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

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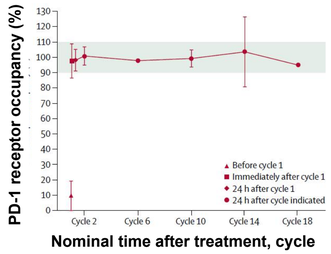
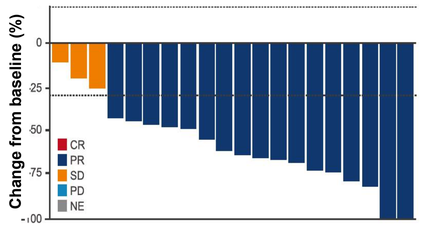
Background

- Concurrent chemoradiotherapy (cCRT) is the standard therapy for locally advanced gastric (G) and gastroesophageal junction (GEJ) adenocarcinoma with poor prognosis[1-2].
- Programmed cell death receptor-1 (PD-1) inhibitor has been approved and recommended to treat ≥ 3 line G/GEJ patients[1-2].
- PACIFIC study demonstrated significant clinical benefits of PD-1 inhibitor in addition to cCRT in locally advanced lung cancer[3].
- Sintilimab, a humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1[4], has shown promising efficacy with an overall response rate of 85% in combination with chemotherapy in gastric cancer in a phase Ib study (NCT02937116)[5].

Pharmacodynamic analysis [4]



Best response of target lesions [5]



- The phase III RCT ORIENT-16 trial of sintilimab in combination of XELOX in first-line treatment of G/GEJ carcinoma is ongoing.

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.

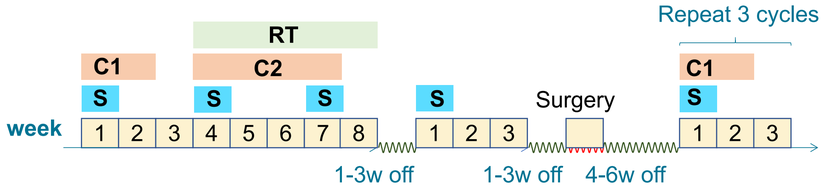
Statistics Consideration

- A Simon optimal two-stage design was employed in this trial. 9 patients were enrolled at the first stage and only if ≥ 1 patient achieved pCR, the other 25 could participate.
- For the primary objective (pCR), the alternative hypothesis of 35% will be tested against a null hypothesis of historical 15% with Chi-square test, resulting in total sample size of 34.
- No formal hypothesis testing will be performed for all the secondary endpoints given the nature of exploratory analysis.

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

Trial Schema



RT: Radiotherapy, 45Gy/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

Key Eligibility Criteria

Key Inclusion Criteria	Key Exclusion 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	• CT/MR/EUS 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.

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.
3. S.J. Antonia, et al. N Eng J Med 2018, 379: 2342-2350.
4. Yuankan Shi, et al. Lancet Haematol 2019, 6(1): e12-19.
5. Haiping Jiang, et al. BMC Cancer 2020, 20(1): 760.

Disclosures

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- All other authors have declared no conflicts of interest.

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