A PHASE 2 RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY OF SIMTUZUMAB OR PLACEBO IN COMBINATION WITH GEMCITABINE FOR THE FIRST LINE TREATMENT OF PANCREATIC ADENOCARCINOMA

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Aim: Simtuzumab (SIM) is a humanized antibody that inhibits lysyl oxidase-like molecule 2 (LOXL2), an extracellular matrix enzyme that catalyzes the covalent cross-linking of collagen and is widely expressed across desmoplastic tumors. Inhibiting LOXL2 is expected to block formation of desmoplasia, which is thought to play an important role in tumor progression and metastasis. In the Phase 1 study, SIM was safe and well-tolerated in patients (pts) with advanced solid tumors and showed early evidence of efficacy. Based on these results, a randomized, double-blind, placebo-controlled phase 2 study of SIM + gemcitabine (Gem) vs. placebo (pbo) + Gem in pts with metastatic pancreatic adenocarcinoma was initiated.

Methods: Eligible pts had no prior systemic therapy for advanced disease and Eastern Cooperative Oncology Group performance status of 0 or 1. The primary endpoint was progression free survival (PFS). Pts were randomized to 200 mg SIM, 700 mg SIM, or pbo at a 1:1:1 ratio in combination with Gem in cycles of 28 days. In each cycle, pts received IV SIM or pbo infused on Days 1 and 15, and IV Gem (1000 mg/m2) on Days 1, 8, and 15.

Results: Between 3/28/12 and 5/15/13, 236 pts were randomized and treated; 76 pts (200 mg SIM/Gem), 79 pts (700 mg SIM/Gem), and 81 pts (pbo/Gem). Median PFS was 3.5 (HR 1.12; p = 0.63 vs pbo), 3.7 (HR 1.08; p = 0.75 vs pbo), and 3.7 months for 200 mg SIM/Gem, 700 mg SIM/Gem, and pbo/Gem arms, respectively. Median overall survival (OS) was 5.9 (HR 1.05; p = 0.76 vs pbo), 7.6 (HR 0.83; p = 0.26 vs pbo), and 5.7 months, respectively. Gemcitabine-related expected toxicities included anemia, thrombocytopenia, neutropenia, and nausea. There were no differences in the safety profile of the SIM plus Gem groups versus pbo plus Gem group.

Conclusions: The addition of SIM to Gem does not improve PFS or OS in advanced pancreatic cancer pts.

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