INSIGHT 2: a Phase II study of tepotinib plus osimertinib in *MET*-amplified NSCLC and first-line osimertinib resistance

Primary objectives/rationale

Primary objective

To assess the efficacy of tepotinib + osimertinib in patients with advanced or metastatic *EGFR*-mutant NSCLC and *MET*amp, determined centrally by FISH, who have progressed on first-line osimertinib

Key secondary objectives

To assess the efficacy of tepotinib + osimertinib in patients with *MET*amp determined centrally by liquid biopsy and in patients with *MET*amp determined centrally by FISH or NGS in liquid biopsy

Article details

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Article URL
www.futuremedicine.com/doi/10.2217/fon-2021-1406

Trial registration number
NCT03940703

Key eligibility criteria

- ≥18 years of age
- Presence of ≥1 independently verified measurable lesion
- ECOG PS 0–1
- Life expectancy ≥12 weeks
- Locally advanced or metastatic NSCLC with activating *EGFR* mutation
- Received only first line therapy with osimertinib for advanced or metastatic NSCLC and acquired resistance on previous first line osimertinib
- Normal organ function
- *MET*amp determined by central or local FISH testing (GCN ≥5 and/or *MET/CEP7* ratio ≥2) by tissue biopsy, or NGS (GCN ≥2.3) by liquid biopsy

Study design and treatment

INSIGHT 2 is a global, open-label, Phase II trial of tepotinib + osimertinib in *MET*amp NSCLC and first-line osimertinib resistance

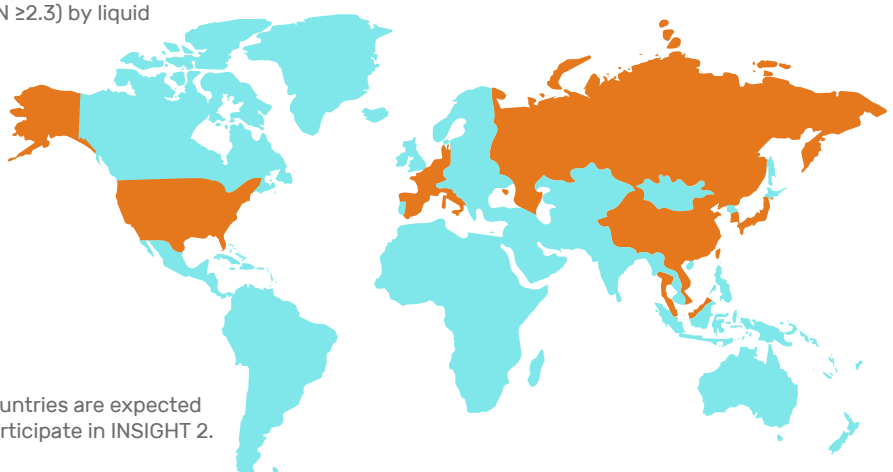
Study period:
- Enrolment began: September 2019
- Estimated study end date: March 2023

Expected total number of patients:

N =~120

Study procedures:
Treatment:

Tepotinib 500 mg QD (450 mg active moiety) + Osimertinib 80 mg QD → Treatment continues until progressive disease, unmanageable adverse event, withdrawal or death



17 countries are expected to participate in INSIGHT 2.

Outcome measures/end points

Primary endpoint:
- Objective response (including confirmed complete response or partial response), by IRC using RECIST v1.1

Secondary endpoints:
- Objective response by IA
- DOR by IRC and IA
- PFS by IRC and IA
- OS
- HRQoL
- Safety and tolerability

Glossary

DOR: Duration of response; EGFR: Epidermal growth factor receptor; FISH: fluorescence *in situ* hybridization; GCN: Gene copy number; HRQoL: Health-related quality of life; IA: investigator assessment; IRC: independent review committee; MET: mesenchymal-epithelial transition factor; *MET*amp: *MET* amplification; NGS: Next-generation sequencing; NSCLC; Non-small-cell lung cancer; OS: Overall survival; PFS: Progression-free survival; RECIST v.1.1: Response Evaluation Criteria in Solid Tumours version 1.1; QD: Once daily.

Job code: GL-TEP-00160