Online supplement to: Seasonal Influence on the Risk for a Relapse at a Rise of Antineutrophil Cytoplasmic Antibodies in Vasculitis Patients with Renal Involvement. *The Journal of Rheumatology.* doi:10.3899/jrheum.160066

ONLINE SUPPLEMENT

Corticosteroid maintenance therapy

Corticosteroid maintenance therapy may also influence serial ANCA measurements. To analyse this, we compared the risk for a relapse after an ANCA rise in patients who were still on corticosteroids versus the risk in patients who were no longer taking corticosteroids. Thirty-two patients were still on corticosteroids, of whom 23 (71.9%) relapsed. The remaining 28 patients were no longer on corticosteroids, of whom 13 (46.4%) relapsed. No difference in time to relapse was observed between the two groups (X2=3.082, log-rank p=0.079).

In particular, a withdrawal of corticosteroid therapy may provoke an ANCA rise. It can be hypothesized that these rises may not be followed by a relapse and are therefore false positive ANCA rises. In order to investigate this, we divided the patients who were no longer taking corticosteroids in two subgroups: patients who were weaned off corticosteroids in the previous 3 months and patients who were off corticosteroids for longer than 3 months. Twenty patients were no longer taking corticosteroids for longer than 3 months, of whom 8 (46.4%) relapsed. The remaining 8 patients were weaned off corticosteroids in the previous 3 months, of whom 5 (62.5%) relapsed. No difference in time to relapse was observed between the two groups (X2=0.299, log-rank p=0.585).

Risk factors of a major and renal relapse

In an additional analysis, we wanted to verify that the risk factors for a relapse were also predictive for a major relapse. Hereto, we limited the endpoint of the multivariate survival analysis to a major relapse (n=20) and we censored the patients who remained in remission and patients who experienced a minor relapse during follow-up. An extended rise and an ANCA rise during the fall season remained significant risk factors for a major relapse, while induction regimen lacking CYC/RTX was no longer predictive of a major relapse (Supplementary Table 1).

We performed the same analysis for renal relapses (n=27), wherein we censored the patients who remained in remission and patients who experienced a non-renal relapse during follow-up. An extended rise and induction regimen lacking CYC/RTX remained significant risk factors for a renal relapse, while an ANCA rise during the fall season was no longer predictive of a renal relapse (Supplementary Table 2).

Supplementary Table 1. Results of the multivariate analysis of risk factors for a **major** relapse from the time of an ANCA rise (patients are censored at a minor relapse). Hazard ratios are shown with 95% confidence intervals.

Risk factor for a major relapse	**Multivariate**		
	HR	95%-CI	p
Induction regimen lacking CYC/RTX	2.06	(0.66 - 6.42)	0.215
Extended rise	7.24	(1.99 - 26.36)	**0.003**
Season			
Spring	*Reference*		
Summer	2.43	(0.70 - 8.44)	0.164
Fall	4.31	(1.17 - 15.86)	**0.028**
Winter	0.83	(0.19 - 3.54)	0.800

Supplementary Table 2. Results of the multivariate analysis of risk factors for a **renal** relapse from the time of an ANCA rise (patients are censored at a non-renal relapse). Hazard ratios are shown with 95% confidence intervals.

Risk factor for a renal relapse	**Multivariate**		
	HR	95%-CI	p
Induction regimen lacking CYC/RTX	3.61	(1.49 - 8.72)	**0.004**
Extended rise	3.72	(1.37 - 10.10)	**0.010**
Season			
Spring	*Reference*		
Summer	1.82	(0.60 - 5.56)	0.292
Fall	2.66	(0.88 - 8.09)	0.084
Winter	1.32	(1.49 - 8.72)	0.627