1365TiP | A RANDOMIZED, PHASE II, MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ONARTUZUMAB (METMAB) IN COMBINATION WITH PACLITAXEL + CISPLATIN (OR CARBOPLATIN) AS FIRST-LINE TREATMENT FOR PATIENTS (PTS) WITH STAGE IIIB OR IV SQUAMOUS NON-SM

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Background

Dysregulation of the HGF/Met pathway has been associated with tumorigenesis in many malignancies, including NSCLC. Onartuzumab (MetMAb) is a recombinant, humanized, monovalent monoclonal antibody directed against Met. By binding to the extracellular domain of Met, onartuzumab selectively blocks ligand binding and subsequent activation by HGF. Current data support a strategy of combining onartuzumab with numerous chemotherapies and targeted agents (bevacizumab, erlotinib). In a phase Ia/Ib study, onartuzumab (monotherapy and in combination with bevacizumab) was shown to be well tolerated in pts with advanced solid tumors (Moss et al. Ann Oncol 2010;21(Suppl. 8):Abstr. 504P). A phase II study of onartuzumab in combination with erlotinib in pts with previously treated NSCLC reported a significant benefit in PFS (HR 0.53; p = 0.04) and OS (HR 0.37; p = 0.002) in pts with Met-positive (Met IHC diagnostic positive) tumors (Spigel et al. J Clin Oncol 2011;29 (Suppl.):Abstr. 7505). Pts with Met-negative tumors who received onartuzumab + erlotinib reported worse outcomes compared with erlotinib alone (PFS HR 1.82; p = 0.05; OS HR 1.78; p = 0.16). The most commonly reported adverse events associated with onartuzumab are peripheral edema and fatigue.

Methods

In this phase II study, pts with squamous NSCLC are randomized (1:1) to receive 4 cycles of paclitaxel, cisplatin (or carboplatin) and either placebo or onartuzumab. Pts without disease progression may continue to receive placebo or onartuzumab as maintenance therapy until disease progression, unacceptable toxicity, or death. The primary study endpoint is PFS in all pts. PFS by Met IHC diagnostic status (Met positive vs Met negative) will also be analyzed. Secondary endpoints include OS, ORR, safety, and PK. A minimum of 110 pts will be randomized to achieve 55 pts with Met-positive squamous NSCLC. A maximum of 55 pts with Met-negative squamous NSCLC will be enrolled. This study is open for accrual; further details can be found on ClinicalTrials.gov (NCT01519804).

Disclosure

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V.E. Paton: Dr Paton is a full-time employee of Genentech, Inc. and minor stockholder of Hoffmann-La

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W. Yu: Dr Yu is a full-time employee of Genentech, Inc. and minor stockholder of Hoffmann-La Roche, Inc.

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