axSpA, and –20 for patients with PsA; figure 1). Quality of life improved by –5 for patients with axSpA and PsA, and by –7 for patients with RA.

Abstract FRI0108 – Figure 1. WPAI questionnaire – Changes from baseline after 3 months of golimumab treatment

Conclusions: This interim analysis shows that golimumab treatment is effective in improving work productivity, daily activities as well as quality of life already within the first 3 months of treatment in RA, axSpA and PsA patients.

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FRI0109 DRUG IMMUNOGENICITY AND THE DEVELOPMENT OF PARADOXICAL ADVERSE EVENTS WITH BIOLOGIC THERAPIES

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Background: Defined as *de novo* or exacerbation of pathologies that usually responds to biologic agents, paradoxical reactions encompass for a wide spectrum of manifestations (cutaneous, intestinal, ocular) reported during biological therapy (TNF and non-TNF medications) regardless of the underlying rheumatic or non-rheumatic disorder.

Objectives: To assess drug levels (DL) and anti-drug antibodies (ADA) in patients with paradoxical reactions (*de novo* or exacerbation of psoriasis, uveitis, Crohn's disease) induced by biological drugs (bDMARS) in Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA).

Methods: We performed a retrospective observational study in cohorts of consecutive RA (267), PSA (65) and AS (145) undergoing TNF (i-TNF) or non-TNF biologics according to the local recommendations for initiation and monitoring, attending a single academic rheumatology department.

All patients were assessed at every 24 weeks months for disease activity and outcomes; supplementary, drug immunogenicity (ADA and DL) was systematically evaluated in patients developing paradoxical adverse events.

DL and ADA were measured with an ELISA assay and antibody binding test, respectively. Serum drug levels were considered positive for infliximab if >0.035 µg/mL, for adalimumab >0.024 µg/mL, for etanercept >0.035 µg/mL, rituximab >0.75 µg/mL, while the cut-offs for ADA positivity to infliximab was established at 5AU/mL, for adalimumab at 10AU/mL, etanercept at 142 AU/mL, rituximab 140 AU/mL (ELISA, Progenika)

Results: 42 patients with paradoxical psoriasis (30 with *de novo* lesions, 18 with palmo-plantar pustulosis, 12 with exacerbation of pre-existent lesions), 12 with paradoxical uveitis (5 with a new onset uveitis) and 3 with paradoxical Crohn's were included in the final analysis. Paradoxical events related to abatacept, certolizumab (one *de novo* psoriasis per agent) or golimumab (2 new onset uveitis, one flare of Chron's disease) were excluded from the final analysis as no immunogenicity lab tests were provided.

Drug induced paradoxical events were described not only with all TNF inhibitors but also with rituximab. DL was in normal range in all these patients; in addition,

ADA were either negative, or, if present, had no impact on drug concentration. Furthermore, we found no significant differences in drug levels of TNF inhibitors for RA, PsA and AS.

Moreover, no statistical significant differences were observed in the detection of ADA between the three groups.

Conclusions: Patients who develop either true or borderline paradoxical AE have adequate drug levels, with normal ADA concentrations.

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FRI0110 THE IMPACT OF SEROPOSITIVITY ON THE EFFECTIVENESS OF ABATACEPT VERSUS TNF INHIBITORS IN RHEUMATOID ARTHRITIS. REAL LIFE DATA FROM SEVERAL EUROPEAN REGISTRIES (THE PAN-ABA STUDY)

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Background: Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) are used as diagnostic tools, but may also be used as prognostic factors, as these biomarkers have been associated with better clinical responses to some biologic agents in rheumatoid arthritis (RA).

Objectives: To compare the impact of seropositivity on drug discontinuation and effectiveness for abatacept (ABA) and TNF inhibitors (TNFi) in patients (pts) with RA.

Methods: Pooled analysis of 13 observational RA registries from countries (FR, IT, CZ, DK, NO, PT, RO, ES, SE, CH, NL, JP, CA) where both ABA and TNFi were available concomitantly. Inclusion criteria were RA diagnosis, treatment with ABA or TNFi, and available RF or ACPA status. Main exposure was seropositivity: positive if RF or ACPA were positive, negative if both were negative, and missing if one was missing and the other was negative. Primary endpoint was drug discontinuation, analysed using Cox models, including treatment, seropositivity, and their interaction, adjusting for patient-, treatment-, and disease-characteristics, using strata terms for country and calendar year. We first tested for effect modification by country by additionally including an interaction term between treatment, seropositivity and country. Since we found no effect modification, we took out the interaction term. Effectiveness was analysed using DAS28 remission and low disease activity (LDA) at 1 year, corrected for attrition using Lundex¹.

Results: Using data from 39 266 treatment-courses, in crude analyses, seronegativity was associated with higher drug discontinuation for pts on ABA but not on TNFi (*p* interaction <0.001), with a hazard ratio (HR) for seropositive vs seronegative of 0.74 (95%CI: 0.66–0.82) for pts on ABA and 0.96 (95%CI: 0.92–1.01) for

pts on TNFi. On average, pts on ABA were older and had more prior bDMARDs. Adjusting for potential confounding factors did not modify the results qualitatively (figure 1), with significantly longer time before discontinuation in seropositive vs seronegative pts on ABA (adj. HR: 0.74 (95% CI: 0.67–0.84) but not on TNFi (adj. HR: 0.99 (95% CI: 0.94–1.04)).

The proportion of pts reaching DAS28 remission or LDA at 1 year was significantly higher for seropositive vs seronegative pts on ABA (difference in proportion: remission: 5.0%; LDA: 9.7%), but similar for seropositive vs seronegative pts on TNFi (difference in proportion: remission: –2.7%; LDA: –2.3%).

Conclusions: Data from this large pooled registry suggests that seropositivity in RA pts is associated with increased drug retention and effectiveness for ABA but not for TNFi.

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FRIO111

ANALYSIS OF REAL-LIFE INFLIXIMAB AND ADALIMUMAB DATA: DRUG SWITCHING AND FATE OF ANTIDRUG ANTIBODIES AND TROUGH LEVELS OVER TIME

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Background: Infliximab (IFX) and adalimumab (ADL) are biological drugs used in the treatment of rheumatoid arthritis (RA), spondyloarthritis (SpA), and juvenile idiopathic arthritis (JIA). Development of antidrug antibodies (ADAb) may lead to increased drug clearance and loss of therapeutic drug trough levels (TL). Switching to another drug may be necessary after ADAb development.

Objectives: To use real-life data from a large Finnish rheumatology patient cohort to determine the association between drug switching and ADAbs and the fate of ADAbs and TLs after ADAb development.

Methods: Serum samples for IFX or ADL ADAb and TL measurements from 1345 (567 RA, 479 SpA, and 299 JIA) rheumatology patients were taken on a clinical basis in daily practice in 20 Finnish referral hospitals. ADAb analyses were performed at Sanquin laboratories (Amsterdam, The Netherlands) using radioimmunoassays; TL analyses were performed at United Medix Laboratories (Helsinki, Finland) using commercial methods (Promonitor ELISA, Progenika Biopharma). Samples were collected and analysed from January 2012 until September 2017. ADAb values ≥ 12 AU/ml were considered positive; ADAb values were classified as low (12–30 AU/ml), intermediate (30–100 AU/ml) and high (≥ 100 AU/ml).

Results: On the basis of TL data, we identified 67 patients (5%) who switched drugs. Of these patients, 47 (70.2%) provided ADAb measurements for the first drug; 33 (49.3%) patients were ADAb positive. Most (22 patients, 63.6%) had high ADAbs. Forty-nine (73.1%) patients provided ADAb measurements for the second drug. Of these patients, 11 (16.4%) were ADAb positive against the second drug; seven (63.6%) had high ADAbs. We identified 48 (3.6%) ADAb-positive patients who provided at least one follow-up ADAb measurement. Of these patients, 32 (66.7%) experienced ADAb loss; most (24 patients, 50%) experienced complete ADAb loss (most recent ADAb value ≤ 12 AU/ml). Twenty-five

patients that experienced ADAb loss had available TL measurements both before and after ADAb loss; 23 (92%) had increased TL after ADAb loss. Of the 16 patients that experienced ADAb gain, only 3/11 (27.3%) patients that had available TL measurements both before and after ADAb gain had increased TL after ADAb gain.

Conclusions: ADAb positivity is associated with drug switching; ADAb development against a second biologic drug is common. A significant proportion of ADAb-positive patients lose ADAbs over time. ADAb loss is associated with TL increase.

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FRIO112

PERSISTENCE ON TUMOUR NECROSIS FACTOR INHIBITOR (TNFI) MONOTHERAPY AFTER ACHIEVING REMISSION OR LOW DISEASE ACTIVITY (LDA) ON COMBINATION THERAPY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: Combination therapy with TNFis and conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) is standard for moderate to severe RA.

Objectives: To estimate persistence with etanercept (ETN) or other TNFi monotherapy among RA patients who achieved remission/LDA on combination TNFi +csDMARD therapy and then discontinued the csDMARD.

Methods: Data from RA patients in the Corrona registry during 10/1/2001–8/31/2017 were analysed. All patients had to be treated with TNFi +csDMARD combination therapy and to have reached Clinical Disease Activity Index remission/LDA and then discontinued the csDMARD (index date). ETN (fusion protein comprising TNF receptor and human IgG1 Fc) and other TNFi therapies (monoclonal antibodies: adalimumab, certolizumab pegol, golimumab, and infliximab) were analysed separately. Outcomes were percentages of patients persistent on index TNFi monotherapy, discontinued index TNFi, switched (to another biologic or to csDMARD monotherapy), or added csDMARD therapy (to receive combination therapy) at 6 months (primary analysis) and 12 months post-index.

Results: Data from 617 patients were analysed (182 ETN, 435 other TNFi); mean age (standard deviation [SD]) was 57.4 (13.3) years, 73% were female. Mean time (SD) in remission/LDA before csDMARD discontinuation was 17.0 (24.3) months. Rates of monotherapy persistence at 6 months were 56% for ETN and 45% for other TNFi (table 1). Patients with ≥ 6 month persistence on monotherapy had mean duration (SD) of 28.2 (22.1) months on ETN monotherapy or 27.8 (23.3) months on other TNFi monotherapy. Rates of persistence for all patients at 12 months were 46% for ETN and 33% for other TNFi. Patients with ≥ 12 month persistence had mean duration (SD) of 35.9 (22.6) months on ETN monotherapy or 39.3 (24.4) months on other TNFi monotherapy. For a subset of patients with < 6 months in remission/LDA before index date (44% of patients), rates of monotherapy persistence at 6 months were 60% for ETN and 42% for other TNFi.

	Treatment pattern, n (%)			
	Persistent on index TNFi monotherapy		Not persistent on index TNFi monotherapy	
	Discontinued index TNFi	Switched to new biologic or csDMARD	Added csDMARD	
6 months				
ETN (n=182)	102 (56)	6 (3)	10 (6)	64
Other TNFi (n=435)	195 (45)	21 (5)	23 (5)	(35) 196 (45)
12 months				
ETN (n=120)	55 (46)	1 (1)	8 (7)	56
Other TNFi (n=307)	102 (33)	22 (7)	19 (7)	(47) 164 (53)

Conclusions: Monotherapy with ETN or other TNFi is an option for patients in remission/LDA; $> 50\%$ of patients on ETN remained on monotherapy 6 months after discontinuing their csDMARD.

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