This is because certain clinical subgroups were underpowered in PEXIVAS to be able to assess the safety and efficacy of this reduce dose taper, for example, those receiving RTX induction. A clinician could choose either one of these regimens, but the importance is to follow one, and you can see that by 4 months, in both cases patients are taking less than 10 mg of prednisone daily.

In terms of choice of induction therapy for organ-threatening disease, there appears to be no difference between RTX and CYC for remission at 6 months, relapse at 12 months, death, or serious adverse events, including infections.

There may be reasons to favor RTX including avoiding the risks of female or male infertility, or premature ovarian failure, and there may be reasons to favor CYC in certain circumstances as well.

In the largest clinical trial ever conducted in ANCA vasculitis, there was no difference in the primary outcome of end-stage renal disease or death between patients receiving or not receiving plasma exchange for severe ANCA vasculitis.

And a Cochrane Metaanalysis found no difference and sustained remission, total adverse events, or death at any time point.

Of note, it found that a 26% increase in the relative risk of serious infections with plasma exchange. Thus, we do not recommend that it be used first-line in patients presenting with severe ANCA vasculitis.

Based on 2 major randomized control trials, it is clear that in both CYC- and RTX-treated patients, relapsing and with new disease, RTX is a superior maintenance agent compared to azathioprine, and thus we recommend it as first-line maintenance. Of note, we recognize RTX is not available for maintenance everywhere in Canada, which will hopefully change soon.

Our recommendations have a section dedicated to eosinophilic granulomatosis with polyangiitis or EGPA.

One of our statements is that mepolizumab add can be a treatment option in nonsevere, steroid-dependent, and relapsing EGPA. Of note, patients with newly diagnosed and or severe EGPA were not included in this main trial for which the recommendation is based.

The working group felt that more data was needed before recommending it as a first-line therapy for newly diagnosed EGPA.

Of note, mepolizumab at this dose is not available to most patients in Canada.

The last recommendation I'll mention is from the monitoring and prevention section of those recommendations, which I encourage readers to review.

We recommend that trimethoprim sulfamethoxazole or Septra prophylaxis be continued in all patients receiving RTX or CYC induction therapy to continue for 3 months after

finishing CYC, and to continue until 6 months has passed since the last RTX dose was received.

Aside from preventing pneumocystis pneumonia, there is data that trimethoprim sulfamethoxazole specifically may reduce all-cause infections and patients receiving RTX maintenance, which is one of the reasons we made this recommendation.

There are of course other indications for specifically PJP prophylaxis, including the use of high-dose corticosteroids.

In summary, we hope our new and revised recommendations will continue to help physicians make therapeutic choices for optimal treatment of patients with ANCA vasculitis, which will minimize relapses, infections, glucocorticoid toxicity, and ultimately, we hope, reducing damage.

Since the initial publication of these recommendations in September 2020, there are already new high impact publications which further promise to change the therapeutic landscape in AAV. We anticipate updating these recommendations, therefore, in the next few years.

As I mentioned, we discussed some of these anticipated changes in the text, especially in the full-length article, which is contained in data supplement 1.

An important next step in Canada will be to evaluate the real-world safety and effectiveness of ANCA vasculitis treatments, including RTX biosimilars as they compare to the originator.

And I'd like to acknowledge all the CanVasc contributors to this publication and recommendations, and a special mention to Dr. Daniel Ennis, Dr. Ellen Go, and Dr. Christian Pagnoux.

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Thank you.