

# INPLASY PROTOCOL

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The authors declare there are no conflicts of interest regarding the publication of this paper.

## Meta-analysis on efficacy and safety of novel chemotherapy drugs in the treatment of advanced metastatic colorectal cancer

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**Review question / Objective:** 1. Whether the new chemotherapy drug can prolong the patient's total survival time. 2. Whether the new chemotherapy drug can prolong the patient's progression-free survival. 3. Which chemotherapy drug is the most effective of the new drugs available.

**Condition being studied:** Currently, there are few chemotherapy drugs available for patients with advanced metastatic colorectal cancer. Regorafenib, TAS-102, and Fruquintinib, as new drugs for the treatment of advanced colorectal cancer, are expected to change this situation. A number of existing clinical trials have shown that the single use of these drugs in the treatment of advanced metastatic colorectal cancer can prolong the indicators such as PFS and OS in patients, but there is a lack of direct comparison of the three drugs to provide clinical guidance for doctors.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 November 2020 and was last updated on 05 November 2020 (registration number INPLASY2020110016).

### INTRODUCTION

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## METHODS

**Participant or population:** Patients with advanced metastatic colorectal cancer who have failed to respond to multiple lines of treatment.

**Intervention:** Regorafenib or TAS-102 or Fruquintinib.

**Comparator:** Placebo.

**Study designs to be included:** Double-blind randomized controlled trial; Studies published in English; Phase II and above clinical trials.

**Eligibility criteria:** Studies with insufficient data; Studies not published in English; studies not a randomized controlled trial.

**Information sources:** Computer retrieval of Cochrane, PubMed, Google School, Embase, CNKI, and other databases was performed from the date of database establishment to December 30, 2020.

**Main outcome(s):** The primary outcome was the patient's overall survival and progression-free survival and the number of adverse events occurring.

**Quality assessment / Risk of bias analysis:** The strategy of data synthesis: Statistical heterogeneity of data was evaluated by using Cochran's Q statistic. If statistical Q statistic ( $P < 0.10$ ) was considered to be significant heterogeneous among studies random-effects model was performed. If not a fixed-effects model was used.

**Strategy of data synthesis:** Data extraction in this study was conducted by two researchers, who independently retrieved and screened all the full-text citations considered qualified. If there is disagreement, a third researcher will make the choice. The data extraction process is as follows. 1. This study will use Review Manager to directly compare OS, PFS, and ADR variables 2. ITC software was used for indirect comparison between variables. 3. For the dichotomous variables, we will calculate the risk ratio.

**Subgroup analysis:** A subgroup analysis of populations in different regions, such as Asia, is planned; the European population; African people.

**Sensibility analysis:** If the analysis result is too heterogeneous, use sensitivity analysis to find the source of the heterogeneity.

**Country(ies) involved:** China.

**Keywords:** Comparative effectiveness; Regorafenib; metastatic colorectal cancer; TAS-102; Fruquintinib.

### Contributions of each author:

Author 1 - Fang Ying Li.

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Author 3 - Wang WenZheng.