A85 SINGLE NUCLEOTIDE POLYMORPHISM 25-TGF β ₁ AS A POSSIBLE MARKER OF RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS

C I Daien, S Fabre, C Rittore, S Soler, V Daien, N Molinari, I Touitou, C Jorgensen *INSERM, U844, Montpellier, France*

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Background The individual response to biological agents in severe rheumatoid arthritis (RA) is unpredictable in daily clinical practice. Despite improving our knowledge on genetic association using GWS in a large RA cohort, no genetic indicators predictive of clinical response to anti-CD20 treatment (rituximab) have been described.

Objectives To analyse the association of several candidate gene polymorphisms with responsiveness to rituximab in patients with severe RA.

Methods The clinical response of 47 French Caucasian RA patients was determined according to the European League Against Rheumatism criteria during the first 6 months after rituximab treatment (intravenously 1000mg one time at day 0, day 15). The clinical response was assessed at months 3 and 6 using the DAS-28 score. Twelve single nucleotide polymorphisms (SNPs) were genotyped: interleukin 10 (IL10) (−1087 IL-10), lymphotoxin A (LTA) (249-LTA and 720-LTA), transforming growth factor β (TGF β 1) (codon 25 TGF β 1), tumour necrosis factor α (TNF α) (−308 TNF α , −488 TNF α and −857 TNF α), TNF receptor II (−196 TNFR2), receptor-associated factor 1 (−C5 TRAF1), signal transducer and activator of transcription 4 (STAT4), TNF α -induced protein 3 (TNF α IP3) and protein tyrosine phosphatase non-receptor type 22 (PTPN22). The Fisher test was used to analyse the impact of specific polymorphisms on treatment response.

Results Eighteen patients were defined as good responders, 13 as moderate responders and 16 as non-responders. The three groups were comparable in terms of gender, rheumatoid

factor and anti-CCP positivity, hand and wrist erosions, previous therapy including methotrexate and number of biological agents used. Baseline DAS-28 tended to be slightly higher in moderate responders (mean DAS-28 respectively 5.0, 5.6 and 5.1) and RA duration was longer in moderate responders (median duration respectively 13, 5, 18 and 10). -25 G/C TGF β SNP was associated with a good response compared with a moderate response and no response ($p=0.0012$ and $p=0.043$ after Bonferroni correction).

Conclusion The 25 G/C TGF β SNP seems to be associated with a good response to rituximab therapy and could become a useful genetic biomarker to predict response to rituximab. This encouraging result needs to be confirmed in a larger number of patients with multivariate analysis.