PSORIATIC ARTHRITIS
Posters and Abstracts from San Diego

POSTER perspectives

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OVERVIEW

Philip J. Mease, MD, clinical professor at the University of Washington School of Medicine in Seattle, Washington, and director of the Rheumatology Clinical Research Division at Swedish Medical Center, provides his perspectives on key posters, presented at the American College of Rheumatology annual meeting, on the treatment of patients with psoriatic arthritis.

FACULTY

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CONTENT AREAS

- Psoriatic arthritis
- L-17 antagonists
- IL-12/23 antagonists
- JAK inhibitor

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CE/CME Information

Target Audience

This activity was developed for rheumatologists, dermatologists, primary care physicians, physician assistants, advanced nurse practitioners, and other health care professionals who have an interest in psoriatic arthritis.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Summarize the latest research developments in the treatment of psoriatic arthritis
- Incorporate evidence-based research into clinical practice

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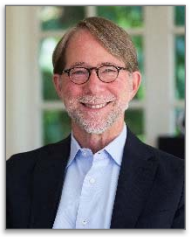
Introduction



Philip J. Mease, MD: Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center, and clinical professor at the University of Washington School of Medicine in Seattle, Washington.

Join me as I review 7 abstracts from the annual meeting of the American College of Rheumatology 2017, hosted in San Diego, California. These selected abstracts assess the latest clinical data from evidence-based research, involving various classes of agents, to help you select the most appropriate treatment and management of psoriatic arthritis to incorporate into your clinical practice.

There remains a challenge among clinicians to stay abreast of optimal treatment strategies for patients with psoriatic arthritis (PsA). A clinical trial is intended to show how a drug works in practice and to provide confidence, or a better sense of the number of patients it will work on, as we employ these agents in our patients. The goal of any study is to increase knowledge and understanding to use in practice.

With this review of several studies presented at ACR 2017, we provide an integrated approach to therapeutic intervention with best practice, stepwise recommendations needed to achieve remission or low disease activity status with the use of appropriate therapy to improve overall health outcomes in the PsA patient. Thank you for joining us for this activity.

[17L] Subcutaneous Secukinumab Inhibits Radiographic Progression in Psoriatic Arthritis: Primary Results from a Large Randomized, Controlled, Double-Blind Phase 3 Study.

Mease PJ, van der Heijde D, Landewé RBM, et al.

Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center, and clinical professor at the University of Washington School of Medicine in Seattle, Washington.

I am discussing the abstract, Subcutaneous Secukinumab Inhibits Radiographic Progression in Psoriatic Arthritis: Primary Results from a Large Randomized, Controlled, Double-Blind Phase 3 Study, authored by myself, along with Drs. van der Heijde, Landewé, and colleagues. This abstract was presented at the American College of Rheumatology meeting in November 2017.

I selected this abstract to review because it discusses the primary results of the FUTURE 5 study—the largest randomized controlled trial of a biologic conducted to date in psoriatic arthritis—to assess the efficacy of subcutaneous secukinumab with dosing at 300 mg and 150 mg, including radiographically assessed structural damage progression.

A total of 996 adults with active psoriatic arthritis (PsA), stratified by previous anti-TNF use, were randomized to subcutaneous secukinumab with 300 mg and 150 mg, with a loading-dose regimen of 5 weekly injections, followed by monthly injections. A third arm was 150 mg without a loading dose, just monthly dosing from baseline. And then a fourth arm was placebo.

Baseline characteristics were balanced across arms. Approximately 30% of patients had experienced an inadequate response or intolerance to previous anti-TNF therapy. At week 16, placebo nonresponders—patients with less than 20% improvement from baseline, and tender or swollen joint counts—were switched to secukinumab 300 mg or 150 mg. The remaining placebo patients were switched at week 24. Primary endpoint was ACR20, at week 16. Secondary endpoints included radiographically assessed structural damage progression measured by modified total van der

Heijde Sharp score assessed by blinded readers, based on hand, wrist, and foot X-rays obtained at baseline, at week 16 for the nonresponders, and at week 24, as well as other key outcome measures, such as enthesitis, dactylitis, patient-reported outcomes, and so on.

What were the key findings?

Secukinumab significantly improved ACR20 at week 16 vs placebo. Radiographic progression was significantly inhibited at week 24 in all secukinumab arms vs placebo. A greater proportion of patients had no radiographic progression change from baseline in modified totals Sharp score of less than or equal to 0.5 with secukinumab vs placebo; 88% in the 300 mg dose arm, 79% in the 150 mg with load; 83% in the 150 mg without load; and 73% in the placebo arm.

All hierarchical endpoints were significant for secukinumab vs placebo at week 16, except for enthesitis and dactylitis resolution for the 150 mg without loading dose. Enthesitis and dactylitis resolution, which arguably are more difficult clinical domains to treat and see rapid results in, showed highly significant improvement in the secukinumab-dose arms with a loading regimen, compared to placebo.

Subcutaneous secukinumab 300 mg with loading dosage and 150 mg, with and without loading dosage, inhibited radiographic structural progression and provided rapid and clinically significant improvements in the signs, symptoms, and physical functions of patients with PsA.

The best effect and key endpoints was achieved utilizing the loading-dose regimen. The safety profile was consistent with previously reported, with no new safety signals identified.

As lead author, here are my additional thoughts and analysis of this study.

This large study shows that secukinumab inhibits progression of structural damage, as well as showing efficacy data for all key clinical domains of PsA that have been shown in previous phase 3 studies, such as FUTURE 1 and 2; including arthritis, as measured by ACR response, and highly significant efficacy in resolution of enthesitis and dactylitis, and improvement of patient-reported outcomes, such as function and quality of life.

The FUTURE 1 study, which also showed inhibition of radiographically assessed structural damage progression had 2 intravenous infusions as a loading dose vs subcutaneous. So, for this FUTURE 5 study, we conducted a large trial to show the subcutaneous loading-dose method of administration would also inhibit structural damage progression.

Another question addressed in this trial was whether having a 5-weekly loading dose is helpful. The outcome with loading dose was slightly better in several key clinical domains.

This study is consistent with previous trials; the safety is consistent, and it is now a popularly used drug that can be used with confidence regarding efficacy and safety.

[1826] Secukinumab Achievement of Psoriatic Arthritis Disease Activity Score (PASDAS) Related Remission: 2-Year Results from a Phase 3 Study.

Coates LC, Gladman DD, Nash P, et al.

Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center and clinical professor at the University of Washington School of Medicine in Seattle, Washington. I will be discussing the abstract, Secukinumab Achievement of Psoriatic Arthritis Disease Activity Score (PASDAS) Related Remission: 2-Year Results from a Phase 3 Study, by Laura Coates and colleagues.

This abstract was presented at the American College of Rheumatology meeting, in November 2017, and subsequently published in *Annals of the Rheumatic Diseases* in 2017.

I selected this abstract because it emphasizes Psoriatic Arthritis Disease Activity Score, or (PASDAS), as a continuous measure of disease activity. Thresholds of remission or low disease activity in this competent measure, which holistically assesses the multiple clinical domains of psoriatic arthritis (PsA), may be a target of therapy in patients with PsA.

This *post hoc* analysis of the FUTURE 2 study assessed the ability of the IL-17, antagonist, secukinumab, to achieve low disease activity or remission, using PASDAS through 104 weeks. [Previously published, the FUTURE 2 study showed secukinumab significantly improved the science and symptoms of PsA over 104 weeks.]

This *post hoc* analysis of the FUTURE 2 study used the PASDAS as a measurement to distinguish treatment effect, noting that performance is better in statistical terms than traditional joint-only indices, such as the ACR score or DAS scoring systems.

The PASDAS index is derived from physician's global visual analog scale (VAS), patient's global VAS taking in both arthritis and skin disease impact, SF-36 Physical Component Score (PCS), tender-and swollen joint counts, Leeds enthesitis count—so, taking into account enthesitis, as well—dactylitis count, and CRP level with validated cutpoints for high disease activity (HDA ≥5.4), moderate disease activity (3.2< MoDA <5.4), and low disease activity (1.9 < LDA ≤3.2), and remission (≤1.9).

PASDAS was assessed in the overall population and in patients stratified by prior anti-TNF use, and disease duration (≤2 years vs >2 years since first PsA diagnosis) and reported using mutually exclusive categories at group level and as observed analysis.

In the FUTURE 2 study, 397 patients with active PsA were randomized to subcutaneous secukinumab at 300 mg, 150 mg, or 75 mg, or placebo at baseline, weeks 1, 2, and 3, and every 4 weeks from week 4. Placebo nonresponder and responder patients were randomized to secukinumab at 300 mg or 150 mg, subcutaneously every 4 weeks, from week 16, if they were nonresponders, and week 24, respectively.

What were the key findings?

PASDAS remission and low disease activity were achieved in 38.5% and 34.4% of patients treated with secukinumab, 300 and 150 mg, respectively, vs 16.1% in the placebo group at week 16. Approximately 50% of patients achieved PASDAS remission and low disease activity in both secukinumab groups at week 104.

A higher proportion of anti–TNF-naïve patients treated with secukinumab achieved PASDAS remission or low disease activity than anti–TNF-inadequate response patients through week 104. Secukinumab treated patients achieving PASDAS remission had significantly greater improvements in function, quality of life, and fatigue.

This study shows that the holistic [approach]—meaning measuring all clinical domains in PsA including, for example, enthesitis, dactylitis, and skin disease as a continuous measure that is specific for PsA—is being used increasingly in trials and shows good utility.

Before beginning my analysis, let's hear about some of the study's highlights from the lead author's perspective, Laura Coates.

I think the abstract highlighted the importance of achieving remission for maximizing patient benefit, in terms of work disability, function, and quality of life. It gave further support to the use of PASDAS as a measure of disease activity, and specifically as a definition of remission or low disease activity, from the patient's perspective.

I am not sure that this will have a direct impact on care that much now, although it does highlight the potential benefits, alongside other data, of achieving a target to improve outcomes and support the use [of a] treat-to-target approach. The other benefit it has is to allow us to translate research findings into what they mean for patients.

Here are my own thoughts and analysis of this study.

This study, the index portion, focuses on the measurement and how it focuses on the quantitation of disease activity. The Psoriatic Arthritis Disease Activity Score, or PASDAS, worked very well as a composite index to measure disease activity. As such, PASDAS is a worthy and reliable, holistic, measure for use in clinical trials to measure PsA.

The threshold of remission and low disease rate were met by approximately one third of the patients in treatment groups as early as week 16. The long-term observation was also positive. By week 104, 50% were in PASDAS state of low disease activity.

For rheumatoid arthritis, increasingly, rheumatologists are using a treat-to-target strategy, using quantitative measures of disease activity to maximize achieving low disease activity or remission. We are also finding this methodology to be so in the management of PsA. We are introducing holistic, quantitative measures that point the way to a treat-to-target strategy for patient care.

Some may argue PASDAS is a complex instrument. However, it is quite easy to plug in the numbers to do the measurements. There remains the question of how readily a treat-to-target strategy, including an assessment of skin disease, will be taken up by rheumatologists in practice. But I would hope that increasingly, in the future, that this will be the case.

[606] Secukinumab Demonstrates Consistent Safety over Long-Term Exposure in Patients with Psoriatic Arthritis and Moderate to Severe Plaque Psoriasis: Updated Pooled Safety Analyses.

Mease PJ, McInnes LB, Reich K, et al.

Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center and clinical professor at the University of Washington School of Medicine in Seattle, Washington.

I will be discussing the abstract, Secukinumab Demonstrates Consistent Safety Over Long-Term Exposure in Patients With Psoriatic Arthritis and Moderate to Severe Plaque Psoriasis: Updated Pooled Safety Analyses, by myself, along with Drs. McInnes and Reich and colleagues. This abstract was presented at the American College of Rheumatology meeting in November 2017.

I selected this abstract to discuss because it reported updates on longer-term safety data of secukinumab exposure from pooled data of psoriasis and psoriatic arthritis studies. Results were derived from pooled psoriasis data from 9 phase 3 studies in moderate-to-severe plaque psoriasis (3893 subjects), and pooled data from 3 phase 3 studies in active psoriatic arthritis (PsA) (1380 subjects).

Secukinumab doses differed, and included intravenous, up to 10 mg per kilogram, or subcutaneous loading, followed by subcutaneous maintenance dosing of 300 [mg], 150 [mg], or 75 mg. Placebo patients were rerandomized to secukinumab at 12 to 24 weeks, depending on study design.

What were the key findings?

Common adverse events included nasopharyngitis, headache, upper respiratory tract infection, and arthralgia. These are common side effects seen in most clinical trials.

Serious adverse events for PsA patients were as follows:

- Serious infections, 1.7%
- *Candida* infections, 1.7%
- Inflammatory bowel disease, 0.4%,
- Crohn's disease and ulcerative colitis, each 0.1%
- Major adverse cardiac events, or MACE, 0.4%.

Secukinumab demonstrated a favorable safety profile during long-term treatment. Up to 2841-patient years of exposure for PsA and patients with moderate-to-severe PsA, consistent with previous reports. Safety was comparable across psoriasis and PsA patient populations, supporting long-term use in these chronic conditions.

As lead author, here are my thoughts and analysis of this study.

This study is the largest compilation of safety data for secukinumab and psoriasis in psoriatic arthritis (PsA) to date, which means that the results will reliably teach us about safety in a large population of patients. We see that safety outcomes are similar between patients who only have the skin disease psoriasis and those with the broader impact of PsA, in which musculoskeletal manifestations exist as well. Although secukinumab does slightly increase the rate of serious infection, as is expected from a biologic agent, we see that the frequency of such infections is low.

We also see some increase of a specific infection, *Candida*, which is to be expected since IL-17 protects against *Candida* infection, and thus inhibition of this cytokine may lower this protection. Fortunately, this adverse event tended to be mild to moderate and relatively easily controlled with topical treatment or, on rare occasions, systemic treatment. There was also a small signal for either recurrent inflammatory bowel disease in patients with known inflammatory bowel disease or in new occurrence. Fortunately, the rate of this was small. It is not known if this is due to the agent not protecting against such an occurrence, or possibly facilitating it. Keep in mind that inflammatory bowel disease is genetically associated with psoriasis and PsA, so we expect it, to a certain extent, in higher frequency in this patient population.

There was no clear signal for a relationship with either malignancy or major adverse cardiovascular events. This study supports the point that secukinumab can be used with confidence regarding safety in patients with psoriasis and PsA over the long term. I do avoid use of this medicine in patients with currently active inflammatory bowel disease.

[605] Ixekizumab Exhibits a Favorable Safety Profile during 24 Weeks of Treatment in Subjects with Active Psoriatic Arthritis: Integrated Safety Analysis of Two Randomized, Placebo Controlled, Phase III Clinical Trials

Mease PJ, Burmester GR, Moriarty S, et al.

Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center and clinical professor at the University of Washington School of Medicine in Seattle, Washington. I will be discussing the abstract, Ixekizumab Exhibits a Favorable Safety Profile During 24 Weeks of Treatment in Subjects with Active Psoriatic Arthritis:

Integrated Safety Analysis of Two Randomized, Placebo Controlled, Phase III Clinical Trials, by myself, along with Drs. Burmester and Moriarty and colleagues. This abstract was presented at the American College of Rheumatology meeting in November 2017.

I selected this abstract because it highlights the most recently FDA-approved (December of 2017) IL-17A antagonist, ixekizumab, for psoriatic arthritis (PsA). This study shows the safety profile of ixekizumab during the placebo-control treatment period was consistent with published findings in patients who received ixekizumab for moderate-to-severe plaque psoriasis.

A total of 678 adults with active PsA were randomized to 80 mg of ixekizumab every 4 weeks, or 2 weeks after a 160 mg starting dose, or placebo. Safety data are presented from the placebo-control treatment periods, weeks 0 to 24, for patients who received at least 1 dose of the study drug. At week 16, patients deemed inadequate responders received rescue therapy and were included in this dataset only up to week 16.

Primary outcome was the integrated safety of 2 pivotal trials in patients with active PsA. SPIRIT phase 3 trials consisted of patients with active PsA who were biologic disease-modifying antirheumatic drug (DMARD)-naïve or inadequate responders to TNF inhibitors. Data was analyzed using the Cochran-Mantel-Haenszel test stratified by trial.

What were the key findings?

There was no clear difference between groups for the percentage of patients with greater than or equal to one serious adverse event or discontinued early from study drug.

Adverse events of special interest from 0 to 24 weeks included infection-related serious adverse events, with the overall frequency being quite low, 1% in the total ixekizumab group vs zero in the placebo group. The rate of *Candida* infection was slightly higher in the ixekizumab group than placebo, 3% compared to <1%. There was no case of Crohn's disease or ulcerative colitis.

Two cases of malignancy (prostate cancer and basal cell carcinoma) were reported in the ixekizumab Q4-week arm; however, there was, overall, no specific malignancy signal, and the rate of malignancy was quite low, less than 1%. There were no major adverse cardiac events, and there were no deaths or reports of suicide or suicidal ideation. The safety profile of ixekizumab was consistent with published findings in patients receiving ixekizumab for moderate-to-severe plaque psoriasis.

As lead author, here are my thoughts and analysis of this study.

This study showed a range of serious adverse events of 1.5% to 2.5%, which is relatively low compared to many other trials of biologic agents. None of the studies are head-to-head trials. That said, the overall rate of serious infection is less than that observed in trials of TNF inhibitors. The serious infection rate was higher than placebo; therefore, clinicians should speak to their patients about the risk, even while understanding that the potential for serious infection is low. There was no specific malignancy signal and the rate of malignancy was low. There was no adverse cardiovascular signal.

Although there were no cases of Crohn's or ulcerative colitis flares in these studies, IL-17 inhibitors in general do not seem to protect against flares of inflammatory bowel disease (IBD). This is important because we know that there is a genetic greater risk for IBD in patients with psoriasis and psoriatic arthritis.

In the psoriasis studies with this agent, a few cases of IBD flares occurred, both in patients with known IBD, as well as new

onset—more in the treatment group than placebo. So, we know that this can occur, but it just wasn't seen in these psoriatic arthritis trials.

These results underline the point that IL-17 inhibitors seem to be overall quite safe and can be used with confidence from this perspective. We see a slightly higher rate of serious infections than placebo. There is a slight increase of *Candida* infection, which is expected because IL-17 is a known protector against *Candida*; however, this adverse event was typically mild to moderate and easily managed.

[2L] Efficacy and Safety Results from a Phase 2 Trial of Risankizumab, a Selective IL-23p19 Inhibitor, in Patients with Active Psoriatic Arthritis.

Mease PJ, Kellner H, Morita A, et al.

Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center and clinical professor at the University of Washington School of Medicine in Seattle, Washington. I will be discussing the abstract, Efficacy and Safety Results from a Phase 2 Trial of Risankizumab, a Selective IL-23p19 Inhibitor, in Patients with Active Psoriatic Arthritis, by myself, along with Drs. Kellner and Morita and colleagues. This abstract was presented at the American College of Rheumatology meeting in November 2017.

I selected this abstract to discuss because it reviews an IL-23 antagonist agent, risankizumab, although not yet approved, but in the pipeline for treatment of patients with psoriatic arthritis (PsA).

We are learning that the IL-23/IL-17/TH-17 cell axis is especially important in psoriasis and PsA, as previously demonstrated with the IL-12/23 inhibitor, ustekinumab; the IL-17a inhibitors, secukinumab and ixekizumab; the IL-17A and F inhibitor, bimekizumab; the pure IL-23 inhibitor, guselkumab; and now a newer, pure IL-23 inhibitor, risankizumab.

In this phase 2 study, risankizumab significantly improved joint and skin symptoms in patients with active PsA. It was well tolerated with no new or unexpected safety findings, and it underscores the continued effort to provide additional treatment options for PsA.

In this 5-arm study, 185 patients with active PsA were randomized to receive risankizumab in an ongoing, double-blind, parallel-design, dose-ranging, phase 2 study. There were several different dose arms, including 150 mg at week 0, 4, 8, 12, and 16; 150 mg at weeks 0, 4, and 16; 150 mg at week 0 and 12; 75 mg single dose at week 0; or matching placebo.

Patients were stratified at randomization by prior anti-TNF use and concurrent methotrexate use. Baseline demographics and disease characteristics were similar across treatment arms. The median age was 51 years; 43% were female. And 49% had psoriasis covering greater than or equal to 3% body surface area, and thus could have PASI scores. The primary endpoint was ACR20 response at week 16. Additional efficacy endpoints included ACR50 and 70, minimal disease activity assessment, DAS28(CRP), dactylitis count, SPARCC enthesitis index, pain, and HAQ-DI.

What were the key findings?

At week 16, ACR20 responses were significantly greater in patients receiving risankizumab across all arms, 57% to 65% compared with placebo at 37%.

ACR50 responses were numerically higher. Improvement in HAQ scores and enthesitis from baseline were numerically greater in risankizumab arms. At week 16, risankizumab-treated patients received significantly higher ACR70 and minimal disease activity responses, as well as greater

improvements in DAS28 and pain VAS. Treatment emergent adverse events were comparable across treatment arms. The most common was infection. There were no deaths or cases of TB in risankizumab-treated patients.

As lead author, here are my thoughts and analysis of this study.

Risankizumab is 1 of 3 pure IL-23 inhibitors that are advancing in psoriasis and PsA. These agents work by interacting with the p19 subunit of IL-23, preventing receptor activation and thereby disrupting the IL-23/IL-17 axis. This trial is the first demonstration of risankizumab effectiveness in PsA with multiple arms studying different dose-frequency regimens. All doses and dose frequencies worked equally well, including the 75 mg single-dose arm. The drug in each of the dose arms and frequency was effective, demonstrating ACR20 response with very good skin responses, as well as a good safety profile. This is a proof of concept study. IL-23 inhibition is an appropriate target in the management of psoriasis and PsA. This study provides clinicians confidence in its use as this agent moves into phase 3.

We know from this study that risankizumab works and has a good safety profile. Providing continued study results remain constant, it will share this stage with the IL-12/23 inhibitor, ustekinumab, as well as other pure IL-23 inhibitors, such as guselkumab, as well as the IL-17 inhibitors.

[881] Ustekinumab Is Superior to TNF Inhibitor Treatment in Resolving Enthesitis in PsA Patients with Active Enthesitis—Results from the Enthesial Clearance in Psoriatic Arthritis Study.

Araujo E, Englbrecht M, Hoepken S, et al.

Hello, this is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center and clinical professor at the University of Washington School of Medicine in Seattle, Washington. I will be discussing the abstract, Ustekinumab Is Superior to TNF Inhibitor Treatment in Resolving Enthesitis in PsA Patients With Active Enthesitis—Results From the Enthesial Clearance in Psoriatic Arthritis Study, by Elizabeth Araujo and colleagues. This abstract was presented at the American College of Rheumatology meeting in November 2017.

I selected this abstract because this study focuses on the theory that inhibition of IL-23 is effective in enthesitis-driven psoriatic arthritis (PsA) patients. Ustekinumab is a combined inhibitor of IL-12 and 23 (FDA approved for PsA in 2013). This study provides a new and statistical response to the pathway of the IL-23, highlighting the enthesitis response, and compares the efficacy of ustekinumab with TNF-inhibitor treatment to clear enthesitis in PsA patients.

Patients with PsA and active enthesitis (at least 1 painful enthesis on SPARCC, Leeds, or MASES indices) were enrolled 1:1, receiving either standard doses of ustekinumab or tumor necrosis factor (TNF) inhibitor. There were 23 patients in the ustekinumab-treated arm, and 24 in the TNF-inhibitor-treatment arm. The primary endpoint was SPARCC enthesitis resolution after 6 months. Patients were seen every 3 months and followed for a total of 6 months.

What were the key findings?

After 6 months, 70.8% of ustekinumab-treated patients and 38.4% of TNF-inhibitor-treated patients reached the primary endpoint defined as clearance of enthesitis or a SPARCC score of zero. The results suggest that ustekinumab may be superior to a TNF inhibitor in resolving the enthesitis component of disease in a population of PsA patients characterized by active enthesial disease. The SPARCC enthesitis scoring system was more discriminative in ability to show statistically significant response than the Leeds Enthesitis Index.

Before beginning my analysis, let's hear about some of the study's highlights from Dr. Araujo's perspective.

First, it is fair to say that most studies conducted in PsA to date focused on patients with predominately polyarticular joint disease. Despite the fact that enthesitis is a common manifestation of this disease, and reason for disability in these patients, it doesn't get much attention in clinical trials. We conducted this study in a group of PsA patients who had enthesitis as their predominant musculoskeletal manifestation and compared their response to 2 different types of cytokine blockage.

Secondly, enthesitis was measured in this study through 3 different scoring systems—the Maastricht Ankylosing Spondylitis Enthesis Score [MASES], SPARCC, and Leeds Enthesitis indices [see Abbreviations for details and differentiation of scoring tests]—giving a very good assessment of the enthesial burden on these patients.

Finally, our results support the concept that the IL-23/IL-17 pathway has a pivotal role in the development of enthesitis. In countries like Germany, where both classes of biologics are approved for the treatment of PsA, it will allow physicians to take a more targeted approach while treating patients with this condition, including enthesitis. Our study shows that in patients who have a more enthesial-driven disease, the response to blocking the IL-12/23 pathway seems to have a superior effect as opposed to using a TNF blocker.

Here are my own thoughts and analysis of the study.

My first take-home from this trial is a methodological one. It seems that the SPARCC Enthesitis Index, which assesses 18 different enthesial sites, is more discriminative than the Leeds Enthesitis Index, which measures just 6. On average, the baseline score in this study was just over 4 sites being tendered with the SPARCC index, and just over 1 with the Leeds. So, simply by assessing more sites, it appears to be statistically better, at least in this relatively small study.

In this comment, I'm focusing on the SPARCC and the Leeds because these are the 2 enthesial indices that are now most commonly used in PsA trials, whereas the Maastricht is used most commonly in trials of axial spondyloarthritis.

When one couples the results of IL-17 inhibitor trials, wherein there is very good data on enthesitis resolution, one wonders whether there may be some differentiation of effectiveness between blockade of the IL-23/IL-17 access vs other treatment mechanisms for the clinical domain of enthesitis. This question will be better addressed in the future when we see the results of larger head-to-head studies with differing classes of agents.

[620] Safety and Efficacy of Tofacitinib, an Oral Janus Kinase Inhibitor, up to 36 Months in Patients with Active Psoriatic Arthritis: Data from the Second Interim Analysis of OPAL Balance, an Open-Label, Long-Term Extension Study.

Nash P, Coates LC, Kivitz AJ, et al.

Hello. This is Dr. Philip Mease, director of rheumatology research at Swedish Medical Center and clinical professor at the University of Washington School of Medicine in Seattle, Washington. I will be discussing the abstract, Safety and Efficacy of Tofacitinib, an Oral Janus Kinase Inhibitor, up to 36 Months in Patients with Active Psoriatic Arthritis: Data from the Second Interim Analysis of OPAL Balance, an Open-Label, Long-Term Extension Study, by Dr. Peter Nash and colleagues.

This abstract was presented at the American College of Rheumatology meeting in November of 2017. I selected this abstract to discuss because it provides confirmation on recently

approved—in December of 2017—tofacitinib, an oral Janus kinase inhibitor, reporting safety, tolerability, efficacy, and sustained responses in all the key domains in psoriatic arthritis for patients with active PsA.

Results were derived from a 36-month, open-label, long-term extension study, OPAL Balance. Eligible patients were included from 2 previous pivotal phase 3 tofacitinib PsA studies, OPAL Broaden and OPAL Beyond, both of which were randomized, double-blind, clinical trials comparing tofacitinib, 5 mg or 10 mg compared to placebo in active PsA.

All patients entered on a background of a conventional synthetic DMARD, as was mandated by the previous qualifying studies. Dosing continued as either 5 mg or 10 mg. based on dosing in the primary studies. After 1 month, patients in the 5-mg arm were allowed to increase to 10 mg twice a day for efficacy reasons or reduce to 5 mg for safety reasons. Primary endpoints included incidence and severity of adverse events, as well as change from baseline in laboratory values, [were] in addition to efficacy endpoints.

What were the key findings?

Six hundred eighty-six patients entered the study. 10.5% of patients had serious adverse events, and 7.6% discontinued due to adverse events. 1.6% reported serious infections. 2.8% reported herpes zoster events. 0.3% reported major adverse cardiovascular events, and 1.9% reported malignancies. There were no adverse events of gastrointestinal perforation or inflammatory bowel disease, and few patients experienced elevated liver enzymes. In terms of efficacy, 67% of patients had ACR20 response at 24 months. Efficacy was achieved in key secondary endpoints, including enthesitis, dactylitis, skin manifestations of psoriasis, function, and quality of life.

Here are my thoughts and analysis of this study.

The study showed a low rate, 1.6%, of serious infections. Over 36 months, the safety profile of tofacitinib was similar to the pivotal phase 3 OPAL studies, as well as previous trials in rheumatoid arthritis. No new or different emerging adverse events were identified. These results support the sustained efficacy and relative safety of tofacitinib in psoriatic arthritis.