## INPLASY PROTOCOL

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Corresponding author: Yuanyang Jin

jyy572@qq.com

Author Affiliation: Henan university

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## INTRODUCTION

Review question / Objective: Gastric cancer is one of the most common malignant tumors of the digestive system. Due to its rapid progression, more than 60% of patients are locally advanced or advanced when they visit the hospital. The

Immunocheckpoint inhibitors for advanced gastric cancer or gastroesophageal junction cancer with different microsatellite stability: a systematic review and meta-analysis

Jin, YY<sup>1</sup>; Suo, ZM<sup>2</sup>.

Review question / Objective: Gastric cancer is one of the most common malignant tumors of the digestive system. Due to its rapid progression, more than 60% of patients are locally advanced or advanced when they visit the hospital. The 5year survival rate is only 2%-15%, and the median OS is difficult to exceed two years. In recent years, immunotherapy has made great breakthroughs in malignant tumors. Recently published trials have highlighted the high activity of ICI in dMMR/MSI-H tumors, and there is a clinical need for specific data on the efficacy and activity of immunotherapy in patients with advanced gastric or gastroesophageal junction cancer with high MSI. This systematic review aims to accurately evaluate the significance of microsatellite instability as a positive predictor of immunotherapy in GC/GEJC patients. P: Patients with advanced gastric cancer or combined gastroesophageal cancer who could be evaluated for microsatellite status I: Immune checkpoint inhibitors C: Chemotherapy or placebo O: ORR, OS S: RCT.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2022 and was last updated on 26 October 2022 (registration number INPLASY2022100106).

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advanced gastric or gastroesophageal junction cancer with high MSI. This systematic review aims to accurately evaluate the significance of microsatellite instability as a positive predictor of immunotherapy in GC/GEJC patients. P: Patients with advanced gastric cancer or combined gastroesophageal cancer who could be evaluated for microsatellite status I: Immune checkpoint inhibitors C: Chemotherapy or placebo O: ORR, OS S: RCT.

Condition being studied: Gastric cancer is one of the most common malignant tumors of the digestive system. Due to its rapid progression, more than 60% of patients are locally advanced or advanced when they visit the hospital. The 5-year survival rate is only 2%-15%, and the median OS is difficult to exceed two years. In recent years, immunotherapy has made great breakthroughs in malignant tumors. Recently published trials have highlighted the high activity of ICI in dMMR/MSI-H tumors, and there is a clinical need for specific data on the efficacy and activity of immunotherapy in patients with advanced gastric or gastroesophageal junction cancer with high MSI.

## **METHODS**

Participant or population: Advanced gastric cancer or gastroesophageal junction cancer can be evaluated for microsatellite status

Intervention: Immune checkpoint inhibitors.

Comparator: Chemotherapy or placebo.

Study designs to be included: RCT.

Eligibility criteria: (1) Locally advanced gastric or gastroesophageal junction adenocarcinoma confirmed by pathology or cytology;(2) Estimated survival time >3 months;(3) RCTS published in English and Chinese, in which treatment with immune checkpoint inhibitors, either alone or in combination with standard therapy, was compared with the same standard therapy in patients with advanced GC/GEJC(4) If

multiple reports refer to the same data, the report containing the (largest and) most recent data will be included in the review and these data will be cross-checked with other reports.

Information sources: Embase, Cochrane, pubmed, obvious, China CNKI.

Main outcome(s): OS.

Additional outcome(s): ORR.

Data management: Document collection, record and management are realized by NoteExpress software.

Quality assessment / Risk of bias analysis: Cochrane TOOL.

Strategy of data synthesis: Heterogeneity between studies was assessed with Cochrane's Q statistic and I2 statistic, as measured by HR for the efficacy of anti-PD-1 treatment. Due to the large amount of clinical heterogeneity between studies, random effects models were used for analysis regardless of statistical heterogeneity. Evidence for assessment of treatment effect according to the MSI pattern is by means of interaction tests (reported as P-values for subgroup differences). The risk of publication bias was determined by funnel plots and visual inspection Egger's linear regression test. All reported p-values are two-sided. RevMan software (version 5.3; Cochrane Collaboration, Copenhagen, Denmark) for all pooled analyses.

Subgroup analysis: Patients were divided into subgroups according to their microsatellite status.

Sensitivity analysis: After deleting any one of the papers, the combined results of the remaining papers are not much different from those without deletion, which means that sensitivity analysis has been passed

Country(ies) involved: China.

**Keywords:** Immune checkpoint inhibitors (ICI), Advanced gastric cancer, Advanced

gastroesophageal junction carcinoma, Microsatellite instability.

## **Contributions of each author:**

Author 1 - Yuanyang Jin. Email: jyy572@qq.com Author 2 - Zhimin Suo.