INPLASY PROTOCOL

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None declared.

Efficacy and safety of copanlisib in relapse/refractory B-cell non-Hodgkin lymphoma: A meta-analysis of prospective clinical trials

Wang, JJ[1].

Review question / Objective: **Populations: patients with relapse/refractory B-cell non-Hodgkin lymphoma interventions: copanlisib monotherapy or combination therapy with rituximab no comparator due to single-arm meta-analysis outcomes: efficacy (CR, PR, SDR, ORR, DCR, PDR, PFS, OS) and safety (any grade and grade≥3 adverse reactions). study design: prospective clinical trials.**
Eligibility criteria: **The inclusion criteria: 1) prospective clinical trials at any stage; 2) studies including patients diagnosed with R/R B-NHL; 3) articles containing copanlisib monotherapy or combination therapy with rituximab; 4) clinical trials reporting the data involving efficacy or safety. The exclusion criteria: 1) no available data of efficacy or safety; 2) reviews, case reports, news, editorials, meta-analyses, and meeting/conference abstracts.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 October 2022 and was last updated on 02 October 2022 (registration number INPLASY2022100008).

INTRODUCTION

Review question / Objective: **Populations: patients with relapse/refractory B-cell non-Hodgkin lymphoma interventions: copanlisib monotherapy or combination therapy with rituximab no comparator due to single-arm meta-analysis outcomes: efficacy (CR, PR, SDR, ORR, DCR, PDR, PFS, OS) and safety (any grade and grade≥3 adverse reactions). study design: prospective clinical trials.**

Condition being studied: **Phosphatidylinositol 3-kinase (PI3K) is a lipid kinase that plays an important role in cell proliferation, differentiation and other processes. PI3K is abnormally activated in**

tumors, so PI3K inhibitors are a promising drug for the treatment of tumors. Currently, oral PI3K inhibitors approved by the Food and Drug Administration (FDA) for the treatment of lymphoma include idelalisib and duvelisib. However, the FDA gave a black box warning for the adverse reactions caused by the two drugs. Copanlisib is an intravenously administered pan-class I PI3K inhibitor that has been approved for relapsed follicular lymphoma in 2017. Various clinical trials have been or are investigating the efficacy and safety of copanlisib-containing regimens in the treatment of patients with relapsed/refractory B-cell non-Hodgkin lymphoma. Therefore, it is necessary to comprehensively evaluate the efficacy and safety of copanlisib in relapse/refractory B-cell non-Hodgkin lymphoma. Our study found that the efficacy of both copanlisib monotherapy and combination therapy with rituximab in patients with relapsed/refractory B-cell non-Hodgkin lymphoma were satisfactory, while treatment-related AEs were tolerable.

METHODS

Search strategy: Pubmed, Web of science, Embase, and Cochrane Central Register of Controlled Trials.

Participant or population: Relapse/refractory B-cell non-Hodgkin lymphoma.

Intervention: Copanlisib monotherapy or combination therapy with rituximab.

Comparator: No.

Study designs to be included: Prospective clinical trials.

Eligibility criteria: The inclusion criteria: 1) prospective clinical trials at any stage; 2) studies including patients diagnosed with R/R B-NHL; 3) articles containing copanlisib monotherapy or combination therapy with rituximab; 4) clinical trials reporting the data involving efficacy or safety. The exclusion criteria: 1) no available data of efficacy or safety; 2) reviews, case reports, news, editorials, meta-analyses, and meeting/conference abstracts.

Information sources: Pubmed, Web of science, Embase, and Cochrane Central Register of Controlled Trials.

Main outcome(s): Efficacy evaluation included complete response rate (CR), partial response rate (PR), rate of stable disease (SDR), overall response rate (ORR), disease control rate (DCR), rate of progressive disease (PDR), median progression-free survival (PFS), and median overall survival (OS). Safety evaluation included any grade adverse reactions (AEs) and grade≥3 AEs.

Quality assessment / Risk of bias analysis: For the involved randomized controlled trials (RCT), the quality was estimated by Cochrane Collaboration Risk of Bias Tool. The methodological index for non-randomized studies (MINORS) was utilized to assessed the quality of the enrolled non-RCT.

Strategy of data synthesis: Statistical analysis of data was processed on R 4.1.1 software. The I^2 statistic test were applied to appraise heterogeneity among studies. The value of I^2 statistic is 0 to 100%. $I^2$50% manifests obvious heterogeneity. A fixed-effect model was employed if I2 statistics was low (I2≤50%), while the random-effect was utilized with I2>50%.

Subgroup analysis: Subgroup analysis (copanlisib vs including copanlisib plus rituximab; R/R indolent B-NHL vs R/R aggressive B-NHL) was employed to address heterogeneity.

Sensitivity analysis: Sensitivity analysis was carried out by using different effect models.

Country(ies) involved: China.

Keywords: coapnlisib, rituximab, R/R B-NHL, efficacy, safety, meta-analysis.

Contributions of each author:

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