A153 INDUCTION OF IFN TYPE I BIOLOGY FOLLOWING THERAPY DETERMINES CLINICAL RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS

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Objective Despite the fact that rituximab depletes B cells in all treated rheumatoid arthritis (RA) patients, not all patients show a favorable clinical response. The goal of this study was to provide insight into the pharmacological changes in the peripheral blood that are associated with clinical response to rituximab using genome-wide gene expression profiling.

Methods Gene-expression profiling was performed on peripheral blood RNA from 13 RA patients (test group) using Illumina HumanHT beadchip microarrays. An independent group of nine patients was used for validation using Taq-man qPCR. Clinical responder status was determined after 6 months using ΔDAS28 and EULAR response criteria. Significance analysis of microarrays, gene set enrichment analysis and metacore ontology analysis were used for data analysis and interpretation.

Results Pharmacogenomic studies in 13 RA patients demonstrated marked interindividual differences in the pharmacological responses at 3 months after the start of therapy with rituximab. Interestingly, only differences in the regulation of the type I interferon (IFN) -response genes at 3 months after therapy correlated with the ΔDAS28 response. Good responders (ΔDAS >1.2; n=7) exhibited a selective increase in the expression of type I IFN-response genes, whereas this activity was not or hardly changed in non-responders (ΔDAS <1.2; n=6) after 3 months ($p = 0.0040$ at a cut-off of 0.15 fold (log2 based) induction). Similar results were obtained using EULAR response criteria. The increase in type I IFN-activity in the good responders correlated with a low baseline level. The association between an increased type I IFN-response activity and clinical response is validated in an independent cohort of nine patients (four responders and five non-responders, $p = 0.0317$).

Conclusions A good clinical response to rituximab in RA is associated with a selective increase in type I IFN-response

activity in RA patients. This finding may provide insight in the biological mechanism underlying the therapeutic response of rituximab.

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