TNF CONCENTRATIONS DURING TREATMENT OF INFLAMMATORY DISEASES WITH GOLIMUB

Femke Hoogberg1, Lea C. Berkhout2,3, Merel J. I. Lam1, Sadaf Atiq1, Michael Nurmohamed1, Annick de Vries1, Charlotte L. Kriekerta2, Theo Rispens2,3, Gert-Jan Wolbink1,2,3.

Background: Golimumab is a monoclonal antibody that binds TNF, countering 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 nonresponse. 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 66 (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, however detailed knowledge of patients' treatment history was sparse.

Objectives: To gain insight into bDMARD-induced ADRs and their burden from the RA patients' perspective.

Methods: The Dutch Biologic Monitor is an AD-DR patient-inclusive ADR-tracking system. Patients were asked to complete questionnaires bi-monthly about used bDMARDs, indication and bDMARD-induced ADRs. ADRs were coded according to MedDRA terminology and their impact was measured on a 5-point scale, ranging from 1 (no burden) to 5 (very high burden). Per patient, every recurrent unique ADR was included as one ADR. ADRs regarding infections (INF), skin (SK), gastrointestinal (GI) and injection site (INS) were clustered and analyzed for the reported prevalence and burden. Fatigue and headache were separately analyzed for prevalence and burden. The prevalence of clustered ADRs versus the number of bDMARDs was compared using a γ²-test and the average burden was compared using a Mann-Whitney U test.

Results: In the Dutch Biologic Monitor 583 consecutive (44.8%) RA patients were included (71.2% female, average age 59 years, SD±12.4) using the originator or a biosimilar of etanercept (ETN, 265), adalimumab (ADA, 196), tocilizumab (41), abatacept (35), certolizumab pegol (23), rituximab (19), infliximab (18), golimumab (15), sarilumab (2), secukinumab (1), anakinra (1). Almost half of the patients (276; 47.3%) reported at least one bDMARD-induced ADR with a total of 703 ADRs in 2,550 completed questionnaires. Patients reported 129 INJ reactions (129 ADRs/583 pts, prevalence of 22.1%, reported by 86 pts) with an average...