CADTH RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

Rituximab for Granulomatosis with Polyangiitis or Microscopic Polyangiitis: A Review of the Clinical effectiveness, Cost-effectiveness, and Guidelines
**Authors:** Chuong Ho, Carolyn Spry

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**Funding:** CADTH receives funding from Canada’s federal, provincial, and territorial governments, with the exception of Quebec.
Context and Policy Issues
Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) belong to a group of rare autoimmune diseases called anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, characterized by inflammatory cell infiltration leading to necrosis of the blood vessels.\textsuperscript{1,2}

Treatment of GPA and MPA includes remission induction and remission maintenance. Currently, rituximab, a monoclonal antibody, is one of the therapeutic options approved for the induction phase.\textsuperscript{1,3,4} Recently, a number of uncontrolled studies have suggested that rituximab can also be of value in maintaining remission.\textsuperscript{5-10}

This Rapid Response report aims to review the clinical effectiveness of rituximab compared to other immunosuppressive drugs. Cost-effectiveness and evidence-based guidelines regarding the use of rituximab for patients with GPA and MPA will also be examined. This review is an update of a previous CADTH review that found no evidence on the comparative clinical effectiveness of rituximab for remission maintenance in patients with GPA and MPA.\textsuperscript{11}

Research Questions
1. What is the clinical effectiveness regarding the use of rituximab for patients with granulomatosis with polyangiitis and microscopic polyangiitis to maintain remission?
2. What is the cost-effectiveness regarding the use of rituximab for patients with granulomatosis with polyangiitis and microscopic polyangiitis to maintain remission?
3. What are the evidence-based guidelines regarding the use of rituximab, including dosing strategies, for patients with granulomatosis with polyangiitis and microscopic polyangiitis?

Key Findings
No evidence on the clinical effectiveness of rituximab, compared with other active treatment or no treatment, for remission maintenance in patients with GPA and MPA was identified. There were no cost-effectiveness and guidelines found regarding the use of rituximab for remission maintenance for GPA and MPA.

Methods
Literature Search Methods
A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. A filter was applied to limit retrieval to guidelines for articles published between January 1, 2012 and December 1, 2014. No filters were applied to limit the retrieval by study type for articles published between December 1, 2014 and April 17, 2017. The search was limited to English language documents.
Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods
One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients with GPA and MPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Rituximab beyond an initial course of weekly intravenous treatment for 4 weeks</td>
</tr>
<tr>
<td>Comparator</td>
<td>Cyclophosphamide, glucocorticoids, any comparator, placebo, and no extended treatment (for safety only)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Clinical effectiveness, safety, cost-effectiveness, guidelines</td>
</tr>
<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews (SRs), meta-analyses, randomized controlled trials (RCTs), non-RCTs, economic evaluations, guidelines</td>
</tr>
</tbody>
</table>

Exclusion Criteria
Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2012 for guidelines, and prior to 2014 for clinical and economic studies. Studies included in the selected systematic reviews were also excluded.

Summary of Evidence

Quantity of Research Available
A total of 147 citations were identified in the literature search. Following screening of titles and abstracts, 136 citations were excluded and 11 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publication was retrieved from the grey literature search. Of these potentially relevant articles, no publication met the inclusion criteria to be included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Findings

What is the clinical effectiveness regarding the use of rituximab for patients with GPA and MPA to maintain remission?
No evidence was found on the clinical effectiveness regarding the use of rituximab for patients with GPA MPA to maintain remission.

What is the cost-effectiveness regarding the use of rituximab for patients with GPA and MPA to maintain remission?
No evidence was found on the cost-effectiveness regarding the use of rituximab for patients with GPA and MPA to maintain remission.
What are the evidence-based guidelines regarding the use of rituximab, including dosing strategies, for patients with GPA and MPA?

No evidence was found on the evidence-based guidelines regarding the use of rituximab for patients with GPA and MPA.

Conclusions and Implications for Decision or Policy Making

There is no additional evidence found since a previous 2015 CADTH review that found no evidence on the clinical effectiveness and the cost-effectiveness of rituximab compared with active or no treatment for remission maintenance in patients with GPA and MPA. Similar to uncontrolled studies reported in the previous CADTH review, recent uncontrolled studies (Appendix 2) on the use of rituximab as maintenance therapy for GPA and MPA found some value of rituximab in reducing relapses and maintaining remission, but the lack of a comparator group made comparison to other immunosuppressive drugs impossible. Randomized controlled trials comparing rituximab to other immunosuppressive drugs for remission maintenance in patients with GPA and MPA are needed. No evidence was found on cost-effectiveness and no evidence-based guidelines regarding the use of rituximab for patients with GPA and MPA were identified.
References


Appendix 1: Selection of Included Studies

147 citations identified from electronic literature search and screened

136 citations excluded

11 potentially relevant articles retrieved for scrutiny (full text, if available)

11 potentially relevant reports

0 potentially relevant reports retrieved from other sources (grey literature, hand search)

11 reports excluded:
- no comparator (1)
- irrelevant outcomes (1)
- other (review articles) (9)

0 reports included in review
Appendix 2: Additional References of potential interest


