SAT0152 REAL-LIFE INFLIXIMAB AND ADALIMUMAB TROUGH LEVEL AND ANTI-DRUG ANTIBODY MEASUREMENTS IN RHEUMATOLOGY: THE FINNISH EXPERIENCE

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Background: Therapeutic drug monitoring of TNF inhibitors (TNFi) may optimize clinical benefits while at the same time reducing financial costs and risk of adverse events^{1,2}. Monitoring the TNFi trough levels (TLs) and the anti-drug antibodies (ADABs) can provide relevant information to make rational adjustments to therapy if indicated.

Objectives: To identify distributions and trends in infliximab (IFX) and adalimumab (ADL) TLs and ADABs from clinically requested, real-life samples from Finnish patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA), or juvenile idiopathic arthritis (JIA).

Methods: Samples for TL and ADABs were taken on a clinical basis in daily practice from four university hospitals and 15 central hospitals in Finland and sent for analysis to United Medix Laboratories. Samples were collected and analyzed from January 2012 to February 2016. TL measurements were performed by enzyme-linked immunosorbent assay (either at Sanquin laboratories, Amsterdam, The Netherlands, or in Helsinki, Finland using Promonitor ELISA, Progenika Biopharma). TLs from 2–10 µg/ml (IFX) or 5–10 µg/ml (ADL) were considered as general target ranges. ADAB measurements were performed by radioimmunoassay (Sanquin). 1762 TL (1241 patients), 1598 ADAB (1203 patients), and 860 combined TL and ADAB samples (718 patients) were analyzed. Statistical analyses were performed by SPSS (IBM, Armonk, NY). $p < 0.05$ was considered statistically significant.

Results: The highest proportions of samples with very low TLs (< 0.1 µg/ml) were seen in IFX-treated RA patients (14.5%) and ADL-treated SpA patients (12.6%). The proportion of all samples in the general target range was 51.3% (IFX) and 33.4% (ADL). A greater proportion of ADL RA and SpA samples had possibly supratherapeutic (> 10 µg/ml) TLs (RA: ADL, 22.9% vs IFX, 10.4%, $p < 0.01$ and SpA: ADL, 21.4% vs IFX, 15.0%, $p = 0.05$). A greater proportion of ADL JIA samples had TLs > 10 µg/ml (ADL, 54.5% vs IFX, 36.3%, $p < 0.01$). Proportions of samples with ADABs (> 12 AU/ml) ranged from 18.0% (IFX RA) to 28.6% (ADL SpA). A greater proportion of ADL samples with TLs of 2–5 µg/ml and detectable ADABs (> 12 AU/ml) (RA: ADL, 3.3% vs IFX, 0%; SpA: ADL, 5.6% vs IFX, 0%; JIA: ADL, 3.4% vs IFX, 0.9%) was observed.

Conclusions: IFX RA and ADL SpA samples had the highest proportions of very low TLs. Compared to IFX, greater proportions of ADL samples (all indications, particularly JIA) had TLs > 10 µg/ml. Proportions of samples with ADABs > 12 AU/ml ranged from 18.0% to 28.6%. Compared to IFX, a greater proportion of ADL samples with possibly therapeutic TLs had detectable ADABs.

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SAT0153 EFFECTIVENESS OF LOW AND HIGH DOSE METHOTREXATE IN COMBINATION WITH ADALIMUMAB IN A REAL WORLD SETTING: RESULTS FROM THE CORRONA RHEUMATOID ARTHRITIS REGISTRY

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Background: Combination therapy of methotrexate (MTX) with biologics results in superior outcomes vs. monotherapy. Recent clinical trials have shown that lower MTX doses may be sufficient in patients with rheumatoid arthritis (RA) to achieve similar clinical and patient reported outcomes (PROs)^{1,2}.

Objectives: To evaluate whether high MTX dose in combination with adalimumab (ADA) results in improved clinical and PROs compared with low MTX dose.

Methods: Adult RA subjects naïve to other monoclonal antibodies, initiating standard dose ADA (40mg q2w) in combination with oral MTX (low dose: ≤ 12.5 mgs and high dose: ≥ 15 mgs) during 2003–2016 and had a 6 month follow-up visit were included. The primary outcomes were mean change in clinical disease activity index (CDAI), and PROs (mHAQ, pain, fatigue, morning stiffness) from baseline to 6 months. Secondary outcomes included achievement of remission (CDAI ≤ 2.8)/low disease activity (CDAI ≤ 10). Outcomes were evaluated adjusting for covariates that differed at baseline using mixed model linear regression. Persistency of ADA between the two groups was examined using Kaplan-Meier survival analysis.

Results: A total of 519 patients were included: N=101 and N=418 initiated ADA with low and high dose MTX respectively. Patients on high dose MTX were

significantly younger (53.3 vs 59.7 years), with lower disease duration of RA (8.8 vs 11.2 years) compared to low dose MTX group. Patients in the high dose group also had higher disease activity (mean CDAI: 20.8 vs 15.4) and more likely to be biologic-naïve (71.3% vs 55.4%), compared to the low dose group (all $p < 0.05$). Unadjusted and adjusted analyses found no sufficient evidence that patients on high dose MTX had a better improvement in the outcomes selected (table). Persistency of ADA did not differ between the two groups.

Table: Outcomes at 6 months among ADA plus low (≤ 12 mg) vs. high dose (≥ 15 mg) combination MTX therapy

	ADA + ≤ 12.5 mg (low dose)	ADA + ≥ 15 mg (high dose)	Unadjusted*	Adjusted**
6 month outcomes	Mean (SD)	Mean (SD)	β (95% CI)	β (95% CI)
Change in CDAI	-5.1 (13.1)	-8.0 (14.2)	-2.65 (-5.68, 0.38)	2.70 (0.27, 5.12)
Change in mHAQ	-0.04 (0.30)	-0.09 (0.43)	-0.05 (-0.14, 0.04)	0.03 (-0.06, 0.13)
Change in pain	-3.3 (26.9)	-9.0 (28.1)	-5.59 (-11.65, 0.46)	2.25 (-3.21, 7.72)
Change in fatigue	1.8 (23.3)	-3 (27.6)	-4.81 (-12.54, 2.92)	-1.99 (-9.96, 5.98)
	Response rate n (%)	Response rate n (%)	Odds Ratio* (95% CI)	Odds Ratio** (95% CI)
Achievement of Remission (CDAI ≤ 2.8)	7 (11.7%)	47 (15.1%)	1.17 (0.47, 2.88)	0.92 (0.36, 2.4)
Achievement of LDA (CDAI ≤ 10)	28 (46.7%)	135 (43.3%)	0.841 (0.47, 1.49)	0.63 (0.31, 1.26)

mHAQ: modified Health Assessment Questionnaire; LDA: Low Disease Activity; * Compared with low dose MTX group as a reference; ** Adjusted for age, duration of RA, work status, insurance status, prior biologic count, MTX continuation, baseline CDAI and patient pain.

Conclusions: In this real world study, improvements in PROs and achievement of LDA/remission at 6 months were similar in the groups initiating ADA in combination with either low dose or high dose MTX.

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SAT0154 EFFECTIVENESS AND SAFETY OF CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND PLAQUE PSORIASIS: OBSERVATIONAL STUDY IN REPUBLIC OF KOREA

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Background: CT-P13 is approved as a biosimilar of innovator infliximab for marketing in 79 countries around the world. After approval, observational study has been conducted in Republic of Korea in patients with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA) and Plaque Psoriasis (PS).

Objectives: To evaluate the effectiveness and safety of CT-P13 under routine care in Republic of Korea.

Methods: This observational study included both biologic naïve patients (Naïve group) and patients who switched from other anti-tumor necrosis factor (TNF) to CT-P13 (Switch group). Effectiveness were evaluated based on remission (DAS28 ≤ 2.6 in RA, BASDAI ≤ 3 in AS and absence of swollen and tender joint counts in PsA), and response (BASDAI 20/50/70 in AS and PASI 50/75 in PS). Adverse events (AEs) were collected over 6 month period.

Results: Total 940 patients (400 with RA, 531 with AS, 3 with PsA and 6 with PS) were registered and 338 (36.0%) patients (108 with RA, 228 with AS, 2 with PS) who switched to CT-P13 were included.

The proportion of patients achieving remission was similar between Naïve and Switch groups in both RA and AS during post-baseline visits (Table 1). In RA, the proportion of patients achieving each disease activity category by DAS28 was similar between Naïve and Switch groups (Figure 1). The proportion of patients

who achieved BASDAI 20/50/70 response gradually increased from week 6 to week 24 or 30 in Naïve group with AS (Figure 1).

Fifty percent of naïve patients with PsA achieved clinical remission. The proportions of both PASI 50 and 75 responses were 50% at Week 22 in Naïve group and were 100% and 50% in Switch group, respectively during post-baseline visits in PS patients.

Throughout this study, treatment-emergent adverse events (TEAE) and treatment-emergent serious adverse events (TESAE) were reported as Table 2. Only 11% of patients experienced infection.

Table 1. Clinical remission in RA and AS

		Naïve		Switch	
		Baseline	Post-baseline	Baseline	Post-baseline
RA	DAS28 (ESR)	0/181 (0.0%)	24/182 (13.1%)	0/25 (0.0%)	5/25 (20.0%)
	DAS28 (CRP)	0/180 (0.0%)	43/179 (24.0%)	2/25 (8.0%)	6/24 (25.0%)
AS	BASDAI	2/292 (0.7%)	199/292 (68.2%)	112/209 (53.6%)	150/210 (71.4%)

Table 2. Summary of safety results

n/N (%)	RA	AS	PsA	PS
TEAE	198/400 (49.5)	183/531 (34.5)	1/3 (33.3)	3/6 (50.0)
TEAE related with CT-P13	73/400 (18.3)	64/531 (12.1)	0/3 (0.0)	2/6 (33.3)
TESAE	52/400 (13.0)	14/531 (2.6)	0/3 (0.0)	1/6 (16.7)
TESAE related with CT-P13	15/400 (3.8)	6/531 (1.1)	0/3 (0.0)	0/6 (0.0)
Infusion-related reactions	28/400 (7.0)	11/531 (2.1)	0/3 (0.0)	0/6 (0.0)

Figure 1. Clinical response of RA and AS

Conclusions: CT-P13 is efficacious and well-tolerated in RA/AS/PsA/PS patients. Efficacy and safety results in patients treated with CT-P13 were clinically consistent to historical data [1,2,3]. Especially, Switch group results showed that CT-P13 provides a useful alternative to other anti-TNFs.

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SAT0155 ADALIMUMAB IN COMBINATION WITH NON-METHOTREXATE CONVENTIONAL SYNTHETIC DISEASE MODIFYING RHEUMATIC DRUGS IN A CLINICAL TRIAL SETTING

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Background: Biologics in combination with methotrexate (MTX) are associated with improved outcomes versus monotherapy. However, few data exist regarding the use of non-MTX conventional synthetic disease modifying rheumatic drugs (csDMARDs) with biologics.

Objectives: To assess the effectiveness and safety of adalimumab (ADA) in combination with MTX and non-MTX csDMARDs through 6 months.

Methods: This post hoc analysis used data from the 24-week (wk) placebo-controlled trial of ADA (STAR), assessing safety and efficacy of ADA+csDMARDs in patients (pts) with moderate to severe RA.¹ For those pts receiving 1 csDMARD, pts were subgrouped according to csDMARD. The most frequently used csDMARDs assessed were MTX, sulfasalazine (SSZ), hydroxychloroquine (HCQ), and leflunomide (LEF). Nineteen pts who received parenteral gold in combination with ADA were excluded from this analysis. Baseline demographics and disease characteristics were summarized across csDMARD groups. 20/50/70% improvement in American College of Rheumatology (ACR) response criteria were assessed for each subgroup. Other clinical and functional endpoints were assessed using ANCOVA within subgroups as the least square (LS) means of the mean change from baseline to wk 24. Adverse events (AEs) were monitored throughout.

Results: Of the 290 pts randomized to receive ADA, 237 (82%) received ≥1 csDMARD [174 (60%) and 63 (22%) received ADA in combination with 1 and ≥2 csDMARDs, respectively]. Of the 63 pts who received ≥2 csDMARDs in combination with ADA, 55 (87%) received concomitant MTX therapy. Similarly, most of the pts receiving ADA in combination with a single csDMARD received

MTX [114 (66%)], while 60 pts received ADA in combination with a single non-MTX csDMARD. Pts receiving non-MTX csDMARDs were slightly younger, on average, than those receiving MTX (mean age: 51.4 vs 56.4 years), but demonstrated slightly higher mean HAQ-DI (1.37 vs 1.26) and CRP (2.4 vs 1.3) at baseline. Following 6 months of combination therapy, pts receiving ADA+MTX experienced numerically better clinical and functional outcomes to pts receiving ADA+non-MTX csDMARDs (Table). The lower response in the non-MTX DMARD group appeared to be driven by pts receiving LEF, who tended to experience lower levels of response in combination with ADA. Overall, frequencies of AEs were similar between combination therapy with MTX and non-MTX csDMARDs (~90% in both groups). Serious AEs were observed in 10% of pts receiving non-MTX csDMARDs and 5% of pts receiving MTX. A total of 42% in the non-MTX csDMARD and 60% in the MTX group experienced infections during the course of the study. There were 3 serious infections, all occurring in the MTX group.

Table. Week 24 Clinical and Functional Outcomes Among Patients Receiving Adalimumab in Combination With a Single csDMARD

Variable	ADA+MTX n=114	ADA+non-MTX csDMARD n=60			
		Pooled n=60	LEF n=25	SSZ n=12	HCQ n=23
ACR20	69 (61)	27 (45)	8 (32)	7 (58)	12 (52)
ACR 50	40 (35)	14 (23)	3 (12)	4 (33)	7 (30)
ACR70	22 (19)	7 (12)	0 (0)	3 (25)	4 (17)
DAS28(CRP)	-1.912 ^a	-1.923 ^b	-1.516 ^c	-1.579 ^d	-2.206 ^e
SDAI	-22.60 ^a	-22.21 ^b	-18.41 ^c	-23.80 ^d	-24.61 ^e
CDAI	-21.90 ^f	-20.95 ^g	-18.05 ^h	-23.79 ^d	-22.02 ⁱ
HAQ-DI	-0.509 ^j	-0.435 ^k	-0.251 ^l	-0.595 ^d	-0.524 ^k

Discrete variables are summarized as n (%).

All continuous variables are within group LS means in mean change from baseline to week 24 using ANCOVA, with csDMARD subgroup as a factor and baseline value as covariate, with the exception of the pooled group, which is mean change from baseline.

^an=105; ^bn=52; ^cn=20; ^dn=11; ^en=21; ^fn=106; ^gn=53; ^hn=22; ⁱn=54.

csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; ADA, adalimumab; MTX, methotrexate; LEF, leflunomide; SSZ, sulfasalazine; HCQ, hydroxychloroquine; ACR, American College of Rheumatology; DAS28(CRP), 28-joint disease activity score based on C-reactive protein; SDAI, simplified disease activity index; CDAI, composite disease activity index; HAQ-DI, health assessment questionnaire disability index.

Conclusions: MTX administered in combination with biologics, like ADA, leads to superior outcomes vs monotherapy. For pts who can't tolerate MTX, non-MTX csDMARDs, specifically HCQ and SSZ but not LEF, may be good alternatives, as outcomes were largely comparable with those of pts receiving MTX when combined with ADA. The limited sample size examined in this analysis should be confirmed in a larger pt population.

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SAT0156 EXPOSITION TO BIOLOGICAL THERAPY DURING PREGNANCY: A SINGLE-CENTRE STUDY OF PREGNANCY OUTCOME IN MOTHERS WITH RHEUMATIC DISEASES

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Background: Biologic DMARDs fall within the FDA category B or C. However many case series and registry data are available about women exposed during pregnancy.

Objectives: to extend information on this topic by the contribution of a tertiary single centre case series

Methods: Data were collected from a single-centre cohort of outpatients followed between 2006 and 2016. Women with rheumatic diseases (RD) exposed to biological (BE) agent during pregnancy or in the 3 months before conception were included. Outcomes in the BE group were compared with an age-matched group of pregnant women with RD non-exposed to biological agent (NE). Demographic and clinical data, obstetric outcome and neonatal complications were recorded.

Results: 34 pregnancies in 28 patients were included: 14 Rheumatoid Arthritis (RA), 6 ankylosing spondylitis (AS), 2 Psoriatic arthritis (PsA), 4 Undifferentiated spondyloarthritis (uSpA), 1 Dermatomyositis (DM), 1 Adult Onset Still's disease