Aim: Endosialin is a cell surface glycoprotein that is expressed on cells involved in the development of tumor vasculature, primarily pericytes and stromal fibroblasts. Ontuxizumab is humanized immunoglobulin G1-kappa (IgG1/κ) monoclonal antibody that is the first clinical-stage agent to target endosialin. The antibody has shown antitumor activity in a variety of models and its pharmacologic activity have shown distinct non-disease activities as compared to other anti-vascular therapies, such as no observed impact on wound healing.

Methods: Patients (pts) with solid tumor who have no other appropriate treatment were eligible in the study. Each cycle consisted of four weeks. Ontuxizumab was administered weekly until disease progression or occurrence of a DLT and administered to 4 cohorts at 2, 4, 8 and 12 mg/kg weekly schedule in a stepwise dose escalation manner.

Results: Fifteen pts were enrolled including three gastric cancer, two gastrointestinal stromal tumor, two breast cancer and a patient with lung cancer, malignant pheochromocytoma, adrenocortical cancer, hypopharyngeal cancer, extraskeletal chondrosarcoma, thymic carcinoma, renal pelvis cancer and intrahepatic cholangiocarcinoma. No DLT was observed. Treatment related adverse events were observed in 5 of 15 pts and the most common events were grade 1 constipation (two pts), grade 2 hyperkalaemia (two pts), grade 2 infusion related reaction (two pts). Cmax and AUC values of ontuxizumab after single administration increased in a dose-related manner. Mean t1/2 was 85.2 - 219 hours after multiple administrations. Human anti-human antibody was not detected. Of eight pts with stable disease, one pt with GIST after failure of imatinib and sunitinib showed tumor shrinkage by CT evaluation based on Choi’s criteria at 12 mg/kg. The longest duration of ontuxizumab treatment was 32 weeks for one gastric cancer pt in 4 mg/kg.

Conclusions: Ontuxizumab was well tolerated in pts with advanced solid tumors at up to 12 mg/kg. Ontuxizumab is currently being investigated in Ph2 studies for its potential treatment of melanoma, metastatic colorectal carcinoma and soft tissue sarcoma.

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