

Letter

Use of Rituximab for the Treatment of Antineutrophil Cytoplasm Antibody–associated Vasculitis in Canada, 2010–2020

To the Editor:

Rituximab (RTX) is the only biologic approved to date for the treatment of antineutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV).^{1,2,3} The Canadian Vasculitis Research Network (CanVasc) has recommended RTX as first-line therapy for remission induction,⁴ and recently, as the preferred maintenance agent in severe granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).⁵ However, patterns in the use of RTX for AAV treatment across Canada are unknown.

We aimed to describe the use of RTX in Canada for the treatment of GPA or MPA during the decade following the publication of the Rituximab in ANCA-Associated Vasculitis (RAVE)¹ and the rituximab versus cyclophosphamide in ANCA-associated vasculitis (RITUXVAS)² trials, which demonstrated that RTX had comparable efficacy to cyclophosphamide (CYC) for severe disease induction. A second objective was to describe the population currently receiving RTX for GPA or MPA.

We obtained aggregate-level data of patients aged ≥ 18 years who received RTX for GPA or MPA from January 2010

to December 2020 from the Rituxan patient support program database (Jointeffort; Roche Canada). The database covers approximately 90% of outpatient RTX prescriptions in Canada until late 2020, when biosimilars of RTX became available. Inpatient RTX administration is not captured, nor is the indication (induction or maintenance). Patients with exceptional circumstances receiving compassionate (free) RTX through the program were excluded (proprietary information). We determined the annual number of patients starting RTX, the total number of applications to provincial or private insurance plans for coverage (multiple applications may be submitted per patient over time, including periodic renewals), and the number of patients who were ultimately not approved for RTX coverage by any payor (“denials”). Among prevalent RTX users, we assessed sex, age, geographic region, and coverage (private insurance or public provincial formulary) as counts and percentages. The Mount Sinai Hospital Research Ethics Board approved this study (#19-0073-C).

From January 2010 to December 2020, 1646 patients started RTX for GPA or MPA. The annual number of patients starting RTX increased 7-fold, from 35 in 2010 to 248 in 2020. Total applications increased nearly 12-fold, from 38 to 451, and denials increased from 18 (2010) to 60 (2020; Figure 1). Patients of reproductive age (18–39 yrs) represented 17% of new RTX starts, which remained stable over time.

Among the 710 prevalent RTX users (January 2021),

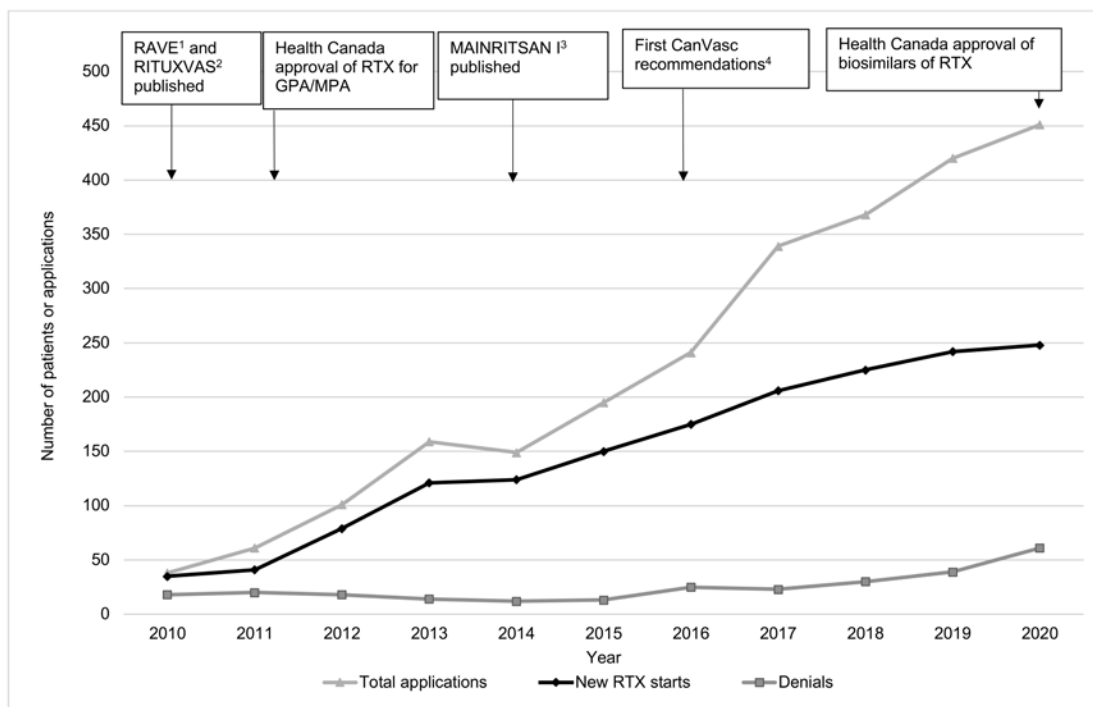




Figure 1. Annual RTX initiation, total applications, and denials for GPA and MPA in Canada (2010–2020). Although Health Canada has not officially approved RTX for maintenance, several individual Canadian provinces approved RTX for maintenance coverage starting in the fall of 2018. CanVasc: Canadian Vasculitis Research Network; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; RAVE: Rituximab in ANCA-Associated Vasculitis trial; RTX: rituximab.

383 (54%) patients were female, 126 (18%) were aged 18–39 years, 260 (37%) were aged 40–59 years, and 324 (46%) were aged \geq 60 years. The distribution of RTX users across Canada was proportional to the general population in these regions,⁶ with 264 (37%) from Ontario, 188 (26%) from Western provinces (British Columbia, Alberta, Manitoba, Saskatchewan), 185 (26%) from Quebec, and 73 (10%) from Atlantic provinces (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador). RTX was publicly funded (or combination of public/private) for 47% (95% CI 41–53) of Ontario patients, 50% (95% CI 43–57) of Quebec patients, 60% (95% CI 52–66) of patients in Western provinces, and 8% (95% CI 4–17) of patients in Atlantic provinces. Following Health Canada approval of RTX induction (end of 2011), the average wait time from initial application to approval was 50 days (SD 34), and the average time from approval to infusion was 9 days (SD 2; data not shown).

The use of RTX for GPA and MPA has increased steadily since clinical trials established its efficacy.^{1,2} One of the advantages of RTX over CYC is the lack of risk to fertility. Patients of reproductive age have remained a minority of RTX users, possibly reflecting the lower incidence of GPA and MPA in this group.⁷ Between Canadian regions, the proportion of patients receiving public (vs private) coverage for RTX varied, and was lowest in Atlantic provinces; this is consistent with known differences in provincial drug programs.⁸ Patients without access to publicly funded RTX and without private insurance nor access to compassionate programs have to take alternative immunosuppressants, which could be less effective or have a higher risk of adverse effects.

A limitation to this work is that only aggregate data, and no disease-specific characteristics, were available. Further, data on inpatient RTX were not available. However, a large Quebec hospital reported only 4 inpatient infusions for GPA in 2016,⁹ and discharged patients generally still require further applications for the remainder of their infusions. Thus, we consider our study to have captured the majority of RTX starts in Canada for GPA or MPA. Second, the denominator of patients with an indication for RTX is not known. However, extrapolating from a study from Saskatchewan¹⁰ and Canadian population estimates for 2020,⁶ approximately 443 (95% CI 296–603) new diagnoses of renal AAV might occur in Canada each year, whereas we found that 248 patients (i.e., over half of this figure) started RTX as part of treatment for GPA or MPA in 2020.

In conclusion, RTX is increasingly used in Canada for AAV treatment. Further work should examine whether availability of biosimilars of RTX (approved in Canada in May 2020; uptake across provinces by late 2020) will increase RTX use further, and whether less costly biosimilars will facilitate expanded access to RTX.

Arielle Mendel¹ , MD, MSc, Assistant Professor
Christian Pagnoux² , MD, MSc, MPH, Associate Professor
¹Division of Rheumatology, McGill University Health Centre and Centre for Outcomes Research and Evaluation, Montreal, Quebec;

²Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada.

The authors declare no conflicts of interest relevant to this article.

Address correspondence to Dr. A. Mendel, Montreal General Hospital, 1650 Cedar Avenue, Montreal, QC H3G 1A4, Canada.

Email: arielle.mendel@mcgill.ca.

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