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THE RELATIONSHIP BETWEEN THE TYPE I INTERFERON SIGNATURE AND THE RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS

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10.1136/ard.2010.129585k

Objectives To analyse the relationship between the type I interferon (IFN) signature and the response to rituximab in rheumatoid arthritis (RA) patients.

Methods Twenty RA patients were treated with rituximab (cohort 1). As a read out for clinical response the decrease in disease activity score (DAS28) between week 0 and 24 was used. In peripheral blood mononuclear cells from baseline the presence of an IFN signature was analysed by measuring the expression levels of three IFN response genes by quantitative PCR. After comparison with healthy controls, patients were qualified as IFN high or IFN low. The data were confirmed in a second independent cohort (n=1). Serum IFN α bioactivity was analysed using a reporter assay. Twenty-four patients underwent synovial biopsy before and 4 weeks after rituximab. Synovial IFN α and IFN β expression and B cells were detected using immunohistochemistry. The relationship with the clinical response (at week 24) was analysed using regression analysis.

Results In cohort 1, the decrease in DAS28 tended to be lower in the IFN high group (n=compared to the IFN low group (n=14; $-0.67 (\pm 0.9)$ compared to $-1.7 (\pm 1.6)$; $p=0.085$). In the second cohort IFN high patients (n=8) experienced a significantly lower decrease in DAS28 at week 24 compared to IFN low patients (n=3; mean ($\pm$ SD) $-0.98 (\pm 1.6)$ compared to $-2.3 (\pm 1.3)$; $p=0.027$). The pooled data of the two cohorts also showed a significant lower decrease in DAS28 in the IFN low patients (n') at week 24 compared to the IFN high group (n=24; mean ($\pm$ SD) $-1.96 (\pm 1.4)$ compared to $-0.90 (\pm 1.5)$; $p=0.012$). Serum IFN α bioactivity at baseline tended to negatively predicted the decrease in DAS28 at week 24 (n=0, $R^2=0.09$, $p=0.107$). Synovial expression of IFN α and IFN β and B cell numbers did not differ between IFN high and IFN low patients. IFN high and low patients had similar depletion of synovial B cells after treatment.

Conclusion The type I IFN signature negatively predicts the clinical response to rituximab treatment in RA. These data support the notion that IFN signalling plays a role in RA immunopathology.

Comments Funding: Dr Gerlag was supported by the Dutch Arthritis Association (Reumafonds). This research was supported by the European Community's FP6 funding (Autocure). This publication reflects only the author's views; the European Community is not liable for any use that may be made of the information herein.