REFERENCES:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.1858

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 transition 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 2.6–8.3) 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 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 event occurred.

Disclosure of Interest: None declared

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. In 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 (2) was used to evaluate large joint 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;
MILD AND MODERATE HEPATIC IMPAIRMENT HAVE
CHARACTERISATION OF THE EFFECT OF RENAL
ARASHI change score in symptomatic knee joints and that in non-symptomatic
performed in evaluated joints during study periods. Influence of symptoms at
joints) [9.6, 65.4, 25.0]. Ankles (53 joints) [3.8, 91.6, 5.7]. Joint surgery was not
years. Evaluation using ARASHI change score from baseline to two years was as
release formulation have been evaluated in Phase 3 trials in RA.

Influence of hepatic impairment on upadacitinib exposure is of key clinical rele-
potential for upadacitinib use in some patients with hepatic impairment, evaluation
ARASHI change score in symptomatic knee joints and that in non-symptomatic
joints (−0.5 vs. 0.1, p<0.01).

Abstract AB0477 – Figure 1. Evaluation of large joint destruction using ARASHI score
during two-year tocilizumab treatment

Conclusions: Over 90% of large joints was not destroyed during two-year TCZ
treatment. Improvement was frequently observed in knees and elbows. Major rea-
sions of improvement of joint destruction were stabilisation of joints by osteophyte
formation and repair of bone erosions.

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Disclosure of Interest: Y. Hirano Speakers bureau: Chugai Pharma., K. Hattori:
None declared, R. Yamada: None declared

Rheumatoid arthritis – non biologic treatment and small molecules

AB0478

MILD AND MODERATE HEPATIC IMPAIRMENT HAVE
NO CLINICALLY RELEVANT IMPACT ON UPADACITINIB
PHARMACOKINETICS: RESULTS FROM A DEDICATED
PHASE 1 STUDY

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Background: Upadacitinib is a selective inhibitor of Janus kinase 1 (JAK1) which is
currently being evaluated for the treatment of several autoimmune disorders, includ-
ing rheumatoid arthritis (RA). Although renal elimination plays a minor role in
upadacitinib clearance (≤20% of upadacitinib dose is eliminated unchanged in
urine), a considerable number of RA patients have renal dysfunction. As such,
characterisation of the effect of different degrees of renal impairment on upadaci-
tib plasma exposures is important for this patient population.

Objectives: The objective of this study was to assess the pharmacokinetics of
upadacitinib in subjects with mild, moderate, and severe renal impairment com-
pared to subjects with normal renal function.

Methods: This Phase 1 study was conducted in 24 adult subjects, who were
assigned to one of four groups (six subjects per group) according to the estimated
glomerular filtration rate (eGFR) as calculated by the Modification of Diet in Renal
Disease (MDRD) equation: normal renal function (eGFR of ≥90 mL/min/1.73 m²),
mild renal impairment (60–89 mL/min/1.73 m²), moderate renal impairment (30–
59 mL/min/1.73 m²), and severe renal impairment (15–29 mL/min/1.73 m²). Sub-
jects received a single 15 mg dose of upadacitinib extended-release formulation
under fasting conditions. Blood samples for pharmacokinetic assessments were
collected for 120 hours after dosing. The effect of renal impairment on upadaci-
tib plasma exposures was assessed through regression analysis as well as anal-
ysis of covariance across the renal impairment categories.

Results: The point estimates for upadacitinib plasma exposure ratios [90% confi-
dence interval] in subjects with mild, moderate, and severe renal impairment were
1.8 [1.06–3.3], 1.3 [1.11–1.59], and 1.4 [1.14–1.82] for AUC and 1.08 [0.92–
1.23], 1.11 [0.88–1.40], and 1.14 [0.84–1.56] for Cmax, respectively, relative to
subjects with normal renal function. In this analysis, one subject with moderate
renal function showed exposures significantly lower than subjects with normal

AB0479

CHARACTERISATION OF THE EFFECT OF RENAL
IMPAIRMENT ON UPADACITINIB PHARMACOKINETICS

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Background: Upadacitinib is a selective inhibitor of Janus kinase 1 (JAK1) which is
currently being evaluated for the treatment of several autoimmune disorders, includ-
ing rheumatoid arthritis (RA). Although renal elimination plays a minor role in
upadacitinib clearance (≤20% of upadacitinib dose is eliminated unchanged in
urine), a considerable number of RA patients have renal dysfunction. As such,
characterisation of the effect of different degrees of renal impairment on upadaci-
tib plasma exposures is important for this patient population.

Objectives: To evaluate the effect of mild and moderate hepatic impairment on the
pharmacokinetics of upadacitinib.

Methods: This was a Phase 1, open-label study in subjects with mild (n=8) or
moderate (n=8) hepatic impairment, according to the Child-Pugh classification,
and demographically-matched healthy subjects (n=6). Subjects received a single
15 mg dose of upadacitinib extended-release formulation under fasting condi-
tions. Blood samples for upadacitinib assay were collected over 120 hours after
administration. Upadacitinib maximum observed plasma concentration (Cmax),
area under the plasma concentration curve (AUC), and terminal phase elimination
half-life (t1/2) were calculated using non-compartmental analyses. Analyses of
covariance were conducted to estimate upadacitinib exposure in subjects with
hepatic impairment relative to subjects with normal hepatic function.

Results: There was no statistically significant difference in upadacitinib Cmax or
AUC in subjects with mild and moderate hepatic impairment compared to subjects
with normal hepatic function. One subject with moderate hepatic impairment
showed significantly lower upadacitinib exposures than subjects with normal hep-
tic functions and was excluded as an outlier to ensure a conservative estimate for
effect of hepatic impairment on exposure. Upadacitinib exposure ratio central values
and 90% confidence intervals) in subjects with mild and moderate hepatic impairment
were 1.28 [0.91–1.79] and 1.24 [0.87–1.76] for AUC and 1.04 [0.77–
1.39] and 1.43 [1.05–1.95] for Cmax, respectively, compared to subjects with nor-
mal hepatic function. Upadacitinib terminal elimination half-life (harmonic mean
spesudo standard deviation) was 7.99±4.60 and 4.14±1.46 in subjects with mild
and moderate hepatic impairment relative to 8.93±4.87 in subjects with normal
hepatic function. Upadacitinib was generally well tolerated by the subjects in the
study.

Conclusions: Mild and moderate hepatic impairment result in only a very limited
effect on upadacitinib plasma exposures (<30% increase in upadacitinib AUC).
Therefore, in clinical trials, dose adjustments in subjects with mild or moderate
hepatic impairment are not warranted.

Acknowledgements: The studies presented were funded by AbbVie. AbbVie
contributed to the study design, research, and interpretation of data, reviewing,
and approving the publication. All authors are employees and shareholders of
AbbVie.

Disclosure of Interest: M.-E. Mohamed Shareholder of: AbbVie, Employee of:
AbbVie, S. Coppola Shareholder of: AbbVie, Employee of: AbbVie, T. Feng
Shareholder of: AbbVie, Employee of: AbbVie, A. P. Lacerda Shareholder of: AbbVie,
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AbbVie
DOI: 10.1136/annrheumdis-2018-eular.3530

AB0479