FRI0130

CERTOLIZUMAB PEGOL EXPOSURE DURING PREGNANCY IN WOMEN WITH RHEUMATOID ARTHRITIS: EVALUATION OF THE LONG-TERM NEWBORN OUTCOMES

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Background: Increased TNF alpha (TNF α) levels have been associated to pregnancy complications such as intra-uterine growth retardation and fetal loss. Even if pregnancy has classically been considered as having a positive impact on RA, disease flares potentially leading to poor obstetrical outcomes are not uncommon, raising the challenge of RA management in the early stages of pregnancy. Among TNF α inhibitors indicated for rheumatoid arthritis (RA), the use of certolizumab pegol (CTZ) has been reported as safe during pregnancy. As such, CTZ is allowed during pregnancy as provided by the factory-issued product's sheet.

Objectives: To assess the CTZ use safety during RA pregnancies, including maternal-fetal outcomes.

Methods: We retrospectively evaluated twelve women with RA, fulfilling the 2010 ACR/EULAR criteria, who had been exposed to CTZ throughout pregnancy. All women had signed an informed consent prior to treatment initiation.

Results: All cases were free from any potentially teratogenic drug, stopped at least 6 months before conceiving. Due to the underlying disease activity, and thanks to the approval for CTZ to be continued throughout the whole pregnancy, we carried on the treatment. Mean maternal age at conception was 31.6 $\pm$ 40 months; mean disease duration dated of 51 $\pm$ 26 months. All patients were on low-dose daily oral prednisone ranging from 2.5 to 5 mg; four subjects were on sulfasalazine 500 mg TID and four others on hydroxychloroquine 200 mg TID. We observed 12 singleton pregnancies; 8/12 mothers were primiparous. Mean gestational duration was 37 $\pm$ 3 weeks and mean birth weight 3.037 $\pm$ 0.58 grams. No stillbirths or fetal deaths were recorded. Five patients experienced elective caesarean section, while the others had vaginal delivery (four labour were induced by intravenous oxytocin; no dystocic births were reported). Mean APGAR scores after 1, 5 and 10 min from delivery were, respectively, 8 $\pm$ 2; 8 $\pm$ 1 and 9 $\pm$ 1. No obstetric, perinatal or neonatal complications were observed. Eight/12 newborns were breastfed. After a 12 months observational gap, all babies were healthy and the development index above the 75th percentile. All children underwent the Italian scheduled vaccine program, without complications. Their antibody vaccine response is nowadays being investigated by our Research team.

Conclusions: The data from our case series confirm the safety of CTZ administration during pregnancy in women with RA, regarding both the mothers and the offspring. No infection rate increase, neither major maternal-fetal issue were reported. The higher caesarean section rate in our patients, in comparison to the average of northern Italy (20%), could have a iatrogenic explanation, as suggested by the fact that all had been scheduled ahead of time. Similarly, the relative low rate of breastfeeding could be justified by the lack of information given to mothers. Further large data collection and perspective, controlled studies are needed to confirm this statement.

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FRI0131

POTENTIAL FACTORS ASSOCIATED WITH LONG-TERM CONTINUATION OF ETANERCEPT

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Background: With the advent of biologic agents, it has become possible to prevent progression of symptoms and joint destruction in rheumatoid arthritis (RA). However, less than half of patients achieve remission. The patient subgroup that benefits from a specific biologic agent remains unclear. Etanercept has been repeatedly reported to have a high long-term continuation rate, and can also be tapered once the therapeutic goal has been achieved. Identification of a patient

subgroup that benefits from long-term use of etanercept would not only benefit the patients but would also reduce healthcare costs.

Objectives: The purpose of this study was to evaluate the characteristics of patients who benefited from long-term use of etanercept and patients who discontinued the drug due to loss of efficacy using our hospital records, and evaluated factors that may predict the difference in efficacy.

Methods: We compared RA patients who continued etanercept treatment for at least 3 years, without interruption for 3 months or longer for reasons other than remission, including patients who switched from other biologics (continuation group), and patients who discontinued treatment within 3 years of treatment initiation due to loss of efficacy (discontinuation group). All patients were treated at our hospital before October 31, 2017. Multiple regression analysis was used to determine factors that may predict long-term etanercept efficacy, using 10 patient background characteristics, including age at initiation of etanercept and DAS28ESR, as explanatory variables.

Results: At the time of evaluation, the 3 year continuation rate of etanercept by the Kaplan-Meier method was 49.7%. Reasons for discontinuation included adverse events (33.3%), loss of efficacy (50%), and patient preference (17.3%). The continuation group comprised 87 cases, including 5 cases where etanercept was discontinued due to remission. Initial dose was 50 mg, and relative dose intensity was 0.78 (95% confidence interval 0.66–0.89). The discontinuation group included 51 cases. Regarding patient characteristics at the time of etanercept initiation, age (continuation group 60.1 vs. discontinuation group 66.7, $p=0.019$), number of previously used biologics (continuation group 1.24 vs. discontinuation group 1.45, $p=0.016$), and disease duration (continuation group 110.2 months vs. discontinuation group 74.2 months, $p=0.035$) were statistically significant with $\alpha=0.05$, suggesting potential utility in predicting long-term response. In contrast, combination therapy with methotrexate ($p=0.259$), rheumatoid factor, or anti-cyclic citrullinated peptide antibody positivity ($p=0.086$), and DAS28ESR ($p=0.056$) were not statistically significant.

Conclusions: Although this was a retrospective study, the results showed that young RA patients who have previously used few biologics, with long disease duration, may be more likely to benefit long-term from etanercept without loss of efficacy.

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FRI0132

FACTORS INFLUENCING SATISFACTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOLICIZUMAB

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Background: Biologics are effective for improving disease activity in patients with rheumatoid arthritis (RA). However, improved disease activity of RA alone does not always lead to high patient satisfaction.

Objectives: We evaluate which factors among items of disease activity and health status are correlated with improvement of patient satisfaction in patients with RA treated with biological agent.

Methods: Patients with RA who were planning to be treated with tocilizumab (TCZ) were enrolled in this study. Satisfaction, disease activity, and health status were assessed at week 0 and week 24 of TCZ therapy. Disease activity was evaluated using SJC, TJC, PGA, EGA and CDAl. Pain was also assessed using Visual Analogue Scale (VAS). Satisfaction and health status were assessed using the patient satisfaction score and the 5 components of the Arthritis Impact Measurement Scale 2 (AIMS-2).

Multiple linear regression analysis was used to assess the correlation between changes in satisfaction, disease activity and health status adjusted for CDAl at week 0. Also, Wilcoxon signed rank test was used to evaluate effect of TCZ on satisfaction, disease activity, and health status.

Results: Nineteen patients (male/female: 4/15) were evaluated. Patients' data at baseline were as follows: mean of age (51.3), disease duration (7.6 years), SJC (12.2), TJC (9.6), PGA (47.9 mm), EGA (51.4 mm), CRP (2.9 mg/dl) and CDAl (10.2), respectively. SJC, TJC, PGA, CDAl and RA-pain showed a statistically significant decrease at week 24 compared to the baseline ($p<0.001$, for each of all items). Out of the 5 components of AIMS-2, "physical", "symptom", "role" and "affect" improved statistically significantly at week 24 compared to the baseline ($p<0.0001$, $p=0.0179$, $p<0.0005$, $p=0.0056$, respectively), while there was no statistically significant improvement for "social interaction". Patient satisfaction was also statistically significantly higher compared to the baseline ($p=0.00038$).

After adjusting for CDAl at week 0, the change in satisfaction from week 0 to week 24 showed statistically significant correlation with changes in PGA and pain-VAS (all p -values <0.05), but not with changes in TJC, SJC EGA. Regarding

health status, the change in patient satisfaction adjusted for CDAI at week 0 was statistically significantly correlated with changes in "symptom" and "affect" (all p -values < 0.05). However, there were no statistically significant correlations between change in patient satisfaction and change in "physical", "role", and "social interaction".

Conclusions: Satisfaction was correlated with pain, PGA and psychological state in patients with RA treated with tocilizumab. On the other hand, satisfaction was not correlated with TJC, SJC and EGA. In other words, it appears that patient satisfaction is more closely linked with how symptoms are experienced physically and mentally. Further research into specific factors influencing the patients' experience could shed more light on conditions for improving patients' satisfaction and QOL.

Disclosure of Interest: None declared

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FRI0133 CENTRAL ROLE OF TOCILIZUMAB IN FIBROBLAST DOMINATED MODELS OF INFLAMMATORY AUTOIMMUNE ARTHRITIS

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Background: Immune mediated inflammatory arthritis including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) all characterised by joint synovitis. Disease-modifying antirheumatic drugs (bDMARDs) targeting specific components of the pathogenesis have radically improved the treatment of the diseases. However, a fair proportion of patients are non-responders.

Today, the first choice of DMARD is dependent on market pricing, regardless of the immunological target. This is due to the rather similar efficacy profile of the different DMARDs. Therefore, there is a need for stratification of patients suffering from Immune mediated inflammatory arthritis in order to reduce the fraction of DMARD non-responders.

Objectives: The objective of this study was to study the effects of various DMARDs on different synovial cell subsets using several human *ex vivo* models of immune mediated inflammatory arthritis. This could potentially guide future studies of personalising DMARDs in these diseases.

Methods: Synovial fluid was obtained from a study population of patients with active rheumatoid arthritis (RA) or peripheral spondyloarthritis (SpA). Synovial fluid mononuclear cells (SFMCs) containing primarily synovial monocytes and lymphocytes cultured for 48 hours ("Macrophage and Lymphocyte model") were used to study the effect of different biological agents on secretion of monocyte chemoattractant protein-1 (MCP-1) ($n=14$). Further, fibroblast-like synovial cells (FLSs) were co-cultured with autologous PBMCs ("FLS model") to study the effects of the same biological agents ($n=6$) in cultures dominated by synovial FLSs. Finally, SFMCs cultured for 21 days ("Osteoclast model") were studied to assess the effects on inflammatory osteoclastogenesis ($n=10$) measured by tartrate-resistant acid phosphatase (TRAP). The DMARDs investigated are shown in table 1.

Results: "Macrophage and Lymphocyte model"; In SFMCs cultured for 48 hours, all DMARDs included, except anakinra, had the ability to decrease the production of MCP-1. The two TNF inhibitors (adalimumab and etanercept) ($p<0.05$ and $p<0.01$) and baricitinib ($p<0.05$) had the most pronounced effects and reduced the production of MCP-1 by approximately 25%. Tocilizumab had in this culture a non-significant reduction of MCP-1 production.

"FLS model"; In the FLS+PBMCs cultured for 48 hours, tocilizumab ($p<0.001$) and the two JAK inhibitors (tofacitinib and baricitinib, $p<0.05$ and $p<0.05$) were exclusive in decreasing the cytokine production of MCP-1 by around 50%.

"Osteoclast model"; In SFMCs cultured for 21 days, only the two TNF inhibitors, adalimumab and etanercept were able to significantly reduce the secretion of TRAP from adherent macrophage like synovial cells by roughly 25% ($p<0.01$, $p<0.001$).

Abstract FRI0133 – Table 1

Generic name:

Adalimumab
Etanercept
Tocilizumab
Anakinra
Ustekinumab
Secukinumab
Tofacitinib
Baricitinib

Conclusions: This study reveals that most DMARDs have effects in the "Macrophage and Lymphocyte model" whereas tocilizumab, tofacitinib and baricitinib were superior in the "FLS model" and only the two TNF inhibitors were effective in

the "Osteoclast model". The findings in the "FLS model" reveals a possible beneficial effect of tocilizumab and JAK inhibitors to patients with fibroblast dominated arthritis. This study could potentially guide future studies of personalising DMARDs to treat immune mediated inflammatory arthritis.

Disclosure of Interest: None declared

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FRI0134 IS THERE ANY DIFFERENCE IN RA PATIENTS FOR METHOTREXATE USE VS. LEFLUNOMIDE USE AS A CONCOMITANT TREATMENT WITH BIOLOGICAL AND TARGETED SYNTHETIC DMARDs IN TURKIBO REGISTRY?

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Background: TURKIBO registry is the Turkish version of Danish DANBIO rheumatologic database which has been established in 2011. Demographics and previous or current treatment with conventional (csDMARD) and targeted synthetic (tsDMARD), and biological DMARDs (bDMARDs) were collected.

Objectives: We aimed to investigate the efficacy and safety status of methotrexate (MTX) vs. leflunomide (LEF) use as a concomitant treatment with bDMARDs and tsDMARD in this registry.

Methods: Frequencies of achievement of remission or remission +low disease activity (LDA) at the 6th month of bDMARD or tsDMARD treatment were compared between patients who were on these medications with MTX vs. LEF as a concomitant treatment. Drug survival and switch rates of bDMARDs and tsDMARD treatments either with MTX or LEF were compared. The adverse effects with MTX and LEF concomitant use were evaluated as well.

Results: The study included 725 bDMARD or tsDMARD receiving RA patients from 8 participating centres of the TURKIBO registry. Of these patients, 462 (63.7%) were receiving concomitant MTX and 263 (36.3%) LEF. Demographic findings are given in the table 1. Achievement of remission and remission +LDA at the 6th month of bDMARD or tsDMARD initiation was similar in concomitant MTX vs LEF groups (51.4% vs. 53%, $p=0.683$). When each bDMARD and tsDMARD was evaluated separately, achievement of remission were again similar in MTX and LEF concomitant users (TNFi: 53% vs. 54%; ABA: 50% vs. 59%; RTX: 53% vs. 61%; TCZ: 42% vs. 35%; $p>0.05$ for all). For TOFA, although remission +LDA rate was numerically higher in MTX concomitant group than LEF group (42% vs. 21%), the difference was not statistically significant due to the smaller sample size of TOFA ($n=33$). The results were similar for all DMARD groups when remission was evaluated alone. Drug survival (17±12 vs. 16±11 months, $p>0.05$) and drug discontinuation (42,2 vs 38, $p>0.05$) rates of bDMARDs or tsDMARD were also not different in MTX vs. LEF concomitant users. Adverse effects rate (19.5% vs 20.5%, $p>0.05$) were similar between MTX vs. LEF concomitant users as well.

Abstract FRI0134 – Table 1. Demographic findings of patients.

Sex, n (%)	Female	596 (82,2)
	Male	129 (17,8)
Age, Median (Q1-Q3)		55 (45-62)
Age, Mean±SD		54±13
Disease duration, Orntaca (Q1-Q3)		12 (8-17)
Disease duration, OrttSD		13±8
Biological and targeted synthetic drugs, n (%)	TNFi*	354 (48,8)
	RITUXIMAB	144 (19,9)
	ABATACEPT	127 (17,5)
	TOCILIZUMAB	61 (8,4)
	TOFACITINIB	36 (5,0)
	ANAKINRA	3 (0,4)
Biological+MTX, n (%)		462 (63,7)
Biological+LEF, n (%)		263 (36,3)

*TNFi: ETANERCEPT, ADALIMUMAB, CERTOLIZUMAB, GOLIMUMAB, INFILIXIMAB, REMSIMA.

Conclusions: Achievement of remission or remission +LDA was not different with the concomitant use of MTX vs. LEF with any bDMARD or tsDMARD treatment in RA patients with a similar safety profile. LEF might be an alternative as a concomitant DMARD in MTX-intolerant RA patients initiating bDMARDs or tsDMARD.

Disclosure of Interest: None declared