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