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

good/moderate E-resp rate was higher in switchers to a nonTNF-i (70% in TNF-i, 8.3% in nonTNF-i, p=0.006). In ADA+ subpopulation (n=34), no differences were found in clinical response at v-end in DAS28 (3.7±1.2 TNF-i, 3.9±1.1 non-TNF-i, p=0.64), ΔDAS28 (0,63±1,6 in TNF-i, 1,4±1,4 in nonTNF-i, p=0,35) and good/moderate E-resp rate (30% in TNF-i, 91% in nonTNF-i, p=0,703). In pts who changed to a 2nd TNF-i, those with ADA to 1st TNF-i had a higher good response rate than ADA- pts (65% in ADA +, 30% in ADA-, p=0.07)

Demographic characteristics	ADA+ subpopulation	ADA- Subpopulation	p
Age (years)	62,3±14,6	65,7±14,9	0,203
Sex (female)	28 (82%)	23 (88%)	0,719
Smokers	7 (20,6%)	4 (26%)	0,537
BMI	26,9±8,9	23,9±4,2	0,39
Disease duration (years)	19,3±8,05	24,1±8,2	0,844
RF +	32 (94%)	20 (77%)	0,067
Anti-CCP +	32 (94%)	22 (88%)	0,641
Basal CPR	15,1±18,2	20,4±21,7	0,46
Basal ESR	41±27,9	38±20	0,28
Basal DAS	5,31±1,4	5,51±1,3	0,18

Conclusions: The development of ADA to the first TNF-i entails a better response when switching to a 2nd TNF-i, with a similar efficacy to the pts who switched to a nonTNF-i. In those pts who did not develop immunogenicity to the 1st TNF-I, there is a better response when changing therapeutic target. The ADA measurement can help to select the pts who can benefit from a 2nd TNF-i

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FRI0187 RADIOGRAPHIC PROGRESSION BY DISEASE ACTIVITY STATES IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB2 OR REFERENCE INFLIXIMAB

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Background: Based on the totality of evidence, SB2 has shown to be similar with reference infliximab (INF) and has been approved as a biosimilar by the European Medical Agency. It is, however, hitherto unknown, if SB2 also shares similar structural efficacy in the different disease activity states when compared with INF.

Objectives: To evaluate the disease activity by simplified disease activity index (SDAI) and clinical disease activity index (CDAI) at weeks 14, 30 and 54 in patients with rheumatoid arthritis (RA) treated with SB2 or INF from a phase III study and to assess the radiographic progression at week 54 in patients by disease activity states (remission, low disease activity [LDA], moderate disease activity [MDA], or high disease activity [HDA]).

Methods: Patients with RA were randomised to receive either SB2 or INF 3 mg/kg at weeks 0, 2, 6, and then every 8 weeks thereafter until week 46 with background methotrexate. Dose increments were allowed after week 30 by 1.5 mg/kg up to a maximum dose of 7.5 mg/kg. Disease activities by SDAI, and CDAI were compared at weeks 14, 30, and 54. The radiographic progression was measured by modified Total Sharp Score (mTSS) at weeks 0 and 54.

Results: Up to week 54, comparable proportions of patients achieved ACR-EULAR-index remission between SB2 and INF (by SDAI: 13/279 [4.7%] vs. 13/283 [4.6%] at week 14; 24/250 [9.6%] vs. 29/263 [11.0%] at week 30; 34/226 [15.0%] vs. 24/224 [10.7%] at week 54; by CDAI: 12/279 [4.3%] vs. 12/283 [4.2%] at week 14; 22/253 [8.7%] vs. 31/265 [11.7%] at week 30; 33/227 [14.5%] vs. 24/225 [10.7%] at week 54 in SB2 and INF, respectively). The proportions of radiographic non-progressors (defined as change in mTSS ≤0) by disease activity were comparable between SB2 and INF at week 14, 30 and 54 (Table 1). Patients treated with SB2 as well as INF also exhibited the lowest progression of radiographic damage in remission and the largest progression in HDA, but also very small increases in mTSS in LDA and MDA, in line with previous findings on INF.

Table 1. The proportion of radiographic non-progressors (mTSS progression ≤ 0) and mean change from baseline in mTSS at week 54 by disease activity states at weeks 14, 30, and 54

Disease activity state at each visit		CDAI				SDAI			
		SB2		INF		SB2		INF	
		Radiographic non-progressors	Mean change	Radiographic non-progressors	Mean change	Radiographic non-progressors	Mean change	Radiographic non-progressors	Mean change
Week 14	HDA	43/62 (69.4)	0.44	42/59 (71.2)	0.61	25/41 (61.0)	0.80	31/45 (68.9)	1.03
	MDA	64/86 (74.4)	0.27	57/82 (69.5)	0.64	81/105 (77.1)	0.10	63/89 (70.8)	0.45
	LDA	43/56 (76.8)	0.54	49/58 (84.5)	-0.38	44/58 (75.9)	0.63	53/64 (82.8)	-0.27
	Remission	7/9 (77.8)	0.17	6/8 (75.0)	1.44	7/9 (77.8)	0.17	7/9 (77.8)	1.00
Week 30	HDA	29/43 (67.4)	0.93	33/47 (70.2)	1.20	25/37 (67.6)	0.79	24/33 (72.7)	1.32
	MDA	57/76 (75.0)	0.14	49/71 (69.0)	0.43	59/80 (73.8)	0.24	58/84 (69.0)	0.54
	LDA	55/74 (74.3)	0.40	52/67 (77.6)	-0.10	56/74 (75.7)	0.42	54/69 (78.3)	-0.23
	Remission	16/20 (80.0)	0.05	22/24 (91.7)	-0.13	17/21 (81.0)	0.07	20/22 (90.9)	0.07
Week 54	HDA	31/43 (72.1)	0.39	25/42 (59.5)	1.59	25/36 (69.4)	0.65	23/36 (63.9)	1.71
	MDA	47/69 (68.1)	0.69	46/66 (69.7)	0.30	50/73 (68.5)	0.57	44/68 (64.7)	0.35
	LDA	51/67 (76.1)	0.20	62/78 (79.5)	0.29	54/69 (78.3)	0.18	66/82 (80.5)	0.24
	Remission	28/33 (84.8)	-0.11	23/23 (100.0)	-1.39	27/33 (81.8)	-0.08	23/23 (100.0)	-1.22

Disease activity was defined as following:
by CDAI: remission, CDAI ≤ 2.8; LDA, 2.8 < CDAI ≤ 10.0; MDA, 10 < CDAI ≤ 22.0; HDA, 22.0 < CDAI
by SDAI: remission, SDAI ≤ 3.3; LDA, 3.3 < SDAI ≤ 11.0; MDA, 11 < SDAI ≤ 26.0; HDA, 26.0 < SDAI
Patients with available mTSS at both baseline and week 54 were included.

Conclusions: The proportion of patients achieving remission or LDA was comparable up to week 54 upon treatment with both SB2 and INF. Inhibition of radiographic progression was also comparable in each disease activity state. The proportion of radiographic non-progressors was also similarly high in patients achieving remission, and overall very low radiographic progression rates were seen even in LDA and MDA in both treatment arms. These data further confirm the comparability of SB2 and INF.

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FRI0188 EFFECTIVENESS OF ADALIMUMAB COMBINATION THERAPY WITH METHOTREXATE AND NON-METHOTREXATE CSDMARDS: RESULTS FROM THE CORRONA RHEUMATOID ARTHRITIS REGISTRY

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Background: Combination therapy of methotrexate (MTX) with biologics results in superior outcomes vs. monotherapy. However, little is known on the effectiveness of adalimumab (ADA) combination therapy with non-MTX conventional synthetic disease modifying anti-rheumatic drugs (csDMARD).

Objectives: To evaluate whether ADA in combination with non-MTX csDMARD has similar effectiveness as MTX combination therapy on clinical and patient report outcomes (PROs).

Methods: Adult RA patients, naïve to other monoclonal antibodies, who initiated standard dose ADA (40mg q2w) in combination with MTX or ≥1 non-MTX csDMARD between 2003–2016 and had a 6 month follow-up visit were included. The primary outcomes were mean change in clinical disease activity index (CDAI) and mean change in PROs (mHAQ, pain, fatigue, morning stiffness) from baseline to 6 months. Secondary outcomes included achievement of remission (CDAI≤2.8)/low disease activity (LDA: CDAI≤10). Outcomes were evaluated adjusting for covariates that differed at the time of initiation using mixed model linear regression. Kaplan-Meier survival analysis was used to examine the persistency of ADA between the two groups.

Results: A total of 754 patients were included: N=519 ADA+MTX and N=235 ADA+non-MTX csDMARD. Patients on ADA+MTX were slightly younger (mean age: 54.5 vs 57.4 years), with shorter disease duration (median: 3 vs 5 years), more likely to be biologic naïve (77% vs 69%) compared to patients on ADA+nonMTX csDMARD (all p<0.05). Disease activity and PROs were comparable in both groups at the time of initiation (mean CDAI: 20.4 vs 22.8; mean pain: 45.3 vs 45.9; mean fatigue: 46.3 vs 47.8; mean patient global assessment: 42.8 vs 42.9 (on a VAS 0–100) in ADA+MTX and ADA+nonMTX csDMARD group respectively. Adjusted analysis showed that patients on ADA+MTX had significantly lower mean CDAI at 6 months and higher change in CDAI vs patients in the ADA+non-MTX csDMARD group (p<0.05). In addition, patients on ADA+MTX were more likely to achieve LDA compared to the ADA+non-MTX csDMARD group (Table). Change in PROs and persistency of ADA was comparable in both groups.

Table: Outcomes at 6 months among ADA+MTX and ADA+nonMTX csDMARD therapy

	ADA +MTX	ADA + nonMTX csDMARD[a]	Unadjusted[b]	Adjusted[b,c]
6 month outcomes	Mean (SD)	Mean (SD)	β (95% CI)	β (95% CI)
Mean CDAI at 6 months	11.9 (11.5)	15.7 (13.1)	4.07 (2.09 to 6.04)	3.15 (1.11 to 5.18)
Change in CDAI	-8.8 (13.4)	-7.4 (13.4)	1.72 (-0.85 to 4.29)	3.15 (1.11 to 5.18)
Change in mHAQ	-0.11 (0.39)	-0.1 (0.4)	0.01 (-0.07 to 0.08)	0.01 (-0.07 to 0.08)
Change in pain	-10.1 (26.5)	-9.7 (30.7)	0.68 (-4.51 to 5.88)	1.61 (-3.58 to 6.80)
Change in fatigue	-2.7 (25.9)	-5.3 (25.1)	-2.64 (-9.13 to 3.84)	-2.58 (-9.22 to 4.07)
	Response rate n (%)	Response rate n (%)	Odds Ratio[†] (95% CI)	Odds Ratio[††] (95% CI)
Achievement of Remission (CDAI≤2.8)	46 (15.5%)	13 (8.6%)	0.52 (0.26, 1.06)	0.58 (0.27, 1.26)
Achievement of LDA (CDAI≤10)	136 (45.9%)	47 (31.1%)	0.51 (0.32, 0.80)	0.59 (0.37, 0.96)

mHAQ: modified Health Assessment Questionnaire; LDA: Low Disease Activity; nonMTX csDMARD: non-methotrexate conventional synthetic disease modifying anti-rheumatic drug. [a] Includes leflunomide, sulfasalazine, and hydroxychloroquine. [b] Compared with MTX combination therapy as a reference; [c]Adjusted for age, duration of RA, work status (part-time, full-time, disabled, retired, other), insurance status (none, private, Medicare), prior biologic count, MTX continuation, baseline CDAI, baseline patient pain.

Conclusions: In this real world study, patients on ADA+MTX had significantly greater improvements in disease activity compared to patients on ADA+nonMTX