Adenocarcinoma of the Stomach or Gastroesophageal Junction

Background: Gastric cancer is the fifth most common cancer and the third leading cause of cancer deaths. HER2/neu is overexpressed in 15% - 25% of patients with gastric cancer. Monotherapy with the anti-HER2 antibody IMU-131 and 2 patients received a dose on day 182. alternatives are needed due to cost and global availability. IMU-131 is a B-cell peptide vac- cine composed of a fusion of 3 epitopes from the extracellular domain of HER2/neu conjugated to CRM197 with the adjuvant Montanide. Polyclonal antibodies against IMU-131 and 2 peptides elicited antitumor activity in vitro and a phase I study demonstrated safety and immunogenicity in Her2/+ breast cancer patients.

Methods: IMU-131 was given to patients with HER2/neu overexpressing gastric or gastroesophageal junctional (GEJ) adenocarcinoma in an international open-label, Phase Ib dose escalation trial performed in 14 Asian and Eastern Europe centers assessing safety, tolerability, and immunogenicity. Each patient received IMU-131 on Days 0, 14, and 35, accompanied by cisplatin and 5-fluorouracil or capecitabine every 21 days.

Results: 14 patients were enrolled with advanced stage IIIb or IV with 10 HER2 overexpressing tumors (7 x HER2++, 3 x HER2++ FISH positive) and 4 HER2++ expressing tumors. Mean age was 57 years (range of 21 - 79) with ECOG scores of 0 or 1 in 7 patients each. There were 9 Asian and 5 Caucasian patients with 5 females and 9 males. Dose levels were 10, 30 and 50 µg with 6, 5 and 6 patients receiving those dose levels each. 11 patients received all 3 doses with 3 patients who received only 2 doses and 1 patient who discontinued due to dose progression. 3 patients received a dose on day 182. Of the 14 patients dosed 11 were evaluable for tumor progression at day 56 and later. Of those patients, the best response was IC 1 CR 4 PR 5 SD, with no dose levels achieving a CR. No 10 µg dose group reached a CR. The only 2 patients who achieved a CR were both patients with a dose level of 50 µg in the 30 µg group. 9 patients with HER2 overexpression had 1 CR, 4 PR, 2 SD, and 1 PD in the 30 µg group, while 2 PR and 1 SD in the 50 µg group. In patients with HER2 overexpression there was 1 CR, 4 PR, 2 SD, and 1 PD, and in patients with HER2+ expression there was 3 SD. There were no SAEs related to IMU-131 and 1 patient had a mild injection site reaction.

Conclusions: IMU-131 is a promising B-cell vaccine against HER2. Further work in a controlled phase 2 trial is ongoing.