patients with satisfactory response to RSV in one joint required radioisotope treatment in another joint (between 2 and 4 different joints were treated in each patient – 13 patients in 2 joints, 5/3 and 2/4). Median patient age was 50 years (21 – 72). Duration of continuous bDMARD treatment preceding RSV was between 1 and 72 months. The intervals between bDMARD administration and RSV ranged from below 24 hours to 4 weeks. Satisfactory effects of RSV, defined as absence of clinical and ultrasound symptoms of inflammation, were observed after 55 (72.4%) interventions. In 11 (14.4%) cases after initial improvement, the inflammation symptoms recurred less than 6 months after RSV. In 10 (13.2%) cases RSV had no effect.

No side effects or adverse events occurred after RSV and, most importantly, there were no local or systemic infections observed up to 6 months after the procedure.

Conclusion: RSV seems to be an effective single joint treatment method in patients with active synovitis refractory to bDMARDs. Despite increased susceptibility to infection in patients partially immunocompromised and biological treatment, no septic complications were observed after RSV. RSV does not require discontinuation of biological treatment, unlike surgical synovectomy.

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FRI0090 SINGLE CENTRE COHORT OF REFRACTORY RHEUMATOID ARTHRITIS ALSO IDENTIFIES A RARE SUBGROUP OF MULTIPLE TARGETED THERAPY CLASS NON-RESPONSE

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Background: Refractory Rheumatoid Arthritis (RefRA) has emerged as an area of unmet need in the biologic era (1). Failure of 3 or more classes of targeted therapy or failure of both an anti-cytokine and a cell-targeted treatment have been proposed as possible definitions (1, 2). The BSRBR-RA reported 6% fulfil RefRA criteria (due to lack of efficacy and/or toxicity; but only including a first line TNF inhibitor bDMARD cohort) (2).

Objectives: To evaluate the extent of multi-targeted therapy RefRA in our tertiary RA single-centre experience, and identify any patterns of drug sequencing associated with development of RefRA.

Methods: We used a prospective database of RA patients established on targeted therapy, supplemented with information from individual funding requests and a review of our specialised biologic clinic patient notes to identify those who have been prescribed 2 or more classes of targeted therapies. Data on number and type of targeted therapy, and where available, reason for failure has been recorded. Disease activity state and functional outcomes are currently being evaluated

Results: Of a cohort of over 1500 RA patients that have received at least 1 targeted therapy, 172 patients have received 3 classes of targeted therapies (reasons for each drug discontinuation has been identified in 166 cases). An additional 50 patients have received multiple (2 or more) TNFi and at least 1 other class of targeted therapy. Table 1 details numbers in each category of RefRA.

	2 class bDMARD	3 or all 4 classes bDMARD	Multi bDMARD (min. 2 class) + JAKi
Number of patients (n=166)	64*	76	26
RF and/or CCP+ (n= 134)	48 (75%)	66 (87%)	20 (77%)
1st Targeted Therapy			
TNFi	54	61	24
Rituximab	5	9	1
Tocilizumab	3	1	0
Abatacept	2	5	1
Reason for drug discontinuation			
Primary NR only	5	3	2
Secondary NR only	7	6	0
Mixed primary/secondary NR	31	28	6
Mixed NR and toxicity	19	36	17
Multiple toxicity	2	3	1

*49 patients received one anti-cytokine and one cell-targeted bDMARD, 12 received two anti-cytokine bDMARD (TNFi and tocilizumab) and 3 received two cell targeted treatments (rituximab and abatacept).

In those who had failed multiple anti-TNF drugs 39 were switched to a cell-targeted therapy (31 Rituximab, 7 Abatacept), the rest were switched from a TNFi to tocilizumab. 36 out of 39 patients have maintained a response to their cell-targeted therapy after failing multiple anti-cytokines. 5 Patients demonstrate at least 3 primary non-responses with a further 4 further patients with multiple primary non-response and only 1 adverse event.
Conclusion: Over 10% of our single-centre targeted therapy exposed cohort demonstrate multi-targeted therapy RefRA. The majority comprise mixed non-response, loss of response and drug toxicity. A rare subgroup of 6% of RefRA demonstrate lack of efficacy to multiple therapies. On-going investigations aim to identify the clinical phenotype, predictors and underlying biology.

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FRI0091 UNEMPLOYED FEMALE RHEUMATOID ARTHRITIS PATIENTS ARE LESS ADHERENT TO THE BIOLOGIC DMARD TREATMENT

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Background: The 5-item Compliance Questionnaire for Rheumatology (CQR5) allows the identification of patients likely to be high adherers (HAs) to anti-rheumatic treatment (i.e. taking ≥80% of their medications correctly), or “low” adherers (LAs). An Italian version of the questionnaire was validated (I-CQR5) [1].

Objectives: The objective was to investigate what factors are associated with high treatment adherence according to I-CQR5 in RA patients treated with biologic DMARDs (bDMARDs).

Methods: RA patients (with disease duration >1 year, undergoing treatment with ≥1 self-administered biological disease-modifying anti-rheumatic drug (bDMARD), willing and capable of completing the questionnaire unaided) were enrolled in the study. I-CQR5 were anonymous and clinical data were collected from the local database. Factors included were demographic, social characteristics of the patients, clinical and treatment variables. Factors achieving a p<0.10 in univariate analysis were included in a multivariate regression analysis.

Results: Among 604 RA patients, 193 patients were included in the validation analysis. Median age of the patients was 57 years (46-65), 142 (73.4%) were females, median disease duration was 15 years (9-21); 82 (42.7%) patients were treated with low dose bDMARDs; 174 (91.1%) patients were in low disease activity or remission (Fig.1). HAs were 40.9% (79/193) of patients: 100% (193/193) of patients treated with bDMARDs and 22.4% (57/193) of those treated with bDMARDs in combination with conventional synthetic DMARDs. Female gender, no employment, lower education level, positive Rheumatoid Factor and/or Anti-Citrullinated Peptides Antibodies, low bDMARD dose, higher patient-VAS were significantly more frequent in LAs compared with HAs. In the multivariate analysis, employment was also positively and significantly associated with high adherence: OR 2.89 (1.3-6.44), p=0.009 (Tab.1).

Conclusion: As previously reported only one third of RA patients treated with bDMARDs were found to be HAs to treatment according to the I-CQR5. Employment status was the major determinant, increasing by almost 3-fold the likelihood of being adherent. Education level and female gender might be also taken into account as factors influencing treatment adherence.

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Univariate analysis. Demographics and clinical variables according to high and low adherence to treatment defined by I-CQR5.				
	Total	HA	LA	p value
No.	193	79 (40.9)	114 (59.1)	
HA, n (%)	79 (40.9)	-	-	-
Females (%)	142 (73.4)	52 (65.8)	90 (80.4)	0.024*
Age, years, median (IQR)	57 (46-65)	54 (50-62)	57 (51-66.3)	0.491
BMI, median (IQR)	24 (22-28)	25 (23-28)	24 (21-27.8)	0.545
Smokers, n (%)	28 (17.6)	12 (15.1)	16 (15.7)	0.394
Employed, n (%)	81 (47.1)	41 (64.1)	40 (37)	0.001*
Education level				0.147
Primary school, n (%)	20 (11)	8 (10.3)	12 (11.5)	
Median school, n (%)	65 (33.7)	21 (26.9)	44 (42.3)	
Secondary school, n (%)	88 (47.4)	34 (43.8)	54 (52.3)	
University, n (%)	29 (15.9)	15 (19.2)	14 (13.5)	
Primary/middle school education, n (%)	85 (46.7)	29 (37.2)	56 (53.8)	0.026*
Social status				0.567
Living with parents and family, n (%)	13 (8.7)	5 (9.3)	8 (8.3)	
Living alone, n (%)	16 (10.7)	6 (11.1)	10 (10.4)	
Living with partner and family, n (%)	113 (75.3)	38 (70.4)	75 (78.1)	
Other, n (%)	6 (4)	4 (7.4)	2 (2.1)	
Positive RF and/or ACPA, n (%)	79 (42.2)	27 (34.6)	52 (47.7)	0.074*
Disease duration, years, median (IQR)	15 (9-21)	14 (10-21)	15 (9-21.5)	0.762
Fibromyalgia, n (%)	38 (20.8)	12 (15.6)	26 (24.5)	0.141
csDMARD treatment, n (%)	57 (30.5)	19 (24.4)	38 (34.9)	0.124
Methotrexate, n (%)	41 (21.9)	16 (20.5)	25 (22.9)	0.693
Leflunomide, n (%)	12 (6.4)	3 (3.8)	9 (8.3)	0.225
Other DMARD, n (%)	7 (3.7)	0 (0)	7 (6.4)	0.023
bDMARD treatment, n (%)	193 (100)	79 (100)	114 (100)	-
bDMARD				0.541
Abatacept, n (%)	13 (8.7)	8 (7)	5 (6.3)	
Adalimumab, n (%)	35 (18.1)	19 (16.7)	16 (20.3)	
Anakinra, n (%)	11 (6.7)	7 (6.1)	4 (5.1)	
Certolizumab pegol, n (%)	15 (7.8)	9 (7.9)	6 (7.6)	
Etanercept, n (%)	101 (52.3)	62 (54.4)	39 (49.4)	
Golimumab, n (%)	8 (4.1)	6 (5.3)	2 (2.5)	
Tocilizumab, n (%)	10 (5.2)	3 (2.6)	7 (8.9)	
bDMARD treatment administered < 1 week, n (%)	110 (57)	43 (54.4)	67 (62.8)	0.549
Low dose bDMARD, n (%)	82 (42.7)	29 (49.4)	43 (37.7)	0.091*
Previous bDMARD failure treatment, n (%)	62 (38.5)	29 (38.7)	33 (38.4)	0.969
Duration bDMARD treatment, months, median (IQR)	88 (45-61.8)	88 (47-130)	86 (41.5-120)	0.992
Associated treatment, n (%)	57 (30.5)	19 (24.4)	38 (34.9)	0.124
Disease duration > 24 months, n (%)	149 (83.7)	63 (82.9)	86 (84.3)	0.8
PON daily dose, median (IQR)	1.5 (0.5)	0.6 (0.1)	2.5 (0.5)	0.13
NSAIDs, n (%)	111 (66.1)	47 (67.1)	64 (65.3)	0.804
Painkillers, n (%)	50 (31.4)	22 (31.9)	28 (31.1)	0.917
Concomitant chronic treatment, n (%)	91 (49.7)	38 (50.7)	53 (49.1)	0.832
DAS28, median (IQR)	2.3 (1.8-2.8)	2.3 (1.7-2.8)	2.4 (1.8-3.0)	0.441
Remission, n (%)	101 (52.9)	39 (49.4)	62 (55.4)	0.414
Low disease activity, n (%)	174 (91.1)	73 (92.4)	101 (90.2)	0.595
Patient-VAS, median (IQR)	38 (20-66)	30 (10-50)	45 (28-69)	0.034
Physician-VAS, median (IQR)	10 (5-15)	10 (0-15)	10 (6-20)	0.988
HAQ, median (IQR)	0.6 (0.1-1.1)	0.5 (0.1-1)	0.8 (0.3-1.1)	0.14
Disease flares, median (IQR)	11 (2.6-2)	5 (3.3)	6 (2.2-2)	0.433
No. of assessments per year, median (IQR)	4 (3-4)	4 (3-4)	4 (3-4)	0.98
Distance from clinic, km, median (IQR)	32 (18-50)	30 (20-50)	35 (18-50)	0.948

Defined as DAS28 < 2.6, defined as DAS28 < 3.2; *variables included in the analysis in patients treated with bDMARDs as achieving a p value < 0.10.

bDMARD biologic DMARD, IQR interquartile range, BMI body mass index, ACPA anti-citrullinated peptides, RF rheumatoid factor, PON prednisone, NSAIDs non-steroidal antiinflammatory drugs, HAQ Health Assessment Questionnaire, DAS28 disease activity score in 28 joints, VAS visual analogic scale.

Table. Multivariate regression analysis. Factors associated with HA to anti-rheumatic treatment according to I-CQR5.

	OR (95% C.I.)	p
Male gender	2.05 (0.9-4.66)	0.086
Employment	2.89 (1.3-6.44)	0.009
Patient-VAS (per 10-unite increase)	0.95 (0.83-1.09)	0.453
Model constant		0.035

OR odds ratio, C.I. confidence interval, VAS visual analogic scale.

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FRI0092

SAFETY AND EFFICACY OF FILGOTINIB IN ACTIVE RHEUMATOID ARTHRITIS BY PRIOR BIOLOGICAL DMARD EXPOSURE IN PATIENTS WITH PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS (bDMARD-IR)

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Background: Filgotinib (FIL), an oral selective Janus kinase 1 (JAK1) inhibitor, significantly improved the signs and symptoms of rheumatoid arthritis (RA) with a favorable safety profile in a global phase 3 study in bDMARD-IR patients with active RA (FINCH2).¹

Objectives: To assess the safety and efficacy of FIL in the FINCH2 study by the number and type of prior bDMARDs.

Methods: FINCH2 enrolled 449 bDMARD-IR patients with moderate-to-severe active RA. Patients were randomized 1:1:1 to FIL 200 mg, FIL 100 mg or placebo (PBO) on a background of csDMARDs for 24 weeks. In this prespecified subgroup analysis, efficacy and safety were analyzed according to the number (<3 vs ≥3) of previous bDMARDs used.

Results: 448 patients received ≥1 dose of study drugs. Of these, 343 were previously exposed to <3 bDMARDs, while 105 were previously exposed to ≥3 bDMARDs. Table 1 shows demographics and baseline (BL) characteristics of patients in these 2 groups; efficacy and safety parameters (Table 2) were similar for both groups. There were no cases of opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death.

Table 1. BL Demographics and characteristics

	<3 bDMARDs (n=343)			≥3 bDMARDs (n=105)		
	FIL 200 (n=110)	FIL 100 (n=119)	PBO (n=114)	FIL 200 (n=37)	FIL 100 (n=34)	PBO (n=34)
Female, n (%)	90 (82)	92 (77)	93 (82)	30 (81)	27 (79)	28 (82)
Mean (SD) age, yrs	54 (13)	55 (13)	56 (12)	59 (9)	54 (9)	56 (12)
Concurrent steroids, n (%)	46 (42)	49 (41)	54 (47)	22 (60)	19 (56)	17 (50)
Concurrent MTX, n (%)	98 (89)	101 (85)	96 (84)	26 (70)	26 (77)	20 (59)
Mean (SD) DAS28 (CRP)	6.0 (1.0)	5.8 (1.0)	5.9 (0.9)	5.8 (1.0)	6.1 (1.0)	5.9 (0.9)
Mean (SD) HAQ-DI	1.66 (0.65)	1.62 (0.70)	1.63 (0.65)	1.84 (0.66)	1.72 (0.61)	1.74 (0.57)
Mean (SD) hsCRP (mg/L)	17.04 (16.80)	21.82 (28.49)	16.08 (19.16)	17.70 (22.36)	20.31 (27.58)	17.56 (15.37)

Table 2. Key week 24 efficacy and safety outcomes

	<3 bDMARDs (n=343)			≥3 bDMARDs (n=105)		
	FIL 200 (n=110)	FIL 100 (n=119)	PBO (n=114)	FIL 200 (n=37)	FIL 100 (n=34)	PBO (n=34)
ACR20 n (%) ^a	Δ34.9%	Δ21.2%		Δ35.2%	Δ17.6%	
DAS28(CRP)≤3.2 n (%) ^a	Δ27.3%	Δ15.8%		Δ29.0%	Δ20.6%	
DAS28(CRP)≤2.6 n (%) ^a	Δ19.6%	Δ12.9%		Δ15.7%	Δ17.6%	
HAQ-DI mean CFB (SD)	-0.74 (0.631) [‡]	-0.61 (0.668)*	-0.42 (0.618)	-0.77 (0.596) [‡]	-0.54 (0.635)	-0.44 (0.525)
SF-36 PCS mean CFB (SD)	9.4 (8.45) [‡]	8.9 (8.72)*	6.4 (8.44)	9.4 (7.65)	9.1 (7.36)	7.2 (5.44)
FACIT-Fatigue mean CFB (SD)	11.3 (11.99) [‡]	9.7 (10.44)*	6.7 (10.68)	12.6 (10.78) [‡]	10.2 (10.42) [‡]	8.4 (8.12)
TEAE	75 (68.2%)	73 (61.3)	76 (66.7%)	27 (73.0%)	24 (70.6%)	24 (70.6%)
TEAE leading to study drug discontinuation	4 (3.6%)	3 (2.5%)	2 (1.8%)	1 (2.7%)	3 (8.8)	1 (2.9%)

CFB, change from BL. *p<0.05, †p<0.01, ‡p<0.001; Δ, difference vs PBO.

^aFIL values are PBO-corrected.

Conclusion: In bDMARD-IR patients with active RA, FIL treatment for 24 weeks significantly improved the signs and symptoms of RA with a favorable safety profile; notably, efficacy and safety results were similar for patients with <3 or ≥3 prior bDMARDs.

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