AB0407

HIGH REMISSION RATES IN PATIENTS WITH RHEUMATOID ARTHRITIS USING BIOLOGICS UNDER A TREAT TO TARGET STRATEGY AND A COMPREHENSIVE DISEASE-MANAGEMENT MODEL. FIVE YEAR FOLLOW-UP RESULTS FROM A REAL-LIFE SETTING

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Background: Treat to target (T2T) strategy for rheumatoid arthritis (RA) aims to achieve remission or low disease activity. On the other hand, biological disease-modifying antirheumatic drugs (bDMARDs) have shown to be effective to achieve clinical remission or, at least, low disease activity in patients with RA. On the other hand, comprehensive healthcare programs have demonstrated good clinical outcomes in patients with chronic conditions.

Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) in patients receiving biological therapy during 5 years, and who were subjected to a multidisciplinary care program.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 ≥ 3.1 and ≤ 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient's conditions don't permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a physiatrist, psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.

Results: 747 patients meet our inclusion criteria, 85% of our patients were women, median age was 57 years RIQ (50-64); The most prescribed bDMARD was certolizumab 25% followed by etanercept 14%, tocilizumab 12%, abatacept 12%, golimumab 10% rituximab 8%, adalimumab 7%, infliximab 6% and Tofacitinib 6%. At beginning 53% of patients were in moderate disease activity and, 25% in high disease activity while at the end of follow up 89% of patients had achieved remission. See Table 1. It was established statistical significance between changes in median DAS28 at beginning and, at the end of follow-up (P<0.05).

Table 1. Comparison of DAS28

ACTIVITY LEVEL	BASELINE		5 YEAR FOLLOW-UP	
	n	%	n	%
REM			653	88.60
LDA	177	23	37	5.02
MDA	388	53	47	5.97
HDA	182	24	3	0.41

Conclusion: Biological therapy is effective for treating patients with RA, there was an evident global improvement of DAS28 in a cohort of RA patients. Also, our findings agree with other studies where T2T programs have shown improvements in disease activity in patients with RA. Thus, multidisciplinary T2T comprehensive healthcare programs should be widely implemented in patients with RA.

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AB0408

FIXED-INTERVAL VERSUS ON-DEMAND RETREATMENT STRATEGY WITH RITUXIMAB IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Rituximab (RTX), a monoclonal anti CD20 B-cell antibody is safe and effective in the treatment of Rheumatoid Arthritis (RA). The most optimal retreatment strategy in responding patients is still unclear.

A recent study by Chatzidionysiou et al suggests that RTX retreatment with Fixed-Interval (FI) strategy is better than retreatment with an On-Demand (OD) strategy. [1] However, whether FI treatment strategy is also superior in a treat to target setting is not known.

At our centre (Sint Maartenskliniek, the Netherlands), patients were retreated with RTX using the FI strategy and the OD strategy, by discretion of the rheumatologist, and using treat to target of DAS28CRP <2.9 in all patients.

In the FI strategy, patients receive retreatment after a predefined fixed period, mostly every 6 months. In the OD strategy, patients receive retreatment in case they experience increase in disease activity. In our hospital, most of the OD strategy patients were switched to the FI strategy in 2014 based on best evidence at that time, enabling us to retrospectively compare effectivity of these strategies.

Objectives: To compare the effectivity of retreatment of RA patients with RTX following the FI or OD retreatment strategy.

Methods: Adult (≥18) RA patients (clinical diagnosis) who started RTX treatment (1 or 2 x 1000mg or 2 x 500mg intravenous) between 1-1-2008 and 1-6-2016 and received at least 3 infusion cycles were included. Patients were treated with either FI or OD strategy, or crossed over from OD to FI. For on demand treatment, RTX retreatment could be planned at the daycare within 2-4 weeks.

Primary outcome was DAS28-CRP, secondary outcome was mean yearly dose of RTX. Baseline characteristics and follow up data (DAS28-CRP scores, information on RTX infusions, and steroid injections) were retrospectively extracted from patients' health records.

A linear mixed model was used to analyse the influence of the strategies on DAS28-CRP score. Time since start of RTX, calendar year, RTX dose, intra-articular (IA) or intramuscular (IM) steroid injection <6 weeks ago, concomitant csDMARD use at start of treatment and RF status were added to the model as fixed effects. Data was analysed using Stata 13.1.

Table 1. Baseline patient characteristics

Age, mean (sd)	59.6 (12.4)
Disease duration at RTX start, median (IQR)	11 (5-17)
csDMARD use at RTX start, n (%)	124 (58%)
Rheumatoid factor positivity, n (%)	166 (78%)
Anti-CCP positivity, n (%)	152 (72%)
Baseline DAS28CRP, mean (sd)	4.0 (1.2)
Strategy, n (%)	154 (72%)
Fixed interval	25 (12%)
On demand	34 (16%)
Both strategies	

Results: 213 patients were included. 154 following FI strategy, 25 following the OD strategy and 34 switching from OD to FI. Median duration of follow up was 38 months (IQR: 23-64), with a median number of 8 (IQR 5-12) DAS28-CRP measurements per patient. Patient characteristics are shown in Table 1. The OD strategy was not associated with higher DAS28-CRP score compared to FI strategy: adjusted difference was 0.09 DAS28-CRP point (95% CI: -0.08 to 0.26). Regardless of used strategy, DAS28-CRP improved significantly both over year of treatment, and by time from the start of RTX treatment. Furthermore was rheumatoid factor positivity associated with an lower DAS28-CRP in all patients, with adjusted difference of -0.37 (95%CI: -0.60 to -0.14). Average yearly RTX dose was 1899mg/yr (SD: 604) under the FI strategy and 1740mg/yr (SD: 732) under the OD strategy (95% CI difference: -336 to 34mg/yr).

Conclusion: Retreatment of RA patients with a fixed interval strategy does not seem to lead to better disease control or more drug use compared to an on demand strategy. A possible explanation might be the use of treat to target in our centre. Our study suggests that either strategy might be chosen in shared decision making and following treat to target.

REFERENCES

[1] Chatzidionysiou, et al. J Rheumatol. 2017 Feb;44(2):162-169.

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AB0409

B CELLS PROFILE AS A BIOMARKER FOR EARLY IDENTIFICATION OF OPTIMAL RESPONDERS TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS

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Background: The most common biological agents used as disease-modifying treatment in rheumatoid arthritis (RA) are TNF inhibitors (TNFi). Although these new strategies to treat RA have improved the course of the disease, approximately 30-50% of patients do not respond to this therapy. Early identification of optimal responders is crucial in the clinical setting.

Objectives: The aim of this study was to investigate if baseline percentages of different leukocyte subsets in peripheral blood (PBMCs) can contribute to identify RA patients who will respond to TNFi.

Methods: This was a prospective bi-center pilot study including 100 RA patients under TNFi therapy. Clinical activity was assessed at baseline and 6 months of treatment by disease activity score 28 (DAS28), considering optimal responders if they reached remission at 6 months (DAS28≤2.6). PBMCs were obtained before treatment and different leukocyte subsets were evaluated by flow cytometry (FACSCantoII instrument). The association between the percentage of PBMCs at baseline and clinical response at 6 months was evaluated through logistic regression models (odds ratio; 95% CI). All the analyses were adjusted by sex, age, disease duration, concomitant methotrexate, baseline DAS28 and seropositivity (ACPA and/or RF).

Results: Demographic characteristics are shown in Table 1. After 6m of TNFi treatment, 40% of the patients achieved clinical remission. A significant association between higher percentage of total B cells (OR=1.19; 95% CI:1.05-1.35; p=0.007) and naïve B cells (Bn; OR=1.32; 95% CI:1.08-1.61; p=0.007) at baseline and clinical response was found. The other PBMC subsets (monocytes, NK cells, CD4+ and CD8+ T cells subtypes) did not show statistical differences (Figure 1).

Conclusion: Our results suggest that basal B cells profile may contribute to identify optimal responders to TNFi in RA. (Funding: ISCIII (PI16/01092, PI16/00474).

Figure 1. legend: Association between the percentage of PBMC subset before TNFi and the clinical remission. Multivariate logistic regression analysis was performed for each PBMC subset. The percentage of total B cells and in naïve B cells were independently associated with the clinical response. No association was found in other PBMC subsets. The analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity and baseline-DAS28.

Baseline patients' characteristics	Total patients (n=100)
Age (years); mean±SD	53±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 (%)	
no	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±SD	4.8±1.2
CRP (mg/L); median (IQR)	5.7 (2.2-12.4)
Previous TNFi treatment; n (%)	13 (13)
TNFi type; n (%)	
Monoclonal antibodies	55 (55)
Etanercept	45 (45)
TNFi monotherapy	4 (4)
Concomitant csDMARD; n (%)	96 (96)
OnlyMethotrexate (MTX)	51 (51)
OnlyothercsDMARDs (OD)*	18 (18)
MTX + OD	27 (27)
Prednisone; n (%)	57 (57)

Table 1

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AB0410

DISCONTINUATION OF ORAL GLUCOCORTICOID AFTER INITIATION OF BIOLOGICAL DMARD DUE TO A HIGHER DOSE OF METHOTREXATE; A RETROSPECTIVE OBSERVATIONAL STUDY BASED ON DATA FROM A JAPANESE MULTICENTER REGISTRY STUDY

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Background: In the treatment of rheumatoid arthritis, glucocorticoid that provide anti-inflammatory effects in the early stage of treatment is an important drug. We recommend discontinuing of glucocorticoid as much