HERTHENA-Lung 02 (Daiichi)

A Study of Patritumab Deruxtecan Versus Platinum-based Chemotherapy in Metastatic or Locally Advanced EGFRm NSCLC After Failure of EGFR TKI Therapy.

This is the trial summary as assessed on clinicaltrials.gov on 19/01//2023.

Minor changes in the protocol may occur. You can check this on this direct link: https://clinicaltrials.gov/ct2/show/NCT05338970.

Trial Design:

ARM	INTERVENTION
Experimental: Patritumab deruxtecan. Participants who will be randomized to receive patritumab deruxtecan (HER3-DXd) 5.6 mg/kg q3W.	IV, 5.6 mg/kg q3w
Active comparator: Platinum-based chemotherapy: 4 cycles. Participants without disease progression after 4 cycles of platinum plus pemetrexed therapy may continue treatment with maintenance pemetrexed with no restriction on the number of cycles.	IV, pemetrexed 500 mg/m^2 plus either cisplatin (75 mg/m^2) or carboplatin (target area under the curve 5 [AUC5] by using the Calvert formula) q3W

Inclusion criteria:

- Is a male or female subject aged ≥18 years (follow local regulatory requirements if the legal age of consent for study participation is >18 years old).
- Has histologically or cytologically documented metastatic or locally advanced non-squamous NSCLC not amenable to curative surgery or radiation.
- Has documentation of an EGFR-activating mutation detected from tumor tissue or blood sample: exon 19 deletion or L858R at diagnosis or thereafter.
- Received 1 or 2 prior line(s) of an approved EGFR TKI treatment in the metastatic or locally advanced setting, which must include a third -generation EGFR TKI
- May have received either neoadjuvant and/or adjuvant treatment if progression to metastatic or locally advanced disease occurred at least 12 months after the last dose of such therapy and subsequently experienced disease progression on or after third-generation EGFR TKI treatment administered in the metastatic or locally advanced setting.
- Has not received any other prior systemic therapies in the metastatic or locally advanced setting (including chemotherapy, immunotherapy etc) (even if administered in combination with EGFR TKI).
- Has documentation of radiographic disease progression while receiving or after receiving a third generation EGFR TKI for metastatic or locally advanced disease.
- Has at least 1 measurable lesion as per RECIST v1.1 by Investigator assessment.
- Is willing to have a tumor biopsy or provide recently obtained tumor tissue.

- Has an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 at Screening.
- Has adequate bone marrow reserve and organ function based on local laboratory evaluation within 14 days prior to randomization:
    - Platelet count: ≥100,000/mm^3 or ≥100 × 10^9/L
    - Absolute neutrophil count: ≥1500/mm^3 or ≥1.5 × 10^9/L
    - Hemoglobin (Hgb): ≥9.0 g/dL
    - Creatine clearance (CrCl): CrCl ≥45 mL/min calculated by using the Cockcroft-Gault equation or measured CrCl
    - Aspartate aminotransferase (AST)/Alanine aminotransferase (ALT): AST/ALT ≤3× Upper limit of normal (ULN)
    - Total bilirubin (TBL): TBL ≤1.5 × ULN
    - Serum albumin: ≥2.5 g/dL
    - Prothrombin time (PT) or Prothrombin time-International normalized ratio (PT-INR) and activated partial thromboplastin time (aPTT)/partial thromboplastin time (PTT): ≤1.5 × ULN, except for participants receiving coumarin-derivative anticoagulants or other similar anticoagulant therapy who must have PT-INR within therapeutic range as deemed appropriate by the Investigator

Exclusion criteria:

- Has any previous histologic or cytologic evidence of small cell OR combined small cell/non-small cell disease in the archival tumor tissue or pretreatment tumor biopsy, or squamous NSCLC histology
- Has any history of interstitial lung disease (ILD) (including pulmonary fibrosis or radiation pneumonitis), has current ILD, or is suspected to have such disease by imaging during Screening
- Has clinically severe respiratory compromise (based on the Investigator's assessment) resulting from intercurrent pulmonary illnesses including, but not limited to the following:
- Any underlying pulmonary disorder, restrictive lung disease, or pleural effusion
- Any autoimmune, connective tissue, or inflammatory disorders where there is documented, or a suspicion of pulmonary involvement at the time of Screening
- OR prior complete pneumonectomy
- Is receiving chronic systemic corticosteroids dosed at >10 mg prednisone or equivalent anti-inflammatory activity or any form of immunosuppressive therapy prior to randomization
- Has evidence of any leptomeningeal disease
- Has evidence of clinically active spinal cord compression or brain metastases, defined as being symptomatic and untreated, or requiring therapy with corticosteroids or anticonvulsants to control associated symptoms
- Any prior treatment with any agent including an antibody drug conjugate (ADC) containing a chemotherapeutic agent targeting topoisomerase I, human epidermal growth factor receptor 3 (HER3) antibody, and any systemic therapies (other than EGFR TKIs) in the metastatic/locally advanced setting, including chemotherapy or any other systemic therapy in combination with an EGFR TKI
- Has history of other active malignancy within 3 years prior to randomization, except for adequately resected nonmelanoma skin cancer, adequately treated intraepithelial carcinoma of the cervix, and any other curatively treated in situ disease
- Has uncontrolled or significant cardiovascular disease prior to randomization
- Has active hepatitis B and/or hepatitis C infection, such as those with serologic evidence of active viral infection within 28 days of randomization

- Has a known human immunodeficiency virus (HIV) infection that is not well controlled
- Has clinically significant corneal disease