Title: Evaluation of changes in skin and joint outcomes and associated treatment changes in PsA: Experience from the Corrona PsA/SpA Registry

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Abstract **(Word Count: 242)**

Objective: To characterize skin severity and joint activity outcomes and associated treatment changes in patients with PsA through 12 months of follow-up after enrollment in the Corrona Psoriatic Arthritis/ Spondyloarthritis (PsA/SpA) Registry.

Methods: Patients ≥18 years of age with a diagnosis of PsA and a history of PsO between 3/21/13 and 9/30/16 were enrolled (n=647). Demographics, clinical features, and treatment characteristics were collected and stratified by skin severity and joint activity. Change in joint and skin from enrollment to the 12-month visit was classified by change in category of CDAI or BSA. Tests of association evaluated the relationship between changes in therapy and changes in skin severity and joint activity.

Results: Patients with improvement in both joint activity and skin severity saw the largest median reduction in both CDAI and BSA, while those who worsened in both had the greatest median increase in both CDAI and BSA. The majority of PsA patients (>50%) had no change in skin severity regardless if they had reduced therapy (50%), no therapy changes (54%), or increased therapy (56%; p=0.5875). However, there was a significant association between changes in therapy and changes in joint activity (p<0.0001). Patients who increased therapy were more likely to have improvement in joint activity (32% of these patients) compared to patients who reduced therapy (22%) or had no therapy changes (11%).

Conclusion: The clinical implication for our findings suggests the assessment and incorporation of both skin and joint components may be advisable.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease, with manifestations that include inflammation of the joints, periarticular structures, and skin (1). Psoriasis (PsO) affects up to 3.2% of the population in the United States (US) (2) and up to 30% of patients with moderate to severe PsO have PsA (3). Previous studies of patients with PsA have shown a higher impairment of quality of life measures and an increase in overall comorbidities compared to PsO (4, 5). The assessment of patients with PsA requires the consideration of major disease domains, including peripheral arthritis, axial disease, enthesitis, dactylitis, nail disease, and skin disease. Patient treatment decisions should be tailored to the individual and may be based upon disease activity, prognostic factors, access to therapy, and comorbidities (6).

Many biologic treatments used in PsO are also effective in PsA. New and emerging biologics such as IL-17A inhibitors (ixekizumab and secukinumab) and IL-23 inhibitors (guselkumab and risankizumab) have shown encouraging clinical results in treating PsA and PsO, with the IL-17A inhibitors (ixekizumab and secukinumab) currently being used in the treatment of both diseases. Collaborative efforts between dermatologists and rheumatologists along with further research into patient stratification are needed to enable clinicians to make the best use of the myriad of biologic treatment options available (7)(8). Given the relationship between PsA and PsO, treatment of both joint and skin symptoms is important for overall disease management of patients with PsA (7)(9). Managing patients with PsA requires a greater understanding of how joints and skin may respond differently to available therapies.

To our knowledge, no studies have investigated the relationship between changes in drug therapy and changes in skin and joint outcomes in PsA patients. Understanding the outcomes seen in skin disease severity and joint disease activity may identify existing treatment gaps. Therefore, the objective of our study was to characterize skin and joint outcomes and associated treatment changes in

patients with PsA through 12 months of follow-up after enrollment in the Corrona Psoriatic Arthritis/ Spondyloarthritis (PsA/SpA) Registry.

MATERIALS AND METHODS

Study setting. The Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry is an independent, prospective, observational cohort of patients with PsA recruited by rheumatologists at 40 private and academic practice sites across 25 states in the United States. As of March 31, 2018, the Corrona PsA/SpA registry database included information on 2827 patients. Data on 11,525 patient visits and approximately 6,278 patient-years of follow-up observation time had been collected. The mean time of patient follow-up was 3.1 years (median, 3.5 years). Information on disease duration, prognosis, disease severity and activity, medical comorbidities, use of medications including biologics, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and prednisone, and adverse events were collected from both patients and their treating rheumatologists.

Institutional review board approval. The Corrona registry was established according to the Declaration of Helsinki. All participating investigators were required to obtain full board approval for conducting non-interventional research involving human subjects. Sponsor approval and continuing review were obtained through a central IRB (New England Independent Review Board, NEIRB No. 120160610). Respective IRBs supplied full board approval for those academic investigative sites that did not receive a waiver to use the central IRB. Documentation of approval was submitted to Corrona before initiating any study procedures. All registry patients provided written informed consent and authorization before participating.

Study population. Our study population included 647 patients from the Corrona PsA/SpA Registry. These patients were continuously enrolled following an index date defined as enrollment into the Corrona PsA/SpA Registry between March 21, 2013, and September 30, 2016. Enrolled patients included those ≥18 years of age with a diagnosis of PsA (with or without SpA) and with a history of PsO

before or at the time of enrollment into the registry. Patients must have had 12 months of follow-up with Body Surface Area (BSA) and Clinical Disease Activity Index (CDAI) assessments available at enrollment and their 12-month visit.

Data analyses. Demographic characteristics, duration of PsA and PsO, clinical characteristics, patient-reported outcomes, history of PsA drug therapy, and current drug therapy at enrollment were collected. Patients were entered into one of 12 cohorts based on joint disease activity and skin disease severity. Skin disease severity and joint disease activity were categorized as follows: *low skin* (BSA 0 to 1%); *mild skin* (BSA >1 to 3%); *moderate skin* (BSA >3 to 10%), or *high skin* (BSA >10%); and *low joint* (CDAI ≤10); *moderate joint* (10<CDAI≤22), and *high joint* (CDAI >22). We compared baseline patient characteristics, clinical and disease characteristics, and patient-reported factors among the 12 stratified skin disease severity-joint disease activity groups using appropriate methods: analysis of variance (ANOVA) for continuous variables and Chi-square test of association [for categorical variables; Fisher's test used if a cell count was <5].

Improvement in skin disease severity and joint disease activity. Patients were defined as improving in skin disease severity if they were in a lower skin disease severity category at the 12-month follow-up visit compared to status at enrollment. Likewise, patients were defined as worsening in skin disease severity if they were in a higher skin disease severity category at the 12-month follow-up visit compared to status at enrollment. Patients who remained in the same skin disease severity category were defined as no change. Similar definitions were used to define improvement/worsening/no change in joint disease activity. Patients were then categorized into one of nine combined skin/joint improvement groups: improve in both skin and joint, worsen in both skin and joint, no change in both skin and joint, improve in skin/no change in joint, improve in joint/no change in skin, worsen in skin/improve in joint, worsen in joint/improve in skin, worsen in skin/no change in joint, and worsen in

joint/no change in skin. Improvement in skin disease severity and joint disease activity was evaluated in all patients and stratified subgroups by minimal disease activity (MDA) status at baseline.

Changes in drug therapy. Patients were categorized into the following drug status groups: no change in therapy or change in therapy. Changes in therapy that occurred between enrollment and the 12 month visit were captured. Change in therapy included a reduction (patient reducing number of DMARDs) or an increase (patient adding to number of DMARDs or switching from one DMARD to another). Reasons for discontinuation were categorized as efficacy, safety, tolerability, other, or unreported. Change in joint disease activity and skin disease severity from enrollment to the 12-month visit was classified by change in category of CDAI or BSA. P-values from Chi-square tests of association or Fisher's exact test (if cell counts were ≤5) were calculated to evaluate the association between changes in therapy and changes in skin disease severity and joint disease activity. The association between changes in drug therapy and change in joint disease activity and skin disease activity was evaluated in all patients and within stratified subgroups by minimal disease activity (MDA) status at baseline.

RESULTS

Patient baseline demographics and clinical characteristics are presented in Table 1. For our study, 647 patients were included, mean (Standard Deviation, SD) age for all patients was 55.1 (12.6) years, 95% of the patients were white and 52% were females. Of the 647 patients, 47% were categorized as low skin (BSA 0 to 1%); 19% mild skin (BSA >1 to 3%); 21% moderate skin (BSA >3 to 10%), 13% high skin (BSA >10%); 66% low joint (CDAI ≤10); 26% moderate joint (10<CDAI≤22), and 8% high joint (CDAI > 22). For PsA the mean (SD) disease duration was 11.8 (9.7) years for all patients with the longest duration of 15.0 (10.4) years in the high skin/low joint subgroup. Those with the highest skin severity had the longest duration of PsA. The mean duration of PsO was 21.2 (14.7) years for all patients with the longest duration of 28.0 (17.4) years in the high skin/moderate joint subgroup. As with PsA, those in the highest skin subgroup (>10%), had the longest duration of PsO, compared to other skin

subgroups. Furthermore, there were significant differences between subgroups for duration of PsA (p=0.030). Only 17.0% of patients were normal weight (BMI<25), 32.5% were overweight (25≤BMI<30), and 50.6% were obese (BMI≥30). The mean BMI for all patients was 31.2 (obese), 40% of all patients had hypertension, nearly 14% of all patients had diabetes and a similar percentage (14%) suffered from depression. However, except for depression (p=0.036), there were no significant differences among the subgroups for these characteristics. Overall, about ¼ of all patients had enthesitis. There was a significant difference in proportion of patients with enthesitis across BSA/CDAI categories. Within BSA categories, patients in low joint disease activity had a lower proportion of patients with enthesitis compared to patients in moderate or high joint disease activity. Although the data in Table 1 do suggest there may be proportionally higher enthesitis in patients with low skin disease activity in this registry, we compared patients with low BSA (n=306) to those with high BSA (n=81) and found the proportions of enthesitis to be 27.1% and 16.1%, respectively. However, the mean (SD) SPARCC scores, among those with enthesis, was 4.3 (2.7) and 6.4 (4.5) for low and high BSA. We also found similar proportions of patients with dactylitis (5.9 and 8.6%, respectively). Therefore, given these data and the small sample sizes (306 vs 81), we are reluctant to overemphasize this finding until multiple and larger sample sizes are evaluated. We believe this would be an interesting question to answer in a larger data set.

The subgroup mean SPARCC scores for those with enthesitis were significantly different across all subgroups (p=0.048). Patients in the high skin/high joint subgroup had the highest Nail PsO visual analog scale (VAS) with a mean (SD) score of 38.1 (23.4). Overall, 8% of patients had dactylitis. There was a significant difference in the proportion of patients with dactylitis across BSA/CDAI categories. Within BSA categories, patients in low joint disease activity had a lower proportion of patients with dactylitis compared to patients in moderate or high joint disease activity. Among patients with dactylitis, the mean Nail VAS score was 15.0 (SD=18.2). There was a significant difference in mean Nail VAS score among the BSA/CDAI categories. Within BSA categories, patients in high joint disease activity had the

highest mean Nail VAS scores. Over 47% of all patients were in minimal disease activity (MDA) at baseline, with the number of patients in MDA decreasing with increasing BSA and CDAI. Within subgroups, 73% (low skin/low joint), 65% (mild skin/low joint), 51% (moderate skin/low joint), and 37% (high skin/low joint) had achieved MDA ($p<0.001$). When pooling the means of the summarized results of patient global skin assessment in Table 1, we found the results show that patient global skin VAS increases with BSA. The high BSA group had a smaller number of patients, but in general, the patient global skin assessment was lower in the low BSA group and higher in the moderate and high groups. For low BSA, mild BSA, moderate BSA, and high BSA, the pooled patient global VAS score means were 37.9, 41.4, 43.8, and 45.9, respectively.

Table 1 also presents patient-reported outcome measures (PROM) at the time of enrollment. The mean (SD) HAQ was 0.6 (0.7) for all patients with the highest mean (SD) HAQ of 1.9 (0.5) among patients in the high skin/high joint subgroup. Patient-reported EuroQuol Group 5 Dimensional (EQ-5D) VAS was 72.4 (20.9) for all patients and lowest (worst health state) among patients in the high skin/high joint subgroup (mean (SD) of 34.8 [25.8]). There were statistically significant differences between all subgroups for HAQ and EQ-5D VAS scores (both $p<0.001$). Patient-reported pain was 36.3 (29.4) for all patients with the worst pain rating (mean (SD) of 83.5 [12.0]) in the high skin/high joint subgroup.

Overall, 55% of patients had no change in skin disease severity (remained in same severity group at 12 month follow-up visit compared to enrollment visit) while 30% saw improvement in skin disease severity and 16% had worsening skin disease severity. Likewise, 69% of patients had no change in joint disease activity while 19% saw improvement and 12% had worsening joint disease activity (data not shown). Table 2 presents the change in CDAI and BSA by skin disease severity and joint disease activity status. When examining the entire population of 647 patients, we found that 8% of patients had improvement over 12 months in both domains, 41% had no improvement in either domain, with the remainder of patients having improvement of one domain with no change or worsening of the other

domain. Improvement in skin disease severity was seen in 30% of patients (median decrease in BSA ranging between 2-5%) and worsening in skin disease severity was seen in 16% of patients (median increase in BSA ranging from 2-3%). Improvement in joint disease activity was seen in 19% of patients (median decrease in CDAI ≥5.5) and worsening of joint disease activity was seen in 12% of patients (median increase in CDAI ≥6.5). Patients with improvement in both joint disease activity and skin disease severity saw the largest median reduction in both CDAI and BSA, while those who worsened in both had the greatest median increase in both CDAI and BSA.

Table 3 presents the relationship between improvement in skin disease severity or joint disease activity and changes in drug therapy from baseline to 12-month follow-up visit among all patients. The majority (57%) had no change in therapy within the first 12 months after enrollment while 35% had an increase in therapy and 8% had a reduction in therapy. Among the 21 patients that had worsened in both joint disease activity and skin disease severity, 38% had no change in therapy, 14% reduced therapy, and 48% had at least one change in therapy. Of the 54 patients who had improvement in both domains, 37% had no change in therapy, 11% reduced therapy, and 52% had at least one change in therapy. A larger percent of patients who saw joint improvement (58%) had at least one change in therapy versus those with skin improvement (31%). Of the 194 patients who improved in skin disease severity alone (not taking into account of changes in joints), 60% had no change in therapy, 9% reduced therapy, and 41% had at least one change in therapy. Among the 120 patients who improved in joint disease activity alone (not taking into account changes in skin), 33% had no change in therapy, 10% reduced therapy, and 58% had at least one change in therapy. Of the 100 patients that worsened in skin alone, the majority (52%) had no change in therapy while 43% of the 79 patients who worsened in joint alone had no change in therapy. Among patients with a reason for changing therapy lack of efficacy was the most frequently identified reason for therapy change (Table 3).

As noted, the majority (57%) of patients did not have a change in therapy within the first year after enrollment; however, 284 (47%) patients were in minimal disease activity (MDA) at time of enrollment. When evaluating changes in therapy stratified by MDA status at enrollment, we observed that 71% of patients who were in MDA at enrollment had no therapy changes versus only 45% of patients who were not in MDA at enrollment (Table 4). Similarly, only 19% of patients in MDA at enrollment had an increase in therapy versus 48% of patients not in MDA at enrollment had an increase in therapy.

We observed that those patients who had an increase in therapy, were more likely to have improvement in joint disease activity but not skin disease severity. Figure 1a summarizes changes in skin disease severity and Figure 1b summarizes changes in joint disease activity, with therapy decisions for all patients stratified by MDA status at baseline. The majority of PsA patients (>50%) had no change in skin disease severity (remained in same severity category) regardless if they had reduced therapy (50%), had no therapy changes (54%), or increased therapy (56%; p=0.5875, Figure 1a). However, there was a significant association between changes in therapy and changes in joint disease activity (p<0.001; Figure 1b). Patients who increased therapy were more likely to have improvement in joint disease activity (32% of these patients) compared to patients who reduced therapy (22%) or had no therapy changes (11%).

For patients in MDA at baseline, the vast majority (>50%) of patients had no change in skin disease severity or joint disease activity (even if therapy changes had occurred) and there was no association between changes in therapy and changes in skin disease severity (P=0.2953, Figure 1a) or changes in joint disease activity (p=0.0961, Figure 1b). Among patients not in MDA at baseline, patients who experienced some type of therapy changes (increased therapy or reduction of therapy) had similar improvement in joint disease activity (39%) which was higher compared to those with no change in therapy (only 17% improved; p<0.0001, Figure 1b). On the other hand, there was no association of the change in therapy with change in skin disease severity for the patients not in MDA (p=0.3057, Figure 1a).

DISCUSSION

To our knowledge many of these analyses have not been performed in a real-world setting of PsA patients. In addition, comparisons in 12 cohorts based on skin severity and joint disease activity have not been shown previously. We believe our study is the first to simultaneously investigate skin and joint outcomes in association with treatment changes in PsA patients. A large number of our patients were in low skin activity at the beginning of the study and subsequently had no change in therapy. However, when patients did have an increase in therapy, they were more likely to have improvement in joint disease activity rather than skin disease severity. These findings may be due, in part, to an increased emphasis on joint rather than skin assessment and improvement. The study cohort was derived from patients seen by rheumatologists; therefore, the care may have been focused on arthritic symptoms rather than skin manifestations. It is conceivable that therapies chosen for treatment were selected based on their effectiveness for arthritis rather than skin.

Patients with improvement in both joint disease activity and skin disease severity saw the largest median reduction in both CDAI and BSA, while those who worsened in both had the greatest median increase in both CDAI and BSA. We believe our results underscore the need for a Treat-to-Target (T2T) strategy in PsA, addressing both joint disease activity and skin disease severity (10). The Tight Control of Psoriatic Arthritis (TICOPA) study was the first to test the T2T concept in PsA. Results from the TICOPA study showed patients in the tight control group were nearly two times more likely to achieve the American College of Rheumatology 20% response (ACR20) (Odds Ratio (OR), 1.91, 95% Confidence Interval (CI) 1.03-3.55; p=0.04) and nearly three times more likely to achieve a PASI75 response (OR, 2.92, 95% CI: 1.51-5.65, p=0.02) at 48 weeks than the standard care group, thus suggesting that a T2T strategy is appropriate for PsA (11).

To achieve better results in both skin disease severity and joint disease activity, the importance of collaborative care among rheumatologists and dermatologist is increasingly being recognized.

International organizations such as the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and those members of the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN) in North America are working towards simultaneously improving care for PsO and PsA patients and recognizing arthritis at an early stage (12). Our findings that some patients with severe skin and/or joint involvement did not see improvement highlights the need for rheumatologists and dermatologists to work collaboratively over the long term in the management of both domains of PsA (13-18). Psoriasis typically presents years before symptoms of PsA with a lag time of 7-12 years from the onset of PsO to diagnosis of PsA. Since most PsA patients present to a dermatologist before the onset of joint symptoms, routinely screening PsO patients for PsA gives the dermatologist the opportunity to refer the patients to a rheumatologist earlier in the disease leading to improved outcomes (7). Early diagnosis of PsA will limit its progression leading to less joint damage and improvement in the patient's quality of life.

Our study is not without limitations. The findings are descriptive, and some characteristics may be highly correlated as no statistical adjustments were made. Rheumatology practices collect data for this registry and information on topical therapy for psoriasis or light therapy is not collected. In addition, this is a cross-section of an observational study where we evaluated the association between change in therapy and change in skin severity and joint activity but it does not evaluate causation. The data source is from a North American registry and the results may not be generalizable to others outside the US. Our study population offered little ethnic diversity and most of our patients were white. Moreover, only a small number of patients had reasons for change in therapies and the follow-up period was only for one year. Future studies with a more diverse ethnic population and longer follow-up are needed to address these shortcomings.

The clinical implication for our findings suggests a T2T approach, requiring the assessment and incorporation of both skin and joint components, may be advisable. Similar studies can help bolster

efforts to educate both patients and providers on the need for serial evaluation of disease activity and changes in therapy until the target disease activity is achieved.

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FIGURE LEGENDS

Figure 1a. Changes in Therapy and Changes in Skin Disease Severity among All Patients and Stratified by MDA Status at Baseline

Figure 1b. Changes in Therapy and Changes in Joint Disease Activity among All Patients and Stratified by MDA Status at Baseline

Table 1. Patient baseline demographic and clinical characteristics of all PsA patients at time of enrollment; stratified by levels of BSA and CDAI

BSA / CDAI	All Patients	PsA Patients Categorized by Skin & Joint activity												
		Low (0 to 1%)			Mild (>1 to 3%)			Moderate (>3 to ≤10%)			High (>10%)			P-Value
		Low	Moderate	High	Low	Moderate	High	Low	Moderate	High	Low	Moderate	High	
	647	225	63	18	82	29	12	78	45	14	42	29	10	
Age (yrs): Mean (SD)	55.1 (12.6)	55.3 (12.4)	60.1 (11.7)	58.4 (8.1)	54.4 (12.7)	58.0 (11.3)	59.1 (15.7)	53.6 (13.1)	52.4 (12.3)	49.2 (15.9)	55.0 (13.2)	51.8 (12.5)	45.5 (9.3)	<0.001
Sex: *n* (%) Female	337 (52.4%)	113 (50.7%)	33 (52.4%)	11 (61.11%)	49 (59.8%)	15 (51.7%)	7 (58.3%)	29 (37.2%)	29 (64.4%)	9 (64.3%)	18 (45.0%)	16 (55.12%)	8 (80.0%)	0.095
Race: *n* (%) White	594 (94.7%)	208 (95.9%)	58 (95.1%)	16 (94.11%)	76 (95.0%)	27 (96.4%)	10 (90.9%)	74 (97.4%)	42 (93.3%)	12 (92.3%)	41 (100.0%)	21 (75%)	9 (90.0%)	0.005
BMI: Mean (SD)	31.2 (7.0)	30.0 (6.4)	31.5 (8.3)	34.1 (6.9)	31.5 (7.3)	30.8 (5.4)	32.0 (6.6)	30.8 (6.3)	33.8 (8.8)	30.1 (6.9)	30.7 (6.3)	33.8 (6.3)	36.0 (10.2)	0.006
BMI Categories:														
Normal (BMI<25)	106 (17.0%)	40 (18.7%)	14 (22.6%)	1 (5.6%)	17 (21.0%)	3 (11.1%)	1 (9.1%)	12 (15.6%)	5 (11.6%)	2 (15.4%)	8 (19.5%)	2 (7.1%)	1 (10.0%)	0.62
Overweight (25≤BMI<30)	203 (32.5%)	84 (39.3%)	18 (29.0%)	5 (27.8%)	17 (21.0%)	7 (25.9%)	4 (36.4%)	28 (36.4%)	12 (27.9%)	5 (38.5%)	14 (34.2%)	8 (28.6%)	1 (10.0%)	0.22
Obese (BMI≥30)	316 (50.6%)	90 (42.1%)	30 (48.4%)	12 (66.7%)	47 (58.0%)	17 (3.0%)	6 (54.6%)	37 (48.1%)	26 (60.5%)	6 (46.2%)	19 (46.3%)	18 (64.3%)	8 (80.0%)	0.05
PsA Disease Duration (yrs): Mean (SD)	11.8 (9.7)	12.9 (10.1)	11.6 (8.7)	8.6 (6.2)	9.3 (7.6)	13.0 (11.3)	10.7 (7.6)	11.4 (8.1)	9.2 (10.0)	6.5 (5.6)	15.0 (10.4)	13.9 (13.3)	14.6 (12.6)	0.0256
PsO Disease Duration (yrs): Mean (SD)	21.2 (14.7)	21.8 (15.5)	19.9 (15.5)	14.4 (11.5)	19.4 (14.9)	22.7 (12.8)	24.5 (10.2)	20.9 (12.3)	18.8 (14.3)	15.4 (10.1)	23.2 (14.8)	28.0 (17.4)	23.2 (11.0)	0.1768
Renal Disease *n* (%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.268
Hypertension *n* (%)	259 (40.0%)	80 (35.6%)	31 (49.2%)	8 (44.4%)	32 (39.0%)	12 (41.4%)	5 (41.8%)	35 (44.9%)	17 (37.8%)	3 (21.4%)	17 (40.5%)	14 (48.3%)	5 (50.0%)	0.676
Hyperlipidemia *n* (%)	176 (27.2%)	53 (23.6%)	19 (30.2%)	4 (22.2%)	23 (28.1%)	11 (37.9%)	5 (41.7%)	24 (30.8%)	9 (20.0%)	2 (14.3%)	12 (28.6%)	13 (44.8%)	1 (10.0%)	0.233
Any CVD: *n* (%)	89 (13.8%)	29 (12.9%)	12 (19.1%)	1 (5.6%)	10 (12.2%)	4 (13.8%)	3 (25.0%)	11 (14.1%)	7 (15.6%)	1 (7.1%)	3 (7.1%)	7 (24.1%)	1 (10.0%)	0.613
Any Cancer: *n* (%)	50 (7.7%)	17 (7.6%)	4 (6.4%)	1 (5.6%)	7 (8.5%)	0 (0.0%)	1 (8.3%)	7 (9.0%)	3 (6.7%)	1 (7.1%)	5 (11.9%)	3 (10.3%)	1 (10.0%)	0.956
Diabetes Mellitus: *n* (%)	90 (13.9%)	27 (12.0%)	11 (17.5%)	2 (11.1%)	7 (8.5%)	3 (10.3%)	2 (16.7%)	9 (11.5%)	9 (20.0%)	1 (7.1%)	8 (19.1%)	8 (27.6%)	3 (30.0%)	0.244
Uveitis/Iritis: *n* (%)	20 (3.1%)	6 (2.7%)	2 (3.2%)	0 (0.0%)	5 (6.1%)	1 (3.5%)	1 (8.3%)	2 (2.6%)	1 (2.2%)	1 (7.1%)	1 (2.4%)	0 (0.0%)	0 (0.0%)	0.831
Asthma: *n* (%)	51 (7.9%)	12 (5.3%)	7 (11.1%)	2 (11.1%)	7 (8.5%)	5 (17.2%)	1 (8.3%)	6 (7.7%)	4 (8.9%)	2 (14.3%)	3 (7.1%)	2 (6.9%)	0 (0.0%)	0.667
Depression: *n* (%)	89 (13.8%)	25 (11.1%)	6 (9.5%)	4 (22.2%)	11 (13.4%)	6 (20.7%)	1 (8.33%)	8 (10.3%)	12 (26.7%)	1 (7.1%)	4 (9.5%)	9 (31.0%)	2 (20.0%)	0.036
Fibromyalgia: *n* (%)	35 (5.4%)	8 (3.6%)	1 (1.6%)	6 (33.3%)	5 (6.1%)	3 (10.3%)	1 (8.3%)	1 (1.3%)	4 (8.9%)	2 (14.3%)	1 (2.4%)	2 (6.9%)	1 (10.0%)	<0.001
Serious Infections *n* (%)	30 (4.6%)	11 (4.9%)	3 (4.8%)	0 (0.0%)	1 (1.2%)	3 (10.3%)	1 (8.3%)	4 (5.1%)	3 (6.7%)	0 (0.0%)	2 (4.8%)	2 (6.9%)	0 (0.0%)	0.753
Enthesitis: n(%)	153 (23.7%)	53 (23.6%)	21 (33.3%)	9 (50.0%)	14 (17.1%)	8 (27.6%)	3 (25.0%)	7 (9.0%)	16 (35.6%)	9 (64.3%)	2 (4.8%)	9 (31.0%)	2 (20.0%)	<0.001

SPARCC Score (among those with Enthesitis): Mean (SD)	4.7 (3.2)	3.5 (2.6)	4.4 (2.3)	6.6 (3.0)	3.3 (2.5)	4.1 (2.9)	5.7 (2.1)	6.7 (3.1)	3.7 (2.1)	7.7 (4.7)	6.5 (0.7)	6.1 (5.0)	7.0 (7.0)	0.0482
Dactylitis: *n* (%)	52 (8.0%)	8 (3.6%)	8 (12.7%)	2 (11.1%)	2 (2.4%)	5 (17.2%)	3 (25.0%)	3 (3.9%)	11 (24.4%)	3 (21.4%)	1 (2.4%)	3 (10.3%)	3 (30.0%)	<0.001
Nail Involvement: n(%)	293 (45.3%)	75 (33.3%)	32 (50.8%)	8 (44.4%)	31 (37.8%)	17 (58.6%)	4 (33.3%)	41 (52.6%)	25 (55.6%)	13 (92.7%)	19 (45.2%)	20 (69.0%)	8 (80.0%)	<0.001
Nail PsO VAS (among those with Nail Involvement): Mean (SD)	15.0 (18.2)	9.8 (11.1)	9.5 (9.0)	23.1 (22.3)	10.6 (12.4)	10.5 (12.4)	24.5 (20.3)	13.3 (18.0)	21.8 (22.0)	28.8 (34.9)	17.0 (20.8)	24.4 (20.6)	38.1 (23.4)	<0.001
MDA: *n* (%)	284 (47.3%)	158 (72.8%)	14 (25.5%)	0 (0.0%)	49 (65.3%)	8 (30.8%)	1 (10.0%)	38 (51.4%)	0 (0.0%)	0 (0.0%)	14 (36.8%)	2 (7.7%)	0 (0.0%)	<0.001
Patient Global Joint Assessment VAS (0-100): N_o	647	225	63	18	82	29	12	78	45	14	42	29	10	<0.001
Mean (SD)	42.2 (31.0)	31.8 (29.7)	62.5 (29.4)	71.7 (23.4)	34.4 (27.9)	58.9 (30.0)	55.8 (21.9)	35.7 (27.0)	57.2 (25.3)	58.0 (21.4)	30.6 (25.1)	57.8 (31.4)	62.5 (29.1)	
Patient Global Skin Assessment VAS (0-100): N_o	645	224	62	18	82	29	12	78	45	14	42	29	10	<0.001
Mean (SD)	40.8 (30.6)	30.4 (29.6)	56.0 (29.4)	68.3 (23.3)	35.1 (27.5)	52.4 (30.8)	57.5 (20.9)	32.6 (26.3)	59.6 (24.4)	55.6 (23.4)	34.7 (26.3)	54.2 (31.9)	68.5 (33.9)	
HAQ: N_o	608	219	57	15	76	28	10	74	41	14	38	26	10	<0.001
Mean (SD)	0.6 (0.7)	0.4 (0.6)	0.8 (0.7)	1.3 (0.7)	0.5 (0.6)	0.6 (0.6)	1.1 (0.8)	0.3 (0.4)	1.0 (0.6)	1.2 (0.7)	0.4 (0.5)	1.0 (0.8)	1.9 (0.5)	
Patient Pain VAS (0-100): N_o	603	218	56	16	75	26	10	74	40	14	38	26	10	<0.001
Mean (SD)	36.3 (29.4)	26.2 (26.0)	42.9 (27.0)	67.1 (30.2)	30.9 (25.6)	39.2 (31.0)	51.0 (25.3)	30.1 (27.0)	58.1 (26.5)	56.7 (25.0)	35.0 (27.9)	51.8 (28.8)	83.5 (12.0)	
EQ5D VAS (0-100): N_o	641	221	63	18	82	29	12	77	44	14	42	29	10	<0.001
Mean (SD)	72.4 (20.9)	79.0 (17.8)	66.3 (19.8)	42.1 (20.1)	73.9 (19.3)	76.9 (16.0)	64.9 (19.9)	78.4 (16.3)	63.8 (24.2)	67.3 (18.2)	76.0 (16.2)	55.0 (20.3)	34.8 (25.8)	
Morning Stiffness: N_o	618	218	60	14	78	28	11	72	45	14	40	28	10	<0.001
0 hrs: n (%)	77 (12.5%)	38 (17.4%)	5 (8.3%)	0 (0.0%)	11 (14.1%)	2 (7.1%)	0 (0.0%)	10 (13.9%)	2 (4.44)	0 (0.0%)	5 (12.5%)	4 (14.3%)	0 (0.0%)	
1-29 mins: n (%)	156 (25.2%)	69 (31.7%)	14 (23.3%)	1 (7.1%)	20 (25.6%)	4 (14.3%)	1 (9.1%)	23 (31.9%)	8 (17.8%)	3 (21.4%)	11 (27.5%)	2 (7.1%)	0 (0.0%)	
30 mins to <1 hr: n (%)	146 (23.6%)	51 (23.4%)	17 (28.3%)	1 (7.1%)	17 (21.8%)	8 (28.6%)	1 (9.1%)	21 (29.2%)	7 (15.6%)	3 (21.4%)	13 (32.5%)	7 (25.0%)	0 (0.0%)	
1hr to <1.5hrs: n (%)	113 (18.3%)	35 (16.1%)	12 (20.0%)	4 (28.6%)	15 (19.2%)	10 (35.7%)	3 (27.23%)	10 (13.9%)	12 (26.7%)	3 (21.4%)	3 (7.5%)	6 (21.4%)	0 (0.0%)	

P-value represents comparisons between CDAI/BSA subgroups analyzed using ANOVA (continuous variables) or chi-square tests (or Fisher's exact tests for continuous variables), as appropriate; Low joint (CDAI ≤10); moderate joint (10<CDAI≤22), and high joint (CDAI > 22); BMI, body mass index; BSA, body surface area; CDAI, Clinical Disease Activity Index; CVD, cardiovascular disease; EQ5D, EuroQuol Group EQ-5D descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression; HAQ, Health Assessment Questionnaire; hrs, hours; MDA, minimal disease activity; PsA, psoriatic arthritis; PsO, psoriasis; SPARCC, Spondyloarthritis Research Consortium of Canada; SD, standard deviation; VAS, visual analog scale; yrs, years

Table 2: Median change in CDAI and BSA by skin disease severity and joint disease activity status

	All Patients			
	n	**%**	Δ in CDAI median (IQR)	Δ in BSA median (IQR)
Improvement				
Improve on both	54	8.3	-11.5 (-15.5, -8.5)	-5 (-12, -2)
Improve in Skin, no change in Joints	118	18.2	-0.8 (-3.5, 1)	-4 (-9, -2)
Improve in Joints, no change in Skin	54	8.3	-8.5 (-11.4, -5.5)	0 (-1, 0)
No Change in both	263	40.7	0 (-2.1, 1.5)	0 (0, 0)
Worsen in Skin, Improve in Joints	12	1.9	-9.3 (-12.2, -4.5)	2 (1.5, 4)
Worsen in Joints, Improve in Skin	22	3.4	7.7 (5, 12.5)	-3 (-10, -1)
Worsen in Skin, No change in Joints	67	10.4	0 (-1.2, 2.7)	2 (2, 5)
Worsen in Joints, No change in Skin	36	5.6	10.2 (5.5, 13.1)	0 (-1, 0)
Worsen in Both	21	3.2	10.3 (8, 16)	2 (2, 5)
TOTAL	647	100.0	-0.5 (-4.5, 2.5)	0.0 (-2.0, 0.0)

Δ, change; CDAI, Clinical Disease Activity Index; IQR, interquartile range; BSA, Body Surface Area

Table 3. Treatment changes among the 647 patients by improvement group for skin disease severity and joint disease activity

	All Patients	No Change in Therapy*	Reduced Therapy*	At least 1 Change in Therapy*	Patients with at least 1 Change in Therapy that Provided a Reason for Change	Due to Efficacy†	Due to Other Reason†	Due to Safety†	Due to Tolerability†
Changes in Skin Severity and Joint Activity									
Improved in both	54	20 (37.0)	6 (11.1)	28 (51.9)	11	2 (18.2)	4 (36.4)	3 (27.3)	2 (18.2)
Improve on Skin, No Change in Joints	118	84 (71.2)	9 (7.6)	25 (21.2)	15	6 (40.0)	5 (33.3)	3 (20.0)	1 (6.7)
Improve on Joints, No Change in Skin	54	14 (25.9)	6 (11.1)	34 (63.0)	12	5 (41.7)	5 (41.7)	1 (8.3)	1 (8.3)
No Change in Either	263	173 (65.8)	18 (6.8)	72 (27.4)	44	27 (61.4)	7 (15.9)	7 (15.9)	3 (6.8)
Worsen in Skin, Improve in Joints	12	5 (41.7)	0 (0.0)	7 (58.3)	2	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)
Worsen in Joints, Improve in Skin	22	12 (54.5)	3 (13.6)	7 (31.8)	7	6 (85.7)	0 (0.0)	0 (0.0)	1 (14.3)
Worsen in Skin, No Change in Joints	67	39 (58.2)	6 (9.0)	22 (32.8)	15	6 (40.0)	3 (20.0)	2 (13.3)	4 (26.7)
Worsen in Joints, No Change in Skin	36	14 (38.9)	3 (8.3)	12 (66.7)	20	12 (60.0)	3 (15.0)	4 (20.0)	1 (5.0)
Worsen in Both	21	8 (38.1)	3 (14.3)	10 (47.6)	11	8 (72.7)	1 (9.1)	2 (18.2)	0 (0.0)
Total	647	369 (57.0)	54 (8.3)	224 (34.6)	137	73 (53.3)	29 (21.2)	22 (16.1)	13 (9.5)
Changes in Skin Severity Alone									
Improved	194	116 (59.8)	18 (9.3)	60 (41.2)	33	14 (42.4)	9 (27.3)	6 (18.2)	4 (12.1)
No Change	353	201 (56.9)	27 (7.6)	125 (35.4)	76	44 (57.9)	15 (19.7)	12 (15.8)	5 (6.6)
Worsened	100	52 (52.0)	9 (9.0)	39 (39.0)	28	15 (53.6)	5 (17.9)	4 (14.3)	4 (14.3)
Changes in Joint Activity Alone									
Improved	120	39 (32.5)	12 (10.0)	69 (57.5)	25	8 (32.0)	10 (40.0)	4 (16.0)	3 (12.0)
No Change	448	296 (66.1)	33 (7.4)	119 (26.6)	74	39 (52.7)	15 (20.3)	12 (16.2)	8 (10.8)
Worsened	79	34 (43.0)	9 (11.4)	39 (45.6)	38	26 (68.4)	4 (10.5)	6 (15.8)	2 (5.3)

*Frequency (percentages) for columns (no change, reduced, or at least one change in therapy) are based on a denominator of all patients.

†Frequency (percentages) for columns (reasons due to efficacy, safety, other reason, and tolerability) are calculated based on the number of patients with at least one change in therapy and have at least one reason given for change. Those that have at least one change in therapy and don't give a reason for changing therapy are not included in the denominator for calculating the percentage.

Table 4: Changes in therapy and improvement in skin disease severity and joint disease activity stratified by baseline Minimal Disease Activity (MDA) status

	All Patients	Reduced Therapy	No Change in Therapy	Increased Therapy
In MDA at Baseline	N=284	N=28	N=201	N=55
Changes in Skin Severity Alone		n (% of N)	n (% of N)	n (% of N)
Improved	65	4 (14.3)	53 (26.4)	8 (14.5)
No Change	173	20 (71.4)	116 (57.7)	37 (67.3)
Worsened	46	4 (14.3)	32 (15.9)	10 (18.2)
Changes in Joint Activity Alone				
Improved	18	2 (7.1)	11 (5.4)	5 (9.1)
No Change	234	21 (75.0)	173 (86.1)	40 (72.7)
Worsened	32	5 (17.9)	17 (8.4)	10 (18.2)
Not In MDA at Baseline	N=316	N=23	N=141	N=152
Changes in Skin Severity Alone		n (% of N)	n (% of N)	n (% of N)
Improved	118	12 (52.2)	56 (39.7)	50 (32.8)
No Change	149	7 (30.4)	66 (46.8))	76 (50.0)
Worsened	49	4 (14.3)	19 (13.4)	26 (17.1)
Changes in Joint Activity Alone				
Improved	93	9 (39.1)	24 (17.0)	60 (39.5)
No Change	178	10 (43.4)	101 (71.6)	67 (44.1)
Worsened	45	4 (17.4)	16 (11.3)	25 (16.4)

MDA: Minimal Disease Activity

47 patients had unknown MDA status at time of enrollment (baseline)

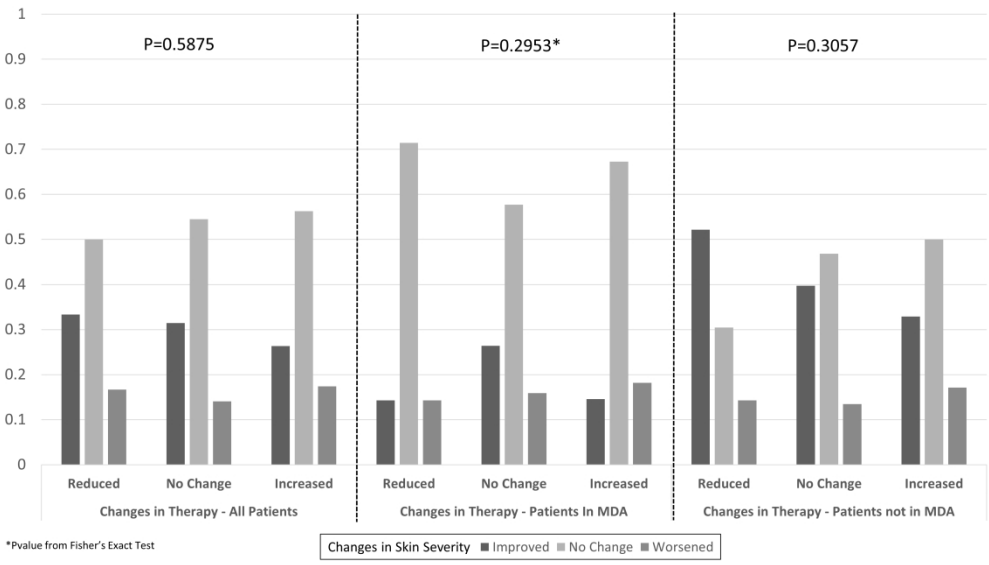

Figure 1a. Changes in Therapy and Changes in Skin Disease Severity among All Patients and Stratified by MDA Status at Baseline

338x190mm (300 x 300 DPI)

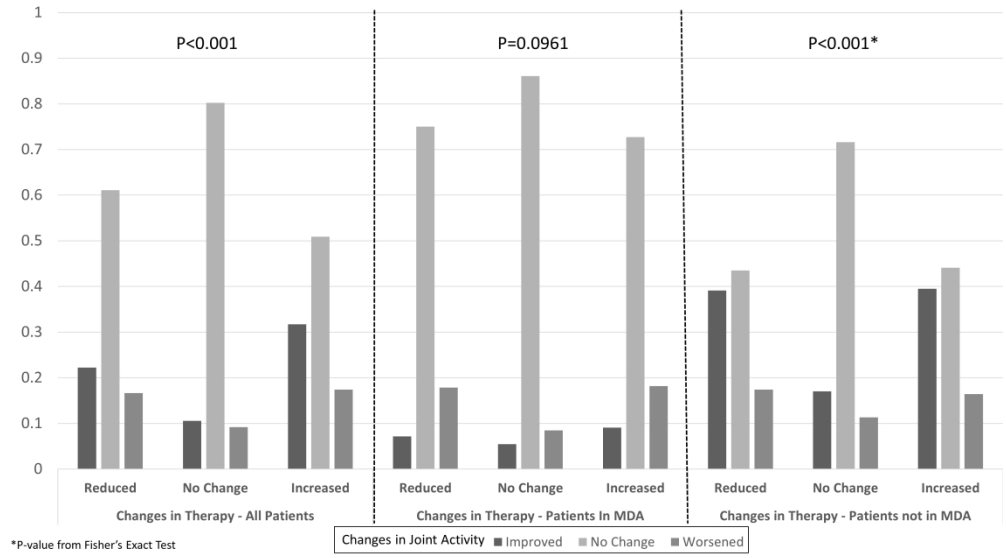

Figure 1b. Changes in Therapy and Changes in Joint Disease Activity among All Patients and Stratified by MDA Status at Baseline

338x190mm (300 x 300 DPI)