

Administration of Amivantamab

Center for Medicare & Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting
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Non-Small Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Exon 20 Insertion Mutations

- An estimated 4-10% of epidermal growth factor receptor (EGFR) mutated non-small cell lung cancer (NSCLC) harbors Exon 20 insertion (Exon20ins) mutations.¹
- No products are FDA approved for the treatment of NSCLC with Exon20ins mutations.
- Therapies currently employed in this patient population, such as EGFR tyrosine kinase inhibitors (TKIs) and chemotherapy, have limited effectiveness.^{1,2}
- Treatment options are limited for patients with Exon20ins mutation who progress after platinum-based chemotherapy, with no clear standard of care (SOC) in this treatment setting.
- 5-year survival is 8%.³

1 Vyse, 2019. 2. Zhao, WCLC, 2019. 3. Girard, WCLC, 2020.

Outcomes for 2nd Line EGFR Exon-20 Insertion Mutation Patients are Very Poor

- Among EGFR Exon-20 Insertion patients receiving mix of 2nd Line therapies* in the Flatiron Core NSCLC Registry:
 - Real-world Tumor Response (surrogate for ORR) was **13%**¹
 - Real-world Progression Free Survival was **3.5 months**¹
 - Real-world Overall Survival was **<12 months**²

* Therapies include tyrosine kinase inhibitors, checkpoint inhibitors, VEGF inhibitors and chemotherapy

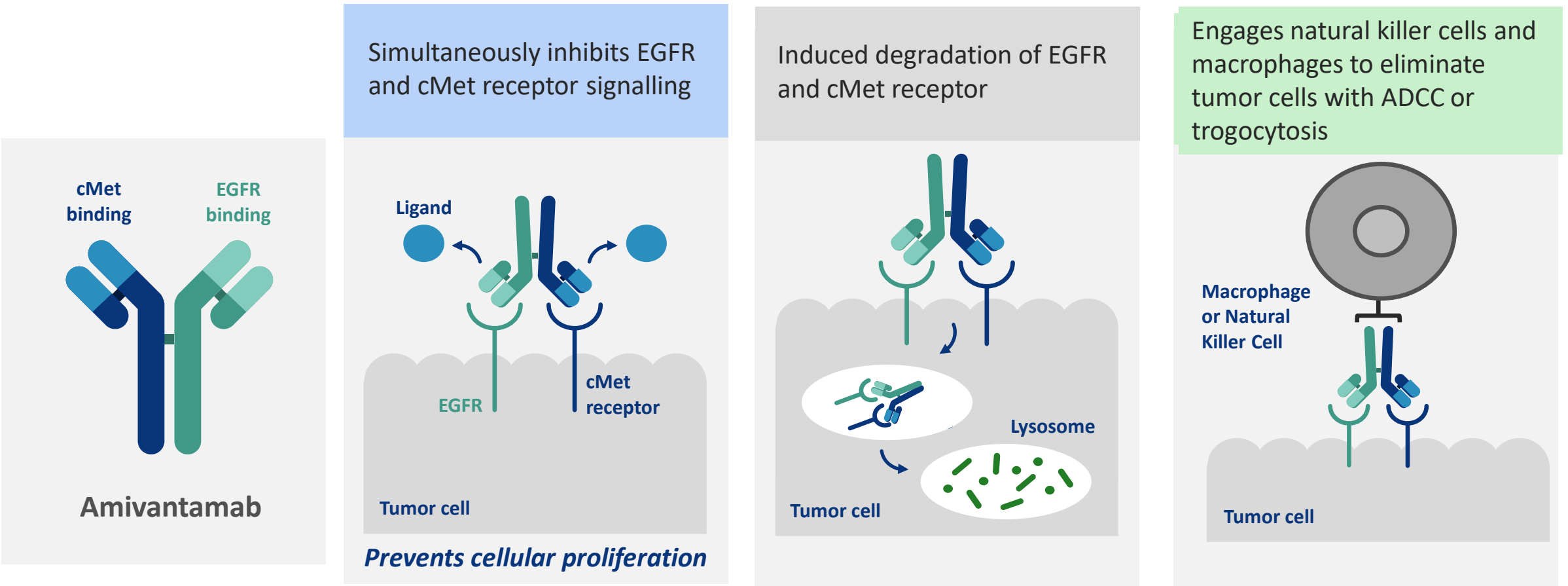
1. Horne, et al. ASCO 2020. 2. DerSarkissian, et al. WCLC 2019.

Amivantamab Product Overview

- Amivantamab is a fully human bispecific antibody that binds to the extracellular domains of the epidermal growth factor (EGF) and mesenchymal epithelial transition (MET) receptors.
- Amivantamab is currently under investigation in patients with metastatic NSCLC with EGFR Exon 20 insertion (Exon20ins) mutations, whose disease has progressed on or after platinum-based chemotherapy.
 - On March 10, 2020, amivantamab was granted FDA Breakthrough Therapy Designation.¹
 - The submission of a Biologics License Application to the FDA was announced on December 3, 2020.²
- Amivantamab (JNJ-372) will have a trade name upon FDA approval. Currently, it has no other identifiers.

1. Janssen announces U.S. FDA Breakthrough Therapy Designation granted for JNJ-6372 for the treatment of non-small cell lung cancer. March 10, 2020. <https://www.jnj.com/janssen-announces-u-s-fda-breakthrough-therapy-designation-granted-for-jnj-6372-for-the-treatment-of-non-small-cell-lung-cancer>. 2. Janssen Submits Application to U.S. FDA Seeking Approval of Amivantamab for the Treatment of Patients with Metastatic Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations <https://www.jnj.com/janssen-submits-application-to-u-s-fda-seeking-approval-of-amivantamab-for-the-treatment-of-patients-with-metastatic-non-small-cell-lung-cancer-with-egfr-exon-20-insertion-mutations>

Amivantamab Mechanism of Action¹



Amivantamab is anticipated to be the first FDA-approved bispecific antibody therapy targeting EGFR and MET mutations simultaneously.

ADCC, antibody-dependent cellular cytotoxicity; cMET, mesenchymal-epithelial transition factor; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

1. Park K, et al. Poster presented at: American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program; May 29-31, 2020.

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NOTE: Amivantamab has been built by Janssen R&D using Genmab DuoBody® technology.

CHRYSALIS Study Design

Phase 1 Study

Key Objectives

- Part 1: Establish RP2D(s)
- Part 2: Safety and preliminary efficacy at RP2D(s)
- PK and immunogenicity

Key Eligibility Criteria

- Metastatic/unresectable NSCLC
- Progressed on prior therapy or ineligible for or refused current therapies
- ECOG PS ≤1
- Evaluable (Part 1) or measurable disease (Part 2)
- Activating EGFR or MET mutations or amplifications and progressed on previous SOC (Part 2)
- Previously definitively treated brain metastases allowed

Part 1 Dose Escalation (28-day cycle)

1750 mg

1400 mg

1050 mg

700 mg

350 mg

140 mg

RP2D

1050 mg (<80 kg)
1400 mg (≥80 kg)

C1 weekly
C2+ biweekly

Part 2 Dose Expansion (28-day cycle)

Cohort C:
Post-EGFR-3GTLI,
C797S+

Cohort D:
EGFR Exon20ins

Cohort MET-1:
MET amp,
post-EGFR-TKI

Cohort MET-2:
MET Exon14
skipping

- The analysis presented here includes all enrolled patients with Exon20ins mutations who received the recommended phase 2 dose (RP2D)

- The safety population (N=50) included all patients who received amivantamab at the RP2D
- The response-evaluable population (n=39) included patients who had at least 2 disease assessments or had discontinued therapy

3GTLI, 3rd generation tyrosine kinase inhibitor; Amp, amplification; C, cycle; ECOG PS, Eastern Cooperative Oncology Group performance status; Exon20ins, Exon 20 insertion; NSCLC, non-small cell lung cancer; PK, pharmacokinetics; RP2D, recommended phase 2 dose; SOC, standard of care.

Demographics

	Total (N=39)
Median age, years (range)	61 (40–78)
Male, n (%)	19 (49)
Race, n (%)	
Asian	25 (64)
Black	1 (3)
White	11 (28)
Not reported	2 (5)
ECOG PS, n (%)	
0	14 (36)
1	24 (62)
2	1 (3)
Median time from initial diagnosis, months (range)	12 (1–56)
Adenocarcinoma, n (%)	39 (100)
Exon20ins mutation, n (%)	39 (100)
Median prior lines, n (range)	1 (0–7)
Prior systemic therapies, n (%)	33 (85)
Platinum-based chemotherapy	29 (74)
Immuno-oncology therapy*	13 (33)
EGFR TKI	9 (23)
Bevacizumab	4 (10)
No prior therapy	6 (15)

*Nivolumab, atezolizumab, pembrolizumab, durvalumab.

- 29/39 (74%) response-evaluable patients had received prior platinum-based chemotherapy in the metastatic setting

EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.

Safety

AEs in Patients Treated at the RP2D, n (%)	Total (N=50) ¹
Adverse Events in the Safety Population	
Any AE	48 (96)
Serious AE	14 (28)
Grade ≥3 AE	18 (36)
AEs leading to death (all unrelated to amivantamab)	4 (8)
AEs leading to discontinuation	3 (6)
AEs leading to dose reduction	5 (10)
AEs leading to dose interruption*	15 (30)
All-grade AEs (≥15%)	
Rash [†]	36 (72)
Infusion related reaction	30 (60)
Paronychia	17 (34)
Constipation	13 (26)
Hypoalbuminemia	11 (22)
Dyspnea	10 (20)
Fatigue	9 (18)
Back pain	8 (16)
Stomatitis	8 (16)

*Excludes infusion related reactions.

[†]Includes dermatitis acneiform, rash, rash generalized, rash maculo-popular, rash pustular, rash papular, erythema, generalized erythema, rash erythematous, macule, perineal rash, rash pruritic, dermatitis

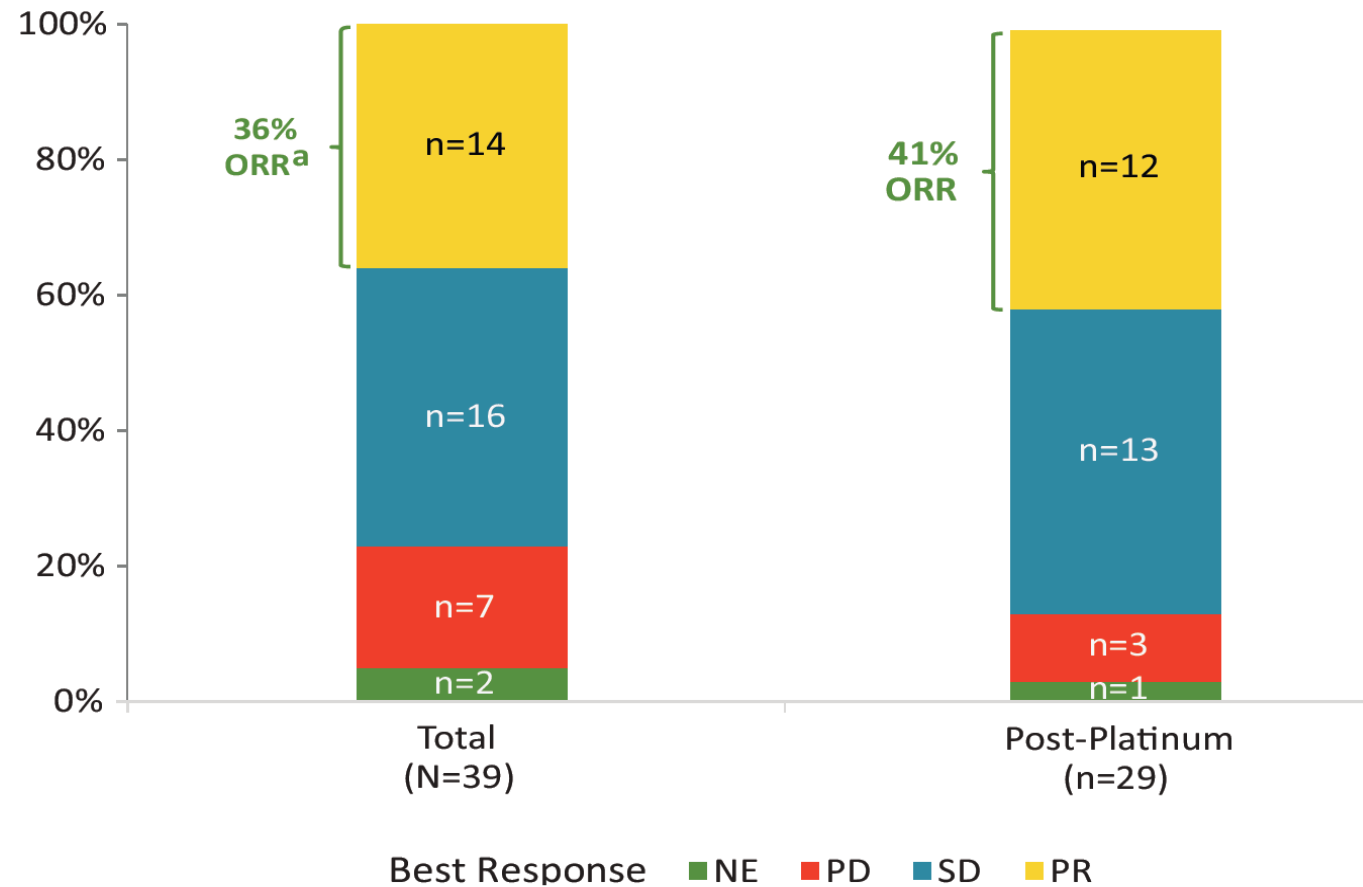
AE, adverse event.

- AEs were reported in 96% of patients treated at the RP2D and were mostly grade 1 to 2 (60%)
- Dose reduction (5 [10%]) and discontinuation (3 [6%]) due to AEs were infrequent
- Most common all-grade AEs were rash, infusion related reaction (IRR), and paronychia
 - IRR occurred predominantly on the first infusion and did not prevent subsequent treatments.
- No grade ≥3 rash was reported, and 1 patient reported grade 3 diarrhea (3 [6%] patients had diarrhea of any grade)
- Treatment-related serious AEs of cellulitis, interstitial lung disease, and shoulder/chest pain were reported in 3 (6%) patients
- AEs leading to death were not considered treatment-related

¹The safety population (N=50) included all patients who received amivantamab at the RP2D

Efficacy

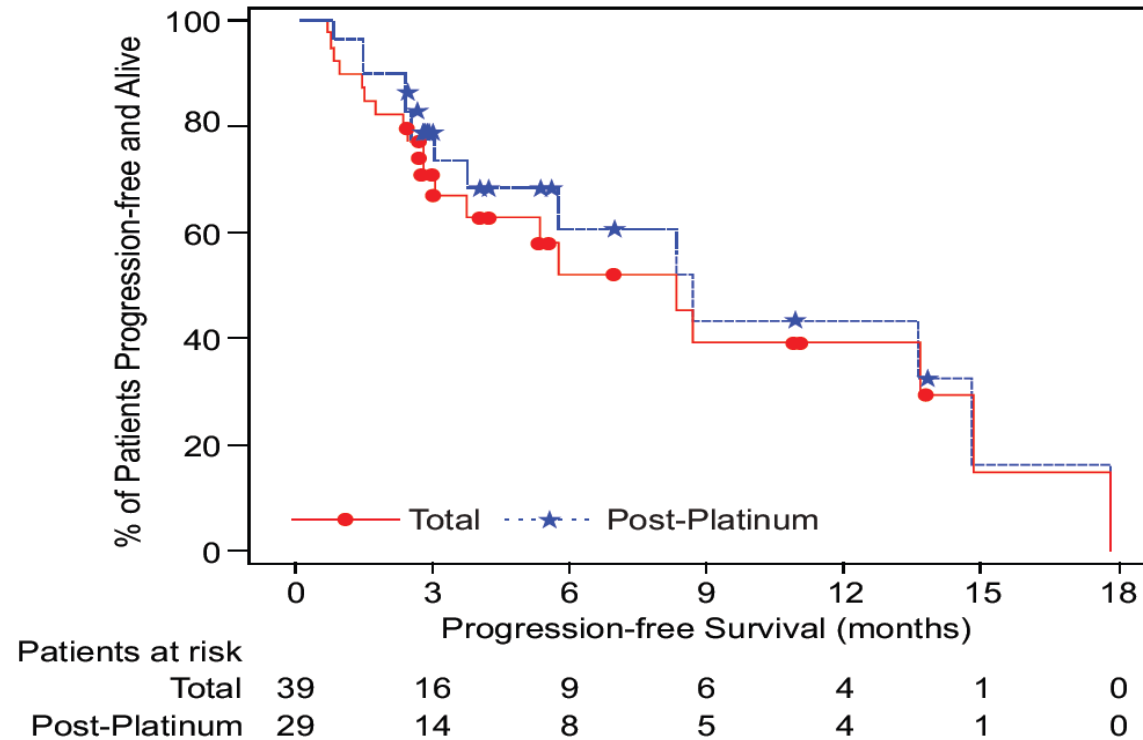
Best Response



- ORR, confirmed responses only, was 36% (95% CI, 21–53), with 14/39 patients achieving a partial response
- The ORR in post-platinum patients was 41% [95% CI, 24–61])
- The clinical benefit rate (PR or better or SD of at least 12 weeks [2 disease assessments]) was 67% (95% CI, 50–81) for all patients and 72% (95% CI, 53–87) for post-platinum patients

CI, confidence interval; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Progression Free Survival



- mPFS was 8.3 months (95% CI, 3.0–14.8) among all patients, with significant early censoring
- Post-platinum patients had mPFS of 8.6 months (95% CI, 3.7–14.8)

mDOR, median duration of response; mPFS, median progression-free survival.

Preparation and Administration

- A vial of amivantamab contains 350mg of the drug.
- The proposed dosing for amivantamab is 1050 mg (3 vials) for patients who weigh less than 80 kg and 1400 mg (4 vials) for patients who weigh 80 kg or more, given as an intravenous infusion administered through the central or peripheral vein primarily as a standalone procedure.
- Amivantamab is administered on a 28-day cycle. It is administered weekly for the first cycle, and every 2 weeks thereafter.
- The first dose will be split between two infusions such that 1 vial is administered on day 1 with the other vials administered on day 2.
- Amivantamab must be diluted for intravenous use (in a 250 mL infusion bag of 5% dextrose solution or 0.9% saline).
- Amivantamab will typically be administered in the outpatient setting. However, if a patient is admitted for inpatient care, the patient may need to receive amivantamab during the inpatient stay (depending on the patient's treatment schedule).

Documentation of Administration

- Amivantamab administration should be documented consistent with the documentation associated with other intravenous infusions.
- Documentation of administration within the medical record would most commonly be found in the Medication Administration Record (MAR), physician orders, and progress notes.

Summary

- No products are FDA approved for the treatment of NSCLC with Exon20ins mutations.
- Existing therapies, such as TKIs and chemotherapy, have limited effectiveness.^{1,2}
- There is no standard of care for patients who progress after platinum-based chemotherapy.
- Amivantamab has been designated as a breakthrough therapy by the FDA in patients with metastatic NSCLC with EGFR Exon20ins mutations, whose disease has progressed on or after platinum-based chemotherapy.³
- Amivantamab has a unique mechanism of action and is anticipated to be the first FDA-approved bispecific antibody therapy targeting EGFR and MET mutations simultaneously.
- Currently, there is no ICD-10-PCS code for the use of amivantamab.