MAINRITSAN 1

MAINTENANCE OF REMISSION USING RITUXIMAB IN SYSTEMIC ANCA-ASSOCIATED VASCULITIS (AAV)

RTX IS MORE EFFECTIVE THAN AZA FOR MAINTENANCE OF REMISSION, BUT GC USE AND RELAPSE REMAIN COMMON[1-4]

- RTX was shown to be a more effective maintenance therapy than AZA for newly diagnosed AAV patients
- Minor and major relapses occurred throughout the maintenance phase of treatment. By month 28, 17% of patients suffered a major relapse, increasing to 38% by month 60
- GC use remained common amongst all patients throughout the 60-month follow-up period

VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

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INTRODUCTION

MAINRITSAN 1 assessed the long-term effectiveness of RTX treatment for remission maintenance in AAV. Results from retrospective studies have suggested that RTX infusion might be an effective maintenance therapy, but these findings have not been thoroughly investigated, with limited long-term data available.[1,2]

STUDY AIM

Compare RTX and AZA maintenance therapy for preventing major relapse rates in newly diagnosed AAV patients.[1]

The sponsor of this study was:
Assistance Publique - Hôpitaux de Paris

STUDY DESIGN: MAINTENANCE PHASE[1,2]

Randomised, open-label, control study[1]

Prednisone use continued throughout the 60-month period[3]

At time of remission and within maximum of 1 month after last CYC pulse, patients randomly assigned 1:1 to receive maintenance therapy (N=115)[1]

MAJOR RELAPSE:
Reappearance or worsening of disease with BVAS >0 and involvement of ≥1 major organ, a life-threatening manifestation or both[1,2]

Patients with newly diagnosed or relapsing GPA, MPA or RLV receiving remission-induction therapy until remission attained after 4–6 months[1]

Prednisone 1 mg/kg/day, gradually tapered (preceded in some patients by 500–1000 mg/day methylprednisolone pulses for 1–3 consecutive days)

PLUS

Pulse CYC (0.6 g/m^2 on days 0, 14 and 28, then 0.7 g/m^2 every 3 weeks for 3–6 additional pulses)

MONTH 0	MONTH 28[1] (Primary endpoint: percentage of patients with major relapse)	MONTH 60[2] (Primary endpoint: time to first major relapse)
AZA (n=58) (2 mg/kg/day until month 12, 1.5 mg/kg/day until month 18 & 1 mg/kg/day until month 22)	**58 patients analysed for study endpoints** (17 had major relapse, 2 died)	**58 patients analysed for study endpoints** (11 had major relapse, 2 died,1 lost to follow-up)
RTX (n=57) (500 mg on days 0 and 14, then months 6, 12 and 18)	**57 patients analysed for study endpoints** (3 had major relapse)	**57 patients analysed for study endpoints** (13 had major relapse)

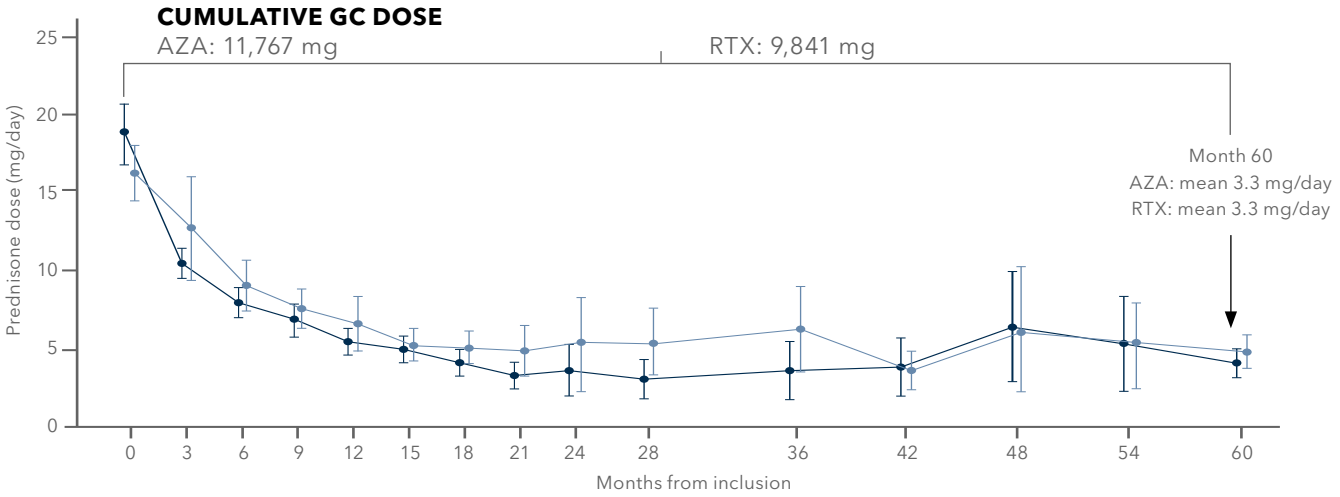
RESULTS

RTX patients suffered significantly fewer major relapses ($p<0.05$) at month 28 compared to patients treated with AZA, with similar frequencies of AEs between the two groups.[1] At month 60 major relapse-free survival was significantly higher in the RTX group compared to the AZA group, 72% vs 49% ($p<0.01$), with no difference in rates of AEs.[2] Use of GCs remained common throughout the 60 month follow-up, with no difference in the mean cumulative dose between the groups, 3.3 mg/day.[2-4]

RESULTS – CONTINUED

MONTH 28	MONTH 28–60
Major relapse (p=0.002)[1] **29%** of AZA patients (within 12 months: n=8; month 12–22: n=2; month 24–28: n=7) **5%** of RTX patients (month 8: n=1; month 22: n=1; month 24: n=1)	**Major relapse (previously major relapse free)[1]** **19%** of AZA patients **23%** of RTX patients Major relapse-free survival rate: p=0.003
Minor relapse (p=0.43)[1] **16%** of AZA patients **11%** of RTX patients	**Minor relapse (p=0.43)[1]** **5%** of AZA patients **12%** of RTX patients All relapse-free survival rate: p=0.012

5 YEAR FOLLOW-UP: GC DOSE IN PATIENTS OVER TIME[2]



CONCLUSION

RTX was shown to be superior to AZA at maintaining remission and preventing major relapse at 28 months.[1] This benefit was sustained post-treatment over 60 months with significantly better major relapse-free survival in the RTX group and a comparable safety profile.[2] Irrespective of these benefits, GC use remained common amongst all patients throughout the 60 month study period.[2-4] In summary, RTX was shown to be a more effective maintenance therapy than AZA for newly diagnosed AAV patients.[1,2]

RELAPSES REMAIN COMMON IN THE MAINTENANCE PHASE OF TREATMENT WITH MANY PATIENTS STILL USING GCS[1-4]

References & footnotes

AAV, ANCA-associated vasculitis; AEs, adverse events; AZA, azathioprine; BVAS, Birmingham Vasculitis Activity Score; CYC, cyclophosphamide; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RLV, renal-limited vasculitis; RTX, rituximab

*Patients with newly diagnosed or relapsing AAV in complete remission after a GC plus CYC regimen were enrolled between October 2008 and June 2010 and randomised to receive maintenance therapy with RTX (GPA: 82%, MPA: 14%; renal-limited AAV: 4%; mean age: 54 years; male: 65%) or AZA (GPA: 69%; MPA: 26%; renal-limited AAV: 5%; mean age: 56 years; male: 48%). Prednisone was gradually tapered and then kept at a low dose (~5 mg/day) for at least 18 months after randomisation. Patients were followed every 3 months for 28 months and then prospectively until month 60.[1,2]

1. Guillevin L, et al. *N Engl J Med* 2014;371(19):1771–80.
2. Terrier B, et al. *Ann Rheum Dis* 2018;77(8):1150–6.
3. Terrier B, et al. *Ann Rheum Dis* 2018;77(8): 1150–6. [Supplementary appendix].
4. Guillevin L, et al. *N Engl J Med* 2014;371(19):1771–80. [Supplementary appendix].