INPLASY PROTOCOL

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Corresponding author:
Hongyu Jin

jinhongyu@stu.scu.edu.cn

Author Affiliation:
West China Hospital

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Conflicts of interest:
None declared.

Adjuvant targeted therapy combined with surgery for advanced and metastatic renal cell carcinoma: Protocol for a systematic review and meta-analysis

Jin, H[1]; Zhang, M[2].

Review question / Objective: **What is the efficacy and safety of peri-operative use of sunitinib combined with radical surgery in patients with advanced or metastatic renal carcinoma. What are incidence rates of all-grade or grade≥3 adverse effects.**
Condition being studied: **Renal cell carcinoma (RCC) is one of the most common types of malignancies of the genitourinary tract originating from the cells in proximal convoluted tubule. Accordingly, the global mortality nearly doubled in 15 years from 1985 to 2000. Clinically, the majority of patients are asymptomatic during the early stages of RCC thus only a fraction of patients is efficiently diagnosed and subsequently managed. Due to the rapid development and invasiveness of RCC, patients who are only correctly managed during late stage have a comparatively low possibility of complete recovery.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2020 and was last updated on 21 November 2020 (registration number INPLASY2020110093).

INTRODUCTION

Review question / Objective: **What is the efficacy and safety of peri-operative use of sunitinib combined with radical surgery in patients with advanced or metastatic renal carcinoma. What are incidence rates of all-grade or grade≥3 adverse effects.**

Rationale: **This study will evaluate the treating efficacy and occurrence rate of post-operative adverse effects of peri-operative use of sunitinib combine with radical surgery with advanced or metastatic renal cancer, the conclusion of which will help introduce a novel therapeutic pattern or patients with advanced or metastatic RCC.**

Condition being studied: Renal cell carcinoma (RCC) is one of the most common types of malignancies of the genitourinary tract originating from the cells in proximal convoluted tubule. Accordingly, the global mortality nearly doubled in 15 years from 1985 to 2000. Clinically, the majority of patients are asymptomatic during the early stages of RCC thus only a fraction of patients is efficiently diagnosed and subsequently managed. Due to the rapid development and invasiveness of RCC, patients who are only correctly managed during late stage have a comparatively low possibility of complete recovery.

METHODS

Search strategy: PubMed/MEDLINE, Web of Science, Cochrane Library, ClinicalTrials.gov (http:// http://www.ClinicalTrials.gov), China National Knowledge Infrastructure (CNKI). The inclusion criteria will include: first, reported at least either indicators for survival analysis or data concerning the AEs; and second, randomized controlled trials and any observational design, including cross-sectional, case-control, and cohort designs. The study needs to be published between January 2008 to May 2018. There's no language restriction. The search phases are as follows: ((((((sunitinib[Title]) AND (renal cell carcinoma[Title])) OR (RCC[Title])) OR (advanced RCC[Title])) OR (metastatic RCC[Title])) OR (advanced renal cell carcinoma[Title])) OR (metastatic renal cell carcinoma[Title]).

Participant or population: Patients pathologically diagnosed with metastatic or advanced RCC.

Intervention: The intervention is the combined treatment of surgery and adjuvant therapy by sunitinib.

Comparator: Patients with suspected symptoms but without pathologically diagnosed metastatic or advanced RCC.

Study designs to be included: The inclusion criteria will include: first, reported at least either indicators for survival analysis or data concerning the AEs; and second, randomized controlled trials and any observational design, including cross-sectional, case-control, and cohort designs. And case reports, reviews, letters and meeting proceedings will be excluded.

Eligibility criteria: The inclusion criteria will include: first, reported at least either indicators for survival analysis or data concerning the AEs; and second, randomized controlled trials and any observational design, including cross-sectional, case-control, and cohort designs. And case reports, reviews, letters and meeting proceedings will be excluded.

Information sources: PubMed/MEDLINE, Web of Science, Cochrane Library, ClinicalTrials.gov (http:// http://www.ClinicalTrials.gov), China National Knowledge Infrastructure (CNKI).

Main outcome(s): The outcomes include efficacy analysis, including objective response rate, OS and PFS, etc and safety analysis manifested by occurrence rate of adverse effect.

Additional outcome(s): None.

Data management: The information mainly includes the basic details of the articles, patients' demographic characteristics, data concerning the efficacy and safety. More specifically, the key parameters will include OS in 10, 20, 30, and 40 months, PFS in 10, 20, and 30 months, objective response rate (ORR), stable disease (SD) rate, progressive disease (PD) rate, median OS and PFS, types of AEs and their occurrence rates, etc. The baseline characteristics of the articles will include title, first author, nationality, department, study design and enrollment year. Finally, sex and median age, ethnicity of the patients will also be carefully extracted as the demographic features.

Quality assessment / Risk of bias analysis: We will perform standard quality assessment of the included study based on Quadas-2 tool. And this will be done

through RevMan 5.3 (The Cochrane Collaboration). By Quadas-2, The articles will be evaluated in the following processes: sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and others.

Strategy of data synthesis: After selecting qualified articles, we will extract important information from these articles. The information will mainly include the basic details of the articles, patients' demographic characteristics, data concerning the efficacy and safety. More specifically, key parameters will include OS in 10, 20, 30, and 40 months, PFS in 10, 20, and 30months, objective response rate (ORR), stable disease (SD) rate, progressive disease (PD) rate, median OS and PFS, types of AEs and their occurrence rates, etc. The baseline characteristics of the articles will include title, first author, nationality, department, study design and enrollment year. Finally, sex and median age, ethnicity of the patients will also be carefully extracted as the demographic features. The aforementioned parameters are described narratively. The occurrence rate of AEs, including AEs of all grades and of grades ≥3 AEs as well as their 95% confidential interval (CIs) will be calculated based on data collected from these single-arm trials. All the analyses and calculations mentioned above will be conducted using comprehensive meta-analysis (CMA) (Biostat, Englewood, NJ). The minimum number of studies we set is 7articles with medium to high consistency.

Subgroup analysis: None.

Sensibility analysis: No sensibility is planned in this study.

Language: No language limits are intended to be imposed.

Country(ies) involved: China.

Other relevant information: None.

Keywords: adverse effects, efficacy, perioperative use of sunitinib, safety.

Dissemination plans: We intend to publish the protocol onto scientific journals.

Contributions of each author:

Author 1 - Hongyu Jin is responsible for article searching, data extraction and manuscript writing.
Email: jinhongyu@stu.scu.edu.cn
Author 2 - Man Zhang is responsible for aiding the data extraction process and cross-checking the results. Moreover, Man Zhang is in charge of article quality assessment, publication bias evaluation and heterogeneity evaluation.
Email: jinhongyu@stu.scu.edu.cn