

# INPLASY PROTOCOL

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**Support:** No

**Review Stage at time of this  
submission:** The review has  
not yet started.

**Conflicts of interest:**  
None.

## Effectiveness of rituximab in myelin oligodendrocyte glycoprotein antibody-associated disease: A protocol for systematic review and meta-analysis

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**Review question / Objective:** This review will assess the efficacy of rituximab (RTX) in patients with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).

**Condition being studied:** Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is increasingly regarded as a distinct entity from multiple sclerosis (MS) and aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG-NMOSD). To date, there are no standardised international guidelines for the management of MOGAD, resulting in heterogeneous policies not only in the type of maintenance therapy used, but also in the time to initiate treatment. Rituximab (RTX) was initially approved for the treatment of B-cell lymphoma and has become the first-line therapy for AQP4-IgG-NMOSD in many countries. So far, the experience of using RTX in MOGAD is still based on single-cohort studies. To our knowledge, there is a lack of data on the efficacy of RTX in MOGAD and the influence of disease duration and severity on clinical response. Therefore, we will conduct a systematic review and a meta-analysis to evaluate the efficacy and safety of RTX use for the treatment of MOGAD.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 August 2020 and was last updated on 14 August 2020 (registration number INPLASY202080057).

### INTRODUCTION

**Review question / Objective:** This review will assess the efficacy of rituximab (RTX) in patients with myelin oligodendrocyte

glycoprotein antibody-associated disease (MOGAD).

**Rationale:** Previous studies on the response to MOGAD treatment included a smaller number of patients treated with

RTX. They also observed a decrease in the recurrence rate after RTX treatment. Compared with AQP4-IgG-NMOSD, RTX does not seem to have the expected benefits of MOGAD, which supports the observation of small case series. Recently, the largest international research on the effectiveness of RTX in MOGAD has been conducted. We hope that this.

**Condition being studied:** Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is increasingly regarded as a distinct entity from multiple sclerosis (MS) and aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG-NMOSD). To date, there are no standardised international guidelines for the management of MOGAD, resulting in heterogeneous policies not only in the type of maintenance therapy used, but also in the time to initiate treatment. Rituximab (RTX) was initially approved for the treatment of B-cell lymphoma and has become the first-line therapy for AQP4-IgG-NMOSD in many countries. So far, the experience of using RTX in MOGAD is still based on single-cohort studies. To our knowledge, there is a lack of data on the efficacy of RTX in MOGAD and the influence of disease duration and severity on clinical response. Therefore, we will conduct a systematic review and a meta-analysis to evaluate the efficacy and safety of RTX use for the treatment of MOGAD.

## METHODS

**Search strategy:** This study will search the following electronic databases until October 31, 2020: PUBMED, Web of Science, EMBASE, Cochrane Library, China National Knowledge Infrastructure Database (CNKI), Wan fang Database, China Science and Technology Journal database (VIP), and Chinese Biomedical Literature Database (CBM), without language restriction. We will combine Medical Subject Heading (MeSH) and free text terms with database-specific controlled vocabulary and text words to implement search strategies. Besides, we will also search other resources, such as

thesis, conference papers, and reference lists of related reviews.

**Participant or population:** We will include studies on patients who have been diagnosed with MOGAD according to the recognized diagnostic criteria, regardless of age, race, sex, and nationality.

**Intervention:** This study included all MOGAD patients receiving RTX treatment.

**Comparator:** All patients who have received other treatments for MOGAD will be considered for inclusion in the study.

**Study designs to be included:** This study includes all studies about the use of RTX in patients with MOGAD.

**Eligibility criteria:** This study will include all studies about the use of RTX in MOGAD patients without language restrictions. We will exclude some studies, such as animal studies, review, case reports < 2 patients.

**Information sources:** PUBMED, Web of Science, EMBASE, Cochrane Library, China National Knowledge Infrastructure Database (CNKI), Wan fang Database, China Science and Technology Journal database (VIP), and Chinese Biomedical Literature Database (CBM). Besides, we will also search other resources, such as thesis, conference papers, and reference lists of related reviews.

**Main outcome(s):** Primary outcomes include the difference in the annualized relapse rate (ARR) ratio and the mean expanded disability status scales (EDSS) score before and after RTX therapy.

**Additional outcome(s):** Secondary outcomes include the proportion of adverse effects and death.

**Data management:** Two reviewers will extract data independently using a predefined data extraction form. Any differences between 2 reviewers will be solved by a third reviewer through discussion. For each study, the following data will be extracted: the first author,

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publication year, country, number of participants, mean age and gender of participants, interventions details in treatment and control groups, duration, main outcomes, additional outcomes and adverse events. Any insufficient or missing data will be required from original trial authors by email, fax, or telephone.

annualized relapse rate, expanded disability status scale.

**Contributions of each author:**

Author 1 - Honglu Song.

Author 2 - Yucai Chuai.

Author 3 - Tao Jin.

**Quality assessment / Risk of bias analysis:**

Two reviewers will use the Cochrane Risk of Bias tool to independently assess the risk of bias for each trial. This tool covers 7 domains and each aspect is further rated as high, unclear, or low risk of bias. With the help of a third reviewer, the differences between 2 reviewers will be resolved through discussion.

**Strategy of data synthesis:** In this study, RevMan 5.3 software will be used for statistical analysis. If the trials are homogeneous and the data are similar and synthesizable, we will conduct a meta-analysis based on the study information, patient characteristics, details of interventions and controls, and outcome indicators. However, if we find significant heterogeneity, we will perform subgroup analysis and meta-regression test to investigate the sources of significant heterogeneity.

**Subgroup analysis:** We will conduct a subgroup analysis to check for obvious heterogeneity based on the different types of study characteristics, the details of treatments and comparators, and outcome indicators.

**Sensibility analysis:** We will conduct a sensitivity analysis to check the robustness of merged outcome results by deleting low quality trials. The main decision includes sample size, study quality, methods and missing data.

**Language:** No language restriction.

**Country(ies) involved:** China.

**Keywords:** myelin oligodendrocyte glycoprotein antibody, rituximab,