HLAB27 positive. In the table selected disease measures at baseline are shown.

	RA	PsA	Ax-SpA
DAS28	2.6 (1.2)	2.2 (1.1)	-
ESR mm/hr	15.9 (15.1)	12.2 (13.9)	12.0 (15.1)
CRP mg/l	4.9 (8.6)	4.3 (7.6)	5.5 (10.3)
Fatigue (VAS 0-100)	34.7 (30.7)	35.8 (29.3)	40.9 (30.0)
Pain (VAS 0-100)	31.3 (23.8)	31.2 (24.1)	33.7 (24.6)
MHAQ	0.42 (0.47)	0.37 (0.40)	0.40 (0.40)
BASDAI	-	-	3.1 (2.3)
BASFI	-	-	2.6 (2.3)

No significant difference ($p=0.97$) in drug survival for SB4 was seen between RA, PsA and ax-SpA patients. Mean (95% CI) SB4 drug survival time (years) was for RA 2.3 (2.2-2.4), for PsA 2.3 (2.2-2.4) and for ax-SpA 2.4 (2.3-2.5). In the figure below Kaplan-Meier drug survival curves are shown. Men had a statistically significant longer mean drug survival than women (2.5 (2.4-2.6) vs 2.2 (2.1-2.3), $p=0.001$).

Conclusion: Our long term real life data show that the majority of patients with a non-medical switch from originator etanercept to biosimilar etanercept SB4 remained on the drug. No significant difference in drug survival was seen between RA, PsA and ax-SpA patients. Men however had a significantly longer drug survival than women. Further analyses are needed to explore reasons for cessation across gender and patient groups.

REFERENCE:

[1] Glinborg B et al. Ann Rheum Dis 2018;0:1-9

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FRI0095

CHANGES IN B CELL PROFILE AS INDICATOR OF CLINICAL REMISSION TO TNF INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with the typical characteristic of synovitis of small-sized and medium-sized joints that leads to cartilage and bone damage. TNF inhibitors (TNFi) are widely used for the treatment of rheumatoid arthritis (RA) however, there are still no objective indicators of clinical response to TNFi therapy.

Objectives: To analyse the change of peripheral blood mononuclear cells (PBMC) profile after 6 months (m) of treatment with TNFi in order to find cellular indicators of response.

Methods: Prospective bi-center pilot study including 100 RA patients receiving TNFi therapy. PBMC were isolated from patients at baseline and 6m of treatment, and were analysed by flow-cytometry. Clinical activity at baseline and 6m of TNFi treatment was assessed by DAS28. Clinical remission ($DAS28 \leq 2.6$) after 6m of treatment was considered as optimal response. The association between clinical remission and the percentage of change (Δ , 6m-0m) within each PBMC subset was analysed through univariate logistic regression model (odds ratio; 95% CI; β ; p-value). All the analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity (ACPA and/or Rheumatoid factor) and baseline-DAS28.

Results: Demographic characteristics before starting TNFi therapy are shown in Table 1. After 6m of TNFi treatment, 40% patients achieved clinical remission. Decreased percentage of B cells ($\Delta CD19+$) was found after 6m of TNFi treatment in optimal responders, while suboptimal responders did not show differences with the baseline (OR: 0.78; 95% CI: 0.63-0.97; β : -0.25; p: 0.027) (Figure 1). This effect was essentially owing to a reduction of naïve B cells (OR: 0.76; 95% IC: 0.62-0.94; β : -0.27; p: 0.011) (Figure 1). No significant association was found between the other PBMC subsets (monocytes, NK cells, CD4+ T cells and CD8+ T cells) and clinical remission (Figure 1).

Table 1

Baseline patients' characteristics	Total patients (n=100)
Age (years); mean $\pm$ SD	53 $\pm$ 13
Female; n (%)	84 (84)
Disease duration (years); median (IQR)	8 (4-12)
Rheumatoid factor positive; n (%)	77 (77)
ACPA positive; n (%)	83 (83)
Smoking habit; n (%)	
non-smoker	46 (46)
smoker	20 (20)
ex-smoker	34 (34)
Body mass index (kg/m ²); median (IQR)	24.8 (22.9-29.6)
DAS28; mean $\pm$ SD	4.8 $\pm$ 1.2
Previous TNFi treatment; n (%)	13 (13)
TNFi type; n (%)	13 (13)
Monoclonal antibodies	55 (55)
Etanercept	45 (45)
Concomitant csDMARD; n (%)	96 (96)
Only Methotrexate (MTX)	51 (51)
Only other csDMARDs (OD)*	18 (18)
MTX + OD	27 (27)

* Other csDMARDs: leflunomide, sulphasalazine, hydroxychloroquine

Figure 1. Association between the percentage of change (Δ PBMC, 6m-0m) within each PBMC subset and the clinical remission. Univariate logistic regression analysis was performed for each PBMC subset. The analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity and baseline-DAS28. The percentage of changes (Δ , 6m-0m) in total B cells and in naïve B cells were independently associated with the clinical response. No association was found in other PBMC subsets.

Conclusion: Our results suggest that B cells may be useful as a cellular indicator of response to TNFi in RA patients.

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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 naïve, 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.

REFERENCE:

- [1] L.C. Berkhout, M.J. l'Ami, J. Ruwaard, M.H. Hart, P.O.-d. Heer, K. Bloem, M.T. Nurmohamed, R.F. Vollenhoven, M. Boers, D.F. Alvarez, C.H. Smith, G.J. Wolbink, T. Rispens, Dynamics of circulating TNF during adalimumab treatment using a drug-tolerant TNF assay. *Sci. Transl. Med.* 11, eaat3356 (2019).

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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 $\pm$ 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