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)	24 (22-30.7)	24 (22-28.5)
Disease duration, years	13 (8-17)	12 (8-16)	11 (5-20)
Infliximab, n (%)	14 (11%)	24 (31%)	20 (40%)
Discontinued prior treatment, n (%)	107 (84)	70 (91%)	47 (94%)
Anti-CDP positive, n (%)	107 (84)	66 (86)	41 (82)
DAS28-CRP at baseline	3.3 (2.2)	3.3 (2.1)	3.3 (2.1)
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 (%)	31 (24)	47 (62)	24 (48)
-Leflunomide, n (%)	41 (32)	31 (40)	18 (36)
-Chloroquine, n (%)	14 (11)	5 (7)	2 (4)
-Methotrexate, n (%)	14 (11)	9 (12)	5 (10)
Duration of previous TNF inhibitor (years)	12.2 (3.3)	13.4 (3.1)	12.3 (3.1)
Reason for discontinuation of previous TNF inhibitor	117 (92)	118 (153)	118 (153)
-Primary inefficacy, n (%)	30 (24)	31 (40)	21 (42)
-Secondary inefficacy, n (%)	30 (24)	40 (52)	38 (76)
-Adverse effects, n (%)	4 (3)	4 (5)	4 (8)
-Other causes, n (%)	4 (3)	4 (5)	4 (8)

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FRI0080

SURVIVAL ON SECOND-LINE BIOLOGIC THERAPY AFTER THE WITHDRAWAL OF AN ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: EXPERIENCE IN A SPANISH TERTIARY HOSPITAL

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Background: Patients with Rheumatoid Arthritis (RA) have been traditionally treated with other TNF inhibitors (TNFi) after the withdrawal of a first TNFi (cycling). However, due to the increase in the biological therapy options, changing to a biologic agent with different mechanism of action (switching) is an alternative choice. More studies are needed to clarify the role of both strategies in order to guide treatment decisions.

Objectives: To analyze the survival of the second biological drug, TNFi or biologic with a different mechanism of action, in patients with RA non-responders to the first TNFi. To evaluate factors associated with the survival of the second-line therapy.

Methods: A retrospective, longitudinal, observational study was performed, which included patients diagnosed of RA and treated with biological therapies between 2008 and 2017, who discontinued a first-line TNFi and started a second-line biological therapy. The demographic and clinical data were obtained from their medical records. Kaplan Meier and Log-rank survival analysis were performed, as well as Cox regression to identify related factors.

Results: 69 patients were identified, 14 men (20.3%) with a mean age at the beginning of the treatment of 52.68 ± 19.79 years. Demographic and clinical data are shown in the table. The main cause of withdrawal of the first TNFi was secondary failure (47.8%), followed by side effects (34.8%) and primary failure (13%). Cycling was performed in 34 patients (49.3%) and switching in 35 (50.7%). During the follow-up, the main causes of withdrawal of the second-line treatment were primary and secondary failure (10.1% in both cases). The survival analysis of the 42 patients who presented a primary or secondary failure to the first TNFi was stratified according to the cause of withdrawal of the second biological therapy. When cycling was chosen, the average treatment survival was 8.8 months (CI95%:4.8-12.8) whereas for the switching option it was 23 months (CI95%:5.4-40.5), being the differences statistically significant ($p=0.049$). Age was shown as a protective factor (HR=0.86, CI95%:0.76-98) and the positivity of Rheumatoid Factor (RF) as a risk factor (HR=4.76, CI95%:1.39-16.30) for the withdrawal of the second biological therapy. No differences were found in the withdrawal rate due to adverse effects among patients who performed switching or cycling (11.42% vs 5.88%, $p=0.41$).

	n= 69 (mean $\pm$ SD or%)	Switching (n=35)	Cycling (n=34)	p-value
Age (years)	52.68 $\pm$ 12.79	54.37 $\pm$ 12.48	50.91 $\pm$ 13.07	0.354
Gender				
Male	14 (20.3%)	8 (22.9%)	6 (17.6%)	0.591
Female	55 (79.7%)	27 (77.1%)	28 (82.4%)	
BMI (kg/m ²)	25.42 $\pm$ 4.62	24.99 $\pm$ 4.03	25.98 $\pm$ 5.40	0.362
First treatment duration (months)	23.85 $\pm$ 22.70	23.1 $\pm$ 20.5	24.7 $\pm$ 25.1	0.856
Smokers	18 (26.1%)	9 (25.7%)	9 (25.5%)	0.943
RF (+)	56 (81.2%)	31 (88.6%)	25 (73.5%)	0.227
ACPA (+)	61 (88.4%)	32 (91.4%)	29 (85.3%)	0.189
Erosions	38 (55.1%)	20 (57.1%)	18 (52.9%)	0.198
Joint space narrowing	44 (63.8%)	22 (62.9%)	22 (64.7%)	0.569
Rheumatoid nodules	10 (14.5%)	5 (14.3%)	5 (14.7%)	0.823
Ocular manifestations	7 (10.1%)	4 (11.4%)	3 (8.8%)	0.938
Sjögren's syndrome	9 (13%)	6 (17.1%)	3 (8.8%)	0.305

SD: Standard Deviation; BMI: Body Mass Index; RF: Rheumatoid Factor; ACPA: Anti-Citrullinated Peptide Antibodies

Conclusion: Switching strategy showed a greater drug survival time and was considered as a better option after the failure of a first TNFi. RF positivity was associated with an increased risk for the withdrawal of the second-line biological therapy.

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FRI0081

WITHDRAWAL OF CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN THE SARILUMAB OPEN-LABEL EXTEND STUDY: EFFICACY AND SAFETY ANALYSIS

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Background: The EXTEND open-label extension study (NCT01146652) is collecting data on long-term treatment of RA with sarilumab as monotherapy and in combination with conventional synthetic (cs)DMARDs, predominantly methotrexate.

Objectives: Post hoc analysis to compare outcomes between patients (pts) who received sarilumab monotherapy, received sarilumab +csDMARDs, or who discontinued csDMARDs during sarilumab treatment.

Methods: Pts enrolled in four trials of sarilumab SC 150 or 200 mg q2w +csDMARDs (MOBILITY, NCT01061736; TARGET, NCT01709578; ASCERTAIN, NCT01768572; and NCT01217814) and an open-label sarilumab monotherapy study (ONE, NCT02121210) were eligible to receive open-label sarilumab SC 200 mg q2w in EXTEND, +csDMARDs if given in the parent trial. In EXTEND, csDMARDs could be stopped at investigator discretion (reasons for csDMARD withdrawal were not recorded). Post hoc analyses were conducted on three pt groups: Group 1 permanently discontinued csDMARDs at any time during Wks 0-96 of EXTEND and subsequently received sarilumab monotherapy; Group 2 continued csDMARDs; and Group 3 enrolled from the monotherapy study and never received csDMARDs. A subgroup of Group 1, comprising pts who received csDMARDs during Wks 0-12 and discontinued csDMARDs during Wks >12-96, was used for sensitivity analysis.

Results: There were 42 pts in Group 1, 1851 in Group 2, and 111 in Group 3 with minor differences between groups in demographics and disease characteristics at entry into EXTEND. The proportion of pts remaining on study at 96 wks was 69%, 80% and 83% in Groups 1, 2 and 3, respectively. Similar substantial and durable response rates (CDAI $\leq$ 2.8, CDAI $\leq$ 10, DAS28-CRP $<$ 2.6, and DAS28-CRP $<$ 3.2) were observed between pts who discontinued csDMARDs, pts who continued csDMARDs, and pts who never received csDMARDs (Fig). Results for the sensitivity analysis subgroup (n=27) were consistent with Group 1. The adverse event (AE) profile was as expected for these groups. Incidence of AEs was greater in Group 1 than Groups 2 and 3 (Table), including hepatic disorders (21, 7 and 3 per 100 pt-years [PYs], respectively) and leucopenia (43, 13 and 20 per 100 PYs, respectively). Rates of infection and serious infection were lowest in pts receiving monotherapy.

Conclusion: Over the 120-wk study period, pts initially on sarilumab +csDMARDs who subsequently discontinued csDMARDs maintained similar clinical responses as pts who continued sarilumab +csDMARDs or received sarilumab monotherapy throughout. The AE profile was as expected, with no new safety signals.