

1364TiP | A RANDOMIZED, PHASE II, MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ONARTUZUMAB (METMAB) WITH EITHER BEVACIZUMAB + PLATINUM + PACLITAXEL OR PEMETREXED + PLATINUM AS FIRST-LINE TREATMENT FOR PATIENTS

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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. In a phase Ia/Ib study, onartuzumab (+/- bevacizumab) was well tolerated in pts with advanced solid tumors (Moss et al. Ann Oncol 2010;21(Suppl. 8):Abstr. 504P). In a phase II study of pts with previously treated NSCLC, onartuzumab + erlotinib was associated with a significant benefit in PFS (HR 0.53; p = 0.04) and OS (HR 0.37; p = 0.002) compared with erlotinib alone in pts with Met IHC diagnostic-positive (Met-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). An interaction between onartuzumab and erlotinib could explain this outcome and therefore may not be seen in this study with chemotherapy. The most commonly reported adverse events associated with onartuzumab are peripheral edema and fatigue. An early safety review is planned for this study.

Methods

In this study the treating physician will assign appropriate chemotherapy for each pt (Cohort 1: bevacizumab + platinum + paclitaxel; Cohort 2: pemetrexed + platinum). Eligible pts within cohorts will be stratified by Met IHC status (positive vs negative) and randomized (1:1) to receive 4 cycles of chemotherapy + onartuzumab or placebo. Thereafter, pts without disease progression may continue to receive placebo or onartuzumab (+ cohort-assigned chemotherapy, without platinum or paclitaxel) until disease progression, unacceptable toxicity, or death. The co-primary endpoints are PFS in all pts and by Met status. Secondary endpoints include OS, ORR, safety, and PK. Approximately 260 pts will be randomized until 130 pts with Met-positive NSCLC are enrolled. This study is open for accrual; further details can be found on ClinicalTrials.gov (NCT01496742).

Disclosure

H. Wakelee: Dr. Wakelee reports an uncompensated consultancy/advisory relationship with Genentech-Roche. Dr Wakelee receives research funding (through Stanford University) from Genentech-Roche.

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

K. Rittweger: Mrs Rittweger is a full-time employee of Hoffmann-La Roche, Inc.

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