INPLASY

Efficacy of Different Biologics in the Treatment of Moderate-to-Severe Allergic Asthma: A Systematic Review and Network Meta-Analysis

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Li, YL; Zong, H; Fan, XM; Luo, D; Song, ZY; Chen, WB.

Corresponding author:
Yuelu Li

liyuelu121@163.com

Author Affiliation:
Southwest Medical University.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

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 30 March 2025 and was last updated on 30 March 2025.

INTRODUCTION

Review question / Objective This study aims to analyze clinical randomized controlled trial data on the efficacy of different biologics in treating moderate-to-severe allergic asthma using a network meta-analysis method based on a frequentist framework. The goal is to compare the effectiveness of various biologics in the treatment of moderate-to-severe allergic asthma and to rank and evaluate their efficacy. This research seeks to provide evidence-based medical guidance for biologic-targeted therapy in moderate-to-severe allergic asthma.

Condition being studied Asthma is a complex and heterogeneous disease that exhibits various phenotypes based on underlying clinical and inflammatory mechanisms. Among them, allergic asthma is the most common clinical phenotype of asthma, characterized by asthma triggered by allergens, primarily driven by T-helper cell type 2 (Th2) immune responses. In recent years, the prevalence of allergic asthma has been rising annually, accounting for approximately 62% of the overall asthma prevalence, with a proportion of 58% among uncontrolled asthma patients and 60% among those with severe asthma, leading to significant increases in emergency visits and hospitalization rates, thereby greatly increasing the burden on healthcare resources. Currently, approximately 5%-10% of patients with moderate to severe allergic asthma still exhibit poor control of asthma symptoms despite standardized treatment with corticosteroids combined with long-acting β2-adrenergic agonists, and some even showing a tendency towards corticosteroid dependence.To effectively control asthma symptoms and reduce the future risk of adverse outcomes, various biologics targeting asthma have been developed.Among these, four types of biologics have been successively approved for marketing: anti- immunoglobulin E (IgE) monoclonal antibody (Omalizumab), anti -interleukin (IL)-5 monoclonal antibodies (Mepolizumab, Reslizumab) /anti-IL-5 receptor monoclonal antibody (Benralizumab), anti-IL-4/ IL-13 monoclonal antibody (Dupilumab), and anti-

thymic stromal lymphopoietin (TSLP) monoclonal antibody (Tezepelumab).An increasing number of clinical randomized controlled trials (RCTs) have indicated that, compared to conventional treatment alone, certain biologics used as adjunctive therapy demonstrate significant clinical advantages in reducing acute exacerbations of moderate to severe allergic asthma, effectively controlling asthma symptoms, improving lung function, and enhancing quality of life. How to select the appropriate biologics based on the clinical phenotypes of asthma has become a central issue of concern in asthma biotherapy.However, due to the varying definitions of treatment response and outcome measurement methods for biologics in clinical trials, it is challenging to assess the relative efficacy of different biologics in the absence of direct comparative studies.

METHODS

Search strategy We searched the PubMed, Embase, Cochrane Library, and Web of Science for randomized controlled trials of approved biologics for the treatment of moderate-to-severe allergic asthma from database inception to July 2024. Our search terms primarily included: “asthma”,“lung allerg*”,“bronchial asthma”, “Omalizumab,” “Benralizumab,” “Dupilumab,” “Tezepelumab,” “Mepolizumab,” “Reslizumab,” “randomized controlled trial,” “random*,” and others.

Participant or population Individuals aged 12 years and older, regardless of gender or race, who fulfill the diagnostic criteria for moderate to severe allergic asthma according to the asthma management guidelines.

Intervention The experimental group received biologic injection therapy in addition to the standard treatment for moderate to severe allergic asthma, with appropriate dosage and frequency of administration determined based on the approved dosage.

Comparator The control group received standard therapy with or without a placebo, with the administration of the placebo being identical to that of the biologic.

Study designs to be included Only randomized controlled trials (RCTs) will be included in this study.

Eligibility criteria 1. Inclusion criteria: (1) Study type: Clinical randomized controlled trials on biologic therapy for moderate to severe allergic asthma, limited to English-language literature;(2) Study participants: Adolescents and adults aged 12 years or older, meeting the diagnostic criteria for moderate to severe allergic asthma according to the asthma management guidelines, regardless of gender or race;(3) Intervention: The experimental group received biologic injection therapy in addition to the standard treatment for moderate to severe allergic asthma; the control group received standard therapy with or without a placebo, with the placebo administered in the same way as the biologic.(4) Efficacy outcomes : The primary efficacy outcomes include the frequency of asthma exacerbations, Forced Expiratory Volume in 1 second (FEV1), Asthma Control Questionnaire (ACQ) score, and Asthma Quality of Life Questionnaire (standardized) +12 (AQLQ[S]+12) score.
2. Exclusion criteria: (1) For multiple publications based on the same trial, only the most complete or most recent publication is included;(2) Exclude conference abstracts, single-arm studies, and studies without important efficacy endpoints, or those with incomplete or missing data.

Information sources We searched the PubMed, Embase, Cochrane Library, and Web of Science for randomized controlled trials of approved biologics for the treatment of moderate-to-severe allergic asthma from database inception to December 2024.

Main outcome(s) The annualized mean number of asthma exacerbations, the change from baseline in forced expiratory volume in 1 second (FEV1), the Asthma Control Questionnaire (ACQ) scores, and Asthma Quality of Life Questionnaire (standardized) +12 scores (AQLQ[S]+12).

Quality assessment / Risk of bias analysis Methodological quality and specifically risk of bias, of included studies, will be assessed independently by two reviewers according to the risk of bias (ROB) tool as described in the Cochrane Hand book.

Strategy of data synthesis We conducted network meta-analyses (NMA) using Stata 18.0 on randomized controlled trials assessing biologic treatments for moderate to severe allergic asthma. In the quantitative synthesis, we performed a random-effects network meta-analysis (NMA) utilizing a frequentist approach to aggregate the available data and estimate the comparative efficacy of all treatment pairs. We estimated mean differences (MD) and calculated the associated 95% credible intervals (CIs) for continuous outcomes. For each intervention, the cumulative

probability was computed to derive the surface under the cumulative ranking curve (SUCRA) value and plotted the cumulative probability. A larger area under the curve indicates a higher ranking for that intervention, suggesting a greater likelihood of it being the optimal treatment option.We computed each study effect size against the standard error and generated comparison-adjusted funnel plots using Stata 18.0 to assess the existence of publication bias or small sample effects .Since there were no head-to-head randomized controlled trials among the biological agents, all evidence network diagrams lacked closed loops, and thus, the side-splitting method was not employed to evaluate statistical inconsistency.

Subgroup analysis None.

Sensitivity analysis To verify the robustness of our analysis conclusions, sensitivity analysis of outcomes will be executed according to different levels of methodological quality, study quality, sample size, effect of missing data as well as the analysis methods.

Language restriction English.

Country(ies) involved China.

Keywords Moderate-to-severe allergic asthma; Biologics; Efficacy; Network meta-analysis.

Contributions of each author
Author 1 - Yuelu Li.
Author 2 - Xianming Fan.
Author 3 - Dan Luo.
Author 4 - Huan Zong.
Author 5 - Zhangyong Song.
Author 6 - Wenbi Chen.