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# Efficacy of Rituximab as Second-Line Therapy for Autoimmune Encephalitis: A systematic review and meta-analysis

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# **ADMINISTRATIVE INFORMATION**

**Support** - The author(s) received no financial support for the research.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

**INPLASY registration number:** INPLASY202490012

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 September 2024 and was last updated on 3 September 2024.

## **INTRODUCTION**

Review question / Objective This study aimed to evaluate rituximab's efficacy in AE patients unresponsive or inadequately responsive to first-line therapies via a systematic review and meta-analysis, aiming to enhance AE treatment protocols.

Condition being studied Approximately 20%-50% of patients with autoimmune encephalitis (AE) exhibit suboptimal responses to first-line therapy, resulting in ongoing neurological deficits and necessitating second-line interventions. Despite some indication of rituximab's effectiveness in AE, comprehensive evidence remains lacking.

# **METHODS**

**Participant or population** AE patients treated with rituximab.

**Intervention** Intravenous rituximab at any dose, cycle, and duration.

**Comparator** Conventional immunomodulatory therapy is administered for treatment.

**Study designs to be included** Prospective or retrospective studies published in English or Chinese.

Eligibility criteria (1) study patients: AE patients treated with rituximab; (2) study interventions: intravenous rituximab at any dose, cycle, and duration; (3) study type: prospective or retrospective studies published in English or Chinese; (4) study outcomes: favorable function.

Information sources Two authors independently conducted searches across six databases: PubMed, Google Scholar, Web of Science, EBSCO, CNKI, and Wanfang, covering the period from database inception to 2024. Additionally, preprint servers and paper databases were

examined for unpublished studies. Studies meeting the inclusion and exclusion criteria from both methods were included. The search primarily employed two sets of subject terms: "Rituximab", "Rituxan", "Mabthera", "RTX", "Mab", "Ma", "AE", "encephalitis", "Anti-NMDAR encephalitis", and "autoimmune encephalitis". Boolean logic operators "OR" were used to connect terms within subject groups, while "AND" linked the subject term groups, as detailed in the supplementary material "Search Strategy".

Main outcome(s) Efficacy of rituximab as secondline therapy for autoimmune encephalitis.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa Scale (NOS) assessed cohort study quality, focusing on study population selection, between-group comparability, and outcome measures.

Strategy of data synthesis Statistical analyses were executed using R 4.3.3 software. The favorable prognosis rate served as the effect analysis statistic, with interval estimation employing a 95% confidence interval (95%-CI). Heterogeneity was measured by I2. P  $\geq$  0.10 and I2  $\leq$  50% indicated low heterogeneity, warranting the use of a fixed effects model; P 50% indicated high heterogeneity, necessitating a random effects model. Publication bias was assessed via a funnel plot. The significance threshold was set at  $\alpha$  = 0.05.

**Subgroup analysis** 1 Age subgroup; 2 Disease duration subgroup.

**Sensitivity analysis** A meta-analysis was conducted excluding one article to assess robustness.

**Country(ies) involved** China /Department of Emergency Medicine, Dali Bai Autonomous Prefecture People's Hospital.

**Keywords** rituximab, autoimmune encephalitis, treatment effects, N-methyl-D-aspartate receptor, Meta-analysis.

## Contributions of each author

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