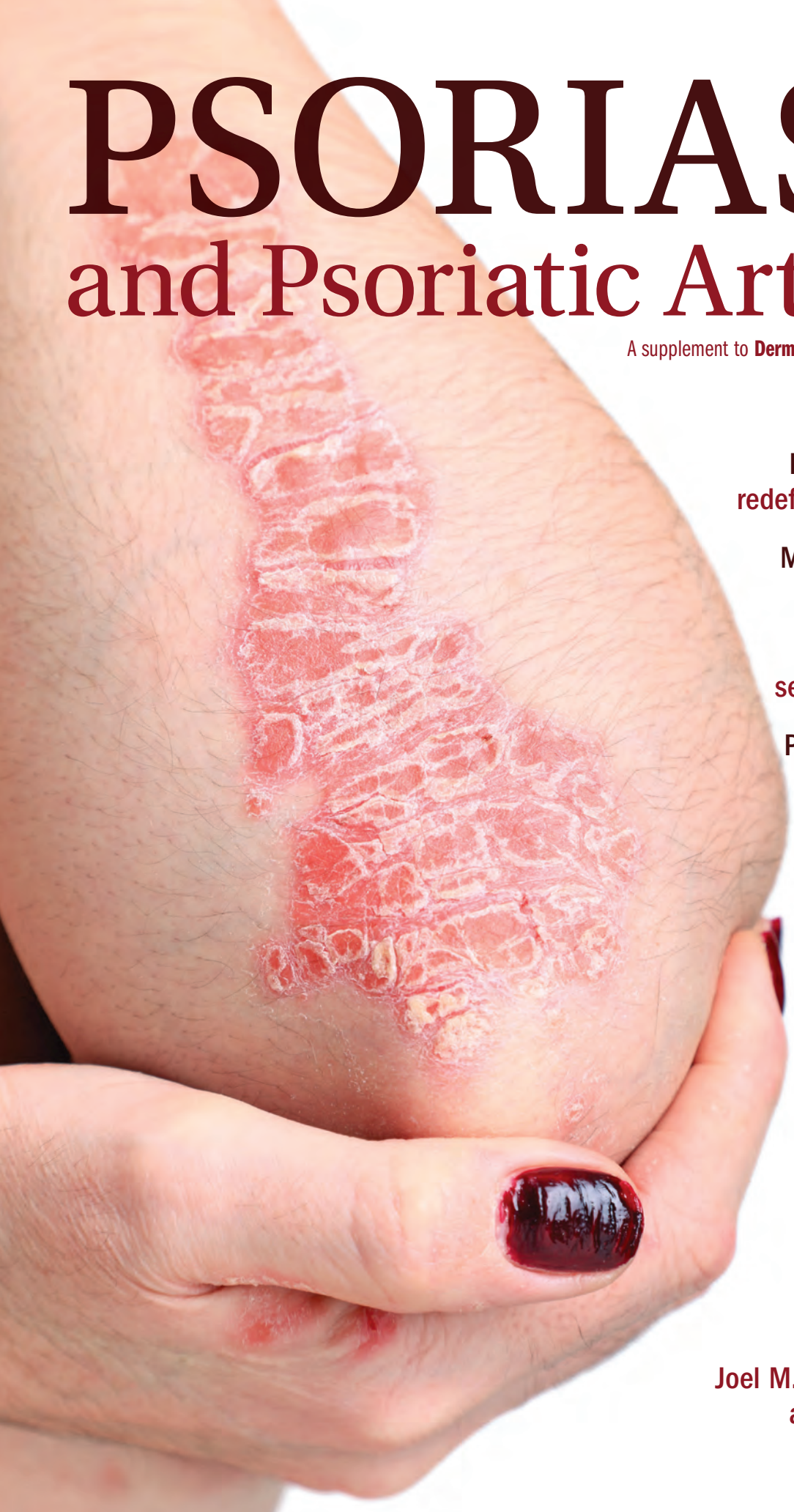
PSORIASIS
and Psoriatic Arthritis

A supplement to **Dermatology News** | **October 2021**



PSORIASIS SEVERITY
redefined by expert group

MITIGATING PSA RISK
with biologic therapy

LACK OF DIVERSITY
seen in psoriasis trials

PSA COMORBIDITIES:
effect on treatment responses

And more...

COMMENTARIES BY
Joel M. Gelfand, MD, MSCE
and Alan Menter, MD

Advances in treatment, diversity challenges, and unanswered questions

BY JOEL M. GELFAND, MD, MSCE


Dr. Gelfand

So much progress is being made in the treatment of psoriasis that our treatment paradigms are shifting in profound ways. A new classification system by the International Psoriasis Council broadens greatly the types of patients now considered eligible for pills, biologics, or phototherapy (see page 7). The decades-long search for treatments that induce clinically important remissions in psoriasis is finally paying dividends (page 8). As our treatments for psoriasis expand, the need to ensure equity in the inclusion of diverse patient populations in our clinical trials is coming under scrutiny. New research in this area challenges us to reflect on how diversity, equity, and inclusion need to be considered when designing, executing, and interpreting data from clinical trials (page 12). Finally, the COVID-19 pandemic continues to affect us all in profound ways. Data on the impact of psoriasis treatments on COVID-19 risk and efficacy of COVID-19 vaccines are rapidly expanding (page 10). Keep up with the latest recommendations from the COVID-19 Task Force (full disclosure, I cochair this effort) at www.psoriasis.org/covid-19-task-force-guidance-statements/. To keep up with the latest publications about psoriasis, I invite you to follow me on Twitter (@DrJoelGelfand) or LinkedIn (www.linkedin.com/in/drjoelgelfand/).

Dr. Gelfand is professor of dermatology and of epidemiology; vice chair of clinical research and medical director, dermatology clinical studies unit; and director of the Psoriasis and Phototherapy Treatment Center at the University of Pennsylvania, Philadelphia. His disclosures relevant to this supplement are serving as a consultant for Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Lilly (DMC), Janssen Biologics, Novartis, UCB (DSMB); receiving honoraria; and receiving research grants (to the Trustees of the University of Pennsylvania) from Boehringer Ingelheim and Pfizer. Dr. Gelfand is also deputy editor for the Journal of Investigative Dermatology receiving honoraria from the Society for Investigative Dermatology, is chief medical editor for Healio Psoriatic Disease (receiving honoraria), and is a member of the board of directors for the International Psoriasis Council, receiving no honoraria.

BY ALAN MENTER, MD


Dr. Menter

In this year's supplement, the articles on psoriatic arthritis focus on the highly important topics of reducing risk of PsA in our patients with psoriasis (page 9), and addressing comorbidities in our patients with PsA (page 14). Another article addresses concerns about COVID-19 in patients with psoriasis and PsA.

As for some of the newer biologics approved for treatment of psoriasis and/or PsA, we now have six interleukin-17 inhibitors and IL-23 inhibitors, and more biologics in the pipeline. Since a biologic that works well for psoriasis may not work as well for psoriatic joint disease – and vice versa – one of the big questions is whether biologics effective for psoriasis will be equally effective for psoriatic joint disease – and will they be any more effective than the tumor necrosis alpha inhibitors on American College of Rheumatology 20 scores in these patients. Another important question that has not yet been answered is whether any of the biologic drugs that are so effective for treating skin and joints will reduce inflammation in the coronary arteries and reduce coronary artery disease in patients with psoriasis and PsA – those answers are still to come.

Dr. Menter is chairman of dermatology at Baylor Scott & White Health and clinical professor of dermatology at the University of Texas, both in Dallas. He is cochair of the American Academy of Dermatology Psoriasis Guideline Work Group. He is an adviser, a consultant, an investigator, and/or a speaker for Abbott Labs, Amgen, Boehringer Ingelheim, Celgene, Janssen Biotech, LEO Pharma, Eli Lilly, Merck, Novartis, Sun Pharma, and UCB; and he has received grants and/or honoraria from these companies. He is also an investigator for Pfizer.

Dermatology News

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Psoriasis and Psoriatic Arthritis is a supplement to *Dermatology News*, an independent newspaper that provides practicing dermatologists with timely and relevant news and commentary about clinical developments in the field and about the impact of health care policy on the specialty and the physician's practice.

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Otezla® (apremilast) 30mg tablets

— ACCESSING OTEZLA —
IS EASIER THAN EVER BEFORE

9 out of 10

commercial patients with plaque psoriasis or psoriatic arthritis have preferred access to Otezla with **no biologic-step** required[1]

74% of commercially insured lives in the US have **no DMARD- and no biologic-step** for plaque psoriasis[1]

Contact your Otezla representative or visit OtezlaPro.com

DMARD, disease-modifying antirheumatic drug.

INDICATIONS

Otezla® (apremilast) is indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Otezla is indicated for the treatment of adult patients with active psoriatic arthritis.

IMPORTANT SAFETY INFORMATION

Contraindications

- Otezla® (apremilast) is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation

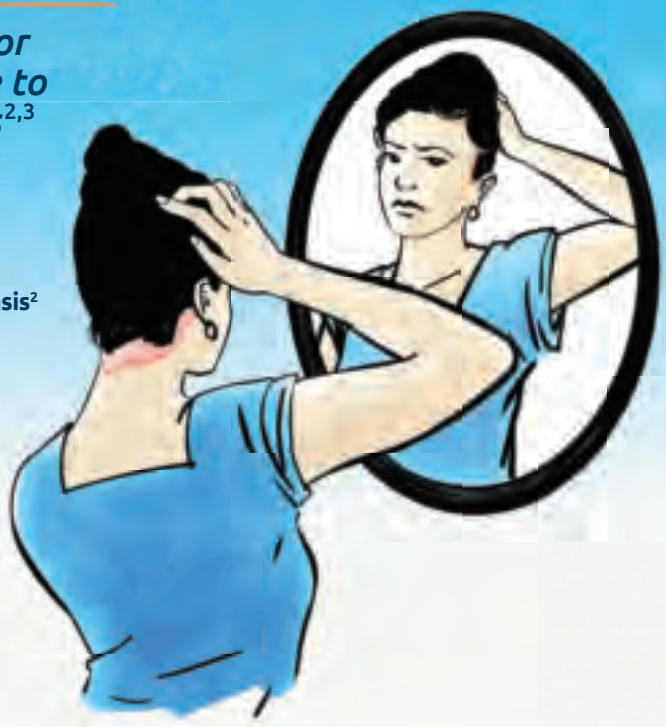
Please see additional Important Safety Information and Brief Summary of Full Prescribing Information on the following pages.

THE *ONLY*

ORAL THERAPY

indicated for
plaque psoriasis
and
psoriatic arthritis[1]

Otezla Clinical Data for Adults with Moderate to Severe Scalp Psoriasis[2,3]



For adult patients with moderate to severe plaque psoriasis[2]

THE ONLY ORAL THERAPY WITH DATA IN THE LABEL FOR SCALP PSORIASIS[1]

- **A FIRST STEP TO SYSTEMIC THERAPY FOR MODERATE TO SEVERE SCALP PSORIASIS[2]**
- **OTEZLA IS A NON-BIOLOGIC THERAPY WITH ORAL DOSING, A PROVEN EFFICACY AND ESTABLISHED SAFETY PROFILE, AND NO LABEL-REQUIRED LAB MONITORING[2]**

STYLE clinical trial

Study design: Phase 3 multicenter, randomized, double-blind, placebo-controlled study of 303 patients with moderate to severe plaque psoriasis of the scalp. Patients were randomized 2:1 to Otezla® (apremilast) 30 mg twice daily (n=201) or placebo (n=102) for the placebo-controlled phase through week 16, then continued or switched to Otezla for the open-label extension phase through week 32. Treatment groups were stratified by baseline ScPGA score (3 [moderate] or 4 [severe]).[2,3]
Selected inclusion criteria: Patients had moderate to severe plaque psoriasis of the scalp (ScPGA ≥3, SSA ≥20%), inadequate response or intolerance to ≥1 topical therapy for plaque psoriasis of the scalp, and moderate to severe plaque psoriasis (BSA involvement of ≥10%, sPGA ≥3, PASI score ≥12).[2]

BSA, body surface area; PASI, Psoriasis Area and Severity Index; ScPGA, Scalp Physician Global Assessment; sPGA, static Physician Global Assessment; SSA, scalp surface area.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

- Diarrhea, Nausea, and Vomiting: Cases of severe diarrhea, nausea, and vomiting have been reported with the use of Otezla. Most events occurred within the first few weeks of treatment. In some cases patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting; advise patients to contact their healthcare provider. Consider Otezla dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting
- Depression: Treatment with Otezla is associated with an increase in depression. During clinical trials 1.3% (12/920) of patients reported depression, compared to 0.4% (2/506) on placebo. Suicidal behavior was observed in 0.1% (1/1308) of patients on Otezla, compared to 0.2% (1/506) on placebo. Carefully weigh the risks and benefits of treatment with Otezla for patients with a history of depression and/or suicidal thoughts/behavior, or in patients who develop such symptoms while on Otezla. Patients, caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and they should contact their healthcare provider if such changes occur
- Weight Decrease: Body weight loss of 5-10% occurred in 12% (96/784) of patients treated with Otezla and in 5% (19/382) of patients treated with placebo. Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of Otezla
- Drug Interactions: Apremilast exposure was decreased when Otezla was co-administered with rifampin, a strong CYP450 enzyme inducer; loss of Otezla efficacy may occur. Concomitant use of Otezla with CYP450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended

OTEZLA SIGNIFICANTLY IMPROVES SCALP RESPONSE[2,3]

STYLE primary endpoint: proportion of patients achieving an ScPGA response at week 16[1,2,*]

Otezla patients **3x** achieved scalp improvement at week 16 *vs placebo in the STYLE study*

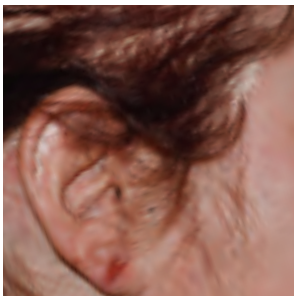
43% with Otezla® (apremilast) 30 mg BID (n=201)

vs (*P*<0.0001)

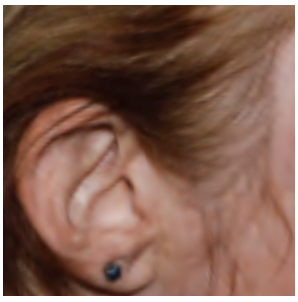
14% with placebo (n=102)

*ScPGA response was defined as the proportion of patients achieving an ScPGA score of 0 (clear) or 1 (almost clear) with at least a 2-point reduction from baseline.[2]

Results seen in an Otezla patient (scalp response)



Baseline



Week 16
ScPGA: 0†
3-point improvement in ScPGA score

†Actual clinical trial patient from STYLE.[1] **Individual results may vary.**

Adverse reactions

- The most commonly reported adverse reactions that occurred at a higher rate in Otezla patients than in the placebo were: diarrhea (31% vs 11%), nausea (22% vs 6%), headache (12% vs 5%), and vomiting (6% vs 2%)[2]
- The proportion of patients who discontinued treatment because of any adverse reaction was 6% for patients who received Otezla 30 mg twice daily and 3% for patients who received placebo[2]
- Gastrointestinal adverse reactions that led to discontinuation of treatment were diarrhea (3% vs 0%), nausea (1.5% vs 1%), and vomiting (1.5% vs 0%) in the Otezla group, compared to placebo[2]

Visit OtezlaPro.com for additional information

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions

- Adverse reactions reported in ≥5% of patients were (Otezla%, placebo%): diarrhea (17, 6), nausea (17, 7), upper respiratory tract infection (9, 6), tension headache (8, 4), and headache (6, 4)

Use in Specific Populations

- Pregnancy: Otezla has not been studied in pregnant women. Advise pregnant women of the potential risk of fetal loss. Consider pregnancy planning and prevention for females of reproductive potential. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Otezla during pregnancy. Information about the registry can be obtained by calling 1-877-311-8972 or visiting https://mothertobaby.org/ongoing-study/otezla/
- Lactation: There are no data on the presence of apremilast or its metabolites in human milk, the effects of apremilast on the breastfed infant, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Otezla and any potential adverse effects on the breastfed child from Otezla or from the underlying maternal condition
- Renal Impairment: Otezla dosage should be reduced in patients with severe renal impairment (creatinine clearance less than 30 mL/min); for details, see Dosage and Administration, Section 2, in the full Prescribing Information

References: 1. Data on file, Amgen Inc. **2.** Otezla [package insert]. Thousand Oaks, CA: Amgen Inc. **3.** Van Voorhees AS, Gold LS, Lebwohl M, et al. *J Am Acad Dermatol.* 2020;83(1):96-103.

Please turn the page for Brief Summary of Full Prescribing Information.

AMGEN®
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03/21 USA-407-80469

Otezla® (apremilast) 30mg tablets

Brief Summary of Prescribing Information

OTEZLA® (apremilast) tablets, for oral use

PLEASE SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

CONTRAINDICATIONS

OTEZLA is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation *[see Adverse Reactions (6.1)]*.

WARNINGS AND PRECAUTIONS

Diarrhea, Nausea, and Vomiting

There have been postmarketing reports of severe diarrhea, nausea, and vomiting associated with the use of OTEZLA. Most events occurred within the first few weeks of treatment. In some cases patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting. Patients who reduced dosage or discontinued OTEZLA generally improved quickly. Consider OTEZLA dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting.

Depression

Treatment with OTEZLA is associated with an increase in adverse reactions of depression. Before using OTEZLA in patients with a history of depression and/or suicidal thoughts or behavior prescribers should carefully weigh the risks and benefits of treatment with OTEZLA in such patients. Patients, their caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and if such changes occur to contact their healthcare provider. Prescribers should carefully evaluate the risks and benefits of continuing treatment with OTEZLA if such events occur.

Psoriatic arthritis: During the 0 to 16 week placebo-controlled period of the 3 controlled clinical trials, 1.0% (10/998) of subjects treated with OTEZLA reported depression or depressed mood compared to 0.8% (4/495) treated with placebo. During the clinical trials, 0.3% (4/1441) of subjects treated with OTEZLA discontinued treatment due to depression or depressed mood compared with none in placebo treated subjects (0/495). Depression was reported as serious in 0.2% (3/1441) of subjects exposed to OTEZLA, compared to none in placebo-treated subjects (0/495). Instances of suicidal ideation and behavior have been observed in 0.2% (3/1441) of subjects while receiving OTEZLA, compared to none in placebo treated subjects (0/495). In the clinical trials, 2 subjects who received placebo committed suicide compared to none in OTEZLA-treated subjects.

Psoriasis: During the 0 to 16 week placebo-controlled period of the 3 controlled clinical trials, 1.3% (12/920) of subjects treated with OTEZLA reported depression compared to 0.4% (2/506) treated with placebo. During the clinical trials, 0.1% (1/1308) of subjects treated with OTEZLA discontinued treatment due to depression compared with none in placebo-treated subjects (0/506). Depression was reported as serious in 0.1% (1/1308) of subjects exposed to OTEZLA, compared to none in placebo-treated subjects (0/506). Instances of suicidal behavior have been observed in 0.1% (1/1308) of subjects while receiving OTEZLA, compared to 0.2% (1/506) in placebo-treated subjects. In the clinical trials, one subject treated with OTEZLA attempted suicide while one who received placebo committed suicide.

Weight Decrease

During the controlled period of the studies in psoriatic arthritis (PsA), weight decrease between 5%-10% of body weight was reported in 10% (49/497) of subjects treated with OTEZLA 30 mg twice daily compared to 3.3% (16/495) treated with placebo.

During the controlled period of the trials in psoriasis, weight decrease between 5%-10% of body weight occurred in 12% (96/784) of subjects treated with OTEZLA compared to 5% (19/382) treated with placebo. Weight decrease of ≥10% of body weight occurred in 2% (16/784) of subjects treated with OTEZLA 30 mg twice daily compared to 1% (3/382) subjects treated with placebo.

Patients treated with OTEZLA should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated, and discontinuation of OTEZLA should be considered *[see Adverse Reactions (6.1)]*.

Drug Interactions

Co-administration of strong cytochrome P450 enzyme inducer, rifampin, resulted in a reduction of systemic exposure of apremilast, which may result in a loss of efficacy of OTEZLA. Therefore, the use of cytochrome P450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) with OTEZLA is not recommended *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]*.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Psoriatic Arthritis Clinical Trials: OTEZLA was evaluated in 3 multicenter, randomized, double-blind, placebo-controlled trials [Studies PsA-1, PsA-2, and PsA-3] of similar design in adult patients with active psoriatic arthritis *[see Clinical Studies (14.1)]*. Across the 3 studies, there were 1493 patients randomized equally to placebo, OTEZLA 20 mg twice daily or OTEZLA 30 mg twice daily. Titration was used over the first 5 days [see Dosage and Administration (2.1)]. Placebo patients whose tender and swollen joint counts had not improved by at least 20% were re-randomized 1:1 in a blinded fashion to either OTEZLA 20 mg twice daily or 30 mg twice daily at week 16 while OTEZLA patients remained on their initial treatment. Patients ranged in age from 18 to 83 years, with an overall median age of 51 years.

The majority of the most common adverse reactions presented below occurred within the first 2 weeks of treatment and tended to resolve over time with continued dosing. Diarrhea, headache, and nausea were the most commonly reported adverse reactions. The most common adverse reactions leading to discontinuation for patients taking OTEZLA were nausea (1.8%), diarrhea (1.8%), and headache (1.2%). The proportion of patients with psoriatic arthritis who discontinued treatment due to any adverse reaction was 4.6% for patients taking OTEZLA 30 mg twice daily and 1.2% for placebo-treated patients.

Adverse Reactions Reported in ≥2% of Patients on OTEZLA 30 mg Twice Daily and ≥1% Than That Observed in Patients on Placebo on Day 1-5 (Placebo %, OTEZLA %): Diarrhea[a] (1.2%, 9.3%), Nausea[a] (1.4%, 7.4%), Headache[a] (1.8%, 4.8%), Upper respiratory tract infection[b] (0.6%, 0.6%), Vomiting[a] (0.4%, 0.8%), Nasopharyngitis[b] (0.2%, 0.2%), Abdominal pain upper[b] (0.0%, 0.6%).

Adverse Reactions Reported in ≥2% of Patients on OTEZLA 30 mg Twice Daily and ≥1% Than That Observed in Patients on Placebo on Day 6-112 (Week 16) (Placebo %, OTEZLA %): Diarrhea[a] (1.6%, 7.7%), Nausea[a] (3.1%, 8.9%), Headache[a] (2.2%, 5.9%), Upper respiratory tract infection[b] (1.8%, 3.9%), Vomiting[a] (0.4%, 3.2%), Nasopharyngitis[b] (1.6%, 2.6%), Abdominal pain upper[b] (0.2%, 2.0%).

[a] Of the reported gastrointestinal adverse reactions, 1 subject experienced a serious adverse reaction of nausea and vomiting in OTEZLA 30 mg twice daily; 1 subject treated with OTEZLA 20 mg twice daily experienced a serious adverse reaction of diarrhea; 1 patient treated with OTEZLA 30 mg twice daily experienced a serious adverse reaction of headache.

[b] Of the reported adverse drug reactions none were serious.

Other adverse reactions reported in patients on OTEZLA in clinical studies including extension studies: **Immune system disorders:** Hypersensitivity, **Investigations:** Weight decrease, **Gastrointestinal Disorders:** Frequent bowel movement, gastroesophageal reflux disease, dyspepsia, **Metabolism and Nutrition Disorders:** Decreased appetite*, **Nervous System Disorders:** Migraine, **Respiratory, Thoracic, and Mediastinal Disorders:** Cough, **Skin and Subcutaneous Tissue Disorders:** Rash
*1 patient treated with OTEZLA 30 mg twice daily experienced a serious adverse reaction.

Psoriasis Clinical Trials

The safety of OTEZLA was assessed in 1426 subjects in 3 randomized, double-blind, placebo-controlled trials in adult subjects with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy. Subjects were randomized to receive OTEZLA 30 mg twice daily or placebo twice daily. Titration was used over the first 5 days *[see Dosage and Administration (2.1)]*. Subjects ranged in age from 18 to 83 years, with an overall median age of 46 years.

Diarrhea, nausea, and upper respiratory tract infection were the most commonly reported adverse reactions. The most common adverse reactions leading to discontinuation for subjects taking OTEZLA were nausea (1.6%), diarrhea (1.0%), and headache (0.8%). The proportion of subjects with psoriasis who discontinued treatment due to any adverse reaction was 6.1% for subjects treated with OTEZLA 30 mg twice daily and 4.1% for placebo-treated subjects.

Adverse Reactions Reported in ≥1% of Subjects on OTEZLA and With Greater Frequency Than in Subjects on Placebo; up to Day 112 (Week 16) (Placebo %, OTEZLA %):
Diarrhea (6%, 17%), Nausea (7%, 17%), Upper respiratory tract infection (6%, 9%), Tension headache (4%, 8%), Headache (4%, 6%), Abdominal pain* (2%, 4%), Vomiting (2%, 4%), Fatigue (2%, 3%), Dyspepsia (1%, 3%), Decreased appetite (1%, 3%), Insomnia (1%, 2%), Back pain (1%, 2%), Migraine (1%, 2%), Frequent bowel movements (0%, 2%), Depression (0%, 1%), Bronchitis (0%, 1%), Tooth abscess (0%, 1%), Folliculitis (0%, 1%), Sinus headache (0%, 1%).
*Two subjects treated with OTEZLA experienced serious adverse reaction of abdominal pain.
Severe worsening of psoriasis (rebound) occurred in 0.3% (4/1184) subjects following discontinuation of treatment with OTEZLA.

OTEZLA was evaluated in a Phase 3, multicenter, randomized, placebo-controlled study (PSOR-3) in adults with moderate to severe psoriasis of the scalp *[see Clinical Studies (14.2)]*. A total of 302 subjects were randomized to receive OTEZLA 30 mg twice daily or placebo twice daily. The most commonly reported adverse reactions that occurred at a higher rate in the OTEZLA group than in the placebo group were: diarrhea (31% vs. 11%), nausea (22% vs. 6%), headache (12% vs. 5%), and vomiting (6% vs. 2%). The proportion of subjects who discontinued treatment because of any adverse reaction during the 16-week placebo-controlled period of the study was 6% for subjects who received OTEZLA 30 mg twice daily and 3% for subjects who received placebo. Gastrointestinal adverse reactions that led to discontinuation of treatment were diarrhea (3% vs 0%), nausea (1.5% vs 1%), and vomiting (1.5% vs 0 %) in the OTEZLA group compared to placebo.

DRUG INTERACTIONS

Strong CYP450 Inducers

Apremilast exposure is decreased when OTEZLA is co-administered with strong CYP450 inducers (such as rifampin) and may result in loss of efficacy *[see Warnings and Precautions (5.3)] and Clinical Pharmacology (12.3)]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to OTEZLA during pregnancy. Information about the registry can be obtained by calling 1-877-311-8972 or visiting https://mothertobaby.org/ongoing-study/otezla/.

Risk Summary

Available pharmacovigilance data with OTEZLA use in pregnant women have not established a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes, but these data are extremely limited. Advise pregnant women of the potential risk of fetal loss. Consider pregnancy planning and prevention for females of reproductive potential.

Lactation

Risk Summary

There are no data on the presence of apremilast or its metabolites in human milk, the effects of apremilast on the breastfed infant, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OTEZLA and any potential adverse effects on the breastfed child from OTEZLA or from the underlying maternal condition.

Pediatric Use

The safety and effectiveness of OTEZLA in pediatric patients less than 18 years of age have not been established.

Geriatric Use

Of the 1493 patients who enrolled in Studies PsA-1, PsA-2, and PsA-3 a total of 146 psoriatic arthritis patients were 65 years of age and older, including 19 patients 75 years and older. No overall differences were observed in the safety profile of elderly patients ≥ 65 years of age and younger adult patients < 65 years of age in the clinical studies.

Of the 1257 subjects who enrolled in two placebo-controlled psoriasis trials (PSOR 1 and PSOR 2), a total of 108 psoriasis subjects were 65 years of age and older, including 9 subjects who were 75 years of age and older. No overall differences were observed in the efficacy and safety in elderly subjects ≥65 years of age and younger adult subjects <65 years of age in the clinical trials.

Renal Impairment

Apremilast pharmacokinetics were characterized in subjects with mild, moderate, and severe renal impairment as defined by a creatinine clearance of 60-89, 30-59, and less than 30 mL per minute, respectively, by the Cockcroft–Gault equation. While no dose adjustment is needed in patients with mild or moderate renal impairment, the dose of OTEZLA should be reduced to 30 mg once daily in patients with severe renal impairment *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

Hepatic Impairment

Apremilast pharmacokinetics were characterized in subjects with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment. No dose adjustment is necessary in these patients.

OVERDOSAGE

In case of overdose, patients should seek immediate medical help. Patients should be managed by symptomatic and supportive care should there be an overdose.

The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www.OTEZLA.com or contact Amgen Medical Information at 1-800-772-6436.

Manufactured for:

Amgen Inc.
Thousand Oaks, CA 91320-1799 U.S.A

https://pat.amgen.com/otezla

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USA-407-80469

International expert group agrees on redefining psoriasis severity

BY BRUCE JANCIN
FROM MEDSCAPELIVE LAS VEGAS DERMATOLOGY SEMINAR

It's high time to say farewell to the traditional categorization of psoriasis severity into mild, moderate, or severe disease, according to the International Psoriasis Council.

The mild/moderate/severe categorization is vague and defined differently by different organizations and in different countries. It often underestimates disease severity because it ignores psoriasis involvement in particularly tough-to-treat special areas, including the scalp, palms, soles, face, nails, and genitalia, Bruce E. Strober, MD, PhD, asserted at MedscapeLive's annual Las Vegas Dermatology Seminar. He chaired an IPC project in which prominent psoriasis experts in 32 countries employed a Delphi consensus approach aimed at achieving agreement on a more practical recategorization of psoriasis severity for use in both daily clinical practice and enrolling appropriate participants in clinical trials. What emerged was a simplified dichotomous categorization system.

"What we came up with is a very sensible approach to defining whether patients should get either topical or systemic therapy. In fact, there are only two groups of patients in psoriasis: those who should get topicals alone, and those who should get systemic therapy. It's topicals or systemics," explained Dr. Strober, a dermatologist at Yale University, New Haven, Conn., who also works in private practice in Cromwell, Conn.

Under the IPC classification, psoriasis patients are candidates for systemic therapy if they meet at least one of three criteria: body surface area of involvement greater than 10%, disease involving the previously mentioned special areas, or failure of topical therapy.

"This approach is about practically treating patients who are in need," Dr. Strober said. "If patients meet just one of these three criteria they can move on to our current toolbox of systemic therapies, be they older systemic treatments, apremilast, phototherapy, or 1 of the 11 biologics currently approved for the treatment of psoriasis. The key point is that for patients with moderate to severe psoriasis – or should I say, systemic therapy–appropriate psoriasis – treatment should be based on individual patient characteristics. We don't work on a stepwise approach. If a patient walks in with more than 10% body surface area involved, don't make them fail topicals; you can go right to systemics."

European dermatologists often use the Psoriasis Area and Severity Index (PASI) score to characterize disease severity and monitor response to therapy. In contrast, American dermatologists generally find PASI too complex and time-consuming for use in clinical practice, relying instead on the amount of body surface area involved with psoriasis. Neither of these measures incorporates disease involvement in special areas, which when present ought to automatically place a patient in the systemic therapy–appropriate category, according to Dr. Strober.

"I find this [IPC recategorization] a very practical approach. I hope you write this down and use this in your own practice," Dr. Strober said.

The full IPC report was published in the Journal of the American Academy of Dermatology (J Am Acad Dermatol. 2020 Jan;82[1]:117-22).

The IPC psoriasis severity reclassification project was unfunded. Dr. Strober reported receiving institutional research funding from and serving as a paid consultant to more than two dozen pharmaceutical companies. MedscapeLive and this news organization are owned by the same parent company.

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COMMENTARY BY DR. GELFAND: Clinicians like to think in a series of dichotomous yes-or-no decisions. Pregnant or not pregnant? White blood cell count elevated or normal? Admit or discharge? With this in mind, the International Psoriasis Foundation aims to simplify the classification of psoriasis to define patients for being candidates for topical or systemic and phototherapy. (Full disclosure: I am a member of the IPC board of directors.) The new classification scheme does away with prior classifications, which focused on body surface area categorized into mild, moderate, or severe disease to a system designed to identify candidates for systemic treatment. This new classification system identifies many subgroups of patients with psoriasis with limited body surface area who should be considered for systemic agents, such as people with sensitive areas involved (that is, scalp or genitals), or even patients with localized psoriasis that doesn't respond to topical treatment. A patient from my practice exemplifies this approach. She had thick patches only on her elbows involving just 2% of her body surface area. She failed ultrapotent corticosteroids, did well with excimer laser, but had rapid recurrence of her disease, which then no longer responded to targeted phototherapy. Her psoriasis is now in remission on a biologic. Still, we must remember that psoriasis is a dynamic and often unpredictable disease and that simple classifications are just guidance that clinicians should use to support shared decision-making with patients to achieve the best patient-centered outcome. Moreover, continuous measures of psoriasis activity remain useful as we have demonstrated that, for every 10% increase in body surface area affected by psoriasis, there is an additional 20% increase in risk of diabetes – an example of why body surface area is still relevant as a measure of severity (J Am Acad Dermatol. 2018 Feb;78[2]:315-22.e1).

Guselkumab maintains psoriasis efficacy long after discontinuation

BY BRUCE JANCIN
FROM THE EADV CONGRESS

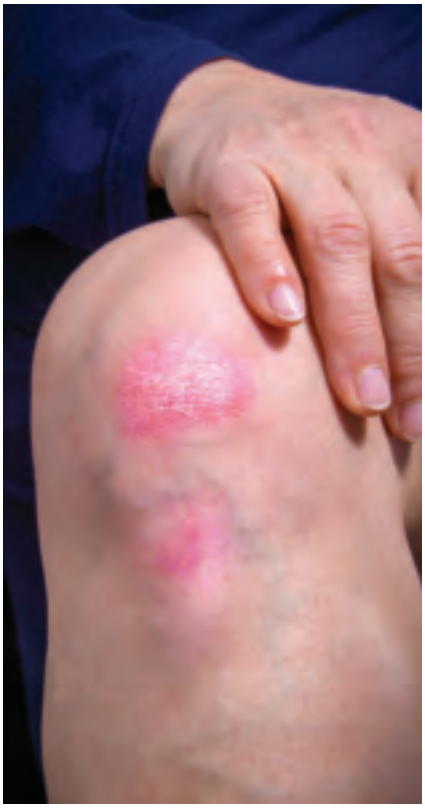
Fully half of patients with moderate to severe psoriasis who achieve complete clearance after their first four doses of guselkumab continue to maintain a PASI 90 response nearly 6 months after withdrawal of the biologic, according to a post hoc analysis of the pivotal phase 3 VOYAGE 2 trial.

"That's impressive maintenance of efficacy," said Curdin Conrad, MD, who presented the data at the annual congress of the European Academy of Dermatology and Venereology.

"These findings are reassuring when you have to interrupt guselkumab therapy – for example, due to acute infection, pregnancy, or surgery. But it might also help when considering in the future a flexible dosing interval, particularly for patients who had complete clearance," added Dr. Conrad, professor of dermatology and head of the polyclinic and the Center of Excellence for Psoriasis at Lausanne (Switzerland) University Hospital.

The intriguing implication from VOYAGE 2 that guselkumab (Tremfya) might lend itself to flexible dosing featuring lengthy drug-free intervals is being prospectively examined in the ongoing phase 3b GUIDE trial. This is a double-blind, placebo-controlled trial including 888 French and German patients with moderate to severe psoriasis and a study hypothesis that those who have a Psoriasis Area and Severity Index score of 0 at weeks 20 and 28 in response to on-label dosing – the so-called "super responders" – will maintain disease control until week 68 if their dosing is reduced to 100 mg of guselkumab every 16 weeks instead of the standard 8-week intervals.

Dr. Conrad reported that in VOYAGE 2, 106 patients on standard-dose guselkumab who had a PASI score of 0 at weeks 20 and 28 were randomized to discontinue the interleukin-23 inhibitor after receiving their fourth dose at week 20. It took 25 weeks for 50% of them to lose their PASI 90 response as defined by regression to a PASI score of 1 or greater. Using a less stringent definition of maintenance of efficacy, the super responders' median time off guselkumab until reaching a PASI score of 3 or more was 30.7 weeks, with a median of 35.4 weeks to a PASI score of 5 or more.



PositiveFocus/Getty Images

In addition, 34 other VOYAGE 2 participants who were almost clear on guselkumab at weeks 20 and 28, with a PASI score of more than 0 but less than 1, were randomized to guselkumab withdrawal after their week-20 dose. Median time to loss of their PASI 90 response was shorter than that of the super responders – not surprising because their mean PASI score when the biologic was halted was 0.5, rather than 0 as for the super responders. But Dr. Conrad said the maintenance of response was still impressive: A median of 16.2 weeks to reach a PASI score of 1 or more, 27.2 weeks for a PASI 3, and 33.7 weeks for a PASI score of 5.

He reported receiving research funding from and serving as a scientific adviser to Janssen, the study sponsor, as well as to more than a dozen other pharmaceutical companies.

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COMMENTARY BY DR. GELFAND: The search for truly remittive treatment for psoriasis has been long and arduous. In the 1990s, bath PUVA was identified as having remittive properties for psoriasis but this treatment is seldom used (Arch Dermatol. 1998;134[10]:1263-8). Alefacept, a biologic targeting T cells, was claimed to be remittive only to be withdrawn from the market because of a lack of clinically significant efficacy (J Cutan Med Surg. 2004 Dec;8 Suppl 2:10-3). Emerging data on IL-23 inhibitors suggest that perhaps we finally have a remittive treatment that is clinically useful. In this post hoc analysis of VOYAGE 2 results, remarkably half of patients who achieved complete skin clearance with guselkumab maintained 90% improvement in PASI 6 months after withdrawal of the biologic. Clinically, remittive effects are very helpful as patients often experience treatment interruptions because of adherence issues, insurance barriers, and intercurrent illness. Thus, patients can typically expect a "soft landing" when interrupting a remittive treatment, with disease slowly coming back over an extended time period. Now the major question is which patients are likely to experience highly remittive effects of treatment so that their dosing can be adjusted accordingly. Such knowledge will be critical so we can stratify patients, personalize their treatment, and improve the cost-to-benefit ratio of our treatment decisions.

Biologic treatment mitigates PsA risk in psoriasis patients, study finds

BY HEIDI SPLETE
FROM ANNALS OF THE RHEUMATIC DISEASES

Psoriasis patients treated with biological disease-modifying antirheumatic drugs had a significantly lower incidence of psoriatic arthritis (PsA) compared with those treated with phototherapy, in a study of 464 adults.

Epidemiologic data show that PsA may be diagnosed as long as 5-10 years after a diagnosis of plaque psoriasis, but PsA ultimately occurs in up to 25% of cases, wrote the study investigators, Paolo Gisondi, MD, of the section of dermatology and venereology, department of medicine, at Università degli Studi di Verona, Italy, and colleagues.

"The delay between the onset of skin manifestations of psoriasis and joint disease may provide a therapeutic window of clinical opportunity for preventing the progression from psoriasis to PsA," but the impact of continuous systemic treatment with biological disease-modifying antirheumatic drugs (DMARDs) has not been well studied, the researchers said (Ann Rheum Dis. 2021 Jun 18. doi: 10.1136/annrheumdis-2021-219961).

In the retrospective, nonrandomized study published in Annals of the Rheumatic Diseases, the researchers reviewed data from adults with moderate to severe plaque psoriasis who received continuous treatment with biologic DMARDs, compared with those who received narrow-band ultraviolet light B (nb-UVB) phototherapy, between January 2012 and September 2020.

Larger prospective and intervention studies are needed to validate the results.

Patients with a past or present PsA diagnosis were excluded from the study. A total of 234 patients were treated with biologic DMARDs for at least 5 years and 230 were treated with at least three courses of nb-UVB phototherapy; all patients were followed for an average of 7 years. PsA was determined based on the Classification for Psoriatic Arthritis criteria. Incidence was defined in terms of cases per 100 patients per year.

During the follow-up period, 51 patients (11%) developed incident PsA: 19 (8%) in the biologic DMARDs group and 32 (14%) in the nb-UVB phototherapy group. The annual incidence rate of PsA was 1.20 cases per 100 patients per year in the biologic DMARDs group compared with 2.17 cases per 100 patients per year in the phototherapy group ($P = .006$).

In a multivariate analysis, independent risk factors for PsA were older age (adjusted hazard ratio, 1.04; $P < .001$), nail psoriasis (aHR 3.15; $P = .001$), and psoriasis duration greater than 10 years (aHR, 2.02; $P = .001$). Most other baseline demographics, including smoking status, baseline Psoriasis Area and Severity Index (PASI) scores, and comorbidities, were similar in patients who did and did not develop PsA.

Of the patients taking biologic DMARDs, 39 (17%) were treated with infliximab, 17 (7%) with etanercept, 67 (29%) with adalimumab, 50 (21%) with ustekinumab, and 61 (26%) with secukinumab; 35 of these patients switched biologics during the study period.

The study findings were limited by several factors including the retrospective design and the resulting potential for biases, notably the potential con-

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COMMENTARY BY DR. MENTER: The importance of early diagnosis is highly significant with dermatologists playing an important role, as the majority of patients who develop psoriatic arthritis (PsA) have had skin involvement for up to 10 years or longer. Thus, dermatologists should always be evaluating their psoriasis patients for early morning joint stiffness, enthesitis, dactylitis, sacroiliitis, and ankylosing spondylitis to identify joint involvement and help ensure patients do not develop permanent joint destruction later.

This study is of importance, with 464 patients evaluated, of whom 234 were treated with biologic agents, and 230 with a minimum of three courses of Narrowband UVB over an average of 5-7 years.

While phototherapy is still fairly commonly used in our psoriasis population with moderate to good clinical responses, its ability to prevent future PsA is negligible, as shown in this review of 230 patients who received a minimum of three courses of NB-UVB.

It is interesting to review the specific biologic therapies used in 234 patients over the 5-year period: Fifty-three percent received TNF-alpha biologics (infliximab, etanercept, and adalimumab), 21% received the IL-12/23 antagonist (ustekinumab), and 26% received the newer IL-17 antagonist (secukinumab). It is important to recognize that data have shown that both the TNF-alpha and the IL-17 biologic agents have excellent PsA responses, with the proportion of those achieving ACR20 (20% improvement in American College of Rheumatology response criteria) responses in the 50s to mid-60s, compared with the IL-12/23 agent ustekinumab (with ACR20 responses in the mid-40s).

In summary, it is of significant importance, as mentioned earlier, for our dermatology colleagues to diagnose PsA early, work with our rheumatology colleagues to prescribe the correct biologic agent, and prevent permanent joint destruction caused by PsA.

Data on potential risks of COVID-19 in psoriasis patients limited, but reassuring

BY TED BOSWORTH
FROM COASTAL DERM

The available data suggest that the risks posed by COVID-19 infection to patients with psoriasis, including those on therapies that affect immune function, are modest at most, according to a summary of published studies and expert opinions summarized at the annual Coastal Dermatology Symposium.


Dr. Duffin

For patients with psoriasis concerned about their outcome if infected with COVID-19, "there is no evidence to support stopping biologics or systemic agents, so I am asking my patients to continue," Kristina C. Duffin, MD, professor and chair of dermatology at the University of Utah, Salt Lake City, said at the meeting.

The National Psoriasis Foundation, which created a COVID-19 task force and maintains a COVID-19 Resource Center on its website, has provided similar advice. Many statements are phrased cautiously and clinicians are encouraged to practice shared decision-making, but the NPF guidance supports continuing effective therapy – or, in newly diagnosed patients, starting effective therapy – among those who are not infected with SARS-CoV2.

Patients with a new diagnosis of psoriasis "should be aware that untreated psoriatic disease is associated with serious impact on physical and emotional health, and in the case of psoriatic arthritis, can lead to permanent joint damage and disability," according to the NPF guidance.

Overall, the "existing data generally suggest" that most treatments for psoriasis and psoriatic arthritis "do not meaningfully alter the risks of contracting SARS-CoV2 or having a worse course of COVID-19 illness," the current guidance states. Yet, because of limited data this "is not known with certainty."

Chronic systemic steroids are an exception. In a review of recently published studies evaluating whether psoriasis or its therapies increase risk of adverse outcomes in patients with COVID-19 infection, Dr. Duffin pointed to several that associated systemic steroids with hospitalization or other markers of severe disease.

The NPF guidance also recommends avoiding chronic systemic steroids in patients with psoriasis during the current COVID-19 era "if possible." In patients with psoriatic arthritis who require systemic steroids, the guidance recommends "the lowest dose necessary to achieve the desired therapeutic effect."

This is not necessarily true in patients with psoriasis and COVID-19 infection. Based on the potential for systemic steroids to improve outcomes in hospitalized COVID-19 patients requiring oxygen, steroids "should not be withheld" even when the justification is concern about the potential risk of flares with withdrawal, according to the NPF guidance statement.

Shared decision-making with patients is ... critical to help patients navigate these uncertain times.

The NPF guidance specifically cautions against use of hydroxychloroquine or chloroquine for prevention or treatment of COVID-19. In addition to an uncertain benefit, these antimalarial drugs have been associated previously with flares of psoriasis.

Dr. Duffin agreed and went on to warn that COVID-19 infection itself is a potential trigger for flares. She cited two published case reports of flares associated with psoriasis. Although one patient had also been exposed to hydroxychloroquine, she said the risk of psoriasis-induced flare "makes sense" based on previous associations made between flares and other viral infections and stress.

In patients with psoriasis who contract COVID-19 infection, Dr. Duffin

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founding bias by indication because of the lack of randomization, the researchers noted. Another limitation was the inability to perform a subgroup analysis of biologic DMARD classes because of the small sample size, the authors said.

However, they added, the findings were strengthened by the complete database and accurate PsA diagnoses supported by an expert rheumatologist.

Larger prospective and intervention studies are needed to validate the results, the researchers emphasized. However, data from the current study suggest that continued treatment with biologic DMARDs "may reduce the risk of incident PsA in patients with moderate to severe chronic plaque psoriasis," they concluded.

The study was supported by the European Union's Horizon 2020 Research and Innovation Program. Dr. Gisondi and several coauthors disclosed relationships with Abbvie, Almirall, Amgen, Janssen, Leo Pharma, Eli Lilly, Novartis, Pierre Fabre, Sandoz, Sanofi, and UCB. The study was supported by the European Union's Horizon 2020 Research and Innovation Program.

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Analysis puts U.S. psoriasis prevalence at 3%

BY RICHARD FRANKI
FROM JAMA DERMATOLOGY

Psoriasis affects over 7.5 million adults in the United States, with prevalence nearly twice as high among Whites as non-Whites, according to an analysis of national survey data from 2011 to 2014.

"The adult prevalence rate of 3.0% continues to place psoriasis as one of the most common immune-mediated diseases affecting adults" in the United States, April W. Armstrong, MD, MPH, and associates said in a report published in JAMA Dermatology (2021 Jun 30. doi: 10.1001/jamadermatol.2021.2007). At that rate, approximately 7,560,000 Americans aged 20

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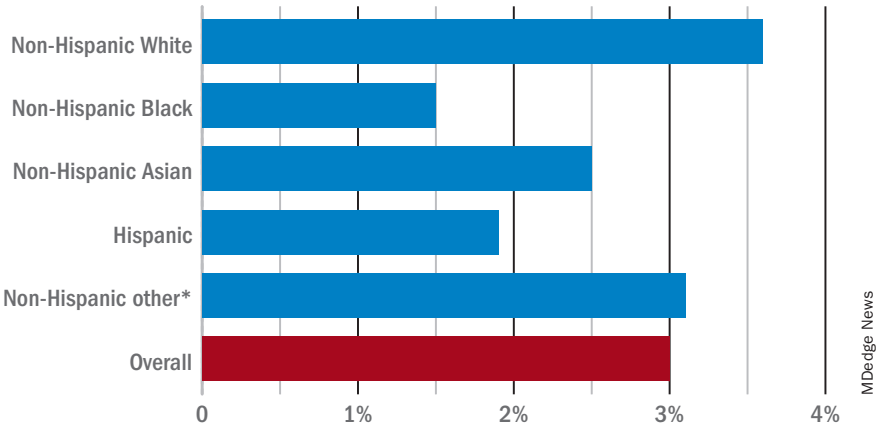
Psoriasis prevalence in U.S. adults by race/ethnicity



*Includes multiracial persons

Note: Based on data for 12,625 respondents aged 20 years and older from the 2011-2012 and 2013-2014 National Health and Nutrition Examination Survey cycles.

Source: JAMA Dermatol. 2021 Jun 30. doi: 10.1001/jamadermatol.2021.2007

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concurred with the NPF guidance that management decisions should be made on a "case-by-case basis." Although the NPF guidance states that "most patients can restart psoriasis and/or psoriatic arthritis treatments after complete resolution of COVID-19 symptoms," no specific advice was offered on the decision to stop treatments.

For protecting psoriasis patients from infection and managing COVID-19 in those who become infected, much of the NPF advice is consistent with that offered to patients without psoriasis. This involves practicing infection control that reduces risk of transmission. Both the NPF guidance and Dr. Duffin suggested telemedicine is appropriate for limiting in-patient visits under pandemic conditions.

Although patients with psoriasis are more likely than the general population to have the comorbidities associated with bad COVID-19 infection outcomes, according to the NPF guidance, Dr. Duffin called the overall data evaluating susceptibility among psoriasis patients "reassuring." She cautioned that the data are still limited, but the evidence so far suggests that neither psoriasis nor biologics are independent risk factors for acquiring COVID-19 or having a worse outcome if infected.

Yet, more definitive data are needed, and Dr. Duffin advised clinicians and patients to consult the NPF website for updates.

The meeting was jointly presented by the University of Louisville (Ky.) and MedscapeLive.

Dr. Duffin reported financial relationships with Amgen, AbbVie, Bristol-Myers Squibb, Boehringer-Ingelheim, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Siena, and UCB.

This publication and MedscapeLive are owned by the same parent company.

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COMMENTARY BY DR. GELFAND: Despite major breakthroughs in the development of highly effective and safe COVID-19 vaccines since Dr. Duffin spoke at this meeting in October 2020, the pandemic rages on with the emergence of the highly contagious Delta variant, a relaxing of and resistance to nonpharmaceutical interventions such as masks and distancing, and vaccine hesitancy or outright refusal in millions of people. I cochair the National Psoriasis COVID-19 Task Force. Our current position is that "Existing data generally suggest that treatments for psoriasis and/or psoriatic arthritis do not meaningfully alter the risk of acquiring SARS-CoV-2 infection or having worse COVID-19 outcomes" (J Am Acad Dermatol. 2021 May;84[5]:1254-68). It is important for clinicians and patients to recognize that uncertainty remains and data continue to evolve. For example, a recent study from France observed no impact of biologics for psoriasis on COVID-19 hospitalization in the first wave but did observe a 44% increased risk in hospitalizations for COVID-19 in the second wave (Br J Dermatol. 2021 Jul 26. doi: 10.1111/bjd.20659). While most studies have not shown adverse effects of psoriasis treatment on COVID-19, we must recognize that the existing studies are often limited by small sample sizes, lumping of treatments with different mechanisms of action, incomplete control for confounding variables, and incomplete case ascertainment (J Invest Dermatol. 2021 Jul 28. doi: 10.1016/j.jid.2021.04.036). Shared decision-making with patients is therefore critical to help patients navigate these uncertain times. Keep up with our recommendations at: www.psoriasis.org/covid-19-task-force-guidance-statements/.

Non-Whites remain sorely underrepresented in phase 3 psoriasis trials

BY TED BOSWORTH
FROM THE BRITISH JOURNAL OF DERMATOLOGY

Non-White patient participation in phase 3 therapeutic trials for plaque psoriasis is less than 15%, according to a recently published analysis of data from the ClinicalTrials.gov database.

The exact figure drawn from the survey of 82 trials was 14.2%, but 20 (24%) of the trials did not include ethnoracial data at all, and only 65% of those with data had complete data, according to a report by a team of investigators from the department of dermatology at the University of California, San Francisco (Br J Dermatol. 2021 Feb;184[2]:348-50).

"The remaining studies reported the percentage of White participants only or White participants and one additional ethnoracial group," reported the investigators, led by Vidhatha D. Reddy, a medical student at UCSF.

The investigators broke down participation by race in all phase 3 plaque psoriasis trials that enrolled adults and had posted results by May 2020. Data from trials of medications yet to be approved were excluded.

Most trials were multinational. The medications evaluated included 11 biologics, 10 topicals, 2 oral systemic agents, and a phosphodiesterase type-4 inhibitor. The 82 trials included in this analysis enrolled 48,846 collectively.

From trials that identified race, 85.8% of 39,161 participants were White, 3.09% of 25,565 patients were Black, 19.55% of 11,364 patients were Hispanic or Latino, and 9.21% of 30,009 patients were Asian. Of trials that included Native Americans or Pacific Islanders, fewer than 2% of participants represented this category.

Non-White patients remain underrepresented even when recognizing differences in the prevalence of psoriasis. For example, one recent survey (J Am Acad Dermatol. 2014;70:512-6) found the U.S, prevalence of psoriasis to be about half as great in Blacks as it is in Whites (1.9% vs. 3.9%), but the representation of Blacks in the phase 3 trials evaluated by Mr. Reddy and colleagues was more than 20 times lower.

There are many reasons to suspect that lack of diversification in psoriasis trials is impeding optimal care in those underrepresented. Of several examples offered by the authors, one involved differential responses to adalimumab among patients with hidradenitis suppurativa with genetic variants in the BCL2 gene (J Invest Dermatol. 2020;140[3]:574-82), but the authors reported racially associated genetic differences are not uncommon.

"Estimates have shown that approximately one-fifth of newly developed medications demonstrate interracial/ethnic variability in regard to various factors, such as pharmacokinetics, safety and efficacy profiles, dosing, and pharmacogenetics," Mr. Reddy and his coinvestigators stated.

Although racial diversity in the design and recruitment for clinical trials has not been a priority in trials involving psoriasis, other skin diseases, or most diseases in general, the authors cited some evidence that this is changing.

"Since 2017, research funded by the

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years or older have psoriasis.

That overall rate among adults aged 20 years and older, based on data from the 2011-2012 and 2013-2014 cycles of the National Health and Nutrition Examination Survey (NHANES), did not change significantly when compared with the 2003-2004 NHANES, when it was 3.15% among those aged 20-59, said Dr. Armstrong, professor of dermatology, University of Southern California, Los Angeles, and associates.

For the 2011-2014 period, psoriasis prevalence was similar between women (3.2%) and men (2.8%) but was significantly associated with older age and White/non-White status. Those aged 50-59 years had the highest prevalence of any age group at 4.3% and those aged 70 and older had a rate of 3.9%, while those aged 20-29 were the lowest at 1.6%, the investigators reported.

The prevalence in non-Hispanic Whites in the United States was 3.6% over the study period, and their odds ratio for having psoriasis was 1.92, compared with non-White individuals. Asian respondents had a prevalence of 2.5%, with the Hispanic population at 1.9%, non-Hispanic Black respondents at 1.5%, and those identifying as other (including multiracial persons) at 3.1%, they said.

The NHANES sample consisted of 12,638 people who had participated in the question that asked if they had ever been diagnosed with psoriasis by a physician or other health care professional, of whom 12,625 gave a definitive yes or no answer, the investigators noted.

A much smaller number, 329, also answered a question about the severity of their disease: Fifty-six percent had little or no psoriasis, almost 22% reported 1-2 palms of involvement, 16% had 3-10 palms of involvement, and 5.5% said the coverage was more than 10 palms. Since the survey did not distinguish between treated and untreated patients, however, some "of those reporting low body surface area involvement may be receiving treatments that are controlling their otherwise more extensive disease," they wrote.

Dr. Armstrong and another investigator said that they have received grants, personal fees, and honoraria from a number of pharmaceutical companies; two other investigators are employees of the National Psoriasis Foundation.

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National Institutes of Health has been required to report race and ethnicity of participants following an amendment to the Health Revitalization Act," according to the authors, who suggested that other such initiatives are needed. They advocated "explicit goals to increase recruitment of people of color" as a standard step in clinical trial conduct.

Dr. Takeshita

Hypertension trials were cited as an example in which diversity has made a difference.

"Although Black patients are at an elevated risk of developing hypertension, it was not until the enrollment of a substantial proportion of black participants in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) that enough data on Black patients were available to make specific treatment recommendations in this population," they noted.

Without clinical trials that include a substantial proportion of Blacks or patients from other racial and ethnic groups, the study investigators concluded that it is impossible to determine whether response to patients of different races and ethnicities benefit similarly. This concern seems particularly apt for diseases of the skin.

Another investigator who has considered this issue, Junko Takeshita, MD, PhD, an assistant professor of dermatology at the University of Pennsylvania, Philadelphia, agreed.

"Lack of diversity ... in phase 3 clinical trials for psoriasis is a problem."

"Lack of diversity among participants in phase 3 clinical trials for psoriasis is a problem," said Dr. Takeshita, who led a study of racial differences in perceptions of psoriasis therapies that was published last year (J Invest Dermatol. 2019;139[8]:1672-9).

In that study, "my research group not only found differences in perceptions about biologics between Black and White patients with psoriasis, but we have also shown that Black patients with psoriasis are less likely to receive biologic treatment," she reported. There are many explanations. For example, she found in another study that Black patients are underrepresented in direct-to-consumer advertisements for biologics.

This problem is not unique to psoriasis. Underrepresentation of Blacks and other ethnoracial groups is true of other skin diseases and many diseases in general, according to Dr. Takeshita. However, she cautioned that the 3% figure for Black participation in psoriasis trials reported by Mr. Reddy and colleagues is not necessarily reflective of trials in the United States.

"This study included international study sites that are recruiting patients from populations with different demographics than the U.S.," she noted. By including sites with only Asian patients or countries with few Blacks in the population, it dilutes Black representation. She would expect the exact proportion of Black participants to be somewhat higher even if they are "still likely to be underrepresented" if the analysis had been limited to U.S. data.

The research had no funding source. Three of the nine authors reported financial relationships with pharmaceutical companies.

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COMMENTARY BY DR. GELFAND: A large analysis of 82 phase 3 psoriasis trials suggests that non-Whites make up just 14.2% of study subjects. This analysis is just the tip of the iceberg when it comes to addressing such a complex and important issue. The first question is, are minority populations underrepresented in psoriasis clinical trials based on the epidemiology of the disease and the makeup of the population? For example, we demonstrated that the prevalence of psoriasis is about 50% lower in Blacks, compared with Whites, based on a U.S. nationwide study (J Am Acad Dermatol. 2005 Jan;52[1]:23-6).

It is estimated that 13.4% of Americans are Black. In order to maintain the ethical underpinnings of justice as defined by the landmark Belmont Report, it is important that there be fairness in the benefits and burdens of participating in research ("The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research," U.S. Department of Health, Education, and Welfare, April 18, 1979). Therefore, in the United States, it would be expected that the percent of Black individuals in psoriasis trials would be low and this could be appropriate. However, a second question pertains to whether the treatment has a different risk-benefit profile in patient subgroups, and to answer this question, low representation of minority populations can be scientifically, and ultimately, ethically problematic.

For example, we are conducting the LITE study, a pragmatic trial of 1,050 patient with psoriasis (thelitestudy.com). From a statistical point of view, we need only 350 patients to test our hypothesis that home phototherapy works as well as office phototherapy. However, skin type may affect our findings (fair-skin patients may be more likely to burn; dark-skin patients may be less likely to respond because of decreased penetration of ultraviolet light). As a result, we designed the study to have equal representation of fair, medium complected, and darker skin types requiring a tripling of the sample size in order to ensure that we can provide the robust data patients need to make decisions based on their unique individualized circumstances (J Invest Dermatol. 2019 Jun;139[6]:1217-20).

To improve PsA outcomes, address common comorbidities

BY BRUCE JANCIN
FROM RWCS 2021

Only about 30% or fewer of patients with psoriatic arthritis (PsA) on therapy achieve disease remission by any definition. One reason for this may be inadequate attention to common comorbid conditions, Alexis Ogdie, MD, MSCE, declared at the 2021 Rheumatology Winter Clinical Symposium.

"I believe that addressing off-target aspects of disease is really important to improving the patient experience of their disease. We might need to target these directly in order to improve outcomes," said Dr. Ogdie, a rheumatologist and epidemiologist at the University of Pennsylvania, Philadelphia, who coauthored the current American College of Rheumatology/National Psoriasis Foundation PsA guidelines (Arthritis Rheumatol. 2019 Jan;71[1]:5-32).

Since rheumatologists are by now well informed about the increased cardiovascular risk associated with PsA, she focused on two common comorbidities that get less attention, both of which are associated with worse clinical outcomes in PsA: obesity and mental health issues.

Anxiety and depression

Dr. Ogdie was first author of a large, population-based, longitudinal cohort study of cause-specific mortality in 8,706 U.K. patients with PsA, 41,752 with RA, and more than 81,000 controls. Particularly striking was the finding of elevated mortality because of suicide in the rheumatic disease patients: a 203% increased risk in the PsA population, compared with the general population, and a 147% greater risk in patients with RA (Rheumatology. 2017 Jun 1;56[6]:907-11).

Overall, 30%-40% of PsA patients have comorbid depression and/or anxiety. "That's pretty striking. It's also true for rheumatoid arthritis and axial spondyloarthritis. And if you're depressed, you're much less likely to respond to therapy in the way that we are measuring response to therapy," Dr. Ogdie said.

Her approach to screening for depression and anxiety in her PsA patients, and indeed in all her other patients, is to begin by normalizing the topic, explaining to them that these affective disorders are common among these patients. She lets her patients know they can talk to her about it. And she informs them that, while effective treatment of their rheumatic disease may improve their depression or anxiety, managing those is also important for improving their disease. Additionally, understanding whether depression is present is important prior to prescribing certain medications. Apremilast (Otezla), for example, can worsen preexisting depression.

"Ask about signs and symptoms of

COMMENTARY BY DR. MENTER: Comorbidities in our patients with moderate to severe psoriasis and those with psoriatic arthritis (PsA) are of significant importance to dermatologists and rheumatologists. The management of 12 comorbidities in the psoriasis population is addressed in the joint American Academy of Dermatology–National Psoriasis Foundation guidelines published in 2019 (J Am Acad Dermatol. 2019 Apr;80[4]:1073-113). In this important review by Dr. Alexis Ogdie, two major comorbid conditions – anxiety and depression, and obesity – in patients with PsA are fully discussed. Of significance in her review is the extremely high risk of suicide in the PsA population: 203% greater compared with the general population, with 30%-40% of PsA patients having comorbid depression and/or anxiety in the study she cited. She stresses how important it is to screen for depression or anxiety in the PsA population. This is of equal importance in the psoriasis population, especially younger patients with active psoriasis who frequently are chronically depressed. Screening tools are listed in Dr. Ogdie's review, with the PROMIS-29 tool screening for depression and anxiety, sleep, fatigue, pain, and physical function, providing significant information.

Obesity in our psoriasis and PsA patients is also of significant importance, especially related to the increased risk of cardiovascular disease in these two groups. Almost 15 years ago, a report on obesity in the psoriasis population, on behalf of the International Psoriasis Council, noted that a review of over 10,000 patients with psoriasis in phase 2 and 3 clinical trials found that the average body mass index of psoriasis patients was 30.6 kg/m^2, the obese category (Br J Dermatol. 2007 Oct;157[4]:649-55).

In 2016, my colleagues and I published a study of patients with moderate to severe psoriasis, and found that patients with psoriasis and those with type 2 diabetes had similar coronary artery calcium scores that were significantly greater than scores among healthy controls (JAMA Dermatol. 2016 Nov 1;152[11]:1244-53). Moderate to severe coronary calcification was about fivefold higher among those with psoriasis (and those with diabetes), compared with controls, and in the psoriasis population, the presence of coronary calcium was associated with cardiovascular and cardiometabolic risk factors.

Thus, again, it is important for us as dermatologists to screen for coronary artery disease in collaboration with our cardiology colleagues in our patients with moderate to severe psoriasis and PsA.

depression," Dr. Ogdie urged her colleagues. "I do this at every single visit in my review of symptoms. This is one I don't skip. I ask: 'Do you have any symptoms of depression or anxiety?'"

Structured evidence-based screening tools, many of which are well suited for completion during a patient's pre-appointment check-in survey, include the Patient Health Questionnaire–2, the PHQ-9, the Patient-Reported Outcomes Measure Information System–10, PROMIS–Depression, and Routine Assessment of Patient Index Data 3.

"I also really like the PROMIS-29. It covers many domains of interest: depression and anxiety, sleep, fatigue, pain, physical function. It gives a lot of information about what's going on in a patient's life right now," according to the rheumatologist.

The main thing is to regularly screen for anxiety and depression and then refer symptomatic patients for further assessment and treatment.

Obesity

Dr. Ogdie was lead author of a national CORRONA Registry study which concluded that obese patients with PsA were only half as likely to achieve remission on a tumor necrosis factor (TNF) inhibitor, compared with nonobese patients (J Rheumatol. 2019 May;46[5]:475-82). She believes the same holds true for all other types of therapy: Across the board, obesity is associated with a poor response. And obesity is much more common in PsA patients than the general population in every age group. Moreover, obesity is associated with risk factors for cardiovascular disease and is associated with fatty liver disease, two other major comorbid conditions in the PsA population.

The CORRONA Registry findings are supportive of an earlier Italian prospective, observational study of 135 obese and an equal number of normal-weight PsA patients, all of whom started on a TNF inhibitor and were followed for 24 months (Arthritis Care Res. 2013 Jan;65[1]:141-7). In a multivariate-adjusted analysis, obesity was independently associated with a 390% higher risk of not achieving minimal disease activity.

The same Italian group subsequently conducted a prospective dietary intervention study in 138 overweight or obese patients with PsA starting anti-TNF therapy (Ann Rheum Dis. 2014 Jun;73[6]:1157-62). A total of 59% of participants randomized to either of the two dietary interventions experienced at least a 5% weight loss at 6 months. The key study finding: Compared with the subjects with less than 5% weight loss, those with 5%-10% weight loss were 275% more likely to achieve minimal disease activity at 6 months, and in those with greater than 10% weight loss the likelihood of attaining minimal disease activity increased by 567%.

Overall, 30%-40% of PsA patients have comorbid depression and/or anxiety.

"We're talking about a disease where treatments tested in clinical trials have odds ratios in the 1.2 range, compared with other therapies, so this is a really striking difference," she observed.

Several studies have demonstrated that obesity in psoriasis patients is a risk factor for developing PsA. Recently, U.K. investigators took things a step further, reporting in a huge observational study that obese or overweight psoriasis patients who reduced their body mass index over a 10-year period had a corresponding reduction in the risk of developing PsA, compared with overweight or obese psoriasis patients whose BMI remained steady over the same period (Br J Dermatol. 2020 Mar;182[3]:714-20).

What's needed now is access to programs to help patients with PsA lose weight. Health insurers are often unwilling to provide coverage. "We have a really tough time getting the patients in to see a nutritionist unless they're willing to pay out of pocket," Dr. Ogdie said.

Physical activity is an important element in successful weight loss. It also is recommended in practice guidelines for patients with inflammatory arthritis because of its salutary effects on disease activity scores, pain and stiffness, sleep, and quality of life. But a recent survey conducted by Dr. Ogdie and coworkers concluded that patients with PsA and other forms of inflammatory arthritis don't receive much exercise guidance from their rheumatologists (ACR Open Rheumatol. 2020 Oct;2[10]:582-7). About 60% of subjects were inactive. Those who were physically active typically engaged in aerobic exercise but were much less likely to do the other guideline-recommended forms of exercise, namely flexibility, balance, and resistance training. The patients' report of low engagement of their physicians "suggests an opportunity for more prescriptive exercise discussions," according to the investigators.


Dr. Ogdie

Diabetes, a critical risk factor for cardiovascular disease, occurs at an increased incidence in PsA. This was demonstrated in a U.K. cohort study coauthored by Dr. Ogdie. The study, which included nearly 4,200 individuals with PsA, concluded that they had a 43% greater incidence of diabetes than the general population in an analysis adjusted for body mass index, smoking, alcohol use, and demographics (Rheumatology. 2014 Feb;53[2]:346-52).

Dr. Ogdie reported receiving research grants and/or consulting fees from numerous pharmaceutical companies. Her research is also funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the Rheumatology Research Foundation, and the National Psoriasis Foundation.

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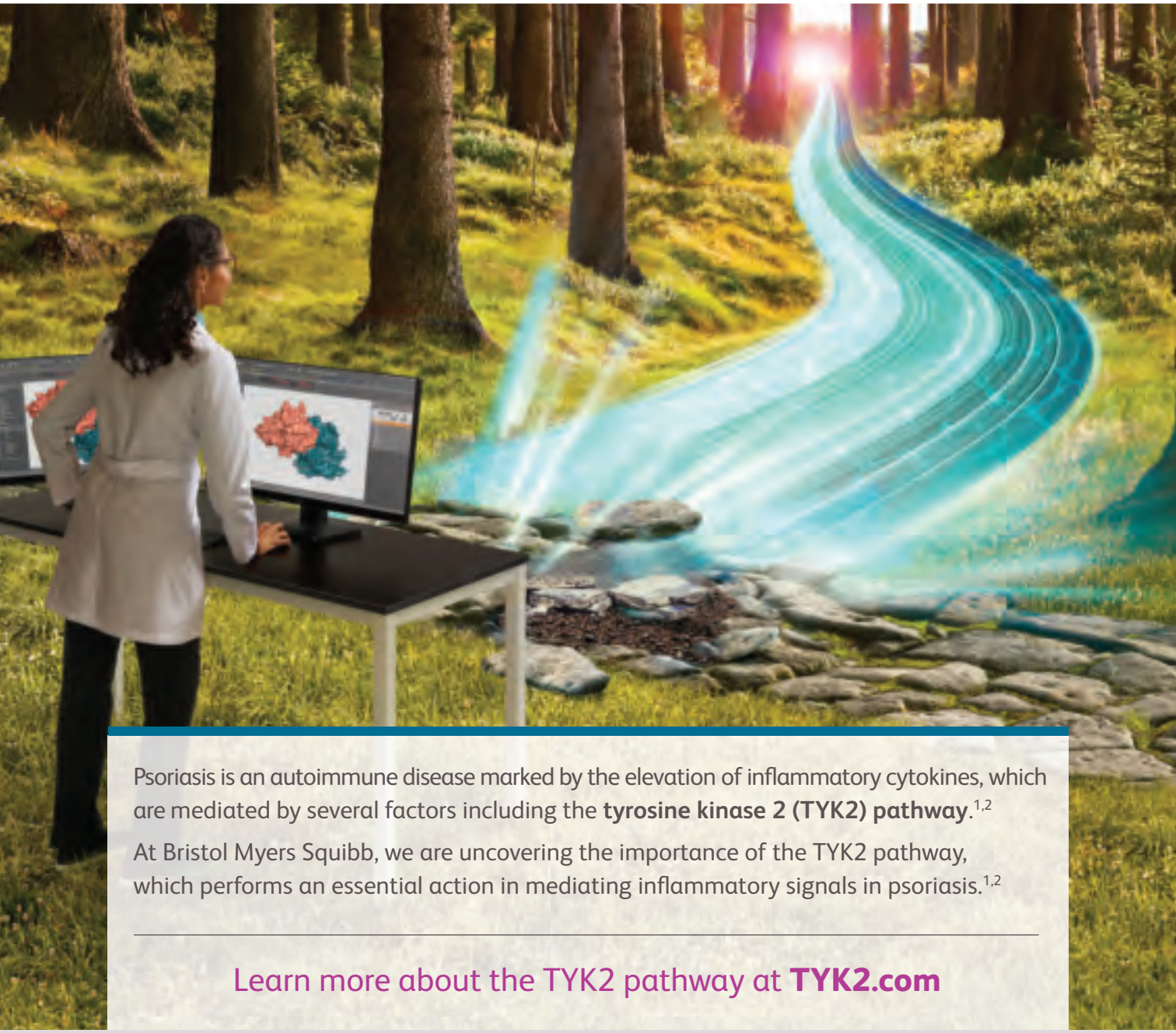

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