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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.

Table. Summary of treatment-emergent AEs

n (%)	Group 1 Withdrawn csDMARD during Wks 0–96 (N=42) [PYs=104]	Group 2 Continued csDMARD during Wks 0–96 (N=1851) [PYs=5870]	Group 3 Sarilumab monotherapy (N=111) [PYs=230]
Any AE	41 (97.6) [225]	1626 (87.8) [184]	83 (74.8) [138]
Serious AE	17 (40.5) [17]	475 (25.7) [13]	16 (14.4) [10]
AEs leading to sarilumab discontinuation	15 (35.7) [16]	382 (20.6) [7]	8 (7.2) [3]

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Figure. Percentage of patients achieving CDAI ≤10 (low disease activity), CDAI ≤2.8 (remission), DAS28-CRP <3.2 (low disease activity), and DAS28-CRP <2.6 (remission). Last observation carried forward (LOCF) was used to impute missing values and/or for patients who discontinued treatment

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FRI0082

EFFECTIVENESS OF TNF INHIBITORS VS. NON-TNF INHIBITORS (ABATACEPT, TOCILIZUMAB AND RITUXIMAB) AFTER FAILURE OF NON-TNFI BIOLOGIC DMARD IN RHEUMATOID ARTHRITIS – COLLABORATION BETWEEN FIVE NATIONAL REGISTERS

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Table 1. Baseline (=start of 2nd bDMARD) characteristics of RA patients who switched to a 2nd bDMARD after a non-TNFi and clinical effectiveness. Results are not shown when N<20.

1 st → 2 nd bDMARD	N. patients	Age, years (mean, SD)	Sex (%) female	Disease duration, years (median, IQR)	RF (%) (pos)	Anti-CCP (%) (pos)	Concomitant csDMARDs (%)	Concomitant GCs (%)	DAS28 baseline (mean, SD)	DAS28 6 months (mean, SD)	DeltaDAS28 0-6m	N (%) of patients still on drug at month 6 from start of 2 nd bDMARD
ABA→TNFi	185	56.1 (13.1)	77.8	4 (2-10)	73.5	64.1	74.1	21.1	4.4 (1.3)	3.5 (1.3)	-0.9 (1.5) N=126	109 (59%)
ABA→RTX	22	57.7 (17.9)	72.7	4.3 (2-7.6)	71.4	100	40.9	31.8	4.5 (1.0)	N<20		19 (86%)
ABA→TCZ	37	59.4 (11.1)	86.5	6.3 (2.6-11.9)	73.5	54.5	29.7	32.4	4.9 (1.3)	3.3 (1.3)	N<20	21 (57%)
RTX→ABA	56	64.3 (12.6)	83.9	12.3 (4.9-21.4)	83.6	57.1	50.0	39.3	4.4 (1.3)	3.8 (1.4)	-0.7 (0.9) N=22	35 (63%)
RTX→TNFi	99	60.1 (12.9)	76.8	8.1 (3-14.2)	76.8	82.4	53.5	42.4	5.2 (1.3)	3.6 (1.4)	-1.5 (1.4) N=44	64 (65%)
RTX→TCZ	31	60.2 (11.6)	87.1	6.7 (3-21.5)	75	66.7	41.9	58.1	5.6 (1.1)	3.3 (1.1)	N<20	21 (68%)
TCZ→ABA	29	55.9 (14.6)	86.2	5.0 (2.3-14.8)	65.5	80	31.0	20.7	4.5 (1.4)	3.9 (1.3)	N<20	18 (62%)
TCZ→TNFi	131	57.6 (12.8)	84	4.0 (2-8.1)	77	71.4	36.6	24.4	3.9 (1.4)	3.5 (1.4)	-0.5 (1.6) N=80	83 (64%)
TCZ→RTX	15	60.8 (14.6)	73.3	4.0 (1.9-13.8)	92.9	100	40.0	26.7	4.4 (2.3)	N<20		11 (73%)