SAT0194

SIGNIFICANT OVERTREATMENT WITH BIOLOGICAL DRUGS IS COMMON IN ROUTINE CARE FOR PATIENTS WHERE SERUM DRUG LEVELS ARE MONITORED

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Background: Current challenges in treating rheumatic disease include using the right drug at right dose for the right length of time. Measuring serum drug levels can help prevent over-treatment, inform regarding secondary drug failure on account of immunogenicity and improve confidence to extend the interval of drug dosing.¹ This pilot work was a prelude to the implementation of the first national monitoring service worldwide within the relatively endogenous Scottish population.

Objectives: 1. To develop skill and familiarity with TDM at a Scottish laboratory prior to a business case for a national service
2. To understand the reasons why a clinician would use the service as part of clinical practice
3. To understand the current extent of over and undertreatment in an endogenous population

Methods: ELISA assays (Promonitor) were supplied by GRIFOLS (Barcelona) for the detection of serum levels of adalimumab (ADA), infliximab (IFX), Golimumab (GOL), Etanercept (ETA) and Rituximab (RIX). A single laboratory site was selected and laboratory training was provided. A bespoke clinical request form was developed. Adult & paediatric rheumatologists across Scotland were invited to send serum biological drug trough samples for analysis. The clinical indication for testing was also captured.

Reference ranges for free drug levels and anti-drug antibody levels: Analyte: Lower limit of measurement-Upper limit of measurement. Units ug/mL: Adalimumab 0.024–12, Infliximab 0.2–14.4, Etanercept 0.035–40, Golimumab 0.036–12.8, Rituximab 0.75–204.

Results: Internal calibration and quality control for the assays were established. A total of 39 IFX, 26 ADA, 14 ETA, 3 RIX, 14 GOL samples were received (total n=96). Only 4 (4%) of patients had serum levels below the reference range and of these just one had anti drug antibodies, suggesting that immunogenicity was not a significant clinical factor in this population. Overtreatment was common: 19 patients (20%) had drug levels greater than the maximum value in the reference range. 12 patients had anti-drug antibodies, but only one of these had poor disease control, suggesting a high proportion had non-neutralising antibodies. Based on this study, if all overtreated patients had dosing interval extended by 33%, this would produce a drug budget reduction of 6–7 %, easily dwarfing the setup and running costs of a biologic drug monitoring service.

Clinicians requested samples to help assess flaring patients to determine if immunogenicity had occurred or drug levels were too low (n=36) confidence around tapering drug (n=28), switching to biosimilar (n=6) and miscellaneous other reasons (n=15)

Conclusions: In this population, immunogenicity was not clinically relevant. Overtreatment with biological drugs was common, highlighting potential longer term safety risk and opportunity for cost reduction by dose interval prolongation. Clinicians primarily indicate the usefulness of serum biological drug testing in determining if secondary failure has occurred or to aid decisions about drug dose tapering.

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SAT0195

OPTIMIZATION OF BIOLOGIC THERAPIES IN RHEUMATOID AND PSORIASIS ARTHRITIS: A SINGLE-CENTRE EXPERIENCE

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Background: A timely diagnosis and a suitable therapy allow a better control of disease activity and limit joint damage in autoimmune arthritis. Biological therapies played a key role, modifying disease natural history. However, the use of these drugs implies several risks and increases health-care costs [1]. This has

raised a question: could be possible, in patients in a state of sustained remission or low disease activity (LDA), choose an optimized regimen of treatment? Recommendations provided by EULAR in 2013 includes this possibility, especially if biologic therapy is in association with DMARDs [2]. While optimized regimen has been attempted in different clinical trials with good results, strong evidences are currently lacking [3].

Objectives: The aim of our study was to analyse the effectiveness of optimization of biologic therapies in a cohort of patients with Rheumatoid and Psoriatic Arthritis (RA and PA).

Methods: We retrospectively included patients undergoing optimized therapy in a cohort of 328 outpatients (190 RA, 128 PA) treated with first-line biologic therapy from 2006 to 2017. Optimization was considered as predefined dose down-titration and/or expansion of dose interval in patients with a sustained remission or LDA (DAS 28 -ESR <2.6 or 2.6–3.2 respectively, for at least 24 months). Relapse was defined by an increase in DAS28-ESR >20% over baseline or by the onset of at least one tender and swollen joint. Our principal end-points were: (I) estimate the proportion of subjects able to optimize therapy (II) define the rate of relapse at 6–12 and 24 months follow-up (FU) in patients undergoing optimization (III) compare the effectiveness of optimized therapy in RA and PA patients and value the rate of optimization in relation to different biologic drugs. Survival analysis (Kaplan-Meier Curves) and Chi Square test were used and a p value <0.05 was considered as statistically significant.

Results: During FU, 15/190 (8%) RA patients and 16/138 (12%) PA patients reached a persistent LDA or remission and started the optimized biologic therapy. In survival analysis, rates of relapse at 6 months were 10 % and 0% in RA ad PA respectively, increasing to 21% and 8% at 12 months and finally to 48 % and 34% at 24 months. No significant differences emerged between the two groups. The use of Etanercept was associated with higher possibility to optimize biologic treatment (p=0.007).

Conclusions: Biologic therapy optimization is a workable option in RA ad PA patients who reached persistent remission or LDA. In our cohort Etanercept seems to be the most promising drug. Further studies are needed to better define the predictive factors of response in order to identify eligible patients.

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SAT0196

TIME TO DISCONTINUATION OF BIOLOGIC THERAPY BY MECHANISM OF ACTION IN RHEUMATOID ARTHRITIS: RESULTS FROM THE ONTARIO BEST PRACTICE RESEARCH INITIATIVE (OBRI) COHORT

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Background: Patients with rheumatoid arthritis (RA) may discontinue their biologic disease modifying antirheumatic drug (bDMARDs) due to non-response, loss of response or adverse events. However, time to discontinuation may be related to mechanism of action.

Objectives: We aimed to compare drug survival of tumor necrosis factor inhibitors (TNFi) versus non-TNFi in patients initiating bDMARD treatment in a Canadian (Ontario) observational cohort.

Methods: Patients enrolled in the Ontario Best Practice Research Initiative (OBRI) who started bDMARD therapy within 30 days before or any time after OBRI enrolment were included in the primary analysis. Patients were followed from bDMARD start until discontinuation/switching, death, lost to follow-up, or last visit, whichever came first. Time to discontinuation/switching of bDMARD due to (i) any reason, (ii) non-response or loss of response, and (iii) adverse events (AEs), were assessed using Kaplan-Meier survival analysis for TNFi versus non-TNFi users.

Results: Among the 943 patients included in the primary analysis, 187 (19.8%) received non-TNFi and 756 (80.2%) TNFi. Mean (SD) age and disease duration were 56.4 (12.7) years and 9.6 (9.8) years, respectively, and the majority were females (79.1%) and biologic naïve (84.4%). TNFi included Etanercept,

Adalimumab, Certolizumab, Golimumab, and Infliximab; and non-TNFi included Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

Over a mean (SD) follow-up of 2.4 (2.0) years, bDMARD discontinuation/switching was reported for 37.6% of patients, with significant difference in time to discontinuation between TNFi and non-TNFi users (Logrank $p=0.01$). However, there was no significant difference due to non-response or loss of response (Logrank $p=0.67$) between the two groups. At 2 years, more patients remained on TNFi (71.0%) compared to non-TNFi (57.0%). At 5 years, 51.0% and 44.0% of patients still remained on TNFi and non-TNFi, respectively.

Conclusions: The overall retention rate for biologics was comparable to finding in European registries. We found that patients stay on TNFi longer compared to non-TNFi. However, no significant difference was found between the two groups, for discontinuation or switching of bDMARDs due to non-response or loss of response. Further analyses are required to adjust for the effect of potential confounders (e.g. age, sex, disease activity, and other treatment regimens) on biologic discontinuation.

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SAT0197

ADHERENCE TO BIOLOGIC THERAPY OF RHEUMATOID ARTHRITIS PATIENTS – IS THERE ANY RELATION WITH DISEASE ACTIVITY?

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Background: In the last years, there has been an increase interest in using Patient Reported Outcomes (PROs) in clinical trials and daily clinical practice in Rheumatology to provide patient-centered care. The most frequently reported PROs are patient's pain, patient's global assessment (PGA) of disease activity and reports of functional capacity, fatigue, anxiety and depression. To date, studies that explore patient adherence to rheumatic medications are scarce.

Objectives: To study the level of adherence to biologic therapy of Rheumatoid Arthritis (RA) patients, followed at a day care hospital of Rheumatology.

Methods: Observational and cross-sectional study which took place in two months of consultation of day care hospital (5 periods per week). Patients with a diagnosis of RA according to 1987 American College of Rheumatology (ACR) and/or 2010 ACR/European League Against Rheumatism criteria, on biologic therapy, able to complete a questionnaire autonomously and who agreed to participate were included. Demographic and clinical data (DAS28, CDAI and SDAI to assess RA disease activity, HADS-A for anxiety, HADS-D for depression, FACIT-F for fatigue) were collected. To assess adherence, a Portuguese version of the Morisky Medication Adherence Scale (MMAS-8) was used and the patients were asked to apply it only to biologic therapy. Three levels of adherence were considered based on the following scores: 0 to <6 (low); 6 to <8 (medium); 8 (high). Statistics: Kruskal-Wallis and Mann-Whitney tests, $p<0.05$, SPSS® v.23.

Results: In total, 61 patients were included, 91.8% female, 82.0% on anti-Tumor Necrosis Factor (anti-TNF), the others on Tocilizumab (16.4%) or Abatacept (1.6%). Table 1 reports the means and medians of demographic and clinical variables included. The mean MMAS-8 score was 7.0 ± 1.2 , the median 7.0 (6.8–8.0), with a minimum of 2.5 and a maximum of 8. The adherence was medium in 50.8%, high in 36.1% and low in 13.1% patients. The median of current age was significantly higher for patients with high and medium levels of adherence compared to those with low levels ($p=0.030$). The time on treatment with the current biologic therapy was significantly different between the levels of adherence ($p=0.028$); the median of time on treatment for patients with medium levels of

adherence was significantly higher comparatively to the other patients ($p=0.009$). No other significant difference was found among the levels of adherence for the studied variables.

Conclusions: The adherence to biologic therapy was at least medium for 86.9% of patients. Differences between levels of adherence were found only for current age and time on treatment. Disease activity of RA does not seem to influence the levels of adherence.

Table 1 Means and medians of demographic and clinical variables.

	Mean ±SD	Median (IQR)
Current age – years	56.1 ±11.1	58.1 (48.1– 62.8)
Disease duration – years	15.0±7.5	13.1 (10.1– 18.2)
Time on treatment with the current biologic therapy – years	3.5±2.7	2.8 (1.0–5.6)
DAS28–4V	3.4±1.2	3.3 (2.6–4.2)
CDAI	9.7±7.8	7.0 (3.6–15.1)
SDAI	10.1±8.0	7.0 (4.0–15.7)
HAQ	0.9±0.6	0.9 (0.4–1.4)
HADS-A	6.5±3.9	6.0 (3.0–9.0)
HADS-D	5.4±3.7	5.0 (2.0–8.0)
FACIT-F	36.5±8.8	37.0 (29.1– 43.5)

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SAT0198

DRUG SURVIVAL AND EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS PATIENTS IN ROUTINE CARE – 7 YEAR EXPERIENCE FROM A SINGLE CENTRE IN THE UNITED KINGDOM

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Background: Even after the advent of multiple biologic drugs, optimum treatment of rheumatoid arthritis (RA) in a real-world situation continues to be challenging. The data on long-term drug survival of biologic drugs in routine clinical practice is lacking. We extended our earlier analysis of abatacept use in RA patients^{1,2} from a single centre in the United Kingdom over 7 years.

Objectives: To assess the efficacy, tolerability and drug survival of abatacept use in RA patients in a routine clinical setting like ours.

Methods: From November 2010 to December 2017, all RA patients with at least 6 months of follow up after abatacept initiation were included in the analysis. Data on demographics, disease duration, previous biologics, mode of administration, reasons for discontinuation and length of abatacept therapy were retrospectively collected from biologics database and medical records. Effectiveness was assessed by change in Disease activity scores (DAS 28) and European League Against Rheumatism response criteria (EULAR) after 6 months of therapy.

Results: 220 patients had received abatacept with at least 6 months follow up until December 2017. 176 were females and 44 males with mean age of 67.83 years (SD = 10.32). Mean disease duration in these patients was 14.42 years (SD = 8.11). 152 (69%) patients were seropositive (Rheumatoid factor and/or anti-CCP antibody). 207 (94%) patients had received a prior biologic and only 13 (6%) patients were biologic naïve. 193 (87.7%) patients were initiated on intravenous (iv) abatacept and 27 (12.2%) patients on subcutaneous (s/c) abatacept. 90 (40.9%) patients were successfully switched from iv to s/c abatacept.

The mean number of prior biologic drugs use per patient was 1.70 (SD = 1.03). 83.6% patients were co-prescribed DMARDs at the initiation of abatacept therapy. Mean baseline DAS 28 score was 6.02 (SD = 3.11). Average DAS 28 change at 6 months was -1.5 (95% CI -1.27, -1.33). 75% patients had a positive EULAR response (38% good, 37% moderate) and 25% had no response at 6 months.

Overall 57 (25.9%) patients discontinued treatment. 43 (19.5%) patients discontinued abatacept early (<9 months) due to primary inefficacy (10.9%) and adverse reactions (8.6%). 24 (10.9%) patients discontinued abatacept later, after a mean 27.46 (SD = 12.9) months of use, due to secondary loss of efficacy (6.3%) and adverse reactions (4.5%).

82% (180/220) of RA patients continued taking abatacept beyond 6 months. 61.5% (91/148) patients were still adherent at 2 years, 51.3% (39/76) retained the drug beyond 48 months.