Transcript Details

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Taking a Multidisciplinary Approach to Treating Active Psoriatic Arthritis

Announcer:
You're listening to ReachMD.

This medical industry feature, titled "Taking a Multidisciplinary Approach to Treating Active Psoriatic Arthritis", is sponsored by Janssen Pharmaceuticals, Inc. This program is intended for physicians.

Your host today is Dr. John Russell and your guests are Dr. Philip Mease and Dr. April Armstrong, who are paid speakers for Janssen Pharmaceuticals, Inc.

John Russell, MD:
Psoriasis and psoriatic arthritis, or PsA, are chronic inflammatory diseases that affect millions of Americans. Today, more than eight million Americans are living with psoriasis, and up to 30 percent of psoriasis patients go on to develop PsA. Early recognition and treatment of PsA are critical, so we are here to discuss some key strategies from both rheumatology and dermatology perspectives.

This is ReachMD, and I'm Dr. John Russell. Joining me today are Dr. Philip Mease and Dr. April Armstrong.

Dr. Philip Mease is Director of Rheumatology Research at the Swedish Medical Center/Providence St. Joseph Health and Clinical Professor at the University of Washington School of Medicine in Seattle, WA. Dr. Mease, thanks for being here today.

Philip Mease, MD:
Thank you for having me, John.

John Russell, MD:
And Dr. April Armstrong is Professor of Dermatology and the Associate Dean of Clinical Research at Keck School of Medicine at University of Southern California. Dr. Armstrong, it's great to have you with us.

April Armstrong, MD, MPH:
I'm excited to be here to talk with you, Dr. Russell and Dr. Mease.

John Russell, MD:
Let's start off with a higher-level look at this disease space and its patients. How do each of you partner with other physicians outside of your specialty to diagnose and treat psoriatic arthritis? Dr. Armstrong, let's hear from you first.

April Armstrong, MD, MPH:
That's an important question, Dr. Russell, as the treatment of diseases like psoriatic arthritis can benefit from a multidisciplinary approach. For example, at my institution I am very fortunate to have access to other rheumatologists who are very interested and knowledgeable about caring for patients with psoriatic arthritis. While we do have a joint rheum-derm clinic that we work within, we also are in frequent contact with other physicians outside of that joint clinic with regards to the co-management of our patients with psoriasis and psoriatic arthritis. For many of our dermatology colleagues, establishing a relationship with a rheumatologist who has demonstrated knowledge in psoriatic arthritis is crucial for informed disease co-management – be it designing a treatment plan that would address both the skin and joints, or just even general questions that we'd appreciate a different perspective on. This is especially true, as we need to think through the colleague interaction in a clinic like ours, where we see patients with overlapping conditions. We learn as much from the rheumatologists as the other way around. It's really a great resource for our trainees as well to be learning in that environment and it paves the way for some valuable teaching moments.

John Russell, MD:
And how about you, Dr. Mease?

Philip Mease, MD:
I think that April raises a great point about the co-management of disease, and I would take it even a step further to emphasize that it all boils down to a constant process of education back and forth, either through the electronic medical record, or exchange of notes or telephone conversations with the referring clinician – be it primary care or dermatology. Oftentimes, it's striking how the clinician isn't even aware of the relationship between psoriasis and psoriatic arthritis. The constant education that April and I refer to is something that rheumatologists need to work on at a clinical exam, history, and family history level. The presentations we observe can provide complicated issues to sort through, and because of the complexity of the clinical domains of psoriatic arthritis, and the varying types of patients we see, I often will use the metaphor of an orchestra when I'm explaining the illness to patients or to other clinicians. One patient may have all the sections playing at once; but in another patient, it may just be the piccolo section, or the trombones that are playing, the skin plaques, or peripheral arthritis. Every time you see a patient, it's an opportunity to teach the person who's doing the referral, and so the next time, they may think about it when diagnosing. Then the treatment is another matter, and that's where all of the close relationships that April has described come into play.

John Russell, MD:
Dr. Mease, I really love the orchestra metaphor you provided. Now, you've organized all the sounds in that orchestra, let's look deeper at treatment. Dr. Armstrong, what does the treatment landscape currently look like for patients with active PsA?

April Armstrong, MD, MPH:
Today, we have essentially four different classes of biologics that can be used for patients with active PsA, as well as some oral systemic medications. From a dermatologist perspective, I'd say that what we now understand of the different classes of biologics, and their clinical attributes, is critical knowledge for healthcare providers and patients. There has also been expanded understanding of the IL-23 pathway. The IL-23 pathway is a mechanism in the overactive inflammatory and immune responses that lead to the symptoms of psoriatic arthritis.

John Russell, MD:
I understand there are several FDA-approved biologics for active PsA. And given the amount of treatments already available, Dr. Armstrong, why is it important to have more treatment options?

April Armstrong, MD, MPH:
Psoriatic arthritis impacts each patient differently in terms of disease extent, severity and response to treatment, so it's important for each patient to have an individualized treatment plan. We do our best to have a more directed approach for treating each patient, and therefore we continue to place value on having a breadth of options available to evaluate.

John Russell, MD:
For those just tuning in, you're listening to ReachMD.

I'm Dr. John Russell, and today I'm speaking with Drs. Philip Mease and April Armstrong about taking a multidisciplinary approach to treating active psoriatic arthritis. We spoke a bit earlier about the current treatment landscape for this condition, but now let's shift over to learn more about a treatment option available to adults with active PsA.

Announcer:
TREMFYA® (guselkumab) was approved for the treatment of adults with active PsA in July 2020 and was previously approved for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

TREMFYA is administered as a 100 mg subcutaneous injection once every 8 weeks, after starter doses at weeks 0 and 4. In active PsA, TREMFYA may be administered alone or in combination with a cDMARD such as methotrexate.

TREMFYA is intended for use under the guidance and supervision of a physician. Patients may self-inject with TREMFYA after physician approval and proper training.

TREMFYA is the first and only biologic approved to treat active PsA that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. The clinical significance of these findings is unknown.

Before we get into a discussion about this treatment option, I'd like to take a moment to review Selected Important Safety Information: TREMFYA is contraindicated in patients with a history of serious hypersensitivity reaction to guselkumab or to any of the excipients. Serious hypersensitivity reactions, including anaphylaxis, have been reported. TREMFYA may increase the risk of infection. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a clinically important or

serious infection develops, discontinue TREMFYA until infection resolves. Evaluate for tuberculosis before treating with TREMFYA. Avoid use of live vaccines in patients treated with TREMFYA. Please stay tuned in to hear related and other Important Safety Information later in this segment.

John Russell, MD:
For now, let's dive a bit deeper into the data around TREMFYA (guselkumab). Dr. Mease, can you tell us about the clinical trials that support approval by the FDA for adult patients with active PsA?

Philip Mease, MD:
I'm happy to, John. DISCOVER 1 and DISCOVER 2 were Phase 3, multicenter, randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of TREMFYA 100 mg administered once every 8 weeks subcutaneously with starter doses at week 0 and week 4; or placebo with starter dose at week 0, then every 4 weeks in patients with active PsA --fulfilling CASPAR criteria-- and despite standard therapies. In DISCOVER 1, 127 patients were on TREMFYA and 126 were on placebo. In DISCOVER 2, 248 patients were on TREMFYA and 246 were on placebo. A stable dose of one selected nonbiologic DMARD, corticosteroids, and NSAIDs were permitted but not required. In DISCOVER 1, eligible patients 18 years of age and older had active PsA for at least six months and included patients with prior biologic experience of less than or equal to two anti-TNF-alpha treatments. Patients with other inflammatory diseases and those who had previously received Janus kinase inhibitors, or JAK inhibitors, or biologics other than TNF-alpha inhibitors were excluded. In DISCOVER 2, eligible patients 18 years of age or older had active PsA for at least six months and no prior JAK inhibitor or biologic experience. At week 16, patients in all treatment groups who had less than 5% improvement from baseline in both swollen and tender joint counts were considered as meeting early escape and were allowed to initiate or increase the dose of one of the permitted concomitant medications up to the maximum dose allowed. The primary endpoint in DISCOVER 1 and DISCOVER 2 was ACR20 at week 24.

John Russell, MD:
Dr. Mease, what were the data supporting approval?

Philip Mease, MD:
So, John – the data supporting the approval for TREMFYA included the primary endpoint of achievement of ACR20 response at week 24. The DISCOVER-1 study, in which, as mentioned previously, patients had previous exposure to less than or equal to two TNF inhibitors, showed that in patients who received TREMFYA 100 mg every 8 weeks after two starter doses, 52 percent achieved an ACR20 response versus 22 percent treated with placebo at week 24. And in DISCOVER-2, at week 24, where the biologic naïve population was studied, 64 percent of patients who received TREMFYA every 8 weeks achieved an ACR20 response, versus 33 percent treated with placebo.

John Russell, MD:
Thank you, that was a great overview. Just want to add one footnote here. Through Week 24, patients were considered to be nonresponders after meeting treatment failure criteria. After week 24, failure rules were not applied. Moving on, I understand that in particular fatigue is important to patients with active PsA. Dr. Mease, can you talk a little bit more about this patient-reported outcome?

Philip Mease, MD:
Absolutely. On this topic I do want to point out that, as a member of OMERACT or Outcome Measures in Rheumatology Clinical Trials Association, I've seen a real focus on the importance of fatigue as a clinical symptom of psoriatic arthritis. Sometimes, I'll have a patient come in and say, "Improvement of my pain, stiffness and swelling are important to me, but Doc, seeing my fatigue improve matters too." It's been very encouraging to see fatigue measured in clinical trials. TREMFYA is actually the first biologic approved for active PsA to have improvement in fatigue in its US label as measured by FACIT-Fatigue, which stands for Functional Assessment of Chronic Illness Therapy-Fatigue, a questionnaire that asks multiple questions related to patient fatigue. In terms of the data, in DISCOVER 1 at week 24 mean change from baseline in FACIT-Fatigue score was 5.76 for patients receiving TREMFYA with every-8-week dosing and 2.15 for patients receiving placebo. In DISCOVER 2 at week 24 the mean change from baseline in FACIT-Fatigue score was 7.69 for patients receiving TREMFYA every-8-week dosing and 3.73 for patients receiving placebo. Through week 24, patients in this analysis were considered to have no improvement --change equaling zero-- after meeting treatment failure criteria. And after week 24, treatment failure rules were not applied. I would note that the FACIT-Fatigue endpoint was not adjusted for multiplicity, so statistical significance has not been established here.

Announcer:
When evaluating mean change from baseline in FACIT fatigue, in DISCOVER 1 there were 127 patients in the TREMFYA every 8-week dosing group and 126 patients in the placebo group. In DISCOVER 2 there were 246 patients in the TREMFYA every 8-week dosing group and 244 in the placebo group. To provide further detail, treatment failure criteria was defined as discontinuing of study agent

injections for any reason, termination of study participation for any reason, initiated or increased dose of DMARDs or oral corticosteroids over baseline for PsA, or initiation of protocol-prohibited medications or therapies for PsA. With regard to the safety profile of TREMFYA in active PsA, the overall safety profile observed in patients with PsA treated with TREMFYA is generally consistent with the safety profile in patients with plaque psoriasis with the addition of bronchitis and neutrophil count decreased. In the 24-week, placebo-controlled period, combined across the 2 studies:

- Bronchitis occurred in 1.6 percent of patients in the TREMFYA every-8-week dosing group and 1.1 percent of patients in the placebo group.
- Neutrophil count decreased occurred in 0.3 percent of patients in the TREMFYA every-8-week dosing group compared to 0 percent of patients in the placebo group. The majority of events of neutrophil count decreased were mild, transient, not associated with infection, and did not lead to discontinuation.

John Russell, MD:
And just a quick follow up to that, Dr. Mease. I also understand that there are some considerations around axial spine manifestations of active psoriatic arthritis in the pivotal studies. Can you provide some additional insight there as well?

Philip Mease, MD:
Yes; in a post-hoc analysis of pooled data from DISCOVER 1 and 2, at week 24 the mean change from baseline in BASDAI for patients with imaging-confirmed sacroiliitis was -2.67 for the TREMFYA group and -1.35 for the placebo group. Through week 24, patients in this analysis were considered to have no improvement (change equaling zero) after meeting treatment failure criteria – which as a reminder was defined as discontinuing of study agent injections for any reason, termination of study participation for any reason, initiated or increased dose of DMARDs or oral corticosteroids over baseline for PsA, or initiation of protocol-prohibited medications/therapies for PsA. Additionally, patients with missing data were considered non-responders. In this post-hoc analysis, 91 patients were on TREMFYA and 118 patients were on placebo. BASDAI is a subject self-assessment of axial disease, which asks patients to rate their symptoms on a scale of 0 to 10; with higher scores indicating greater disease severity. I would note that the BASDAI endpoints were not adjusted for multiplicity, so statistical significance has not been established here. I did still want to call out these analyses, given the prior considerations you mentioned.

John Russell, MD:
I have just one more specific question specific to TREMFYA, as I recognize it has been evaluated in different domains of PsA. Dr. Armstrong, how does TREMFYA work in the skin in active PsA?

April Armstrong, MD, MPH:
Depending on when you're evaluating the patient and what “section of the orchestra” is playing, you may need to evaluate your treatment options accordingly. So, another area that was evaluated was skin manifestations of psoriasis; and we saw that in adults with active PsA, treatment with TREMFYA resulted in an improvement in the skin manifestations of psoriasis. More specifically, this was in patients with greater than or equal to 3 percent body surface area, or BSA, of psoriatic involvement and IGA score greater than or equal to 2 at baseline. In DISCOVER 1, at week 24, 47 of the 82 patients receiving TREMFYA every-8-week dosing had an IGA score 0 (meaning cleared) or 1 (meaning minimal) and greater than or equal to 2 point reduction from baseline. This was versus 12 of the 78 patients receiving placebo. And in the blinded, placebo-controlled phase of DISCOVER 2, 124 patients out of 176 patients receiving TREMFYA 100 mg every 8 weeks had an IGA score of 0 (meaning cleared) or 1 (meaning minimal) and greater than or equal to 2 grade reduction from baseline. This was versus 35 of the 183 patients receiving placebo. I would like to note that through week 24, patients were considered to be nonresponders after meeting treatment failure criteria. After week 24, treatment failure rules were not applied. Patients with missing data were also considered nonresponders. So options are always an appreciation of the multi-domain nature of the disease; this is a disease where it is important to evaluate each of the domains when you're with a patient, and we always look to treat each patient individually.

John Russell, MD:
That’s great, Dr. Armstrong, thank you very much. Please continue listening as our announcer will now review the indications and Important Safety Information for TREMFYA.

Announcer:
INDICATIONS

TREMFYA® (guselkumab) is indicated for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

TREMFYA® is indicated for the treatment of adults with active psoriatic arthritis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TREMFYA® is contraindicated in patients with a history of serious hypersensitivity reaction to guselkumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, have been reported with postmarket use of TREMFYA®. Some cases required hospitalization. If a serious hypersensitivity reaction occurs, discontinue TREMFYA® and initiate appropriate therapy.

Infections

TREMFYA® may increase the risk of infection. Treatment with TREMFYA® should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated.

Consider the risks and benefits of treatment prior to prescribing TREMFYA® in patients with a chronic infection or a history of recurrent infection. Instruct patients receiving TREMFYA® to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection, or is not responding to standard therapy, closely monitor and discontinue TREMFYA® until the infection resolves.

Pre-Treatment Evaluation for Tuberculosis (TB)

Evaluate patients for TB infection prior to initiating treatment with TREMFYA®. Initiate treatment of latent TB prior to administering TREMFYA®. Monitor patients for signs and symptoms of active TB during and after TREMFYA® treatment. Do not administer TREMFYA® to patients with active TB infection.

Immunizations

Prior to initiating TREMFYA®, consider completion of all age-appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with TREMFYA®.

ADVERSE REACTIONS

Most common (≥1%) adverse reactions associated with TREMFYA® include upper respiratory infections, headache, injection site reactions, arthralgia, bronchitis, diarrhea, gastroenteritis, tinea infections, and herpes simplex infections.

The overall safety profile observed in patients with psoriatic arthritis is generally consistent with the safety profile in patients with plaque psoriasis, with the addition of bronchitis and neutrophil count decreased.

Please read the full Prescribing Information and Medication Guide for TREMFYA®. Provide the Medication Guide to your patients and encourage discussion.

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John Russell, MD:
That is all great context for us to think on as we come to the end of today's program.

I want to thank my guests for helping us better understand taking a multidisciplinary approach to treating active psoriatic arthritis. Dr. Mease, Dr. Armstrong, it was great speaking with you both today.

Philip Mease, MD:
Thanks, John, for having us tonight. I hope our listeners found this information useful for their practice.

April Armstrong, MD, MPH:
I agree with Dr. Mease. It was great discussing this important topic with you, Dr. Russell, as well as Dr. Mease, and thank you very much for having me.

John Russell, MD:
It was really terrific, thank you. I'm Dr. John Russell. Thanks for listening.

Announcer:
This program was sponsored by Janssen Pharmaceuticals, Inc. Please read the full Prescribing Information, including Medication Guide

for TREMFYA at TREMFYAHCP.com. If you missed any part of this discussion, visit ReachMD.com/IndustryFeature. This is ReachMD. Be part of the knowledge.