Q2W than PBO attained ACR50, improvement in HAQ-DI ≥0.35, MDA, DAS28-CRP, and DAPSA ≤14. Improvement persisted on all measures through Week 52.

	1-TNFi Inadequate Responder n/N (%)			2-TNFi Inadequate Responder n/N (%)		
	PBO	Q4W	Q2W	PBO	Q4W	Q2W
ACR50						
Week 24	2/68 (2.9%)	24/71 (33.8%)**	19/65 (29.2%)**	3/41 (7.3%)	15/41 (36.6%)*	16/46 (34.8%)*
Week 52	–	29/71 (40.8%)	20/65 (30.8%)	–	18/41 (43.9%)	13/46 (28.3%)
Improvement in HAQ-DI ≥0.35[a]						
Week 24	9/61 (14.8%)	28/61 (45.9%)**	19/58 (32.8%)*	7/38 (18.4%)	16/36 (44.4%)*	20/41 (48.8%)*
Week 52	–	32/61 (52.5%)	18/58 (31.0%)	–	14/36 (38.9%)	13/41 (31.7%)
MDA						
Week 24	3/68 (4.4%)	22/71 (31.0%)**	14/65 (21.5%)*	1/41 (2.4%)	8/41 (19.5%)*	13/46 (28.3%)**
Week 52	–	26/71 (36.6%)	17/65 (26.2%)	–	11/41 (26.8%)	7/46 (15.2%)
DAPSA ≤14						
Week 24	11/68 (16.2%)	30/71 (42.3%)**	24/65 (36.9%)*	2/41 (4.9%)	14/41 (34.1%)*	12/46 (26.1%)*
Week 52	–	41/71 (57.7%)	26/65 (40.0%)	–	18/41 (43.9%)	14/46 (30.4%)
DAS28-CRP Good Response Criteria[b]						
Week 24	7/68 (10.3%)	33/71 (46.5%)**	24/65 (36.9%)**	2/41 (4.9%)	17/41 (41.5%)**	16/46 (34.8%)**
Week 52	–	38/71 (53.5%)	27/65 (41.5%)	–	19/41 (46.3%)	15/46 (32.6%)

*P<0.05 vs. PBO, **P<0.001 vs. PBO, Fisher's exact test. Missing values imputed using nonresponder imputation.
[a]Patients with ≥0.35 HAQ-DI at baseline.
[b]Good response criteria defined as >1.2 improvement and ≤3.2 present DAS28-CRP.

Conclusion: Both IXE Q4W and Q2W improved the signs and symptoms of PsA in a population of difficult-to-treat patients who have had inadequate response to 1 or 2 TNFi.

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OP0111 A RANDOMIZED, PHASE 3, DOUBLE-BLIND TRIAL EXAMINING METHOTREXATE AND ETANERCEPT AS MONOTHERAPY OR IN COMBINATION FOR TREATING PSORIATIC ARTHRITIS: A COMPARISON OF THE COMPOSITE MEASURES USED TO EVALUATE DISEASE ACTIVITY

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Background: Optimal treatment regimens and measuring outcomes in psoriatic arthritis (PsA) remain key areas of research.
Objectives: To examine methotrexate (MTX) and etanercept (ETN) as monotherapy or in combination in a randomized trial and assess the relative performance of PsA-specific composite measures using trial efficacy data.
Methods: Patients with active PsA naïve to biologic drugs (no prior MTX for PsA) were randomized to 3 groups for 48 weeks: ETN 50mg+MTX 20mg weekly (Combo; N=283); ETN 50mg+placebo weekly (ETN-mono; N=284); or MTX 20mg+placebo weekly (MTX-mono; N=284). At week 24, the American College of Rheumatology (ACR)20 and Minimal Disease Activity (MDA) responses were the primary and key secondary endpoints, respectively. Other PsA-specific composite measures used for disease activity included the Psoriatic Arthritis Disease Activity Score (PASDAS) and Disease Activity Index for Psoriatic Arthritis (DAPSA).
Results: Baseline characteristics were well balanced in the 3 arms. Mean (SD) age was 48.4 (13.1) years and mean/median PsA duration 3.2/0.6 years. ACR20 and MDA responses at week 24 were significantly greater with ETN-mono vs MTX-mono and Combo vs MTX-mono; ETN-mono and Combo had similar results (Table). PASDAS also showed differences between each ETN-containing arm vs MTX-mono and no difference for ETN-mono vs Combo, whereas study arm differences were not seen with DAPSA. PASDAS had a greater effect size and standardized response than DAPSA.
Conclusion: In this large randomized, controlled PsA trial, ETN-mono or Combo had greater efficacy than MTX-mono. Combining ETN and MTX did not improve ETN efficacy. Compared with the joint-focused DAPSA, PASDAS captured a wider range of PsA manifestations and performed better in this trial.

Table: Week 24 Results

	Methotrexate Monotherapy N=284		Etanercept Monotherapy N=284		Methotrexate plus Etanercept N=283	
	Composite endpoint response[a]	ES[c] (SR[d])	Composite endpoint response[a] (P-value)[e]	ES[c] (SR[d])	Composite endpoint response[a] (P-value)[e]	ES[c] (SR[d])
ACR 20, %	50.7	–	60.9 **(P=0.029)**	–	65.0 **(P=0.005)**	–
ACR 50, %	30.6	–	44.4 (P=0.006)	–	45.7 (P<0.001)	–
ACR 70, %	13.8	–	29.2 (P<0.001)	–	27.7 (P<0.001)	–
MDA, %	22.9	–	35.9 **(P=0.005)**	–	35.7 **(P=0.005)**	–
VLDA, %	4.8	–	15.2 (P<0.001)	–	14.3 (P<0.001)	–
PASDAS	-1.98 (0.10)	1.56 (1.26)	-2.64 (0.10) (P<0.001)	2.26 (1.66)	-2.63 (0.11) (P<0.001)	2.15 (1.54)
DAPSA	-22.6 (1.4)	0.92 (1.04)	-25.0 (1.3) (P=0.24)	1.08 (1.25)	-24.9 (1.4) (P=0.23)	1.06 (1.12)

ACR, American College of Rheumatology; DAPSA, Disease Activity Index for Psoriatic Arthritis; ES, effect size; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; SD, standard deviation; SE, standard error; SR, standardized response; VLDA, very low disease activity
[a]Percent patients with response for ACR, MDA, and VLDA; mean change from baseline (SE) for PASDAS and DAPSA
[c]Effect size=(baseline mean−post baseline mean)/SD of baseline mean
[d]Standardized response=(baseline mean−post baseline mean)/SD of change from baseline for that visit, in the same treatment group
[e]P-values are for comparison with methotrexate monotherapy. P-values in bold measured statistical significance; all others are unadjusted

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OP0112 UNACCEPTABLE PAIN DESPITE INFLAMMATION CONTROL AFTER START OF A FIRST ANTI-TNF THERAPY IN PATIENTS WITH PSORIATIC ARTHRITIS AND ITS RELATION TO TREATMENT RESPONSE

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Background: Pain is a major concern of patients with inflammatory arthritides, but while considerable focus has been put on the occurrence and

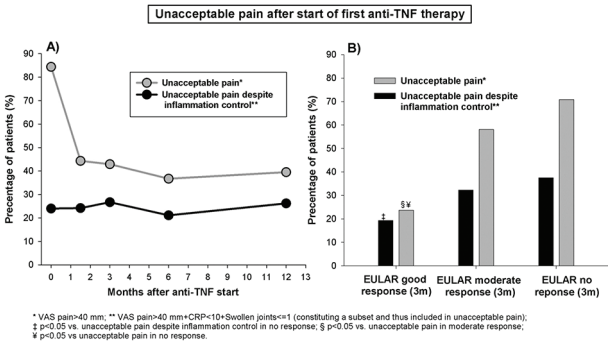
management of pain due to inflammation, less is reported on pain despite inflammation control, with most such reports addressing rheumatoid arthritis (RA).

Objectives: To investigate the prevalence of pain despite inflammation control after start of a first anti-TNF therapy in psoriatic arthritis (PsA) patients and its relation to EULAR treatment response.

To test the feasibility of a network analysis approach to examine associations between clinical variables and mental health symptoms in RA.

Methods: PsA patients starting a first anti-TNF therapy 2004-2010 were identified in the prospective, observational South Swedish Arthritis Group register (n= 352, 48% women), with mean age 47 years and mean disease duration 10 years. At anti-TNF start, 63% of patients had ongoing methotrexate and 68% were on any conventional DMARD(s). Based on the patient acceptable symptom state (PASS) 1, unacceptable pain was defined as >40 mm on a Visual Analogue Scale (VAS) of pain (scale 0-100 mm), and concomitant inflammation control (as in earlier RA studies) was captured through CRP<10 mg/L,2 in combination with <1 swollen joint (of 28).3 Assessments were performed at baseline, 1.5, 3, 6 and 12 months after anti-TNF start. Furthermore, analyses were conducted in relation to EULAR treatment response after 3 months (good, moderate, no response). Differences in pain measures between treatment response groups were estimated by logistic regression.

Results: At start of a first anti-TNF therapy, 84.5% of PsA patients reported unacceptable pain, which declined to 42.9% after 3 months and then remained stable during the rest of the study period, being 39.5% at 12 months (Figure 1A). In contrast, the fraction showing unacceptable pain despite inflammation control was largely unchanged over the study period (24.0 % at treatment start, 26.7% at 3 months and 26.2% at 12 months). Unacceptable pain at 3 months was strongly related to EULAR 3-month response (23.7% of good responders vs. 70.8% of non-responders; p<0.001), whereas for unacceptable pain despite inflammation control the relation was less pronounced (19.3% of EULAR good responders vs 37.5% of non-responders, p=0.016). Among EULAR good responders, unacceptable pain despite inflammation control constituted 81% of all unacceptable pain at 3 months (Figure 1B).



Conclusion: A considerable proportion of PsA patients starting their first biological treatment reported unacceptable pain throughout the first treatment year. Among EULAR good responders non-inflammatory pain made up more than 4/5 of this pain load at 3 months, indicating insufficient effects of biologics on a subset of patients with inflammation-independent pain, and strongly warrants alternative treatment strategies in affected patients.

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OP0113

HISTOLOGICAL AND MOLECULAR PORTRAIT OF THE SYNOVIAL TISSUE IN EARLY TREATMENT-NAÏVE PSORIATIC ARTHRITIS IN COMPARISON WITH RHEUMATOID ARTHRITIS

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Background: Psoriatic Arthritis (PsA) and Rheumatoid Arthritis (RA) are autoimmune joint diseases characterised by chronic inflammation of the synovial tissue (ST). It has been previously suggested that PsA-ST has less marked hyperplasia of the synovial lining and fewer infiltrating T/B cells in comparison with RA. However, several confounders such as treatment, disease duration, sampling techniques and predominance of large joints samples may have influenced these findings.

Objectives: To compare the synovial features of PsA/RA at the beginning of the disease process and prior to any treatment for defining their histological/molecular individual characteristics, and to correlate the histological pattern with clinical parameters.

Methods: 183 consecutive treatment-naïve patients with <12 months symptoms and active synovitis of at least one joint were enrolled into the Pathobiology of Early Arthritis Cohort (PEAC) at the Barts Health NHS Trust, and underwent a baseline US-guided synovial biopsy of an inflamed joint. ST inflammatory infiltrate was evaluated by semi-quantitative score (0-4) of the immunostaining for CD68 (macrophages), CD3 (T cells), CD20 (B cells) and CD138 (plasma cells). Patients were classified as: pauci-immune if CD68sublining (SL)<2 and/or CD3-CD20-CD138<1; diffuse-myeloid if CD68SL≥2, CD20<2 or CD138<2; lymphoid-myeloid if CD20≥2 or CD138>2. RNA sequencing of the ST was performed on 93RA/15PsA patients.

Results: 39/183 patients were diagnosed with PsA (32 polyarticular, 7 oligoarticular) and 144/183 with RA (2010 ACR/EULAR criteria). Age was significantly lower in PsA patients. The comparison of the age-adjusted baseline variables showed: significantly higher number of tender and swollen joints in RA, but no significant differences between ESR, CRP and DAS28; higher US synovial thickening score of the biopsied joint in PsA, but comparable power-doppler. ST was obtained from small joints in 74.4% of PsA and 82% of RA. Histological comparison is summarised in Table 1 and 2. Only in RA, the pauci-immune pathotype associated with significantly lower ESR, CRP and DAS28 compared to lymphoid-myeloid; this association was maintained in a subset of 26 RA patients age- and gender-matched with the PsA population. Transcriptomic profiling showed that PsA-ST has significantly higher expression of the skin fibroblasts, eosinophils and neutrophils cellular gene modules. Genes significantly up regulated in PsA clustered in neutrophil recruitment/enrichment, cell migration and cytoskeleton remodelling modules.

	PsA (n=37)	RA (n=125)	*p value*
CD3	0.9 (1)	1.7 (1.3)	**0.0045***
CD20	0.8 (1.1)	1.4 (1.5)	**0.03***
CD68L	1.5 (1.3)	1.8 (1.2)	0.16
CD68SL	1.8 (1.2)	2.3 (1.2)	**0.04***
CD138	0.8 (1.2)	1.4 (1.5)	**0.02***

	PsA (n=37)	RA (n=125)	*p value*
Pauci-immune	16 (43.2%)	31 (24.8%)	0.056
Diffuse-Myeloid	12 (32.4%)	40 (32%)	
Lymphoid-Myeloid	9 (24.4%)	54 (43.2%)	

Conclusion: The identification of specific histological and molecular signatures characterising early-untreated PsA will help to better understand the disease pathogenesis and explore novel therapeutic targets.

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