IMMUNOGENICITY OF BIOSIMILARS FOR RHEUMATIC DISEASES: AN UPDATED REVIEW FROM REGULATORY DOCUMENTS AND CONFIRMATORY CLINICAL TRIALS

V. Strand1, J. Goncalves2, T.P. Hickling2, H. Jones3, L. Marshall4, J. Isacs5

1Stanford University School of Medicine, Palo Alto CA, USA; 2Med-Research Institute for Medicines, Faculdade de Farmácia da Universidade de Lisboa, Lisboa, Portugal; 3Biomedicine Design, Pfizer, Andover, MA, USA; 4Inflammation and Immunology, Pfizer, Collegeville, PA, USA; 5NIHR Newcastle Biomedical Research Centre, Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle upon Tyne, UK

Background: Several biosimilars have been approved for the treatment of rheumatic diseases by the European Medicines Agency (EMA) or the US Food and Drug Administration (FDA).

Objectives: To summarise immunogenicity data from regulatory documents or confirmatory trials of biosimilars approved by the EMA or FDA for the treatment of rheumatic diseases.

Methods: EMA Public Assessment Reports (EPARs), FDA Clinical Summaries, PubMed records, and EULAR and ACR abstracts were searched for immunogenicity data from confirmatory trials of approved TNFα inhibitors or CD20 inhibitor biosimilars in patients with rheumatic diseases. Data collected included the proportion (%) of patients positive for anti-drug antibodies (ADAbs) among all patients and the proportion (%) of patients with neutralising antibodies (nAbs) among ADAb-positive patients.

Results: We identified 10 biosimilars approved by the EMA or FDA: three each for adalimumab (BI 695501, SBS, and ABP 501) and infliximab (SB2, CT-P13, and infliximab–qfbx) and two each for etanercept (GP2015 and SB4) and rituximab (CT-P10 and GP2013). The duration of treatment periods in the 16 identified trials (which varied in design and methodology of ADA/nAb detection) ranged from 12 weeks to 102 weeks. Across treatment groups in all trials, 0% to 62% of patients were ADAb-positive, of whom 0% to 100% were also nAb-positive. The lowest proportions of ADAb-positive (0%–13%) and nAb-positive patients (0%–3%) were observed in the trials of etanercept and its biosimilars, and the highest in the trials of infliximab and its biosimilars (ADAbs: 20%–62%; nAbs: 88%–100%). Consistent with the biosimilar designation, the proportions of ADAb- and nAb-positive patients in individual trials were similar between the originator and biosimilar products. Of note, in a 52 week trial of etanercept and its biosimilar SB4, the incidence of ADAs by Week 52 was significantly lower with SB4 than with etanercept (1%[3/299] vs 13%[39/296], p<0.001). However, as noted in the SB4 EPAR, this difference, which was not reflected in the incidence of nAbs or efficacy or safety of etanercept, may have been due to an ADA assay bias in samples collected at Weeks 4 and 8, when 37/39 ADAbs in the etanercept group and 2/3 in the SB4 group were detected.

Conclusions: Immunogenicity of the approved biosimilars is generally similar to that of originator products. For ETN, which has been associated with relatively low ADAb levels, there was a discrepancy in ADAb incidence compared with its biosimilar SB4, but those differences were transient and did not affect clinical activity or safety.

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THE CLINICAL EFFECTIVENESS AND COST SAVINGS OF TAPERING BIOLOGIC DMARDs IN PATIENTS WITH INFLAMMATORY ARTHRITIS AT A UK DISTRICT GENERAL HOSPITAL

W.P. Lee, R. Manhas, V. Sebbage, S. Kyle. Rheumatology, North Devon District Hospital, Barnstaple, UK

Background: Biologic DMARDs (bDMARDs) have led to substantial improvement in clinical outcomes for treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial/peripheral spondyloarthritis (SpA), making remission a realistic target. Current guidelines suggest clinicians should consider tapering after achieving remission in RA.1 Nevertheless, the optimal approach for tapering bDMARDs remains unknown and un-standardised across conditions.2

Objectives: To evaluate the tapering strategies on 3 major rheumatological disease entities (RA, PsA, SpA), the number of patients successfully tapered and the total cost saving from successful tapering.

Methods: The study was conducted at North Devon District Hospital in Barnstaple, UK and includes all bDMARDs users up until 31st December 2017. The tapering strategy was identified from hospital notes. Patients who were deceased, lost to follow-up or discontinued bDMARDs due to contraindication or adverse effects were excluded. Successful tapering is defined as patient on tapered dose or had their biologics withdrawn and remains at target treatment level (RA: DAS-28 <2.6; PsA:<3 tender joints and <3 swollen joints; SpA: BASDAI<4).

Results: There are a total of 298 patients: 174 RA; 59 PsA; 57 SpA; 8 other diagnoses. 94 patients (31.5%) had attempted tapering: 52 RA, 18 PsA, 22 SpA, 60 (20.1%) successfully tapered their bDMARDs: 34 RA (56.7%); 13 PsA (21.7%); 13 SpA (21.7%). Out of 34 RA, 30 seropositive; 4 seronegative; 2 co-prescribed with synthetic DMARDs, 10 on monotherapy. Out of 13 PsA; 8 co-prescribed with synthetic DMARDs; 5 on monotherapy.

Tapered by increasing interval of subcutaneous therapy. Only 1 RA patient tapered its IV dose of tocilizumab. This patient is excluded from the final analysis.

Results of bDMARDs therapy by disease and price (table 1). Number rounded to 2 decimal points.

Abstract AB0474 – Table 1

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<th>Mean period of tapering (months)</th>
<th>% saving per unit biologic</th>
<th>Cost per unit biologic (£)</th>
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ADA – adalimumab; TOC – tocilizumab; ETN – etanercept; GOL – golimumab; CDP – certolizumab pegol

Conclusions: In our study, 20% of bDMARDs users successfully tapered their dose. The total cost saving is significant at £359,912.98 over the tapered period, of which £249,321.19 (69%) in RA; £93,171.01 (11%) in PsA; £71,420.78 (20%) in SpA.


REFERENCES:

Disclosure of Interest: None declared
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THE INFLUENCE OF SWITCHING FROM ETANERCEPT ORIGINATOR TO ITS BIOSIMILAR ON EFFECTIVENESS AND THE IMPACT OF SHARED DECISION MAKING ON RETENTION AND WITHDRAWAL RATES

W.D. Müskens, S.A.A. Rongen-van Dartel, E.A. Adang, P.L. van Riel, I.Q. Healthcare, Radboud UMC, Nijmegen; Rheumatology, Bernhoven, Uden; Health Evidence, Radboud UMC, Nijmegen, Netherlands

Background: With biological patents expiring, biosimilars are becoming a realistic, less costly alternative to their originator. The data from numerous randomised clinical trials support that it is safe, effective and cost-saving to switch to a biosimilar. However, real world data about efficacy, safety, and cost-effectiveness of such a switch are lacking.

Since shared decision making (SDM) is a key factor in the treatment of rheumatic diseases, a non-mandatory open label transitioning from Etanercept originator to its biosimilar was performed at the rheumatology department of Bernhoven.

Objectives: The first goal of this study was to investigate the effect of switching from Etanercept originator to its biosimilar on the effectiveness of treatment. The second aim was to analyse the effect of SDM on the 1 year retention rates and reasons for withdrawal in daily clinical practice.

Methods: All patients with rheumatoid arthritis (RA), axial spondyloarthritis (SpA) and psoriatic arthritis (PsA) that were using Etanercept originator between 01–06–2016 and 23–10–2017 were informed by letter of the possibility to switch to its biosimilar. During the next outpatient visit with their rheumatologist the possibility to switch was discussed. Patients had the opportunity to ask questions regarding biosimilars and the switch to a biosimilar. If patients agreed the switch was made, with the reservation that they could switch back to the originator if they encountered difficulties with the biosimilar.

Using the registry of the rheumatology department at Bernhoven data were collected on disease activity (DA), medication use and adverse events from the moment of switch till 23–10–2017. As measure for DA the DAS28 was used for RA and PsA, the ASDAS was used for SpA. Stop reasons for biosimilars were verified using the health record system of the hospital. Reasons for change in disease activity and discontinuation of biosimilar treatment were assessed.

Results: Between 01–06–2016 and 23–10–2017 80% (69 patients) of the Etanercept originator users switched to its biosimilar. These patients switched to bio-
similar after a median time of 5.1 (IQR 2.6–8.3) years. By 23–10–2017, median follow-up of 307 (IQR 196–357) days, the mean DA did not significantly differ from the DA at baseline, 3.1 (95%CI 2.5–3.7) vs. 2.8 (95%CI 2.5–3.1). At end of follow-up 25% of the patients had discontinued their treatment and either switched back to originator (18%), switched to another biological (3%) or stopped treatment with biologicals (4%).

Reasons for switching back to originator were adverse events (18%), lack of effect (17%) and “adverse event and lack of effect” (25%). Only one serious adverse event was reported. This was a drug hypersensitivity reaction. After the patient was recovered, the originator was restarted without any difficulties.

Conclusions: An open label non-mandatory switch from Etanercept originator to its biosimilar showed that around 80% of the patients is willing to perform this switch. Switching did not affect effectiveness of treatment during one year follow-
up. 75% of the patients were able to continue biosimilar therapy. In the 69 patients that switched only one serious adverse effect occurred.

Disclosure of Interest: None declared

INHIBITION OF LARGE JOINT DESTRUCTION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

Y. Hirang, K. Hattori, R. Yamada, Rheumatology, Toyohashi Municipal Hospital, Toyohashi, Japan

Background: Rheumatoid arthritis (RA) causes not only inflammation of small joints, such as hands and feet, but also inflammation of large joints. Destruction of large joints is correlated with impairments of physical activity in RA patients more than destruction of small joints is. We experience strong inhibitory effect of inflammation in synovial joints, not only small joints but also large joints, by treatment with tocilizumab (TCZ), an antibody to IL-6 receptor in RA patients in daily clinical practice. Although inhibitory effects of small joint destruction by TCZ is well known, inhibitory effects of large joint destruction is unknown.

Objectives: This retrospective study investigated inhibitory effect of large joint destruction by TCZ treatment in RA patients.

Methods: Toyohashi RA database (TRAD) was used. TCZ was initiated in 65 RA patients in our institute. 31 cases (23 female and 8 male) who continued TCZ over 2 years were utilised in this study. Baseline characteristics and time course of disease activity were investigated. Delta-modified Sharp score (ΔmTSS) per year was used to evaluate small joint destruction. ARASHI score (3) was used to evaluate large joints destruction. Shoulders, elbows, hips, knees and ankles were evaluated using ARASHI score.

Results: Treatment continuation rate of TCZ was 86.3% at one year and 77.7% at two years in whole 65 cases (Kaplan-Meier methods). Baseline characteristics of 31 cases was as follows. Average age: 56 years old. Average RA duration: 6.6 years. Concomitant rate of MTX: 74.2%. Concomitant rate of prednisolone: