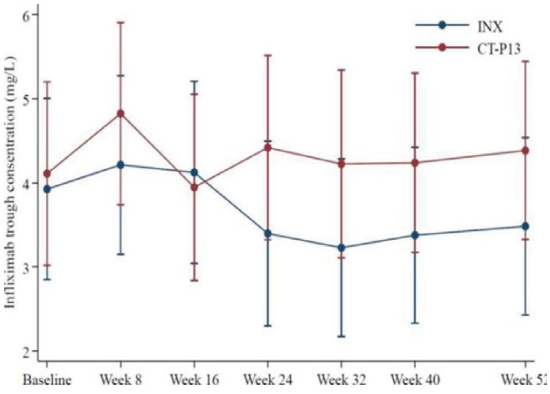
Abstract FRI0182 – Table 1. Demographic and baseline characteristics (FAS), percentage of RA patients with disease worsening and change in disease measures during 52 weeks follow-up (PPS)

Demographics and baseline characteristics	INX	CT-P13	
Total number of RA patients PPS/FAS	30/39	30/38	
Age (years) mean (SD)	59.9 (11.5)	60.4 (11.4)	
Females	31 (79%)	25 (66%)	
Duration of ongoing infliximab treatment (years) mean (SD)	8.2 (3.7)	9.9 (3.4)	
Concomitant immunosuppressive medication	27 (69%)	34 (89%)	
ACPA pos	25 (83%)	20 (74%)	
Disease worsening			95% CI of group difference after 52 weeks
All study patients	53 (26.2%)	61 (29.6%)	-12.7–3.9%
RA	11 (36.7%)	9 (30.0%)	-20.3–29.3%
Change in disease measures from baseline			
Physician Global Assessment of Disease Activity (0–10)	-0.1 (1.3)	0.1 (1.4)	-0.58–0.68
Patient Global Assessment of Disease Activity (0–10)	1.1 (1.4)	0.4 (1.9)	0.21–1.91
Log_{10} erythrocyte sedimentation rate (mm/h)	0.0 (0.3)	0.0 (0.3)	-0.08–0.16
Log_{10} C-reactive protein (mg/L)	0.1 (0.3)	0.0 (0.5)	-0.11–0.22
DAS28	0.2 (0.9)	0.2 (0.9)	-0.30–0.50
TEAE (FAS)	94	62	

Data are n (%), mean (SD) or median (25–75 percentiles). 95% CI, 95% confidence interval of the adjusted treatment difference. DAS28, Disease Activity Score in 28 joints. FAS, Full Analysis Set. PPS, Per Protocol Set. TEAE, treatment emergent adverse events.

endpoint was disease worsening according to disease-specific composite measures and/or consensus between investigator/patient leading to major treatment change. Exploratory subgroup analyses examined disease worsening and safety in RA. The primary endpoint was analysed using logistic regression, adjusted for diagnosis and disease duration.

Results: Demographics, occurence of disease worsening, change in disease measures and treatment-emergent adverse events (TEAE) were similar (Table). Serum drug levels for INX and CT-P13 were similar throughout the study (Figure)



Conclusions: Explorative analyses in the NOR-SWITCH study showed similar efficacy, serum drug levels and safety in RA patients switched to CT-P13 as those on continuous INX. The study was not powered to show non-inferiority within each diagnosis.

References:

[1] Jørgensen KK et al Switching from originator infliximab to biosimimlar CT-P13 compared to maintained treatment with originator infliximab (NOR-SWITCH): a 52-week randomized double-blind non-inferiority trial. The Lancet, in press.

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FRI0183 ASSESSING ADHERENCE OF RA PATIENTS TREATED WITH ETANERCEPT USING ETANERCEPT SERUM TROUGH CONCENTRATIONS AND PATIENT SELF-REPORT

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Background: The EULAR recommendations for the management of rheumatoid arthritis (RA) update 2013 contained the following research question: "How good is patient adherence to biological agents and can lack of adherence be related to loss of efficacy?" [1]. Limited studies are published in which adherence of RA patients treated with biological disease-modifying anti rheumatic drugs (bDMARDs) has been assessed. Previous studies regarding adherence of RA patients treated with etanercept did not take into account that patients are instructed to temporarily discontinue bDMARDs therapy during e.g. a serious infection. In addition, etanercept concentrations have never been utilized in determining adherence to etanercept in RA patients.

Objectives: The aim of our study was to determine the percentage of non-adherent RA patients treated with etanercept, using etanercept concentrations and patient self-report, and to assess the relationship between adherence and clinical outcome during 52 weeks.

Methods: Non-adherence was defined as an etanercept trough concentration <0.1ug/mL at least once and no valid/medical reason to miss an etanercept dose. In this retrospective cohort study patients visited our clinic at baseline and 4, 16, 28, 40 and 52 weeks after initiation of etanercept treatment. At baseline and following visits disease activity score of 28 joints (DAS28) was calculated and blood was drawn to measure etanercept concentrations. During each visit patients were asked if they missed an etanercept dose, at which date and for which reason. Remission was defined as DAS28 <2.6 at least for two consecutive visits. Low disease activity (LDA) was defined as DAS28 <3.2 during a minimal of two consecutive visits.

Results: In total 292 patients were included. Mean age was 53 years (SD 12.7), 82% was women and median disease duration was 8 years (IQR 3–16). In total 24 patients had an etanercept concentration <0.1ug/mL. Most patients had a medical reason to miss an etanercept dose, see table 1.

Table 1. Reasons for patients to miss an etanercept dose

Reason	Number of patients
Medical	10
Did not start	3
Logistical problem	1
Stopped due to inefficacy	1
Unknown	9

Only ten patients (3.4%) were non-adherent during the follow-up of 52 weeks. Of the adherent patients 82 out of 282 (29%) reached LDA versus 1 out of 10 non-adherent patients. A total of 127 of 282 (45%) adherent patients achieved MDA versus 3 out of 10 non-adherent patients.

Conclusions: Most patients had a medical reason to miss an etanercept dose. The percentage of patients who are non-adherent to etanercept therapy is very low (3.4%).

References:

[1] Smolen JS, Landewe R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.

Disclosure of Interest: E. Vogelzang: None declared, R. Hebing: None declared, M. Nurmohamed Speakers bureau: Abbvie, Bristol-Myers Squibb, Merck Sharp & Dohme, Celgene, Pfizer, Roche, Janssen, UCB and Sanofi, M. l'Ami: None declared, C. Krieckaert Speakers bureau: Pfizer and Abbvie, G. Wolbink Grant/research support from: Pfizer, Speakers bureau: Pfizer, UCB and Abbvie

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FRI0184 THE PROFILES OF PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO THEIR BELIEFS IN THEIR BIOLOGICAL DRUGS. ARCO STUDY

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Objectives: To describe profiles of rheumatoid arthritis (RA) patients according to their beliefs in their subcutaneous biological medication (SC).

Abstract FRI0184 – Table 1

		Accepting (n=116)	Ambivalent (n=182)	Indifferent (n=16)	Skeptical (n=7)	p
Mean age (SD)		55.5 (12.6)	54.2 (12.5)	58.8 (13.2)	53.6 (10.2)	0.459
		%	%	%	%	
Sex	Men	19.0	23.1	43.8	43.9	0.090
	Women	81.0	76.9	56.2	57.1	
RA duration	> median	51.8	50.3	43.8	28.6	0.651
	≤ median	48.2	49.7	56.2	71.4	
Satisfaction						
Symptoms control	Very/quite satisfied	93.1	82.9	68.8	85.7	0.009
	Indifferent, quite/very unsatisfied	6.9	17.1	31.2	14.3	
Tolerance/side effects	Very/quite satisfied	79.7	57.0	50.0	57.1	<0.001
	Indifferent, quite/very unsatisfied	20.3	43.0	50.0	42.9	
Expectations						
Effect of the drug on symptoms	Much/quite greater than expected	69.6	53.3	75.0	57.1	0.031
	+/– As expected	23.5	39.0	12.5	28.6	
	Quite/lower than expected	7.0	7.7	12.5	14.3	
Side effects/discomfort	Much/quite greater than expected	7.0	17.0	12.5	0.0	0.004
	+/– As expected	27.0	39.6	25.0	57.1	
	Quite/lower than expected, or no side effects/discomfort	66.0	43.4	62.5	42.9	

Methods: ARCO was a study carried out on RA Spanish patients who initiated a SC biological drug 11–18 months prior to the study visit. Patients completed the Beliefs About Medication Questionnaire (BMQ). According to the scores obtained in the necessity (N) and concerns (C) sub-scales, patients were classified into 4 groups: accepting (high N [>3]/low C [≤3]), ambivalent (N>3/C>3), indifferent (N≤3/C≤3) and skeptical (low N [≤3]/high C [>3]). We studied demographic characteristics, expectations and satisfaction with the treatment by group.
Results: 321 patients (77% women) completed the BMQ, 92.8% scored N>3 and 58.9% C>3. A higher % of men than women scored N≤3 (13.5% vs. 5.2%, p=0.031). The % who scored C>3 was higher in those with low satisfaction with symptom control (71.1% vs. 56.7% in satisfied/very satisfied, p=0.098), or side effects (72.1% vs. 52.0%, p<0.001), and in those with lower fulfillment of expectations of efficacy and tolerance (p=0.006 and p<0.001). The combination of N and C scores identified 116 accepting (36.1%), 182 ambivalent (56.7%), 16 indifferent (5.0%) and 7 skeptical patients (2.2%). There were no differences in age, gender, or RA duration among the groups, but differences were seen in the satisfaction with the treatment and in the fulfillment of the expectations (table). Ambivalent patients showed less satisfaction and lower fulfillment of expectations with the treatment received than accepting patients.
Conclusions: Patients with RA have strong beliefs about the need of their biological SC medication, but a high % also expresses concerns. Beliefs, and especially concerns, seem to relate to the satisfaction and fulfillment of expectations of efficacy and tolerability or the drug, rather than to demographics or RA characteristics. Discussing expectations may be important when initiating a biological treatment.
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FRI0185 A SYSTEMATIC REVIEW AND BIVARIATE META-ANALYSIS OF STUDIES THAT MEASURED ADALIMUMAB DRUG LEVELS BY ELISA TO DETECT TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS

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Background: Previous research has demonstrated an association between circulating drug levels and treatment response in patients with rheumatoid arthritis that received the anti-TNF therapy adalimumab. Commercial ELISA assays are now available for use in routine practice to monitor anti-TNF drug levels at regular intervals. However, the ability to detect treatment response by measuring adalimumab drug levels using an ELISA is uncertain.
Objectives: The objectives of this research were to identify and synthesise all published studies that investigated the accuracy of measuring adalimumab drug levels by ELISA to detect treatment response in patients with rheumatoid arthritis.
Methods: A systematic review identified all published studies that performed a receiver operating characteristic (ROC) analysis to detect treatment response in patients with rheumatoid arthritis by measuring adalimumab drug levels using an ELISA. Medline and Embase were searched electronically from inception to August 2016. Two researchers independently identified studies for the review using a pre-defined inclusion criteria. Assay results were classified as positive if adalimumab drug levels exceeded the cut-point reported in each study. Study design characteristics, sample characteristics, and test outcomes from 2x2 tables (true-positive; false-positive; true-negative; false-negative) were extracted from each study. The quality of each study was assessed using the QUADAS-2. A hierarchical bivariate meta-analysis synthesised the findings of the ROC analyses to account for between-study heterogeneity and correlation between assay sensitivity and specificity.
Results: The search strategy identified 4,006 abstracts and four studies met the inclusion criteria of the systematic review. Patients received 40mg adalimumab every two weeks in all studies. Studies varied in their design and sample characteristics, but had low risk of bias and low concern of applicability to the research objective. The hierarchical bivariate meta-analysis estimated that measuring high adalimumab drug levels by ELISA detected treatment response with an average sensitivity of 0.95 (95% CI: 0.85–0.98) and specificity of 0.68 (95% CI: 0.28–0.92).
Conclusions: Measuring high adalimumab drug levels by ELISA in patients with rheumatoid arthritis appeared to be predictive of treatment response. However, the measurement of low adalimumab drug levels was less predictive of no response to treatment. In practice, test accuracy may be improved by measuring anti-drug antibodies alongside adalimumab drug levels. Given the imperfect accuracy of ELISA assays, the relative cost-effectiveness of drug level monitoring should be evaluated before being recommended for use in routine practice.
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FRI0186 INFLUENCE OF IMMUNOGENICITY TO THE FIRST TNF-I THERAPY ON RESPONSE TO THE SECOND BIOLOGIC AGENT IN RA PATIENTS

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Background: There is currently no consensus on selecting a therapeutic target in patients (pts) non-responsive to their first TNF-inhibitors (TNF-i). The development of anti-drug antibodies (ADA) is a frequent cause of secondary inefficacy in our pts with TNF-i and there is evidence that those who develop ADA at their 1st TNF-i achieve a higher degree of response to the second one, compared to ADA- pts. Thus ADA measurement can help in choosing a therapeutic target in pts who failed to respond to their 1st TNF-i
Objectives: To assess if development of ADA to the 1st TNF-i determines better response when switching to a 2nd TNF-i versus a nonTNF-i. As secondary objective, analyze whether the presence or absence of ADA to a 1st TNF-i influences the efficacy of a 2nd TNF-i
Methods: Of a total of 144 pts that switched from infliximab or Adalimumab to a 2nd biologic agent (Etanercept, Rituximab, Tocilizumab, Adalimumab, Abatacept, Certolizumab and Infliximab), only 60, who had measured drug levels (DL)/ADA at discontinuation of the 1st TNF-I, were included. Clinical response was evaluated with DAS28, Delta-DAS28 (ΔDAS28) and EULAR response (E-resp) at 6 (v-6) and 12 (v-12) months after initiating 2nd biologic agent and at the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the biological therapy (v-end). DL/ADA levels were measured by ELISA. Statistical analysis was performed using SPSS version 20.0
Results: Within the 60 pts who had measured DL/ADA at suspension of the 1st TNF-i, 26 (43%) were ADA- (i.e. DL +). In this ADA- subpopulation, 50% changed to a 2nd TNF-i; at v-6 there were no differences between switchers to a 2nd TNF-i and switchers to a nonTNF-i in DAS28 (3.7±2.1 TNF-i vs 4.2±1.1 nonTNF-i, p=0.286), ΔDAS28 (1,4±2 TNF-i, 1±1,2 nonTNF-i, p=0,374) and resp-E (75% good/moderate resp in TNF-I, 40% in nonTNF-i, p=0,064). At v-12, switchers to a 2nd TNF-i showed a lower DAS28 (2.5±0.6 TNF-i, 3.9±0.9 nonTNF-i, p=0.009) and a higher good E-resp rate with a marginally significant difference (80% in TNF-i, 22% in nonTNF-i, p=0.071). However, at v-end, pts with a 2nd nonTNF-i had better response (DAS28 >5,1 in 50% of TNF-i pts, 0% of nonTNF-i, p=0.044). Likewise ΔDAS28 at v-end was higher in the nonTNF-i group with trend to significance (0,7±1,7 TNF-i, 1,7±0,8 nonTNF-i, p=0,06). Along these lines, the