

Long-term efficacy and safety of pre-emptive maintenance therapy with rituximab in Granulomatosis with Polyangiitis: results from a single centre.

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Objective:

Rituximab (RTX) is an anti-CD20 antibody used successfully in Granulomatosis with Polyangiitis (GPA) for induction and maintenance of remission. Our study aims to evaluate the long term efficacy and safety of chronic pre-emptive RTX therapy in GPA.

Methods:

Retrospective study of 35 GPA patients treated with RTX between April 2004 and September 2011 for active disease and maintenance. RTX was initiated as two 1-gram infusions 2 weeks apart and thereafter 2gr RTX was re-administered annually. Patients were followed for 47 (2-88) months. They received a median RTX dose of 8g (2-13) dealt in 5 (1-10) rounds.

Results:

All patients (35) had a clinical response

30.9 relapses /100 patient-years before RTX
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 6.6 relapses / 100 patient-years with RTX maintenance

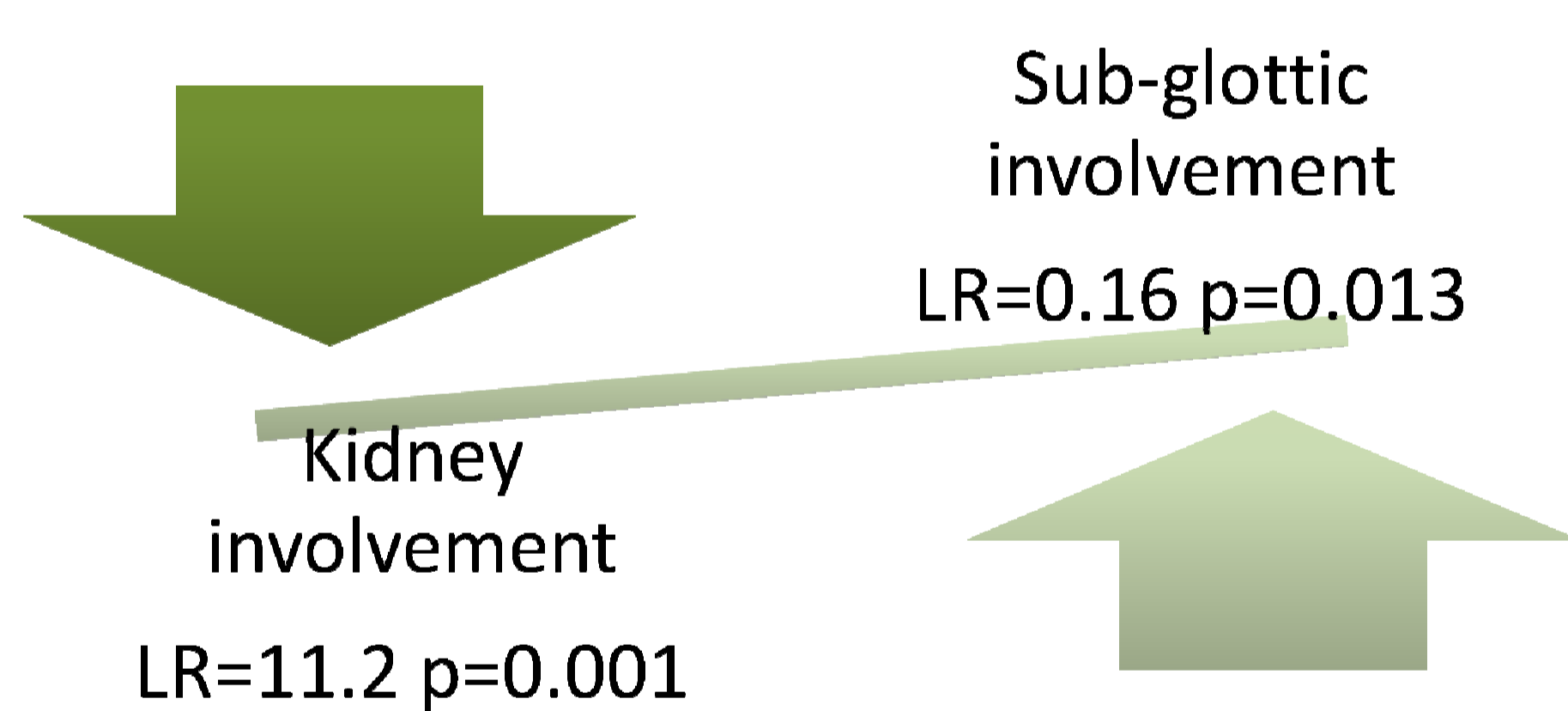
At last visit

63% of the patients still treated with RTX
 37% of the patients had discontinued RTX (62% due to hypogammaglobulinemia)

Risk of infections

26% had SEVERE INFECTION
 6.6 severe infections / 100 patient-years
 29% had CHRONIC INFECTION

Severe infections (necessitating hospitalization and IV antibiotics)



Chronic infections (symptomatic localized infections lasting >3 months and requiring several antibiotics courses)

Lower B cells at RTX initiation in patients with chronic infections compared with patients without chronic infections (Mann-Whitney U test: 0.035 vs. 0.09x10⁹/L, p=0.065)

	Univariate analysis		Multivariate analysis	
	Odds ratio	P-value	Odds ratio	P-value
Age	1.06	0.059		
Cumulative CYC dose (g)	1.04	0.036	1.09	0.037
Prednisolone dose at last visit (mg)	1.18	0.055		
Total Ig decline after 1. round (g/L)	1.81	0.023	2.38	0.040
CD4 count at last visit (x10 ⁹ /L)	0.002	0.016		0.045
IgA level at nadir (g/L)	0.07	0.050		0.341

Risk factors for severe infections determined by univariate and multivariate (backward stepwise) binary logistic regression analysis. All predictor variables in the analysis are continuous.

	Univariate analysis		Multivariate analysis	
	Odds ratio	P-value	Odds ratio	P-value
Cumulative RTX dose (g)	1.30	0.075	1.40	0.095
IgG level at nadir (g/L)	0.48	0.023	0.43	0.026
IgM level at nadir (g/L)	0.001	0.039		0.264
Total Ig at nadir (g/L)	0.62	0.038		

Risk factors for chronic infections determined by univariate and multivariate (backward stepwise) binary logistic regression. All predictors variables in this analysis are continuous.

Conclusion:

Long term pre-emptive RTX maintenance is efficacious in reducing the risk for relapse but was discontinued in a third of the patients.

Kidney involvement and the total CYC cumulative dose are important risk factors for severe infections.

The patients' net state of immunodeficiency under RTX changes over time as low level of total immunoglobulins increases the risk for infections.