Disclosure of Interest: J. Smolen Grant/research support from: Abbvie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Z. Li: None declared, R. Klar Employee of: Quintiles IMS Holdings, Inc., L. Xie Employee of: Eli Lilly and Company, D. Walker Employee of: Eli Lilly and Company, A. Ghizdavescu Employee of: Eli Lilly and Company, R. Ortmann Employee of: Eli Lilly and Company, M. Dougados Grant/research support from: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, Consultant for: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS
DOI: 10.1136/annrheumdis-2017-eular.1311

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

J.A. van der Pol[1], G. Akdemir[1], M. van den Broek[1], L. Dirven[1], P. Kerstens[2], W.F. Lems[3], I.M. Markusse[1], T.W. Huizinga[1], C.F. Allaart[1]. *[1]Department of Rheumatology, Leiden University Medical Center, Leiden; [2]Department of Rheumatology, Westfries Gasthuis, Hoorn; [3]Department of Rheumatology, VU Medical Center, Amsterdam, Netherlands*

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

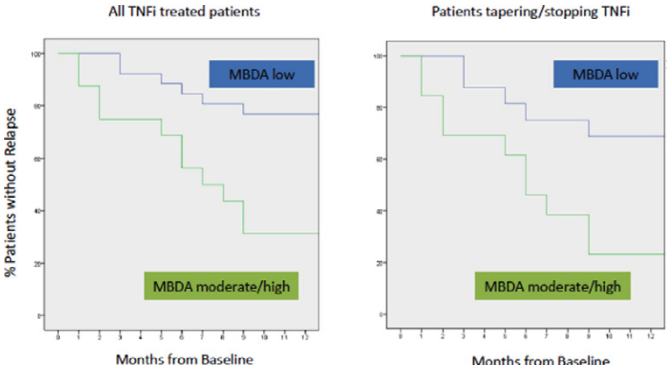
All models were adjusted for mean Sharp/van der Heijde score until repair
DAS: disease activity score, ACPA: anti-citrullinated peptide antibody
*No results due to 100% remission in non-repair comparator group

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.
Disclosure of Interest: J. van der Pol: None declared, G. Akdemir: None declared, M. van den Broek: None declared, L. Dirven: None declared, P. Kerstens: None declared, W. Lems Speakers bureau: Speakersfee/advosory boards Pfizer, MSD, Eli Lilly, Abbvie, I. Markusse: None declared, T. Huizinga: None declared, C. Allaart Grant/research support from: The BeSt study was supported by a government grant from the Dutch Insurance Companies, with additional funding from Schering-Plough B.V. and Janssen B.V.
DOI: 10.1136/annrheumdis-2017-eular.2270

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

J. Rech[1,1], M. Hagen[1], M. Englbrecht[1], J. Haschka[2], M. Reiser[1], A. Kleyer[1], A. Hueber[1], B. Manger[1], C. Figuereido[3], J. Fogagnolo Cobra[3], H.-P. Tony[4], S. Finzel[5], S. Kleinert[6], J. Wendler[6], F. Schuch[6], M. Ronneberger[6], M. Feuchtenberger[7], M. Fleck[8], K. Manger[9], W. Ochs[10], M. Schmitt-Haendle[10], H.-M. Lorenz[11], H. Nuesslein[12], R. Alten[13], J. Henes[14], K. Krueger[15], G. Schett[1]. *[1]University of Erlangen-Nuremberg, Erlangen, Germany; [2]St.Vincent Hospital, Vinforce Study Group, Medical University of Vienna, Vienna, Austria; [3]Institutio de Rheumatologia, Sao Paolo, Brazil; [4]University of Wuerzburg, Internal Medicine 2, Wuerzburg; [5]University Medical Center Freiburg, Rheumatology and Clinical Immunology, Freiburg; [6]Rheumatology Clinical Practice Erlangen, Erlangen; [7]Rheumatology Practice and Department of Internal medicine 2, Clinic Burghausen, Burghausen; [8]Asklepios Medical Center, Department of Rheumatology and clinical Immunology, Bad Abbach; [9]Rheumatology Practice Bamberg, Bamberg; [10]Rheumatology Practice Bayreuth, Bayreuth; [11]University of Heidelberg, Medicine 5, Heidelberg; [12]Rheumatology Practice Nuremberg, Nuremberg; [13]Schlosspark Klinik, Internal Medicine/Rheumatology, Berlin; [14]University of Tuebingen, Centre for Interdisciplinary Clinical Immunolog, Tuebingen; [15]Praxiszentrum St.Bonifatius, Munich, Germany*

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



RA patients with low MBDA scores (N=6 of 16; 37%) but high in those with moderate/high scores (N=10 of 13; 77%) (chi square p=0.015) (Figure; right graph).

Conclusions: These data show that the majority of RA patients in sustained clinical remission with low MBDA scores can successfully taper TNFi. In contrast tapering cannot be recommended in patients with moderate to high MBDA scores, as relapse rates are high in these patients.

References:
[1] Haschka J et al. Ann Rheum Dis 2016,75;45–51.
[2] Curtis JR et al. Arthritis Care Res 2012;64:1794–803.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4787

FRI0099 PAIN REDUCTION IS ASSOCIATED WITH IMPROVED WORK PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Michaud[1,2], B. Zhu[3], C. Gaich[3], A.M. DeLozier[3], V. Arora[3], C. Dickson[3], J.S. Smolen[4]. *[1]University of Nebraska Medical Center, Omaha; [2]NE & National Data Bank for Rheumatic Diseases, Wichita; [3]Eli Lilly and Company, Indianapolis, United States; [4]Division of Rheumatology, Medical University of Vienna, Vienna, Austria*

Background: Patients with rheumatoid arthritis (RA) indicate pain is an important aspect of disease burden and may persist despite control of disease. In a randomized, double-blind phase 3 clinical trial of baricitinib (RA-BEAM),[1] baricitinib provided significant improvement in pain reduction. It is not clear, however, how much reductions in pain impacted other aspects of life, such as work productivity.

Objectives: To assess the relationship between pain reduction and improvements, regardless of treatment, in daily activity and work productivity in patients with RA.

Methods: In this post-hoc analysis of RA-BEAM[1], pain for the intention-to-treat patients was assessed using the patient's assessment of pain (0–100 mm visual analogue scale). The Work Productivity and Activity Impairment Questionnaire-RA (WPAI-RA) instrument was used to evaluate the percentage of activity impairment due to RA (impairment in regular daily activities, N=1302), percentage of work-time missed due to RA (absenteeism, N=521), percentage of impairment while working due to RA (presenteeism, N=490), and percentage of overall work impairment due to RA (impairment in work productivity, N=490). Pain was divided into pain reduction groups (<30%, 30% – <50%, ≥50% at Weeks 12 and 24; ≥30% [Y/N] and ≥50% [Y/N] at Weeks 1 and 2). Pairwise comparisons on improvement in WPAI-RA scores between pain reduction groups at Weeks 12 and 24 were assessed by ANCOVA adjusting for region, baseline joint erosion status, and baseline values of outcome variables. Missing values were imputed using the modified last-observation carried forward method.

Results: At baseline across treatment groups, the mean values ranged from 56–58 for daily activity impairment, 12–13 for absenteeism, 42–46 for presenteeism, and 45–49 for work productivity impairment. A ≥30% reduction in pain as early as Week 1 was associated with significantly greater (p<0.001) improvement than <30% pain reduction in regular daily activity (-22.8 vs -16.0), presenteeism (-17.5 vs. -12.1), and work productivity (-16.8 vs. -11.6) at Week 12. Greater improvement was observed in most WPAI-RA scores in patients who had more pain reduction at Weeks 12 and 24; with a reduction of ≥50% in pain from baseline, the WPAI-RA scores were substantially improved at Weeks 12 or 24 for daily activity, presenteeism, and work productivity (Table).

	Pain (VAS) % reduction from baseline at Week 12			Pain (VAS) % reduction from baseline at Week 24		
Mean (SD)%	**<30%**	**30% - <50%**	**≥50%**	**<30%**	**30% - <50%**	**≥50%**
Improvement in WPAI-RA	**WPAI-RA at Week 12**			**WPAI-RA at Week 24**		
Impairment in Regular Daily Activity	-5.6 (22.2)	-17.8 (21.8)[c]	-30.1 (25.4)[cd]	-3.5 (23.6)	-17.1 (22.4)[c]	-33.2 (25.3)[cd]
Absenteeism	0.7 (28.0)	-5.2 (29.7)[b]	-3.0 (18.2)[c]	-1.8 (28.5)	-2.1 (36.1)	-2.5 (21.8)
Presenteeism	-2.8 (24.6)	-12.9 (21.1)[c]	-23.4 (24.6)[cd]	-0.2 (25.1)	-7.7 (23.1)[a]	-26.0 (25.1)[cd]
Impairment in Work Productivity	-2.3 (24.4)	-11.3 (23.5)[c]	-23.1 (26.5)[cd]	0.5 (25.6)	-5.7 (26.2)	-25.2 (28.1)[cd]

[a]p≤0.05; [b]p≤0.01; [c]p≤0.001 vs. pain reduction <30%; [d]p<0.001 vs. pain reduction 30-<50%

Conclusions: Regardless of treatment, pain reduction was associated with improved regular daily activity and work productivity in patients with RA, with larger levels of reduction related to more improvement.

References:
[1] Taylor PC, Keystone E, van der Heijde D, et al. Baricitinib Versus Placebo or Adalimumab in Patients with Active Rheumatoid Arthritis (RA) and an Inadequate Response to Background Methotrexate Therapy: Results of a Phase 3 Study. Arthritis Rheum 2015;67(Suppl 10):3928.

Disclosure of Interest: K. Michaud Grant/research support from: Pfizer, B. Zhu Employee of: Eli Lilly and Company, C. Gaich Employee of: Eli Lilly and Company, A. DeLozier Employee of: Eli Lilly and Company, V. Arora Employee of: Eli Lilly and Company, C. Dickson Employee of: Eli Lilly and Company, J. Smolen Grant/research support from: Abbvie, Janssen, Lilly, MSD, Pfizer, Roche and has provided expert advice to and/or had speaking engagements for Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB
DOI: 10.1136/annrheumdis-2017-eular.1345

FRI0100 DETERMINING MINIMUM CLINICALLY IMPORTANT CHANGE IN MULTI BIOMARKER DISEASE ACTIVITY SCORE ASSOCIATED WITH CLINICAL IMPROVEMENT IN METHOTREXATE NAÏVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

K. Chatzidionysiou[1], A.H. Hensvold[1], S. Saevarsdottir[1], R.J. Bolce[2], D. Chernoff[2], C.C. Hwang[2], X. Wang[2], A.I. Catrina[1]. *[1]Karolinska University and Institutet, Stockholm, Sweden; [2]Crescendo Bioscience Inc., South San Francisco, United States*

Background: The Multi-Biomarker Disease Activity (MBDA) score is a validated tool that quantifies 12 biomarkers to assess disease activity in rheumatoid arthritis (RA) patients. Many studies have demonstrated usefulness of the score for assessing RA disease activity.

Objectives: To determine minimum clinically important change in MBDA score (ΔMBDA) from baseline (BL) to Month 3 (M3) associated with clinical improvement (decrease in DAS-ESR >1.2) in early RA patients after initiating methotrexate (MTX).

Methods: We evaluated the MBDA test in patients from one of the sites participating in the Solna Epidemiological Investigation of RA (EIRA) cohort. EIRA patients were eligible if they were ≥18 years; RA diagnosis within 12 months of symptom duration; had serum and clinical assessments at BL and M3; and clinical follow-up data in the Swedish Rheumatology Quality Register. Patients naïve to disease modifying anti-rheumatic drugs who received MTX were included. Kruskal-Wallis was used to test the null hypothesis that medians of ΔMBDA scores of 3 EULAR response groups are equal. Receiver operating characteristic (ROC) analysis was performed. The optimal threshold of ΔMBDA associated with DAS28-ESR improvement (decrease in DAS-ESR >1.2 at M3) was determined by Youden criterion maximizing sum of sensitivity and specificity.

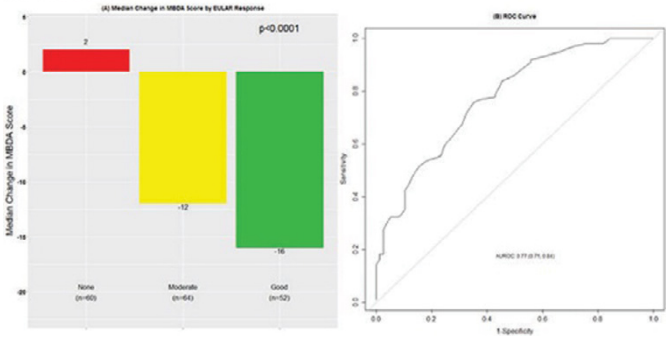
Results: 176 patients were included: 72% women, mean age 51 (SD: 11.7) years, mean DAS28-ESR score 5.6 (SD: 0.99); 51% had ESR <28 mm/hr, 66% were anti-CCP2+, and 22% received prednisone. Mean BL MBDA score was 56.8 (SD: 14.7) with 8 (5%) patients in low (<30), 29 (16%) patients in moderate (30–44) and 139 (79%) patients in high MBDA disease activity categories. Median MBDA scores for patients with no EULAR response worsened by 2 points and for patients with moderate and good response improved by 12 and 16 points, respectively (p<0.0001 across groups, Fig 1A). Median MBDA scores improved by 10 points for all patients and 15 points in patients with a DAS28-ESR decrease >1.2. The best combination of sensitivity and specificity to achieve a DAS28-ESR decrease >1.2 was provided by a ≥8 point MBDA score improvement (Fig 1B). A similar result was obtained using the bootstrap method. AUROC was 0.77 (95% CI: 0.71, 0.84). 125 patients (71%) had concordance between DAS28-ESR improvement and ΔMBDA improvement at the optimal threshold (Table 1).

Table 1. Performance Measures (95% CI) Based on Optimal Threshold of ΔMBDA Score from BL to M3 Associated with DAS28-ESR Improvement

Improvement		DAS28-ESR (decrease >1.2)		
		Yes	No	Total
MBDA (optimal threshold: improvement ≥8 points)	Yes	75	27	102
	No	24	50	74
	Total	99	77	176

Sensitivity: 0.76 (0.66, 0.83); Positive predictive value: 0.74 (0.64, 0.81); Specificity: 0.65 (0.54, 0.75); Negative predictive value: 0.68 (0.56, 0.77).r Concordance rate: 71%.

Figure A) Median Change in MBDA Score by EULAR Response; B) Receiver Operating Curve (ROC) to Determine the Optimal Threshold of Change in the MBDA Score Associated with Clinical Improvement (ΔDAS28-ESR Decrease >1.2)



Conclusions: The optimal threshold of ΔMBDA score associated with a clinically relevant decrease of DAS28 was 8 points. Using this threshold, the MBDA test is informative to detect clinical improvement. Thus, based on these results improvement in MBDA score ≥8 points at M3 after initiating MTX is indicative of meaningful clinical improvement.