Lung Cancer UPDATES
ASCO HIGHLIGTHS
03-07 JUNIO 2022
Chicago, IL

Iniciativa científica de GECP lung cancer research

Innovaciones inmunoterapia CPNCP avanzado

Manuel Cobo
H RU Málaga

Inmunoterapia en CPNCP avanzado 1° linea

Figure 1. Study Design and Statistical Considerations of GEMSTONE-302

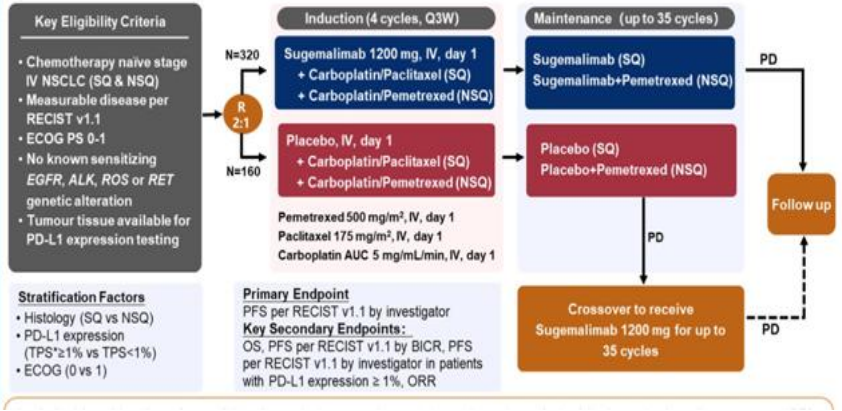
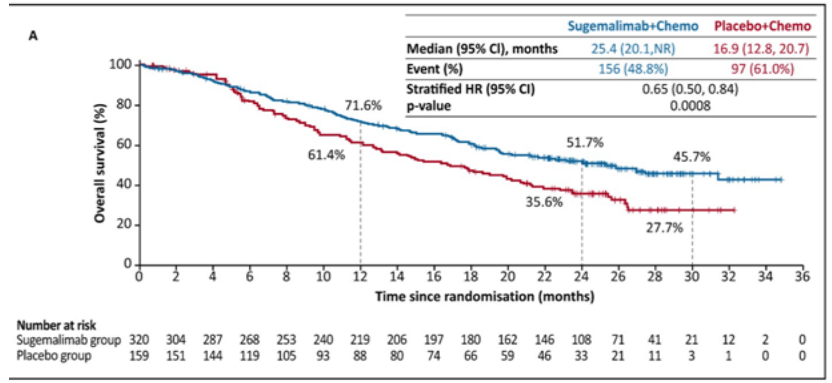
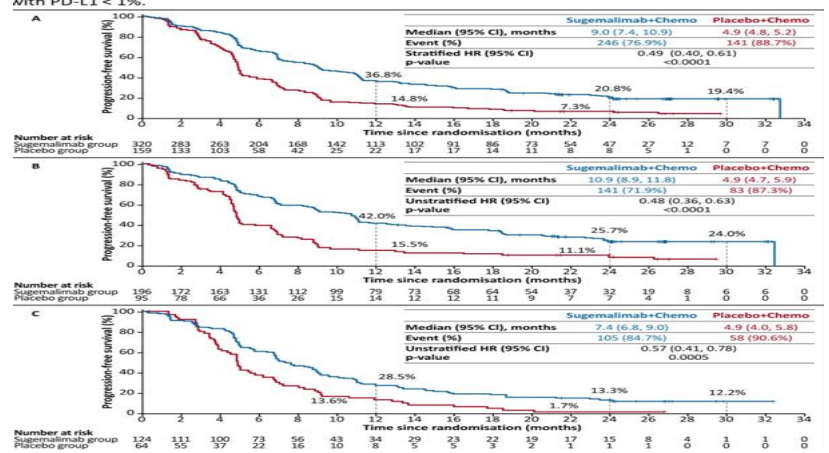


Figure 2. Overall Survival (A) Kaplan–Meier estimates of overall survival in the intent-to-treat (ITT) population

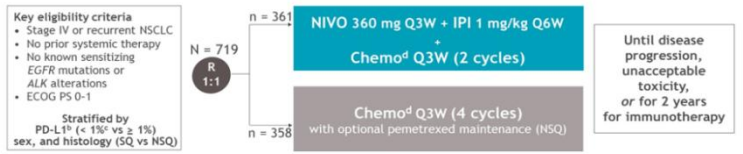




First-line nivolumab + ipilimumab + 2 cycles of chemotherapy vs chemotherapy alone (4 cycles) in patients with metastatic non-small cell lung cancer: 3-year update from CheckMate 9LA

Luis G. Paz-Ares, et al. Poster LBA9026

- In the randomized phase 3 CheckMate 9LA study,[a] 1L NIVO + IPI + 2 cycles of chemo significantly improved OS vs chemo alone (4 cycles), with no new safety signals, in patients with metastatic NSCLC[1,2]
- Here, we present updated efficacy and safety results from CheckMate 9LA with a minimum follow-up of 3 years, and an exploratory analysis of OS by oncogenic driver mutation status

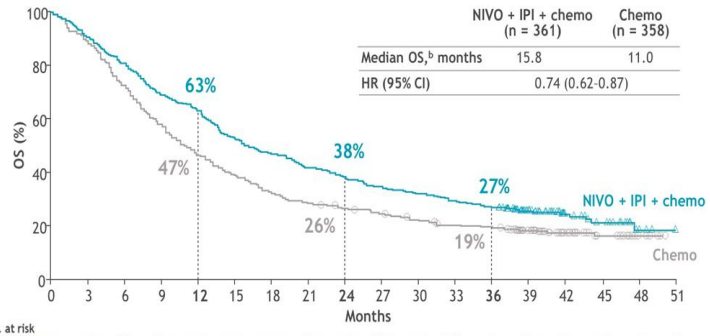


Database lock: February 15, 2022; minimum/median follow-up for OS: 36.1/42.6 months.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

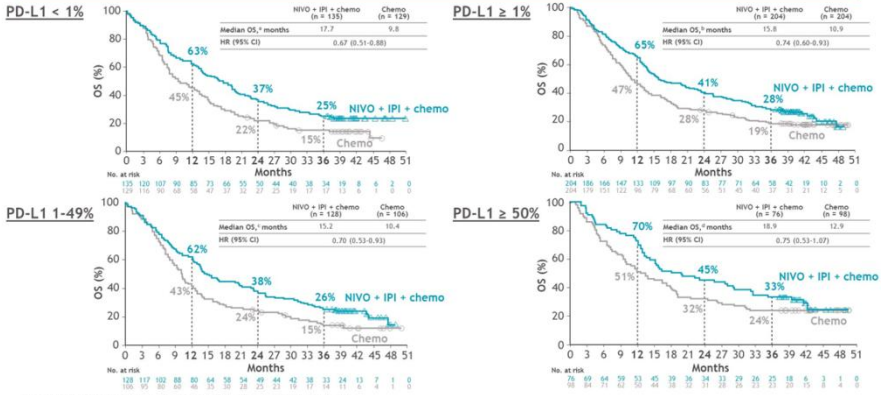
1. Paz-Ares L, et al. *Lancet Oncol* 2021;22:198-211; 2. Reck M, et al. *ESMO Open* 2021;6:100273.

3-year update: OS in all randomized patients[a]



Database lock: February 15, 2022; minimum follow-up: 36.1 months.

OS by PD-L1 expression



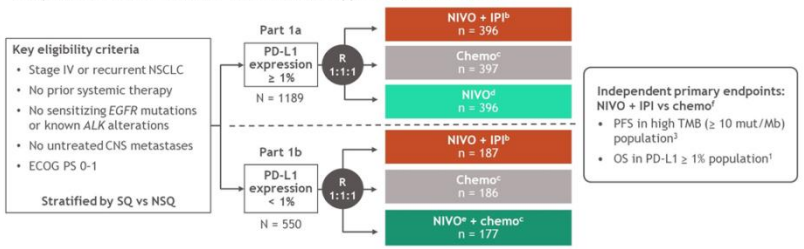
Database lock: February 15, 2022; minimum follow-up: 36.1 months.

[b]95% CI, 13.7-20.3 (NIVO + IPI + chemo) and 7.7-13.5 (chemo); [c]95% CI, 13.8-22.2 (NIVO + IPI + chemo) and 9.5-13.2 (chemo); [d]95% CI, 12.6-21.2 (NIVO + IPI + chemo) and 8.7-12.4 (chemo); [e]95% CI, 13.1-29.1 (NIVO + IPI + chemo) and 9.4-17.6 (chemo).

Five-year survival outcomes with nivolumab + ipilimumab vs chemotherapy as first-line treatment for metastatic non-small cell lung cancer: results from CheckMate 227

Julie Brahmer, et al. Poster #LBA9025

- In CheckMate 227 Part 1, 1L NIVO + IPI demonstrated long-term, durable survival benefit versus platinum-doublet chemo in patients with metastatic NSCLC regardless of tumor PD-L1 expression level[1,2]
- Here, we present the 5-year update of CheckMate 227 Part 1, the longest reported follow-up (minimum 61.3 months) of a phase 3 trial of 1L combination immunotherapy in metastatic NSCLC



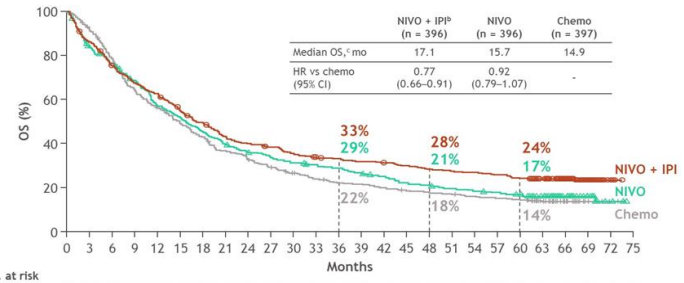
Database lock: February 15, 2022; minimum/median follow-up for OS: 61.3/66.7 months.

Treatment was continued until disease progression, unacceptable toxicity, or for 2 years for immunotherapy; [a]NCT02477826; [b]NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W); [c]NSQ: pemetrexed + cisplatin or carboplatin, Q3W for ≤ 4 cycles, with optional pemetrexed maintenance following chemo or NIVO + pemetrexed maintenance following NIVO + chemo; SQ: gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤ 4 cycles; [d]NIVO (240 mg Q2W); [e]NIVO (360 mg Q3W); [f]Both endpoints were met; results were previously reported.[1]

1L, first-line; chemo, chemotherapy; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; IPI, ipilimumab; mut, mutation; NIVO, nivolumab; NSQ, non-squamous; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; R, randomized; SQ, squamous; TMB, tumor mutational burden.

1. Hellman MD et al. *New Engl J Med*. 2019;381:2020-2031. 2. Paz-Ares LG, et al. *J Thorac Oncol*. 2021;17:289–308. 3. Hellmann MD, et al. *N Engl J Med*. 2018;378:2093-2104.

5-year OS in patients with tumor PD-L1 ≥ 1%[a]

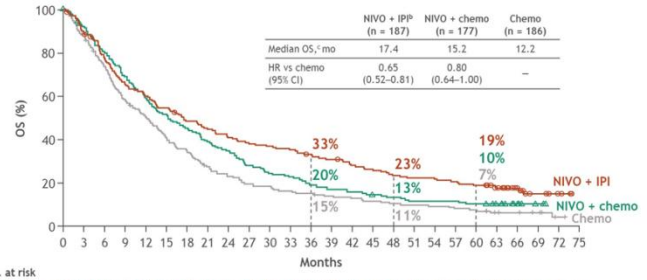


Database lock: February 15, 2022; minimum/median follow-up for OS: 61.3/66.7 months.

[a]In patients with PD-L1 ≥ 1% with a PFS event (per BICR), subsequent systemic therapy was received by 34% in the NIVO + IPI arm, 46% in the NIVO arm, and 48% in the chemo arm; subsequent immunotherapies by 7%, 9%, and 40%; subsequent chemo by 33%, 45%, and 25%, respectively. [b]NIVO + IPI vs NIVO HR was 0.84 (95% CI, 0.72–0.99). [c]Median OS 95% CI are 14.95–20.17 (NIVO + IPI), 13.27–18.14 (NIVO), and 12.71–16.72 (chemo).

BICR, blinded independent central review.

5-year OS in patients with tumor PD-L1 < 1%[a]



Database lock: February 15, 2022; minimum/median follow-up for OS: 61.3/66.7 months.

[a]In patients with PD-L1 < 1% with a PFS event (per BICR), subsequent systemic therapy was received by 44% in the NIVO + IPI arm, 39% in the NIVO + chemo arm, and 48% in the chemo arm; subsequent immunotherapies by 8%, 5%, and 33%; subsequent chemo by 43%, 37%, and 33%, respectively. [b]NIVO + IPI vs NIVO + chemo HR was 0.80 (95% CI, 0.63–1.00). [c]Median OS 95% CI are 13.21–22.05 (NIVO + IPI), 12.29–19.78 (NIVO + chemo), and 9.17–14.32 (chemo).

2022 ASCO ANNUAL MEETING

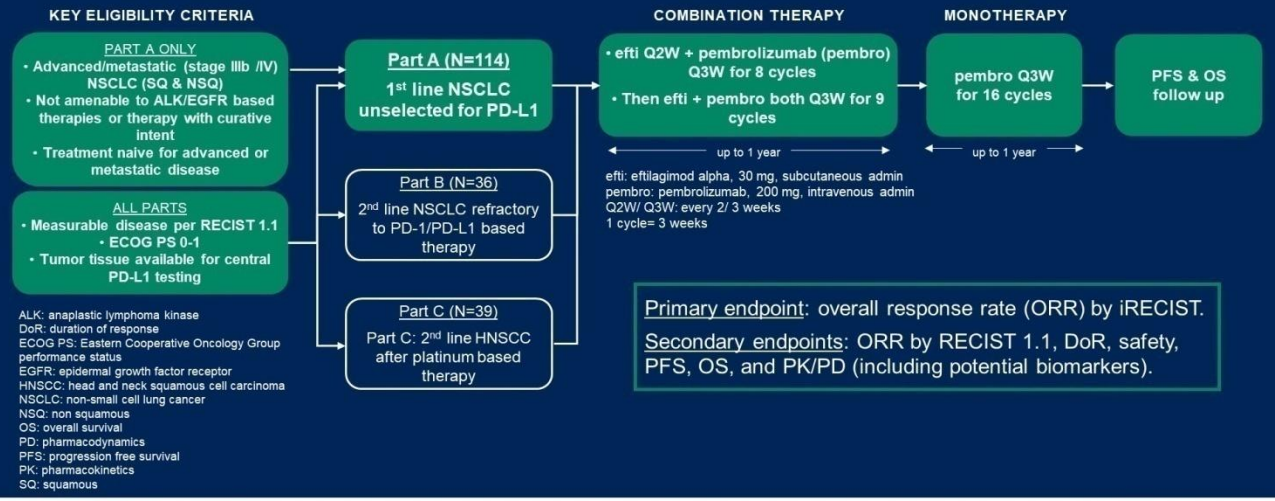
A Phase II study (TACTI-002) in 1st line metastatic non-small cell lung cancer (NSCLC) investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab: updated results from a PD-L1 unselected population

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]

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.

Trial Design – TACTI-002

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



ALK: anaplastic lymphoma kinase
DoR: duration of response
ECOG PS: Eastern Cooperative Oncology Group performance status
EGFR: epidermal growth factor receptor
HNSCC: head and neck squamous cell carcinoma
NSCLC: non-small cell lung cancer
NSQ: non squamous
OS: overall survival
PD: pharmacodynamics
PFS: progression free survival
PK: pharmacokinetics
SQ: squamous

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).

2022 ASCO ANNUAL MEETING #ASCO22

PRESENTED BY: Enriqueta Felip. A Phase II 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

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Efficacy – ORR[1] & DCR[1] by iRECIST/RECIST 1.1 – TACTI-002

Response (Local investigator read, unconfirmed)	iRECIST n (%), N=114	RECIST 1.1 n (%), N=114
Complete Response	2 (1.8)	2 (1.8)
Partial Response	42 (36.8)	41 (36.0)
Stable Disease	40 (35.1)	39 (34.2)
Progression	19 (16.7)	21 (18.4)
Not Evaluable[2]	11 (9.6)	11 (9.6)
ORR, (ITT=114); [95% CI][3]	44 (38.6); [29.6-48.2]	43 (37.7); [28.8-48.3]
DCR (ITT=114); [95% CI][3]	84 (73.7); [64.6-81.5]	82 (71.9); [62.7-80.0]
ORR (EVAL[4]=103); [95% CI][3]	44 (42.7) [33.0-52.9]	43 (41.8); [32.1-51.9]
DCR (EVAL[4]=103); [95% CI][3]	84 (81.5); [72.7-88.5]	82 (79.6); [70.5-86.9]

N = 114

- ORR (iRECIST - primary endpoint) of 38.6% (95% CI: 29.6-48.2) in the ITT.
- ORR (RECIST 1.1) 37.7% (95% CI: 28.8-48.3) in the ITT.
- ORR of 42.7% (iRECIST) and 41.8% (RECIST 1.1) in the EVAL[4] population.

[1] local investigator read, unconfirmed.
[2] patients with no on-study post baseline tumor staging for any reason.
[3] 95% CIs calculated using Clopper-Pearson method.
[4] all patients with ≥1 on-study post baseline tumor staging.
ITT: intention-to-treat population
EVAL: evaluable population

Data cut-off date: April 15, 2022

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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 [95% CI][4]	9 (28.1) [13.8-46.8]	15 (41.7) [25.5-59.2]	10 (52.6) [28.9-75.6]	25 (45.5) [32.0-59.5]	24 (35.3) [24.1-47.8]
DCR [95% CI][4]	22 (68.8) [50.0-83.9]	28 (77.8) [60.9-89.9]	15 (79.0) [54.4-94.0]	43 (78.2) [65.0-88.2]	50 (73.5) [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 [95% CI][4]	9 (24.3) [11.8-41.2]	16 (40.0) [24.9-56.7]	16 (51.6) [33.1-69.9]	32 (45.1) [33.2-57.3]	25 (32.5) [22.2-44.1]
DCR [95% CI][4]	26 (70.3) [53.2-84.1]	30 (75.0) [58.8-87.3]	24 (77.4) [58.9-90.4]	54 (76.1) [64.5-85.4]	56 (72.7) [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

2022 ASCO ANNUAL MEETING #ASCO22

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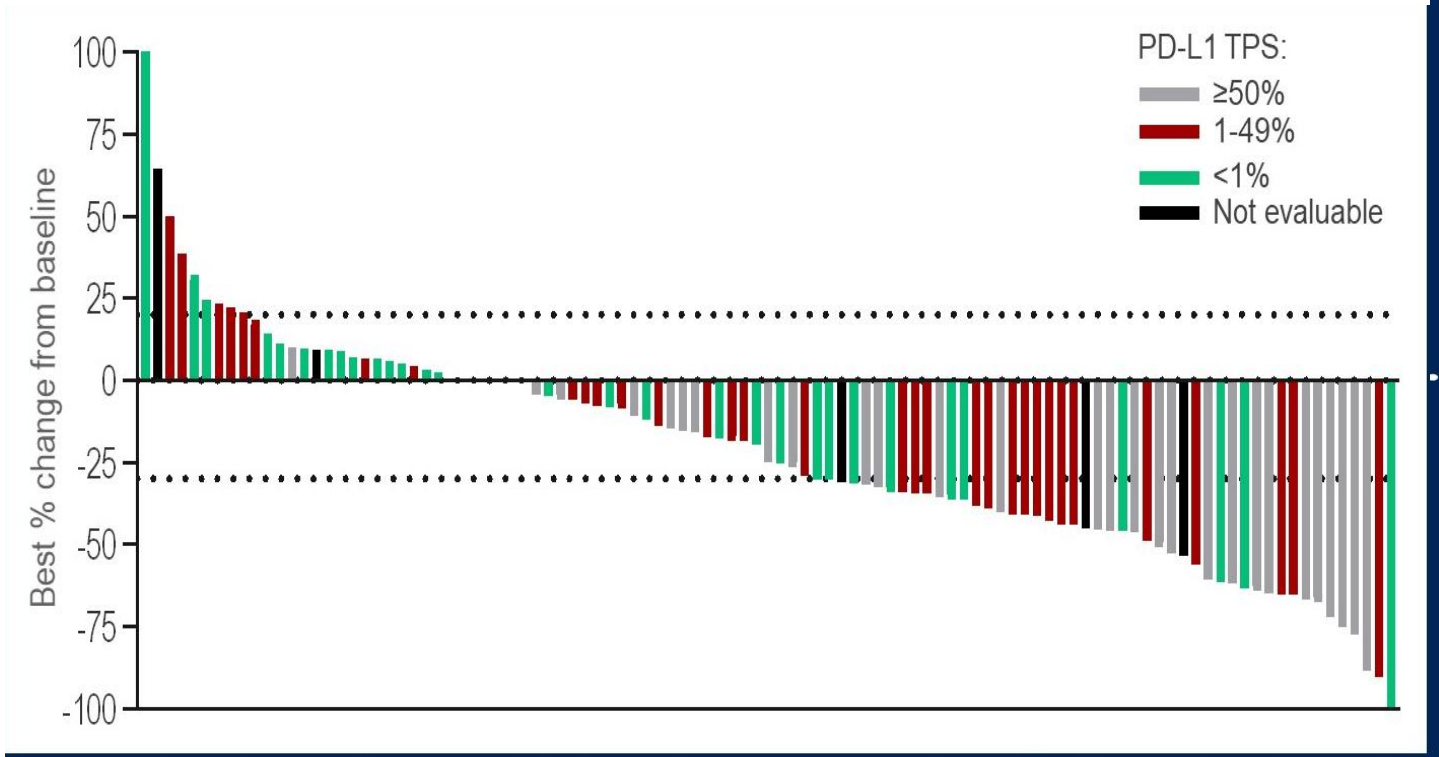
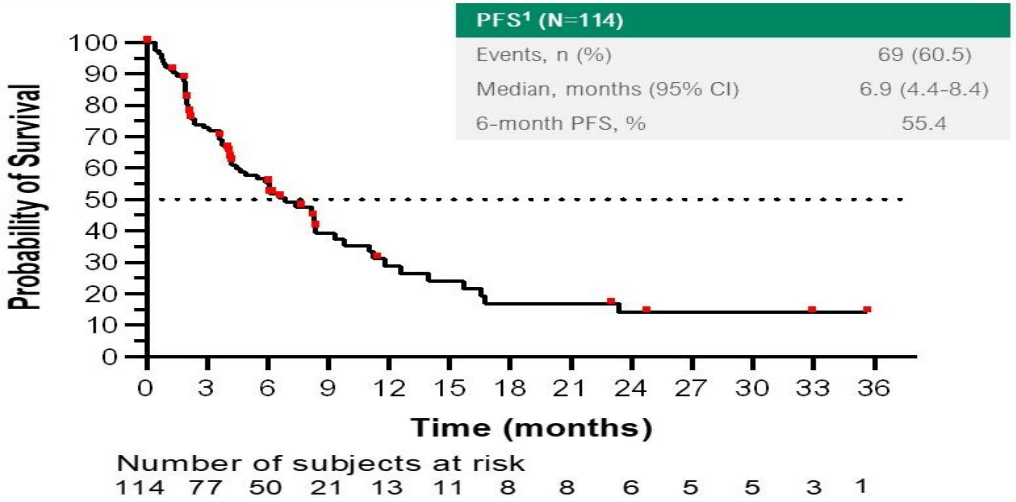


[1] all patients with ≥1 post-baseline CT scan n=103; [2] PD-L1 assessed by central assessment (Dako kit); n=79; [3] local assessment included due to non evaluable central assessment results, n=19; [4] no results available for neither central nor local testing, n=5.

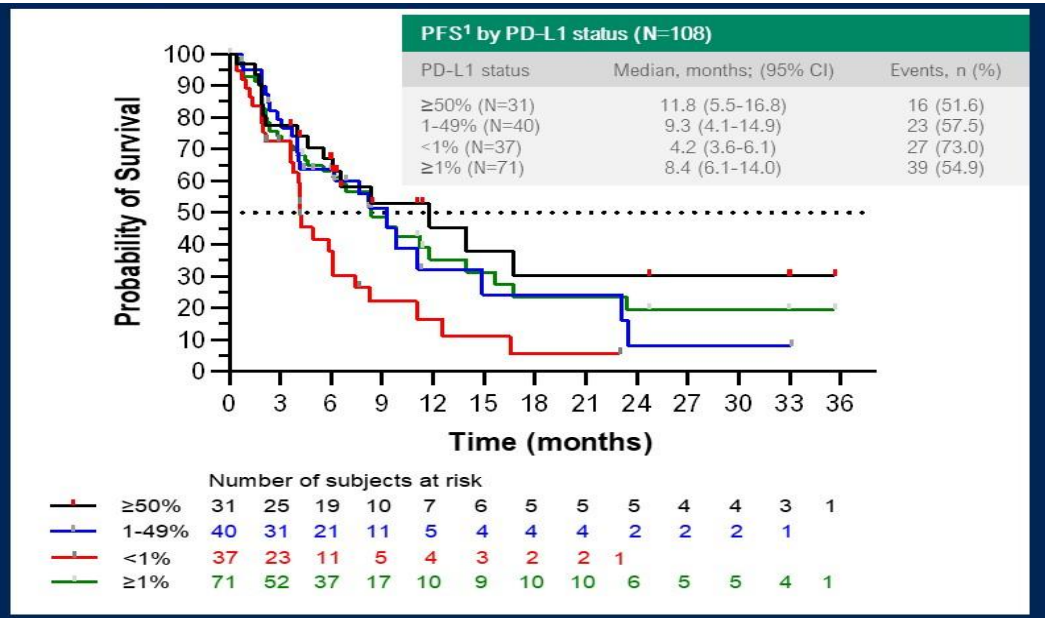
- 2 complete responses and 19.4% of patients with a target lesion decrease ≥50%.
- 68/103 (66.0%) of patients with a post-baseline assessment had a decrease in target lesions.

Data



- 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: Apr

#ASCO22

PRESENTED BY:
Enriqueta Felip, A Phase II 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[2]	*10 (8.8)*
Any Grade ≥3 TEAE	59 (51.8)
Grade ≥3 TEAE related to study treatment[2]	*12 (10.5)*
Any Grade 4 TEAE	5 (4.4)
Any Grade 5 TEAE	12 (10.5)
Grade 5 TEAE related to study treatment[2]	*3 (2.6)*
Any TEAEs leading to discontinuation of study treatment[2]	23 (20.2)
TEAEs leading to discontinuation related to study treatment[2]	*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 (v5.0).
[2] Study treatment= efti and/or pembrolizumab.

Data cut-off date: April 15, 2022

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.

2022 ASCO ANNUAL MEETING

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]

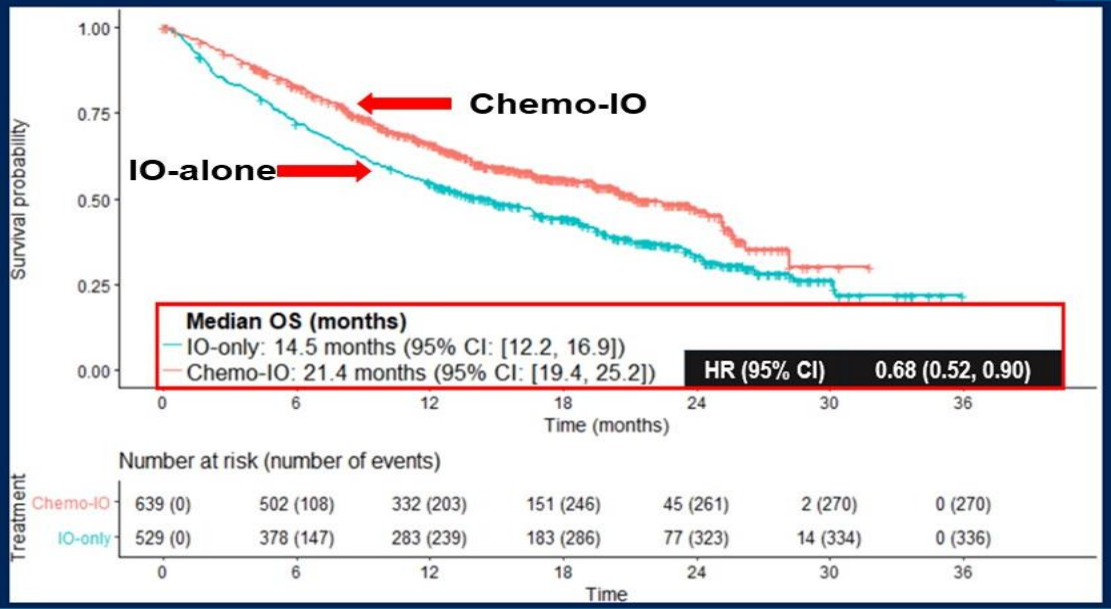
[1]Center for Drug Evaluation and Research, U.S. Food and Drug Administration

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

Oladimeji Akinboro, MD, MPH

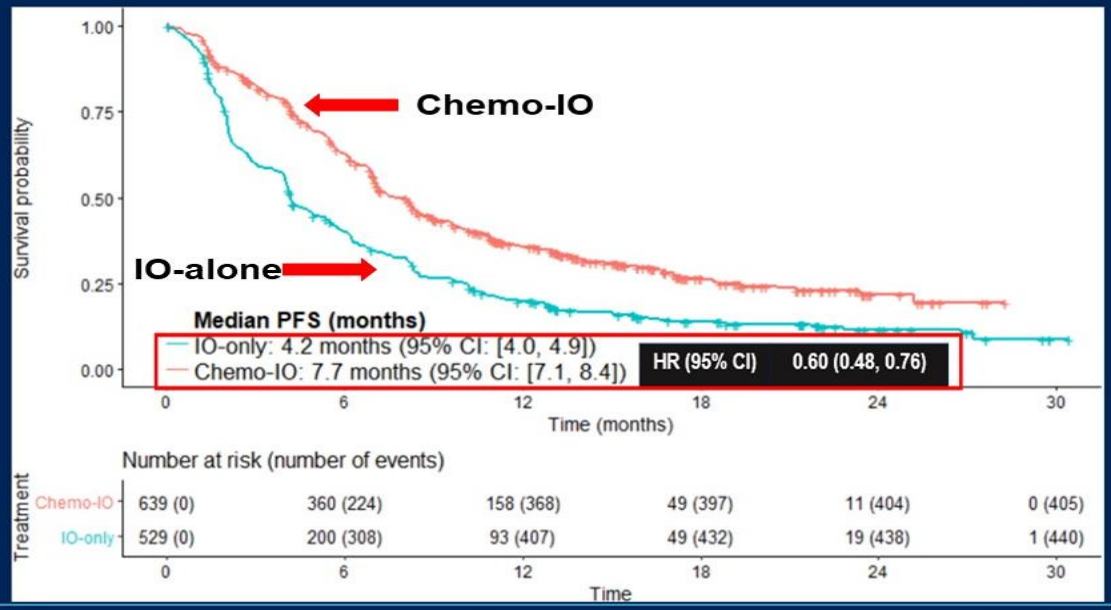
Exploratory OS: NSCLC PDL1 1-49%

FDA



Exploratory PFS: NSCLC PDL1 1-49%

FDA



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*

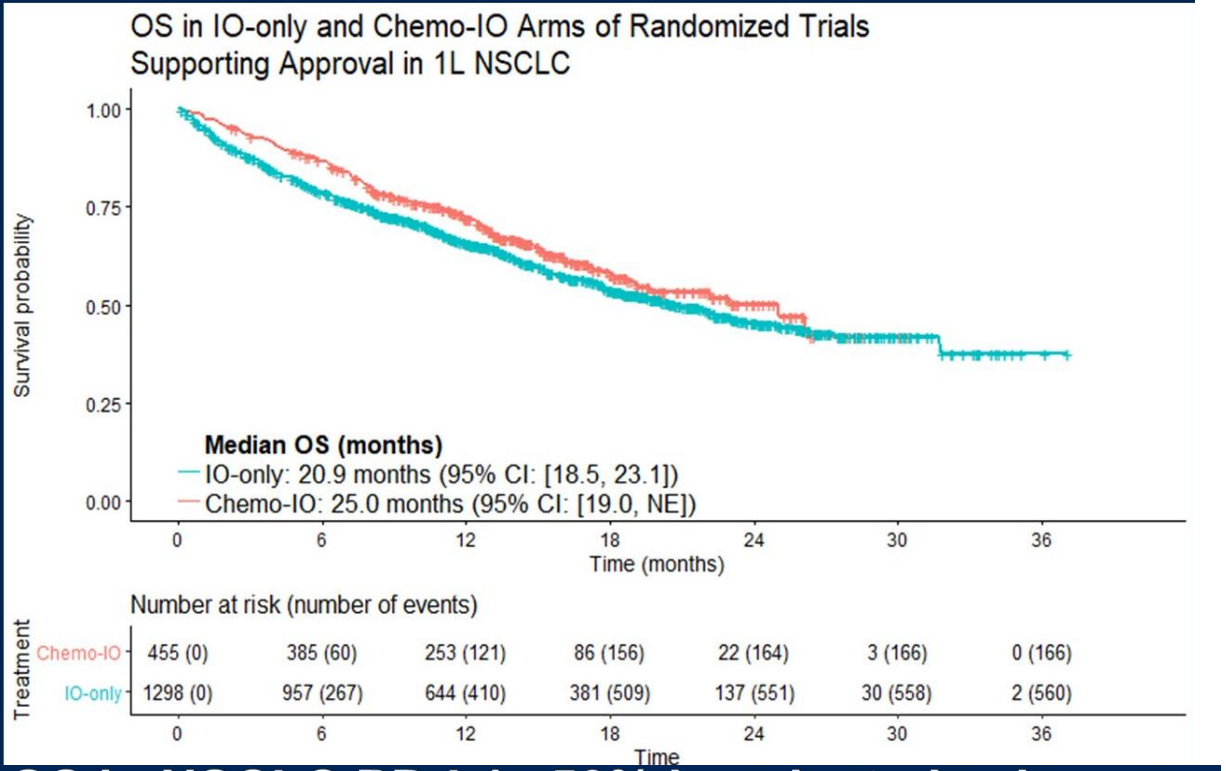
		Chemo-IO (*N*=455)	IO alone (*N*=1,298)	Chemo (*N*=1,436)	Overall (*N*=3,189)
Age	Median, years	65	64	64	64
	<65 years, %	49	53	50	51
	65-74 years, %	41	36	39	38
	≥75 years, %	10	11	11	11
Sex	Female	37	29	31	31
Race	White, %	91	77	80	80
	Black, %	1	1	2	1
	Asian, %	8	20	16	16
Smoking history	Ever smoked, %	87	89	88	89
ECOG PS	≥1, %	59	68	67	66
Histology	Non-squamous, %	78	69	68	70

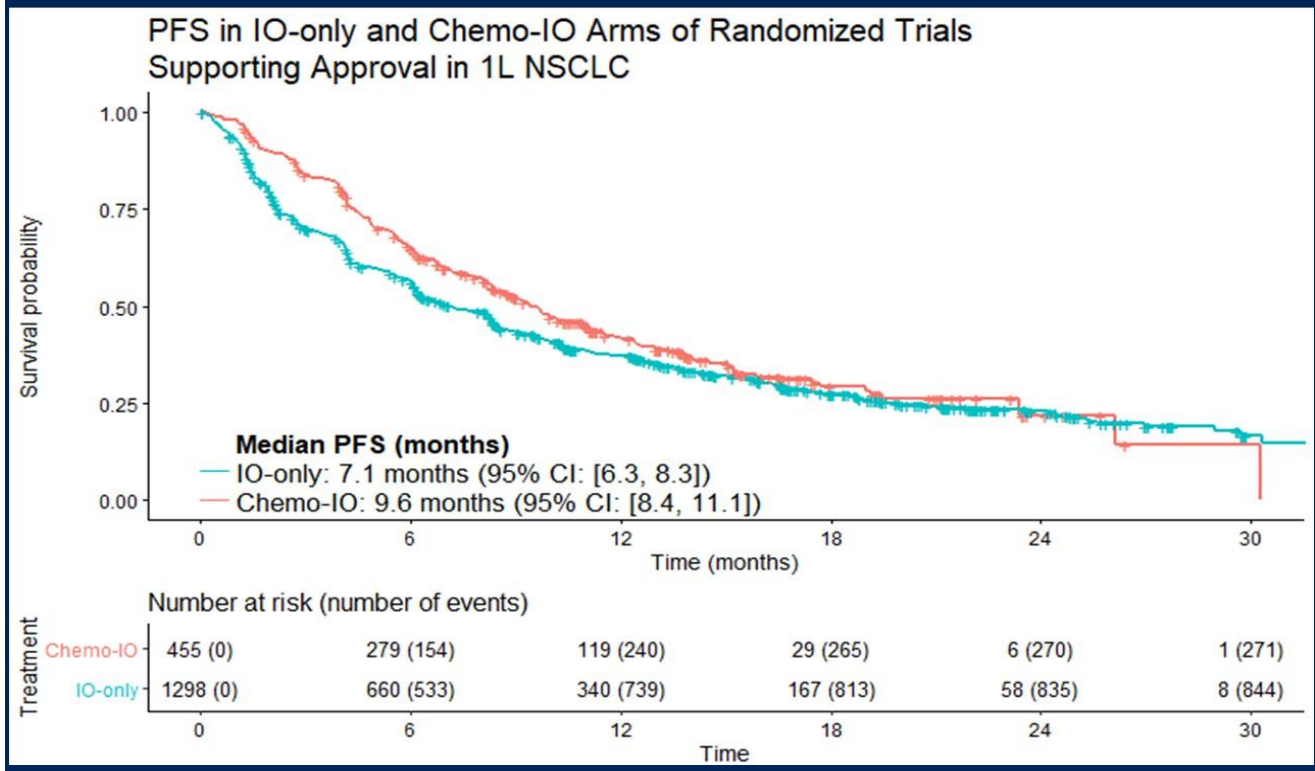
Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IO=immunotherapy; *N*=number.

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

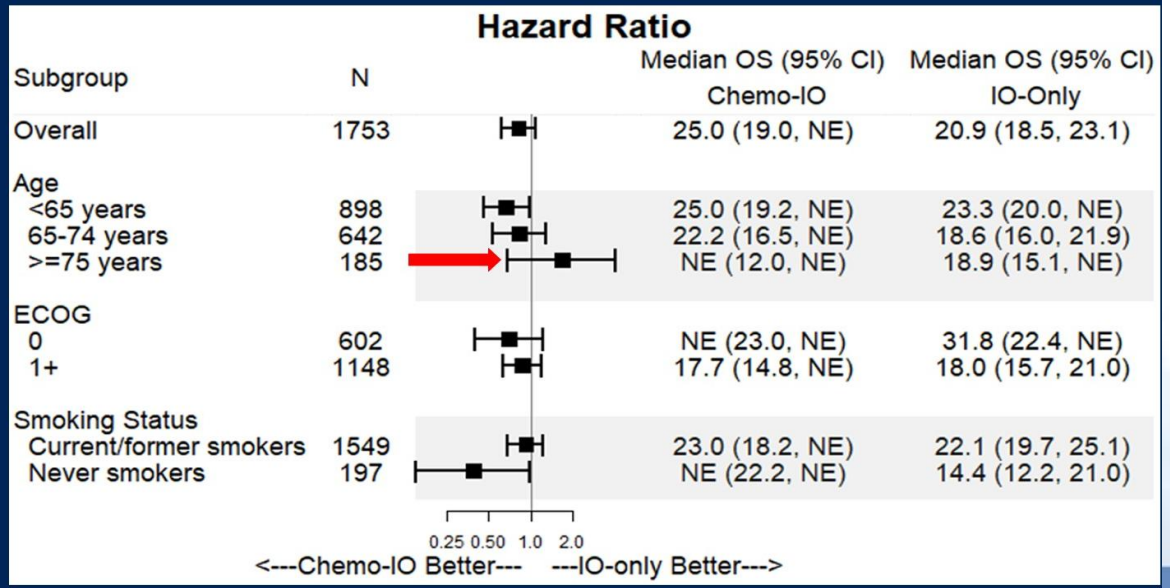
	Chemo-IO (*N*=455)	IO-alone (*N*=1,298)
OS		
Median, months (95% CI)	25.0 (19.0, NE)	20.9 (18.5, 23.1)
HR (95% CI)	0.82 (0.62, 1.08)	
PFS		
Median, months (95% CI)	9.6 (8.4, 11.1)	7.1 (6.3, 8.3)
HR (95% CI)	0.69 (0.55, 0.87)	
ORR		
% (95% CI)	61 (56, 66)	43 (41, 46)
Odds ratio	1.2 (1.1, 1.3)	

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.

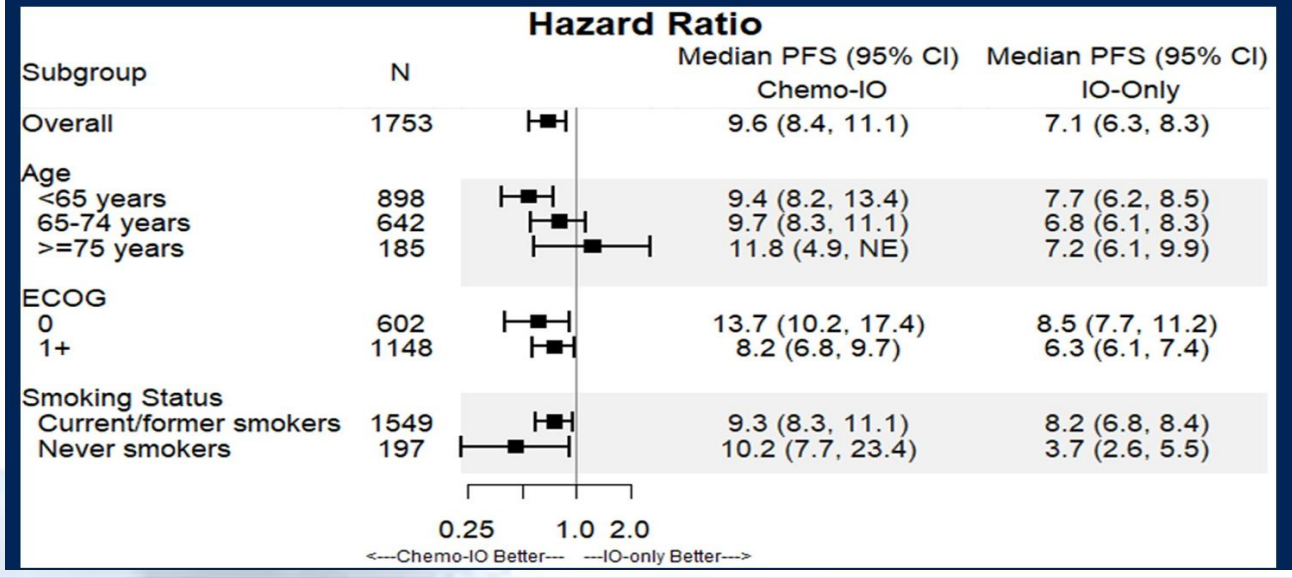




OS in NSCLC PD-L1 ≥50% in selected subgroups



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



2022 ASCO ANNUAL MEETING

Poster #9019: A phase II study of AK112 (PD-1/VEGF Bispecific) in combination with chemotherapy in patients with advanced non-small cell lung cancer (NSCLC)

Yuanyuan Zhao[1], Wenfeng Fang[1], Yunpeng Yang[1], Jianhua Chen[2], Li Zhuang[3], Yingying Du[4], Qitao Yu[5], Wu Zhuang[6], Yanqiu Zhao[7], Ming Zhou[8], Weidong Zhang[9], Yu Zhang[10], Yixin Wan[11], Ziping Wang[12], Lin Wang[13], Yu Xia[14], Baiyong Li[14], Zhongmin Maxwell Wang[14], Weifeng Song[14], Li Zhang[1]

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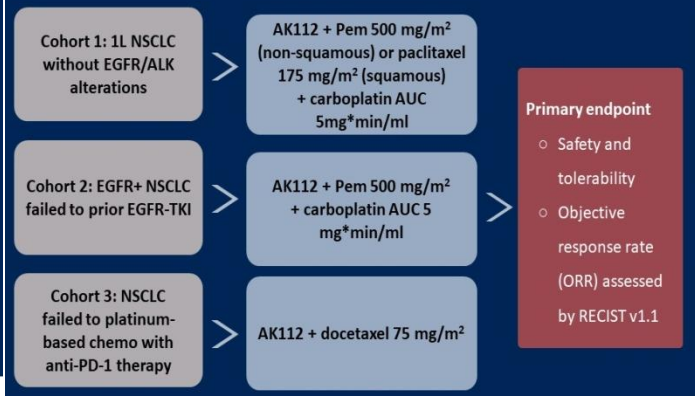
Study Design

- Patients with advanced NSCLC were Enrolled into 3 cohorts and treated with 10 or 20mg/kg AK112 plus chemotherapy once every 3 weeks.

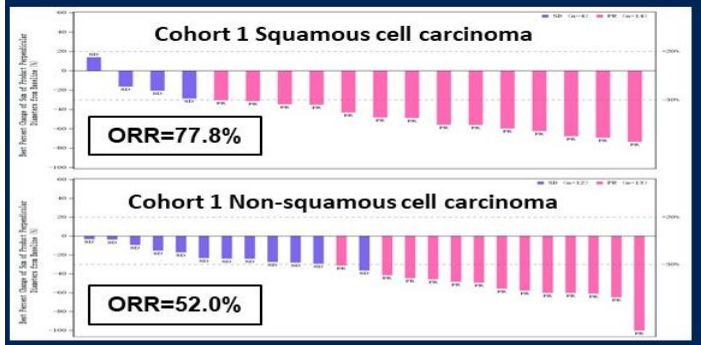


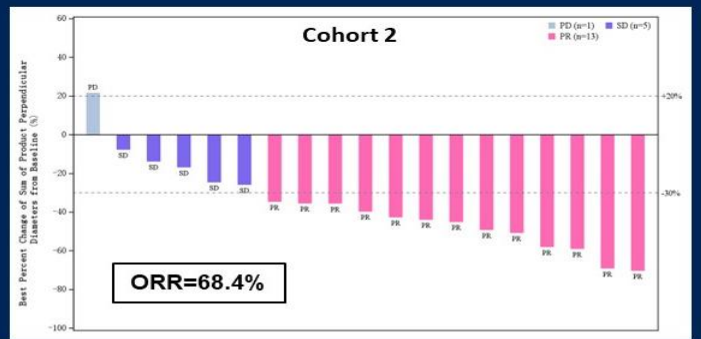
Enrollment

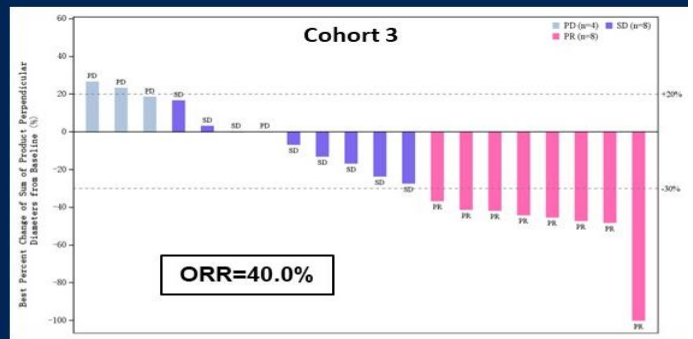
- 83 pts were enrolled from Feb 2021 to Mar 2022 to cohorts 1-3. Baseline characteristics are shown in the following table.

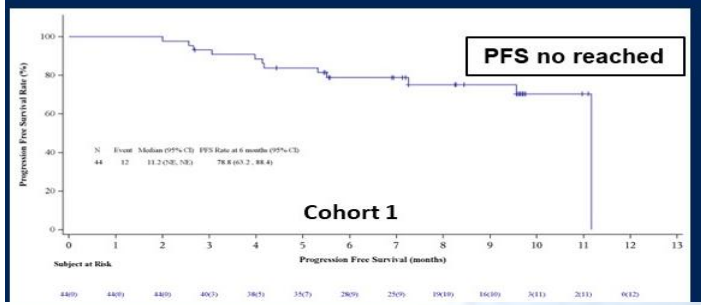
Characteristics	Cohort 1 (N = 44)	Cohort 2 (N = 19)	Cohort 3 (N = 20)	Overall (N = 83)
Age, median (range), years	57.6 (44.3, 73.0)	60.2 (34.7 - 64.9)	60.0 (31.6 - 73.4)	58.03 (31.6 - 73.4)
Male, n(%)	28 (63.6)	6 (31.6)	16 (80.0)	50 (60.2)
ECOG performance status, n(%)				
1	42 (95.5)	14 (73.7)	19 (95.0)	75 (90.4)
Smoking status, n(%)				
Former or Current	24 (54.5)	4 (21.1)	15 (75.0)	43 (51.8)
Never	20 (45.5)	15 (78.9)	5 (25.0)	40 (48.2)
PD-L1 TPS, n(%)				
<1%	20 (45.5)	10 (52.6)	6 (30.0)	36 (43.4)
1-49%	16 (36.4)	6 (31.6)	8 (40.0)	30 (36.1)
≥50%	6 (13.6)	3 (15.8)	4 (20.0)	13 (15.7)
NE	2 (4.5)	0 (0.0)	2 (10.0)	4 (4.8)
Clinical Stage at Study Entry, n(%)				
IIIB/IIIC	4 (9.1)	0 (0.0)	3 (15.0)	7 (8.4)
IV	40 (90.9)	19 (100.0)	17 (85.0)	76 (91.6)
Histology, n(%)				
Squamous	18 (40.9)	0 (0.0)	7 (35.0)	25 (30.1)
Non-squamous	26 (59.1)	19 (100.0)	13 (65.0)	58 (69.9)
Brain metastasis, n(%)	8 (18.2)	7 (36.8)	1 (5.0)	16 (19.3)

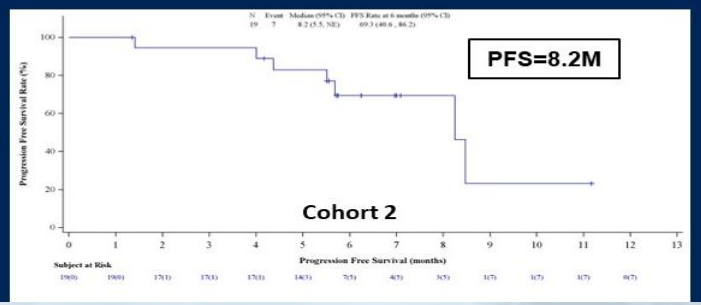
- As of Mar 20, 2022, median duration of follow-up (95% CI) was 9.2 months (range: 7.7 - 9.7) for Cohort 1; 7.0 months (range: 5.6 - 7.1) for Cohort 2; and 5.9 months (range: 4.4 - 6.9) for Cohort 3.

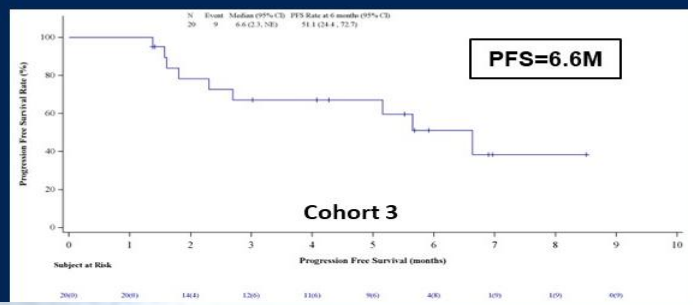












Phase 1/2a trial of nadunolimab, a first-in-class fully humanized monoclonal antibody against IL1RAP, in combination with cisplatin and gemcitabine (CG) in patients with non-small cell lung cancer (NSCLC)

A Paulus[1]; S Cicenas[2]; Z Zvirbule[3]; L Paz-Ares[4]; A Awada[5]; I Garcia Ribas[6]; N Losic[6]; M Zemaitis[7]

[1]CHU de Liège, Liege, Belgium; [2]National Cancer Institute, Vilnius, Lithuania; [3]Riga East Clinical University Hospital, Riga, Latvia; [4]Hospital Universitario 12 de Octubre, Madrid, Spain; [5]Institut Jules Bordet, Brussels, Belgium; [6]Cantargia AB, Lund, Sweden; [7]Department of Pulmonology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

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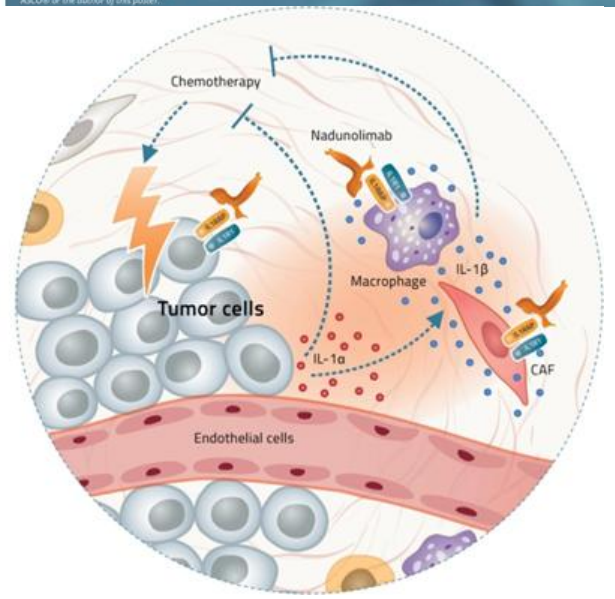
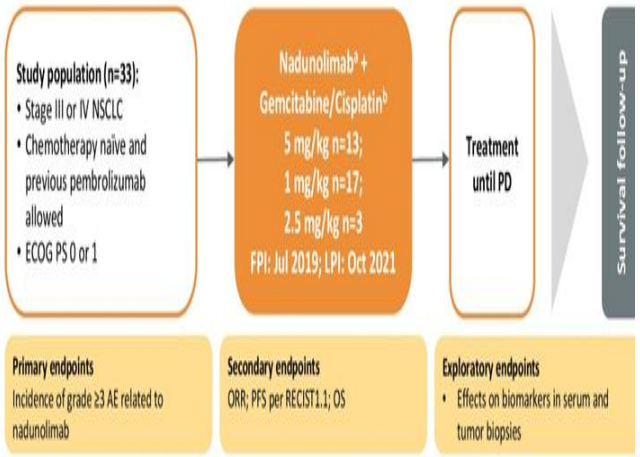
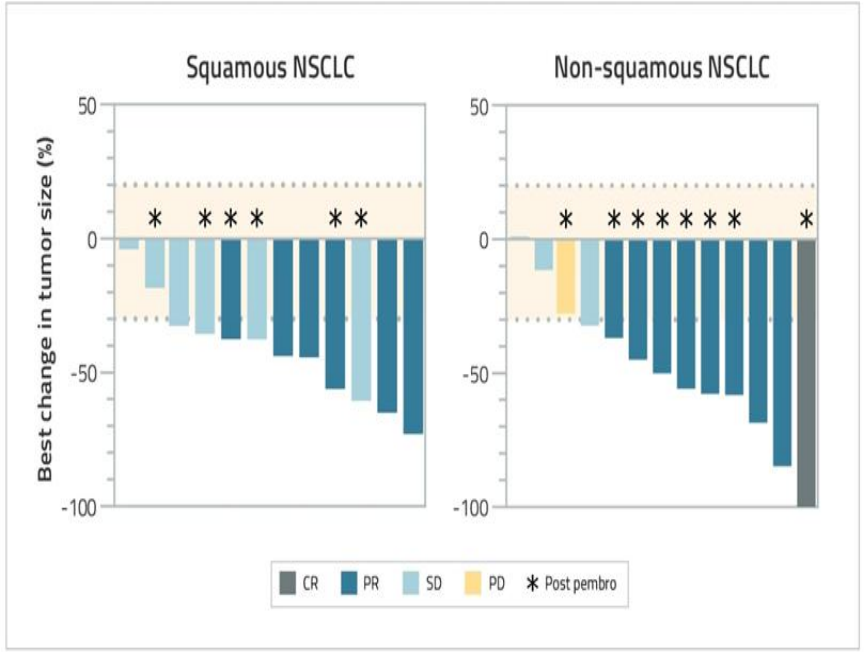


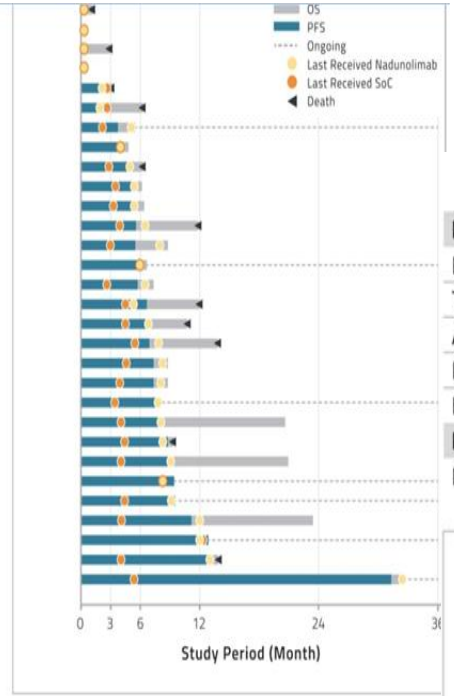
Study Design

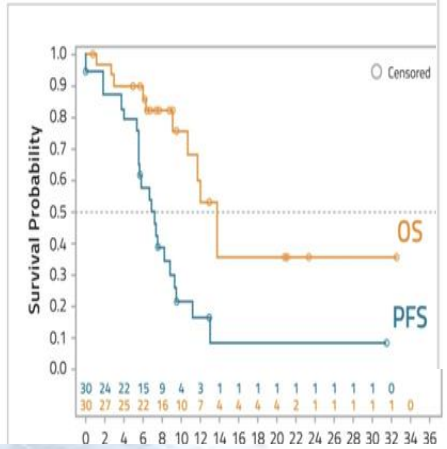


Efficacy parameter*	All (n=30)**	Non-squamous (n=16)	Squamous (n=13)
ORR [95% CI]	53% [34-72]	56% [30-80]	46% [19-75]
Disease control rate*** (CR+PR+SD) [95% CI]	83% [65-94]	75% [48-93]	92% [64-100]
Median duration of response [95% CI]	5.8 months [3.7-11.2]	11.2 months [NA]	4.1 months [3.4-5.8]
PFS [95% CI]	6.8 months [5.5-8.8]	7.3 months [5.3-13.0]	5.8 months [3.7-7.4]
Median OS [95% CI]	13.7 months**** [NA]	NA	NA
1-year survival [95% CI]	53%**** [26-73%]	NA	NA

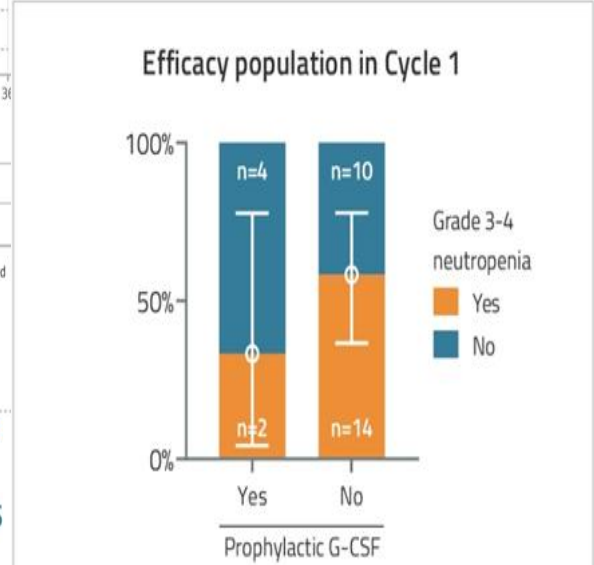
*Responses according to RECIST1.1 criteria
**One tumor of unknown histology
***Two patients withdrew early in association with COVID-19
****Based on 37% of events







	Grade 3-4	All grade
Hematological TEAE; n (%)		
Neutropenia	19 (58%)	24 (73%)
Thrombocytopenia	16 (49%)	24 (73%)
Anemia	10 (30%)	18 (55%)
Febrile neutropenia	4 (12%)	4 (12%)
Leukopenia/WBC decreased	3 (9%)	3 (9%)
Non-hematological TEAE; n (%)		
Pneumonia	3 (9%)	5 (15%)



A phase Ib/II study of AK112, a PD-1/VEGF bispecific antibody, as first or second-line therapy for advanced non-small cell lung cancer (NSCLC)

Caicun Zhou[1], Shengxiang Ren[1], Yongzhong Luo[2], Lei Wang[1], Anwen Xiong[1], Chunxia Su[1], Zhihong Zhang[3], Wei Li[1], Jin Zhou[4], Xinmin Yu[5], Yanping Hu[6], Xiaodong Zhang[7], Xiaorong Dong[8], Xiaoming Hou[9], Yuanrong Dai[10], Weifeng Song[11], Baiyong Li[11], Zhongmin Maxwell Wang[11], Yu Xia[11]

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Figure 2. Study design (Ib)

Key eligibility criteria

- 18-75 years old
- ECOG PS 0 or 1
- Life expectancy ≥ 3 months
- Histologically/cytologically-confirmed diagnosis of advanced NSCLC (stage IIIB/C that were unsuitable for radical therapy or IV)
- Treatment-naïve or with disease progression after platinum-containing chemotherapy
- No sensitizing EGFR mutations or ALK translocation
- At least one measurable lesion as defined by RECIST v1.1
- Adequate organ function

AK112 IV
10 mg/kg Q3W,
20 mg/kg Q2W,
20 mg/kg Q3W,
or 30 mg/kg Q3W

End of treatment
whichever occurs first:
- Disease progression as determined by the investigator according to RECIST v1.1
- Intolerable toxicity
- A maximum of 24 months

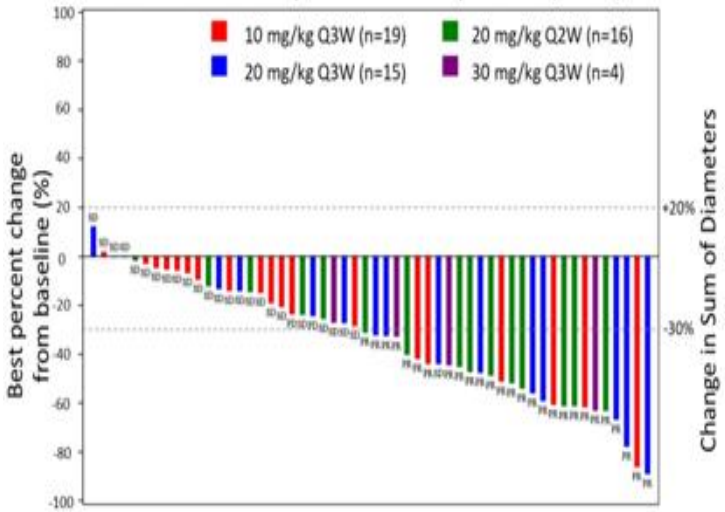
Primary endpoints
- Safety (graded according to NCI-CTCAE v5.0)
- ORR (investigator assessed) per RECIST v1.1

Secondary endpoints
- DoR, DCR, TTR and PFS per RECIST v1.1, and OS
- Pharmacokinetics
- ADA assessment
- Correlation between PD-L1 level and efficacy

Categories, n (%)	AK112 (N=96)
Grade 3/4 TRAEs	13 (13.5)
Pneumonia	3 (3.1)
Hypertension	1 (1.0)
Proteinuria	1 (1.0)
Diarrhoea	1 (1.0)
Pyrexia	1 (1.0)
Urticaria chronic	1 (1.0)
Rhabdomyolysis	1 (1.0)
Hepatic failure	1 (1.0)
Lacunar infarction	1 (1.0)
Cognitive disorder	1 (1.0)
Tracheo-oesophageal fistula	1 (1.0)
Most frequent TRAEs (incidence ≥10%)	
Proteinuria	19 (19.8)
Hypertension	15 (15.6)
Blood urea increased	15 (15.6)
Blood cholesterol increased	14 (14.6)
Hyperglycaemia	14 (14.6)
Lipase increased	13 (13.5)
Apolipoprotein E increased	13 (13.5)
Alanine aminotransferase increased	12 (12.5)
C-reactive protein increased	11 (11.5)
Aspartate aminotransferase increased	11 (11.5)
Amylase increased	10 (10.4)

Best percentage change in tumor size from baseline

Treatment-naïve pts with PD-L1 positive (N=54)



Spider Plot of Percentage Change from Baseline

Treatment-naïve pts with PD-L1 positive (N=54)

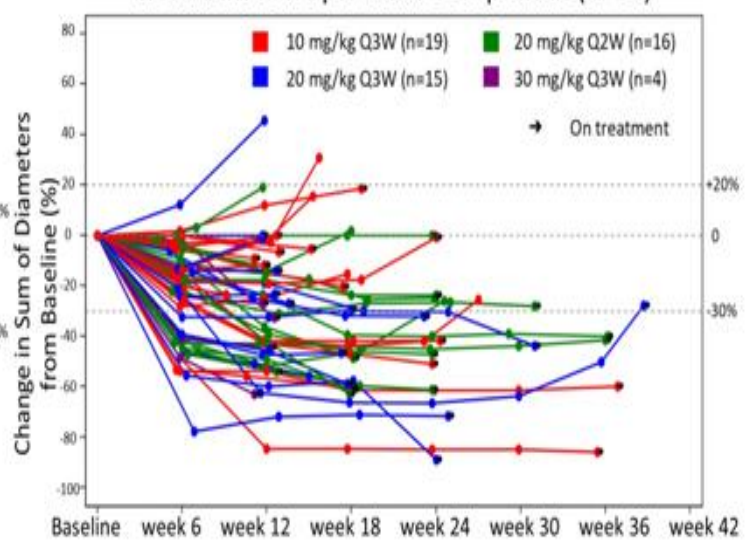


Table 3. Response rate of treatment-naïve pts (AK112 > 10mg/kg Q3W)

PD-L1 TPS	≥ 1% (N=35)	1-49% (N=22)	≥ 50% (N=13)	< 1% (N=15)	Total (N=50)
ORR, %	60.0	50.0	76.9	13.3	46.0
DCR, %	97.1	95.5	100.0	66.7	88.0
CR, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PR, n (%)	21 (60.0)	11 (50.0)	10 (76.9)	2 (13.3)	23 (46.0)
SD, n (%)	13 (37.1)	10 (45.5)	3 (23.1)	8 (53.3)	21 (42.0)
PD, n (%)	1 (2.9)	1 (4.5)	0 (0.0)	5 (33.3)	6 (12.0)
NE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)