TNF CONCENTRATIONS DURING TREATMENT OF INFILAMMATORY DISEASES WITH GOLIMUMAB

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Background: Golimumab is a monoclonal antibody that binds TNF, counteracting its pro-inflammatory effects. Berkhou et al. (2019) described the development of a novel drug-tolerant assay to quantify TNF during TNF inhibitor treatment. Using this assay, they analyzed the dynamics of TNF during treatment of rheumatoid arthritis (RA) patients with adalimumab and found that TNF levels shortly after treatment initiation predict non-response (1). Our study is the first to measure TNF levels during golimumab treatment, using the same drug-tolerant assay.

Objectives: To describe the dynamics of TNF in patients with RA, ankylosing spondylitis (AS) or psoriatic arthritis (PsA) during golimumab treatment.

Methods: Consecutive patients with RA, AS, or PsA starting golimumab treatment were included in this prospective observational cohort study, named the Reade Rheumatology Registry. Serum samples drawn during the study visits were analyzed for drug levels, anti-drug antibody (ADA) formation, and TNF concentrations using a regular enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay, and a drug-tolerant competition ELISA, respectively. Regression analyses were used to analyze the data. Missing data was imputed using last observation carried forward.

Results: In total, 304 serum samples from 69 patients were included in this study. The median follow-up period was 52 (interquartile range (IQR) 16-130) weeks. Median TNF concentration at baseline was 4 (IQR 3-105) pg/ml and this increased to 68 (37-127) pg/ml four weeks after treatment initiation. During follow-up, TNF concentrations remained stable for the majority of patients (Figure 1). TNF levels at baseline were already high (>30 pg/ml) in 25% of the patients. These patients used a previous TNF-inhibitor with a median of 19 (IQR 11-32) days before start of golimumab. In contrast, patients with low baseline TNF concentrations were TNF-inhibitor naive, used a TNF-inhibitor longer before the start of golimumab treatment (median 489 (IQR 56-916) days), or used a biologic with a different target. A trend was found for the association between drug level and TNF concentration during follow-up; patients with low TNF concentrations (<30 pg/ml) had median drug levels of 0.32 (IQR 0.03-1.00) μg/ml, while patients with high TNF concentrations (>30 pg/ml) reached a median drug level of 1.45 (0.80-2.47) μg/ml (odds ratio (OR) 1.51, CI: 0.97-2.37, p=0.071). No association was found between TNF concentrations at week 4 and low disease activity at week 52, defined as DAS28 ≤3.2 or ASDAS <2.1 (OR 1.00, CI: 1.00-1.00, p=0.309). Four patients (6%) developed detectable ADAs.

Conclusion: Golimumab therapy was found to induce an increase in TNF concentrations, independent of disease activity. This is in line with what has been found for adalimumab treatment. However, TNF concentrations measured in this study were at least twice as low as TNF concentrations during adalimumab treatment (1). The high baseline TNF concentrations in 25% of the patients were also surprising, as it indicates that patients switch to golimumab while their TNF is still in complex with a previous TNF-inhibitor.

REFERENCE:


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