INSIGHT2

Referring patients to the INSIGHT 2 Study

We would be very grateful if you would consider referring any patients who may be interested and potentially eligible for participation in the INSIGHT 2 Study. If you have any questions about the study, please contact us.

Further information can be found on clinicaltrials.gov, using the NCT number **NCT03940703**.

Physician Referral Brochure, 06 Jan 2021 [V02 Global(en)]

Information for Referring Physicians

US-TEP-00326

About the INSIGHT 2 Study

We are currently recruiting for the INSIGHT 2 Study, a Phase 2 study investigating the efficacy, safety, and tolerability of an investigational medication, tepotinib, alone or in combination with osimertinib in patients with MET-amplified, advanced or metastatic non-small cell lung cancer (NSCLC).

Eligible participants must be diagnosed with NSCLC harboring epidermal growth factor receptor (EGFR) mutations and having relapsed on prior first-line osimertinib therapy. The study will involve approximately 120 patients in Europe, Asia, and North America.

We would like to ask you for your help in referring any patients who may be eligible, with their permission. Please feel free to discuss any information about the INSIGHT 2 Study with your patients first.

Study objectives

Primary objective

- To assess the efficacy of tepotinib combined with osimertinib in participants with advanced or metastatic EGFRm+ NSCLC

Key secondary objectives

- To assess tolerability and safety
- To further assess efficacy
- To assess health-related quality of life
- To assess pharmacokinetics

The study has additional secondary and tertiary/exploratory objectives.

Why is the INSIGHT 2 Study being conducted?

Targeted therapies, such as EGFR tyrosine kinase inhibitors (TKIs), that interfere with specific molecular signaling pathways have emerged as a standard option for selected NSCLC patients with EGFR mutations. Many patients eventually develop resistance to EGFR TKIs, and MET amplification has been identified as the most common acquired resistance mechanism in 15% to 19% of these patients.[1,2]

Tepotinib is a MET inhibitor that has shown clinical efficacy in a previous study with MET-amplified, EGFR TKI-relapsed NSCLC patients in combination with the first-generation EGFR TKI gefitinib.[3] The third-generation EGFR TKI osimertinib has shown clinical efficacy in EGFR-mutant NSCLC patients who relapsed on previous EGFR TKIs.[4]

Currently, there are no personalized treatment options available for patients who have relapsed on previous osimertinib treatment when used as a first-line EGFR TKI. The INSIGHT 2 Study will assess whether the combination of tepotinib and osimertinib may be beneficial.

References:

1. Ramalingam SS, Cheng Y, Zhou C, *et al*. Mechanisms of acquired resistance to first-line osimertinib: preliminary data from the phase III FLAURA study. *Annals of Oncology*, Volume 29, Issue suppl_8, October 2018, mdy424.063.
2. Papadimitrakopoulou VA, Wu YL, Han JY, *et al*. Analysis of resistance mechanisms to osimertinib in patients with EGFR T790M advanced NSCLC from the AURA3 study. *Annals of Oncology*, Volume 29, Issue suppl_8, October 2018, mdy424.064.
3. Wu YL, Zhou J, Lu S, *et al*. Tepotinib + gefitinib (TEP+GEF) in MET+/epidermal growth factor receptor (EGFR)-mutant non-small lung cancer (NSCLC): Phase II data. *Annals of Oncology*, Volume 29, Issue suppl_9, November 2018, mdy425.026.
4. Mok TS, Wu Y-L, Ahn M-J, *et al*. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. *N Engl J Med*. 2017;376:629–640.

Study overview

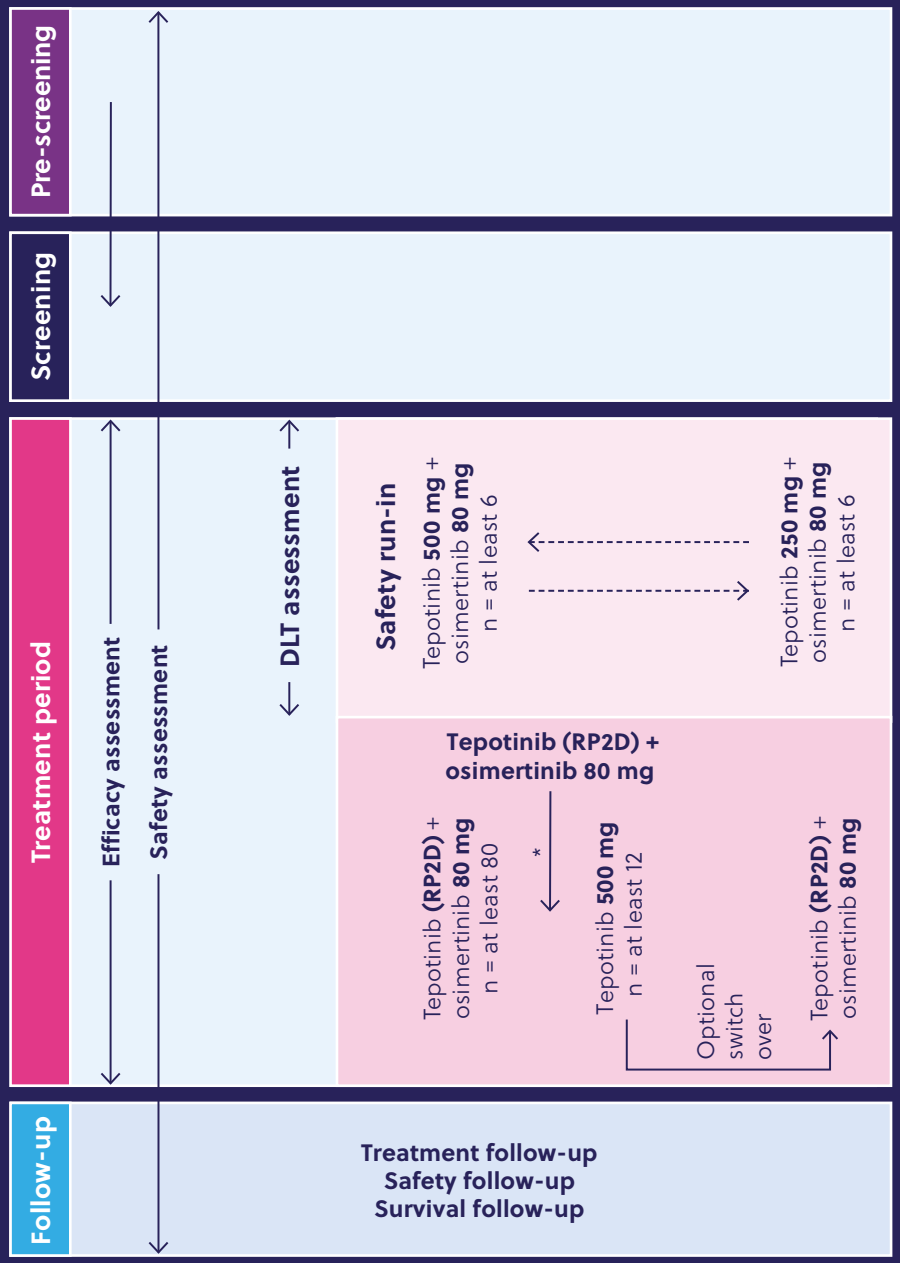
The INSIGHT 2 Study will involve study visits about every 3 weeks for the first 9 months, then every 6 weeks. The study is open-label. Participants will receive tepotinib and osimertinib. Eligible participants with MET amplification will be randomly assigned in a 2:1 ratio to either the combination of tepotinib and osimertinib or tepotinib alone. Randomization to the 2 arms of the study will continue until 12 participants are enrolled in the monotherapy arm. After this, all participants will be assigned to the combination of tepotinib plus osimertinib. Participants who are randomized to tepotinib monotherapy will have the opportunity to switch over to the combination of tepotinib plus osimertinib once they experience disease progression.

The study consists of:

- a pre-screening period to confirm the presence of MET amplification
- a screening period (up to 4 weeks before start of study treatment) to confirm eligibility
- a treatment period
- a follow-up period (including survival follow-up visits or phone calls every 1.5 or 3 months).

A safety run-in period has been completed.

Study design



DLT: dose-limiting toxicity ; RP2D: recommended Phase 2 dose.

*As soon as 12 participants are enrolled in the monotherapy arm, all further participants will receive combination treatment.

Eligibility criteria

Key inclusion criteria

- ≥18 years of age (or having reached the age of majority if it is >18 years)
- Locally advanced or metastatic NSCLC histology with documented activating EGFR mutation
- MET amplification as determined by either fluorescence in situ hybridization (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 pre-screening.
  - Submission of tumor tissue and blood samples obtained after progression on first-line osimertinib is mandatory for all patients for MET amplification testing.
  - Submission of tumor tissue during pre-screening 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.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and minimum life expectancy of 12 weeks
- Acquired resistance on previous first-line osimertinib

Key exclusion criteria

- Spinal cord compression or brain metastasis unless asymptomatic, stable, or not requiring steroids for at least 2 weeks prior to the 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 mmHg)
- Contraindication to the administration of osimertinib