FRI0095 PILOT STUDY OF THE EARLY RHEUMATOID ARTHRITIS DIAGNOSIS PROGRAM WITH A STRUCTURED REFERRAL FORMAT

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Background: The delay in referral of patients with suspicion of Undifferentiated Inflammatory Arthritis (UIA), especially the Rheumatoid Arthritis (RA), from the primary care physician (PCP) to the Rheumatologist prevents diagnosing and treatment in a timely manner. Early diagnosis and treatment decreases progression and permanent joint damage. Several strategies have been proposed to improve the time to referral of patients with UIA, however there is none for early RA in specific.
Objectives: We present a pilot study for the use of a weighted construct format for the improvement of the time to referral of patients with suspicion of early RA.
Methods: Since June 2005, in clinics and hospitals, PCPs were trained for the use of the weighted construct format tool. Adult patients with less than 1year of symptoms were considered for the referral. The criteria for reference of suspicion of early RA are shown in Table 1. The patient referral was made through the counter-reference system, including the complete format and laboratory results. The patient's appointment was given within 15 business days. Once the patients were evaluated and studied in the Department of Rheumatology, they were classified with RA according to 2010 ACR/EULAR criteria when was available this criteria classification. For the demographic variables, we used descriptive and inferential statistics and for the format validation we verified the reliability, and validity of the construct and criterion tool.
Results: Between July 2005 and July 2015, 298 patients were referred to our clinic. The average referral time in the first year (2005–2006) was 34.3±20.4 days, maintaining an average of 32.1±16.8 days until 2015. There was a reduction of 74% of referral time compared to a historical reference (mean time of referral was 127.4±51.8 days, in 122 patients). 182 (62%) patients filled out the 2010 ACR/EULAR criteria. The referral format for early RA had a Cronbach alpha of 0.49, Sensitivity 85.1%, Specificity 93.5% and PPV 92.2%. The correlation between patients with early RA and the 2010 ACR/EULAR criteria was 0.765 with a $p<0.000$.
Conclusions: In this pilot study, we observed that the construct had a suitable sensitivity, specificity and PPV for a referral format. Therefore, on suspicion of early RA the referral format could be useful as a simple clinical tool for the timely referral to the Rheumatologist. On the other hand, the program implementation allowed the reduction in the referral time substantially. To implement the use of this tool in the daily clinical practice it needs to be validated with an open population and an adequate sample size

Table 1

	Criteria	Score	Total
Clinical	Polyarticular arthritis: >5 joints Small joints: proximal interphalangeal joints, metacarpophalangeal joints, metatarsophalangeal or wrist joints+ any large joint (shoulders, elbows, knees or ankles)	4	
	Morning stiffness greater than 30 minutes (>30').	3	
	Oligoarticular arthritis: < 5 joints (small and large joints).	0	
Laboratory	Rheumatoid factor (+): dilution > 1:160 or 20 IU for nephelometry or turbidimetry.	4	
	Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP): positive (> than normal reference parameter).	3	
	Anemia: hemoglobin (Hb) ≤12.5g/dl or thrombocytosis>40x10 ^{3}/µl platelets.	1	
	Total	15	

≤ 5points low suspect, between ≥6 and ≤10 suspect, and ≥11 points highly suspect.
Clinical criteria: obtained through complete clinical history (morning stiffness: time it takes to mobilize a joint after waking up). Musculoskeletal examination should show joint swelling (swelling, tenderness, temperature increase and difficulty to mobilize).
Laboratory: obtained within the protocol that caused the patient's visit (no > 2 weeks) results must be attached.

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FRI0096 DURABILITY AND MAINTENANCE OF EFFICACY FOLLOWING PROLONGED TREATMENT WITH BARICITINIB

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Background: Baricitinib (bari) demonstrated clinical efficacy in Ph3 trials in RA patients (pts) naïve to DMARDs (RA-BEGIN[1]); and in RA pts with inadequate response to conventional synthetic DMARDs (RA-BEAM[2] and RA-BUILD[3]) or biologic DMARDs (RA-BEACON[4]).
Objectives: To evaluate durability and maintenance of efficacy over an additional 96 weeks (wks) of bari treatment.
Methods: Pts included were those randomised to bari in an originating study (OS), completed that study without rescue (52 wks in RA-BEGIN or RA-BEAM; 24 wks in RA-BUILD or RA-BEACON), and entered the long-term extension (LTE) study ≥96 wks prior to data cut-off. Durability of response was evaluated as pts achieving low disease activity (LDA) of SDAI ≤11 and minimal clinically important difference (MCID) of HAQ-DI improvement ≥0.22. Maintenance of response was evaluated as proportion of pts who had responded to bari at entry into LTE and maintained response at wk 96. Data are also provided for pts who had not responded to bari at entry into LTE who achieved response.
Results: Approximately half the pts in the durability analyses were categorised as LDA by wk 24 and the proportion of pts in the LDA category were similar or higher at wk 96. Three quarters of pts across groups demonstrated HAQ-DI improvement by wk 12 and more than half achieved MCID at wk 96. Most responders at entry into LTE maintained their response through wk 96. More than 25% of SDAI and HAQ-DI nonresponders at entry into LTE achieved response after 96 wks of treatment.
Conclusions: These data provide further evidence of the effectiveness of bari treatment in achievement of meaningful clinical control of disease activity long term.

References:
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Abstract FRI0096 – Table 1

		RA-BEGIN Bari 4mg N=30	RA-BEAM Bari 4mg N=104	RA-BUILD Bari 2mg N=154	RA-BUILD Bari 4mg N=164	RA-BEACON Bari 2mg N=117	RA-BEACON Bari 4mg N=124
Durability of Response, n (%)							
SDAI ≤11	Wk12 OS	13 (43.3)	48 (46.2)	59 (38.3)	69 (42.1)	31 (26.5)	46 (37.1)
	Wk24 OS	18 (60.0)	59 (56.7)	87 (56.5)	106 (64.6)	40 (34.2)	56 (45.2)
	Wk52 OS	23 (76.7)	74 (71.2)				
	Wk48 LTE	23 (76.7)	77 (74.0)	98 (63.6)	106 (64.6)	54 (46.2)	62 (50.0)
	Wk96 LTE	25 (83.3)	73 (70.2)	86 (55.8)	92 (56.1)	54 (46.2)	62 (50.0)
HAQ-DI imp≥0.22	Wk12 OS	28 (93.3)	80 (76.9)	118 (76.6)	118 (72.0)	85 (72.6)	97 (78.2)
	Wk24 OS	27 (90.0)	85 (81.7)	121 (78.6)	121 (73.8)	88 (75.2)	92 (74.2)
	Wk52 OS	24 (80.0)	86 (82.7)				
	Wk48 LTE	25 (83.3)	77 (74.0)	113 (73.4)	115 (70.1)	75 (64.1)	80 (64.5)
	Wk96 LTE	26 (86.7)	80 (76.9)	98 (63.6)	105 (64.0)	58 (49.6)	79 (63.7)
Maintenance of Response at 96 wks, % (n/N')							
SDAI ≤11	R	82.6 (19/23)	81.1 (60/74)	70.9 (61/86)	66.7 (68/102)	77.5 (31/40)	77.8 (42/54)
	NR	85.7 (6/7)	43.3 (13/30)	36.9 (24/65)	36.2 (21/58)	27.8 (20/72)	27.7 (18/65)
HAQ-DI imp≥0.22	R	87.5 (21/24)	84.9 (73/86)	72.7 (88/121)	71.9 (87/121)	56.8 (50/88)	71.7 (66/92)
	NR	83.3 (5/6)	38.9 (7/18)	30.3 (10/33)	39.0 (16/41)	27.6 (8/29)	40.6 (13/32)

Data were analysed using nonresponder imputation without considering rescue status in LTE. N = number of mITT pts; N' = number of responders (R) or nonresponders (NR) at entry into LTE; n = number of pts in the specific category.

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FRI0097 REPAIR OF JOINT DAMAGE IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS OCCURS BUT DOES NOT RELATE TO PREVIOUS SUPPRESSION OF INFLAMMATION; AN 8-YEARS SUB ANALYSIS IN THE BEST-COHORT

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Background: Joint damage in rheumatoid arthritis (RA) is thought to be irreparable. We hypothesized that in patients where inflammation is well suppressed for a long time, repair may be possible.
Objectives: To investigate whether reversal of erosions and joint space narrowing (JSN) in RA occurs and whether clinical variables predict repair.
Methods: In the BeSt study, patients with active early RA (ACR 1987 criteria, arthritis symptoms <2 years) were randomized to 4 treatment strategies, each with the aim to ensure and maintain suppression of disease activity by adjusting medication based on three-monthly calculations of the 44-joint Disease Activity Score (DAS), target ≤2.4. Radiographic joint damage was assessed yearly, using the Sharp/van der Heijde score (SHS). In this analysis, 8-years data of the study were used. Repair of erosions or JSN was defined at the individual joint level as a reduction of ≥1 SHS point compared to the previous available X-ray, present in ≥2 consecutive visits and with ≥3 out of 4 independent scorers agreeing. Radiographs were scored in random order per patient, blind for patient identity and treatment arm. Multiple logistic regressions were applied at the patient level for associations between achieving repair and maximum duration of previous remission, mean DAS until repair, previous prednisone use, previous infliximab use, anti-citrullinated protein antibody (ACPA), gender, age and randomization arm. All models were adjusted for mean joint damage over time in the group with repair. In the group without repair, the models were corrected for mean damage over time until mean time point of repair in the group with repair.
Results: Seven out of 508 patients did not have any X-ray images taken in the study. Of the remaining 501 patients, 320 had damage in at least 1 joint and thus could potentially show repair. In total, 2395 X-rays were available, on average 7.5 per patient (range 2–9). Median SHS after 8 years in these patients was 10 (IQR 4–21, range 0–234), and mean (SD) DAS from month 3 was 2.00 (0.67). Repair was seen in 17 patients, 3.3%; 10 had reduction of JSN, 6 of erosions, 1 had repair of both JSN and erosions. In 14 patients repair was seen in 1 joint, in 3 patients repair was seen in 2 joints (same time point). Mean (SD) time to repair was 44.1 (20.1) months. Ten of 17 patients (59%) had previously achieved DAS-remission, compared to 100% of the patients who at a matching time point showed no repair. Adjusted for mean SHS until repair, we found no associations with repair for duration of remission, mean DAS until repair, gender, age, presence of ACPA, or previous exposure to prednisone or infliximab (table 1). Apart from a trend towards fewer patients with repair in the initial infliximab study arm, there were no differences in any of the groups in any of the regression analyses.

Table 1. Results of multiple logistic regression models to investigate associations with repair (n=17)

	OR	95% CI	P
Duration of previous remission*	-	-	-
Mean DAS from month 3 to time of repair	1.39	0.77 - 2.51	0.270
Previous prednisone	1.09	0.385 - 3.09	0.871
Previous infliximab	0.599	0.206 - 1.74	0.347
ACPA	1.51	0.413 - 5.53	0.533
Gender	1.13	0.401 - 3.16	0.822
Baseline age	1.01	0.975 - 1.05	0.548
Randomization arm			
Sequential monotherapy	ref	-	-
Step-up combination therapy	0.797	0.231 - 2.75	0.721
Initial combination with prednisone	0.597	0.158 - 2.26	0.448
Initial combination with infliximab	0.147	0.0173 - 1.25	0.080

All models were adjusted for mean Sharp/van der Heijde score until repair
DAS: disease activity score, ACPA: anti-citrullinated peptide antibody
*No results due to 100% remission in non-repair comparator group

Conclusions: In this early RA cohort, during 8 years treated to target DAS ≤2.4, repair of JSN and erosions was seen in 17 patients (3.3%), which supports that repair occurs in early RA. However, repair is a rare phenomenon, and does not seem to relate to previous inflammation or other predictors in this cohort.
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FRI0098 ELEVATED MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) PREDICTS RELAPSES IN RA PATIENTS IN SUSTAINED REMISSION TAPERING TUMOUR NECROSIS FACTOR INHIBITOR THERAPY- RESULTS FROM THE RANDOMIZED CONTROLLED RETRO STUDY

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Background: Tumor necrosis factor inhibitors (TNFi) are the most frequently used bDMARDs in RA patients. TNFi induces remission in a substantial numbers of patients. Once remission, particularly sustained remission is achieved the question arises whether TNFi can be successfully tapered. To date biomarkers, which can help to predict if TNFi can be tapered or stopped, remain to be developed.
Objectives: To test whether residual subclinical inflammation assessed by multi-biomarker disease activity (MBDA) predicts the risk of disease relapse after tapering or stopping TNFi treatment in RA patients in sustained remission.
Methods: Sub-analysis of TNFi treated patients of the RETRO study, a randomized-controlled study in RA patients in sustained (>6 month) DAS28 remission comparing 3 different DMARD treatment strategies (continuation of full dose, 50% dose tapering, stopping after 50% dose tapering). Patients were followed over one year for the occurrence of relapses as defined by leaving DAS28-ESR remission (>2.6 units) (1). Vectra-DA tests were done in the baseline samples of all patients included into the RETRO study. MBDA score was calculated according to previously defined algorithms with low MBDA score defined as <30 units and moderate to high scores as ≥30 units (2).
Results: Of the 151 patients included in the RETRO study, 42 received TNFi treatment (mean age: 56 ys, 25 (60%) females, 78% concomitant csDMARDs; 69% ACPA/RF positive. Baseline demographic and disease specific characteristics of these patients were comparable to the non-TNFi treated patients of the RETRO study. 26/42 patients (62%) had low MBDA scores at baseline, while 16/42 (38%) had moderate/high scores. Relapse rates were significantly (chi square p=0.016) lower in RA patients with low MBDA scores (N=8 of 26; 31%) than in those with moderate/high scores (N=11 of 16; 69%) (Figure; left graph). When separately analyzing only patients tapering TNFi (N=29), relapse rates were moderate in