elcc European Lung Cancer Congress 2023

Long-term efficacy, safety and predictors of response to amivantamab among patients with post-platinum EGFR Ex20ins-mutated advanced NSCLC

Pilar Garrido,[1] Nicolas Girard,[2] Byoung Chul Cho,[3] Joshua K Sabari,[4] Alexander I Spira,[5] Rachel E Sanborn,[6] Koichi Goto,[7] James Chih-Hsin Yang,[8] Joshua C Curtin,[9] Xuesong Lyu,[10] Andy He,[11] James Penton,[12] Joanne Edwards,[12] Grace Low,[13] Karen Xia,[9] Marc Chioda,[9] Meena Thayu,[9] Roland E Knoblauch,[9] Parthiv Mahadevia,[9] Natasha B Leighl[14]

[1]University Hospital Ramón y Cajal, Madrid, Spain; [2]Institut Curie, Paris, France; [3]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [4]NYU Langone Health, New York, NY, USA; [5]Virginia Health Specialists, Fairfax, VA, USA; [6]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; [7]National Cancer Center Hospital East, Kashiwa, Japan; [8]National Taiwan University Cancer Center, Taipei, Taiwan; [9]Janssen R&D, Spring House, PA, USA; [10]Janssen R&D, Shanghai, China; [11]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [12]Janssen EMEA, High Wycombe, UK; [13]Janssen Asia-Pacific, Singapore; [14]Princess Margaret Cancer Centre, Toronto, ON, Canada

Organisers

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

IASLC

Partners

ESTRO

ESTS

etop Information | Research

DECLARATION OF INTERESTS

Pilar Garrido

Personal financial interests

Consultancy/honoraria from AbbVie, Amgen, AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Daiichi Sankyo, GlaxoSmithKline, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi and Takeda

Direct funding from Medscape and Touch Medical

Institutional research funding

Amgen, AstraZeneca, Blueprint, Bristol Myers Squibb, Boehringer Ingelheim, Daiichi Sankyo, GlaxoSmithKline, Janssen, IO Biotech, Lilly, MSD, Novartis, Pharmamar, Pfizer, Roche, Sanofi, Takeda, and Theradex Oncology

Nonfinancial interests

ESMO Council Member as Women for Oncology Committee Chair

ESMO Faculty for Lung and Other Thoracic Tumours

IASLC Academy and Educational Committee Member

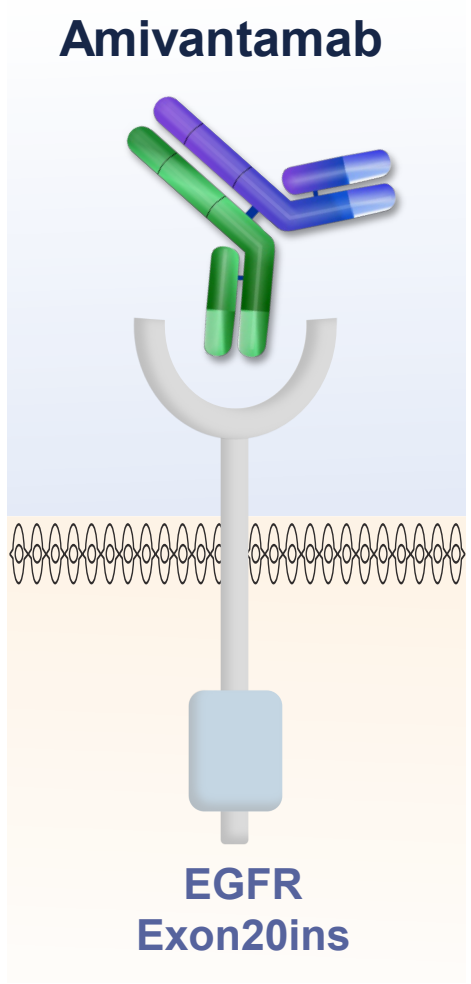
Former President of Spanish Medical Oncology Society and Spanish Federation of Medical Societies (FACME)

Member of the Spanish National Health Advisory Board

President of the Technical Committee and Member of the Scientific Committee of the Spanish Against Cancer Research Foundation (AECC)

EGFR Exon 20 Insertion Mutations (Ex20ins) NSCLC

- Ex20ins are the third most frequent EGFR mutation after the common mutations[a]
- **Amivantamab**, an EGFR and MET bispecific antibody with immune cell-directing activity, is approved to treat patients with EGFR Ex20ins advanced NSCLC whose disease progressed on platinum-based chemotherapy
- The CHRYSALIS study (ClinicalTrials.gov Identifier: NCT02609776) evaluated amivantamab monotherapy among post-platinum patients at the recommended phase 2 dose (1050 mg <80 kg; 1400 mg ≥80kg)
    - The initial (WCLC 2020) presentation,[b] with a median follow-up of 9.7 months, showed a BICR-assessed overall response rate of 40% with a duration of response of 11.1 months[1]
- This report presents long-term results for the patients with EGFR Ex20ins advanced NSCLC whose disease progressed on platinum-based chemotherapy



elcc European Lung Cancer Congress 2023

[a]Common mutations defined as Exon 19 deletions and Exon 21 L858R.[2,3]
[b]Included patients had ≥1 dose of amivantamab monotherapy at the RP2D (administered intravenously weekly for the first 4 weeks [Cycle 1] and then biweekly thereafter) and were exposed by 8 June 2020.
BICR, blinded independent central review; EGFR, epidermal factor growth receptor; Ex20ins, Exon 20 insertion mutations; MET, mesenchymal-epithelial transition factor; NSCLC, non–small cell lung cancer; RP2D, recommended phase 2 dose.

1. Sabari JK, et al. Oral presentation at: International Association for the Study of Lung Cancer (IASLC) 2020 World Conference on Lung Cancer; 28-31 January 2021; Singapore. Accessed 3 March 2023.
2. Riess JW, et al. *J Thorac Oncol*. 2018;13(10):1560-1568; 3. Vyse S, et al. *Signal Transduct Target Ther*. 2019;4:5.

Demographics and Baseline Disease Characteristics

- A total of 114 heavily-pretreated patients were included in this analysis[a]

Characteristic, n (%)	n=114
Median age, years (range)	62 (36–84)
Male / female	44 (39) / 70 (61)
Race	
Asian	59 (52)
White	42 (37)
Black	3 (3)
Not reported	10 (9)
Smoking history	
Nonsmoker	65 (57)
Smoker	49 (43)

Characteristic, n (%)	n=114
Baseline brain metastases	29 (25)
ECOG PS	
0	33 (29)
1	80 (70)
2	1 (1)
Median (range) prior lines	2 (1–7)
Prior platinum chemo	114 (100)
Prior immunotherapy	50 (44)
Prior EGFR TKI	23 (20)

elcc European Lung Cancer Congress 2023

[a]Data cutoff date: 12 Sept 2022 (median follow-up of 19.2 months).
Note: Percentages may not add to 100 due to rounding.
ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

Safety Profile

	Ex20ins Post-Platinum (n=114)		RP2D (n=474)	
AEs (≥15%) by preferred term, n (%)	**Total**	**Grade ≥3**	**Total**	**Grade ≥3**
EGFR-related				
Paronychia	66 (58)	4 (4)	204 (43)	9 (2)
Dermatitis acneiform	54 (47)	1 (1)	165 (35)	5 (1)
Rash	49 (43)	2 (2)	167 (35)	8 (2)
Stomatitis	29 (25)	1 (1)	97 (20)	2 (0.4)
Pruritus	23 (20)	0	84 (18)	0
Diarrhea	21 (18)	4 (4)	53 (11)	6 (1)
MET-related				
Hypoalbuminemia	45 (39)	5 (4)	153 (32)	11 (2)
Peripheral edema	31 (27)	1 (1)	119 (25)	5 (1)
Other				
Infusion-related reaction	76 (67)	3 (3)	319 (67)	14 (3)
Nausea	32 (28)	1 (1)	111 (23)	3 (1)
Constipation	30 (26)	0	115 (24)	1 (0.2)
Fatigue	30 (26)	4 (4)	100 (21)	9 (2)
Dyspnea	29 (25)	6 (5)	101 (21)	24 (5)
Cough	24 (21)	0	87 (18)	0
Arthralgia	24 (21)	0	53 (11)	1 (0.2)
Back pain	23 (20)	1 (1)	66 (14)	4 (1)
Decreased appetite	23 (20)	1 (1)	83 (18)	2 (0.4)
Alanine aminotransferase increased	20 (18)	4 (4)	80 (17)	10 (2)
Dry skin	19 (17)	0	59 (12)	0
Vomiting	19 (17)	1 (1)	59 (12)	2 (0.4)
AEs of special interest by grouped term, n (%)				
Rash[a]	102 (89)	5 (4)	349 (74)	17 (4)
Interstitial lung disease[b]	8 (7)	0	16 (3)	4 (1)
Venous thromboembolism[c]	13 (11)	7 (6)	50 (11)	25 (5)

- No new safety signals were detected
- Treatment-related dose interruptions, reductions and discontinuations were seen in 33 (29%), 20 (18%), and 8 (7%) patients, respectively
- Cumulative grouped rash[a] and infusion-related reactions remained the most frequent toxicities

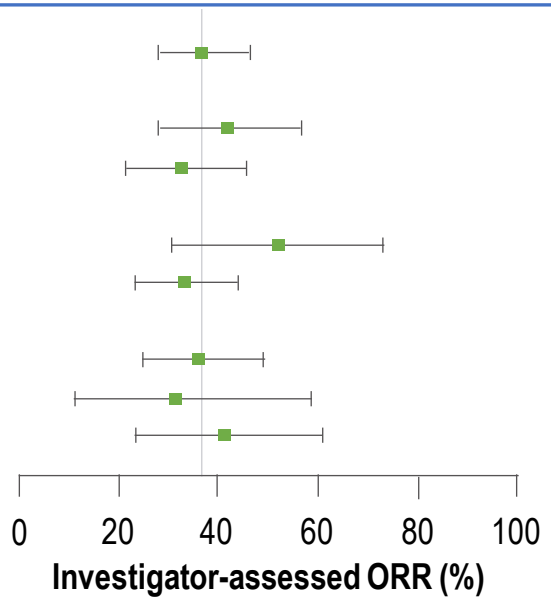
[a]Grouping includes the following related preferred terms: rash, dermatitis acneiform, rash maculo-papular, folliculitis, erythema, rash pustular, acne, palmar-plantar erythrodysaesthesia syndrome, rash erythematous, rash papular, skin lesion, rash pruritic, dermatitis, skin exfoliation, dermatitis exfoliative generalized, macule, pustule, blister, dermatitis atopic, dermatitis bullous, dermatitis infected, eczema asteatotic, erythema multiforme, hand dermatitis, perineal rash, perioral dermatitis, rash macular, rash vesicular, and toxic epidermal necrolysis. [b]Includes interstitial lung disease and pneumonitis. [c]Includes pulmonary embolism, deep vein thrombosis, embolism, thrombophlebitis superficial, venous thrombosis limb, pulmonary thrombosis, and thrombosis.

AE, adverse event; EGFR, epidermal factor growth receptor; MET, mesenchymal-epithelial transition factor; RP2D, recommended phase 2 dose.

Subgroup Efficacy Based on Prior Therapies

- As of 12 Sept 2022, the investigator-assessed ORR was 37% (95% CI, 28–46), with a median duration of response of 12.5 months (95% CI, 6.9–19.3)[a]
- Amivantamab demonstrated consistent efficacy regardless of prior therapies or response to prior platinum chemo

Subgroups	n (%)	No. of responders	ORR (95% CI)
All	114 (100)	42	36.8% (28.0–46.4)
Prior immunotherapies?			
Y	50 (43.9)	21	42.0% (28.2–56.8)
N	64 (56.1)	21	32.8% (21.6–45.7)
Prior EGFR TKI(s)?			
Y	23 (20.2)	12	52.2% (30.6–73.2)
N	91 (79.8)	30	33.0% (23.5–43.6)
Response to prior platinum chemo			
CR, PR, or SD	69 (60.5)	25	36.2% (25.0–48.7)
PD	16 (14.0)	5	31.2% (11.0–58.7)
Unknown/NA	29 (25.4)	12	41.4% (23.5–61.1)



- As previously presented,[1] there were no differences for the subgroups by age, sex, race, baseline ECOG PS, number of prior lines, smoking history, or baseline brain metastases

elcc European Lung Cancer Congress 2023

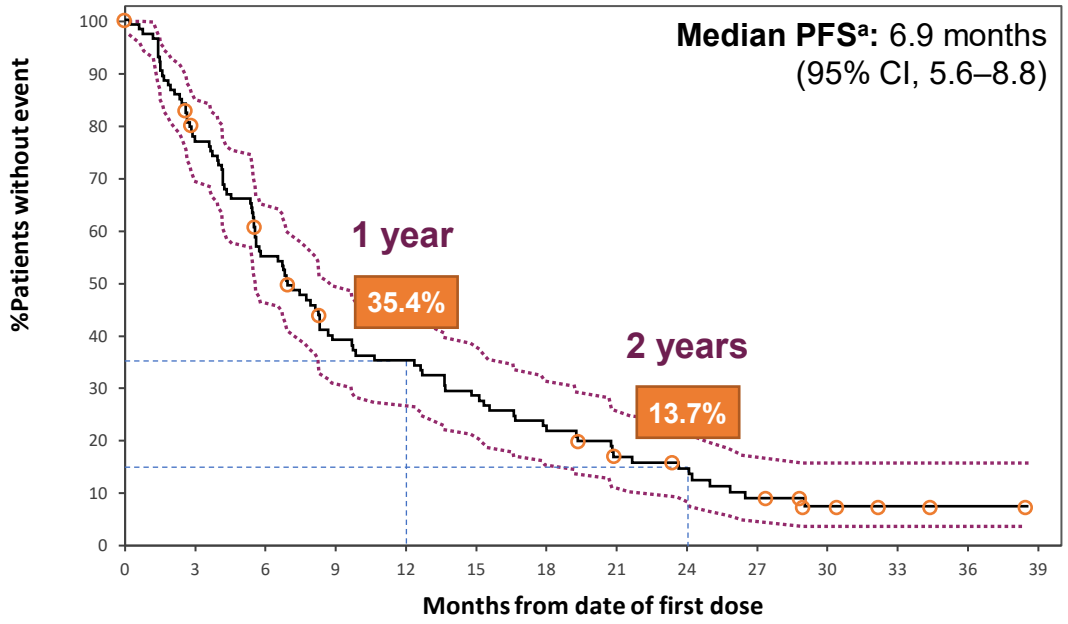
[a]As of 30 March 2021, ORR by blinded independent central review was 43%, with a median duration of response of 10.8 months.[1]

CI, confidence interval; chemo, chemotherapy; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal factor growth receptor; ORR, overall response rate; PD, progressive disease; PR, partial response; NA, not available; SD, stable disease; TKI, tyrosine kinase inhibitor.

1. Sabari JK, et al. Oral presentation at: International Association for the Study of Lung Cancer (IASLC) 2020 World Conference on Lung Cancer; 28-31 January 2021; Singapore. Accessed 3 March 2023

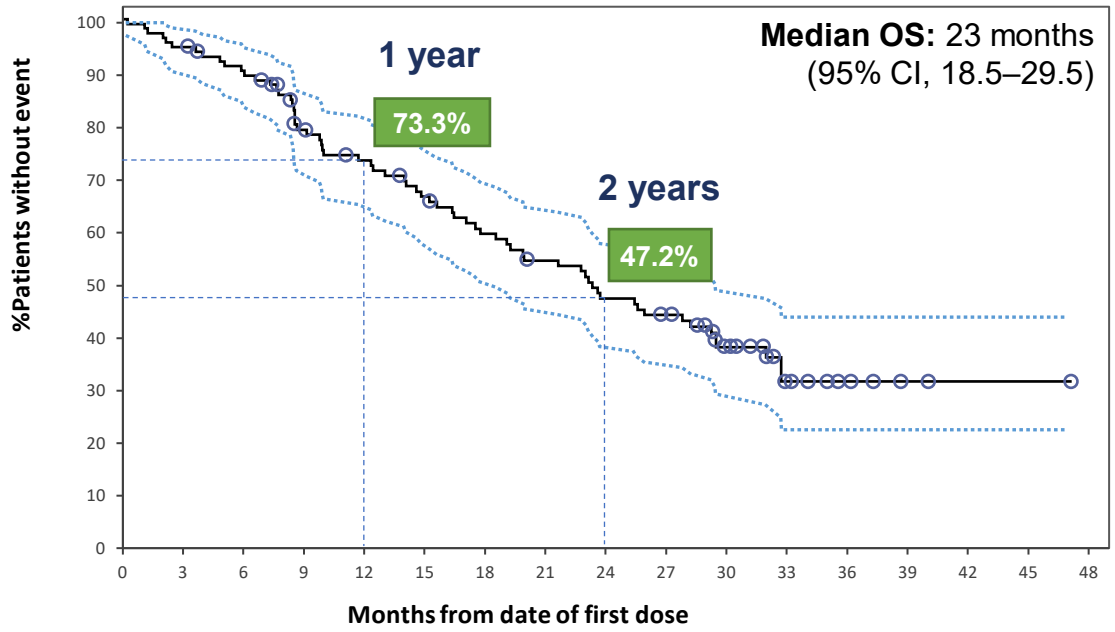
Long-term Outcomes Observed With Amivantamab

Progression-free Survival



Patients at risk														
	114	85	60	41	37	30	23	16	12	8	4	2	1	0

Overall Survival



Patients at risk																
	114	108	101	83	75	67	59	53	46	42	26	13	6	3	2	2	0

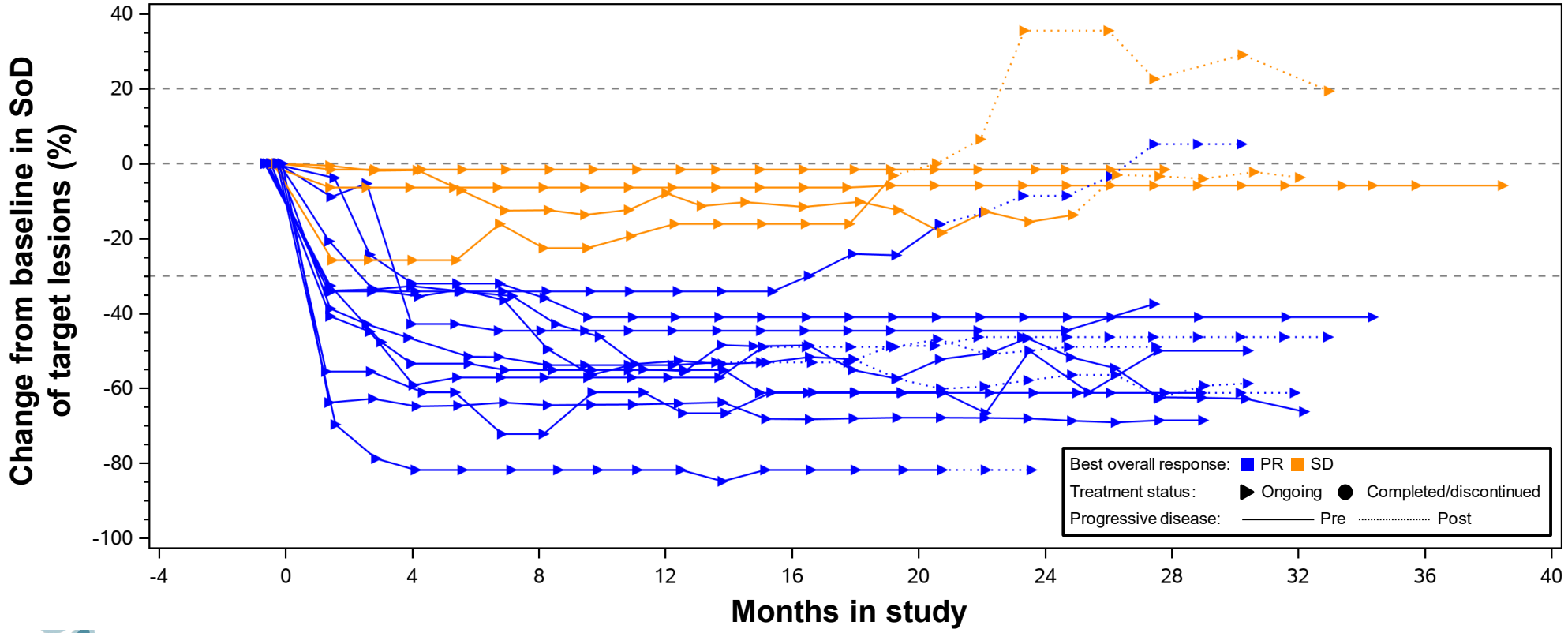
- As of 12 Sept 2022, the median follow-up was 19.2 months and median duration of treatment was 7.5 months, with 48 of 114 (42%) patients alive

elcc European Lung Cancer Congress 2023

[a]As assessed by the investigator.
CI, confidence interval; PFS, progression-free survival; OS, overall survival.

Long-term Clinical Benefit of Amivantamab

- There were 48 (42%) patients who had sustained clinical benefit (on amivantamab for ≥12 cycles[a])
- Treatment is ongoing in 15 of 114 (13%) patients who have received amivantamab for a median of 2.6 years
  - Of these, 7 are progression-free and 8 are receiving treatment beyond progression



[a]Cycle duration was 28 days.
PR, partial response; SD, stable disease; SoD, sum of diameters.

Demographic Predictors of Sustained Clinical Benefit

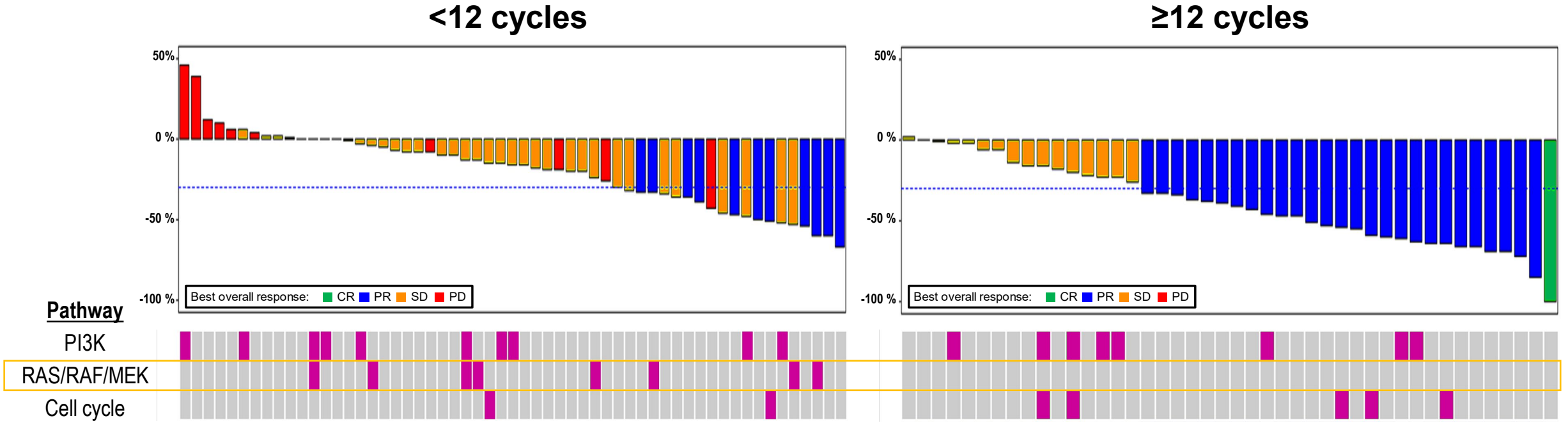
Demographic	<12 cycles (n=66)	≥12 Cycles (n=48)	Nominal *P*-value
Age, median (range), years	62.5 (41–84)	60 (36–84)	0.4
Sex, n (%)			0.2
Female	44 (67)	26 (54)	
Male	22 (33)	22 (46)	
Race, n (%)			0.4
Asian	34 (52)	25 (52)	
Non-Asian	28 (42)	17 (35)	
Unknown	4 (6)	6 (13)	
BMI category, n (%)			0.057
Underweight (<18.5)	10 (15)	1 (2)	
Normal (18.5 to <25)	38 (58)	27 (56)	
Overweight (25 to <30)	13 (20)	12 (25)	
Obese (≥30)	5 (8)	8 (17)	

Characteristic	<12 cycles (n=66)	≥12 Cycles (n=48)	Nominal *P*-value
ECOG PS, n (%)			
0	13 (20)	20 (42)	0.021
1	52 (79)	28 (58)	
2	1 (2)	0	
Brain metastases, n (%)	17 (26)	12 (25)	>0.9
Smoker,[a] n (%)	27 (41)	22 (46)	0.6
Prior lines of therapy, median (range)	2 (1–6)	2 (1–7)	>0.9
Prior platinum chemo as last line	40 (61)	32 (67)	0.5
Prior immunotherapy	31 (47)	19 (40)	0.4
Prior EGFR TKI	14 (21)	9 (19)	0.7

- In univariate analysis, ECOG PS of 0 was associated with sustained clinical benefit
- There was a trend for underweight patients being associated with shorter treatment

[a]Includes current smokers and those with a history of smoking.
Note: Percentages may not add to 100 due to rounding.
BMI, body mass index; chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal factor growth receptor; TKI, tyrosine kinase inhibitor.

Absence of Baseline RAS/RAF/MEK Alterations[a] Was Associated With Sustained Clinical Benefit



- Patients with baseline alterations[a] in the RAS/RAF/MEK pathway were only seen in the <12 treatment cycles group, with none occurring in the ≥12 cycles group
- Having a PR or better was also associated with sustained clinical benefit

Authors would like to acknowledge Clarivate for their contributions to the biomarker analyses.

[a]Genomic profile obtained from plasma ctDNA at baseline prior to starting amivantamab.
CR, complete response; ctDNA, circulating-tumor DNA; PD, progressive disease; PR, partial response; SD, stable disease.

Conclusions

Treatment Benefit

- After a median of 2 prior lines of therapy and a median follow-up of 19.2 months:
  - The median OS of amivantamab was 23 months, with a 2-year landmark OS rate of 47%
  - 13% of patients remain on treatment for a median treatment duration of 2.6 years
- Among post-platinum patients with EGFR Ex20ins advanced NSCLC, amivantamab demonstrated consistent efficacy regardless of prior therapy type
- Sustained clinical benefit (≥12 cycles) was associated with:
  - Good performance status
  - Having a response
  - Not having baseline alterations in the RAS/RAF/MEK pathway

Safety

- No new safety signals were detected, with low rates of treatment-related discontinuations

Next Steps

- The phase 3 PAPILLON study (ClinicalTrials.gov Identifier: NCT04538664) is investigating amivantamab + chemotherapy vs chemotherapy in the frontline EGFR Ex20ins NSCLC setting

EGFR, epidermal factor growth receptor; Ex20ins, Exon 20 insertion mutations; NSCLC, non–small cell lung cancer; OS, overall survival.