Background: Concurrent chemoradiotherapy (cCRT) is the standard therapy for locally advanced gastric and GEJ adenocarcinoma with poor prognosis. Progressed cell death receptor-1 (PD-1) inhibitor has been approved to treat >3 line gastric and GEJ patients (pts). PACIFIC study demonstrated significant clinical benefits of PD-1 inhibitor in addition to cCRT in locally advanced lung cancer. Sintilimab, a humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1, has shown promising efficacy with an overall response rate of 85% in combination with chemotherapy in gastric cancer in a phase Ib study (NCT02937116). A study was therefore designed to explore the efficacy and safety of periperoative cCRT in combination with sintilimab for pts with locally advanced gastric cancer.

Trial design: This is a prospective, open label, multicentric phase II trial which pts with locally advanced (cT3N2-3 or cT4aN0-3) gastric cancer or GEJ adenocarcinoma will receive preoperative 4 cycles sintilimab in combination with S1, nab-paclitaxel (nab-PTX) and radiotherapy (RT) and post-operative 3 cycles sintilimab with S1 and nab-PTX. Sintilimab will be administered intravenously at flat dose of 200 mg every 3 weeks. S1 orally at dose of 40 mg/m² (bid) and nab-PTX intravenously at 100-120 mg/m² on days 1, 8, 15, 22 will be given for 2 cycles between surgery and 3 cycles after. A weekly nab-PTX (80-100 mg/m²,d1, d8, d15, d22) with concurrent RT (45Gy/1.8Gy*25f) will be given in between 2 cycles of S1 and nab-PTX combination. The primary endpoint is the pathological complete response (pCR), and a Simon optimal two-stage design will be employed to achieve the target at 35% from historical 15%. Secondary endpoints include safety, major pathological response (MPR) (defined by tumor residual ≤10%), R0 resection rate, and overall survival. Collaborative translational studies explore the correlation of response with tumor mutational burden or genetic alterations, or biomarkers etc. The trial is now open to enrollment, 13 of planned 34 pts have been enrolled.

Clinical trial identification: ChiCTR1900024428.

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