Transcript Details
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An Rx Option for Adults with Moderate-to-Severe Plaque Psoriasis

Announcer:
This medical industry feature, titled "An Option for Adults with Moderate-to-Severe Plaque Psoriasis" is sponsored by Bristol Myers Squibb.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
An estimated 7.5 million people across the U.S. are impacted by psoriasis[1], and nearly one-quarter of them, or around two million, have cases of plaque psoriasis that are considered moderate-to-severe.[1,2] According to a survey, despite a variety of treatments, many of these patients remain undertreated or untreated.[2,3] Today we will be discussing an oral treatment option for adults with moderate-to-severe plaque psoriasis.

Dr. Caudle:
This is ReachMD, and I'm Dr. Jennifer Caudle.

Joining me to discuss an oral treatment option for adults with moderate-to-severe plaque psoriasis is Dr. Bruce Strober, a Clinical Professor of Dermatology at Yale University School of Medicine. He also is board certified by the American Board of Dermatology and is a Fellow in the American Academy of Dermatology.

Dr. Strober, thanks for being here today.

Dr. Strober:
Thanks for having me.

Dr. Caudle:
Of course, so to start us off, Dr. Strober, how do you approach selecting a treatment option for your adult patients with moderate-to-severe plaque psoriasis?

Dr. Strober:
So there are a lot of over-the-counter products and prescription therapies out there, including oral therapies, injectable therapies, topicals and ultraviolet phototherapy. And with the growing presence of information available on social media, and other online platforms, and television, it may be confusing for patients to understand the available options.

When I consider treatment goals for my patients, I consider three aspects: efficacy, safety, and what fits into my patients' routine. In the case of psoriasis, goals are most often associated with skin clearance.

Efficacy and the safety profile of the drug is important and is something I always consider, and it's also important for me that the patient finds a medicine that works for their routine.

So all three of those things – efficacy, safety, and what fits into my patients' routine – are important to consider when determining whether to prescribe a product to a specific patient.

Dr. Caudle:
Can you tell us about this oral treatment called Sotyktu?

Dr. Strober:
Yes. Sotyktu, also known as deucravacitinib, was approved by the FDA in September of 2022, for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. It is a first-in-class, oral, selective, allosteric tyrosine kinase 2, or TYK2 inhibitor, and the first ever approved TYK2 inhibitor. Before we dive in, let me just say that Sotyktu is not recommended for use in combination with other potent immunosuppressants, and it is contraindicated in patients with a history of hypersensitivity reaction to either deucravacitinib or to any of the excipients of Sotyktu.

ANNOUNCER:
Selected Important Safety Information

Contraindications: SOTYKTU is contraindicated in patients with a history of hypersensitivity reaction to deucravacitinib or to any of the excipients in SOTYKTU

Hypersensitivity: Hypersensitivity reactions such as angioedema have been reported. Discontinue if a clinically significant hypersensitivity reaction occurs

Infections: SOTYKTU may increase the risk of infection. Avoid use in patients with active or serious infection. If a serious infection develops, discontinue SOTYKTU until the infection resolves

Tuberculosis (TB): Evaluate patients for latent and active TB infection prior to initiating treatment with SOTYKTU. Do not administer SOTYKTU to patients with active TB. Initiate treatment of latent TB prior to administering SOTYKTU

Malignancy and Lymphomas: Malignancies, including lymphomas, were observed in clinical trials with SOTYKTU. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with SOTYKTU, particularly in patients with a known malignancy (other than a successfully treated non-melanoma skin cancer) and patients who develop a malignancy when on treatment with SOTYKTU

Rhabdomyolysis and Elevated CPK: Discontinue SOTYKTU if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Instruct patients to promptly report any unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever

Laboratory Abnormalities: Periodically evaluate serum triglycerides. Evaluate liver enzymes at baseline and thereafter in patients with known or suspected liver disease

Immunizations: Avoid use with live vaccines

Potential Risks Related to JAK Inhibition: It is not known whether TYK2 inhibition may be associated with the observed or potential adverse reactions of JAK inhibition. Higher rates of all-cause mortality, including sudden cardiovascular death, major adverse cardiovascular events, overall thrombosis, deep venous thrombosis, pulmonary embolism, and malignancies (excluding non-melanoma skin cancer) were observed in patients treated with a JAK inhibitor compared to those treated with TNF blockers in rheumatoid arthritis (RA) patients. SOTYKTU is not approved for use in RA

Adverse Reactions: The most common adverse reactions (≥1%) are upper respiratory infections, blood creatine phosphokinase increased, herpes simplex, mouth ulcers, folliculitis, and acne

Use in Specific Populations: Use in patients with severe hepatic impairment (Child-Pugh C) is not recommended

Dr. Strober:
I am particularly excited about the availability of Sotyktu. I've actually prescribed it for a lot of my patients who are adults with moderate-to-severe plaque psoriasis because of the safety and efficacy I've seen in the clinical trial data.

And importantly, it's a once daily oral option which some of my patients with moderate-to-severe plaque psoriasis are looking for. They want something that they can fit into their daily routines.

Dr. Caudle:
Can you tell us more about the clinical trial data that led to the approval of Sotyktu?

Dr. Strober:
Yes. The approval is based on the pivotal phase 3, POETYK PSO-1 which had 644 patients in it, and POETYK PSO-2 which had 1,020 patients enrolled, in these clinical trials. And these clinical trials evaluated the efficacy of Sotyktu, a once daily pill, compared to placebo

and Otezla – also known as apremilast – which is a twice daily pill. The studies also evaluated the safety of Sotyktu. I will share those results with you shortly, but let's first consider the study design.

The trials included 1,684 patients, aged 18 years of age or older, with moderate to severe plaque psoriasis, who were eligible for systemic therapy or phototherapy. Both were multinational, multi-center, randomized, double blind, placebo and active controlled, 52-week, phase 3 studies. Patients in the studies were randomized 1:2:1 to placebo, Sotyktu or apremilast in POETYK PSO-1. 166 patients were randomized to placebo, 330 were randomized to Sotyktu, and 168 were randomized to apremilast; and in POETYK PSO-2, 255 patients were randomized to placebo, 511 randomized to Sotyktu, and 254 were randomized to apremilast.

The coprimary endpoints of both studies measured the percentage of patients who achieved 75% improvement in the PASI score – the Psoriasis Area and Severity Index. This is also known as the PASI 75. And, the percentage of patients who achieved a static Physician's Global Assessment score, also known as the sPGA, of 0 or 1 at week 16, versus placebo. The key secondary endpoints included the percentage of patients who achieved PASI 75 and PASI 90, compared to Otezla at week 16 and week 24. Patients enrolled in these studies had to be adults with moderate to severe plaque psoriasis, who were eligible for systemic therapy or phototherapy, and had a PASI score of greater than or equal to 12, an sPGA greater than or equal to 3, and a BSA of involvement of greater than or equal to 10%.

Dr. Caudle:
Thank you for that. And can you discuss what was seen in clinical trials, in terms of efficacy and safety for Sotyktu?

Dr. Strober:
In the trials, Sotyktu demonstrated superior PASI 75 response rate versus placebo at week 16, a coprimary endpoint. PASI 75 response rates at week 16 were 58% for Sotyktu and 13% for placebo in POETYK PSO-1, and 53% for Sotyktu, versus 9% for placebo in POETYK PSO-2. Sotyktu also demonstrated superior sPGA 0-1 response rates versus placebo at week 16, another coprimary endpoint. sPGA 0-1 response rates for Sotyktu at week 16 was 54% versus 7% for placebo in POETYK PSO-1; and 50% for Sotyktu versus 9% for placebo in POETYK PSO-2.

Sotyktu also showed superior PASI 75 response rate vs apremilast at Weeks 16, a secondary endpoint. PASI 75 response rates at week 16 were 58% for *Sotyktu* vs 35% for apremilast in POETYK PSO-1, and 53% for *Sotyktu* and 40% for apremilast in POETYK PSO-2.

Sotyktu also achieved superior PASI 90 response rate compared with apremilast at week 24, another key secondary endpoint. For Sotyktu, PASI 90 response rate was 42% versus 22% for apremilast, in POETYK PSO-1; and 32% for Sotyktu versus 20% for apremilast in POETYK PSO-2.

Across both trials, Sotyktu and placebo had the following discontinuation rates due to adverse events: at Week 16, 2.4 percent of patients on Sotyktu and 3.8 percent of patients on placebo.[4]

Studies were not designed to compare the safety of apremilast to Sotyktu. Some of the observed safety rates for apremilast may differ from those previously reported. Please refer to the apremilast full Prescribing Information.

The most common adverse reactions – defined as greater than or equal to 1 percent and higher than placebo – were upper respiratory tract infections, blood creatine phosphokinase increase that's CPK increase, herpes simplex, mouth ulcers, folliculitis, and acne.[4]

So, this reminds me of a patient I saw recently. A 25-year-old woman with fairly extensive psoriasis. About 15% of her body surface area was affected. It involved her scalp, her elbows, her trunk, her legs, and importantly, involved a lot of itch. And she told me she had been seeing other dermatologists, who had prescribed her numerous various, topical therapeutics. And she was just looking for something different. So, I offered her Sotyktu, and explained to her Sotyktu's characteristics, namely it's a 6 milligram, once daily, pill. She just takes one pill a day. And it would require, test at the baseline for TB, either latent or active, throughout her therapy, she would be tested periodically for her triglycerides. But otherwise, a fairly straightforward approach – once daily pill, she has to stick with it.

There are some potential adverse events that were seen in the clinical trials, such as upper respiratory tract infection, acne, folliculitis, herpes or, oral ulcers. I told her those occurred in a group of patients, in the clinical trials, and she should let me know if she experiences any of those side effects. She came back to me, after a period of time, and noted that she had significantly improved. In fact, about 80% of her psoriasis had, gone away, particularly on her scalp and her upper trunk, and for the most part on her lower extremities, too. There was a much lessened severity. And, really important was the itch had gone away completely. So, she expressed to me her desire to continue taking the therapy, which I said of course, it's something that we would like her to do, and that we would continue to monitor her periodically over time.

Dr. Caudle:
Thank you for that. And how does *Sotyktu* work and what makes its mechanism of action unique?

Dr. Strober:
Sotyktu is the first in a class of systemic therapies called TYK2 inhibitors. Sotyktu is an oral, selective, allosteric inhibitor of TYK2.[4,5]

TYK2 is a member of the Janus kinase, or, also called JAK, family. Sotyktu selectively inhibits activation of TYK2 and its downstream activation of STATs.[5] The precise mechanism linking inhibition of TYK2 enzyme to therapeutic effectiveness in the treatment of adults with moderate to severe plaque psoriasis is not currently known.[4]

Dr. Caudle:
Now that we have a better understanding of the safety and efficacy profile of *Sotyktu* in clinical trials – how can practitioners get their appropriate patients started?

Dr. Strober:
Well, if you have a patient appropriate for *Sotyktu* treatment, there are a few things to keep in mind when starting treatment. Beyond a TB evaluation, no tests are required to start *Sotyktu*, unless patients have known or suspected liver disease. In patients with known or suspected liver disease, practitioners should evaluate liver enzymes at baseline and thereafter according to routine management. After starting *Sotyktu* in appropriate patients, serum triglyceride levels should be evaluated periodically according to clinical guidelines for hyperlipidemia. *Sotyktu* importantly requires no dose titration, with once-daily dosing right from the start.

Clinicians may be familiar with certain standards of practice in the plaque psoriasis treatment journey, such as screenings and TB treatment, so the requirement to evaluate for TB prior to starting treatment with *Sotyktu* may not be something new for them.

Dr. Caudle:
And before we close, Dr. Strober, can you tell us what Sotyktu could mean for appropriate patients?

Dr. Strober:
With a product like Sotyktu, that offers the possibility of clearer skin for my appropriate patients - it's something that my patients and I are really enthusiastic about.

And while no treatment is right for everyone. For patients who have wanted or preferred an oral treatment, we have a once daily oral option with proven superior skin clearance to twice daily Otezla, as demonstrated by the PASI 75 and PASI 90 results I mentioned earlier.

Dr. Caudle:
That’s a great way to round out our discussion on this treatment option.

I’d like to thank my guest, Dr. Bruce Strober, for helping us better understand an emerging oral therapy for adult patients living with moderate-to-severe plaque psoriasis. Dr. Strober, it was great speaking with you today.

Dr. Strober:
It was my pleasure speaking with you today also.

Dr. Caudle:
And before we close, let’s take a moment to review some important safety information.

INDICATION

SOTYKTU™ (deucravacitinib) is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

Limitations of Use: SOTYKTU is not recommended for use in combination with other potent immunosuppressants.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

SOTYKTU is contraindicated in patients with a history of hypersensitivity reaction to deucravacitinib or to any of the excipients in SOTYKTU.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions such as angioedema have been reported. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue SOTYKTU.

Infections: SOTYKTU may increase the risk of infections. Serious infections have been reported in patients with psoriasis who received SOTYKTU. The most common serious infections reported with SOTYKTU included pneumonia and COVID-19. Avoid use of SOTYKTU in patients with an active or serious infection. Consider the risks and benefits of treatment prior to the initiation SOTYKTU in patients:

- with chronic or recurrent infection
- who have been exposed to tuberculosis
- with a history of a serious or an opportunistic infection

with underlying conditions that may predispose them to infection.

Closely monitor patients for the development of signs and symptoms of infection during and after treatment. A patient who develops a new infection during treatment should undergo prompt and complete diagnostic testing, have appropriate antimicrobial therapy initiated and be closely monitored. Interrupt SOTYKTU if a patient develops a serious infection. Do not resume SOTYKTU until the infection resolves or is adequately treated.

Viral Reactivation

Herpes virus reactivation (e.g., herpes zoster, herpes simplex) was reported in clinical trials with SOTYKTU. Through Week 16, herpes simplex infections were reported in 17 patients (6.8 per 100 patient-years) treated with SOTYKTU, and 1 patient (0.8 per 100 patient-years) treated with placebo. Multidermatomal herpes zoster was reported in an immunocompetent patient. During PSO-1, PSO-2, and the open-label extension trial, the majority of patients who reported events of herpes zoster while receiving SOTYKTU were under 50 years of age. The impact of SOTYKTU on chronic viral hepatitis reactivation is unknown. Consider viral hepatitis screening and monitoring for reactivation in accordance with clinical guidelines before starting and during therapy with SOTYKTU. If signs of reactivation occur, consult a hepatitis specialist. SOTYKTU is not recommended for use in patients with active hepatitis B or hepatitis C.

Tuberculosis (TB): In clinical trials, of 4 patients with latent TB who were treated with SOTYKTU and received appropriate TB prophylaxis, no patients developed active TB (during the mean follow-up of 34 weeks). One patient, who did not have latent TB, developed active TB after receiving 54 weeks of SOTYKTU. Evaluate patients for latent and active TB infection prior to initiating treatment with SOTYKTU. Do not administer SOTYKTU to patients with active TB. Initiate treatment of latent TB prior to administering SOTYKTU. Consider anti-TB therapy prior to initiation of SOTYKTU in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during treatment.

Malignancy including Lymphomas: Malignancies, including lymphomas, were observed in clinical trials with SOTYKTU. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with SOTYKTU, particularly in patients with a known malignancy (other than a successfully treated non-melanoma skin cancer) and patients who develop a malignancy when on treatment with SOTYKTU.

Rhabdomyolysis and Elevated CPK: Treatment with SOTYKTU was associated with an increased incidence of asymptomatic creatine phosphokinase (CPK) elevation and rhabdomyolysis compared to placebo. Discontinue SOTYKTU if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Instruct patients to promptly report unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Laboratory Abnormalities: Treatment with SOTYKTU was associated with increases in triglyceride levels. Periodically evaluate serum triglycerides according to clinical guidelines during treatment. SOTYKTU treatment was associated with an increase in the incidence of liver enzyme elevation compared to placebo. Evaluate liver enzymes at baseline and thereafter in patients with known or suspected liver disease according to routine management. If treatment-related increases in liver enzymes occur and drug-induced liver injury is suspected, interrupt SOTYKTU until a diagnosis of liver injury is excluded.

Immunizations: Prior to initiating therapy with SOTYKTU, consider completion of all age-appropriate immunizations according to current immunization guidelines including prophylactic herpes zoster vaccination. Avoid use of live vaccines in patients treated with SOTYKTU. The response to live or non-live vaccines has not been evaluated.

Potential Risks Related to JAK Inhibition: It is not known whether tyrosine kinase 2 (TYK2) inhibition may be associated with the observed or potential adverse reactions of Janus Kinase (JAK) inhibition. In a large, randomized, postmarketing safety trial of a JAK inhibitor in rheumatoid arthritis (RA), patients 50 years of age and older with at least one cardiovascular risk factor, higher rates of all-

cause mortality, including sudden cardiovascular death, major adverse cardiovascular events, overall thrombosis, deep venous thrombosis, pulmonary embolism, and malignancies (excluding non-melanoma skin cancer) were observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. SOTYKTU is not approved for use in RA.

ADVERSE REACTIONS Most common adverse reactions (≥1% of patients on SOTYKTU and more frequently than with placebo) include upper respiratory infections, blood creatine phosphokinase increased, herpes simplex, mouth ulcers, folliculitis and acne.

SPECIFIC POPULATIONS

Pregnancy: Available data from case reports on SOTYKTU use during pregnancy are insufficient to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Report pregnancies to the Bristol-Myers Squibb Company's Adverse Event reporting line at 1-800-721-5072.

Lactation: There are no data on the presence of SOTYKTU in human milk, the effects on the breastfed infant, or the effects on milk production. SOTYKTU is present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SOTYKTU and any potential adverse effects on the breastfed infant from SOTYKTU or from the underlying maternal condition.

Hepatic Impairment: SOTYKTU is not recommended for use in patients with severe hepatic impairment.

SOTYKTU is available in 6 mg tablets.

Please see Full Prescribing Information, including Medication Guide, available on this site.

Announcer:

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