INPLASY

Efficacy and safety of HAIC-FOLFOX plus tyrosine kinase inhibitors and immune checkpoint inhibitors as first-line treatment for unresectable advanced hepatocellular carcinoma: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 August 2024 and was last updated on 02 August 2024.

INTRODUCTION

Review question / Objective HAIC-FOLFOX plus tyrosine kinase inhibitors and immune checkpoint inhibitors as first-line treatment for unresectable advanced hepatocellular carcinoma has raised great attention in recent years, many clinical studies present more optimal outcomes. We intend to pool and extract datas of high-quality literatures about this triple therapy for advanced hepatocellular carcinoma published in the last 5 years,and then give an account of the efficacy and safety.
Population: unresectable advanced hepatocellular carcinoma with PVTT and/or tumor occupancy≥50% of the liver ,Child-Pugh A or B;ECOG 0-2.
Intervention: HAIC-FOLFOX plus tyrosine kinase inhibitors and immune checkpoint inhibitors.
Comparison: tyrosine kinase inhibitors or immune checkpoint inhibitors or both of them.
Outcome:ORR, DCR, mPFS, mOS, AEs.
Study design: retrospective cohort study or RCT.

Condition being studied Recently, therapeutic strategies for advanced hepatocellular carcinoma (HCC) have been dramatically changing. Treatment guidelines worldwide recommend systemic therapies as the standard treatment for advanced HCC.Various drugs, such as sorafenib, regorafenib, lenvatinib, ramucirumab, cabozantinib, and atezolizumab plus bevacizumab have been approved. However, curative efficacy and prognosis is still unsatisfactory. HAIC is a locoregional treatment, the benefits of HAIC are increasing local concentrations of anti-cancer drugs in the tumor and reducing systemic adverse events due to anti-cancer drugs.In recent years, HAIC combined with targeted therapy and immunotherapy is gradually becoming the focused topic in the treatment of advanced hepatocellular carcinoma.Based on these points, we conduct this systematic review and meta-analysis and aim to explore the efficacy and safety of HAIC-FOLFOX plus tyrosine kinase inhibitors and immune checkpoint inhibitors as first-line treatment for unresectable advanced hepatocellular carcinoma.

METHODS

Participant or population Unresectable advanced hepatocellular carcinoma.

Intervention HAIC-FOLFOX plus tyrosine kinase inhibitors and immune checkpoint inhibitors.

Comparator Tyrosine kinase inhibitors or immune checkpoint inhibitors or both of them.

Study designs to be included Cohort study or randomized controlled trial.

Eligibility criteria Inclusion criteria: 1. Unresectable advanced hepatocellular carcinoma,BCLC stage B or C, Child-Pugh A or B, ECOG 0-2. 2. HAIC-FOLFOX plus tyrosine kinase inhibitors and immune checkpoint inhibitors as first-line treatment.3. The primary outcomes: all studies should report ORR, DCR, PFS and AEs; secondary outcomes :mOS and surgical conversion rate.
Exclusive criteria:1. Case report, meta analysis or systemic review.2. Data incomplete or unable to obtain desired outcomes.3. Studies are inconsistent with the subject of research.

Information sources Four databases (PubMed, Embase, the Cochrane Library, and Web of Science) were comprehensively searched for relevant studies.

Main outcome(s) The interested clinical tumor outcomes, including objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and adverse events (AEs). The tumor response was evaluated using the mRECIST. Toxic effects were evaluated for their incidence and severity using the Common Terminology Criteria for Adverse Events (CTCAE).

Data management Noteexpress.

Quality assessment / Risk of bias analysis All studies involved were the retrospective studies and were assessed by the JBI Critical Appraisal tool,which includes 10 questions addressing the internal validity and risk of bias of case series designs, particularly confounding, selection and information bias, in addition to the importance of clear reporting.

Strategy of data synthesis STATA 17.0 was used to analyze the data. Heterogeneity was measured using the chisquared test and I2 statistic. $p < 0.1$ indicated a statistically significant difference. If significant heterogeneity p50% existed, a random-effect model was performed. Otherwise, the fixed-effects model was used.

Subgroup analysis None.

Sensitivity analysis Remove single study was used to assess Sensitivity, after removal of individual study the Pooled effect sizes was consistent with that before removal,we hold the opinion that the result was stable and sensitivity analysis was negative.The funnel chart was used to detect publication bias.

Country(ies) involved China.

Keywords Hepatic arterial infusion chemotherapy,tyrosine kinase inhibitors, immune checkpoint inhibitors,unresectable advanced hepatocellular carcinoma.

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