TARGETING MET clinicaltrials.targeting-met.com

EMD SERONO

Tepotinib clinical development

Tepotinib is being investigated for the treatment of various diseases. Efficacy of this product is still under investigation in various indications. Regulatory approval is dependent on the completion of the study programs and review by local regulatory authorities and varies from country to country. Please check with your local market authorization label for country-specific information. Clinical trial information is available at www.clinicaltrials.gov.

INSIGHT 2

NOW ENROLLING: **Patients with *MET* amplified advanced or metastatic NSCLC harboring activating *EGFR* mutations with acquired resistance to prior osimertinib**

Visit clinicaltrials.targeting-met.com, or clinicaltrials.gov NCT03940703 for more details.

Purpose of this study

In this Phase II trial the safety and efficacy of tepotinib, an oral once-daily MET inhibitor, is being investigated in combination with osimertinib in patients with *MET* amplified advanced/metastatic NSCLC harboring activating *EGFR* mutations with acquired resistance to prior osimertinib.

Study design

Advanced or metastatic *EGFR*-mutated NSCLC

MET amplification

Acquired resistance to prior first-line osimertinib

N≈120*

Tepotinib
500 mg orally once daily**
+
Osimertinib
80 mg orally once daily

Endpoints

Key endpoints include:

ORR (by independent and investigator review), safety **PFS**, **DOR**, **DC**, **OS**, **HRQoL**, **PK**
- **DLTs** assessed only in safety run-in

Key eligibility criteria

- Histologically confirmed locally advanced or metastatic NSCLC with a documented, activating *EGFR* mutation
- *MET* amplification determined by FISH in tissue biopsy (enrolment based on central or local testing). Samples collected following progression on prior first-line osimertinib
- Acquired resistance to prior first-line osimertinib, and first-line osimertinib as the only prior therapy for advanced/metastatic NSCLC†
- Age ≥18 years
- ECOG PS 0–1

Key exclusion criteria

- Patients with symptomatic brain metastases who are neurologically unstable
- Inadequate hematological, liver, renal or cardiac function, or hypertension uncontrolled by standard therapies
- Any unresolved Grade 2 or higher toxicity from previous therapies

*Target enrollment.

**Initially, eligible participants who are detected to be *MET* amplification positive will be randomly assigned in a ratio of 2:1 to either the combination of tepotinib and osimertinib or tepotinib alone, until 12 are enrolled in the monotherapy arm. After this, all participants will be assigned to the combinati on. Participants who are randomized to the tepotinib monotherapy will have the opportunity to switch over to the combination of tepotinib plus osimertinib at the time of disease progression. Treatment continues until progression of disease, withdrawal of consent, or development of unacceptable toxicities. 500 mg tepotinib refers to 500 mg tepotinib hydrochloride hydrate which is equivalent to 450 mg tepotinib (the free base form).

†Patients must have had a radiologically confirmed response or stable disease (for a least 6 months) to treatment with first-line osimertininb, followed by radiologically documented disease progression. Radiological assessments must be made according to RECIST v1.1

For a full list of all outcome measures, inclusion and exclusion criteria, please visit clinicaltrials.gov NCT03940703.

References

1. Clinicaltrials.gov. A study of tepotinib plus osimertinib in osimertinib relapsed mesenchymal-epithelial transition factor (*MET*) amplified non small cell lung cancer (NSCLC) (INSIGHT 2). https://clinicaltrials.gov/ct2/show/NCT03940703. Last accessed: January 2021.

DC, disease control; DLT, dose limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; HRQoL, health related quality of life; MET, mesenchymal epithelial transition factor; NSCLC, non small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression free survival; PK, pharmacokinetics.

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