CADTH

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

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	May 17, 2017
Report Length:	8 Pages

CADTH

Authors: Chuong Ho, Carolyn Spry

Cite As: Rituximab for granulomatosis with polyangiitis or microscopic polyangiitis: a review of the clinical effectiveness, cost-effectiveness, and guidelines. Ottawa: CADTH; 2017; May. (CADTH rapid response report: summary with critical appraisal).

ISSN: 1922-8147 (online)

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.[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.[1,3,4] Recently, a number of uncontrolled studies have suggested that rituximab can also be of value in maintaining remission.[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.[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

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

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.

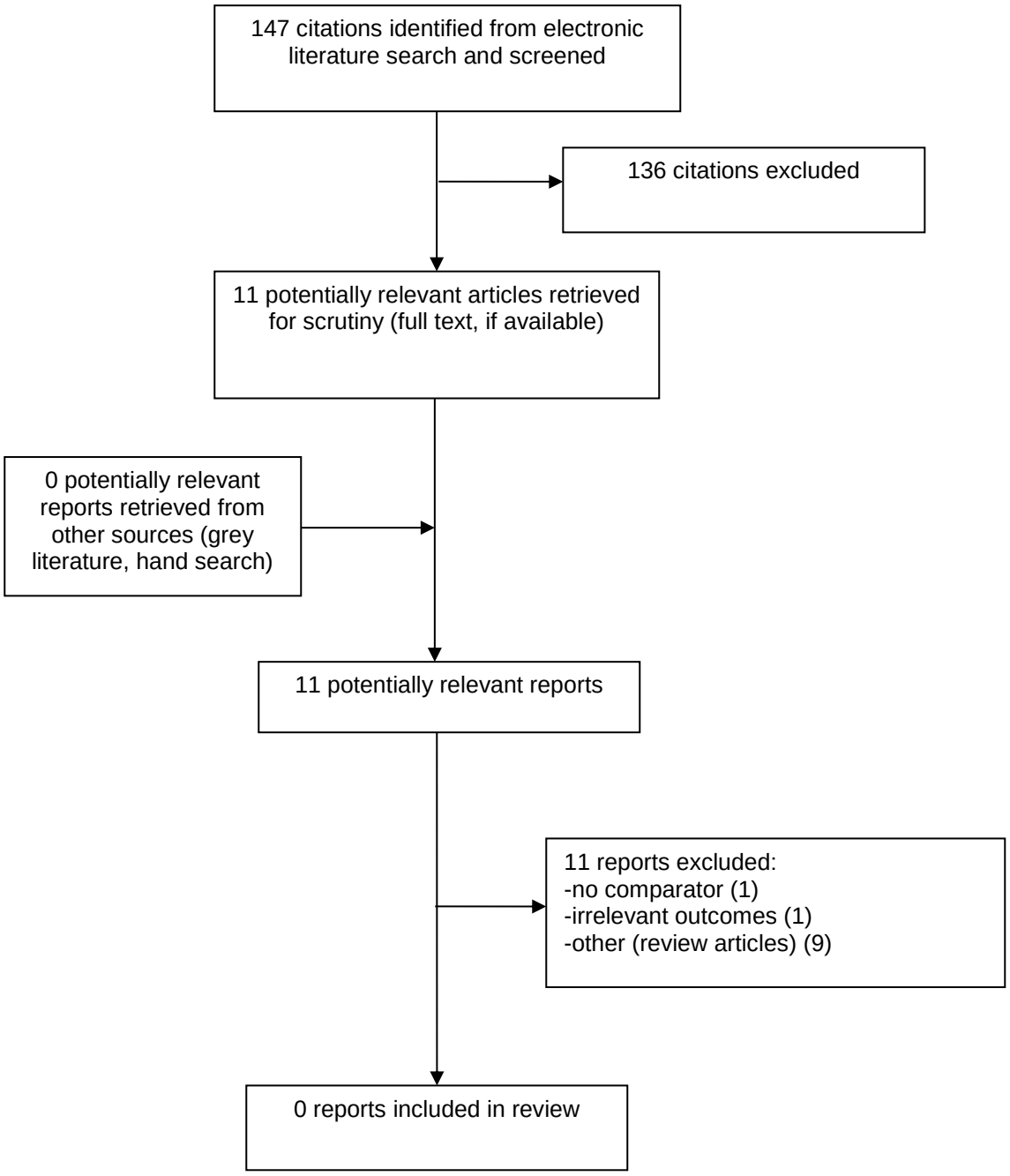
Conclusions and Implications for Decision or Policy Making

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.[11] 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[5,6] 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

1. Yates M, Watts R. ANCA-associated vasculitis. Clin Med (Lond) [Internet]. 2017 Feb [cited 2017 Apr 20];17(1):60-4. Available from: http://www.clinmed.rcpjournal.org/content/17/1/60.full.pdf+html
2. Vasculitis types. In: About vasculitis [Internet]. Toronto: Vasculitis Foundation Canada; 2017 [cited 2017 May 3]. Available from: http://www.vasculitis.ca/?page_id=68
3. Randall KL. Rituximab in autoimmune diseases. Aust Prescr [Internet]. 2016 Aug [cited 2017 Apr 19];39(4):131-4. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4993704/pdf/austprescr-39-131.pdf
4. Moog P, Thuermel K. Spotlight on rituximab in the treatment of antineutrophil cytoplasmic antibody-associated vasculitis: current perspectives. Ther Clin Risk Manag [Internet]. 2015 [cited 2017 Apr 19];11:1749-58. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4669915/pdf/tcrm-11-1749.pdf
5. Besada E, Nossent JC. CD4 cell count and CD4/CD8 ratio increase during rituximab maintenance in granulomatosis with polyangiitis patients. PeerJ [Internet]. 2016 [cited 2017 Apr 19];4:e2487. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5036106/pdf/peerj-04-2487.pdf
6. Alberici F, Smith RM, Jones RB, Roberts DM, Willcocks LC, Chaudhry A, et al. Long-term follow-up of patients who received repeat-dose rituximab as maintenance therapy for ANCA-associated vasculitis. Rheumatology (Oxford) [Internet]. 2015 Jul [cited 2017 Apr 20];54(7):1153-60. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4473766/pdf/keu452.pdf
7. Calich AL, Puechal X, Pugnet G, London J, Terrier B, Charles P, et al. Rituximab for induction and maintenance therapy in granulomatosis with polyangiitis (Wegener's). Results of a single-center cohort study on 66 patients. J Autoimmun. 2014 May;50:135-41.
8. Cartin-Ceba R, Golbin JM, Keogh KA, Peikert T, Sanchez-Menendez M, Ytterberg SR, et al. Rituximab for remission induction and maintenance in refractory granulomatosis with polyangiitis (Wegener's): ten-year experience at a single center. Arthritis Rheum. 2012 Nov;64(11):3770-8.
9. Besada E, Koldingsnes W, Nossent JC. Serum immunoglobulin levels and risk factors for hypogammaglobulinaemia during long-term maintenance therapy with rituximab in patients with granulomatosis with polyangiitis. Rheumatology (Oxford). 2014 Oct;53(10):1818-24.
10. Roubaud-Baudron C, Pagnoux C, Meaux-Ruault N, Grasland A, Zoulim A, LE Guen J, et al. Rituximab maintenance therapy for granulomatosis with polyangiitis and microscopic polyangiitis. J Rheumatol. 2012 Jan;39(1):125-30.
11. Rituximab for granulomatosis with polyangiitis or microscopic polyangiitis: a review of the clinical and cost-effectiveness [Internet]. Ottawa: CADTH; 2015 Jan 28. [cited 2017 Apr 20]. (Rapid response report: summary with critical appraisal). Available from: https://www.cadth.ca/sites/default/files/pdf/htis/feb-2015/RC0631%20Rituximab%20for%20GPA%20or%20MPA%20Final.pdf

Appendix 1: Selection of Included Studies



Appendix 2: Additional References of potential interest

Alberici F, Smith RM, Jones RB, Roberts DM, Willcocks LC, Chaudhry A, et al. Long-term follow-up of patients who received repeat-dose rituximab as maintenance therapy for ANCA-associated vasculitis. Rheumatology (Oxford) [Internet].2015 Jul [cited 2017 Apr 20];54(7):1153-60. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4473766/pdf/keu452.pdf

Besada E, Nossent JC. CD4 cell count and CD4/CD8 ratio increase during rituximab maintenance in granulomatosis with polyangiitis patients. PeerJ [Internet].2016 [cited 2017 Apr 19];4:e2487. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5036106/pdf/peerj-04-2487.pdf

Calich AL, Puechal X, Pugnet G, London J, Terrier B, Charles P, et al. Rituximab for induction and maintenance therapy in granulomatosis with polyangiitis (Wegener's). Results of a single-center cohort study on 66 patients. J Autoimmun.2014 May;50:135-41.

Cartin-Ceba R, Golbin JM, Keogh KA, Peikert T, Sanchez-Menendez M, Ytterberg SR, et al. Rituximab for remission induction and maintenance in refractory granulomatosis with polyangiitis (Wegener's): ten-year experience at a single center. Arthritis Rheum.2012 Nov;64(11):3770-8.

Besada E, Koldingsnes W, Nossent JC. Serum immunoglobulin levels and risk factors for hypogammaglobulinaemia during long term maintenance therapy with rituximab in patients with granulomatosis with polyangiitis. Rheumatology (Oxford).2014 Oct;53(10):1818-24.

Roubaud-Baudron C, Pagnoux C, Meaux-Ruault N, Grasland A, Zoulim A, LE Guen J, et al. Rituximab maintenance therapy for granulomatosis with polyangiitis and microscopic polyangiitis. J Rheumatol.2012 Jan;39(1):125-30.