Are we achieving patient treatment goals with guideline-based therapy for Psoriatic Arthritis?

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Are we achieving patient treatment goals with guideline-based therapy for Psoriatic Arthritis?

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1. Abstract

Psoriatic arthritis (PsA) is a heterogeneous autoimmune disease that occurs in one in three people with the skin disease psoriasis. PsA can cause arthritis (joint inflammation), enthesitis (tendon and ligament inflammation), sausage digits (swollen entire finger or toe), spondyloarthritis (spinal inflammation). Skin involvement by psoriasis is also highly variable in terms of psoriasis type and location. Through combined skin and musculoskeletal involvement, psoriatic disease has a significant life impact with decrease quality of life including uncomfortable symptoms, ability to participate in life and functioning. Medications used to treat PsA have sometimes an uneven effect on the various PsA manifestations where some are more effective for skin while others more effective for the joints. In this context, clinical care and treatment of PsA is a complex process which balances disease activity with medication risks and benefits as well as patient priorities. Professional PsA treatments guidelines state that PsA treatment goals are disease remission or low disease activity. Several studies to date have shown that physicians tend to overestimate remission and low disease activity in PsA patients when compared to disease activity indices. Also patients and physicians frequently do not align on perceptions of remission or low disease activity. In the proposed study we aim to identify predictors of successful treatment from a patient perspective on a range of disease measures including psoriasis, arthritis, enthesitis, dactylitis, patient reported outcomes, and laboratory assessments which are routinely collected in the clinical care of PsA. Secondary endpoints are to quantify longitudinally how stable a state of treatment success is from a patient perspective, and to define score ranges for disease measurements, including health-related quality of life measures, that correspond to treatment success from a patient perspective. **The impact of this research is that we will be able to define parameters predictive of achieving treatment success from a patient perspective, which will then inform goals of care for psoriatic arthritis.**

2. Objectives

Primary objective

To determine predictors of reaching PsA treatment goals/treatment success (primary outcome) from a patient perspective in an academic PsA guideline-based treatment cohort. Conversely, to determine adverse predictors to reaching this desirable state. The primary outcome determination is based on the patients' report of whether they are/are not at goal with their PsA treatment.

Secondary objective(s)

To estimate the following parameters:

A. Prevalence of patients reporting they met PsA treatment goals (successful treatment) from their perspective.

B. Frequency and direction of longitudinal transitions between treatment goals/met not met states: 3 observations/participant.
C. Score ranges that correspond to a status of patients' treatment goals met on a set of PsA outcome measures used in the study, including composite disease activity measures.
D. On the same set of PsA outcome measures, meaningful change values in patients who transition longitudinally to the better and worse categories.

3. Background

Efficacy of therapeutics in PsA is incomplete, considering at most 60% of patients achieve the primary efficacy outcome in clinical trials. More so, treatment goals from the patient perspective, as well as alignment of patient opinion with index-based definitions of treatment success are part of the knowledge gap in PsA. In clinical practice, desirable treatment targets have been defined by experts as Disease Activity in Psoriatic Arthritis (DAPSA) low disease activity or remission, or Minimal Disease Activity (MDA)2. The clinical DAPSA score is computed by adding the sum of tender (out of 68) and swollen (out of 66) joints with patient global assessment and patient reported pain (each on a scale of 0-10). DAPSA remission state is defined by a score≤ 4, and DAPSA low disease activity as ≤ 14. MDA is a checklist based state defined as achieving five out of the following seven criteria: ≤ 1 swollen joint, ≤ 1 tender joint, ≤ 1 tender entheseal point, HAQ-DI score ≤ 0.5 (range 0-3), patient reported pain ≤ 1.5, patient global assessment ≤ 2, body surface area psoriasis ≤ 3%. It is of great interest to ascertain if guideline-based PsA clinical care achieves individual patient goals as articulated by patients, and to identify predictors of achieving individual patient goals from PsA treatment.

4. Study Procedures

All study assessments will be programmed in the electronic medical record (Epic EMR) with the help of the epic physician builder who is co-investigator on the study (Dr. Thomas Grader Beck, MD). Demographics, key comorbidities (cardiovascular disease, hypertension, diabetes, obesity, osteoporosis, thromboembolic disease, cancer), routine laboratories including inflammatory markers, and disease characteristics will be updated **at every visit**. Information that does not change such as disease onset for psoriasis and psoriatic arthritis will be recorded only at baseline. Study visits will occur at 3-4 month intervals in conjunction with clinical care. Disease assessments will comprise physician assessments (Table 1 a,b), laboratories (Table 2), and patient reported outcomes (Table 3 a,b). Medication doses and changes in medications will be recorded longitudinally. Disease activity measures will be programmed in the medical record such that scores are automatically generated from the primary data elements as illustrated in Table 4.

Table 1a. Physician assessments

PsA Phenotype smartform	Elements
CASPAR classification criteria (cumulative)	Psoriasis (active, history, family history), Nail psoriasis, Dactylitis, Negative rheumatoid factor, Juxtaarticular new bone (radiographic PsA)
Extraarticular manifestations (cumulative)	Uveitis, Inflammatory bowel disease, Inflammatory back pain, Psoriasis type (plaque, pustular, inverse, guttate, erythrodermic) and special locations (scalp, palmoplantar, intergluteal cleft/perianal), Elevated CRP
Comorbidities (from problem list)	Cancer of skin (not melanoma), Melanoma skin cancer, Cancer other than skin (fill in), Coronary artery disease, Diabetes, Fatty liver disease, Obesity , Osteoporosis, Stroke, Thyroid disease, Vitiligo

Table 1b. Disease activity measures

Psoriatic arthritis areas/domains	Physician assessments
Musculoskeletal Arthritis Dactylitis Enthesitis Spondyloarthritis	Tender/swollen joint counts 66/68
	Dactylitis index (LDI basic) (0-20)
	Enthesitis index (SPARCC) (0-18)
	Antropometrics (Cervical range of motion anteroposterior and lateral: occiput to wall, degrees lateral rotation; Thoracic expansion; Lumbar spine: Schober 10 and 15 cm, Lateral lumbar flexion)*
Skin and nails	Psoriasis body surface area affected (BSA%)**;** Psoriasis location (scalp, upper extremities, lower extremities, torso, abdomen)**;** Psoriasis phenotype (plaque, pustular, inverse, guttate, erythrodermic) Investigator global assessment (0-4); Nail disease (pitting, onycholysis, and surface area affected)

* assessed only at baseline

Table 2. Laboratory assessments

Psoriatic arthritis areas/domains	Laboratory test
Inflammatory markers	C reactive protein (CRP, mg/dL), ESR

We will also assess complete blood counts and comprehensive metabolic panel at every visit as part of usual clinical care. We will retrospectively abstract serologic information collected as part of usual clinical care from the medical record (rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP) status, HLA-B27, and ANA).

Table 3a. Patient reported treatment success impression

The final questions will be refined with patient research partners to make sure these are formulated such that patients understand we are assessing at each visit whether they have achieved their personal treatment goals for their psoriatic arthritis.

Patient impression of PsA treatment goals met	Response options
1. “Today, considering the level of control of your psoriatic arthritis and psoriasis, do you consider your treatment has been successful?”	1. yes 2. no
2. “If in your opinion, psoriatic arthritis and psoriasis treatments have NOT been successful for you, please choose the three most important manifestations and life impact aspects that are still active for you (from your psoriatic arthritis and psoriasis).”	1. inflamed joints, 2. inflamed tendons, 3. back/spine inflammation, 4. skin psoriasis, 5. nail psoriasis, 6. scalp psoriasis, 7. Pain, 8. Fatigue, 9. Stiffness, 10. Ability to be physically active/exercise, 11. Ability to participate with family activities, 12. Ability to work, 13. Ability to participate in social activities, 14. Emotional impact, 15. Ability to be independent in my daily activities, 16. Other, please fill in.

Patient impression of PsA treatment goals met	Response options
3. Patient acceptable symptom state: "If you were to remain for the next few months as you were during the past week, would this be acceptable or unacceptable for you?"	1. acceptable 2. unacceptable

Table 3b. Patient reported outcomes for disease status and life impact

Psoriatic arthritis areas/domains	Patient reported outcomes
Musculoskeletal	Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
Health related quality of life	Psoriatic Arthritis Impact of Disease (PsAID12, PsA specific)
	PROMIS Profile 29 (generic)
Pain	Pain visual analog scale (VAS, 0-100 mm) PROMIS Pain interference (Profile 29)
Physical function	PROMIS Physical Function 10
PsA patient globals	Patient global Arthritis (GRAPPA) (VAS, 0-100 mm) Patient global Psoriasis (GRAPPA) (VAS, 0-100 mm)
Fatigue	PROMIS Fatigue 8a
Participation, Depression, Anxiety Sleep quality	PROMIS Profile 29

Table 4. Disease activity measures (programmed in EMR and calculated automatically from elementary data)

Disease activity measure	Components and calculation
Disease Activity Psoriatic Arthritis (DAPSA) Cutoffs Remission ≤ 4 Low 4 ≤ 14 Moderate 14 ≤ 28 High ≥ 28	Tender/swollen joint counts: 68/66 Patient global (0-10) Patient pain (0-10) C reactive protein (mg/dL) DAPSA = 68tender joints + 66swollen joints + patient global + pain + CRP (ranges from 0 to more than 154) Clinical DAPSA = 68tender joints + 66swollen joints + patient global + pain (0-154)
Very low disease activity (VLDA) and Minimal disease activity (MDA) VLDA (7/7 criteria met) MDA (5/7 criteria met)	Set of 7 criteria: 1. Tender joint count 68 ≤ 1 2. Swollen joint count 66 ≤ 1 3. Patient global ≤ 2/10 4. Pain ≤ 1.5/10 5. Health assessment questionnaire disability index ≤ 0.5 6. Enthesitis ≤ 1 7 Body surface area psoriasis ≤ 3%

Patients will be enrolled in CRMS and the CRMS study flag in Epic will be used to identify patients for research visits and data extraction. The unique study identifier will be linked to the patients' JHH medical record number and only study staff will have access to the key table. This will allow study staff to keep track of enrollment and study visits and to specify data query parameters to the EPIC team at the stage of data extraction. If the patient signs consent and has a study visit on the same day, the CRMS flag will not be available to trigger specific Epic content, since the update from CRMS to EPIC takes about 24 hours. Because of this, we will institute a patient-level Smartdata element in Epic that will be flagged after the patient signs consent. This will also indicate inclusion in the study and can be used to trigger specific Epic content for the visit.

Safety assessments: All adverse events (AE) will be recorded and managed per usual clinical care. Serious adverse events (SAE) are defined as adverse events that meet any of the following criteria: result in death; are life-threatening (i.e., in the opinion of the Investigator(s) the subject is at immediate risk of death from the AE); require inpatient hospitalization or prolongation of existing hospitalization; result in persistent or significant disability/incapacity (a substantial disruption of the subject's ability to conduct normal life functions); represent a congenital anomaly/birth defect; constitute an important medical event. As part of usual clinical care, some patients participating in the study will be taking apremilast. Any SAE due to apremilast must be reported immediately (i.e., within 24 hours of the Investigators' knowledge of the event) to Amgen Inc Safety by facsimile. A written report (prepared by the Investigator(s) using an SAE Report Form or a 3500A Medwatch form is to be faxed to Safety (see below for contact information).

Amgen Inc Drug Safety Contact Information:
Amgen Inc Corporation
Global Drug Safety and Risk Management
86 Morris Ave.
Summit, NJ 07901
Fax: (908) 673-9115
E-mail: drugsafety@Celgene.com

Pregnancies: Pregnancies and suspected pregnancies (including a positive pregnancy test regardless of age or disease state) of a female subject or the female partner of a male subject occurring while the subject is on apremilast, or within 30 days of the subject's last dose of study drug, are considered immediately reportable events. Apremilast is to be discontinued immediately. The pregnancy, suspected pregnancy, or positive pregnancy test must be reported to Amgen Inc Safety immediately facsimile using the Pregnancy Report form provided by Amgen Inc.

5. Inclusion/Exclusion Criteria

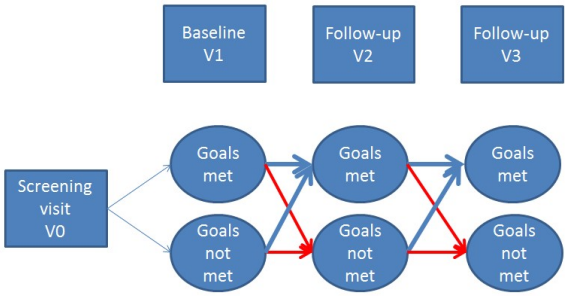
Inclusion criteria: English speaking/reading adults, ages 18 to 95 years who are patients in the Johns Hopkins Arthritis Center and/or the Psoriatic Arthritis Clinical Program (PI, Ana-Maria Orbai MD MHS directs the PsA program) and are followed every 3-4 months. Participants have to meet CASPAR classification criteria for psoriatic arthritis (supplementary material), and be able to interact with touch screen computer.
Exclusion criteria: None

6. Drugs/ Substances/ Devices – Not Applicable

7. Study Statistics

Grouping of treatment goals met or not met is based on the primary outcome at each study visit (Fig1).

Figure 1. Determining patient status in terms of treatment goals met (treatment has been successful from the patient's perspective) or not.



a. Predictors of successful treatment/reaching PsA treatment goals (primary outcome) from a patient perspective: In the longitudinal dataset with up to three visits per participant, we will examine predictors of 'treatment goals met' status using logistic regression with covariates disease characteristics and patient reported variables. We will identify predictors associated with a transition state from unmet to met, a stable status of treatment goals met, as well as predictors of stable status of unmet goals or transition in the negative direction (state variable with 4 categories: unmet to met, stable met, stable unmet, met to unmet). Full visits for this study must be in-person so that the physician assessment of the patient's disease is complete.

b. Prevalence of patients reporting successful treatment/they meet PsA treatment goals from their perspective: We will perform exploratory data analysis to estimate the prevalence of 'patient treatment goals met' status in this longitudinal guideline based therapy cohort. We will then compare characteristics of 'treatment goals met' vs 'not met' patient groups using proportions for binary/categorical (chi square tests) and means for continuous variables (t-tests).

c. Frequency and direction of longitudinal transitions between treatment goals met(successful treatment)/not met states: 3 observations/participant Inperson Visits only: We will determine how patient states change over time to define stability of the notion of successful treatment. Interim Telemedicine visit data will be collected to fill gaps between extended in-person intervals.

d. Score ranges that correspond to a status of patients' treatment goals are met (succesful treatment) on a set of PsA outcome measures used in the study, including composite disease activity measures: We will calculate average score ranges for multiple variables of interest that correspond to a status of successful treatment for patients.

e. Meaningful change values in patients who transition longitudinally to the better and worse categories: We will determine change scores in clinical outcomes corresponding to a meaningful change from the patient perspective (MCII). We will determine MCII for various measures using a predictive approach (logistic regression with ROC and AUC). We will perform a similar analysis in patients who go the other direction (from treatment goals met to treatment goals not met).

f. Telemedicine Visits: Data from telemedicine visits will be collected and used to fill gaps in understanding the changes to the patient's health status over time. This is important do to the length of time between In-Person visits due to COVID-19.

8. Risks

This study is a longitudinal observational study of usual guideline based treatment of psoriatic arthritis. There are no medical risks associated with participating in this research. There are no additional risks to questionnaire completion. Only the investigators will have access to a list linking personal identifying information to study number. There are no known financial or legal risks associated with participation in this study.

9. Benefits

There are no direct benefits to participants from participating in the study. It is possible that some patients will benefit from better communicating their disease experience to their own healthcare providers. Benefits for society include a better understanding of how patients define treatment success, experience and self-manage their disease, and interact with their healthcare providers regarding their disease.

10. Payment and Remuneration

Participants will not receive monetary compensation for their participation. Coupons will be provided to cover the cost of parking at the time of each study visit.

11. Costs

There are no costs associated with participating in this study.