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FRI0096

TNF CONCENTRATIONS DURING TREATMENT OF INFLAMMATORY DISEASES WITH GOLIMUMAB

Femke Hooijberg¹, Lea C. Berkhout^{2,3}, Merel J. L'Ami¹, Sadaf Atiqi¹, Michael Nurmohamed¹, Annick de Vries⁴, Charlotte L. Kriekaert⁵, Theo Rispens^{2,3}, Gert-Jan Wolbink^{1,2,3}. ¹Amsterdam Rheumatology and immunology Center, location Reade, Amsterdam, Netherlands; ²Department of Immunopathology, Sanquin Research, Amsterdam, Netherlands; ³Landsteiner Laboratory, Academic Medical Centre, University of Amsterdam, Amsterdam, Netherlands; ⁴Biologics Lab, Sanquin Diagnostic Services, Amsterdam, Netherlands; ⁵Amsterdam Rheumatology and immunology Center, location VUmc, Amsterdam, Netherlands

Background: Golimumab is a monoclonal antibody that binds TNF, counteracting its pro-inflammatory effects. Berkhout 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 (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 56-816) 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) μ g/ml, while patients with high TNF concentrations (≥ 30 pg/ml) reached a median drug level of 1.45 (0.80-2.47) μ g/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, $p=309$). Four patients (6%) developed detectable ADAs.

Figure 1

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.

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RA PATIENTS' PERSPECTIVES ON BIOLOGICAL DMARD-INDUCED ADVERSE DRUG REACTIONS AND THEIR BURDEN

Jette van Lint¹, Naomi Jessurun¹, Sander W. Tas², Harald Vonkeman³, Bart van den Bemt^{4,5}, Astrid van Tubergen⁶, Michael Nurmohamed^{7,8}, Eugène van Puijenbroek^{1,9}. ¹Netherlands Pharmacovigilance Centre Lareb, 's-Hertogenbosch, Netherlands; ²Amsterdam University Medical Centers, location AMC, Rheumatology and Clinical Immunology, Amsterdam, Netherlands; ³Medisch Spectrum Twente, Rheumatology and Clinical Immunology, Enschede, Netherlands; ⁴Sint Maartenskliniek, Nijmegen, Netherlands; ⁵Radboudumc, Nijmegen, Netherlands; ⁶Maastricht UMC+, Rheumatology, Maastricht, Netherlands; ⁷Amsterdam Rheumatology and Immunology Center Reade, Amsterdam, Netherlands; ⁸Amsterdam University Medical Centers, location VUMC, Rheumatology and Clinical Immunology, Amsterdam, Netherlands; ⁹University of Groningen, Research Institute of Pharmacy, Groningen, Netherlands

Background: Numerous biological DMARDs (bDMARDs) are used in RA treatment, however detailed knowledge of patients' perceptions on drug use and the impact of adverse drug reactions (ADRs) is sparse.

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

Methods: The Dutch Biologic Monitor is an ADR-patient web-based questionnaire used for a prospective, multicentre, event monitoring cohort study including patients using a bDMARD for an immune-mediated inflammatory disease between January 1, 2017 and December 31, 2018. 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 (INJ) were clustered and analysed for the reported prevalence and burden. Fatigue and headache were separately analysed for prevalence and burden. The prevalence of clustered ADRs between the various bDMARDs was compared using a χ^2 -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, $SD \pm 12.4$) 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 2,559 completed questionnaires. Patients reported 129 INJ reactions (129 ADRs/583 pts, prevalence of 22.1%, reported by 86 pts) with an average