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FRI0096 TNF CONCENTRATIONS DURING TREATMENT OF INFLAMMATORY DISEASES WITH GOLIMUMAB

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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) 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=309). Four patients (6%) developed detectable ADAs.

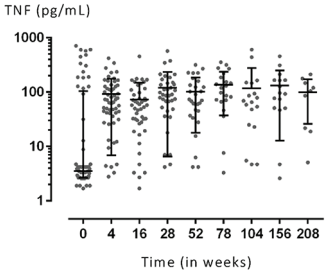

Figure 1

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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FRI0097 RA PATIENTS' PERSPECTIVES ON BIOLOGICAL DMARD-INDUCED ADVERSE DRUG REACTIONS AND THEIR BURDEN

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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±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

burden of 1.7 (SD±0.8), 57 GI reactions (9.8%, 41 pts) with an average burden of 2.9 (SD±1.1), 102 SK reactions (17.5%, 64 pts) with an average burden of 2.9 (SD±1.1) and 109 INFs (18.7%, 79 pts) with an average burden of 3.3 (SD±1.0). Prevalence of INJ and GI reactions was significantly higher among ETN users than among ADA users (INJ: 76 ADRs/265 ETN users (28.7%) vs 30 ADRs/196 ADA users (15.3%), P=0.007; GI: 30/265 (11.3%) vs 9/196 (4.6%), P=0.01). The prevalence of INFs and SK reactions did not differ. The perceived burden of GI reactions was higher for ETN than for ADA users (3.1 ±1.0 vs 2.0 ±0.7, p=0.006) but did not differ for other clustered ADRs. The number of patients using other bDMARDs was too low for further analysis. Prevalence of bDMARD-induced headache was 1.9% (12 ADRs/583 pts) with an average burden of 3.4 (SD±0.9). Prevalence of bDMARD-induced fatigue was 4.3% (25 ADRs) with an average burden of 2.7 (SD±1.0).

Conclusion: Almost half of the RA patients reported bDMARD-induced ADRs. From the patients' perspective INJ reactions have the highest prevalence with a relatively low burden, whereas INFs and headache are less prevalent but give the highest burden of the analysed ADRs. Further studies are required to obtain more insight into the perceived differences in ADRs between bDMARDs.

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FRI0098 SWITCHING RATE OF BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS PATIENTS: TREASURE – REAL LIFE DATA

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Background: In rheumatoid arthritis (RA), biologic DMARDs are important treatment options in resistant patients. Inefficacy or side effects may cause switching between these drugs.

Objectives: This study aimed to determine features of patients switching from one biologic DMARD to another in RA treatment and to investigate associated reasons for switching.

Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of RA and spondyloarthritis patients are being performed in 15 centers across different regions of Turkey. In this study, data of RA patients switching from one biologic agent to another were analyzed. Demographic and clinical data, follow-up duration, time to switch, and reasons for switching were retrieved from the database.

Results: Of the included 2115 RA patients, 829 (39.2%) switched between biologic agents (switched group) and 1286 (60.8%) continued to receive their current therapies (continued group). The median follow-up duration of all patients was 3.7 years and the median time to switch was 1.1 years. In the switched group, the proportion of females and the median HAQ-DI score were higher as well as disease duration was longer (Table 1). Among the biologic agents used at first, 60.9% of the patients were receiving an anti-TNF agent and 39.1% of the patients were receiving other biologic agents (Table 2, figure 1). In the switched group (n=829), the main reasons for switching were secondary inefficacy (n=269), primary inefficacy (n=238), and side effects (n=178) followed by primary or secondary unknown inefficacy (n=30), patient's demand (n=21), physician's request (n=16), willing to be pregnant (n=7), other (n=31), and unknown (n=54).

Table 1. Demographic and clinical features of the study groups

	N	Switched Group	N	Continued Group	p
Age, year, median (min-max)	829	54 (19-84)	1286	55 (18-91)	0.121
Sex, n (%) Female		688 (83.0)		1000 (77.8)	**0.003**
Sex, n (%) Male		141 (17.0)		286 (22.2)	
Body mass index, median (min-max)	823	27.74 (14.33-66.1)	1256	28.05 (15.59-58)	0.640
Disease duration, year, median (min-max)	806	12 (0-43)	1245	8 (0-41)	**<0.001**
ESR, mm/h, median (min-max)	538	34 (2-120)	1029	33 (2-174)	0.311
CRP, mg/dL, median (min-max)	533	15.7 (0.04-335)	1019	14.7 (0-11062)	0.859
RF positivity, n (%)	776	508 (65.5)	1193	785 (65.8)	0.878
Anti-CCP positivity, n (%)	585	345 (59.0)	945	582 (61.6)	0.309
Swollen joint count, median (min-max)	250	3 (0-24)	612	3 (0-32)	0.994
Tender joint count, median (min-max)	253	6 (0-30)	609	7 (0-44)	0.217
PtGA-VAS, median (min-max)	432	70 (0-100)	954	70 (0-100)	0.347
Pain-VAS, median (min-max)	345	70 (0-100)	879	70 (0-100)	0.142
Fatigue-VAS, median (min-max)	337	70 (0-100)	873	70 (0-100)	0.066
HAQ-DI score, median (min-max)	300	1 (0-3)	832	0.9 (0-2.95)	**0.040**
CDAI score, median (min-max)	115	15.5 (0-72)	293	21.5 (0-89)	0.117
SDAI score, median (min-max)	113	37.5 (1.72-137)	290	43 (2-389)	0.057

Table 2. Distribution of the biologic agents used at first and second and the rate of patients switching to another biologic agent

Biologic agents used at first	n (%)	Biologic agents used after switch	n (%)
Etanercept	482 (22.8)	Adalimumab	152 (18.3)
Adalimumab	404 (19.1)	Etanercept	135 (16.3)
Abatacept	265 (12.5)	Rituximab	140 (16.9)
Rituximab	234 (11.1)	Tocilizumab	103 (12.4)
Tofacitinib	209 (9.9)	Abatacept	101 (12.2)
Infliximab	152 (7.2)	Tofacitinib	61 (7.4)
Golimumab	136 (6.4)	Certolizumab	51 (6.2)
Certolizumab	115 (5.4)	Infliximab	44 (5.3)
Tocilizumab	114 (5.4)	Golimumab	38 (4.6)
Anakinra	4 (0.2)	Anakinra	4 (0.5)

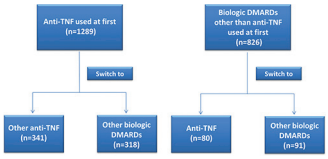

Figure 1. Switching pattern of the switched group

Conclusion: The patients in the Treasure database were followed-up approximately 4 years and about one-third of the patients had to switch from one biologic DMARD to another. The main reasons for this switching were primary (29.2%) and secondary (33.0%) inefficacy and 20% of the patients had to switch due to side effects. According to the switching pattern, about half of the patients using an anti-TNF agent at first switched to another anti-TNF agent and the other half switched to other biologic agents.

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