Introduction: Patients with metastatic gastric cancer have a poor prognosis, despite the use of multi-drug chemotherapy regimens. While in some patients these may provide initial clinical benefit, continued use results in cumulative toxicity. Thus, treatment options that improve upon the initial benefit from chemotherapy while reducing the potential for cumulative toxicity are needed in the first-line (1L) treatment setting. Programmed death-1 receptor ligand (PD-L1) is a key therapeutic target in the reactivation of the immune response against multiple cancers. Avelumab\(^*\) (MSB0010718C) is a fully human anti-PD-L1 IgG1 antibody that has shown promising efficacy and an acceptable safety profile in patients with various tumor types. In the phase 1 JAVELIN Solid Tumor and JAVELIN Solid Tumor JFN trials, avelumab 10 mg/kg administered every 2 weeks (Q2W) showed antitumor activity in patients with advanced gastric cancer or gastroesophageal junction cancer (GC/GEJC) as maintenance therapy in non-progressing patients after first-line chemotherapy and as second-line treatment. A phase 3 trial, JAVELIN Gastric 100 (NCT02625610), has been initiated to compare efficacy and safety of single-agent avelumab as switch maintenance treatment vs continuation of 1L chemotherapy in patients with GC/GEJC.

Methods: JAVELIN Gastric 100 is a randomized, open-label, global, multicenter trial. Primary endpoints are overall survival and progression-free survival. Secondary endpoints are best overall response, quality of life (assessed via EQ-5D-5L, EORTC QLQ-C30, and EORTC QLQ-STO22 questionnaires), and safety. Additional endpoints include duration of response, time to response, and association between PD-L1 expression in tumor cells or immune cells within the tumor microenvironment (measured by immunohistochemistry) and clinical responses. Responses are evaluated according to RECIST 1.1 every 6 weeks and adjudicated by a blinded independent review committee. Adverse events are assessed throughout the trial. Key eligibility criteria are: histologically confirmed, unresectable, locally advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction; age ≥18 years; ECOG performance status score of 0 or 1; no prior therapy with any drug targeting T cell coregulatory proteins; no prior chemotherapy for locally advanced/metastatic disease; and no concurrent anticancer treatment or immunosuppressive agents. Fresh or archival tumor tissue for PD-L1 expression assessment is required for all patients, but patients are not preselected based on PD-L1 expression; patients with HER2+ tumors are excluded. Approximately 666 eligible patients will receive 12-week induction chemotherapy (with either oxaliplatin + 5-fluorouracil + leucovorin or oxaliplatin + capecitabine), and upon completion, approximately 466 patients without disease progression will be randomized to receive treatment in the maintenance phase. Patients entering the maintenance phase are randomized to receive either avelumab 10 mg/kg as a 1-hour intravenous infusion Q2W or to continue 1L chemotherapy. Patients not eligible to receive further chemotherapy will receive best supportive care alone. Patients in the 1L chemotherapy arm are allowed dose adjustments if toxicity would otherwise prohibit continued treatment. Treatment is given until disease progression, unacceptable toxicity, or consent withdrawal. Avelumab therapy may continue past the initial determination of progression if multiple pre-specified criteria are met. Trial enrollment began in December 2015. *Proposed INN.

Results: Conclusion: