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AB0473

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

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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 TNF α 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, SB5, and ABP 501) and infliximab (SB2, CT-P13, and infliximab-qbtz) 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 ADAB/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 ADABs 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 and efficacy or safety of etanercept, may have been due to an ADAB 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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AB0474

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

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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 are 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; 24 co-prescribed with synthetic DMARDs, 10 on monotherapy. Out of 13 PsA, 8 co-prescribed with synthetic DMARDs; 5 on monotherapy.

59 tapered by increasing interval of subcutaneous treatment. Only 1 RA patient tapered its IV dose of tocilizumab. This patient is excluded from the final analysis. Tapering of subcut bDMARDs therapy by disease and price (table 1). Number rounded to 2 decimal points.

Abstract AB0474 – Table 1

Disease	bDMARDs	No. of patients	Usual dose of interval (days)	Mean tapered dose interval (days)	Mean period of tapering (months)	% saving per unit biologic	Cost per unit biologic (£)	Cost Saving per patient (£)	Total cost saving (£)
RA	ADA	12	14	7.00	27.75	50.00	352.14	9771.89	117262.68
	CZP	13	14	6.85	22.92	48.92	357.50	8016.92	10421.96
	ETN	5	7	8.20	34.40	117.14	134.06	21608.41	108042.05
	TOC	3	14	3.00	14.75	42.86	179.20	4531.50	13594.50
Total		33							249321.19
PsA	ADA	7	14	3.14	14.86	22.43	352.14	2347.43	16432.01
	GOL	4	28	10.50	18.25	28.57	701.93	4803.83	19215.32
	ETN	2	7	2.00	11.50	28.57	134.06	1761.84	3523.68
Total		13							39171.01
SpA	ADA	9	14	4.89	20.30	34.93	352.14	4993.90	44945.10
	GOL	2	28	10.50	5.63	37.50	701.93	7121.81	14243.62
	CZP	1	14	10.00	10.00	71.43	357.50	5107.25	5107.25
	ETN	1	7	3.00	31.00	42.86	134.06	7124.81	7124.81
Total		13							71420.78
Grand Total		59							359912.98

ADA – adalimumab; TOC – tocilizumab; ETN – etanercept; GOL – golimumab; CZP – 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; £39,171.01 (11%) in PsA; £71,420.78 (20%) in SpA.

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AB0475

THE INFLUENCE OF SWITCHING FROM ETANERCEPT ORIGINATOR TO ITS BIOSIMILAR ON EFFECTIVENESS AND THE IMPACT OF SHARED DECISION MAKING ON RETENTION AND WITHDRAWAL RATES

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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 biosimilar after a median time of 5.1 (IQR 2.8–8.3) 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 (58%), 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.

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AB0476

THE EFFICACY OF IMMUNOADSORPTION WITH INFliximab THERAPY ON THE MODULATION OF DISEASE ACTIVITY IN PATIENTS WITH SEVERE RHEUMATOID ARTHRITIS

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Background: Active refractory rheumatoid arthritis (RA) is common in real-world. Patients with active refractory RA usually have poor prognosis. And they respond poorly to a variety of therapies. The arrival of remission or low disease activity

(LDA) as soon as possible is an important way to improve their prognosis. We investigated the effectiveness of immunoadsorption therapy, a novel blood purification treatment, as a rapid and sustained disease-modifying therapy for active refractory RA.

Objectives: To evaluate the efficacy of additional immunoadsorption therapy (2 times) besides infliximab (IFX) on disease remission in patients with active refractory RA.

Methods: 90 patients with severe RA were included in this study. 43 patients were treated with basic IFX 3 mg/kg+methotrexate (MTX) therapy, and other different 47 patients, besides of basic therapy, were previous given 2 times additional immunoadsorption therapy. IFX 3 mg/kg was infused at weeks 0, 2, 6, 14, 22 and 30. Age, sex ratio, mean disease duration and core index of disease activity in two treatment groups were collected at weeks 0, 2, 6 and 30 weeks to compare the efficacy and safety of combined immunosorbent therapy in the treatment of severe RA.

Results: The baseline age, sex ratio and core indexes of disease activity were comparable between the two treatment groups ($p>0.05$). After treatment, the core indexes of disease activity of all patients decreased significantly compared with their baseline levels ($p<0.05$). The degree of reduction in the combined therapy group was significantly better than that in the basic treatment group ($p<0.05$), and the proportion of ACR remission patients in the combined treatment group was higher than that in the basic treatment group at different stages after treatment.

Conclusions: Additional immunoadsorption therapy can rapid relieve the disease activity of severe RA patients, and the remission rate of 30 W was significantly higher than only IFX treatment. However, due to the limited sample size of this study, the efficacy of additional immunoadsorption needs further observations.

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AB0477

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

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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 ⁽¹⁾. 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 (Δ mTSS) per year was used to evaluate small joint destruction. ARASHI score ⁽²⁾ 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 followed. Average age: 56 years old. Average RA duration: 6.6 years. Concomitant rate of MTX: 74.2%. Concomitant rate of prednisolone: