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The Performance Characteristics of Composite Measures Used in a Randomized Trial Examining Etanercept and Methotrexate as Monotherapy or in Combination in Patients With Psoriatic Arthritis

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INTRODUCTION

- Psoriatic arthritis (PsA) is a systemic, immune-mediated disease with multiple manifestations (eg, arthritis, psoriasis, enthesitis, and dactylitis)[1]
- Composite measures may be useful for making treatment decisions in PsA since they combine multiple disease domains into a total score that represents disease activity at a specific time point[2,3]
- Composite measures used to evaluate PsA disease activity include:
  - Disease Activity Score 28 (DAS28), Clinical Disease Activity Index (CDAI), and Simplified Disease Activity Index (SDAI), which were developed for rheumatoid arthritis and focus on peripheral arthritis[4-7]
  - Disease Activity Index in PsA (DAPSA), which was developed for PsA and focuses on articular manifestations using 66 joints for a swollen joint count and 68 joints for a tender joint count[8]
  - PsA Disease Activity Score (PASDAS)[9], which was developed to collect data from articular and non-articular PsA manifestations
- It has yet to be determined which measures have the greatest sensitivity for measuring PsA disease activity and have the strongest relationship to patient outcomes
- We examined the relative performance of 5 continuous composite measures (DAS28, CDAI, SDAI, DAPSA, and PASDAS) used in a phase 3, randomized trial[10] in patients with PsA that compared methotrexate monotherapy with etanercept monotherapy and with combination therapy of methotrexate plus etanercept

METHODS

Study Design and Patients

- The Study of Etanercept And Methotrexate in Combination or as Monotherapy in Subjects with Psoriatic Arthritis (SEAM-PsA) was a 48-week, phase 3, double-blind, randomized, multicenter, international, controlled trial
- Key eligibility criteria
  - ≥ 18 years old with active PsA
  - Naïve to etanercept and other biologic agents
  - No prior use of methotrexate for PsA (prior treatment for psoriasis was allowed)
  - ≥ 3 tender and ≥ 3 swollen joints (68/66 joint count)
  - Active psoriatic skin lesion ≥ 2 cm in diameter
- Patients were randomized 1:1:1 to weekly treatments of:
  - Oral methotrexate monotherapy plus subcutaneous placebo
  - Subcutaneous etanercept monotherapy plus oral placebo
  - Combination therapy of subcutaneous etanercept plus oral methotrexate
- Methotrexate was initiated at 10 mg/week and titrated up to 20 mg/week over a 4-week period (the dose could be lowered to as low as 10 mg/week if toxicities occurred)
- Etanercept was administered at 50 mg/week
- At or after week 24, patients with an inadequate response (< 20% improvement in tender and swollen joint counts from baseline) received rescue therapy of etanercept plus methotrexate until week 48
- Dichotomous composite measures utilized: American College of Rheumatology (ACR) 20, ACR 50, ACR 70, Minimal Disease Activity (MDA), and Very Low Disease Activity (VLDA)
- Continuous composite measures utilized: DAS28-C-reactive protein (CRP), CDAI, SDAI, DAPSA, and PASDAS

Study Endpoints

- Previously published study outcomes[10]
  - When compared with methotrexate monotherapy at week 24, a statistically significantly higher number of patients in the etanercept-containing groups achieved an ACR 20 response (primary endpoint) and MDA (key secondary endpoint); more patients in the etanercept-containing groups also achieved ACR 50, ACR 70 responses, and Very Low Disease Activity (VLDA)
  - At week 24, the mean improvement from baseline for the PASDAS score was greater in the etanercept-containing groups compared with methotrexate monotherapy; only modest differences were evident between the 3 treatment groups for the mean changes in DAPSA scores
  - Week 48 safety results indicated no new safety signals associated with etanercept or methotrexate
- Study outcomes not previously published and presented here
  - Mean improvements from baseline to week 24 in DAS28-CRP, CDAI, and SDAI
  - For DAS28-CRP, CDAI, SDAI, DAPSA, and PASDAS, exploratory analyses examined the effect sizes and standardized responses in each treatment group at week 24 and which individual component changes drove the overall change from baseline at week 24 for each composite measure

Statistical Analyses

- Efficacy endpoints (other than the ACR 20 primary and MDA key secondary endpoints) were analyzed as observed and without adjustment for multiplicity; therefore, P-values were descriptive
- The Cochran-Mantel-Haenszel test for all between-treatment comparisons used stratification factors of baseline body mass index status (≤ 30 kg/m^2 or > 30 kg/m^2) and prior use of conventional synthetic disease-modifying antirheumatic drugs
- To calculate the effect size for each continuous composite measure, the following formula was used: (baseline mean − post baseline mean) / standard deviation of baseline mean
- To calculate the standardized response for each composite measure, the following formula was used: (baseline mean − post baseline mean) / standard deviation of change from baseline for that visit in the same treatment group
- The contribution of each component's change to the change in the overall composite score from baseline to week 24 was calculated using the following formula: [change from baseline in each of the component scores / change from baseline in the overall score]

RESULTS

Patient Characteristics

- Of 851 patients enrolled, 284 were randomized to methotrexate monotherapy, 284 to etanercept monotherapy, and 283 to combination therapy. The trial was completed by 691 patients (81.2%)
  - Rescue therapy was received at or after week 24 by 24.3% of patients in the methotrexate monotherapy group, 16.2% in the etanercept monotherapy group, and 12.7% in the combination therapy group
  - During weeks 4 to 24, the mean methotrexate dose in the methotrexate-containing groups was > 18.8 mg (median 20 mg)
- Baseline demographics (**Table 1**) and disease activity (**Table 2**) were generally well balanced across all 3 treatment groups

Table 1. Baseline Demographics

	Methotrexate Monotherapy N = 284	Etanercept Monotherapy N = 284	Combination Therapy N = 283
Age in years, mean (SD)	48.7 (13.1)	48.5 (13.5)	48.1 (12.7)
Female sex, n (%)	160 (56.3)	133 (46.8)	139 (49.1)
White race, n (%)	255 (89.8)	252 (88.7)	265 (93.6)
Duration of PsA in years, mean (SD) [n][a]	3.6 (6.8) [231]	3.1 (6.0) [222]	3.0 (6.0) [231]
Median (Q1, Q3) [n]	0.9 (0.1, 3.3) [231]	0.6 (0.1, 3.0) [222]	0.5 (0.1, 3.0) [231]
Prior use of csDMARD, n (%)	38 (13.4)	26 (9.2)	43 (15.2)
Body mass index (kg/m^2), mean (SD) [n]	30.6 (7.1) [284]	30.4 (6.6) [283]	30.0 (6.7) [283]
≤ 30 kg/m^2, n (%)	146 (51.4)	153 (53.9)	160 (56.5)
> 30 kg/m^2, n (%)	138 (48.6)	130 (45.8)	123 (43.5)

[a]n] is the number of patients analyzed for mean values if different from the full analysis set).
csDMARD: conventional synthetic disease-modifying antirheumatic drug; PsA: psoriatic arthritis; Q1: first quartile; Q3: third quartile; SD: standard deviation.

Table 2. Baseline Disease Activity

	Methotrexate Monotherapy N = 284	Etanercept Monotherapy N = 284	Combination Therapy N = 283
mTSS, mean (SE) [n]*	2.76 (0.12) [269]	2.97 (0.13) [273]	2.70 (0.12) [274]
Psoriasis-affected BSA, mean % (SD)	12.7 (18.8)	10.8 (14.7)	10.7 (15.6)
sPGA, mean (SD) [n]	2.6 (1.1) [281]	2.6 (1.0) [284]	2.5 (1.0) [283]
C-reactive Protein, mean (SD) mg/L [n]	10.5 (16.3) [284]	10.7 (15.6) [282]	8.7 (11.6) [283]
Swollen Joint Count (66 joints), mean (SD) [n]	12.9 (9.9) [284]	11.5 (9.6) [283]	11.2 (9.1) [282]
Tender Joint Count (68 joints), mean (SD) [n]	20.9 (15.0) [284]	18.8 (14.5) [283]	20.0 (15.3) [282]
Swollen Joint Count (28 joints), mean (SD) [n]	7.7 (5.4) [284]	6.8 (5.4) [283]	6.7 (5.0) [282]
Tender Joint Count (28 joints), mean (SD) [n]	10.9 (7.4) [284]	9.5 (7.0) [283]	9.9 (7.4) [282]
Tender Dactylitis Count, mean (SE) [n]	2.3 (0.2) [284]	2.2 (0.2) [283]	2.4 (0.3) [282]
Leeds Dactylitis Index Score > 0 at baseline, n (%) Mean (SE) [n] for patients with > 0 at baseline	98 (34.5) 164.9 (26.9) [98]	96 (33.8) 147.6 (20.8) [96]	90 (31.8) 138.2 (23.9) [90]
Leeds Enthesitis Index Score, mean (SE) [n]	1.5 (0.1) [284]	1.6 (0.1) [283]	1.7 (0.1) [282]
SPARCC Enthesitis Score > 0 at baseline, n (%) Mean (SE) [n] for patients with > 0 at baseline	191 (67.3) 5.7 (0.3) [191]	189 (66.5) 5.5 (0.3) [189]	196 (69.3) 5.9 (0.3) [196]
Physician Global Assessment (0-100), mean (SD) [n]	58.6 (19.4) [284]	58.3 (18.2) [284]	58.0 (17.8) [282]
Patient Global Assessment (0-100), mean (SD) [n]	60.7 (22.5) [283]	62.9 (22.1) [284]	61.0 (20.8) [282]
Patient Global Assessment of pain (0-100), mean (SD) [n]	56.1 (21.7) [283]	56.5 (22.3) [284]	55.7 (21.6) [282]
SF-36 PCS, mean (SD) [n]	35.6 (8.4) [282]	37.8 (8.4) [284]	37.4 (9.2) [282]
Continuous Composite Measures			
DAS28-CRP, mean (SD) [n]; scores range from 2 to 10	4.93 (1.11) [283]	4.80 (1.13) [281]	4.75 (1.12) [281]
CDAI, mean (SD) [n]; scores range from 0 to 76	30.51 (13.26) [283]	28.45 (12.89) [283]	28.55 (12.71) [281]
SDAI, mean (SD) [n]; scores range from 0 to 86	31.56 (13.52) [283]	29.52 (13.19) [281]	29.43 (12.90) [281]
DAPSA, mean (SE) [n]; scores range from 0 to 144 + CRP	46.5 (1.4) [283]	43.4 (1.4) [281]	43.8 (1.4) [281]
PASDAS, mean (SE) [n]; scores range from 0 to 10	6.09 (0.07) [282]	6.05 (0.07) [279]	6.04 (0.07) [280]

*[n] is the number of patients analyzed for mean values (if different from the full analysis set).
BSA: body surface area; CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score (28 joints) using C-reactive protein; mTSS: van der Heijde modified Total Sharp Score; PASDAS: Psoriatic Arthritis Disease Activity Score; SD: standard deviation; SDAI: Simplified Disease Activity Index; SE: standard error; SF-36 PCS: Short Form 36 (health survey) Physical Component Summary; SPARCC: Spondyloarthritis Research Consortium of Canada; sPGA: static Physician Global Assessment.

Efficacy Outcomes From the Dichotomous and Continuous Composite Measures

- More patients achieved ACR, MDA, and VLDA responses at week 24 in the etanercept-containing groups compared with methotrexate monotherapy (**Table 3**)
- The DAS28-CRP and PASDAS continuous composite measures had greater mean changes from baseline to week 24 in the etanercept-containing groups compared with methotrexate monotherapy (**Table 3**). The difference between the etanercept-containing groups and methotrexate monotherapy was most pronounced for PASDAS
- The mean changes from baseline to week 24 for CDAI, SDAI, and DAPSA were similar in all 3 treatment groups, though slightly numerically higher in the etanercept-containing groups (**Table 3**)

Relative Performance of the Continuous Composite Measures

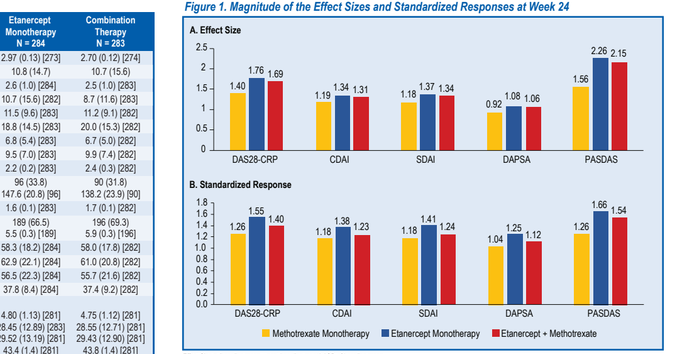
- Across all 5 continuous composite measures, the etanercept-containing groups had numerically larger effect sizes (**Figure 1A**) and standardized responses (**Figure 1B**) than methotrexate monotherapy
- For the effect sizes and standardized responses, PASDAS had the most pronounced difference between the etanercept-containing groups and methotrexate monotherapy (which closely mirrored the efficacy outcomes observed with the dichotomous composite measures) (**Figure 1**)

Table 3. Composite Measure Responses at Week 24

Composite Endpoint Response	Methotrexate Monotherapy N = 284	Etanercept Monotherapy N = 284	P-Value[a] for Methotrexate Monotherapy vs Etanercept Monotherapy	Combination Therapy N = 283	P-Value[a] for Methotrexate Monotherapy vs Combination Therapy
Dichotomous Composite Measures:[b] Percentage of Patients Achieving a Response at Week 24					
ACR 20, n/N (%)	144/284 (50.7)	173/284 (60.9)	**P = 0.029**	184/283 (65.0)	**P = 0.005**
ACR 50, n/N (%)	77/252 (30.6)	114/257 (44.4)	*P = 0.006*	117/256 (45.7)	*P < 0.001*
ACR 70, n/N (%)	35/253 (13.8)	75/257 (29.2)	*P < 0.001*	71/256 (27.7)	*P < 0.001*
MDA, n/N (%)	65/284 (22.9)	102/284 (35.9)	**P = 0.005**	101/283 (35.7)	**P = 0.005**
VLDA, n/N (%)	12/252 (4.8)	39/257 (15.2)	*P < 0.001*	37/258 (14.3)	*P < 0.001*
Continuous Composite Measures: Mean (SE) [n]^c Change From Baseline to Week 24					
DAS28-CRP	−1.55 (0.08) [251]	−1.97 (0.08) [253]	*P < 0.001*	−1.86 (0.08) [256]	*P = 0.01*
CDAI	−15.74 (0.85) [249]	−17.12 (0.78) [257]	*P = 0.26*	−16.43 (0.85) [256]	*P = 0.59*
SDAI	−15.96 (0.86) [248]	−17.75 (0.81) [253]	*P = 0.15*	−17.01 (0.87) [256]	*P = 0.41*
DAPSA	−22.59 (1.4) [251]	−24.99 (1.3) [253]	*P = 0.24*	−24.92 (1.4) [256]	*P = 0.23*
PASDAS	−1.98 (0.10) [246]	−2.64 (0.10) [250]	*P < 0.001*	−2.63 (0.11) [255]	*P < 0.001*

[a]P-values in bold were adjusted for multiplicity and had statistical significance; all others are unadjusted and are italicized.
[b]Data were previously published.[10]
[c]n] is the number of patients examined for mean values if different from the primary analysis set.
ACR: American College of Rheumatology; CDAI: Clinical Disease Activity Index; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score (28 joints) using C-reactive protein; MDA: Minimal Disease Activity; PASDAS: Psoriatic Arthritis Disease Activity Score; SDAI: Simplified Disease Activity Index; SE: standard error; VLDA: Very Low Disease Activity.

Figure 1. Magnitude of the Effect Sizes and Standardized Responses at Week 24



Effect Size = (baseline mean − post baseline mean) / SD of baseline mean.
Standardized Response = (baseline mean − post baseline mean) / SD of change from baseline for that visit in the same treatment group.
CDAI: Clinical Disease Activity Index; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score (28 joints) using C-reactive protein; PASDAS: Psoriatic Arthritis Disease Activity Score; SD: standard deviation; SDAI: Simplified Disease Activity Index.

Degree of Individual Component Contribution to the Continuous Composite Measures

- For DAPSA, DAS28-CRP, CDAI, and SDAI, the main drivers of changes in composite scores from baseline to week 24 were changes in the tender and swollen joint counts (**Table 4**)
- The main drivers of changes in the PASDAS score from baseline to week 24 were changes in the Physician Global Assessment and the Patient Global Assessment; changes in tender and swollen joint counts contributed much less (**Table 5**)
- For PASDAS, changes in the Leeds Enthesitis Index and Tender Dactylitis Count contributed little to the results when analyzing the full analysis set. However, the contribution of changes in the Leeds Enthesitis Index became more prominent in an analysis of a patient subset with Leeds Enthesitis Index of > 0 at baseline (**Table 5**). Similarly, the contribution of changes in Tender Dactylitis Count notably increased in the patient subgroup with Tender Dactylitis Count > 0 at baseline (**Table 5**)
- In contrast to the mean values (which had large confidence intervals), median values for the contribution of each component change to the composite score change from baseline to week 24 were fairly similar between treatment groups (**Tables 4 and 5**)
- To more easily visualize the relative contribution of each component change to the median changes in composite scores from baseline to week 24, pie charts were generated showing percentage contribution of each median value to the overall composite score in each treatment group (**Figure 2**)

Table 4. Contribution of Each Component Measure Change to the Change in Composite Score From Baseline to Week 24 for DAPSA, DAS28-CRP, CDAI, and SDAI

Median (mean; 95% CI) Component Contribution to the Overall Score[a]	DAPSA			DAS28-CRP			CDAI			SDAI		
	MTX N = 251	ETN N = 253	MTX + ETN N = 256	MTX N = 251	ETN N = 253	MTX + ETN N = 256	MTX N = 249	ETN N = 257	MTX + ETN N = 256	MTX N = 248	ETN N = 253	MTX + ETN N = 256
Tender Joint Count[b]	0.46 (0.61: 0.18, 1.03)	0.43 (0.69: 0.26, 1.11)	0.44 (0.4: 0.10, 0.69)	0.48 (0.48: 0.34, 0.61)	0.44 (0.68: 0.32, 1.04)	0.45 (0.55: 0.30, 0.80)	0.36 (0.38: 0.20, 0.56)	0.33 (0.33: 0.29, 0.38)	0.33 (−0.02: −0.46, 0.42)	0.36 (0.43: 0.24, 0.61)	0.32 (0.33: 0.29, 0.38)	0.32 (0.56: −0.13, 1.25)
Swollen Joint Count[b]	0.32 (0.28: 0.02, 0.55)	0.28 (0.20: 0.07, 0.33)	0.30 (0.52: −0.00, 1.03)	0.23 (0.22: 0.17, 0.27)	0.21 (0.32: 0.17, 0.43)	0.21 (0.42: 0.14, 0.69)	0.26 (0.33: 0.25, 0.40)	0.25 (0.31: 0.19, 0.27)	0.24 (0.31: 0.16, 0.47)	0.26 (0.33: 0.25, 0.41)	0.24 (0.23: 0.19, 0.27)	0.22 (0.34: 0.19, 0.49)
Physician Global Assessment	---	---	---	---	---	---	---	0.19 (0.27: 0.15, 0.39)	0.22 (0.28: 0.17, 0.40)	0.20 (0.45: 0.20, 0.70)	0.19 (0.42: 0.20, 0.66)	0.21 (0.11: −0.00, 0.84)	0.20 (−0.02: −0.09, 0.32)	−0.63, 0.59)
Patient Global Assessment	0.09 (0.12: −0.02, 0.27)	0.11 (0.05: −0.15, 0.24)	0.11 (0.04: −0.08, 0.15)	0.19 (0.15: −0.00, 0.30)	0.21 (−0.04: −0.46, 0.37)	0.21 (−0.09: −0.65, 0.46)	0.14 (0.03: −0.19, 0.24)	0.17 (0.15: 0.03, 0.27)	0.16 (0.26: 0.11, 0.40)	0.13 (−0.17: −0.59, 0.26)	0.17 (0.29: 0.10, 0.48)	0.15 (0.07: −0.14, 0.29)
Patient Global Assessment Joint	0.09 (0.09: −0.03, 0.21)	0.09 (0.11: 0.06, 0.16)	0.10 (0.05: −0.08, 0.17)	---	---	---	---	---	---	---	---	---
Pain	---	---	---	---	---	---	---	---	---	---	---	---
C-Reactive Protein	0.0 (−0.11: −0.37, 0.16)	0.01 (−0.04: −0.16, 0.08)	0.01 (0.00: −0.03, 0.04)	0.05 (0.16: 0.05, 0.26)	0.11 (0.07: −0.03, 0.16)	0.11 (0.13: 0.03, 0.23)	---	---	---	0.0 (−0.01: −0.05, 0.04)	0.01 (0.03: 0.01, 0.06)	0.01 (0.05: 0.02, 0.08)

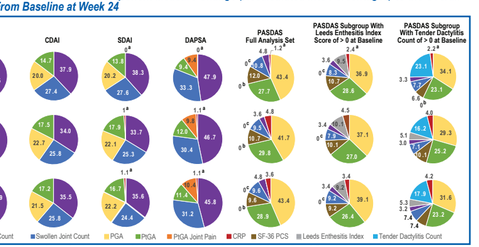
[a]Contributions to the overall score are calculated by [change from baseline in each of the component scores / change from baseline in the overall score]. Positive values indicate changes in the same direction as the change in overall score. Negative values indicate changes in the opposite direction as the change in overall score. Both an individual's [change in scaled component / change in composite score] for all components and the average across all patients for a given treatment group and a visit's [change in scaled component / change in composite score] for all components sum to 1. [b]n = the number of patients examined. [c]Represents a 28-joint count except for DAPSA, which had a 68-joint count. [d]Represents a 28-joint count except for DAPSA, which had a 66-joint count.
CDAI: Clinical Disease Activity Index; CI: confidence interval; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score (28 joints) using C-reactive protein; ETN: etanercept; MTX: methotrexate; SDAI: Simplified Disease Activity Index.

Table 5. Contribution of Each Component Measure Change to the Change in Composite Score From Baseline to Week 24 for PASDAS

Median (mean: 95% CI) Component Contribution to the Overall Score[a]	PASDAS Full Analysis Set			PASDAS: Subgroup With Leeds Enthesitis Index of > 0 at Baseline			PASDAS: Subgroup With Tender Dactylitis Count > 0 at Baseline		
	MTX N = 246	ETN N = 250	MTX + ETN N = 255	MTX N = 161	ETN N = 165	MTX + ETN N = 177	MTX N = 87	ETN N = 86	MTX + ETN N = 86
PGA	0.36 (−0.47: −1.93, 0.99)	0.35 (0.08: −0.48, 0.63)	0.36 (0.41: 0.21, 0.61)	0.31 (−0.90: −3.12, 1.33)	0.33 (−0.08: −0.91, 0.76)	0.34 (0.35: 0.09, 0.61)	0.31 (−1.85: −6.00, 2.29)	0.29 (0.21: 0.11, 0.31)	0.30 (0.29: 0.23, 0.35)
PtGA	0.23 (0.41: −0.13, 0.94)	0.25 (0.31: 0.19, 0.43)	0.24 (0.47: −0.04, 0.99)	0.24 (0.55: −0.27, 1.36)	0.24 (0.28: 0.12, 0.45)	0.23 (0.58: −0.17, 1.32)	0.21 (1.00: −0.44, 2.44)	0.25 (0.26: 0.22, 0.31)	0.22 (0.27: 0.14, 0.39)
SF-36 PCS	0.10 (0.01: −0.26, 0.28)	0.09 (−0.43: −1.24, 0.37)	0.08 (0.15: 0.01, 0.29)	0.09 (−0.06: −0.45, 0.33)	0.09 (−0.69: −1.91, 0.52)	0.08 (0.21: 0.04, 0.39)	0.06 (0.15: 0.04, 0.25)	0.10 (0.10: 0.08, 0.12)	0.07 (0.15: −0.01, 0.31)
Swollen Joint Count (66)	0.09 (0.10: 0.05, 0.15)	0.08 (0.03: −0.07, 0.13)	0.08 (−0.06: −0.33, 0.21)	0.07 (0.07: −0.01, 0.14)	0.07 (−0.01: −0.16, 0.14)	0.08 (−0.11: −0.49, 0.28)	0.07 (0.13: 0.05, 0.20)	0.07 (0.06: 0.04, 0.08)	0.07 (0.12: 0.06, 0.18)
Tender Joint Count (68)	0.04 (0.02: −0.01, 0.05)	0.03 (0.05: −0.02, 0.12)	0.04 (−0.02: −0.18, 0.13)	0.03 (0.03: 0.01, 0.05)	0.03 (0.05: −0.05, 0.16)	0.03 (−0.07: −0.29, 0.15)	0.03 (0.02: −0.01, 0.05)	0.03 (0.02: 0.01, 0.06)	0.03 (0.01: −0.01, 0.04)
Leeds Enthesitis Index	0.0 (0.68: −0.22, 1.58)	0.0 (0.54: −0.48, 1.56)	0.0 (−0.07: −0.32, 0.18)	0.08 (1.04: −0.34, 2.41)	0.09 (0.83: −0.71, 2.37)	0.08 (−0.11: −0.46, 0.25)	0.0 (0.71: −0.68, 2.11)	0.05 (0.04: −0.01, 0.09)	0.05 (0.05: 0.04, 0.07)
Tender Dactylitis Count	0.0 (0.47: −0.13, 1.08)	0.0 (0.25: −0.00, 0.51)	0.0 (0.17: −0.09, 0.43)	0.0 (0.55: −0.32, 1.42)	0.0 (0.37: −0.02, 0.76)	0.0 (0.20: −0.17, 0.58)	0.21 (0.97: −0.65, 2.58)	0.16 (0.27: 0.11, 0.42)	0.17 (0.20: 0.14, 0.25)
C-Reactive Protein	0.01 (−0.23: −0.53, 0.08)	0.04 (0.17: 0.03 (−0.04: −0.15, 0.06)	0.03 (−0.04: −0.74, 0.17)	0.02 (−0.28: −0.03, 0.50)	0.04 (0.24: −0.22, 0.07)	0.03 (−0.07: −0.48, 0.21)	0.02 (−0.13: 0.02, 0.05)	0.04 (0.04: −0.01, 0.36)	0.04 (−0.09: −0.36, 0.18)

[a]Contributions to the overall score are calculated by [change from baseline in each of the component scores / change from baseline in the overall score]. Positive values indicate changes in the same direction as the change in overall score. Negative values indicate changes in the opposite direction as the change in overall score. Both an individual's [change in scaled component / change in composite score] for all components and the average across all patients for a given treatment group and a visit's [change in scaled component / change in composite score] for all components sum to 1. N = the number of patients examined.
CI: confidence interval; ETN: etanercept; MTX: methotrexate; PASDAS: Psoriatic Arthritis Disease Activity Score; PGA: Physician Global Assessment; PtGA: Patient Global Assessment; SF-36 PCS: Short Form 36 (health survey) Physical Component Summary.

Figure 2. Median Contribution of Each Component Measure Change (Recalculated Into Percentages) to the Overall Composite Score From Baseline at Week 24



Contributions to the overall score are calculated by [change from baseline in each of the component scores / change from baseline in the overall score]. For each pie chart, the median values were totaled and then the percentages calculated for how much each component contributed to the whole. Tender Joint Count represents a 28-joint count except for DAPSA, which had a 68-joint count. Swollen Joint count represents a 28-joint count except for DAPSA, which had a 66-joint count.
[a]C-reactive protein. [b]Leeds Enthesitis Index. [c]Tender Dactylitis Count.
CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score (28 joints) using C-reactive protein; ETN: etanercept; MTX: methotrexate; PASDAS: Psoriatic Arthritis Disease Activity Score; PGA: Physician Global Assessment; PtGA: Patient Global Assessment; SDAI: Simplified Disease Activity Index; SF-36 PCS: Short Form 36 (health survey) Physical Component Summary.

SUMMARY

- Of the continuous composite measures examined, PASDAS was the most sensitive and had the highest ability to detect changes in PsA disease activity
- The major contributors to the PASDAS score were the patient and physician global assessments, whereas the swollen and tender joint counts were the major contributors to the DAPSA, DAS28-CRP, CDAI, and SDAI scores

DISCUSSION

- In these analyses, PASDAS was the most sensitive continuous composite measure and had the highest ability to detect treatment-associated differences; these results were consistent with the ACR20 and MDA outcomes. PASDAS also had the largest effect size and standardized response of the 5 continuous composite measures examined
- Composite measures that cover multiple domains, like PASDAS, may be optimal for quantifying PsA disease burden as they appear to show the greatest sensitivity to change and better represent the breadth of disease manifestations
- Key limitations include that the trial was neither designed nor powered for studying the continuous composite outcomes (thus, P-values were descriptive) and did not include a placebo group. In addition, other composite measures used to measure disease activity in patients with PsA (such as Composite Psoriatic Disease Activity Index) were not used in SEAM-PsA. Results may be best applicable to the type of patients included in SEAM-PsA who were early in the course of their disease, methotrexate naïve, and likely to have polyarticular disease
- Though extrapolating findings from a clinical trial to the real-world population of patients with PsA can be challenging, results from this trial can inform planning of future studies (especially active-comparator trials) that use composite measures to evaluate PsA therapies

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