Table 1. Mean baseline PROs and LSM changes to week 12

	Baseline, mean (standard deviation)				12 weeks LSM changes (standard error)			
	OKZ q2w, N=464	OKZ q4w, N=479	ADA q2w, N=462	Placebo, N=243	OKZ q2w, N=464	OKZ q4w, N=479	ADA q2w, N=462	Placebo, N=243
PtGA-VAS	67.5(20.2)	66.8(20.9)	66.7(21.0)	67.4(20.0)	-29.7(1.1)#	-29.5(1.0)#	-31.6(1.1)#	-21.0(1.5)
Pain-VAS	68.4(20.6)	67.1(21.0)	66.8(21.5)	66.5(20.7)	-31.8(1.1)#	-31.7(1.1)#	-32.7(1.1)#	-21.3(1.6)
HAQ-DI*	1.7(0.58)	1.7(0.60)	1.7(0.57)	1.7(0.62)	-0.6(0.03)#	-0.6(0.03)#	-0.6(0.03)#	-0.4(0.04)
Comparison vs. ADA LSM difference [97.5% CI]					-0.03 [-0.12;0.05]	0.00 [-0.08;0.08]		
SF-36 PCS	31.8(7.0)	31.6(7.2)	31.4(7.4)	31.9(7.5)	8.1(0.4)#	7.8(0.4)#	8.1(0.4)#	4.9(0.5)
SF-36 MCS	42.9(11.4)	43.50(11.3)	44.1(11.4)	43.1(11.0)	5.1(0.4)†	4.9(0.4)†	5.0(0.4)†	3.1(0.6)
FACIT-F	26.7(10.7)	27.3(10.4)	27.4(11.3)	27.3(10.2)	8.4(0.4)#	8.1(0.4)ŧ	8.9(0.4)#	5.2(0.6)

Footnotes: LSM difference (SE) 97.5% CI by ANCOVA. NRS imputation.*, secondary endpoint; †p≤0.05, ŧp<0.01, #p<0.001 vs placebo; VAS (mm).

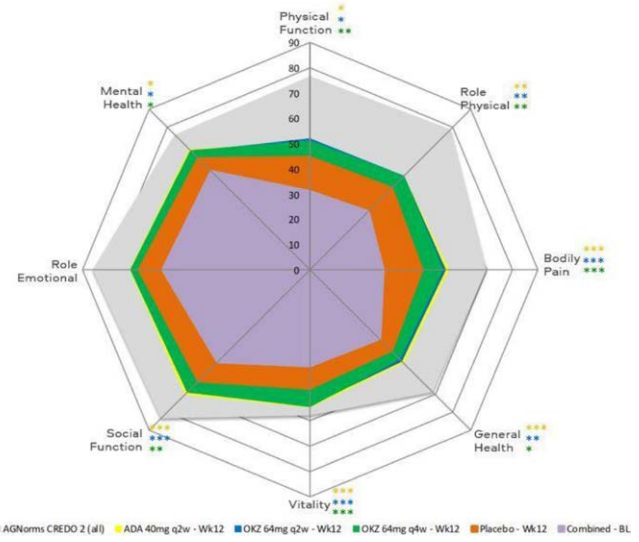

Figure 1. SF-36 domain changes from baseline to week 12. *p≤0.05, **p<0.01, ***p<0.001 ADA vs placebo; *p≤0.05, **p<0.01, ***p<0.001 OKZ q2w vs placebo; *p≤0.05, **p<0.01, ***p<0.001 OKZ q4w vs placebo. AGNorms, age- and gender-matched; BL, baseline.

Conclusion: Treatment with both doses of OKZ resulted in similar, statistically significant improvements across PROs vs placebo in MTX-IR patients with moderate to severely active RA, comparable to ADA, that were clinically meaningful.

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OP0064

FREQUENCY AND PREDICTORS OF MULTIPLE TREATMENT SWITCHING IN RHEUMATOID ARTHRITIS

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Background: Despite the significant improvements in the field of rheumatoid arthritis (RA) treatment, a significant and troubling minority of patients remain refractory to multiple disease modifying antirheumatic drugs (DMARDs). The consequence of this "difficult-to-treat" state is irreversible damage, risk of co-morbid conditions, and substantial loss of quality of life. Early, precise, and actionable identification of this challenging group of RA patients is crucial for optimal prevention and management.

Objectives: To assess the frequency and to identify predictors of switching between multiple biological and targeted synthetic DMARDs (b/tsDMARDs) in RA patients in a large national register.

Methods: Observational cohort study including RA patients starting a first-ever b/tsDMARD 2009-2018, based on data from the Swedish Quality Rheumatology register. Comorbidities were identified through linkage to the national Patient Register. Baseline (time of RA diagnosis) characteristics of the population were described. Three groups were investigated: A) Patients starting ≥3 treatment courses; B) Patients starting ≥4 treatment courses; and C) Patients starting ≥5 treatment courses. Predictors of multi-switching were explored using univariate and multivariable logistic regression analyses.

Results: 23,908 RA patients were identified. Proportions of patients starting ≥3, ≥4 or ≥5 b/tsDMARDs treatment courses were 7%, 3.2% and 1.6%, during a mean (95% CI) of 3.6 (3.5-3.7), 4.3 (4.2-2.5) and 4.9 (4.7-5.2) years from RA diagnosis, respectively. In Table 1 baseline characteristics for each multi-switching group are summarized. For definition A, the following baseline univariate predictors were identified: female sex (OR=1.57, 95% CI=1.39-1.76), younger age (OR=0.96, 95% CI=0.95-0.96), positive RF (OR=1.36, 95% CI=1.22-1.53) and ACPA (OR=1.40,

Table 1. Baseline (time of RA diagnosis) characteristics

		Multi-switching definition		
	All patients	A: ≥3 b/tsDMARDs	B: ≥4 b/tsDMARDs	C: ≥5 b/tsDMARDs
N, %	23 908 (100)	1677 (7)	755 (3.2)	385 (1.6)
Age (years), mean (SD)	59.5 (15.2)	50.3 (14.5)	50.0 (14.6)	47.6 (14.7)
Sex (male) %	30.7%	22.5%	22.4%	21.6%
CRP, mg/L (median, IQR)	8.9 (4-22)	10 (4-24)	10 (4.2-25)	10 (4-29)
ESR (median, IQR)	23 (12-40)	23 (25-39)	23 (11-37.5)	22 (11.8-36.3)
Patient global, VAS 0-100 (mean, SD)	48.8 (26.8)	58.4 (25.3)	59.8 (24.5)	60.8 (24.0)
Patient pain, VAS 0-100 (mean, SD)	50.2 (26.8)	59.2 (25.4)	59.8 (25.2)	59.9 (25.2)
Fatigue, VAS 0-100 (mean, SD)	48.5 (28.8)	61.2 (26.5)	63.1 (25.9)	64.6 (23.6)
HAQ (mean, SD)	0.97 (0.66)	1.1 3(0.64)	1.15 (0.64)	1.13 (0.63)
Swollen joint count (median, IQR)	5 (2-9)	6 (3-10)	6 (3-10)	6 (3-10)
Tender joint count (median, IQR)	5 (2-9)	6 (3-12)	6 (3-12)	7 (3-11.25)
Concomitant csDMARD, %	52.5%	50.4%	51.7%	51.4%
Reumatoid factor positive, %	63.1%	69.6%	69.8%	67.8%
ACPA positive, %	67.0%	73.4%	74.3%	72.7%
DAS28-ESR (mean, SD)	4.62 (1.51)	5.00 (1.41)	5.10 (1.37)	5.12 (1.33)
VAS general health physician (mean, SD)	42.28 (23.02)	45.30 (22.19)	45.68 (20.69)	51.40 (25.83)

95% CI=1.24-1.58), higher DAS28 (OR=1.21, 95% CI=1.15-1.26), HAQ (OR=1.46, 95%=1.33-1.61), pain (OR=1.014, 95% CI=1.012-1.017) and fatigue (OR=1.017, 95% CI=1.014-1.021). In the multivariable logistic regression model, female sex, younger age, higher HAQ, pain and fatigue at baseline were independent predictors of multiple treatment switching. Similar results were found for all three multi-switch definitions. Several comorbidities (i.e. heart failure, ischemic heart disease, malignancy, renal failure) were associated with a lower risk for multiple treatment switching, suggestive of medical contraindications for b/tsDMARDs.

Conclusion: In this large national observational cohort, multiple treatment switching, indicative of difficult to treat RA, was observed in a significant proportion of patients, ranging between around 2 to 7% during the first 5 years from time of diagnosis. Risk factors include female gender, younger age, higher HAQ, pain and fatigue at the time of RA diagnosis, suggesting increased attention to this challenging group of patients.

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OP0065 INFLIXIMAB BIOSIMILAR-TO-BIOSIMILAR SWITCHING IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: CLINICAL OUTCOMES IN REAL-WORLD PATIENTS FROM THE DANBIO REGISTRY

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Background: In routine care, biosimilar-to-biosimilar infliximab switching may occur to save costs (=non-medical switching). Previous studies have investigated the efficacy and safety of switches from originator infliximab to a corresponding biosimilar in patients with inflammatory rheumatic diseases (1). However, the outcomes after switching from one infliximab biosimilar to a second infliximab biosimilar remain scarcely investigated. Denmark has recently conducted a nationwide mandatory infliximab biosimilar-to-biosimilar switch.

Objectives: To investigate the effectiveness of infliximab biosimilar-to-biosimilar switch (CTP-13 to GP1111) among patients with RA, PsA and AxSpA, including patients who had previously switched from originator (originator-experienced) to CT-P13 as well as patients who were originator-naïve.

Methods: Observational cohort study based on DANBIO registry (for clinical data upon switch =baseline) linked with national patient registries (to identify prior comorbidities). Patients with RA, PsA or AxSpA who performed a biosimilar-to-biosimilar switch from CT-P13 to GP1111 between April 1st 2019 and February 1st 2020 were included. Patient were divided into two groups: originator-naïve and originator-experienced. Main outcomes in the two groups were one-year GP1111 treatment retention (Kaplan Meier "drug survival curves") and changes in disease activity 4 months before versus 4 months after switch in individual patients. Also, factors associated with GP1111 treatment retention for both groups combined were explored with Cox proportional hazard regression analyses, stratified by diagnosis (univariate-, age-and gender adjusted and fully adjusted). Analyses were adjusted for relevant clinical factors (for details: see Table 1)

Results: In total, 1,605 patients underwent an infliximab biosimilar-to-biosimilar switch and were included; 1,171 were originator-naïve and 434 were originator-experienced, 685 RA/314 PsA/606 AxSpA, median disease duration was 9 years, 42% were in DAS28/ASDAS remission at the time of switch.

At one year, 83% (95% CI 81-85) of the originator-naive and 92% (95% CI 90-95) of the originator-experienced switchers maintained GP1111 treatment (Figure 1). Changes in disease activity 4 months pre- and post-switch were close to zero for all disease activity measures (e.g. DAS28, ASDAS, VAS pain, not shown).

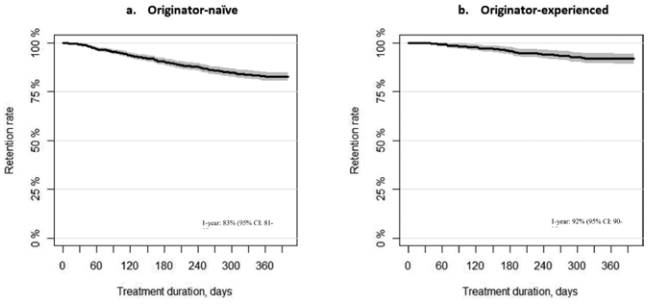

Figure 1. Kaplan-Meier plots of crude GP1111 treatment retention rates after an infliximab biosimilar-to-biosimilar switch among patients with inflammatory arthritis

The risk of GP1111 withdrawal was lower in originator-experienced compared to originator-naïve patients in patients with RA and PsA: HR 0.4 (95% CI 0.2-0.9, p-value 0.01) and HR 0.1 (0.1-0.6, p=0.01), but not significantly for AxSpA 0.56 (0.27-1.13, p=0.1). Across all indications, lower disease activity at baseline (DAS28/ASDAS remission) was associated with higher retention (Table 1).

Conclusion: Biosimilar-to-biosimilar infliximab switch was effective and well-tolerated in >1,500 real-world patients. Retention was higher in originator-experienced switchers and patients, who were in remission at the time of the switch, suggesting retention to be more affected by patient-related than drug-related factors.

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[1] Glintborg *et al*, *ARD*, 2017; 76: 1426–1431

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Table 1. Baseline variables associated with GP1111 withdrawal (RA shown below, similar findings for PsA and AxSpA)

	Univariate		Age- and gender adjusted		Multivariate	
	HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**	**HR (95%CI)**	**p-value**
RA						
Female gender	0.9 (0.6-1.3)	0.4	-		0.7 (0.5-1.2)	0.2
Age, years	1.0 (0.9-1.0)	0.9	-		1.0 (0.9-1.1)	0.6
Originator-experienced versus originator naïve to infliximab	**0.5 (0.3-0.8)**	**0.002**	**0.5 (0.3-0.8)**	**0.002**	**0.4 (0.2-0.9)**	**0.01**
Methotrexate use, yes	**0.5 (0.3-0.7)**	**<0.001**	**0.5 (0.3-0.7)**	**<0.001**	**0.6 (0.4-0.9)**	**0.01**
Comorbidities ≥1	1.1 (0.7-1.5)	0.8	1.1 (0.7-1.5)	0.8	0.9 (0.6-1.4)	0.7
In remission (yes)	**0.4 (0.3-0.6)**	**<0.001**	**0.4 (0.2-0.6)**	**<0.001**	**0.5 (0.3-0.7)**	**<0.001**
DAS28	**1.7 (1.4-1.9)**	**<0.001**	**1.7 (1.5-1.9)**	**<0.001**	-	-
Patient global VAS, mm	**1.0 (1.0-1.1)**	**<0.001**	**1.0 (1.0-1.1)**	**<0.001**	-	-