psoriatic arthritis (PsA) and ankylosing spondylitis (AS) in North East Romania from 2003 to 2018.

Methods: We performed a hospital-based retrospective cohort study in consecutive adult patients receiving their first biologic agent (TNF or non-TNF drugs) according to local recommendations in two academic centers. Patients were classified based on the initial TB/latent TB screening test: the tuberculin skin test (positive if > 5mm, TST group) or interferon gamma release assays (positive if >0.35 IU/mL QuantiFERON-TB gold, QFT group); retesting was done regularly if negative initial.

Data about drug efficacy was recorded every 24-weeks based on standard scores (DAS28-ESR for RA, DAPSA for PsA, ASDAS-CRP for AS), while TB risks at the end of the study or prior to switching were determined as hazard ratio (HR) with 95% confidence interval (CI) using cox regression.

Statistical analysis was performed in SPSS-19, $p < 0.05$, on subgroups of patients depending on whether positive TST or QFT at baseline.

Results: 673 patients (360 RA, 116 PsA, 195 AS) were recruited; 55 of them (33 RA, 13 AS, 9 PsA) had latent TB at baseline and received chemoprophylaxis with isoniazid before starting biologics according to local policy. Fourteen active TB were identified, the majority of them occurred within one year of biologics (ranging 6 to 52 months), as follows: three pulmonary TB in AS (two in etanercept, one adalimumab), one case of pulmonary TB in PsA (infliximab) and ten cases of RA (six pulmonary TB in abatacept, two adalimumab, etanercept and two infliximab; one ganglionic infection with infliximab; one peritoneal under certolizumab; one pulmonary and pleural under infliximab biosimilar; one pulmonary and peritoneal TB under adalimumab). The rate of active TB was 5/321.32 patient-years for infliximab, 4/594.64 for adalimumab, 1/38.39 patient-years for certolizumab, 3/721.51 for etanercept and 1/21.12 patient-years for abatacept, respectively. We reported an increased risk of TB disease in anti-TNF monoclonal antibodies users vs. soluble receptor, with an incidence ratio of 2.66 ($p < 0.05$). Interestingly, no significant TB risk factors were demonstrated in our cohort; baseline latent TB, previous active TB, chronic glucocorticoid use, high disease activity at baseline, comorbidities, concurrent synthetic drugs were not associated with increased risk ($p > 0.05$). In addition, we described 18 new patients with positive QFT when TB retesting as per protocol, classified as latent TB and requiring chemoprophylaxis.

Conclusion: The risk of tuberculosis remains a reality in biologics, despite extensive screening and prevention methods. The risk is variable with different drugs, higher with TNF inhibitors and relatively low in newer biologics, emphasizing a risk-stratification when selecting biologics in such patients.

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FRI0077

SHORT DURATION OF CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (CSDMARDS) BEFORE AND AFTER BECOMING A CSDMARD INADEQUATE RESPONDER IN RHEUMATOID ARTHRITIS PATIENTS

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Background: ACR guidelines recommend starting rheumatoid arthritis (RA) treatment with conventional-synthetic (cs)DMARD monotherapy¹. If disease activity remains moderate or high, the guidelines recommend adding or switching to another csDMARD, biologic (b)DMARD, or janus kinase inhibitors (JAKi) for established RA. In early (<6 months) RA, the guidelines recommend tumor necrosis factor inhibitors TNFi over JAKi and TNFi+methotrexate (MTX) over JAKi+MTX.

Objectives: This study aimed to investigate treatment patterns and duration in csDMARD IR patients.

Methods: In fully-adjudicated commercial medical and pharmacy health insurance claims database with 40 million lives annually, adult RA patients (≥ 2 RA diagnoses ≥ 30 days apart) who started csDMARD (1/1/2012–3/31/2017) and then switched to or added another DMARD (index date, ID) were selected. Real world treatment patterns of patients with

≥ 1 -year continuous enrollment before (baseline) and after ID (index treatment) were assessed.

Results: Among 25,104 csDMARD initiators, 10,091 (40%) demonstrated IR, and 7,816 met all the inclusion and exclusion criteria (median age 54 years, 26% male). The baseline csDMARD treatment lasted for a median of 4.3 months and mostly comprised of monotherapy (96%). Upon treatment regimen change, 62% ($n=4,869$) initiated combination therapy (32% csDMARD+csDMARD, 28% csDMARD+TNFi, 1.4% csDMARD+other bDMARD, 0.5% csDMARD+JAKi) and 38% initiated monotherapy (27% on csDMARD, 10% TNFi, 0.7% other bDMARD, 0.5% JAKi). Post-switch, the median treatment duration was longer for combination therapy than monotherapy: 13.7 vs. 5.2 months ($p < 0.001$). Among next therapies, csDMARD showed the trend towards shortest durability and JAKi – toward longest durability. Among monotherapies the median treatment duration varied: 4.9 (csDMARD), 5.9 (TNFi), and 8.1 (JAKi) months ($p=0.2$, comparing all). The median duration of combination therapies lasted: 12.5 (csDMARD+csDMARD), 14.9 (TNFi+csDMARD), and 17.2 (JAKi+csDMARD) months ($p=0.04$, comparing all).

Characteristics	csDMARD IRs (n=7,816)	
Index therapy allocation after csDMARD IR, (n,%)	N	%
csDMARD Monotherapy	2,095	27
TNFi Monotherapy	757	10
Other bDMARD Monotherapy	55	0.7
JAKi Monotherapy	40	0.5
csDMARD + csDMARD Combination	2,539	32
TNFi + csDMARD Combination	2,178	28
Other bDMARD + csDMARD Combination	112	1.4
JAKi + csDMARD Combination	40	0.5
Index treatment duration after csDMARD IR, months, median (IQR)	Months	(IQR)
Monotherapy	5.2	9.8
csDMARD	4.9	10.1
TNFi	5.9	10.1
JAKi	8.1	11.9
Combination therapy	13.7	15.6
csDMARD+csDMARD	12.5	14.8
TNFi+csDMARD	14.9	15.9
JAKi+csDMARD	17.2	11.3

Conclusion: The real-world evidence suggests that treatment durability may be better for JAKi than TNFi (both monotherapy and combination). The majority of csDMARD patients switched to another csDMARD, which showed short durability of treatment, suggesting that switching MOA may benefit these patients.

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FRI0078

IMPACT OF THE IMPLEMENTATION OF FLUSH SERUM ON TROUGH LEVELS OF INFlixIMAB IN PATIENTS WITH INFLAMMATORY JOINT DISEASE

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Background: The administration of intravenous biological therapies is based on the manufacturer's instructions and the administration guidelines of Spanish Medicine Agency. We observed that a considerable amount of the solution remains in the tubing of the equipment after the administration of the drug. This amount depends on the drug and the solution used for the infusion. In the particular case of Infliximab is around 7% of the total solution to infuse, so it could potentially have a relevant therapeutic impact.

Objectives: To assess the variation in serum trough levels of Infliximab after the systematic application of flush physiological serum after drug administration.

Methods: The study was divided into two phases: a first phase in which the clinical and analytical variables (including the serum trough levels of infliximab) were measured before the application of the flush serum and a second stage in which the same variables were measured after the systematic implementation of an infusion of 50ml of 0.9% sodium chloride following the administration of infliximab.

Results: A total of 35 patients were collected, including 6 rheumatoid arthritis (13.3%), 9 psoriatic arthritis (20%) and 20 ankylosing spondylitis (AS) (44.4%). Overall, 18 patients were women (40%), the mean age was 57.6 years (12.6) and the BMI was 30.5 (13.1). The mean dose of infliximab was 4.3 mg/kg (1.1) and the mean number of years of treatment was 10 (5).

23 patients were taking infliximab on monotherapy (51.1%). The mean serum trough levels of infliximab pre-intervention with the dragging serum was 3.13 mg/dl (3.1), while postintervention levels were 3.66 mg/dl (3.9) ($p = 0.071$). In the subgroup of patients with AS there was a significant decrease in BASDAI between the pre and post intervention visit (3.4 vs 2.6, $p < 0.05$).

Conclusion: The use of flush serum after infliximab infusion increased serum drug levels. In the subgroup of patients with AS there was a clinically significant improvement measured by BASDAI.

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FRI0079

LONG-TERM CLINICAL EFFICACY OF CYCLING VS SWITCHING TO A NON-TNF INHIBITOR IN RA PATIENTS WHO FAILED TO A FIRST TNF INHIBITOR

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Background: In rheumatoid arthritis (RA) patients (pts) after discontinuation of tumour necrosis factor α inhibitors (TNFi) physicians can choose an alternative TNFi or a biological agent with another mode of action (non-TNFi), however little guidance on choosing one or another exists.

Objectives: To compare the long-term clinical response, survival and safety of TNFi versus non-TNFi after discontinuing a previous TNFi in

pts with RA, both in the global cohort and in the subpopulations stratified by reason of discontinuation of 1st TNFi.

Methods: Observational study including 127 pts from La Paz University Hospital biological RA registry, who discontinued a first TNFi between 1999 and 2016 and subsequently were treated with a second biologic. Disease activity was assessed by DAS28 at the beginning of the second biologic and at 6 (m-6), 12 (m-12) and 24 months (m-24) follow-up. Primary outcome was the proportion of pts with good or moderate EULAR response (E-Resp). Sensitivity analysis to evaluate clinical response according to the reasons for discontinuation of the first TNFi was performed too. Pts were classified into primary and secondary failure based on the characteristics of the non-response and if possible on the measure of drug and anti-drug antibodies, which were measured by ELISA after 6 months of the first biologic treatment and before switching. Mann-Whitney U test and Fisher's exact test were used to test statistical differences. Factors associated with clinical response were assessed using univariable and multivariable logistic regression analysis. Drug retention was compared using Cox proportional hazards models.

Results: Seventy-seven (61%) pts received a TNFi and 50 (39%) a non-TNFi as second biologic therapy. Mean age was 56 years, 84% were women and 58% were also treated with methotrexate. At baseline, no significant differences between groups were found, except for significantly higher CRP levels in non-TNFi group (Table 1). No statistical differences were observed in E-resp between groups at m-6 and m-12. Nevertheless, at m-24 more pts achieved E-resp in non-TNFi group (80% vs 52%; $p=0.001$, Figure 1). Likewise, 100% (n=6) of the pts who achieve remission with the second biologic were treated with a non-TNFi. In the univariable analysis, higher baseline DAS28 (OR=1.65, $p=0.06$), being ACPA positive (OR=3.6, $p=0.02$) and treatment with a non-TNFi (OR=3.53, $p=0.01$) were associated with E-resp at m-24. In the multivariable analysis, baseline DAS28 (OR=1.65, $p=0.01$) and non-TNFi treatment (OR=3.7, $p=0.02$) remained associated. Drug survival was similar in both groups (1.6 ± 0.7 in TNFi vs 1.6 ± 0.6 years in non-TNFi, $p=0.5$). In the subgroup of pts who dropped out due to secondary inefficacy (n=76) no differences in response to the second biologic were found, however, pts who stopped the first TNFi for other reasons (primary inefficacy and adverse events) achieved more frequently E-resp after switching to non-TNFi since the beginning of treatment (m-6: 54% in TNFi vs 86% in non-TNFi, $p=0.04$; m-12: 56% in TNFi vs 70% in non-TNFi, $p=0.4$; m-24: 47% in TNFi vs 86% in non-TNFi, $p=0.04$). The overall incidence of AEs was similar between TNFi and non-TNFi groups (21% in TNFi vs 14% in non-TNFi ($p=0.9$)).

Conclusion: In our cohort of patients with RA and failure to a first TNFi, and mainly after primary failure and adverse events, treatment with a non-TNFi was more effective than a second TNFi at 24 months after switch, without significant differences in the survival of the two treatments. In the subgroup of patients who failed the first TNFi due to secondary inefficacy, both treatment options were equally effective. These data reflect how the reason for discontinuation of a first biological can guide the response to a second treatment.

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Baseline Characteristics	Population (n=127)	(n=77)	(n=50)
Age, years	56 (12.4)	55 (10.4)	57 (12.4)
Female, n (%)	107 (84)	67 (87)	40 (80)
Body mass index	25 (21.8-30.1)	26 (22-30.7)	24 (22-28.5)
Disease duration, years	13 (8-17)	12 (8-16)	15 (10-20)
Infliximab, n (%)	14 (11%)	24 (31%)	20 (40%)
Discontinued prior position, n (%)	107 (84)	70 (91%)	37 (74%)
Anti-CDP positive, n (%)	107 (84)	66 (86%)	41 (82%)
DAS28-CRP at baseline	5.3 (4.2-5.8)	5.3 (4.3-5.8)	5.3 (4.3-5.8)
CRP (mg/L) at baseline	31 (18-44)	31 (17-43)	32 (19-44)
CRP (mg/L) at baseline	4 (2-16)	3 (2-12)	4 (2-16)
Concomitant DMARDs:			
-Methotrexate, n (%)	71 (56)	47 (61)	24 (48)
-Leflunomide, n (%)	41 (32)	21 (27)	20 (40)
-Chloroquine, n (%)	14 (11)	9 (12)	5 (10)
-Methotrexate, n (%)	14 (11)	9 (12)	5 (10)
Duration of previous TNF inhibitor (years)	12.2 (6.3-13)	13.1 (7.3-13)	11.3 (6.3-13)
Reason for discontinuation of previous TNF inhibitor	117 (92)	73 (95)	44 (88)
-Primary inefficacy, n (%)	30 (26)	11 (15)	19 (38)
-Secondary inefficacy, n (%)	30 (26)	40 (52)	10 (20)
-Adverse effects, n (%)	4 (3)	4 (5)	0 (0)
-Other causes, n (%)	4 (3)	4 (5)	0 (0)