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Exploring the safety and efficacy of Ripretinib against advanced gastrointestinal stromal tumor: 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 09 June 2024 and was last updated on 09 June 2024.

INTRODUCTION

Review question / Objective The present study aimed to analyze the literature on Ripretinib to assess an effective, safe, and successful treatment strategy against advanced gastrointestinal stromal tumor (GIST) and offer guidelines for managing GIST.

Condition being studied Imatinib (IMA) is approved as the first-line drug for gastrointestinal stromal tumor (GIST) treatment. However, about 50% of advanced GIST patients indicate disease progression after use of IMA. Current second - and third-line drugs have limited effectiveness in treating different GIST secondary mutations. Thus, a high medical need remains for developing kinase inhibitors that broadly inhibit secondary drug-resistant mutations in advanced GIST.

METHODS

Participant or population Advanced gastrointestinal stromal tumor patients.

Intervention Studies on Ripretinib.

Comparator Gastrointestinal stromal tumor patients before the study was initiated.

Study designs to be included cohort studies, randomized controlled trials (RCT), and case reports.

Eligibility criteria To assess the reliability and qualification of selected articles, the intervention (I), population (P), outcome (O), comparator (C), and study design (S) framework were employed. The inclusion parameters based on the described framework included, (P): advanced GIST patients, (I): studies on RPT, (C): GIST patients before the

study was initiated, (O): studies with data of disease control rate (DCR), the adverse reactions rate (ARR), and objective response rate (ORR), and (S): cohort studies, randomized controlled trials (RCT), and case reports.

Information sources For comprehensive analysis, different databases, including Web of Science (https://webofscience.clarivate.cn/), PubMed (http://www.ncbi.nlm.nih.gov/pubmed), ClinicalTrials.gov (clinicaltrials.gov/), Embase (https://www.embase.com/), and Cochrane (https://www.cochranelibrary.com/) were extensively searched.

Main outcome(s) ORR, ARR, DCR, and grade ≥ 3 adverse reactions, as well as the outcomes and corresponding 95% confidence intervals (CIs), were also evaluated.

Quality assessment / Risk of bias analysis The literature screening was carried out by 2 researchers, JL and HZ, who carefully reviewed the topic, picked articles that met the above criteria, and elucidated the selected article's full text and abstract. For RCT, two researchers cross-estimated the literature's quality based on the RCT Jadad method, double-blind method setting, from random allocation, randomized hiding, as well as exit and loss to follow-up (based on 7 point scores, 1 – 3 = inferior quality, 4 – 7 = high-quality literature) . Moreover, they also elucidated the methodological quality of selected articles based on the guidelines of the Cochrane Review handbook. The Newcastle-Ottawa scale (NOS) was employed to elucidate cohort study quality. The NOS is an extensive framework comprising 8 items grouped into 3 domains: exposure or outcome evaluation, population selection, and comparability. A numerical score was assigned to each item between 0 – 9 scale, where > 5 scores represent a high-quality level.

Strategy of data synthesis The I2 statistic and Cochran's Q test were carried out to assess the inter-study heterogeneity, where 50% and 75% values, a sensitivity test was carried out to assess the impact size and research heterogeneity. To ensure the result's stability, studies that significantly influenced heterogeneity were excluded. For combined analysis, a random effect model was employed, while funnel plots were drawn to elucidate publication bias. The potential bias and plot asymmetry were evaluated simultaneously using Begg's and Egger's tests. p-value of < 0.05 was the threshold for the significantdifference.

Subgroup analysis None.

Sensitivity analysis The sensitivity analysis revealed that studies exclusion had no statistically essential variations in the combined analysis data of ORR (Figure 3A), DCR (Figure 3B), and the occurrence of grade ≥ 3 adverse events , suggesting that the results acquired were valid and reliable. However, the sensitivity test of the overall ARR was statistically significant, indicating that the result might not be completely reliable.

Country(ies) involved China.

Keywords gastrointestinal stromal tumor, ripretinib, meta-analysis.

Contributions of each author
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