TTg arthritis model. The association of a short course of IFX to TNFK results in a more rapid clinical efficacy with the same long-term clinical and histological efficacy than solely TNFK immunisation.

A163 COMBINATION OF ACTIVE AND PASSIVE ANTI-TNFα TREATMENTS IN HUMAN-TNFα TRANSGENIC MICE

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Background and objectives Anti-tumour necrosis factor α (TNFα) active immunisation with the heterocomplex TNFα-keyhole limpet hemocyanine (TNFK) proved therapeutic efficacy in human TNFα transgenic (TTg) mice spontaneous arthritis, opening the way for the application of this anti-TNFα targeting strategy in human disease (a phase II clinical trial is ongoing at present in rheumatoid arthritis).
In this animal study the authors compared the clinical and histological efficacy of different anti-TNFα strategies in TTg mice: active anti-TNFα immunisation with TNFK, passive anti-TNFα immunotherapy with infliximab (IFX) and the association of both.
Methods After spontaneous arthritis onset (w0) 48 TTg mice were allocated to receive one of the following treatments: TNFK immunisation at w0, w1, w4 (TNFK) (10 mice), weekly IFX all along the study duration (IFX w0-w15) (10 mice), TNFK immunisation+weekly IFX from w0 to w4 (TNFK+IFX) (10), weekly IFX from w0 to w4 (IFXw0-w4) (8 mice), phosphate-buffered saline (PBS) at w0, w1, w4 (PBS) (10 mice, control group). Animals were killed at w15. Clinical and histological scores were compared for all treatments. Anti-TNFα antibodies levels were assessed by ELISA, the anti-TNF neutralising capacity of sera by L929 bioassay. Histological scores of articular inflammation and destruction (H&E) and of cartilage degradation (safranine O) were quantified after sacrifice.
Results All TNFK immunised mice (TNFK and TNFK+IFX groups) produced neutralising anti-TNFα antibodies. All the treatments had comparable overall clinical efficacy versus PBS ($p<0.05$). All IFX-treated groups had a more rapid clinical improvement versus PBS and TNFK ($p<0.05$).
At the end of the study TNFK, IFXw0-w15 and IFX+TNFK groups had lower clinical scores of arthritis than both IFXw0-w4 and PBS groups ($p<0.05$). Reduced histological scores of inflammation and destruction and of cartilage degradation were evident for TNFK, IFXw0-w15 and TNFK+IFX versus PBS group. TNFK group had less histological inflammation and destruction even compared to IFX w0-w4 group.
Conclusion Active immunisation with TNFK is as effective as weekly IFX on clinical activity and structural damage in