MS200095-0031 / INSIGHT-2 - (dernière mise à jour : 05/02/2020)

http://archimaid.fr/index.php?action=show&id=1032

Informations générales

Titre de l'étude : A Phase II Single-arm Study to Investigate Tepotinib Combined With Osimertinib in MET Amplified, Advanced or Metastatic Non-small Cell Lung Cancer (NSCLC) Harboring Activating EGFR Mutations and Having Acquired Resistance to Prior 1st to 3rd Generation EGFR-tyrosine Kinase Inhibitor Therapy

Traitement : Métastasique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : II **Stade** : Localement avancé à Métastasique **Ligne(s)** : 2

Schéma : 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.

Study arm:
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.
Interventions:
-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.

Current primary outcome:
- Safety run-in: Number of Participants Experiencing Dose Limiting Toxicities (DLT) According to National Cancer Institute Common Terminology Criteria for Adverse Events Version (NCI-CTCAE v 5.0) [Time Frame: Up to Day 21 of Cycle 1 (each Cycle is of 21 days)]
- Objective response determined according to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 as per Independent Review Committee (IRC) [Time Frame: Every 6 weeks following the Cycle 1 Day 1 visit until 9 months; every 12 weeks thereafter until disease progression, death, study withdrawal, or withdrawal of consent (each Cycle is of 21 days) (approximately 21.7 months)]

Current secondary outcomes:
- Number of Participants With Treatment Emergent Adverse Events (TEAEs) And Treatment-Related Adverse Events According to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0, and Deaths [Time Frame: Baseline up to 30 days after the last dose of study treatment (approximately 10.5 months)]
- Percentage of Participants With Abnormal greater Than or Equal to (>=) Grade 3 Laboratory Findings [Time Frame: Baseline up to 30 days after the last dose of study treatment (approximately 10.5 months)]
- Percentage of Participants With Abnormal Vital Signs, Electrocardiograms (ECGs) and Eastern Cooperative Oncology Group (ECOG) Performance Status [Time Frame: Baseline up to 30 days after the last dose of study treatment (approximately 10.5 months)]
- Objective Response According to RECIST 1.1 assessed by Investigator [Time Frame: Every 6 weeks following the Cycle 1 Day 1 visit until 9 months; every 12 weeks thereafter until disease progression, death, study withdrawal, or withdrawal of consent (each Cycle is of 21 days) (approximately 21.7 months)]
- Confirmed Complete Response assessed by Independent Review Committee and by Investigator [Time Frame: Every 6 weeks following the Cycle 1 Day 1 visit until 9 months; every 12 weeks thereafter until disease progression, death, study withdrawal, or withdrawal of consent (each Cycle is of 21 days) (approximately 21.7 months)]
- Duration of Response assessed by Independent Review Committee and by Investigator [Time Frame: Approximately 21.7 months]
- Percentage of Participants With Disease Control as assessed by Independent Review Committee and by Investigator [Time Frame: Approximately 21.7 months]
- Progression-Free Survival Based on Tumor Assessment by the Independent Review Committee and Investigator According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria [Time Frame: Approximately 21.7 months]
- Overall Survival [Time Frame: Approximately 21.7 months]
- Health-Related Quality of Life as Assessed by EuroQol Five Dimension Five Level (EQ-5D-5L) Scale Score [Time Frame:

Approximately 21.7 months]
- Health-Related Quality of Life as assessed by European Organisation For Research And Treatment of Cancer Quality of Life Questionnaire Core 3D (EORTC-QLQ-C30) [Time Frame: Every 6 weeks following the Cycle 1 Day 1 visit until 9 months; every 12 weeks thereafter until disease progression, death, study withdrawal, or withdrawal of consent (each Cycle is of 21 days) (approximately 21.7 months)]
- Health-Related Quality of Life as assessed by Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ) [Time Frame: Every 6 weeks following the Cycle 1 Day 1 visit until 9 months; every 12 weeks thereafter until disease progression, death, study withdrawal, or withdrawal of consent (each Cycle is of 21 days) (approximately 21.7 months)]
- Area Under the Plasma Concentration-Time Curve From Time Zero to the Last Sampling Time (AUC 0-t) of Tepotinib and Osimertinib [Time Frame: Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours after tepotinib and Osimertinib administration at Day 1 of Cycle 1 and Day 15 of Cycle 1 (each Cycle is of 21 days)]
- Maximum Observed Plasma Concentration (Cmax) of Tepotinib and Osimertinib [Time Frame: Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours after tepotinib and Osimertinib administration at Day 1 of Cycle 1 and Day 15 of Cycle 1 (each Cycle is of 21 days)]
- Time to Reach Maximum Observed Plasma Concentration (tmax) of Tepotinib and Osimertinib [Time Frame: Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours after tepotinib and Osimertinib administration at Day 1 of Cycle 1 and Day 15 of Cycle 1 (each Cycle is of 21 days)]
- Apparent Total Body Clearance (CL/f) of Tepotinib and Osimertinib [Time Frame: Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours after tepotinib and Osimertinib administration at Day 1 of Cycle 1 and Day 15 of Cycle 1 (each Cycle is of 21 days)]
- Apparent Volume Of Distribution (Vz/F) of Tepotinib and Osimertinib [Time Frame: Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours after tepotinib and Osimertinib administration at Day 1 of Cycle 1 and Day 15 of Cycle 1 (each Cycle is of 21 days)]
- Percentage of Participants With Epidermal Growth Factor Receptor (EGFR) Mutation [Time Frame: From Day 1 of Cycle 3 up to end of treatment (14 days after last dose) (each Cycle is for 21 days) (approximately 7.5 months)]

Spécialités / Localisations

Spécialité n°1 : Organes respiratoires et intrathoraciques

CIM10 - Localisation n°1 : **C34** - Tumeur maligne des bronches et du poumon

Critères

Critères d'inclusion : - Locally advanced or metastatic Non-small Cell Lung Cancer (NSCLC) histology (confirmed by either histology or cytology) with documented activating mutation of the Epidermal Growth Factor Receptor (EGFR) receptor including T790 mutation status
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and a minimum life expectancy of 12 weeks
- Acquired resistance on previous EGFR-Tyrosine Kinase Inhibitors (EGFR-TKI) therapy.
- MET amplification
- Other protocol defined inclusion criteria could apply

Critères de non-inclusion : - 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

Informations promoteur

Nom du promoteur : EMD Serono Research & Development Institute, Inc.

Type de promoteur : Industriel

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Informations centre investigateur n°1

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Ouverture de l'essai : OUVERT

Liens utiles

ClinicalTrials (anglais) :
https://clinicaltrials.gov/ct2/show/record/NCT03940703?term=tepotinib+combined+with+osimertinib&draw=2&rank=1