INITIAL SAFETY AND EFFICACY FINDINGS WITH BAVITUXIMAB PLUS PEMBROLIZUMAB IN PATIENTS WITH ADVANCED GASTRIC OR GASTROESOPHAGEAL CANCER

Ian Chau1, Haeseong Park2, Jeeyun Lee3, Susan Machnytre4, Hagop Youssoufian4, Laura Benjamin4, Kerry Culm-Merdek4 and Joanna Bendell5

Royal Wender-Mill Foundation Trust, London, England, Washington University School of Medicine, St. Louis, MO, Samsung Medical Center, Seoul, Korea, Oncology, Inc., Watkins, MA, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN

BACKGROUND
- Phosphatidylserine (PS), an amino-sugar-phospholipid present at the outer leaflet of the plasma membrane in apoptotic tumour cells and uninfected cells, is also a ligand for PS receptors on natural killer (NK) cells and tumour-infiltrating lymphocytes (TILs). PS signalling can activate immunosuppressive cells and inhibit tumour cell lysis by NK cells and TILs.

BAVITUXIMAB
- Bavituximab is a monoclonal IgG4 antibody that binds to PS on the tumour cell surface to inhibit PS signaling and activate NK cells, thereby blocking PD-1/PD-L1-mediated immunosuppression.

PEMBROLIZUMAB
- Pembrolizumab is a humanized monoclonal antibody that binds to PD-1 on T cells preventing it from binding to PD-L1 or PD-L2 expressed on tumour cells, thereby inhibiting negative T cell signalling.

Study Design & Objectives
- Phase 2 multicenter, open-label, single arm, global study (NCT04754948) in checkpoint inhibitor naïve, advanced gastric/gastroesophageal junction cancer patients
- Patients with known MSI-H were excluded from the study
- Safety run-in phase 1 (5 day dose finding toxicity observation period, followed by an expansion phase)
- Study population:
  - Primary: Assess safety, tolerability and anti-tumor activity (using RECIST) v1.1 of bavituximab plus pembrolizumab in previously treated advanced non-squamous non-small-cell lung cancer.
  - Secondary: Assess bavituximab concentrations and immunogenicity
  - Tertiary: Evaluate novel biomarker signatures and explore relationships among patient subgroups with efficacy outcomes.

Study Status
- Safety run in phase 1: 3 patients enrolled, recommended dose for expansion phase: 7 mg/kg bavituximab plus 200 mg pembrolizumab monthly.

RESULTS
- 8 patients still on treatment at data cut off date of Aug 14, 2020
- 8 patients had evaluable tumours at visits before Aug 14, 2020
- ORR (CR + PR): 4 (17.4) 0 3 (23.1)
- Stable disease: 2 (8.7) 0 3 (23.1)
- Complete response, n (%): 2 (8.7) 0 3 (23.1)
- Disease progression, n (%): 10 (25.0)
- Safety: No new safety signals have emerged with the treatment combination.

CONCLUSIONS
- The combination of bavituximab and pembrolizumab appears to be well-tolerated in the patient population.
- A dosing escalation was observed in the phase 1 trial with patients receiving lower bavituximab doses experiencing more systemic toxicity.
- A phase 2 trial is planned to be conducted in patients with lower historical CPI response rates, such as MSS (17% ORR) and CPS (20% ORR).
- Safety data support the proposal hypothesis that inhibition of immunosuppressive cells with bavituximab can enhance response rates in combination with checkpoint inhibitors.
- In addition, anti-tumor activity was enhanced in patients with reduced NLR (23% ORR) and in patients whose TME was PD-L1 or PD-L2 positive. TIL expression and infiltration is shown to be associated with PD-L1 expression.
- Overall, the bavituximab/pembrolizumab combination in advanced gastric cancer patient appears promising, especially in TME-1 biomarker positive patients with NLR values above the combined OSR ORR (23% of 7 out of 30).