TPS4155 General Poster Session (Board #33A), Sun, 8:00 AM-11:45 AM

MetGastric: A randomized phase III study of onartuzumab (MetMAb) in combination with mFOLFOX6 in patients with metastatic HER2-negative and MET-positive adenocarcinoma of the stomach or gastroesophageal junction.

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Background: Dysregulation of the HGF/MET pathway in patients with gastroesophageal cancer (GEC) is associated with diminished survival and poor prognostic features, such as nodal and organ metastasis, disease stage and tumor invasiveness. Preclinical data suggest that inhibition of the HGF/MET axis may increase the anti-tumor properties of platinum agents by overcoming HGF-mediated resistance mechanisms. Overexpression and inappropriate activation of the MET pathway has been shown to promote peritoneal metastasis in murine models of GEC. Overexpression of HGF or MET has also been linked to metastatic spread to the liver and peritoneum in patients with GEC. Clinical studies suggest that antibody-based inhibitors of the HGF/MET pathway are active in GEC. Onartuzumab, a monovalent monoclonal antibody, specifically binds to the MET receptor preventing HGF binding thereby inhibiting signal transduction. The most commonly reported adverse events associated with onartuzumab are grade 1–3 peripheral edema, hypoalbuminemia and fatigue. **Methods:** MetGastric is a randomized placebo-controlled, international phase III study in patients with previously untreated metastatic GEC. Only patients with tumors classified as both HER2-negative and MET-positive (by IHC) are eligible. Patients will be randomized (1:1) to receive mFOLFOX6 plus onartuzumab or mFOLFOX6 plus placebo. A maximum of 12 cycles of mFOLFOX6 are permitted. Onartuzumab or placebo will be continued until disease progression. The primary endpoint is overall survival. Secondary endpoints include progression-free survival, overall response rate, safety and correlative biomarker studies. Primary and secondary analyses will include all randomized patients, analyzed according to treatment arm assignment and MET IHC score. Safety will be assessed in all patients who receive at least one dose of study treatment. This study is open for accrual. Clinical trial information: NCT01662869.