Conclusion: The immunogenicity of patients treated with RTX is a rare event with possible clinical and biological consequences, especially in patients with high antibody levels.

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POS0601

DIFFERENCES IN DRUG SURVIVAL BETWEEN ORIGINATOR AND BIOSIMILAR PRODUCTS AMONG FIRST USERS OF EACH MOLECULE

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Background: Biosimilar products of biological disease-modifying antirheumatic drugs (bDMARDs) entered the Swedish market in 2015, with regulatory approvals based on head to head trials of limited duration. Longer-term comparative drug survival, in clinical practice, remains less well documented.

Objectives: To compare survival on drug between biosimilars and their originator products among first starters of etanercept, infliximab, adalimumab and rituximab.

Methods: Data from the Swedish Rheumatology Quality register (SRQ) was used to identify and follow patients who started a first ever treatment with etanercept since April 2015 (originator=ETA, biosimilar= SB4), infliximab since March 2014 (originator=IFX, biosimilar= CT-P13), adalimumab since January 2018 (originator=ADA biosimilars=SB5, ABP501), or rituximab since January 2018 (originator=RIT, biosimilar= GP2013), through December 31st, 2019, date of first discontinuation of the drug, or death. Discontinuation was defined as lack of effectiveness or adverse events, while other reasons for interruption of the drug (including non-medical switch) were considered censoring events. Descriptive characteristics were collected from the SRQ and tabulated. Hazard ratios (HR) of discontinuation were estimated using Cox regression, with each drug analyzed separately, adjusted for age, sex, indication, line of treatment, disease duration, year of treatment start, region and concomitant use of csDMARD.

Results: 9274 patients started etanercept (49% SB4), 3609 started infliximab (64% CT-P13), 3117 started adalimumab (27% SB5, 14% ABP 501), and 763 started rituximab (39% GP2013), Table 1. Patients starting CT-P13 and GP2013 were less likely to be biologics-naïve compared to those starting the originator product. Initiators of SB5, ABP501 and GP2013 were more likely, and those starting CT-P13 were less likely, to be on concomitant csDMARDs compared to those starting the originator products. Patients characteristics of ETA and SB4 were similar.

The introduction of a biosimilar was typically followed by a decrease in the uptake of the originator, but for ETA a change in pricing in 2018 later led to a reversal of this pattern (Figure 1).

For IFX, ADA, and RIT, survival on drug was similar for the originator and its biosimilar(s). For ETA, risk of discontinuation was somewhat lower for the biosimilar than for the originator (adjusted HR: 0.87, 95% confidence interval: 0.79-0.95), Table 1.

Table 1. Hazard ratios of discontinuation and descriptive characteristics of biosimilar vs. originator among first starters of each molecule, until 31st December 2019.

	Etanercept		Infliximab		Adalimumab			Rituximab	
	Originator	SB4	Originator	CT-P13	Originator	SB5	ABP 501	Originator	GP2013
N	4721	4553	1308	2301	1834	852	431	465	298
Discontinuation	1289	1236	582	878	399	139	80	57	26
Adjusted hazard ratios*	Ref	0.87 (0.79-0.95)	Ref	1.14 (0.99-1.31)	Ref	1.02 (0.83-1.26)	1.16 (0.88-1.52)	Ref	1.12 (0.68-1.85)
Age, mean years (std)	51 (16)	51 (15)	49 (16)	49 (16)	48 (15)	52 (15)	51 (15)	59 (15)	60 (15)
Female, %	67%	65%	61%	64%	62%	64%	65%	75%	76%
RA, %	46%	48%	39%	35%	33%	42%	43%	61%	76%
Bionative, %	72%	72%	76%	69%	45%	52%	43%	53%	38%
Disease duration, mean years (std)	11 (12)	11 (11)	11 (11)	11 (11)	12 (13)	12 (11)	14 (15)	14 (19)	15 (11)
DAS28, mean	4.0 (1.3)	4.0 (1.4)	4.1 (1.4)	4.1 (1.4)	3.7 (1.4)	3.8 (1.3)	4.0 (1.3)	4.5 (1.4)	4.7 (1.4)
Concomitant csDMARDs, %	45%	47%	57%	48%	37%	49%	42%	36%	43%

Abbreviations: RA=rheumatoid arthritis. csDMARDs=conventional synthetic DMARD, std=standard deviation.

Figure 1. Number of starts of biosimilars compared to the originator during the follow-up time, by molecule

Conclusion: Despite their identical indications and therapeutic positioning, there are some differences in the baseline characteristics between patients who start ADA, IFX and RIT and their biosimilars. There are no differences in drug survival between originator and biosimilar with the possible exception of etanercept although the observed difference should be interpreted in light of possible unmeasured or residual channeling.

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POS0602

ROLE OF INTRAARTICULAR BIOLOGICS AND METHOTREXATE IN THE MANAGEMENT OF ACTIVE INFLAMMATORY MONOARTHRITIS

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Background: Expansion of immunosuppressive medications has greatly improved disease activity control in rheumatoid arthritis (RA) patients. However, persistent symptomatic monoarthritis can be a problem in some patients who otherwise have satisfactory disease control. Intra-articular (IA) corticosteroid (CS) injections have remained a treatment cornerstone for these patients, but the need for other therapies is clear. Patients can fail such therapy, may develop adverse effects or have comorbidities that are exacerbated by IA CS. 50% of patients relapse after IA CS therapy. Several studies have looked at other agents such as methotrexate (MTX) or tumor necrosis factor inhibitors (TNF-i) as IA treatment options.

Objectives: To systematically review the evidence regarding utility of IA methotrexate and biologics in managing inflammatory monoarthritis in patients with RA.

Methods: A systematic literature review, in accordance with PRISMA guidelines, was conducted looking at trials investigating the use of IA MTX and/or TNF- α against IA CS, in managing inflammatory monoarthritis in patients with RA. A trained librarian conducted search of Ovid MEDLINE, Ovid EMBASE, Scopus, and Web of Science databases. Included studies were assessed for risk of bias as per the Cochrane tool.

Results: A total of 1013 citations were retrieved from the medical database searches. 12 studies were included in the final review. 6 studies investigated IA MTX while 5 studied IA etanercept. One study investigated different biologic agents: infliximab, etanercept, or adalimumab. Multitude of dosing regimens and administration protocols were used in various studies. 5 of the 6 MTX studies only included knees. IA MTX was compared against saline, CS and as combined MTX/CS vs CS alone. There was no evidence to support the use of IA MTX as a superior or equivalent agent to the comparator groups. Unlike MTX, etanercept was investigated in multiple joint types e.g. elbows, knees and wrists. IA etanercept was found to have utility as a successful IA alternative to CS. The only study investigating infliximab and adalimumab found them to be superior to IA CS across multiple joint types. All therapies were generally well tolerated. Etanercept studies had low risk of bias while the MTX studies mostly suffered from higher risk of bias.

Conclusion: Etanercept may be used as an IA agent in select patients with inflammatory arthritis when systemic treatment is not an option and IA corticosteroids cannot be used. Limited data also supports the utility of IA adalimumab and infliximab as better IA agents compared to CS. IA MTX, however, did not have such supporting data.

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POS0603

ANALYSIS OF FACTORS ASSOCIATED WITH THE EFFECTIVENESS OF ABATACEPT IN THE ORIGAMI STUDY

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Background: The ORIGAMI study is a multicenter, observational study to evaluate the effectiveness, safety, and patient-reported outcomes of abatacept (ABA) in Japanese patients with csDMARD-resistant, Simplified Disease Activity Index (SDAI)-moderate, biologic-naïve rheumatoid arthritis (RA). ABA has shown better effectiveness/efficacy in RA patients with anti-cyclic citrullinated peptide antibody (ACPA) positive (1) and high ACPA titer (2) compared to ACPA negative and low ACPA titer, respectively. However, more accurate predictors of effectiveness in clinical practice are needed than ACPA status.

Objectives: This post-hoc analysis is aimed to determine the association between ACPA and ABA effectiveness (disease activity and physical function) or retention rate and to investigate other factors associated with the effectiveness of ABA in patients enrolled in the ORIGAMI study.

Methods: Of the 279 patients in the effectiveness analysis set of the ORIGAMI study, 270 patients with baseline ACPA measurement were analyzed. The patients were divided into the ACPA-positive group (ACPA +ve, ≥ 4.5 U/mL at baseline) and the ACPA-negative group (ACPA -ve, < 4.5 U/mL). Patients' characteristics, changes in disease activity and physical function (Japanese Health Assessment Questionnaire; J-HAQ) through 52 weeks, and retention rates of ABA at week 52 were evaluated. Baseline characteristics and use of concomitant drugs were analyzed as independent variables by multiple regression analysis using a standard linear model adjusted by SDAI at week 0 to identify factors associated with SDAI change at week 52. In addition, the

interaction effects among ACPA status, RF status, and the factor that was significantly associated with SDAI change in multiple regression analysis on changes in SDAI were explored.

Results: The numbers of ACPA +ve and -ve patients were 226 and 44, respectively. ACPA values (mean $\pm$ SD, U/mL) were 280.3 ± 376.8 and 0.9 ± 0.7 , and rheumatoid factor (RF) values were 174.8 ± 302.6 and 20.9 ± 61.7 in the ACPA +ve and -ve groups, respectively. Mean (95% confidence interval) changes in SDAI at week 52 were -11.3 (-12.4 to -10.3) and -8.0 (-10.5 to -5.5), and those in J-HAQ were -0.27 (-0.34 to -0.20) and -0.16 (-0.34 to 0.01) in the ACPA +ve and -ve groups, respectively. In the Kaplan-Meier analysis, the retention rates of ABA at week 52 in the ACPA +ve and -ve groups were 72.1% and 58.7%, (discontinuation for any reason), and 91.6% and 75.7% (discontinuation because of lack of effectiveness), respectively. In a multiple regression analysis, the duration of disease (< 1 year) was associated with the change in SDAI at week 52. With respect to SDAI changes, the estimated difference of ACPA +ve and disease duration (< 1 year), ACPA +ve and disease duration (≥ 1 year), and ACPA -ve and disease duration (< 1 year), versus ACPA -ve and disease duration (≥ 1 year), were -4.26 ($p = 0.022$), -0.82 ($p = 0.618$), and -0.93 ($p = 0.716$), respectively (Fig. 1). The estimated difference of ACPA +ve and RF +ve, ACPA +ve and RF -ve, and ACPA -ve and RF +ve, versus ACPA -ve and RF -ve, were -2.48 ($p = 0.060$), -2.77 ($p = 0.107$), and -5.48 ($p = 0.087$), respectively.

Conclusion: A higher retention rate as well as better effectiveness of ABA on disease activity and physical function in ACPA +ve group versus ACPA -ve group were shown in the simple subgroup analysis. ABA effectiveness on the SDAI change was significantly better in patients with disease duration < 1 year and ACPA +ve compared to those with ACPA -ve and disease duration ≥ 1 year.

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Fig.1 Interaction of ACPA and disease duration with change in SDAI

Interaction analysis adjusted for RF, age, sex, comorbidity, SDAI, J-HAQ, steroid use, MTX use and csDMARDs use (except for MTX) were performed. ACPA, anti-cyclic citrullinated peptide antibody; SDAI, simplified disease activity index; RF, rheumatoid factor; J-HAQ, Japanese Health Assessment Questionnaire; MTX, methotrexate; csDMARDs, conventional synthetic disease modifying anti-rheumatic drugs.

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