Perioperative sintilimab in combination with concurrent chemoradiotherapy for patients with locally advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma

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Background
- Concurrent chemoradiotherapy (cCRT) is the standard therapy for locally advanced gastric (G) and gastroesophageal junction (GEJ) adenocarcinoma with poor prognosis1-2.
- Programmed cell death receptor-1 (PD-1) inhibitor has been approved and recommended to treat ≥ 3 line G/GEJ patients1-2.
- PACIFIC study demonstrated significant clinical benefits of PD-1 inhibitor in addition to cCRT in locally advanced lung cancer3.
- 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)4.

Aim and Design
- The aim of this study is to explore the efficacy and safety of perioperative cCRT in combination with sintilimab for patients with locally advanced G/GEJ adenocarcinoma: a prospective, single arm, multicentric phase II trial.
- This trial was registered at Chinese Clinical Trial Registry as ChiCTR1900024428.

Objectives
- Primary Objective: Pathological complete response (pCR)
- Secondary Objectives: Safety, Major pathological response (MPR) (defined as tumor residual cells ≤10%), R0 resection rate, OS
- Exploratory Objectives: Correlation of response with tumor mutational burden or genetic alterations, or biomarkers, etc

Key Inclusion Criteria
- Histologically confirmed locally advanced G/GEJ adenocarcinoma
- Endoscopic ultrasonography (EUS) or enhanced CT or MRI confirmed cT3N2-3 or cT4aN+ or cT4bN any (AJCC 8th)
- ECOG PS 0-1
- ≥ 18 years old
- At least one measurable lesion per RECIST v1.1

Key Exclusion Criteria
- CT/MR/ESU proven distant metastasis
- Prior anticancer therapy including chemotherapy, radiotherapy and immunotherapy
- Patients with other malignant tumors over the last 5 years
- Allergic to drugs used in this trial
- Active autoimmune diseases

Recruitment
- The first eligible patient was enrolled in 06.2019 at the leading center of Affiliated Drum Tower Hospital to Medical School of Nanjing University.
- The trial is now open for enrollment in total 5 clinical sites in China and 13 patients have been enrolled by 07.2020.

Trial Schema
- RT: Radiotherapy, 450Gy/1.8Gy×25f; C1: S-1 (40mg/m², BID, d1-14) + Nab-PTX 100-120 mg/m², d1, d8; C2: Weekly Nab-PTX: 80-100 mg/m², d1, d8, d15, d22; S: Sintilimab, 200mg, iv, q3w

References
1. 2020 NCCN guidelines in Oncology of Gastric Cancer, vision 3.
2. 2020 NCCN guidelines in Oncology of Esophageal and Esophagogastric Junction Cancers, vision 4.

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