

Cyclophosphamide effect on immunoglobulins levels in AAV patients treated with long-term pre-emptive rituximab maintenance.

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Objective:

Rituximab (RTX) is an anti-CD20 antibody used in ANCA-associated vasculitis (AAV) for induction and maintenance of remission.

The objective of this study is to determine the effects of CYC on Ig levels in patients treated with long-term pre-emptive RTX maintenance.

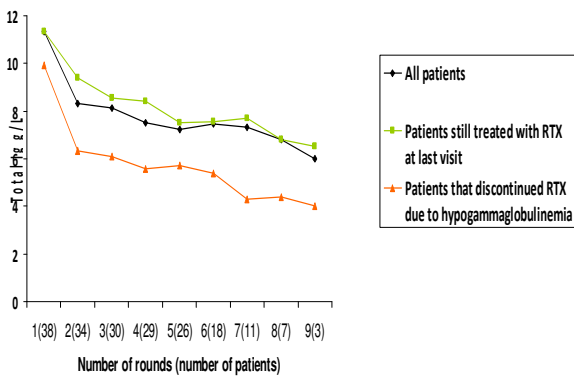
Methods:

Retrospective study of 38 patients (35 with GPA and with 3 with CSS) treated with RTX between April 2004 and September 2011 for active disease. 58% of the patients had renal involvement. The cumulative cyclophosphamide (CYC) dose was 14g (0-250). Twelve patients (32%) were treated with combination CYC-RTX at initiation.

RTX was initiated as two 1g infusion 2 weeks apart (RA protocol) and thereafter 2g RTX was administered annually to achieve long-term B cell depletion. Patients were closely monitored during 46.5 (2-88) months follow-up with clinical and serological surveillance. They received a median of 5 (1-10) rounds of RTX for a cumulative dose of 8g (2-13)

Results:

Median serum Ig levels declined continuously but not in a linear fashion after each RTX re-treatment



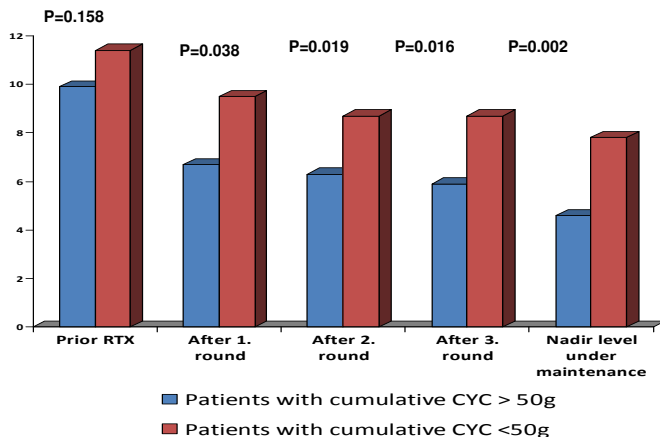
The largest decline in Ig level occurred after the first RTX round.

	Ig decline after first round	Ig decline after second round	Ig decline after third round	Overall decline from baseline to last visit
IgG g/L	1.70	0.20	0.05	2.80
IgA g/L	0.32	0.06	0.03	0.40
IgM g/L	0.25	0.03	0.03	0.39
Total Ig g/L	2.35	0.27	0.39	3.46

Median decrease in immunoglobulins classes and total immunoglobulins after the first (33 patients included), the second (30 patients) and the third round (28 patients) as well at last visit (38 patients).

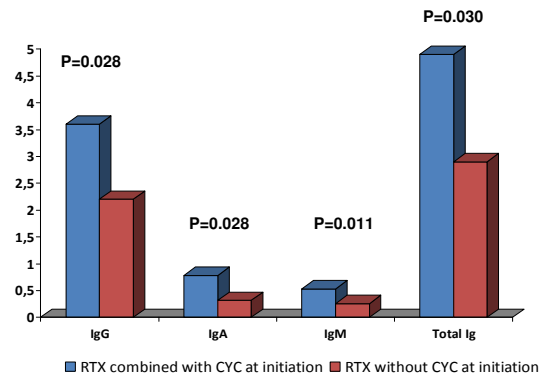
Patients with a cumulative CYC dose > 50g (29%):

Had lower levels of total Ig after the first 3 RTX rounds and had also lower levels during RTX maintenance.



Patients receiving initial RTX in combination with CYC (32%):

Had bigger overall decline from baseline in all Ig classes.



Conclusion:

During RTX maintenance therapy in AAV, the largest Ig decrease occurs after the first infusion round, but Ig levels continue to decrease thereafter albeit at a lower speed.

A high cumulative CYC dose (>50g) as well as combining RTX with CYC at initiation leads to larger decline of Ig during RTX maintenance therapy