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

M. E. Perry1, 1Rheumatology, Royal Alexandra Hospital, Paisley, United Kingdom

Background: Current challenges in treating rheumatic disease include using the right drug at the right dose for the right length of time. Measuring serum drug levels can help prevent overtreatment, inform regarding secondary drug failure on account of immunogenicity and improve confidence to extend the interval of drug dosing.

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 immuno-negativity 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.

REFERENCE:

Acknowledgements: Drs Alan Dunlop, Frank Finlay and Peter Galloway for the laboratory expertise and analysis

Disclosure of Interest: M. Perry Grant/research support from: GRIFOLS


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

M. Sorrenti1, S. Salemi1, R. Di Rosa1, R. Petruccelli1, B. Lagarà1, M. L. Songi1, G. Meneguzzì1, S. Quaglia1, M. Caldon1, A. Piscopo Diamanti1, S. Capussocchio1, G. Salemi1, R. D’Amelio1, 1Dipartimento di Medicina Clinica e Molecolare, Sapienza Università di Roma, Azienda Ospedaliera S. Andrea, ROME, 2Poliecnico Universitario di Monza, Università degli Studi di Cagliari, Cagliari, Italy

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 Psoriatric 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 downtitration 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.

REFERENCES:

Disclosure of Interest: None declared

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

M. Movahedi1, S. COUTA1, A. CESTA1, C. Bombardier1 on behalf of Other OBRI Investigators.1Ontario Best Practices Research Initiative, Toronto General Research Institute, University Health Network, Toronto, Canada

Background: Patients with rheumatoid arthritis (RA) may discontinue their biologic therapy due to reasons, such as loss of response or adverse events. However, time to discontinuation may be related to the 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 (0.9) 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.

REFERENCE:

Disclosure of Interest: M. Movahedi Employee of: OBRI, S. Couta Employee of: OBRI, A. Cesta Employee of: OBRI, C. Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, & UCB. Consultant for: Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology DOI: 10.1136/annrheumdis-2018-eular.2131

SAT0197

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


1Rheumatology, 2Nutrition, 3Nursing, Instituto Português de Reumatologia, Lisboa, Portugal.

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, HAQ 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). Statistical tests: 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 58.1 (48.1–73.2), median (IQR) DAS28 = 5.3 (4.1–6.9), median (IQR) CDAI = 15.1 (11.6–20.7), median (IQR) SDAI = 8.0 (6.2–11.2). 83.6% 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 (SC) abatacept, 90 (40.9%) patients were successfully switched from IV to SC abatacept.

Conclusions: The adherence to biologic therapy was significantly higher 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.