Psoriasis is a common disease affecting approximately 7.5 million patients in the United States, 1.5 million (20%) of which have moderate to severe psoriasis (affecting more than 10% of their body surface area). Dr. Menter, chairman of dermatology, Baylor University Medical Center, Dallas, says that less than 500,000 of 1.5 million patients with moderate to severe psoriasis are currently being treated with any form of systemic or biologic therapy. Therefore, over 1 million patients with moderate to severe psoriasis in the United States are not receiving appropriate therapy. In addition to inappropriate drug selection, Dr. Menter says a patient’s adherence to prescribed therapies can also significantly contribute to inadequate disease control and suboptimal treatment outcomes.

**ADHERENCE**

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**THE PATIENT WEIGHS IN:**

**PSORIASIS SYMPTOM INVENTORY (PSI)**

PSI is designed to allow patients to score their disease severity from zero (not at all severe) to four (very severe) for each of the following eight disease symptoms. A better understanding of the patient’s psychological state regarding their disease can help clinicians choose an appropriate therapeutic plan.

1. **ITCH**
2. **REDNESS**
3. **SCALING**
4. **BURNING**
5. **STINGING**
6. **CRACKING**
7. **FLAKING**
8. **PAIN**

**Take AWAYS**

Less than 500,000 of 1.5 million patients with moderate to severe psoriasis are being treated with systemic or biologic therapy.

Over 1 million patients with moderate to severe psoriasis in the United States are not receiving appropriate therapy.

The right therapeutic vehicle can be instrumental in improving treatment outcomes.

**AUGUST 2018**

Cover Image: Shutterstock / robodread

**COMPREHENSIVE PSORIASIS MANAGEMENT**

Longer consults may improve outcomes

Clinicians must allow more time to assess for comorbidities, improve symptoms, enhance QoL

by Ilya Petrou, M.D. | Staff Correspondent

A recent article in *Seminars in Cutaneous Medicine and Surgery* addressing the mosaic of steps and strategies for optimizing the management of psoriasis confirms a complexity of considerations, including patient adherence to prescribed therapies and the choice of appropriate medicine individualized to each case. Appropriate patient education is important with the overall goal of increasing the patient’s quality of life.

“We have to recognize as dermatologists that we are dealing with a systemic disease. Patients with moderate to severe psoriatic disease will likely also have multiple comorbidities, including cardiovascular disease, that need to be actively addressed alongside the typical skin signs and symptoms. As such, we need to spend more time with our psoriasis patients in clinical practice during the consultation to help improve symptoms, increase the quality of life and assess for comorbidities for a significant number of patients,” said Alan Menter, M.D., an author of the study.

Psoriasis is a complex, chronic, lifelong skin condition that affects around 7.5 million Americans, with approximately 1.5 million having moderate to severe psoriasis, affecting more than 10% of their body surface area. Dr. Alan Menter, chairman of dermatology at Baylor University Medical Center in Dallas, emphasizes the importance of comprehensive care, including patient adherence to prescribed therapies and consideration of comorbidities.

“Psoriasis is a systemic disease, and patients often have multiple comorbidities, including cardiovascular disease,” Dr. Menter said. “Clinicians must spend more time with their patients during consultations to help improve symptoms, enhance quality of life, and assess for comorbidities.”

**THE PATIENT WEIGHS IN:**

**PSORIASIS SYMPTOM INVENTORY (PSI)**

The PSI is a tool designed to allow patients to score their disease severity from zero (not at all severe) to four (very severe) for each of the following eight disease symptoms. A better understanding of the patient’s psychological state regarding their disease can help clinicians choose an appropriate therapeutic plan.

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**Take AWAYS**

- Less than 500,000 of 1.5 million patients with moderate to severe psoriasis are being treated with systemic or biologic therapy.
- Over 1 million patients with moderate to severe psoriasis in the United States are not receiving appropriate therapy.
- The right therapeutic vehicle can be instrumental in improving treatment outcomes.

**ADHERENCE**

Adherence in psoriasis has always been an issue, particularly for patients with mild to moderate symptoms who are typically prescribed topical regimens. As psoriasis is a lifelong disease without cure, many patients over time can become frustrated and indifferent towards a positive outcome for their disease and will not regularly apply therapy as advised by their doctor.

“People are very busy today and find it difficult to...”

**Consult Time** CONTINUED ON PAGE 5
For moderate to severe plaque psoriasis, some roadblocks are a good thing.

**INDICATION**
SILIQ™ injection is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.

**IMPORTANT SAFETY INFORMATION**

**WARNING: SUICIDAL IDEATION AND BEHAVIOR**
Suicidal ideation and behavior, including completed suicides, have occurred in patients treated with SILIQ. Prior to prescribing SILIQ, weigh the potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior. Patients with new or worsening suicidal ideation and behavior should be referred to a mental health professional, as appropriate. Advise patients and caregivers to seek medical attention for manifestations of suicidal ideation or behavior, new onset or worsening depression, anxiety, or other mood changes [see Warnings and Precautions (5.1) in the full Prescribing Information].

Because of the observed suicidal behavior in subjects treated with SILIQ, SILIQ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the SILIQ REMS Program [see Warnings and Precautions (5.2) in the full Prescribing Information].

**Crohn's Disease** SILIQ is contraindicated in patients with Crohn's disease. In clinical trials, which excluded Crohn's patients, one SILIQ-treated patient was withdrawn after developing Crohn's disease.

**SILIQ Risk Evaluation and Mitigation Strategy (REMS) Program** SILIQ is available only through a restricted program called the SILIQ REMS because of observed suicidal ideation and behavior in patients treated with SILIQ. Before prescribing SILIQ, prescribers must be certified with the program, have each patient sign a Patient-Prescriber Agreement Form, and provide the patient a Wallet Card describing symptoms requiring immediate medical evaluation. Pharmacies must be certified and only dispense to patients authorized to receive SILIQ. More information is available at SILIQREMS.com.

Please see Brief Summary of Full Prescribing Information on following pages.
There's no getting around it.

Only SILIQ works by blocking IL-17 Receptor A, tapping the brakes on a key factor in the progression of plaque psoriasis.

If your patients have been around the block with other treatments, maybe it's time to try an alternate route.

INDICATION
SILIQ™ injection is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.

IMPORTANT SAFETY INFORMATION (cont'd)

Infections SILIQ may increase the risk of infections. Serious infections and fungal infections were observed at a higher rate in patients treated with SILIQ than placebo-treated patients in clinical trials, including one case of cryptococcal meningitis that led to discontinuation of therapy.

- Consider risks and benefits prior to prescribing SILIQ in patients with a chronic infection or history of recurrent infection
- Instruct patients to seek treatment if signs or symptoms of a chronic or acute infection occur

Risk for Latent Tuberculosis (TB) Reactivation Evaluate patients for TB prior to initiating treatment with SILIQ and do not treat patients with active TB. Initiate treatment for latent TB prior to starting SILIQ and consider anti-TB therapy prior to initiation in patients with history of latent TB if adequate treatment cannot be confirmed. Monitor closely for symptoms of active TB during and after treatment.

Immunizations Avoid use of live vaccines in patients treated with SILIQ.

Adverse Reactions The most commonly reported adverse reactions in clinical trials were arthralgia, headache, fatigue, diarrhea, oropharyngeal pain, nausea, myalgia, injection site reactions, influenza, neutropenia, and tinea infections.

To report SUSPECTED ADVERSE REACTIONS, contact Valeant Pharmaceuticals at 1-800-321-4576 or FDA at 1-800-FDA-1088, or visit www.fda.gov/MedWatch.

Please see Brief Summary of Full Prescribing Information on following page, including Boxed Warning about suicidal ideation and behavior.

**BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION FOR SILIQ™ (BRODALUMAB) INJECTION**

This Brief Summary does not include all the information needed to use SILIQ safely and effectively. See full prescribing information for SILIQ SILIQ™ (broladumab) injection, for subcutaneous use. Initial U.S. Approval: 2017

**WARNING: SUICIDAL IDEATION AND BEHAVIOR**

Suicidal ideation and behavior, including completed suicides, occurred in subjects treated with SILIQ. Prior to prescribing SILIQ, weigh the potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior. Patients with new or worsening suicidal ideation and behavior should be referred to a mental health professional, as appropriate. Advise patients and caregivers to seek medical attention for manifestations of suicidal ideation or behavior, new onset or worsening depression, anxiety, or other mood changes [see Warnings and Precautions].

Because of the observed suicidal behavior in subjects treated with SILIQ, SILIQ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the SILIQ REMS Program [see Warnings and Precautions].

**CONTRAINDICATIONS**

SILIQ is contraindicated in patients with Crohn’s disease because SILIQ may cause worsening of disease [see Warnings and Precautions].

**WARNINGS AND PRECAUTIONS**

Suicidal Ideation and Behavior: Suicidal ideation and behavior, including 4 completed suicides, occurred in subjects treated with SILIQ in the psoriasis clinical trials. There were no completed suicides in the 12-week placebo-controlled portion of the trials. SILIQ users with a history of suicidality or depression had an increased incidence of suicidal ideation and behavior as compared to users without such a history [see Adverse Reactions]. A causal association between treatment with SILIQ and increased risk of suicidal ideation and behavior has not been established.

Prescribers should weigh the potential risks and benefits before using SILIQ in patients with a history of depression or suicidality. Patients with new or worsening symptoms of depression or suicidality should be referred to a mental health professional, as appropriate. Advise patients and caregivers to seek medical attention for manifestations of suicidal ideation and behavior, new onset or worsening depression, anxiety, or other mood changes. Prescribers should also re-evaluate the risks and benefits of continuing treatment with SILIQ if such events occur.

Because of the observed suicidal ideation and behavior in subjects treated with SILIQ, if an adequate response to SILIQ has not been achieved within 12 to 16 weeks, consider discontinuing therapy.

SILIQ is available only through a restricted program under a REMS [see Warnings and Precautions].

**SILIQ REMS Program:** SILIQ is available only through a restricted program under a REMS called the SILIQ REMS Program because of the observed suicidal ideation and behavior in subjects treated with SILIQ [see Warnings and Precautions].

Notable requirements of the SILIQ REMS Program include the following:

- Prescribers must be certified with the program.
- Patients must sign a Patient- Prescriber Agreement Form.
- Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive SILIQ.

Further information, including a list of qualified pharmacies, is available at www.SILIQREMS.com or by calling the SILIQ REMS Program Call Center at 855-511-6135.

**Infections:** SILIQ may increase the risk of infections. In clinical trials, subjects treated with SILIQ had a higher rate of serious infections than subjects treated with placebo (0.5% versus 0.2%) and higher rates of fungal infections (2.4% versus 0.9%). One case of cryptococcal meningitis occurred in a subject treated with SILIQ during the 12-week randomized treatment period and led to discontinuation of therapy [see Adverse Reactions].

During the course of clinical trials for plaque psoriasis, the exposure-adjusted rates for infections and serious infections were similar in the subjects treated with SILIQ and those treated with ustekinumab.

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

**Risk for Latent Tuberculosis Reactivation:** Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with SILIQ. Do not administer SILIQ to patients with active TB infection. Initiate treatment for latent TB prior to administering SILIQ.

Consider anti-TB therapy prior to initiation of SILIQ in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Closely monitor patients receiving SILIQ for signs and symptoms of active TB during and after treatment.

**Crohn’s Disease:** In psoriasis trials, which excluded subjects with active Crohn’s disease, Crohn’s disease occurred in one subject during treatment with SILIQ and led to discontinuation of therapy. In other trials, exacerbation of Crohn’s disease was observed with SILIQ use.

SILIQ is contraindicated in patients with Crohn’s disease.

Discontinue SILIQ if the patient develops Crohn’s disease while taking SILIQ.

**Immunizations:** Avoid use of live vaccines in patients treated with SILIQ. No data are available on the ability of live or inactive vaccines to elicit an immune response in patients being treated with SILIQ.

**ADVERSE REACTIONS**

The following serious adverse reactions are discussed in greater detail in other sections of labeling:

- **Suicidal Ideation and Behavior** [see Warnings and Precautions]
- **Infections** [see Warnings and Precautions]
- **Crohn’s Disease** [see Contraindications, Warnings and Precautions]

**Clinical Trial 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 practice.

The overall safety population included 4558 subjects (3066 SILIQ, 613 ustekinumab, 879 placebo) in controlled clinical trials and open-label extension studies. The majority of subjects were male (69%), white (91%), and aged 40-64 years old (58%). One-third of subjects reported previous biologic use prior to enrollment. Across the clinical development program, 4464 subjects received at least one dose of SILIQ; 3755 subjects were exposed to SILIQ for at least 1 year.

Weeks 0 to 12: Data from one multicenter, randomized, placebo-controlled trial (Trial 1), two multicenter, randomized, placebo- and active-controlled trials (Trials 2 and 3), and one dose-finding trial (Trial 4) in plaque psoriasis were pooled to evaluate the safety of SILIQ (210 mg weekly at Weeks 0, 1, and 2, followed by treatments every 2 weeks [Q2W]) compared to placebo for up to 12 weeks after treatment initiation.

During the 12-week randomized treatment period, about 1% of the subjects in the treatment groups (SILIQ, ustekinumab and placebo) discontinued treatment because of adverse events. Adverse events leading to discontinuation of SILIQ included neutropenia, arthralgia, and urticaria. The proportion of subjects who developed serious adverse events was similar among the SILIQ, ustekinumab, and placebo groups.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the SILIQ 210 mg Q2W group than in the placebo group during the 12-week randomized treatment period of the pooled trials.

### Table 1: Adverse Reactions Occurring in ≥1% of Subjects in the SILIQ Group and More Frequently than in the Placebo Group in Plaque Psoriasis Trials through Week 12

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Placebo (N=879)</th>
<th>SILIQ 210 mg every 2 weeks* (N=1496)</th>
<th>Ustekinumab (N=613)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>29 (3.3)</td>
<td>71 (4.7)</td>
<td>15 (2.4)</td>
</tr>
<tr>
<td>Headache</td>
<td>31 (3.5)</td>
<td>64 (4.3)</td>
<td>23 (3.8)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>10 (1.1)</td>
<td>39 (2.6)</td>
<td>16 (2.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (1.1)</td>
<td>33 (2.2)</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>Oropharyngeal pain</td>
<td>10 (1.1)</td>
<td>31 (2.1)</td>
<td>8 (1.3)</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (1.1)</td>
<td>28 (1.9)</td>
<td>6 (1.0)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (0.3)</td>
<td>26 (1.7)</td>
<td>4 (0.7)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>11 (1.3)</td>
<td>23 (1.5)</td>
<td>12 (2.0)</td>
</tr>
<tr>
<td>Influenza</td>
<td>4 (0.5)</td>
<td>19 (1.3)</td>
<td>7 (1.1)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>4 (0.5)</td>
<td>15 (1.0)</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>Tinea infections</td>
<td>2 (0.2)</td>
<td>15 (1.0)</td>
<td>3 (0.5)</td>
</tr>
</tbody>
</table>

* subjects receiving 210 mg of SILIQ at Weeks 0, 1, and 2, followed by treatment every two weeks during the 12-week period

**Trials 2 and 3 included the active comparator, ustekinumab.**

Adverse reactions that occurred in less than 1% of subjects in the SILIQ group through Week 12 were conjunctivitis and candida infections (including oral [0.2%], genital [0.1%], and esophageal [0.1%]) versus none in the placebo group.

**Week 0 to End of Trial:** Through Week 52, exposure-adjusted rates of serious adverse events were similar between subjects treated with SILIQ and those treated with ustekinumab. Through the end of the trial, the exposure-adjusted rates of treatment-emergent serious adverse events were similar to those seen in the 52-week period in the subjects treated with SILIQ.

**Specific Adverse Reactions:** Suicidal Ideation and Behavior–During the 12-week randomized treatment period in the pooled trials, one subject in the SILIQ group attempted suicide and none in the placebo or ustekinumab groups. From initiation through Week 52 of the trials, suicidal ideation or behavior occurred in 7 of 4019
subjected subjects (0.2 per 100 subject-years) treated with SILIQ and in 2 of 613 subjects (0.4 per 100 subject-years) treated with ustekinumab.

During the course of the clinical trials for plaque psoriasis, suicidal ideation or behavior occurred in 34 of 4464 subjects treated with SILIQ (0.37 per 100 subject-years). Eight of the 10 subjects who attempted or completed suicide had a history of depression and/or suicidal ideation or behavior [see Warnings and Precautions].

Infections—During the 12-week randomized treatment period, infections occurred in 25.4% of the SILIQ group compared to 23.4% of the placebo group. The majority of infections consisted of nasopharyngitis, upper respiratory tract infection, pharyngitis, urinary tract infections, bronchitis, and influenza, and did not necessitate treatment discontinuation. The SILIQ group had a higher rate of fungal infections compared to the placebo group (1.8% vs 0.9%). The fungal infections were primarily non-serious skin and mucosal candida infections [see Warnings and Precautions].

Neutropenia—During the 12-week randomized treatment period, neutropenia occurred in 0.7% of subjects in the SILIQ group. Most adverse reactions of neutropenia were transient. In subjects with normal absolute neutrophil count (ANC) at baseline, a reduction in ANC occurred in 0.8% of subjects in the SILIQ group, compared to 0.3% in the ustekinumab group, and 3.6% in the placebo group. Neutropenia (ANC 9586500 Issued: February/2017

**NONCLINICAL TOXICOLOGY**

Carcinogenesis, Mutagenesis, Impairment of Fertility: Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of SILIQ. The published literature is mixed on the potential effects on malignancy risk due to the inhibition of the IL-17RA, the pharmacological action of SILIQ. Some published literature suggests that IL-17A directly promotes cancer cell invasion, which suggests a potential beneficial effect of SILIQ. However, other reports indicate IL-17A promotes T-cell mediated tumor rejection, which suggests a potential adverse effect by SILIQ. However, inhibition of the IL-17RA with SILIQ has not been studied in these models. Therefore, the relevance of experimental findings in these models for malignancy risk in humans is unknown.

In cynomolgus monkeys, there were no effects on fertility parameters such as changes in reproductive organs or sperm analysis following subcutaneous administration of brodalumab at dose levels up to 90 mg/kg/week for six months (26 times the MRHD on a mg/kg basis). The monkeys were not mated in this study to evaluate effects on fertility.

**Patient Counseling Information**

[see Patient Counseling Information in full Prescribing Information].

**Manufactured for:** Valeant Pharmaceuticals North America LLC. Bridgewater, NJ 08807 USA

**Manufactured by:** Valeant Pharmaceuticals Luxembourg S.à.r.l. Grand Duchy of Luxembourg, L-1931, Luxembourg

U.S. License Number 2053
U.S. Patents 7,939,070; 7,786,284; 7,833,527; 7,767,206; 8,790,648; 8,545,842; 8,435,518; 9,073,999; 9,096,673

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9586500 Issued: February/2017
find the time or energy to commit and follow through with a long-term therapy, even though they are the ones making the appointment with the dermatologist to address their psoriasis symptoms. We use double the amounts of super potent topical steroids per patient per capita, more than anywhere else in the world because patients want to be over their symptoms as soon as possible. Everyone wants a quick fix, but patients need to understand that psoriasis is a chronic life-long disease,” Dr. Menter says.

Choosing the appropriate vehicle can be instrumental in improving treatment outcomes. Scalp psoriasis, for instance, is known to be very difficult to treat and can be recalcitrant to standard therapies. Here, it is paramount to consider the patient’s type of hairstyle when choosing among the different sprays, gels, and oil-based vehicles. According to Dr. Menter, the clinician needs to have understanding of the individual patient’s particular needs and aim to prescribe the appropriate therapy and vehicle for each individual case, facilitating treatment adherence by the patient.

“I’m not sure all dermatologists take or have the time to do this in their busy daily practices. Nursing staff or physician assistants following appropriate training could or should take the time and explain in greater detail to the patients how, when, and how often a prescribed therapy should be applied, as well as the importance of following through with the therapy. I believe that longer and more in-depth consultations with the dermatologist, nursing staff, or physician assistants could make a difference in improving outcomes,” Dr. Menter says.

“BY FORMING A STRONG THERAPEUTIC ALLIANCE WITH PATIENTS AND BY ASKING THEM ABOUT THEIR EXPECTATIONS FOR TREATMENT, CLINICIANS HAVE A BETTER CHANCE OF PROVIDING PATIENTS WITH MORE EFFECTIVE AND DURABLE RELIEF FROM THEIR PSORIASIS SYMPTOMS.”


QUALITY OF LIFE

Improving the quality of life of patients is one of the central goals in psoriasis therapy. Tracking disease severity is one way the clinician can have a better idea of the of the patient’s status. The Psoriasis Symptom Inventory (PSI) is comprised of eight usual symptoms seen in psoriasis (i.e., itching, scratching, burning, stinging, etc.), and patients rank their status on a 0 to 4-point score basis. According to Dr. Menter, the PSI is proving to be very useful in helping to categorize where patients are in terms of their disease severity, which can often reflect their psychological state regarding their psoriasis. Clinicians can then, perhaps more quickly, adjust treatment to hopefully improve clinical treatment outcomes, leading to a higher quality of life.

“We have to be very aware to carefully assess the symptomatology of our patients and treat them appropriately. The PSI can give the physician some insight into some of the symptoms that patients experience but perhaps seldom talk about. I believe such assessment tools can help clinicians better understand what patients are going through and further help them choose an appropriate therapeutic plan for the typical complex mosaic of psoriasis symptoms,” Dr. Menter says.

REFERENCE


2. Hema N. Viswanathan, PhD; Alex Mutebi, PhD; Cassandra E. Milmont; et al. “Measurement Properties of the Psoriasis Symptom Inventory Electronic Daily Diary in Patients with Moderate to Severe Plaque Psoriasis,” Value in Health Journal. September 2017. DOI: https://doi.org/10.1016/j.jval.2016.11.020
A recent study found that children with psoriasis are at an increased risk of developing comorbidities compared to those without psoriasis, and obesity appears to be an important independent risk factor for the development of these comorbidities.

The study, published in *JAMA Dermatology*, shows that, in addition to needing to manage the cutaneous symptoms of the disease, patients with psoriasis are also at a higher risk for developing comorbidities such as obesity, hyperlipidemia, hypertension, diabetes, metabolic syndrome, polycystic ovarian syndrome, nonalcoholic liver disease, and elevated function enzyme levels.

“The existence of these comorbidities in children with psoriasis is not really new to us. After the associations with these comorbidities were recognized in adult psoriasis patients, we began to recognize these associations in the pediatric population as well. What’s striking is the importance of obesity as an independent risk factor for the development of these comorbidities,” said Megha M. Tollefson, M.D., the study’s corresponding author.

Dr. Tollefson and Mayo Clinic colleagues determined the risk of these comorbidities in children with and without psoriasis, after accounting for obesity. Children with psoriasis were significantly more likely to develop each of the comorbidities than those children without psoriasis, and obesity was found to be a strong risk factor for the development of each comorbidity, even in those children without psoriasis.

“While we found that psoriasis certainly does play a bit of a role in the development of these comorbidities, obesity is a much larger issue in relation to the development of these comorbidities,” Dr. Tollefson says.

In addition to managing symptoms, physicians should focus on other factors associated with preventing and identifying the onset of comorbid conditions. It is important to recognize that obesity is probably a much larger factor in children who have psoriasis and are obese; spending time talking about that with families is paramount. Also, it is very important to bring in the primary care specialist or pediatrician in a multidisciplinary forum to appropriately address the different comorbidities that can occur in this patient population, Dr. Tollefson adds.

**REFERENCE**

Ovarian reserve low in premenopausal women with psoriasis

Study indicates female patients of reproductive age may benefit from additional medical services

by Whitney J. Palmer | Staff Correspondent

Women with psoriasis could have a harder time getting pregnant, according to new research.

Based on a study published in the Taiwanese Journal of Obstetrics & Gynecology, these patients have a diminished ovarian reserve or a number of follicles capable of producing a mature, healthy egg for fertilization.

Current data suggest female hormones released during pregnancy impact the course of psoriasis, and, at the same time, psoriasis affects pregnancy outcomes. However, no previous research exists into the ovarian reserve and function of psoriatic patients.

According to study authors, knowing how psoriasis might affect pregnancy chances can be very important for women interested in having a family.

“Average age of diagnosis in women with psoriasis is 28, a prime age for pregnancy,” the authors wrote.

“Therefore, many female patients with psoriasis are concerned about adverse effects of the disease on their future fertility.”

Although age is a factor in determining whether a woman can get pregnant, it has limited usefulness in predicting individual ovarian performance. Consequently, knowing a woman’s ovarian reserve is increasingly important clinically.

And, the measure of a number of factors can help determine the quality of a woman’s ovarian reserve. These include basal follicle stimulating hormone (FSH), estrogen (E2), FSH/luteinizing hormone (LH) ratio, Inhibin B, and antimullerian hormone (AMH). Ovarian volume (OV) and antral follicle count (AFC) determine ovary size and shape.

THE STUDY
The study, conducted between January and September 2014, occurred in Aksaray University Research and Training hospital in Turkey. It was designed to determine whether women with psoriasis who hadn’t undergone previous treatment had a reduced ovarian reserve compared to women without psoriasis. They also investigated if disease severity was associated with ovarian reserve.

Researchers selected participants based on their type of psoriasis, presence of hair and nail psoriasis, and the severity of disease. Participants were excluded for infertility, pregnancy, gynecological pathologies, polycystic ovarian syndrome, breastfeeding, gynecological surgery history, chronic liver or kidney failure, smoking, cancer, or other dermatological, inflammatory, physical, or psychiatric disorders. Women who previously received any systemic treatment and hormone medication were also excluded due to potential effects on ovarian function.

Researchers enrolled 14 women with psoriasis for this study. Nine had plaque type psoriasis, three had guttate type, and two had palmoplantar type. A control group of 35 women without psoriasis also

Take AWAYS
Average age of psoriasis diagnosis in women is 28.

Measures indicate diminished ovarian reserve in this small group.

Women of reproductive age with psoriasis could benefit from further analysis before starting systemic therapy.

CONTINUED ON PAGE 11
Poor diet, psoriasis flares, often intertwined

by Lisette Hilton | Staff Correspondent

There are two important reasons for physicians to address the role of diet when managing psoriasis patients. One is to limit risks of cardiovascular and metabolic comorbidities. The other is to potentially improve psoriasis severity.

Evidence suggests certain food types can flare psoriasis and losing weight can improve treatment response for some with psoriasis, according to Rajani Katta, M.D., co-author of an article that examines how dietary changes can impact skin diseases — including psoriasis, published earlier this year in *Skin Therapy Letter*.

“We know that patients who have psoriasis are at higher risk for diabetes, high blood pressure, heart disease and a number of metabolic abnormalities. It’s really important that psoriasis patients know that and realize that changing their diet can be an important part of preventing these comorbidities,” said Dr. Katta, a dermatologist with Texas Children’s Hospital in Houston.

DIETARY TRIGGERS

Smoking and high alcohol intake are recognized psoriasis triggers, however, dietary factors may also play a role, she said.

The question about whether what patients eat can make their psoriasis worse needs more research, but there are evidence-based suggestions dermatologists can make about certain food types. “One that has been researched more extensively is the role of gluten,” Dr. Katta says.

Psoriasis patients are bound to ask about gluten because gluten’s role is mentioned extensively and high up on Google searches on diet and psoriasis.

“The gist of it is that gluten-containing foods can act as a trigger in a small percentage of patients, but definitely not all,” she said.

Dr. Katta says an important clue about whether to pursue gluten as a trigger is to ask psoriasis patients about gastrointestinal symptoms, such as abdominal pain, diarrhea, or of evidence of certain nutrient deficiencies, including iron deficiency.

“Those are clues that they may have celiac disease,” she said.

Dr. Katta refers those psoriasis patients to gastroenterology for a workup, and she might order a test for antibodies to gluten.

“There was one large study that found there was about a two-fold higher risk of celiac disease in patients with psoriasis,” Dr. Katta says. “There’s not a high risk of celiac disease baseline, so even a two-fold higher risk is not a huge number, but it’s definitely an increased risk and that’s why we take it seriously when psoriasis patients have gastrointestinal symptoms.”

Researchers have also found patients who have antibodies to gliadin in their bloodstream, but do not have celiac disease, fare better on psoriasis treatment when they’re on a gluten-free diet than matched controls.

APPLYING KNOWLEDGE TO PRACTICE

Physicians should ask psoriasis patients about gastrointestinal symptoms. It’s an easy screening tool for better managing those patients, Dr. Katta said.

Physicians who take patients’ height, weight and blood pressure during office visits, should calculate body mass index (BMI) and consider referring patients who are overweight or obese to a nutritionist. Derma-
Dermatologists can tackle the touchy subject with their patients by mentioning their higher risk of comorbidities. They should also mention that there is evidence to suggest that weight loss can improve psoriasis patients’ treatment response, reflected by improved psoriasis area and severity index, or PASI, scores.

Providers can direct patients to the review published July 2014 in the Journal of the American Academy of Dermatology (JAAD) in which authors concluded that a number of studies have shown weight loss may be a preventative and adjunctive therapy for psoriasis or psoriatic arthritis treatment in patients who are overweight or obese.

“Given the vast body of popular literature available to patients, it is important for clinical providers to familiarize themselves with the evidence supporting various dietary plans. By doing so, they will be able to engage their patients and partner with them to maximize the impact of pharmacologic and non-pharmacologic interventions,” the JAAD authors write.

Disclosures: Dr. Katta is author of the book Glow: The Dermatologist’s Guide to a Whole Foods Younger Skin Diet.

REFERENCES

FOODS THAT TRIGGER SKIN FLARES

Diet can affect skin conditions including acne, atopic dermatitis, psoriasis and rosacea. In a review that focuses on these four conditions, plus aging, Rajani Katta, M.D., and Mary Jo Kramer, B.S., writing in Skin Therapy Letter, highlight trigger foods that should be avoided.

ACNE

Clinical trials have established an association between high-glycemic-load diets and acne. One randomized clinical trial showed that after 12 weeks on a low glycemic load diet, patients experienced a significant improvement after 12 weeks.

Researchers say that the diet may have lowered androgen bioavailability, altered skin sebum production, decreased skin inflammation and reduced sebaceous gland size.

AGING SKIN

The authors write that a diet high in advanced glycation end products (known as AGEs), which are found in deep-fried foods, can promote the loss of elasticity in skin.

ATOPIC DERMATITIS

The consumption of six common foods are milk, eggs, wheat, soy, seafood, and nuts may trigger a flare within minutes to hours.

PSORIASIS

Gluten-containing foods may act as a trigger for some patients. Gluten-containing foods may trigger flares in some patients, but not all. Celiac disease testing is recommended for psoriasis patients with gastrointestinal symptoms. While estimates vary, one large study found a 2.2 fold higher risk of celiac disease in psoriasis patients. The is little evidence that connects certain food types with psoriasis flares, but one observational study suggested benefits from consuming the Mediterranean diet.

ROSACEA

The evidence is sparse in this area, but surveys of patients suggest that some spices and hot sauce can trigger foods as well as tomatoes (30%), chocolate (23%), and citrus (22%). Alcohol was another frequent trigger, including wine (52%) and hard liquor (42%), as well as hot beverages such as coffee (33%) and tea (30%).
Recommendations for individualized biologic therapy

by John Jesitus | Staff Correspondent

A new study advises selecting biologic therapies for psoriasis based on individual factors such as patients’ comorbidities, preferences and clinical situations, as well as the advantages and disadvantages of particular biologic treatments. The study appears in the February issue of the *American Journal of Clinical Dermatology*.

Authors led by Jashin J. Wu, M.D., reviewed available evidence to formulate expert-opinion algorithms for comorbidities, such as psoriatic arthritis (PsA), tuberculosis and hepatitis B, as well as psoriasis in children and women of childbearing potential.

Few patients present with psoriasis and no other health issues, said Dr. Wu, of Kaiser Permanente Los Angeles Medical Center. Probably the most common comorbidity dermatologists see, he said, is psoriatic arthritis, which afflicts around one-third of patients with psoriasis. In such cases, Wu et al. recommend the TNF inhibitors adalimumab, etanercept and infliximab, in that order, as first-line options, as all have been shown to inhibit radiographic progression of PsA, as well as other disease signs and symptoms.

“The efficacy of TNF inhibitors for PsA is comparable. However, infliximab is more effective at clearing skin lesions, followed by adalimumab and then etanercept,” they write.

For patients with PsA who do not respond to TNF inhibitors, the authors recommend as second-line -treatment the interleukin (IL)-17 inhibitor class, which includes secukinumab, ixekizumab and brodalimumab (equal-weight recommendations). If IL-17 inhibition fails, the authors recommend the IL-12/23 inhibitor ustekinumab, especially for patients with severe psoriasis and mild arthritis.

**PSORIASIS WITH PSORIATIC ARTHRITIS**

Psoriatic arthritis affects one-third of psoriasis patients. In these cases, Dr. Wu’s prefers TNF inhibitors as first-line options in this order:

- **FIRST**: adalimumab
- **SECOND**: etanercept
- **THIRD**: infliximab

If TNF inhibitors fail in these cases, his second-line treatment includes IL-17 inhibitors:

- Secukinumab, Ixekizumab, Brodalimumab

If IL-17s fail, third-line treatments include IL-12/23 inhibitors:

- Ustekinumab

**WOMEN WITH PSO**

Approximately one-fourth of patients with psoriasis are females of childbearing potential. For pregnant or nursing women, the authors recommend the following as among possible treatments, but caution these are based on limited data:

- **Certolizumab Pegol.** Approved by the Food and Drug Administration in May, certolizumab pegol is indicated for adults with moderate-to-severe plaque psoriasis. In clinical trials, it was shown to have minimal to no fetal transfer through the placenta or via nursing.

- **Ustekinumab.** With evidence limited to case reports, ustekinumab was found to be relatively safe, with no clear reported safety signals in pregnant women.

**PEDIATRIC PSORIASIS**

“ Usually psoriasis presents in the late teens or early 20s. If it does present in childhood, it’s usually mild, and patients do not need systemic therapies,” Dr. Wu said. But for those rare cases when they are needed, the authors recommend the following as among the leading treatment options:

- **Etanercept** (FDA-approved for treating moderate-to-severe plaque psoriasis in children ages 4-17 years)
Ustekinumab (approved for moderate-to-severe plaque psoriasis in children ages 4-17)

Adalimumab

CASES COMPlicated BY INFECTIONS

For patients with psoriasis and latent tuberculosis infection (LTBI), ustekinumab is first-line and IL-17 inhibitors second.

Multiple cases of serious TB infections have been associated with TNF inhibitor use for chronic inflammatory conditions, so TNF inhibitors are third-line.

Wu et al. also note that physicians must determine patients’ LTBI status and provide anti-TB prophylaxis for positive patients one to two months before initiating biologic therapy.

For psoriasis cases complicated by inflammatory bowel disease, adalimumab, infliximab and ustekinumab are first-line therapies.

LIMITATIONS TO THE STUDY

The study did not include IL-12/23 inhibitors guselkumab and tildrakizumab. When these recommendations were written, there was little data for guselkumab, which was FDA-approved in July 2017, and tildrakizumab, which is not yet approved. The study authors are planning to update algorithms to incorporate these and other recently approved biologics.

REFERENCE

Psoriasis is associated with a small reduction of pulmonary function and those with psoriasis are more likely than people without the disease to report shortness of breath, according to a population-based study published in the *British Journal of Dermatology*.

“Dermatologists are generally well aware that psoriasis is a systemic inflammatory disease with a range of comorbidities, including cardiovascular disease and diabetes. Our results add to evidence that pulmonary disease is part of the deal, and although the magnitude of reduced pulmonary function in patients with psoriasis found in our study was small, it can contribute to shortness of breath in individual patients,” says study author Peter Riis Hansen, M.D., D.M.Sc., Ph.D., of Herlev and Gentofte Hospital, Hellerup, Denmark.

Dermatologists, Dr. Hansen says, play a significant role in screening for psoriasis comorbidities and asking about shortness of breath as a routine part of medical history-taking.

“Our results put pulmonary symptoms a bit more on the clinical radar in patients with psoriasis and they emphasize that smoking cessation remains a fundamental part of psoriasis treatment,” he says.

Until now, there had been only a small study on pulmonary function in psoriasis subjects, which found reduced pulmonary function in psoriasis patients. Other research suggests that smoking is a risk factor for psoriasis. And epidemiological studies have linked psoriasis to increased risk of pulmonary infections, chronic obstructive pulmonary disease (COPD) and asthma.

Dr. Hansen and colleagues studied 20,422 adults older than 20 years of age in the Danish General Suburban Population Study, which included 1,173 people with psoriasis. Participants had pulmonary function tests with handheld spirometers, as well as answered questions about whether they had psoriasis, shortness of breath and pneumonia during the past decade.

At the study’s start, psoriasis patients were more likely than controls to smoke, report shortness of

**Take AWAYS**

- Psoriasis is associated with a small reduction of pulmonary function.
- The findings are an extension of what is known about smoking’s link to psoriasis.
- Psoriasis patients face an increased risks for pulmonary infections, chronic obstructive pulmonary disease and asthma.

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**SCREEN FOR PULMONARY MALFUNCTION AND OTHER COMORBIDITIES**

by Lisette Hilton | Staff Correspondent
breath or prior pneumonia. They also had a higher mean body mass index than those without psoriasis. The increased risks of shortness of breath and pneumonia remained significantly higher in the psoriasis group even after adjusting for smoking.

The researchers found forced expiratory volume in the first second in percent of expected values was reduced, at an average 93.2 in the psoriasis group, versus 94.9 in controls. The forced expiratory volume in the first second- forced vital capacity ratio was also lower among psoriasis patients at an average 0.76 versus 0.77. However, force vital capacity was similar in both groups. And after adjusting for smoking, only the average reduction in forced expiratory volume in the first second remained significant in the psoriasis group.

The finding that forced vital capacity was similar in both groups suggests that psoriasis’s predominate pulmonary effect is on airway obstruction. And the finding related to the forced expiratory volume in the first second- forced vital capacity ratio in the psoriasis group is compatible with COPD or asthma and in line with observational studies that have found an increased risk of COPD in psoriasis patients, the authors note.

The authors write they’re tempted to speculate that psoriasis-related inflammatory airway injury and remodeling plays a role in psoriasis’s potential associations with respiratory infections and more.

“Indeed, psoriasis is considered to be an interleukin 23/T helper cell 17-driven disease and similar inflammatory mechanisms have been implicated in the pathogenesis of airway inflammation,” they write.

Dr. Hansen says these findings are an extension of what is known about smoking’s link to psoriasis, as well as psoriasis patients’ increased risks for pulmonary infections, chronic obstructive pulmonary disease and asthma.

“[Our study demonstrates] a small reduction of pulmonary function in psoriasis. Preliminary studies have suggested that subjects with severe psoriasis have increased subclinical airway inflammation and inflammatory pathways may coincide between psoriasis and obstructive lung disease,” he says. “More research is needed to define these mechanisms and their clinical consequences.”

These results indicate that pulmonary disease should be counted among psoriasis comorbidities, and they underscore that psoriasis is a systemic inflammatory disease and not just a skin disorder, Dr. Hansen says.

REFERENCES
In clinical trials: Candidates for psoriasis

by John Jesitus | Staff Correspondent

New treatment prospects for common and uncommon skin ailments address targets ranging from various forms of interleukin (IL) to eotaxin-1. During this year’s American Academy of Dermatology annual meeting, investigators presented findings from trials for investigational drugs. Here’s an update.

Ustekinumab (Stelera, Janssen) is approved for moderate to severe plaque psoriasis, active psoriatic arthritis and moderately to severely active Crohn’s disease. In October 2017, the FDA approved ustekinumab for adolescents with moderate to severe plaque psoriasis who are candidates for phototherapy.

This IL-23 inhibitor improved psoriasis and reduced vascular inflammation in a phase four crossover study, suggesting that inhibiting IL-12/23 in psoriasis may reduce cardiovascular risk. Researchers randomized 21 patients to placebo and 22 patients to ustekinumab. “We found that at week 12, those who got ustekinumab had a 6.6% reduction in aortic vascular inflammation, while the placebo group saw a 12% increase,” said Joel M. Gelfand, M.D., M.S.C.E., of the University of Pennsylvania. Additionally, “We’ve shown that when you clear the skin with a drug that blocks interleukin 12 and 23, you also have significant improvements in aortic inflammation,” to a level on par with a statin.

Risankizumab (AbbVie) is an investigational IL-23 inhibitor in development for psoriasis, psoriatic arthritis and other inflammatory diseases. In April, AbbVie submitted a biologics license application to the FDA completing a phase three trial in which risankizumab met all primary endpoints in the trial.

It works by inhibiting IL-23’s p19 subunit, reducing psoriatic inflammation. In two phase three psoriasis trials, patients received 150 mg risankizumab, 45 or 90 mg ustekinumab (weight-based) or placebo at weeks 0, 4, 16, 28 and 40, with placebo crossover to risankizumab at week 16. “Across both trials, all primary and ranked secondary endpoints achieved statistical significance, with p values of <0.001 versus placebo and ustekinumab,” said Marek Honczarenko, M.D., Ph.D., vice president, immunology development, AbbVie. At one year, 82% and 81% of risankizumab-treated patients achieved Psoriasis Area and Severity Index (PASI) 90, versus 44% and 51% of ustekinumab-treated patients.

Guselkumab is a monoclonal antibody approved to treat adults with moderate to severe plaque psoriasis. It maintained high efficacy with continuous treatment versus withdrawal in an extension of the VOYAGE 2 phase three trial. At week 28, investigators re-randomized 375 patients who had achieved PASI 90 to receive either continued treatment or withdrawal and possible retreatment upon loss of ≥50% of their week 28 improvement. PASI 90 responses among the respective cohorts at week 72 were 86% and 11.5%. Maintenance of PASI 90 after drug withdrawal was associated with continued suppression of IL-17A, IL-17F and IL-22. Among the withdrawal cohort, 87.6% achieved PASI 90 within 6 months of commencing retreatment.

Bimekizumab (UCB) is an IL-17A and IL-17F inhibitor under investigation for the treatment for psoriasis. In a phase 2b trial for moderate-to-severe psoriasis, it provided rapid, substantial clinical improvements by neutralizing IL-17A and IL-17F. Investigators randomized 250 patients to receive 64 mg, 160 mg, 160 mg with 320 mg loading dose, 320 mg, 480 mg or placebo, given monthly for 3 months. At week 12, 46.2%-79.1% of bimekizumab-treated patients achieved PASI 90, versus 0% of placebo-treated patients (p<0.0001, all doses).

Disclosures: Dr. Thaçi is an investigator and advisor for Galápagos and Morpheus, developers of MORT06, and is an investigator, advisor and speaker for Sanofi-Regeneron. Dr. Fiorino is an employee and shareholder of Immune Pharmaceuticals Inc., developer of bertilimumab. Dr. Gelfand is a consultant to several companies that market psoriasis treatments, including Janssen, which supported his study via a grant to the University of Pennsylvania. Dr. Honczarenko is an AbbVie employee.

REFERENCE