INPLASY PROTOCOL

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None declared.

Efficacy and safety of burosumab in X-linked hypophosphataemia: Systematic review and meta-analysis

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Review question / Objective: **Burosumab, a fully human monoclonal antibody to fibroblast growth factor 23 (FGF23), is approved for the treatment of X-linked hypophosphataemia (XLH), the most common inherited form of rickets. To assess the efficacy and safety of burosumab in patients with XLH, we conducted a systematic review and meta-analysis.X-linked hypophosphataemia.**
Condition being studied: **X-linked hypophosphataemia (XLH) is the most common genetic cause of rickets, which is caused by a loss-of-function mutation in the phosphate regulated endopeptidase homologous gene, X-linked gene[1, 2]. The disease is characterised by the increased concentrations of fibroblast growth factor 23 (FGF23) in the blood, resulting in hypophosphataemia by increasing phosphoruria and inhibiting the synthesis of 1,25-dihydroxyvitamin D (1,25(OH)2 D). Hypophosphataemia and defects in bone mineralisation can result in rickets, osteomalacia, skeletal deformities and short stature, which persists into adulthood and are accompanied by impaired physical function and musculoskeletal pain.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 August 2022 and was last updated on 15 August 2022 (registration number INPLASY202280058).

INTRODUCTION

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METHODS

Search strategy: The literature search was conducted using PubMed, Embase, ClinicalTrials.gov, Web of Science and the Cochrane Library up to August 1, 2022. The medical subject heading keywords including "Burosumab," "KRN23," "X-linked hypophosphataemia," "Hypophosphatemic Rickets, X-Linked." was used to search for burosumab and X-linked hypophosphataemia. To ensure a comprehensive literature search, we also screened reference lists from included articles. The ClinicalTrials.gov website was searched for ongoing but unpublished trials in this field.

Participant or population: Patients with XLH.

Intervention: Burosumab.

Comparator: Placebo or traditional treatment.

Study designs to be included: randomized controlled trials and single-arm trials.

Eligibility criteria: We included trials of all designs, including randomized controlled trials (RCTs), non-randomized controlled trials and single-arm trials(SATs). Studies included in this meta-analysis satisfied the following criteria: (1) interventions using burosumab ; (2) Studies must have been published in peer-reviewed academic journals or as part of scientific conference proceedings. The available data were used to calculate the corresponding statistics. Meeting abstracts, animal studies, and review articles were not included.

Information sources: PubMed, Embase, ClinicalTrials.gov, Web of Science and the Cochrane Library, reference lists from included articles.

Main outcome(s): Overall, 343 articles were found after a multi-database search, and no additional records were found during manual searches of reference lists up to August 1, 2022.

Quality assessment / Risk of bias analysis: We assessed the methodological quality (risk of bias) of each RCT in accordance with the Cochrane Risk of Bias Tool (CCRBT) for the randomized clinical trials. Risk of bias was determined in duplicate, and discrepancies were resolved by consensus in group discussion. The methodological index for non-randomized studies (MINORS) was also used to assess the overall quality of the SATs.

Strategy of data synthesis: We performed separate analyses for randomized controlled trails and single-arm studies. For RCTs, we computed net differences as Net change = (burosumab at final –burosumab at baseline) – (control at final – control at baseline) for outcomes. For single arm trials, we computed change in outcomes as (Change = burosumab at final – burosumab at baseline). The meta-analysis was carried out using the Review Manager (version: 5.4) and Stata platform (version: 15.1), and the combined effect was expressed as a weighted mean difference (WMD) and its 95% confidence interval (CI), that is, WMD (95 percent CI). The heterogeneity test was applied to the studies, and heterogeneity is considered low when I2 is >50%. Moreover, the outcome indicators were combined using the fixed-effect model, and if I2 ≥ 50%, it is considered that there is more than moderate heterogeneity. Additionally, to combine the outcome indicators, the random-effect model is applied.

Subgroup analysis: Based on the administration frequency outcomes were divided to q2w group and q4w group.

Sensitivity analysis: Sensitivity analysis was not performed.

Country(ies) involved: China.

Keywords: Burosumab, X-linked hypophosphataemia, monoclonal antibody, fibroblast growth factor 23, serum phosphorus, adverse event, meta-analysis.

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