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FRI0142

THE COMPARISON OF THE ULTRASONOGRAPHIC SYNOVIAL FINDINGS BETWEEN INTRAVENOUS ADMINISTRATION AND SUBCUTANEOUS INJECTION OF TOCILIZUMAB

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Background: Biologic disease-modifying anti-rheumatic drugs (bDMARDs) that target cytokines and cytokine receptors such as tumour necrosis factor (TNF) alpha and interleukin (IL) 6 have been established as a standard therapy in patients with rheumatoid arthritis (RA). Tocilizumab (TCZ) that targets IL-6 receptors has two administration routes such as intravenous administration (IV) or subcutaneous injection (SC). The effect of TCZ-SC therapy demonstrated comparable efficacy and safety to TCZ-IV therapy in clinical study.^{1,2} However, there have been no reports that evaluate the effect of TCZ-IV and SC for synovitis by imaging modality.

Objectives: The aim of this study was to compare the ultrasound findings between patients with rheumatoid arthritis (RA) treated by TCZ-IV and SC.

Methods: All patients with RA who treated with TCZ in Osaka City University RA registry (1140 patients with RA and 390 patients using bDMARDs) were included in this cross-sectional study. US examination was performed in MCP, PIP, wrist and MTP joints and finger flexor tendon and wrist extensor tendon, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18–6 MHz). The grey scale (GS) and power Doppler (PD) findings were assessed by the semi-quantitative method (0–3). GS score and PD score (both 0–156 points) were defined as the sum total of each score.

Results: We analysed total 76 patients who treated TCZ, 27 patients in IV group and 49 patients in SC group (mean age: 62.9±14.0 vs 66.0±13.2 years, p=0.343, mean duration of RA: 17.1±11.1 vs 13.7±12.3 years, p=0.218). The duration of TCZ use was significantly longer in IV (4.6±2.2 vs 3.0±2.4 years, p=0.004).

Clinically, DAS28-ESR improved from 5.3±1.5 at baseline to 2.4±1.1 at US examination in IV group, and it improved from 5.2±1.4 to 2.8±1.5 in SC group. US findings were not significantly differenced in both groups, GS score: 11.7±12.5 vs 10.9±9.6 (p=0.751), PD score: 5.3±8.1 vs 5.7±6.8 (p=0.832), max PD grade: 1.3±0.9 vs 1.4±0.9 (p=0.571) in IV and SC respectively.

Abstract FRI0142 – Table 1. The comparison of demographic and ultrasonographic findings between TCZ-IV and SC patients with rheumatoid arthritis.

	TCZ-IV group (n=27)	TCZ-SC group (n=49)	P value
Age (years old)	62.9±14.0	66.0±13.2	0.343
Disease duration (years)	17.1±11.1	13.7±12.3	0.218
Duration of TCZ use (years)	4.6±2.2	3.0±2.4	0.004
DAS28-ESR at baseline	5.3±1.5	5.2±1.4	0.780
DAS28-ESR at ultrasound examination	2.4±1.1	2.8±1.5	0.175
CDAI at baseline	21.8±14.5	22.8±14.4	0.787
CDAI at ultrasound examination	7.3±5.9	10.6±10.4	0.082
Total GSUS score	11.7±12.5	10.9±9.6	0.751
Total PDUS score	5.3±8.1	5.7±6.8	0.832
Maximum PDUS grade	1.3±0.9	1.4±0.9	0.571

Conclusions: We compared the ultrasound findings between patients with RA treated by TCZ-IV and SC. Ultrasound findings between IV and SC were not significantly differenced. Both administration routes of TCZ are effective for the treatment in patients with RA.

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FRI0143

INFLUENCE OF LOW-DOSE GLUCOCORTICOID TREATMENT ON PERSISTENCE ON BIOLOGIC DMARDS THERAPY: REAL-LIFE DATA FROM THE ITALIAN GISEA REGISTRY

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Background: The use of glucocorticoid (GC) in Rheumatoid arthritis (RA) is recognised by the current treatment approach as a valid adjunct to DMARDs therapy. Despite its efficacy, safety of GC is still an issue and the best strategy of use is still debated, including patients under bDMARDs therapy

Objectives: To analyse in RA the differences of GC users versus non-users of baseline features, response to therapy and persistence in bDMARDs from the Italian biologics registry GISEA (Italian Group for the Study of Early Arthritis)

Methods: Consenting patients satisfying 1987 or 2010 ACR criteria for RA included in the Italian GISEA registry were enrolled. Data recorded comprehend demographic and clinimetric variables. Data are collected at baseline and 6 monthly during follow-up. To be included in the study patients needed a minimum follow-up time of 12 months and if data were not updated after 2012 patients were considered lost to follow-up. EULAR and HAQ responses were calculated. Statistical analysis included descriptive measures, parametric and nonparametric comparisons between groups and univariate analysis of survival on therapy

Results: A total of 8545 patients were enrolled, of them 4193 (49%) using a variable dose of GC. In 3035 (72%) the dose was ≤5 mg. Baseline demographic and disease-specific features at the start of bDMARD therapy were not different between GC users and non-users, both in 1 st and 2nd line bDMARDs RA patients. EULAR response rates were generally better in GC users at 6 and 12 months, but without statistical significance: good/moderate EULAR responses at 6 months were attained in 76.5% of GC users versus 67% in non users, while at 12 months in 81.5% vs 73% respectively (both Ps not significant). Similarly, HAQ responses (<0.5) were slightly better in users vs non users at 6 (42.5% vs 37.4%) and 12 months (46.5% vs 42%) but again without statistical significance. Finally, mean survival on bDMARDs therapy after 2 years was significantly influenced by GC with better survival curves in steroid-treated patients (55.8% vs 47%, p<0.001). This difference was also maintained subanalysing patients in 1 st or 2nd bDMARD lines of therapy (56.2% in users vs 48% in non users in 1 st line and 55.3% vs 45.9% in 2nd line, both Ps <0.001).

Conclusions: Our data show that GC are used in a high percentage of RA patients on bDMARD therapy. GC significantly improve the persistence on bDMARDs therapy in 1 st and 2nd line. No obvious other differences are evident in baseline, EULAR and HAQ response rates. This fact should be kept in mind when evaluating the persistence on bDMARD treatment reported in different registries. Safety evaluations in individual patients should be further analysed to guide the use of GC in this setting

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FRI0144

PATIENT-REPORTED OUTCOMES WITH SARILUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE SIMILAR REGARDLESS OF PRIMARY OR SECONDARY FAILURE WITH TUMOUR NECROSIS FACTOR INHIBITORS

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Background: Sarilumab is a human monoclonal antibody that binds membrane and soluble IL-6 and was recently approved for the treatment of moderate-to-severe rheumatoid arthritis. Among inadequate responders to a TNF inhibitor (TNFi), patients may respond differently to sarilumab depending on whether they had a primary (1st) failure or initially responded but then subsequently lost response (secondary [2nd] failure).

Objectives: To understand if changes in patient reported outcomes (PROs) differ among patients with 1° or 2° TNFi failure.

Methods: In TARGET (NCT10709758), patients with intolerance or an inadequate response to TNFi were randomised to placebo or sarilumab 150 mg or 200 mg plus csDMARD. For patients with an inadequate response to TNFi (92% of the sample), 1° or 2° failure was investigator-determined at enrollment. The following PROs were assessed at Week 0 (treatment initiation) and Week 24: HAQ-DI, patient global assessment of disease visual analogue scale (VAS), pain VAS, SF-36, morning stiffness VAS, EQ-5D, and Rheumatoid Arthritis Impact of Disease (RAID) scale. All scales produce global (total) scores, except the SF-36 which has eight domains and two summary scores (physical and mental component scores [PCS and MCS]) and the EQ-5D which has a single index utility score and a global health VAS. The PRO change from baseline was analysed through mixed model repeated measures with treatment, region, number of prior TNFis, baseline of the PRO analysed, visit, treatment-by-visit interaction, 1° and 2° subgroup, treatment-by-subgroup interaction, and treatment-by-visit-by-subgroup interaction. *Post-hoc* analysis of the sarilumab 200 mg data are reported here as this is the recommended dose of sarilumab.

Results: In this *post-hoc* analysis, 174 of 181 patients in the placebo group and 167 of 184 in the sarilumab 200 mg group were classified as TNFi 1° or 2° failures (the remaining patients were classed as intolerant or other and not included in this analysis); 75 and 64 were 1° and 99 and 103 were 2° treatment failures in the placebo and the sarilumab 200 mg groups, respectively. At Week 24, changes in all PROs were numerically similar in the 1° or 2° TNFi failures for both the sarilumab 200 mg and placebo groups (table 1). Furthermore, treatment-by-subgroup interaction testing did not show a statistically significant interaction of TNFi failure status and PRO outcome (all interaction *P*-values>0.05). Treatment emergent adverse events occurred in 65.6% of sarilumab 200 mg patients in the 1° failure group and 63.1% in the 2° failure group and were consistent with safety data reported previously.

Abstract FRI0144 – Table 1. Least square mean (SE) change from baseline to Week 24 in patient-reported outcomes with sarilumab 200 mg and placebo following primary and secondary TNFi failure

PRO	Placebo (n=75)	Sarilumab 200 mg (n=64)	Placebo (n=99)	Sarilumab 200 mg (n=103)	Interaction <i>P</i> -value*
Patient global assessment	-25.56 (3.30)	-30.61 (3.43)	-18.91 (2.93)	-32.07 (2.97)	0.2043
Pain VAS	-21.25 (3.56)	-31.81 (3.87)	-21.90 (3.07)	-33.04 (2.70)	0.8399
HAQ-DI	-4.39 (0.28)	-4.52 (0.28)	-4.30 (0.27)	-4.50 (0.28)	0.1672
SF-36 PCS	4.03 (1.01)	8.78 (1.01)	4.61 (0.99)	7.95 (0.90)	0.7237
SF-36 MCS	4.78 (1.41)	5.28 (1.42)	4.84 (1.21)	6.81 (1.10)	0.8526
Physical functioning	5.98 (2.86)	16.09 (3.00)	10.40 (2.78)	14.77 (2.53)	0.2965
Role-physical	9.19 (3.03)	17.97 (3.00)	11.75 (2.76)	20.01 (2.49)	0.0874
Body pain	14.51 (3.99)	25.35 (2.5)	18.32 (2.43)	28.02 (2.36)	0.8947
General health	10.10 (2.29)	18.20 (2.28)	7.00 (2.17)	12.79 (1.98)	0.8198
Vitality	9.19 (2.58)	14.56 (2.58)	9.05 (2.30)	13.47 (2.12)	0.8065
Social functioning	12.50 (3.23)	17.08 (3.22)	12.78 (2.84)	18.86 (2.55)	0.8477
Role emotional	10.46 (3.34)	12.88 (3.29)	10.19 (3.04)	15.55 (2.72)	0.6854
Mental health	6.09 (2.48)	12.15 (2.48)	9.00 (2.13)	11.97 (1.93)	0.5772
FACIT-fatigue	7.19 (1.38)	7.32 (1.37)	6.50 (1.14)	10.95 (1.04)	0.1630
Morning stiffness VAS	-21.83 (3.58)	-32.11 (3.63)	-22.27 (2.38)	-32.22 (2.33)	0.8177
EQ-5D VAS	13.72 (3.32)	18.83 (3.28)	16.51 (2.83)	16.74 (2.45)	0.9919
EQ-5D single index utility	0.16 (0.04)	0.31 (0.04)	0.22 (0.03)	0.35 (0.03)	0.7003
RAID	-1.74 (0.31)	-2.46 (0.32)	-1.84 (0.28)	-2.81 (0.25)	0.0620

EQ-5D, EuroQol; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; MCS, mental component score; PCS, physical component score; RAID, Rheumatoid Arthritis Impact of Disease; SF-36, short form-36; VAS, visual analogue scale.

*Interaction *P*-value tests for a difference in the treatment effect (sarilumab vs placebo) between the TNFi 1° and 2° failure groups

Conclusions: In TNFi inadequate response patients, following treatment with sarilumab 200 mg +csDMARD, changes in PRO outcomes were similar, regardless of whether they had experienced 1° or 2° TNFi failure, suggesting that sarilumab is suitable for both 1° and 2° TNFi failure patients.

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FRI0145

A BAYESIAN NETWORK META-ANALYSIS ON EFFICACY OF BIOLOGICS AND SMALL MOLECULES IN EARLY RHEUMATOID ARTHRITIS

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Background: The use of several biologic drugs as well as small molecules, in combination or not with methotrexate (MTX), is licensed for the treatment of Rheumatoid Arthritis (RA). Treating patients within the 'therapeutic window of opportunity' may reset the disease's long-term trajectory. Which agent would fit better the need of promptly achieving remission of patients affected with early RA is

currently a matter of debate. Ideally head to head comparison are required to estimate which treatment is the most effective. Alternatively, indirect comparisons based on a common comparator may be useful. Previous indirect comparisons did not take into account all the biologics and small molecules approved for the treatment of RA, being also biased, identifying early RA in patients with high variance of disease duration, ranging from 6 months to 2 years.

Objectives: To provide an estimate through a Bayesian Network Meta-Analysis of which biologic or small molecule in association with MTX is more likely to determine a good clinical response in patients affected with early RA (i.e. mean disease duration <1 year).

Methods: A literature search was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement to identify results of Randomised Controlled Trials (RCTs) of biologic agents and small molecules at licensed doses to treat patients affected by early RA. MEDLINE, EMBASE, Cochrane Library, and Clinicaltrials.gov were searched for all published RCTs ranging from 1990 to September 2017. Patients had to fulfil the ACR 1988 revised criteria and/or the 2010 ACR/EULAR criteria for classified RA. We included all completed RCTs of biologics or small molecules in combination with MTX, compared with MTX plus placebo or in combination with other biologics or small molecules, in patients whose RA had mean duration of less than 1 year. American College of Rheumatology (ACR) 50% response and ACR 70% response had to be evaluated after one year of continuous treatment both in examined drug branch and in placebo branch. WinBUGS 1.4 software (MRC Biostatistics Unit, Cambridge, UK) was used to perform the analyses, using a fixed-effect model.

Results: Thirteen studies were included in the analysis. All the biologics as well as Tofacitinib proved to be more effective than MTX plus placebo in inducing an ACR50 response. In this regard, Tofacitinib was the most effective overall (probability of being the best treatment: 75.04%) followed by Etanercept (21.52%). The agent with the highest probability of inducing ACR70 response was Etanercept (52.00%) followed by Abatacept (20.22%). All compared biologics in combination with MTX were superior to MTX alone in inducing ACR70 response.

Conclusions: After one year of continuous treatment, Tofacitinib and Etanercept are the agents with the highest probability of inducing ACR50 response in patients