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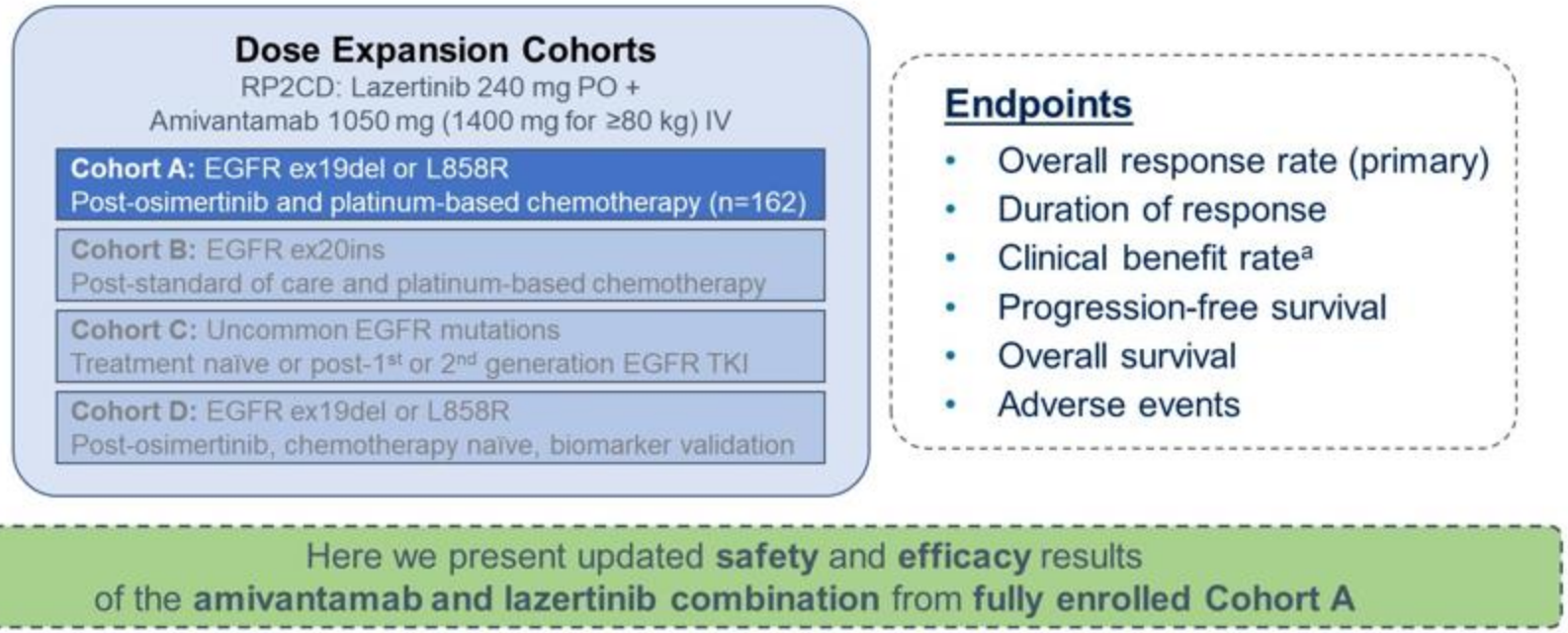
CHRYSALIS-2 (ClinicalTrails.gov Identifier: NCT04077463) Study Design



[a]Percentage of patients with confirmed response or durable stable disease (duration of ≥11 weeks).

EGFR, epidermal growth factor receptor; ex19del, exon 19 deletion; ex20ins, exon 20 insertion; IV, intravenous; PO, per oral; RP2CD, recommended phase 2 combination dose; TKI, tyrosine kinase inhibitor.

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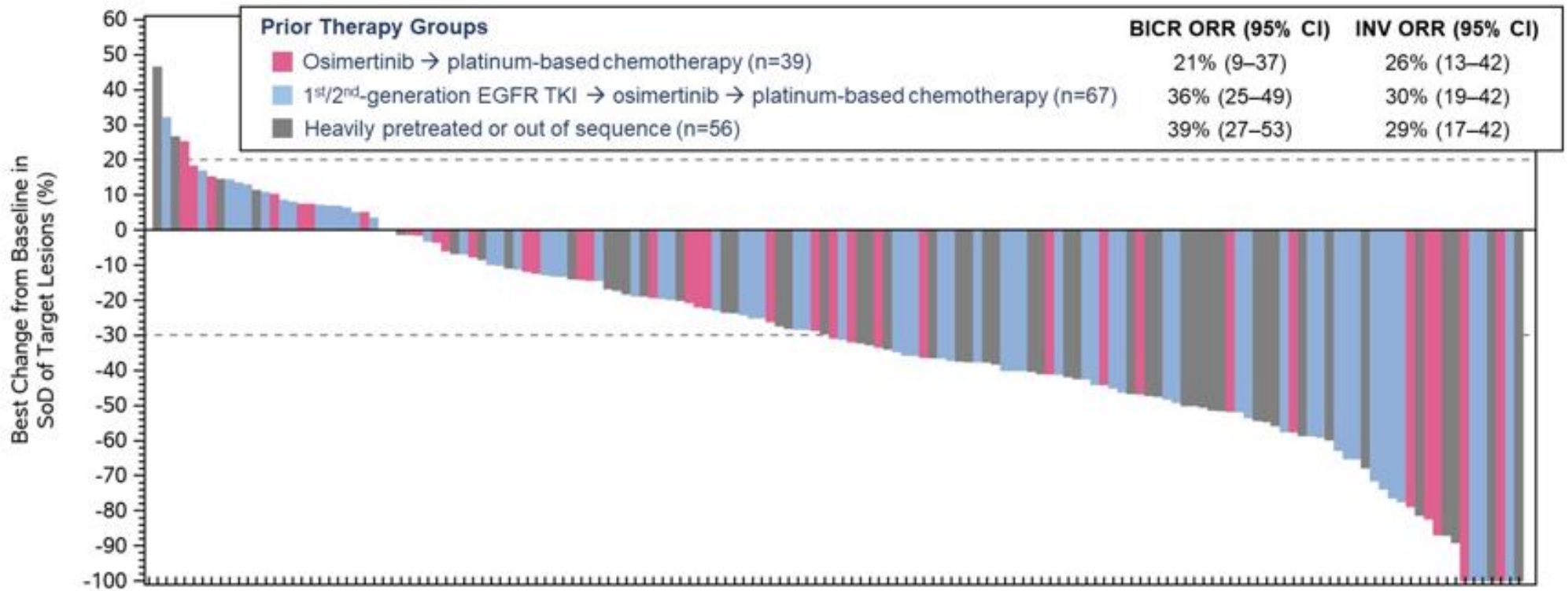
Best Antitumor Response and ORR by Prior Therapy Group



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

BICR, blinded independent central review; CI, confidence interval; EGFR, epidermal growth factor receptor; INV, investigator-assessed; ORR, overall response rate; SoD, sum of diameters; TKI, tyrosine kinase inhibitor.

Shu, C., et al. ASCO Annual Meeting 2022.

Safety Profile of Amivantamab + Lazertinib

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)

- Individual AEs were mostly grade 1-2
- Dose interruptions, reductions, and discontinuations of both amivantamab and lazertinib due to toxicity were seen in 57 (35%), 15 (9%), and 12 (7%) patients, respectively
- Pneumonitis/ILD was seen in 11 (7%) patients, of which 6 (4%) were grade ≥3 (no grade 5)
- Cumulative grouped rash-related AEs[a] occurred in 129 (80%) patients, with 17 grade ≥3 (10%)
- Safety profile consistent with what was previously reported; no new safety signals identified

[a]Rash-related terms include rash, dermatitis acneiform, acne, dermatitis, drug eruption, erythema, erythema multiforme, folliculitis, macule, papule, pustule, rash erythematous, rash macular, rash maculo-papular, rash pustular, rash papular, rash pruritic, rash vesicular, skin exfoliation, and skin lesion.

AE, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EGFR, epidermal growth factor receptor; TEAE, treatment-emergent adverse events.

Shu, C., et al. ASCO Annual Meeting 2022.

Abstract 9013

Phase 1/1b study of telisotuzumab vedotin (Teliso-V) + osimertinib (Osi), after failure on prior Osi, in patients with advanced, c-Met overexpressing, *EGFR*-mutated non-small cell lung cancer (NSCLC)

Presenter: Jonathan W. Goldman

Methods:

Metastatic *EGFR*-mutated,

c-Met overexpression

Progressed on prior Osimertinib

Treatment:

Teliso-V (IV Q2W) + Osi (oral; 80 mg QD).

Teliso-V + Osi is well tolerated with an ORR of 58% (67% at 1.9 mg/kg) in pts with c-Met OE NSCLC who progressed on prior Osi. Clinical trial information: NCT02099058.

		N	ORR,* n (%) [95% CI]
Dose	1.6 mg/kg	7	3 (43) [10, 82]
	1.9 mg/kg	12	8 (67) [35, 90]
	Total	19	11 (58) [34, 80]
c-Met level	High (≥50%, 3+ staining)	10	5 (50) [19, 81]
	Intermediate (25–49%, 3+ staining)	8	5 (63) [25, 92]
	Total	18†	10 (56) [31, 79]
***EGFR* mutation**	L858R	9	5 (56) [21, 86]
	Del19	9	6 (67) [30, 93]
	Total	19‡	11 (58) [34, 80]

*RECIST v1.1; data not mature for duration of response and progression-free survival. †c-Met IHC score < 25% 3+, n = 1. ‡G719S mutation, n = 1.

Goldman, J., et al. ASCO Annual Meeting 2022.

2022 ASCO ANNUAL MEETING

Phase1/2a Study of CLN-081 in NSCLC Patients with EGFR Exon 20 Insertion (ex20ins) Mutations

Helena Yu[1], Daniel Shao-Weng Tan[2], Egbert F. Smit[3], Alexander I. Spira[4], Ross A. Soo[5], Danny Nguyen[6], Victor Ho-FunLee[7], James Chih-Hsin Yang[8], Vamsidhar Velcheti[9], John M. Wrangle[10], Mark A. Socinski[11], Marianna Koczywas[12], David Witter[13], Asher Page[13], Leigh Zawel[13], John E. Janik[13], Zofia Piotrowska[14]

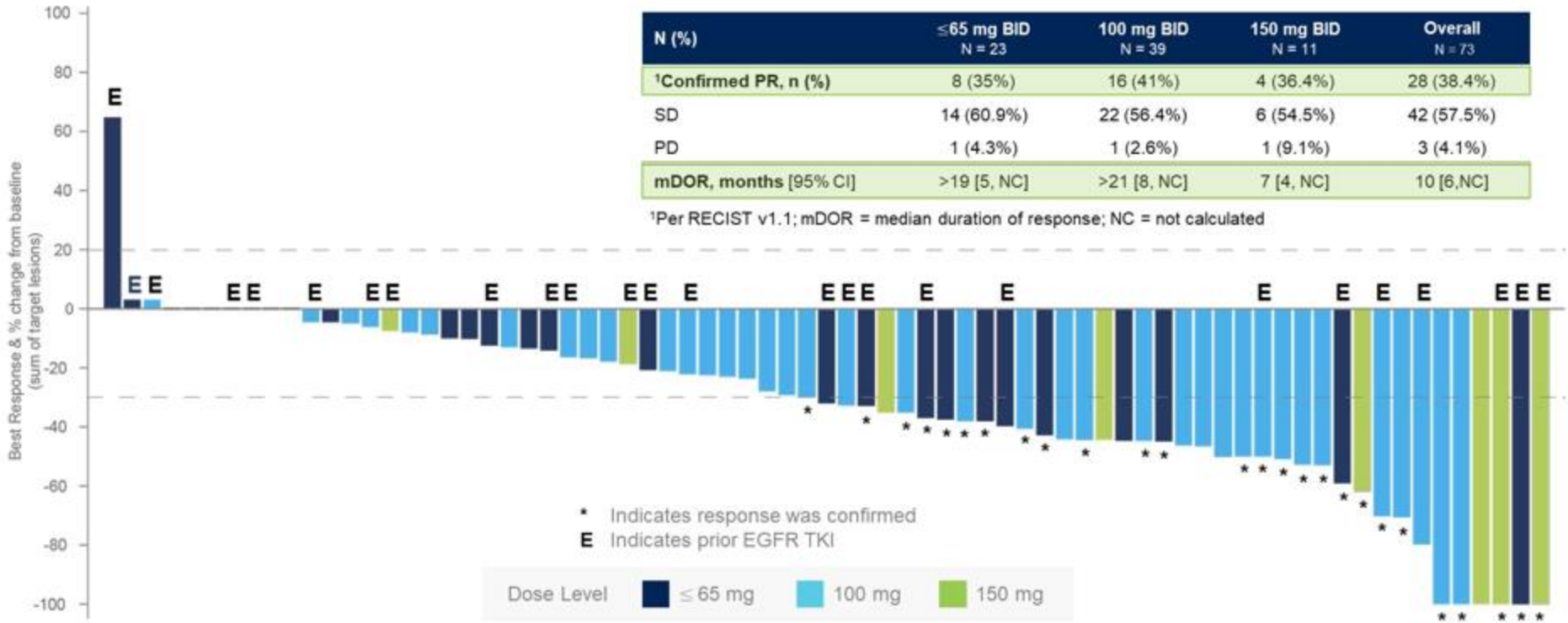
[1]Memorial Sloan Kettering Cancer Center; [2]National Cancer Centre Singapore; [3]The Netherlands Cancer Institute; [4]Virginia Health Specialists; [5]National University Hospital; [6]City of Hope National Medical Center; [7]Queen Mary Hospital, The University of Hong Kong; [8]National Taiwan University Hospital and National Taiwan University Cancer Center; [9]Cleveland Clinic Foundation; [10]Johns Hopkins University School of Medicine; [11]AdventHealth Cancer Institute; [12]Department of Medical Oncology and Therapeutics Research, City of Hope; [13]Cullinan Oncology, LLC; [14]Massachusetts General Hospital

Yu, H., et al. ASCO Annual Meeting 2022.

CLN-081-001: Best percentage change from baseline in target lesion dimensions and confirmed response by dose level

N (%)	≤65 mg BID N = 23	100 mg BID N = 39	150 mg BID N = 11	Overall N = 73
[1]Confirmed PR, n (%)	8 (35%)	16 (41%)	4 (36.4%)	28 (38.4%)
SD	14 (60.9%)	22 (56.4%)	6 (54.5%)	42 (57.5%)
PD	1 (4.3%)	1 (2.6%)	1 (9.1%)	3 (4.1%)
mDOR, months [95% CI]	>19 [5, NC]	>21 [8, NC]	7 [4, NC]	10 [6,NC]

[1]Per RECIST v1.1; mDOR = median duration of response; NC = not calculated



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Key comparisons: *EGFR ex20ins* trials

	Amivantamab[1]	Mobocertinib[2]	CLN-081[3]
Study	CHRYSALIS Phase I expansion (n=81)	Plt-Pre-treated Phase II (n=114) EXCLAIM Phase II (n=96)	Phase I (n=39)
Drug	Bispecific IgG antibody	Pyrimidine-based small molecule	Pyrimidine-based small molecule
Dose	1050 mg / 1400 mg (if > 80 kg)	160 mg OD	100 mg/150 mg BID
Schedule	Intravenous, q1wk C1, q2wk C2	Oral, Daily	Oral, Twice daily
Efficacy	ORR 40% (29-51) PFS 8.3 m (6.5-10.9) DoR 11.1 m (6.9-NR)	ORR 28% (20-37) PFS 7.3 m (5.5-9.2) DoR 17.5 m (7.4-20.3)	ORR 38.4% PFS 10 m (6-12) DoR 10 m (6-NR)
Toxicity (at RP2D)	83% G1-2 rash (4% G3) 63% G1-2 Infusion reactions (3% G3) 44% G1-2 paronychia (1%G3) 24% G1-2 hypoalbumin (3% G3) 9% G1-2 diarrhoea (4% G3) 18% peripheral edema (2% G3) 13% dose reductions	45% G1-2 rash/ 18% acneiform/ 14% maculopapular; (2% G3) 38% G1-2 paronychia (1% G3) 23% G1-2 Creatinine rise (2% G3) 70% G1-2 diarrhoea (21% G3) 18% G1-2 anaemia (1% G3) 25% dose reductions	82% G1-2 rash (no G3) 36% G1-2 diarrhoea 31% G1-2 paronychia 3% G3 anaemia/ AST elevation 13% dose reductions
Potential liabilities	? CNS activity Infusion reactions 93% C1 Long term *i.v.* infusion	CNS activity (38% intracranial PD in all patients who progressed) ? Long term chronic AE	? Long term chronic AE ? CNS activity

[1]Park K et al, JCO 2021;[2]Zhou C et al, JAMA Onc 2021; [3]Yu et al. ASCO 2022

PRESENTED BY:
Dr Daniel SW Tan, National Cancer Centre Singapore

Yu, H., et al. ASCO Annual Meeting 2022.

2022 ASCO ANNUAL MEETING

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

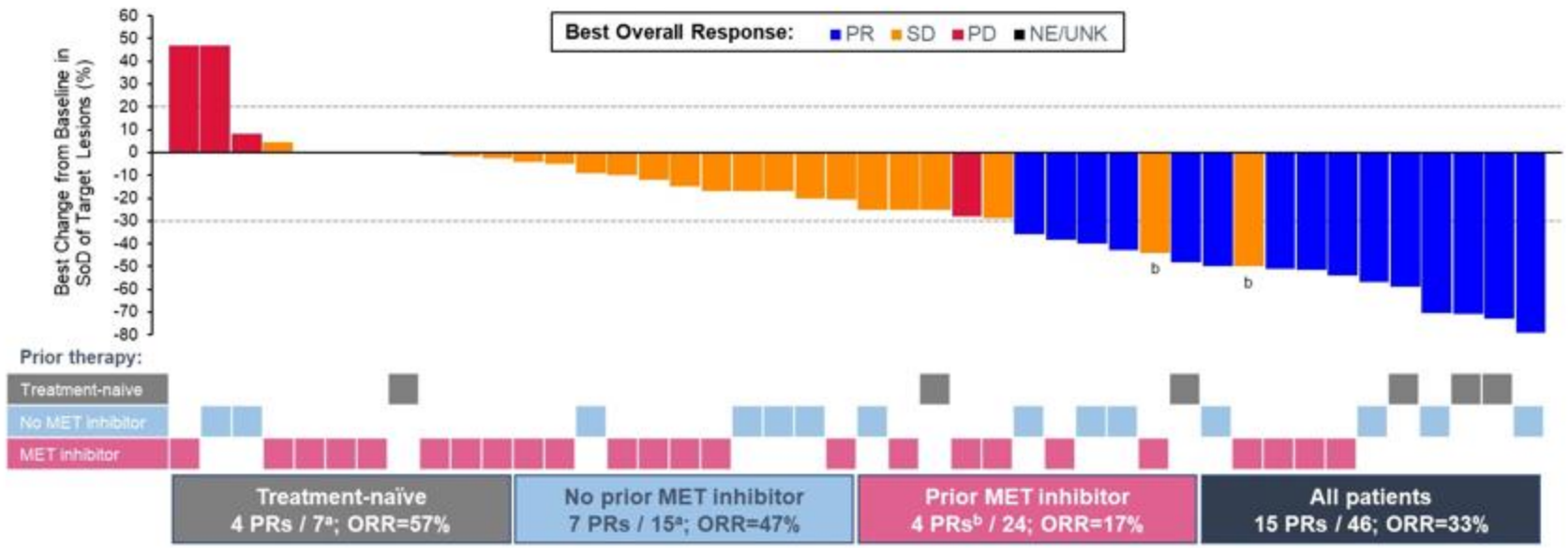
Matthew G. Krebs,[1] Alexander I. Spira,[2] Byoung Chul Cho,[3] Benjamin Besse,[4] Jonathan W. Goldman,[5] Pasi A. Jänne,[6] Zhiyong Ma,[7] Aaron S. Mansfield,[8] Anna Minchom,[9] Sai-Hong Ignatius Ou,[10] Ravi Salgia,[11] Zhijie Wang,[12] Casilda Llacer Perez,[13] Grace Gao,[14] Joshua C. Curtin,[14] Amy Roshak,[14] Robert W. Schnepp,[14] Meena Thayu,[14] Roland E. Knoblauch,[14] Chee Khoon Lee[15]

[1]Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [2]Virginia Cancer Specialists Research Institute, US Oncology Research, Fairfax VA; [3]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [4]Institut Gustave Roussy, Villejuif, France; [5]David Geffen School of Medicine at UCLA, Los Angeles, CA; [6]Dana Farber Cancer Institute, Boston, MA; [7]Henan Cancer Hospital, Zhengzhou, China; [8]Mayo Clinic, Rochester, MN; [9]Drug Development Unit, Royal Marsden/Institute of Cancer Research, Sutton, UK; [10]University of California Irvine, Orange, CA; [11]City of Hope, Duarte, CA; [12]Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China; [13]Medical Oncology Intercenter Unit, Regional and Virgen de la Victoria University Hospitals, IBIMA, Málaga, Spain; [14]Janssen R&D, Spring House, PA; [15]St George Hospital, Kogarah, Australia

Krebs, M., et al. ASCO Annual Meeting 2022.

Antitumor Activity of Amivantamab Monotherapy

- A total of 46 patients were efficacy evaluable



[a]Two patients discontinued prior to completing their secondpostbaseline disease assessment (1 in treatment naïve group and 1 in no prior MET inhibitor group). [b]Two additional patients had a best timepoint response of PR but did not confirm. NE/UNK, not evaluable/unknown; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters; TKI, tyrosine kinase inhibitor.

Krebs, M., et al. ASCO Annual Meeting 2022.

2022 ASCO® ANNUAL MEETING

SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab + carboplatin + etoposide with or without tiragolumab in patients with untreated extensive-stage small cell lung cancer

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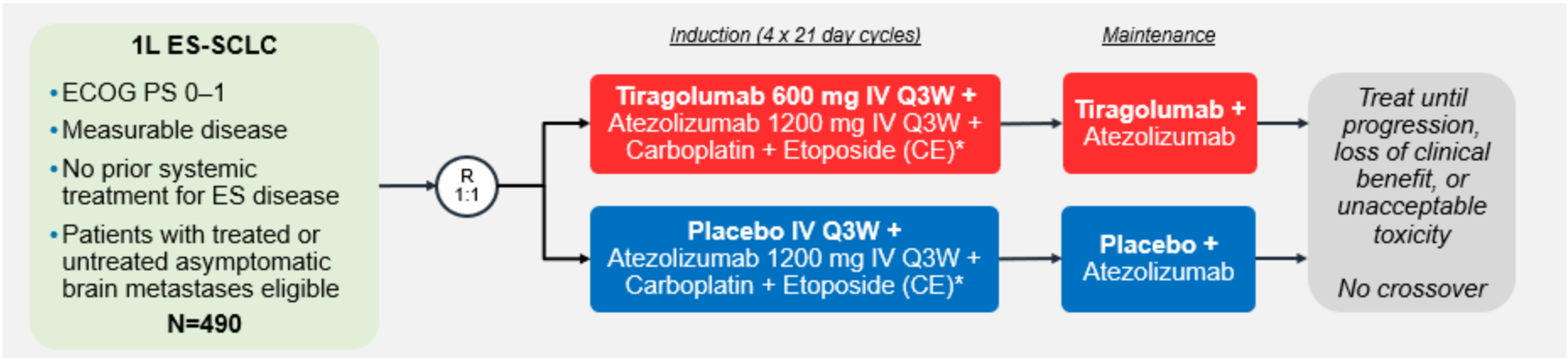
SKYSCRAPER-02: randomized, double-blind, placebo-controlled study of tiragolumab + atezolizumab + chemotherapy in patients with untreated ES-SCLC



Stratification Factors:

- **ECOG PS** (0 vs. 1)
- **Brain metastases** (Yes vs. No)
- **LDH** (≤ ULN vs. > ULN)

Co-Primary Endpoints:

- OS and investigator-assessed PFS in **Primary Analysis Set** (all randomized patients without presence or history of brain metastases at baseline)

Secondary Endpoints:

- PFS and OS in **Full Analysis Set** (all randomized patients)
- Confirmed objective response rate
- Duration of response
- Safety
- Pharmacokinetics
- PROs

Primary analysis

- Cut-off date of 6 February 2022
- Median follow-up of 14.3 months (Primary Analysis Set)

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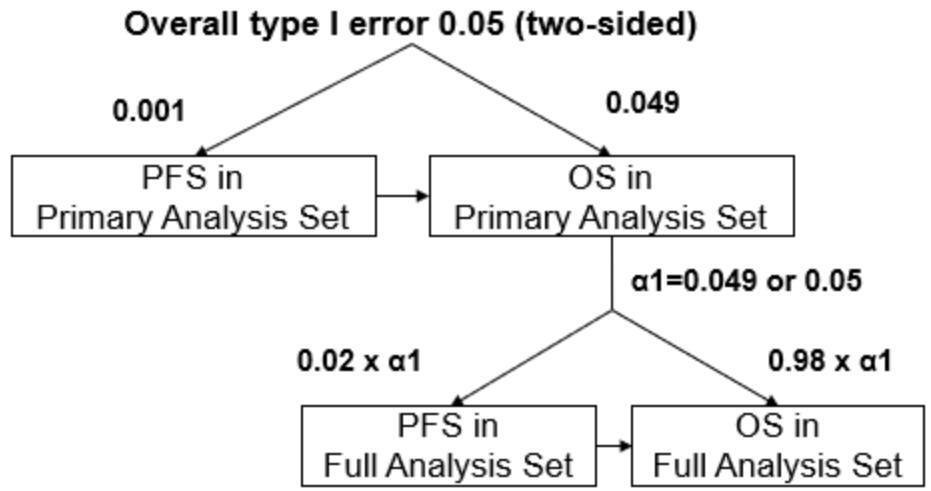
Analysis sets and statistical analysis plan

Primary analysis set: all randomized patients without presence or history of brain metastases at baseline
Full analysis set: all randomized patients, including those with treated or untreated brain metastases

	Tiragolumab + atezolizumab + CE	Placebo + atezolizumab + CE	Total
Primary Analysis Set	196	201	397
Full Analysis Set	243	247	490



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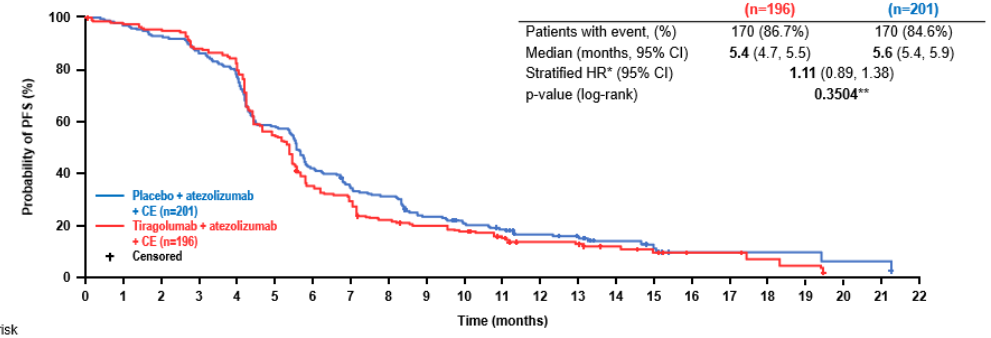
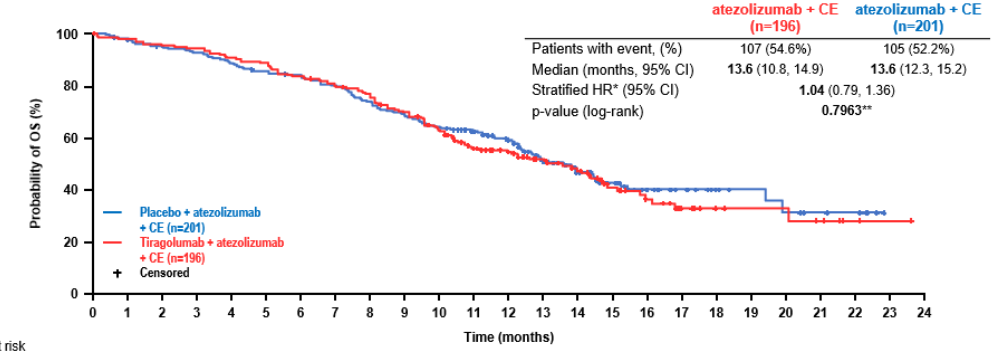
PFS: Primary Analysis Set



	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	170 (86.7%)	170 (84.6%)
Median (months, 95% CI)	**5.4** (4.7, 5.5)	**5.6** (5.4, 5.9)
Stratified HR* (95% CI)	**1.11** (0.89, 1.38)	
p-value (log-rank)	**0.3504****	

No. at risk																						
Placebo + atezo + CE	201	192	184	171	152	115	84	68	62	46	39	34	26	20	11	8	3	3	3	3	2	2	NE
Tiragolumab + atezo + CE	196	189	183	170	154	105	67	54	41	37	33	25	17	17	11	8	5	5	3	2	NE	NE	NE

Interim OS: Primary Analysis Set



	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	107 (54.6%)	105 (52.2%)
Median (months, 95% CI)	**13.6** (10.8, 14.9)	**13.6** (12.3, 15.2)
Stratified HR* (95% CI)	**1.04** (0.79, 1.36)	
p-value (log-rank)	**0.7963****	

No. at risk																							
Placebo + atezo + CE	201	195	188	183	175	168	164	156	144	134	125	115	97	70	47	36	26	19	12	9	7	5	4	NE	NE
Tiragolumab + atezo + CE	196	191	186	184	177	172	162	154	146	133	116	93	80	62	51	32	21	14	9	7	7	5	2	1	NE

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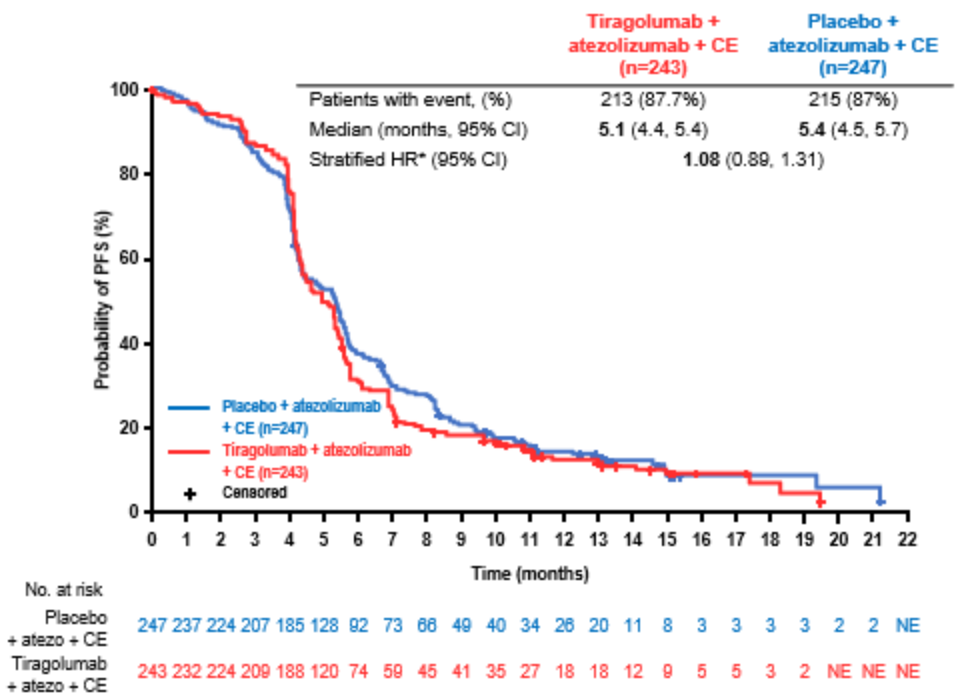
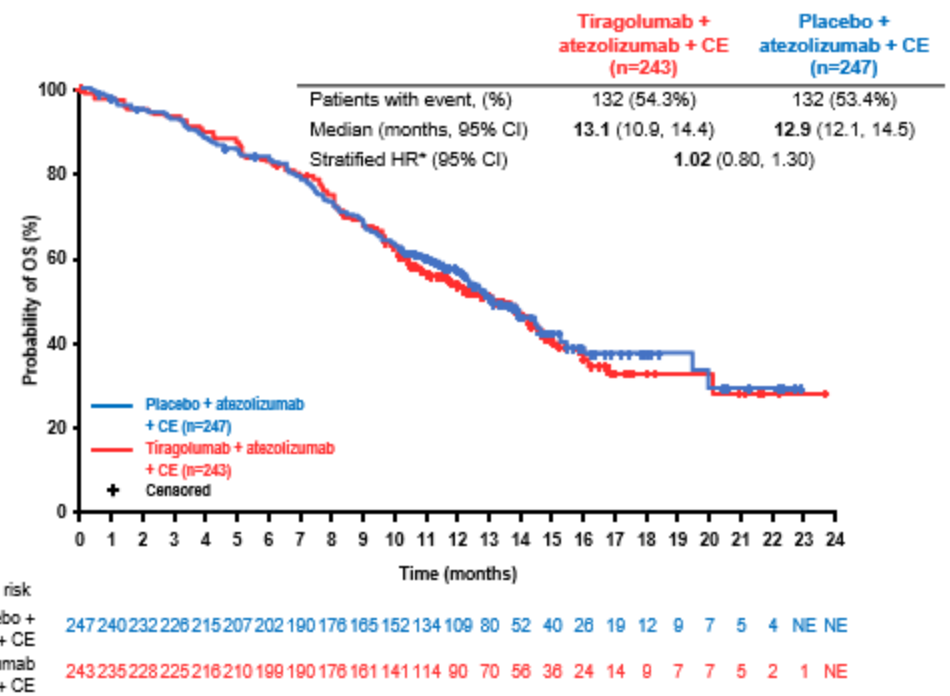
PFS and OS: Full Analysis Set

PFS in the Full Analysis Set



Interim OS in the Full Analysis Set



*Stratification factors are: ECOG, LDH
Data cut-off: 6 February 2022 (median follow-up:13.9 months)

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Extensive Stage Small Cell Lung Cancer

- 8516
  - Sintilimab plus anlotinib as second or further-line therapy
- 8517
  - Primary analysis from the phase II study of continuous talazoparib plus intermittent low-dose temozolomide
- 8518
  - Targeting genomic instability in extrapulmonary small cell neuroendocrine cancers: A phase II study with ATR inhibitor (berzosertib) and topotecan

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Goldman, J., et al. ASCO Annual Meeting, 2022.
Takahashi, N., et al. ASCO Annual Meeting, 2022.

Questions: