INSIGHT-2 (Merck)

A Study of Tepotinib Plus Osimertinib in Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitor (TKI) Relapsed Mesenchymal-epithelial Transition Factor (MET) Amplified Non-small Cell Lung Cancer (NSCLC).

This is the trial summary as assessed on clinicaltrials.gov on 06/10/2020.

Minor changes in the protocol may occur. You can check this on this direct link: https://clinicaltrials.gov/ct2/show/NCT03940703

Trial Design:

This study will assess the antitumor activity, safety, tolerability, and pharmacokinetics (PK) of the MET inhibitor tepotinib combined with the 3rd generation EGFR inhibitor osimertinib in participants with advanced or metastatic NSCLC.

Arm	Intervention
Experimental: Tepotinib and Osimertinib Participants will receive a combination of tepotinib and osimertinib. The combination will be applied in cycles of 21 days until disease progression, death and adverse event leading to discontinuation, study withdrawal or consent withdrawal.	Drug: Tepotinib Participants will be administered Tepotinib orally once daily at an initial dose of 500 milligram (mg). A safety monitoring committee (SMC) may decide to confirm or adapt the dose. Drug: Osimertinib Participants will receive Osimertinib at a dose of 80 mg orally once daily.
Experimental: Teptotinib mono-therapy Participants will receive once daily dose of tepotinib. The mono therapy will be applied in cycles of 21 days until disease progression, death, adverse event leading to discontinuation, study withdrawal or consent withdrawal.	Drug: Tepotinib Participants will be administered Tepotinib orally once daily at an initial dose of 500 milligram (mg). A safety monitoring committee (SMC) may decide to confirm or adapt the dose.

Inclusion criteria:

- Locally advanced or metastatic Non-small Cell Lung Cancer (NSCLC) histology (confirmed by either histology or cytology) with documented activating Epidermal Growth Factor Receptor (EGFR) mutation
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and a minimum life expectancy of 12 weeks
- Acquired resistance on previous first-line osimertinib. Participants must meet both of the following 2 criteria:
- Radiological documentation of disease progression on first-line osimertinib

- Objective clinical benefit documented during previous osimertinib therapy, defined by either partial or complete radiological response, or durable stable disease (SD) (SD should last greater than (>) 6 months after initiation of osimertinib
- Have received only first-line osimertinib as a prior line of therapy in the non curative advanced or metastatic NSCLC setting
- MET amplification as determined by either FISH testing (central or local) on tumor tissue (TBx) or central blood-based next generation sequencing (LBx). Tumor and blood samples must be collected following progression on prior first-line osimertinib at Prescreening
- Submission of tumor tissue and blood sample obtained after progression on first-line osimertinib, is mandatory for all patients for MET amplification testing
- Submission of tumor tissue during Prescreening or Screening is mandatory for patients with tumor tissue tested by local FISH, to confirm MET amplification status. Central confirmation is not mandated prior to the start of study treatment
- Other protocol defined inclusion criteria could apply

Exclusion criteria:

- Spinal cord compression or brain metastasis unless asymptomatic, stable or not requiring steroids for at least 2 weeks prior to start of study intervention
- Any unresolved toxicity Grade 2 or more according to National cancer institute common terminology criteria for adverse events(NCI-CTCAE) version 5, from previous anticancer therapy with the exception of alopecia
- Inadequate hematological, liver and renal function
- Impaired cardiac function
- History of interstitial lung disease(ILD) or interstitial pneumonitis including radiation pneumonitis that required steroid treatment
- Hypertension uncontrolled by standard therapies (not stabilized to < 150/90 millimeter of mercury (mmHg)
- Contraindication to the administration of osimertinib
- Other protocol defined exclusion criteria could apply.