PolyDamas

Amivantamab, an EGFR-MET Bispecific Antibody, With Cetrelimab, an Anti-PD-1 Antibody, in Advanced NSCLC: Phase 1/2 PolyDamas

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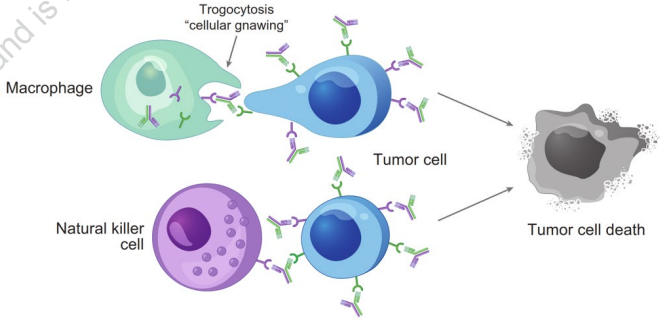
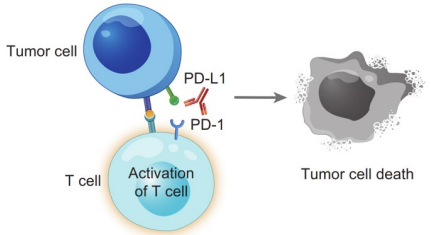
Background

- EGFR activation and EGFR TKI treatment may contribute to upregulation of PD-1/PD-L1, promoting treatment resistance[1,2]
  - Despite this, PD-1/PD-L1 inhibition has had limited activity in patients with *EGFR*-mutated NSCLC[1]
- The combination of anti-EGFR and anti-PD-1 antibodies has shown potentially synergistic efficacy in patients with recurrent and/or metastatic HNSCC in treatment-naïve and treatment-refractory settings[3,4]
- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[5-7]
- Cetrelimab is an anti-PD-1 monoclonal antibody with clinical activity in patients with previously treated NSCLC[8]
- Simultaneous targeting of the innate and adaptive immune systems with amivantamab and cetrelimab may improve antitumor activity versus either agent alone in both *EGFR*-mutated and *EGFR* wild-type NSCLC
- The PolyDamas study (ClinicalTrials.gov Identifier: NCT05908734) aims to identify the RP2CD and evaluate the antitumor effect of amivantamab plus cetrelimab

Amivantamab



Cetrelimab



EGFR, epidermal growth factor receptor; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; RP2CD, recommended phase 2 combination dose; TKI, tyrosine kinase inhibitor.

1. Peng S, et al. *Mol Cancer*. 2019;18(1):165. 2. Akbay EA, et al. *Cancer Discov*. 2013;3(12):1355-1363. 3. Chung CH, et al. *Clin Cancer Res*. 2022;28(11):2329-2338. 4. Sacco AG, et al. *Lancet Oncol*. 2021;22(6):883-892.
5. Moores S, et al. *Cancer Res*. 2016;76(13):3942-3953. 6. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044-2056. 7. Yun J, et al. *Cancer Discov*. 2020;10(8):1194-1209. 8. Felip E, et al. *Cancer Chemother Pharmacol*. 2022;89(4):499-514.

Methods: Study Design

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- PolyDamas is an open-label, multicenter, interventional study with a combination dose selection phase (phase 1) followed by an expansion phase (phase 2) in adult patients with metastatic NSCLC
- Phase 1: dose escalation/de-escalation will be based on DLTs; RP2CD will be selected through a BOIN design with a 3+3 design run-in

Key eligibility criteria

- Histologically/cytologically confirmed metastatic NSCLC
- Progressed on/after SOC systemic anticancer therapy and declined other systemic treatment options
- No prior anti-PD-1/PD-L1 therapy for patients with *EGFR* mutations (phase 1 only)[a]
- ECOG PS score of 0 or 1
- No history or current diagnosis of ILD/pneumonitis

Study design

Phase 1: combination dose selection (n=~20)

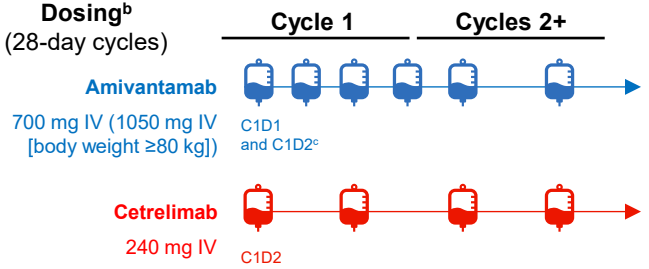
Amivantamab + Cetrelimab

Phase 2: dose expansion (n=~60)

Amivantamab + Cetrelimab

- **Cohort A (n=~30)**: Ex19del/L858R mutations and prior 3rd-generation EGFR TKI and platinum-based chemotherapy
- **Cohort B (n=~30)**: Treatment-naïve, PD-L1 expression ≥50%, no known driver mutations

Dosing[b] (28-day cycles)



- AEs are measured continuously until EOT[d]
- CT and MRI scans are assessed at screening, 6 weeks (+1 week) from C1D1, Q6W (±1 week) for the first 18 months, and then Q12W (±1 week) thereafter until disease progression[e]

PolyDamas (ClinicalTrials.gov Identifier: NCT05908734).

[a]Patients in the phase 2 cohorts must not have received prior amivantamab or anti-PD-1/PD-L1 therapy. [b]Patients will continue study treatment until disease progression, unacceptable toxicity, or another criterion for treatment discontinuation is met. [c]Amivantamab will be administered with a split dose for the first infusion (C1D1 and C1D2) and a prolonged initial infusion in order to mitigate the risk of IRR. [d]Continuous from signing of ICF to 30 days after last dose of amivantamab or 100 days after last dose of cetrelimab (whichever is longer). [e]Brain MRI (or CT if MRI is contraindicated) will be performed at screening, at the EOT visit, and if new disease or progressive disease in the brain is suspected at any time.

AE, adverse event; BOIN, Bayesian optimal interval design; C, Cycle; CT, computed tomography; D, Day; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EOT, end of treatment; Ex19del, exon 19 deletion; ICF, informed consent form; ILD, interstitial lung disease; IRR, infusion-related reaction; IV, intravenously; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; Q6W, every 6 weeks; Q12W, every 12 weeks; RP2CD, recommended phase 2 combination dose; SOC, standard-of-care; TKI, tyrosine kinase inhibitor.

Key Inclusion and Exclusion Criteria

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Inclusion criteria

Inclusion criteria for all cohorts

- Aged ≥18 years
- Histologically/cytologically confirmed metastatic NSCLC
- ECOG PS score of 0 or 1
- May have CNS metastases if definitively treated, stable, and asymptomatic for >2 weeks with/without low-dose corticosteroid treatment (≤10 mg prednisone or equivalent) ≥2 weeks prior
- Adequate organ and bone marrow function

Phase 1 cohort

- Metastatic NSCLC and progression on or after SOC systemic anticancer therapy and patient declined other systemic treatment options

Phase 2 expansion cohorts

- **Cohort A:** Ex19del/L858R mutations and progression on 3rd-generation EGFR TKI and platinum-based chemotherapy
- **Cohort B:** Treatment-naïve in metastatic setting, high PD-L1 expression (≥50% TPS/TC), and no known driver mutations

Exclusion criteria

- History of uncontrolled illness[a] or significant drug allergy[b]
- Prior anti-PD-1/PD-L1 therapy for patients with *EGFR* mutations (phase 1 only)
- Prior amivantamab or anti-PD-1/PD-L1 therapy (phase 2 cohorts only)
- History or current diagnosis of ILD/pneumonitis
- History of clinically significant cardiovascular disease[c]
- Active autoimmune disease or a documented autoimmune disease that requires systemic steroids or immunosuppressive agents

[a]Including, but not limited to, uncontrolled diabetes, ongoing/active infection, active bleeding diathesis, impaired oxygenation requiring continuous oxygen supplementation, psychiatric illness, or other circumstances that would limit compliance with study requirements. [b]Such as anaphylaxis, hepatotoxicity, or immune-mediated thrombocytopenia or anemia or has known allergies, hypersensitivity, or intolerance to amivantamab, cetrelimab, or protein-based therapies. [c]Including, but not limited to, deep vein thrombosis or pulmonary embolism within 1 month prior to administration of the first dose of study treatment, or any of the following within 6 months prior to administration of the first dose: myocardial infarction, unstable angina, stroke, transient ischemic attack, coronary/peripheral artery bypass graft, or any acute coronary syndrome; prolonged QTc interval >480 milliseconds or clinically significant cardiac arrhythmia or electrophysiologic disease; uncontrolled hypertension; congestive heart failure within 6 months of administration of the first dose of study treatment; pericarditis/clinically significant pericardial effusion; left ventricular ejection fraction outside of normal institutional limits during screening; or myocarditis.

CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; SOC, standard-of-care; TC, tumor cell; TKI, tyrosine kinase inhibitor; TPS, tumor proportion score.

Study Objectives and Endpoints

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Primary objective	Primary endpoint
Phase 1 combination dose selection • Identify the RP2CD of amivantamab plus cetrelimab	• Incidence and severity of AEs according to the NCI-CTCAE v5.0, including DLTs
Phase 2 expansion • Evaluate the antitumor effect of amivantamab plus cetrelimab at the selected RP2CD in patients with metastatic NSCLC characterized by EGFR and PD-L1 status	• ORR according to RECIST v1.1 by investigator review[a]
Key secondary objectives	**Key secondary endpoints**
Phase 1 combination dose selection • Evaluate the safety and tolerability of amivantamab plus cetrelimab	• Incidence and severity of AEs according to the NCI-CTCAE v5.0 • Clinical laboratory abnormalities
Phase 2 expansion • Assess the clinical benefit achieved by amivantamab plus cetrelimab • Characterize the safety and tolerability of amivantamab plus cetrelimab	• DoR[a] • DCR • PFS according to RECIST v1.1 by investigator review[a] • OS • Incidence and severity of AEs • Clinical laboratory abnormalities

[a]Confirmatory analysis may be performed using blinded independent central review.

AE, adverse event; DCR, disease control rate; DLT, dose-limiting toxicity; DoR, duration of response; EGFR, epidermal growth factor receptor; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; RP2CD, recommended phase 2 combination dose.

Statistical Analysis

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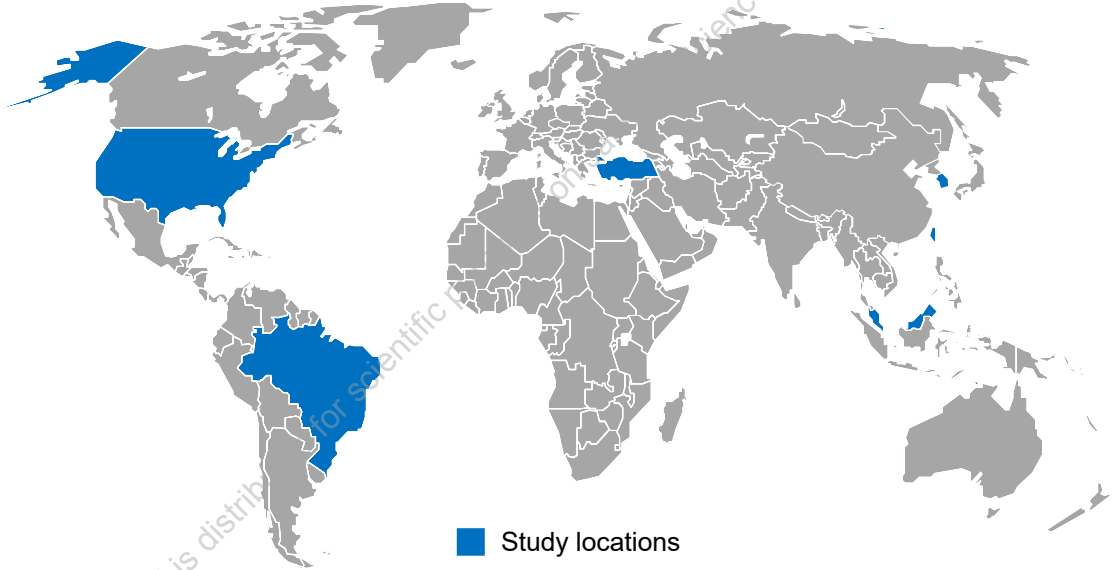
- This study is exploratory in nature and hypothesis generating; no formal statistical hypotheses exist for either phase
- Analyses will be based on the FAS (unless otherwise specified) and will be summarized separately for phases 1 and 2
  - Phase 1 primary endpoint: DLT incidence (based on the DLT-evaluable population)
  - Phase 2 primary endpoint: ORR (based on the response-evaluable population)
- Time-to-event variables (eg, DoR, PFS, and OS) will be analyzed using the Kaplan-Meier method
- A SET will help determine the RP2CD and review phase 2 safety and efficacy data

DLT, dose-limiting toxicity; DoR, duration of response; FAS, full analysis set; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RP2CD, recommended phase 2 combination dose; SET, safety evaluation team.

PolyDamas Enrollment Sites

- Patients are being enrolled at 12 sites across Brazil, Malaysia, the Republic of Korea, Turkey, and the United States



Summary

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- PolyDamas is an open-label, multicenter, interventional study with a combination dose selection phase (phase 1) followed by an expansion phase (phase 2) in adult patients with metastatic NSCLC
- Current status: The study is currently recruiting, with a goal of 80 patients
- Registration information: This study is registered with ClinicalTrials.gov (Identifier: NCT05908734)

NSCLC, non-small cell lung cancer.

Other Amivantamab Presentations at WCLC 2024

PolyDamas

MARIPOSA

Longer follow-up of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 10:47-10:57am

(OA02.03; Gadgeel)

MARIPOSA

Patient-relevant outcomes of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Tuesday, Sep 10 1:55-2:00pm

(MA12.07; Nguyen)

MARIPOSA

Lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 11:07-11:17am

(OA02.05; Lee)

PAPILLON

High-risk biomarker subpopulations from patients with *EGFR* Ex20ins in PAPILLON

Tuesday, Sep 10 1:50-1:55pm

(MA12.06; Goldman)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

Monday, Sep 9 11:07-11:17am

(OA09.05; Alexander)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: primary results

Tuesday, Sep 10 2:00-2:05pm

(MA12.08; Lopes)

EGFResisters

Development of a **patient-friendly lung cancer lexicon**:
Sunday, Sep 8 6:15-7:45pm

(P2.16F.03; Feldman)

Poster tour: Monday, Sep 9 6:45-6:53pm

Additional posters:

- **COCOON TiP:** Enhanced vs standard dermatologic management with amivantamab + lazertinib in advanced NSCLC**:**
  Monday, Sep 9 12:00-2:00pm (P3.12D.04; Cho)
- 5-year survival estimates with 1L osimertinib for *EGFR*-mutant advanced NSCLC in the US: Virtual ePoster (EP.12A.03; Sabari)

Acknowledgments

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