to confirm observations from DE019. Pts were subgrouped by CRP level at entry (CRP <1 mg/dL, ≥1 mg/dL). Baseline (BL) demographics and disease characteristics were summarized for each group. Clinical efficacy was assessed through swollen/tender joint count (S/TJC) at 66/68 joints, pain, patient global assessment (PtGA), physician global assessment (PhGA), CRP, clinical disease activity index (CDAI), 28-joint disease activity score based on CRP (DAS28-CRP), and proportions of pts achieving ACR20/50/70. Functional outcomes were assessed by the disability index of the health assessment questionnaire (HAQ-DI), and radiographic outcomes by the modified total Sharp score (mTSS). Outcomes were assessed in pts with CRP <0.8 mg/dL in DE019, which included pts with CRP levels as low as 0.75 mg/dL Observed data are reported at week 24.

Results: In DE019, 183 pts (89 and 94 in the ADA and PBO arms, respectively) had CRP <1 mg/dL and 224 pts (118 and 106, respectively) had CRP ≥1mg/dL. Pts with elevated CRP had higher BL disease activity compared with those with CRP <1 mg/dL at entry (not shown). After 24 wks of treatment with ADA, pts in both CRP subgroups experienced significant improvements in most clinical and functional outcomes vs PBO (Table). In pts with CRP <0.8 mg/dL, the ACR20 response rate difference (30.4, p<.001) and the difference in ΔmTSS (-1.3, p<.05) for ADA vs PBO treatment were still significant. Compared to pts with CRP <1 mg/dL, pts with elevated CRP experienced greater clinical and functional improvements. However, within the ADA subgroups, pts with elevated CRP had smaller differences vs PBO in mTSS, perhaps reflecting higher joint damage at BL. In general, similar trends were observed in MUSICA (not shown).

Disease characteristics at Week 24 in patients with CRP <1 or ≥1 mg/dL at entry in DE019

	CRP <1			CRP ≥1		
	PBO n=79	ADA n=74	Difference	PBO n=75	ADA n=101	Difference
TJC68	-13.2	-17.2	-3.2	-11.7	-16.5[e]	-6.0***
SJC66	-7.1	-11.3	-4.3**	-6.7	-12.5[e]	-5.0***
Pain	-13.0	-24.5	-11.7***	-20.3[c]	-35.8	-14.4***
PtGA	-11.0	-24.2	-13.2***	-20.7[c]	-35.5	-16.1***
PhGA	-24.4	-35.0	-10.2**	-28.0[c]	-43.2	-14.2***
HAQ-DI	-0.26[f]	-0.49	-0.24**	-0.38	-0.68	-0.31***
CRP	0.1	0.02	-0.08[g]	-0.54	-2.05	-1.08**
DAS28-CRP	-1.19	-1.92	-0.75***	-1.26[c]	-2.33[e]	-1.10***
CDAI	-15.9	-22.7	-7.6***	-15.7[c]	-26.5[e]	-11.1***
ACR20, n/N (%)	32/79 (41)	50/74 (68)	27***	30/72 (42)	82/99 (83)	41***
ACR50, n/N (%)	9/79 (11)	34/74 (46)	35***	11/72 (15)	46/99 (46)	31***
ACR70, n/N (%)	6/79 (8)	19/74 (26)	18**	0/72 (0)	19/99 (19)	19***
mTSS	0.93[a]	-0.32[b]	-1.30**	1.63[g]	0.79[d]	-0.84

Change from baseline values and least square mean differences (using ANCOVA) are reported for continuous endpoints. p-values for binary endpoints are calculated based on chi-square test or Fisher's exact test. ***, **, *: p < .001, .01 and .05, respectively for differences between treatment groups for change from BL. Missing values are not imputed.
[a]n=82, [b]n=76, [c]n=72, [d]n=102, [e]n=99, [f]n=78, [g]n=84 .
TJC68, tender joint count at 68 joints; SJC66, swollen joint count at 66 joints; PtGA, patients global assessment of disease activity; PhGA, physician's global assessment of disease activity; HAQ-DI, disability index of health assessment questionnaire; CRP, C-reactive protein; DAS28-CRP, 28-joint disease activity score based on CRP; CDAI, clinical disease activity index; mTSS, modified total Sharp score; ACR20/50/70, 20, 50 and 70% improvement in the American College of Rheumatology criteria

Conclusions: While pts with elevated CRP at entry experienced larger improvements from BL in clinical and functional outcomes upon treatment, significant improvements in most outcomes were also observed in those without elevated CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not be required to see differences between active and inactive treatment.

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THU0084 AGREEMENT BETWEEN THE DAS28-ESR AND THE DAS28-CRP AND FACTORS RELATED TO THE DISCREPANCIES BETWEEN DISEASE ACTIVITY LEVELS ACCORDING TO THESE 2 SCORES IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE ESPOIR COHORT

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Background: DAS28 is often used as a treatment decision tool in patients with rheumatoid arthritis (RA) in the daily clinic. Although different versions of DAS28 have previously been validated, and although disease activity thresholds are the same, it is not clear whether DAS28-ESR and DAS28-CRP can be used interchangeably in individual patients.

Objectives: The aims of our study were to examine the agreement between these two DAS28 versions in individual early RA patients in the daily clinic and to idenditify factors related to the discrepancies between disease activity levels according to these 2 scores.

Methods: Baseline and 6 months data from 677 patients with early RA (ACR EULAR 2010) were extracted from the French cohort of early arthritis ESPOIR (at least 2 swollen joints for less than 6 months, DMARD naïve) and were used to calculate DAS28-ESR and DAS28-CRP. Disease activity levels according to the DAS thresholds and EULAR responses were assessed. Intraclass correlation coefficient [ICC] and weighted kappa (k) were calculated. The Bland-Altman method was used to examine the bias between the DAS scores and the 95% limits of agreement (LoA). Multivariate logistic regression was used to determine the patient and RA features independently associated with discrepancies between disease activity levels according to DAS28-ESR and DAS28-CRP.

Results: The mean value of DAS28-CRP (5.04±1.16 at M0 and 3.38±1.33 at M6) was smaller than that of mean DAS28-ESR (5.33±1.24 at M0 and 3.51±1.42 at M6). Agreement between the scores was excellent: ICC=0.93 at M0 and M6. Agreement between disease activity levels according to the 2 scores was good: k=0.70 at M0 and 0.75 at M6. Agreement between EULAR responses at M6 according to the 2 scores was good: k=0.78. At M0, the bias of DAS28-CRP was -0.28 (LoA -1.16, 0.59) and -0.14 (LoA -1.17, 0.89) at M6.There were discrepancies between disease activity levels according to the 2 scores in 122 (18.6%) patients at M0 with clear difference in moderate (88 patients for DAS28-CRP vs 29 for DAS28-ESR) and high disease activity (18 patients for DAS28-CRP vs 80 for DAS28-ESR), and in 171 (28.1%) patients at M6 with clear difference in remission (42 patients for DAS28-CRP vs 29 for DAS28-ESR) and high disease activity (9 patients for DAS28-CRP vs 32 for DAS28-ESR). At M0, presence of erosion (OR 95% CI=1.76 [1.07–2.90]), better mental component of the SF36 (OR 95% CI=2.14 [1.38–3.31]), fewer tender joint counts (TJC) and better physical component of the SF36 (PCS) (with significant interaction between TJC and PCS) were associated with discrepancies between disease activity levels according to the 2 scores. At M6, only being male (OR 95% CI=1.62 [1.09–2.41]) was associated with discrepancies.

Conclusions: DAS28-CRP significantly underestimated disease activity compared to DAS28-ESR. Agreement was high between the 2 scores, good for disease activity levels and EULAR responses. In the individual patient, however, the two scores may differ considerably. The scores should not be used interchangeably in the daily clinic without caution.

Disclosure of Interest: None declared

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THU0085 TIME TO REMISSION AND THE ACHIEVEMENT OF SUSTAINED REMISSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: SITE VARIATION ANALYSIS IN THERAPEUTIC STRATEGY FROM THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Background: Treatment response in ERA reflects individual prognostic factors and therapeutic selection which may be influenced by provider experience and beliefs. This may lead to variations in rates of and time to remission across centres involved in multi-site cohorts.

Objectives: We compared therapeutic strategies across Canadian ERA clinics in relation time to CDAI and DAS28 remission, and frequency of attaining sustained remission.

Methods: Data were analyzed for patients with >1 year of follow-up, enrolled at sites with >40 patients at baseline and >30 patients with 2 years of follow-up data. We determined time to remission and frequency of sustained remission (2 consecutive visits at least 6 months apart), using DAS28 and CDAI scores. Treatment strategy was determined as initial and ever use of oral methotrexate monotherapy, subcutaneous methotrexate monotherapy, methotrexate-based combinations, non-methotrexate DMARDs, triple therapy, or biologic therapy.

Results: 1,749 participants from 13 centers with mean age 54 years, 73% female, mean DAS28 4.9 (SD 1.4) and mean CDAI 25.6 (SD 14.6) were included. There were significant differences between centers in participant characteristics (gender, age, symptom duration, body mass index, comorbidities, smoking status, education, ethnicity, marital status, seropositive status, erosions). The

initial therapeutic strategies were oral methotrexate monotherapy 16% (site range 0%>55%), subcutaneous methotrexate monotherapy 15% (0%>45%), methotrexate-based combination therapy 30% (10%>47%), non-methotrexate DMARDs 19% (4%>44%), triple therapy 11% (0%>60%), and biologics 2% (0%>18%). At 60 months of follow-up, the frequency of use of these strategies was relatively stable except for biologics which increased to 21% (0%>80%). The mean and median time to DAS28 remission was 12.4 months (SD 12.1, range 8.6 to 17.2) and 9 (IQR 3, 18) months respectively. The mean and median time to CDAI remission was 14.8 (SD 13.5, range 10.3 to 21.2) and 9 (IQR 6, 18) months respectively. The frequency of sustained DAS28 remission was 50% (site range 20–70%), and CDAI 35% (12–58%). At the two sites with the highest rates of sustained remission and shortest time to remission, patients had fewer comorbidities and the initial treatment strategy was preferentially methotrexate-based combination therapies, and with eventual advancement to biologics in 7 and 39% in patients. In contrast, the patients at the site with the lowest rates of sustained remission and longest time to remission had long symptom duration at treatment initiation, highest body mass index and proportion with ≥2 comorbidities, worse socioeconomic status and higher baseline DAS28. This site also had the highest proportion of patients treated with biologics at the baseline visit, escalating to 80% by 60 months.

Conclusions: Treatment strategy and patient characteristics vary across CATCH sites and contribute to variable rate and frequency of achieving sustained remission.

Disclosure of Interest: None declared

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THU0086 THE USE OF A BLINDED TRUNCATED ULTRASOUND POWER DOPPLER JOINT COUNT VALIDATES EFFICACY DATA FROM AN EARLY PHASE OPEN LABEL DRUG STUDY TREATING RHEUMATOID ARTHRITIS

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Background: Small open label pilot trials generate important information on tolerability, toxicity, pharmacokinetics, and antigenicity in the early phase investigation of new compounds in the treatment of rheumatoid arthritis (RA). However, because the standard disease activity measures (DAMs), such as the disease activity score in 28 joints (DAS28) have a major subjective component, the efficacy data acquired in such trials is generally felt to be much less reliable than that obtained in blinded trials. Incorporating more objective DAMs, and performing them in a blinded fashion, might enhance the validity of efficacy data in such an early clinical setting.

One possible disease activity measure to fulfill this role would be an ultrasound power Doppler joint count (UPD) which has been shown to correlate with conventional clinical measures[1].

Objectives: To determine whether the blinded use of a truncated (low joint count) UPD in an early phase RA trial correlates with other DAMs in the trial and contributes to validation of efficacy of the drug.

Methods: The results of an open label trial in which Staph Protein A (PRTX-100, Protalex Inc.) was given to patients with active RA has been previously reported[2]. Standard disease activity measurements were obtained. In addition, an UPD was performed utilizing a truncated methodology in which three sites at the dorsal wrist and three dorsal metacarpal sites were analyzed bilaterally for a total of twelve sites studied. There were a total of 117 UPDs performed on eleven patients. UPD were acquired in less than five minutes per study. These UPDs were stored digitally and subsequently read in duplicate in a blinded fashion after completion of the study by the investigator (CW). Each joint site was subjectively scored from 0 (normal) to 3 (severe) with a possible total score of 0 -36 Intra-observer reliability was determined by two-way random intra-class correlations (ICC). Significant changes of UPD and clinical DAMs from baseline to single time points were assessed by the Wilcoxon signed rank test and correlations were performed by the Spearman's rho test (p). Effect size was determined by standardized mean difference (SMD).

Clinical assessments and UPDs were obtained weekly for the first month, then monthly for five more months.

Results: Intra-observer UPD score reproducibility was high (ICC =0.886). Significant reductions ($p<0.05$) in UPD and the DAS28 were found at day 22 and on all subsequent visits. Correlations between UPD and DAMs total scores were moderate to strong. However, the total differences from baseline and visits did not correlate, except for CRP (n=67 p=0.471, $p<0.001$). Also, some individual time points showed differences such as baseline vs day 196 (see table). SRMs for both UPD and DAMs were high, but higher for the DAS28 (1.00–2.16) than for the UPD (0.83–1.10).

Absolute Numbers UPD vs Disease Activity Measures / Differeces UPD vs Disease Activity Measures on Visit Day 196

	N	USP vs	Prob	N	USP vs	
DAS28CRP	71	p=.555	***	11	p=.639	*
DAS28ESR	98	p=.521	***	11	p=.542	*
ESR	97	p=.440	***	11	p=.043	NS
CRP	63	p=.540	***	11	p=588	*
Jt Pain	111	p=.466	***	11	p=.152	NS
Jt. Swelling	113	p=.468	***	11	p=.509	*
Pt. Global	113	p=.313	***	11	p=.422	NS
Dr Global	113	p=.634	***	11	p=.342	NS
CDAI	113	p=.502	***	11	p=.365	NS
Vectra	33	p=.525	***	11	p=.093	NS
	prob <0.05 *		prob <0.01 **		prob <0.001 ***	

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THU0087 DAILY AND DIURNAL VARIATION AND DETERMINATION OF THE MINIMALLY IMPORTANT DIFFERENCE IN RHEUMATOID ARTHRITIS PATIENTS WITH MODERATE TO HIGH MULTI-BIOMARKER DISEASE ACTIVITY SCORES

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Background: The Multi-Biomarker Disease Activity (MBDA) score has been validated as a disease activity metric in rheumatoid arthritis (RA) patients. Patients initiating new therapy or changing therapy frequently have moderate to high MBDA scores. Understanding short term biological variation of MBDA scores in these patients is important in order to determine a minimally important difference (MID).

Objectives: To evaluate biological variation in MBDA scores over a 24-hour period and from day to day in patients with clinically stable RA with moderate to high MBDA scores at baseline and to determine the MID in these patients.

Methods: We performed an analysis of 22 RA patients with moderate or high baseline MBDA scores. Adults with clinically stable seropositive RA (>8 weeks without DMARD and/or biologic medication changes and ≤10 mg prednisone per day) who had MBDA scores of moderate (MBDA 30–44) or high (MBDA >44) were eligible. Serum samples were obtained 5 times over the first 24-hour period (8 AM, 12 PM, 4 PM, 8 PM, and 8 AM); at 12 PM in the next 24-hour period; and at 8 AM the next 2 consecutive days, for a total of 8 timepoints. An additional midnight sample was excluded from the analysis because this timepoint is not relevant to normal clinical practice hours. Diurnal variation was calculated using 5 timepoints over the first 24 hours. Daily variation was determined using 4 timepoints taken at 8 AM on successive days. Combined diurnal and daily variation was calculated using 8 timepoints over 4 days. For each patient, absolute changes in MBDA scores were calculated for all possible pairs of timepoints for: a) diurnal variation (total 220 pairs), b) daily variation (total 132 pairs) and c) diurnal and daily variation (total 616 pairs). MID was calculated as the 90th percentile of absolute

Figure 1. Mean (SE) MBDA Scores over Four Days for Patients with Moderate (n=13) or High (n=9) MBDA Scores at Baseline