Methods: Eligible patients, aged ≥ 18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who were IV abatacept-naïve and initiated SC abatacept 125mg once weekly, were enrolled into two cohorts: biologic (b) DMARD-naïve patients and those with ≥ 1 prior bDMARD treatment failure. This *post hoc* analysis assessed the mean change in disease activity (CDAI, SDAI and DAS28 [ESR]) from baseline (BL) at 6, 12, 18 and 24 months in response to treatment with abatacept. Patients were stratified by BL serostatus (all patients, RF/ACPA double positive [+/+] RA; RF/ACPA single positive [+/-; RF+/ACPA- or RF-/ACPA+] RA and RF/ACPA double negative [-/-] RA) and by line of therapy (all patients, patients receiving abatacept as a first-line or $\geq$ second-line therapy and those receiving abatacept following 1 or ≥ 2 prior bDMARDs). Overall patient data, as well as data for patients who were +/- or those who had 1 or ≥ 2 previous bDMARDs, are not shown. Estimates of mean difference are from *t*-test.

Results: Among 2892 eligible patients in ASCORE, 1748 patients with RF/ACPA status available at BL were included in this analysis (1079 +/+ RA, 326 +/- RA and 343 -/- RA). After 6 months, patients with +/+ RA on first-line abatacept therapy had better improvements in CDAI and SDAI scores from BL than patients on $\geq$ second-line abatacept therapy (mean difference [95% CI]: -3.4 [-5.6, -1.1]; $p=0.0032$ and -3.9 [-6.5, -1.3]; $p=0.0035$, respectively); better improvements in SDAI were also seen after 12 months (mean difference [95% CI]: -3.5 [-6.5, -0.5]; $p=0.0207$). Changes in CDAI and SDAI scores were comparable after 18 and 24 months. At 6 and 12 months, patients with +/- RA on first-line therapy had better improvements from BL in DAS28 (ESR) than those on $\geq$ second-line therapy (mean differences [95% CI]: -0.5 [-0.8, -0.2]; $p=0.0002$ and -0.4 [-0.7, -0.0]; $p=0.0317$, respectively); changes were comparable at 18 and 24 months (Figure 1). For patients on $\geq$ second-line therapy, at 18 months those with +/- RA had better improvements from BL in DAS28 (ESR) than those with -/- RA (mean difference [95% CI]: -0.7 [-1.2, -0.1]; $p=0.0232$). For patients not stratified by line of therapy, changes in DAS28 (ESR) were comparable between the +/- and -/- RA subgroups over time, with the exception of 6 months where patients with -/- RA had better improvements from BL compared with patients with +/- RA (mean difference [95% CI]: -0.3 [-0.6, -0.0]; $p=0.0495$).

Conclusion: In this real-world, *post hoc* analysis, patients with +/- RA who received abatacept as a first-line therapy had greater early improvements in disease activity compared with patients who received abatacept as a $\geq$ second-line therapy. Improvements in disease activity at 24 months were comparable between patients who were +/- and those who were -/-. Larger studies are needed to further corroborate these findings.

REFERENCES:

1. Katchamart W, et al. *Rheumatol Int* 2015;35:1693–1699.
2. Malmström V, et al. *Nat Rev Immunol* 2017;17:60–75.
3. Alten R, et al. *Ann Rheum Dis* 2019;78(Suppl 2):A1639.

Figure 1. Mean change from BL in DAS28 (ESR) for patients with RA treated with abatacept

p values are for the mean difference between abatacept as a first-line and abatacept as a $\geq$ second-line therapy, determined by *t*-test.
+/+ RF/ACPA double positive; +/- RF/ACPA double negative; ACPA anti-citrullinated protein antibody.

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POS0600

IMMUNOGENICITY OF RITUXIMAB BIOSIMILAR GP2013: A RARE EVENT, BUT NOT WITHOUT CONSEQUENCES ...

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Background: The bioequivalence between rituximab (RTX) originator and its biosimilar GP2013 has been demonstrated in rheumatoid arthritis (RA) (1). A recent randomized controlled trial suggested in a selected population a very low immunogenicity of GP2013 in RA (<1%) (2).

Objectives: To study in daily practice the risk of immunogenicity of patients treated with GP2013 for their chronic inflammatory rheumatic disorder.

Methods: Prospective routine care study carried out between September 2018 and August 2020 in the Rheumatology department of Cochin Hospital. We consecutively included patients treated with the biosimilar RTX GP2013, systematically used in the department since March 2018. Samples were taken before each infusion in order to detect anti-RTX antibodies (Ab) and RTX residual concentrations by ELISA (Lisa Tracker Duo Rituximab, LTR005, Theradiag).

Results: We included 159 consecutive patients treated with GP2013 (124 women, 78%) with a mean age of 59 $\pm$ 13 years and a mean disease duration of 18 $\pm$ 11 years. Among these 159 patients, 108 (68%) had RA and 51 had another disease (16 systemic sclerosis (SSc), 15 mixed connective tissue disease (MCTD), 5 systemic lupus (SLE), 5 inflammatory myopathies (MI), 5 undifferentiated polyarthritis, 2 juvenile idiopathic arthritis (JIA) and 3 primary Sjögren's syndromes). 137 patients (86%) were receiving associated disease-modifying therapy (DMARD), mainly methotrexate (111/137 patients, 81%). 120 patients (75%) were in maintenance therapy with originator RTX (cumulative dose of RTX: 3.5 $\pm$ 6g) before the switch to GP2013 in March 2018. Originator RTX was not re-established during the entire treatment period. The other 39 patients (25%) treated with GP2013 were naïve of originator RTX.

The analysis of the first sample, performed before the second GP2013 infusion, identified 8 patients (5 RA, 1 SLE, 1 MCTD and 1 SSc) with positive anti-RTX antibodies (prevalence 5%), with rates varying between 6 and >100ng/mL and undetectable residual RTX concentrations. Among these 8 patients, 6 had previously received originator RTX and 2 were RTX-naïve patients. There was a trend for higher body mass index in patients with positive anti-RTX antibodies (28 $\pm$ 7 vs. 25 $\pm$ 6 kg/m², $p=0.12$), and no association was observed between anti-RTX immunization and age, disease duration, combination with conventional DMARD, mean interval between infusions or cumulative RTX dose.

Among the 8 immunized patients, two groups could be isolated: i) a group of 5 patients (3 RA, 1 SLE, 1 SSc) with low antibody levels (6-22ng/mL) and no significant clinical consequences (absence of treatment discontinuation and loss of efficacy after 13 $\pm$ 4 months of follow-up, only one minor allergic reaction) and ii) a group of 3 patients (2 RA, 1 MCTD) with a high antibody levels ($\geq$ 100ng/mL) and meaningful clinical consequences: one severe allergic reaction during the second GP2013 infusion leading to treatment discontinuation, and a loss of efficacy with incomplete B depletion in 2 patients leading to RTX dose escalation from 500 mg to 1 g. Among the 151 patients not immunized at the time of the first sample, no severe allergic reaction and 6 minor allergic reactions were noted under GP2013.

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.

REFERENCES:

[1] Smolen et al, Ann Rheum Dis 2017

[2] Tony et al, Arthritis Care Res 2019

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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%
Bionaiive, %	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.