AB0495

POST-MARKETING SURVEILLANCE OF TOFACITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM REPORT OF SAFETY DATA

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Efficacy and safety of tofacitinib have been shown in patients (pts) with RA in global Phase (P)2, P3 and a long-term extension (LTE) study and in 2 P2 and 1 LTE study in Japanese pts.

Objectives: To evaluate safety of tofacitinib following drug approval in Japanese pts with RA using all-case post-marketing surveillance (PMS) data.

Methods: An interim analysis (IA) of safety data from an ongoing 3 year PMS study was conducted (5 Nov 2017 data-cut). All Japanese RA pts receiving tofacitinib were prospectively registered in the PMS study. All adverse events (AEs) were collected during tofacitinib treatment. Follow-up surveillance after discontinuation was conducted for serious infection events (SIEs; 1 year), malignancy and death (3 years). For all AEs and serious AEs, 6 month IA data was used. For AEs of special interest, all-period data (up to 36 months) was used to calculate cumulative incidence rates (IRs: pts with events/100 pt-years [yrs]) over time for herpes zoster (HZ) and SIEs during treatment +28 days and for malignancies during the full observation period.

Results: Overall, 3929 tofacitinib-treated pts with 1704.1 pt-yrs of exposure were included in the 6 month IA of safety: 80.5% were female, mean age was 62.7 years, with 32.6% of pts ≥70 years. Of these, 892 pts (22.7%) discontinued treatment, mainly due to AEs (351 pts; 8.9%) or lack of effectiveness (335 pts; 8.5%). At least one AE was observed in 1313 pts (33.4%); infections were observed in 493 pts (12.5%). The most frequent AEs were HZ (145 pts; 3.7%) and abnormal hepatic function (72 pts; 1.8%). SAEs occurred in 287 pts (7.3%); the most frequent SAEs were HZ (24 pts; 0.6%) and pneumonia/bacterial pneumonia (33 pts; 0.8%). SIEs occurred in 130 pts (3.3%). Malignancy (all causality) was reported in 25 pts (0.6%); lymphoma/lymphoproliferative disorder occurred in 5 pts (0.1%) and breast cancer in 3 pts (0.08%). There were 21 deaths (0.5%) during the 6 month period. The most common causes of death (including pts with multiple causes listed) were infection (6 cases) and malignancy (5 cases). For AEs of special interest from all-period data the IR of HZ (serious and non-serious) was 6.81 (264 pts; 3876 pt-yrs), the IR of SIEs was 5.38 (212 pts; 3941 pt-yrs) and the IR of malignancy was 1.25 (61 pts; 4874 pt-yrs).

Conclusions: This IA of tofacitinib PMS in Japan did not reveal any new or unexpected safety signals vs the tofacitinib RA clinical trials. IRs for HZ and malignancy were similar to IRs in clinical trials of tofacitinib in Japanese RA pts and the SIE IR was within the range reported in PMS of biologic treatments. Continuous monitoring of SAEs is required until the final PMS results.

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AB0496

T2T WITH SUBCUTANEOUS METHOTREXATE IN VERY EARLY RHEUMATOID ARTHRITIS (RA)

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Objectives: Adherence to foundations T2T and education of patients (pts) according to T2T Connect program increase possibility of favourable outcome of RA

Methods: In open prospective 36 months study of efficacy and safety of subcutaneous methotrexate (MT) 74 pts with definite very early RA (ACR/EULAR 2010) were included: mean age was 45.2±15.9, mean duration of RA – 5.2±3.48 months, mean DAS28 – 5.66±1.99 (max 7.06, min 4.44), RF positivity 73% and ACCP positivity 77% of pts. 3 pts had joint erosions. FK II had 43% and III- 53% of pts. Education conducted by program T2T Connect. Initial dose of MT was 15 mg/week, all pts used 5–10 mg/week folic acid and NSAIDs in therapeutically dose according to comorbidities, systemic glucocorticoids (GK) were not prescribed. 72 pts completed 12 months of treatment, 54–24 months, 29–36 months.

Results: In 88% of pts improvement was observed in first 4–5 weeks. After 3 months low disease activity (LDA) was registered in 18 pts, in over pts therapy wasn't corrected in view with clear tendency to decrease of RA activity, intraarticular injection of GK was performed in 3pts. Changes of DAS28 are in the table 1. After 6 months moderate disease activity was in 49% of pts, LDA – in 51%. After 12 months of study in all pts target of treatment was achieved: LDA in 81% of pts and remission (ACR/EULAR 2010) in 19%; after 24 months 57% and 43% respectively, after 36 months – 36% and 64% respectively (18 pts without treatment). The minimal radiographic progression was observed in 18 pts (24%, mean erosion's score 1.63±1.02), that wasn't cause of firm decrease of functional ability in pts. 3 women with remission after 18 and 20 months of treatment with MT became pregnant and gave birth to normal newborns. Withdraw MT because of AE was in 2 pts (flu-syndrome).

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Abstract AB0496 – Table 1

Months	0	3	6	12	24	36
Mean DAS28±SD	5.66±1.77	4.41±2.09	3.25±1.63	2.72±1.10	2.81±1.75	2.69±1.14

Conclusions: Peculiarity of our group of pts was the beginning of the treatment by MT, in most cases, at the first 6 months of RA onset. It is possible in this case to achieve remission more, than in half of pts without GK treatment. Thus, the subcutaneous form of MT is effective as regards activity and progression in early RA, safety for the long time in case of the using principles of controlled treatment allows achieve target after 6–12 month of therapy in most of pts with RA.

Disclosure of Interest: None declared

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AB0497

EFFECTIVENESS, TOLERABILITY, AND SAFETY OF TOFACITINIB IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE ANALYSIS OF REAL-WORLD DATA FROM THE ST. GALLEN AND AARAU COHORT

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Background: Tofacitinib is an oral JAK inhibitor indicated for the treatment of RA. Efficacy and safety of tofacitinib have been shown in several randomised clinical studies.

Objectives: The study presented here aimed to assess the clinical tolerability and effectiveness of tofacitinib among patients with RA in real life.

Methods: Consecutive patients between June 2013 and April 2017 with RA who fulfilled the American College of Rheumatology/EULAR 2010 criteria were analysed in a prospectively designed analysis of retrospective data. Patients were initiated on tofacitinib 5 mg bid. The primary objective was to analyse safety of tofacitinib in a real life cohort. Safety was assessed by the reasons to stop tofacitinib during follow up and changes of liver enzymes, haemoglobin, and creatinine. The secondary outcome was to analyse the frequency of and time to achieve low disease activity (LDA) and remission as defined by DAS28.

Results: Overall, 144 patients were treated with tofacitinib. 84.9% of the patients were pre-exposed to at least one biological agent. The average DAS 28 at initiation of tofacitinib was 4.43. 50.0% were rheumatoid factor and 49.0% ACPA positive. The mean follow up was 1.22 years (range 10d – 3.7a) after initiation of tofacitinib treatment. 94 (64.4%) patients remained on tofacitinib during follow up. The average time to stop tofacitinib was 190.0 days. Reasons to stop tofacitinib were: insufficient response (n=23), gastrointestinal symptoms (n=18), infection (n=5), myalgia (n=2), remission (n=2), headache,² cough, blue toe syndrome, intolerance, heart burn, psoriasis, and increased liver enzymes (all n=1). Increased ALAT or ASAT >2 x ULN were detected in 3.3% and 4.4%, respectively. These elevated transaminase levels were transient in 50% and 60% of the cases, respectively. Haemoglobin decrease of >10% was detected in 15.1% of the patients and decreased lymphocytes<500/μl in 3.4%. An increase of creatinine >20% was detected in 9.4%.

62.9% and 50.0% of the patients achieved LDA or remission after a median 260 and 616 days, respectively. These rates were significantly higher in patients naïve to biologic agents as compared to patients pre-exposed to biologics (LDA: naïve 100% after median 100d, pre-exposed 57.0% after 359d; remission: naïve 86.7% after 132d, pre-exposed 44.1% after 720)

Conclusions: Tofacitinib is a safe and effective treatment option for patients with RA. Tofacitinib may induce high rates of LDA and remission in patients with active disease, even after use of one or more biologics, though the rate is significantly higher in patients naïve to biologics. Tofacitinib may be a valuable option in a treat to target approach. Our data justify an early use of tofacitinib in the therapeutic strategy.

Disclosure of Interest: None declared

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AB0498

OPTIMISATION OF METHOTREXATE DOSE INDUCED SUCCESSFUL REDUCTION OF GLUCOCORTICOID WITHOUT IMPAIRED DISEASE CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Use of short-term glucocorticoids (GCs) along with methotrexate (MTX) have been recommended for newly onset patients with rheumatoid arthritis (RA) in EULAR recommendation 2016. However, it is not always easy to reduce or withdraw GCs due to patients' fear of relapsed pain or fatigue. As well, some patients are negative to increase MTX dose for fear of adverse events.

Objectives: To clarify whether GCs could be reduced without impaired disease control by optimising MTX dose in RA patients with stable medication in real-world clinical practice setting.

Methods: 70 patients with RA who regularly visit our outpatient clinic for ≥1 year were enrolled. Clinical characters, disease activity, and medications at present and 1 year before were retrospectively collected. Therapeutic strategy was to increase MTX with reducing prednisolone (PSL) based on patient's consent. Initiating bDMARDs was allowed in case of uncontrollable disease. Wilcoxon test and chi-square test were used for statistics.

Results: Clinical characters (median [IQR]) were; age 62^{51, 68} yrs; female 69%; disease duration 6.8 [3.4, 13.7] yrs. Rate of MTX was elevated from 57% to 62%,

and dose (mean ±SD) was increased from 9.8±3.2 to 11.6±3.7 mg/w (p<0.0001) for uses only, whereas PSL was suppressed from 56% to 26%, and decreased from 2.0±3.1 to 0.8±1.8 mg/d (p=0.0004) for all patients. bDMARDs were used for 16 patients, and newly initiated for 2 patients. Although not significant, median CDAI, SDAI, and DAS28 were suppressed from 5.7 to 3.8, 6.2 to 3.9, and 2.92 to 2.77, and remission rate were increased from 24% to 39%, 27% to 41%, and 36% to 41%, respectively.

Abstract AB0498 – Table 1

	Baseline	1 Year	p-value
%MTX	57%	67%	0.2226
MTX[mg/w] for users	9.8±3.2	11.6±3.7	<0.0001
%PSL	56%	26%	0.0003
PSL[mg/d] for all patients	2.0±3.1	0.8±1.8	0.0004
CDAI remission	24%	39%	0.0687
SDAI remission	27%	41%	0.075
DAS28 remission	36%	41%	0.4874

Conclusions: GCs could be reduced or withdrawn without deterioration with appropriately increased MTX. Moreover, disease control rather showed improved tendency.

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AB0499

EVALUATION OF THE EFFECTIVENESS OF METAXODINE IN THE HEPATIC TOXICITY DUE TO METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate inhibits the metabolism of purines resulting in the accumulation of adenosine; it also inhibits the activation of T cells and suppresses the expression of intercellular adhesion molecules for T cells. Side effects may show up during the treatment and among them there is hepatic toxicity, characterised by an increase of AST and ALT; such increase is usually asymptomatic but it may lead to a suspension of the treatment. Metadoxine (MTDX) is a drug which is used in order to treat both acute and chronic alcohol intoxication; it also prevents the inactivation of ATP from acetaldehyde and pyroglutamic acid. MTDX also showed to improve hepatic function markers and to decrease oxidative stress leading to a protective effect against radicals.

Objectives: The aim of this preliminary study was to evaluate the possible effect of MTDX on hepatic function in patients affected by RA in therapy with MTX.

Methods: The study involved the recruitment of patients affected by RA in treatment with MTX; a following random selection of a subgroup of patients who took MTDX (500 mg twice a day for 28 days, from the 5th to the 8th week of therapy with MTX) was performed. All the patients underwent a 12-week-follow up in which these parameters were evaluated: demographics, blood tests required for MTX in accordance with datasheets (especially AST and ALT), CRP, ESR, ACPA, numbers of swollen and tender joints, concomitant medications (NSAIDs and steroids) and the degree of disability (HAQ, table 1).

Results: 24 patients affected by RA (20 women), with an mean age of 51.3 years (±14.1) and mean MTX dose of 12.3±2.6, were recruited. 70.3% took GC with a medium dosage (3.72±2.71). Among these 24, 13 patients were underwent MTDX 500 mg twice a day from the 5th to the 8th week. Patients treated with MTDX+MTX showed a significant decrease of hepatic markers (AST Δ-18.38 p=0.004 – ALT Δ-19.23 p=0.004) compare with patients with MTX only (AST Δ-4.27 p=0.110 – ALT Δ-6.09 p=0.045) after a 12-week-monitoring, with no statistically significant difference concerning disease activity (table 2).