Phase 1b/2 Study of Margetuximab Plus Pembrolizumab in Advanced HER2+ Gastroesophageal Junction or Gastric Adenocarcinoma

Dana-Farber Cancer Institute, Boston, MA; 2Washington University School of Medicine in St. Louis, MO; 3University of Texas MD Anderson Cancer Center, Houston, TX; 4Memorial Sloan Kettering Cancer Center, New York, NY; 5Ihirohara-ina General Hospital, Tokyo, Japan; 6Yale School of Medicine, New Haven, CT; 7Samsung Medical Center, Seoul, Korea; 8Yale University School of Medicine, New Haven, CT; 9University of Chicago Pritzker School of Medicine, Chicago, IL; 10Washington University School of Medicine in St. Louis, MO; 11Memorial Sloan Kettering Cancer Center, New York, NY; 12Ihirohara-ina General Hospital, Tokyo, Japan; 13Korea University College of Medicine, Seoul, Korea; 14Asan Medical Center, University of Ulsan, Seoul, Korea; 15Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; 16National Cancer Center, Singapore, Singapore; 17Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Patient Population
HER2 amplification status assessed in a subset of patients by plasma circulating tumor (ct) DNA post-trastuzumab

Dose escalation evaluated margin 10 and 200 mg pembrolizumab (pembro) for 3rd-line treatment of recurrent PD-L1+ gastric cancer who are initially HER2+

Loss of HER2 amplification may occur after trastuzumab failure in a subset of GEA patients

Phase 1b/2 Clinical Trial
Open label, dose escalation 3+3 design study of margetuximab (marge) in combination with pembrolizumab (pembro) and nivolumab (nivo) in HER2+ gastric or GEJ cancer

Characterize pharmacokinetics and immunogenicity of combination

Investigate preliminary overall survival (OS) and progression-free survival (PFS)

Goal: Develop a chemotherapy-free approach for the treatment of gastroesophageal cancer

Pembrolizumab and nivolumab approved for 3rd-line treatment of recurrent PD-L1+ gastric cancer (Gastric Cancer Patients (IHC 3+))

Open label, dose escalation 3+3 design study of margetuximab (marge) in PD-L1+ gastric (GEJ) and gastroesophageal junction (GEJ) cancer

HER2+ Gastric Cancer Patients (IHC 3+)

Margetuximab + pembrolizumab is a well-tolerated, chemotherapy-free combination that has shown preliminary antitumor activity in 2nd line patients with advanced/ metastatic HER2+ gastric or GEJ cancer

Response rate higher and PFS longer in gastric vs GEJ cancer, particularly in patients with HER2 3+ at time of diagnosis

Margetuximab + pembrolizumab is well-tolerated, chemotherapy-free combination that has shown preliminary antitumor activity in 2nd line patients with advanced/metastatic HER2+ gastric or GEJ cancer

- Response rate higher and PFS longer in gastric vs GEJ cancer, particularly in patients with HER2 3+ at time of diagnosis
- Gastric cancer compared to GEJ tumors has a higher rate of reremorization of ERBB2 amplification as determined by plasma ctDNA
- Retained ERBB2 amplification by ctDNA post-trastuzumab may enrich for treatment benefit
- No clear association between response and ctDNA genotyping
- Higher response rate observed in Asian vs North America
- May be due to higher percent of gastric cancer in Asia cohort

First New Lesion
Change in Target Lesions

Circulating Tumor DNA Results

45 patients evaluated, 51% (22/43), 15% were positive for ERBB2 amplification by ctDNA post-trastuzumab

Response rate in the ctDNA positive post-trastuzumab population was 28% (6/23), while in the ctDNA negative population was 0% (0/22)

- Rates of ERBB2 amplification were higher in gastric cancer vs GEJ cancer

Development of a chemotherapy-free approach for the treatment of gastroesophageal cancer

Preliminary Clinical Activity

Clinical activity (15 mg/kg + Pembro 200 mg – All Patients)

51 evaluable patients to date at dose of 15 mg/mg and 200 mg pembrolizumab (29 North America/22 Asia)

- 37 (55.2) with tumor regression (target lesions)
- 110 (14.9) with tumor shrinkage ≥ 50% (confirmed and/or partial response and/or stable disease)
- Diarrhoea
- Vomiting
- Decreased appetite
- Pruritus

North America
Asia

Change from Baseline (%)Change in Lesions from Baseline (%)