Psoriasis is a crowded space in managed care with many therapeutic options that are often costly; common comorbidities, such as metabolic syndrome, further add to the complexity of treatment. Therefore, strategies for controlling costs, including utilization management, have become a key priority among payers, and the use of claims and electronic medical record (EMR) data is currently being explored to improve understanding of costs and quality of health care and to personalize the approach to psoriasis management. In an AJMC® Peer Exchange™ entitled, “A Personalized Approach to Disease Management in Psoriasis,” managed care decision makers and an expert in psoriasis discussed strategies for using total cost of care data to optimize outcomes and reduce care costs in patients with psoriasis who have comorbidities such as metabolic syndrome. The session was moderated by Ryan Haumschild, PharmD, MS, MBA, director of pharmacy services at Emory Healthcare and Winship Cancer Institute in Atlanta, Georgia.

ECONOMIC IMPACTS OF PSORIASIS

Psoriasis is an immune-mediated, inflammatory skin condition that is characterized by demarcated, scaling, and erythematous plaques. The total costs of care (including direct and indirect costs and costs of medical comorbidities) are substantial for patients with psoriasis. A systematic review of economic studies evaluated the costs of adult psoriasis in the United States; costs were adjusted to 2013 US$ using the Consumer Price Index for All Urban Consumers and multiplied by the estimated number of US patients with psoriasis in 2013 (7.4 million). Estimated annual direct costs (including medical costs related to specialist medical evaluations, hospitalization, prescription medications, phototherapy, administration of medication, laboratory tests and monitoring studies, and nonprescription medications and self-care products) ranged from $51.7 billion to $63.2 billion. The estimated annual indirect costs, as determined by absenteeism (lost work productivity due to missing work for health care appointments, sick leave, or unemployment) and presenteeism (impaired work productivity while working due to disease activity), ranged from $23.9 billion to $35.4 billion. Annual costs...
of medical comorbidities (including costs of medical evaluations, treatment, and laboratory monitoring that are directly attributed to comorbid conditions associated with psoriasis) contributed an estimated $36.4 billion.\(^2\)

The authors of the systematic review noted that the estimated annual costs for those with psoriasis are considerably higher than those for the general population and that defining the economic burden is essential for identifying, developing, and increasing access to cost-effective therapies.\(^2\) The results of 1 study included in the systematic analysis showed that direct costs were higher with increasing psoriasis severity even after excluding the cost of systemic therapy.\(^2\)

The substantial effect of psoriasis on health-related quality of life is particularly evident in occupational function.\(^7\) Data collected from the National Health and Wellness Survey showed that in comparison with a cohort without psoriasis matched for age, sex, region, and race, those with psoriasis were more likely to have missed hours at work for health-related reasons (odds ratio [OR], 1.37; 95% CI, 1.00-1.89; \(P < .05\)), have greater impairment in health-related work productivity (OR, 1.66; 95% CI, 1.28-2.18; \(P < .001\)), experience more overall work impairment (OR, 1.62; 95% CI, 1.25-2.11; \(P < .001\)), and report greater impairment in nonwork activity (OR, 1.59; 95% CI, 1.25-2.03; \(P < .001\)).\(^4\) Impairments in work productivity also contribute to indirect costs, which increase with greater disease severity.\(^4\) An analysis of data from the 2015 Adelphi Real World Psoriasis Disease Specific Programme, which included data from 6 countries (United States, France, Germany, Spain, United Kingdom, and Italy), showed that the average hours of work productivity loss and annual indirect costs associated with total work productivity loss increased with greater disease severity, with the majority of work productivity losses and associated costs attributed to presenteeism.\(^7\)

**Stakeholder Insights**

Psoriasis is a high-cost disease state in terms of both health care resource utilization and drug cost; thus, payers are focused on lowering costs via utilization management. Managing the total costs of care for patients with psoriasis can be challenging, because costs stem from multiple sources, including biologic therapy, hospitalizations, emergency department (ED) visits, specialist visits, laboratory tests, and other medications for comorbidities related to psoriasis. Notably, it may be difficult to obtain a full picture of all costs related to psoriasis care, except in the case of integrated delivery networks (IDNs). The ability of integrated IDNs to see the multiple sources of care costs, including medical and pharmacy costs based on claims as well as data from EMRs, gives them a unique perspective on psoriasis management, noted Bhavesh Shah, PharmD, senior director of specialty pharmacy strategy at Boston Medical Center in Boston, Massachusetts.

In addition to drug costs, another driver of pharmacy costs is switching of medications. Switching therapies is common among patients with psoriasis; however, it can lead to the formation of antibodies directed against the drug (and thus, lower effectiveness) and higher costs due to the additional doses required during the loading phase, according to Mark Lebwohl, MD, dean for clinical therapeutics and professor and chair emeritus of Dermatology at the Icahn School of Medicine at Mount Sinai Hospital in New York, New York. “These are very expensive treatments, so you’re now increasing the cost of the treatment for that year by giving an extra dose that you didn’t need before,” he said.

Poor adherence and patient perceptions may also drive the switching of medications. Shah noted that, for example, many patients discontinued their biologic therapies early in the COVID-19 pandemic based on a perceived negative effect of the drugs on their immune systems, even though later studies demonstrated that most of the biologic therapies did not affect the immune response to COVID-19 vaccination or to COVID-19 itself and may have even been protective against advanced lung disease. Alternatively, switching medications and needing to understand a new adverse effect profile and specifics on monitoring required can also decrease adherence, according to Haumschild.

Lebwohl said that, in his experience, adherence is substantially improved with drugs that are administered in the office or hospital, “... because the doctor is directly determining when [the drug is] given, so the ability of a patient to depart from their protocol is reduced.” Also, drugs administered in the office

(Continued on Page 5)
A Personalized Approach to Disease Management in Psoriasis

or hospital are covered by a patient’s medical benefit, as opposed to a self-administered drug that is covered by the pharmacy benefit and may incur a large copay. Lebwohl noted that pharmaceutical companies often cover the copay of self-administered medications for patients with commercial insurance. Finding medications that can be given in the office may be particularly important for patients on Medicare so they can have their medication covered fully under the medical benefit.

The considerable impact of psoriasis on quality of life and work absenteeism and presenteeism can incur substantial indirect costs through loss of productivity and have downstream effects on employer payers, according to Shah. “We definitely need to look at that from a value perspective in terms of how this disease can really impact the quality of life. [W]hat is the downstream impact of that? How is that really driving our cost to be unfavorable indirectly?” he asked.

PSORIASIS AND METABOLIC SYNDROME

Although psoriasis is commonly thought of as a condition affecting the skin and joints, it is increasingly recognized as a systemic inflammatory condition, and it poses an increased risk for inflammatory cardiometabolic comorbidities in affected patients. Metabolic syndrome is defined as the presence of 3 or more of the following aberrations that increase the risks of atherosclerotic cardiovascular disease, insulin resistance, diabetes, and vascular and neurologic complications: increased waist circumference, elevated triglyceride level, reduced high-density lipoprotein cholesterol level, elevated fasting glucose results, and elevated blood pressure measurements (Table).

Metabolic syndrome is strongly associated with psoriasis. A population-based study showed that metabolic syndrome was more prevalent among patients with psoriasis (34% vs 26% of matched controls; OR, 1.50; 95% CI, 1.40–1.61). Moreover, the severity of psoriasis was related to the degree of association, with metabolic syndrome observed in 32% of patients with mild psoriasis (adjusted OR, 1.22; 95% CI, 1.11–1.35), 36% of patients with moderate psoriasis (adjusted OR, 1.56; 95% CI, 1.38–1.76), and 40% of patients with severe psoriasis (adjusted OR, 1.98; 95% CI, 1.62–2.43). Additionally, a cohort study of a population derived from the General Practice Research Database in the United Kingdom showed that severe psoriasis is also an independent risk factor for death related to cardiovascular disease (HR, 1.57; 95% CI, 1.26–1.96) after adjusting for other known cardiovascular risk factors (eg, age, sex, hyperlipidemia, hypertension, smoking, and diabetes).

<table>
<thead>
<tr>
<th>TABLE. Definition of Metabolic Syndrome</th>
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<tbody>
<tr>
<td><strong>Metabolic syndrome defined as ≥3 of the following:</strong></td>
</tr>
<tr>
<td>• Waist circumference: ≥ 40 in. for men or ≥ 35 in. for women</td>
</tr>
<tr>
<td>• Triglyceride level: ≥ 150 mg/dL</td>
</tr>
<tr>
<td>• High density lipoprotein–cholesterol level: &lt; 40 mg/dL for men or &lt; 50 mg/dL for women</td>
</tr>
<tr>
<td>• Fasting blood glucose level: ≥ 100 mg/dL</td>
</tr>
<tr>
<td>• Blood pressure measurement: systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg</td>
</tr>
</tbody>
</table>

Although the exact pathophysiologic mechanisms explaining the relationship between psoriasis, metabolic syndrome, and cardiovascular-related death are not fully understood, the increase in proinflammatory cytokines (eg, TNFα, IL-1, and IL-6) mediated by type 1 T-helper cells likely affects insulin signaling, lipid metabolism, and adipogenesis, which are involved in the pathogenesis of atherosclerosis and myocardial infarction. Furthermore, shared genetic risk factors contributing to psoriasis, metabolic disorders, and cardiovascular disease also may play a role in the link between psoriasis, metabolic syndrome, and cardiovascular death.

Effects of Metabolic Syndrome on Treatment Efficacy

Multiple biologic therapies have been developed that target specific cytokines involved in the pathogenesis of psoriasis. First-generation biologics include the TNFα inhibitors adalimumab, infliximab, certolizumab-pegol, golimumab, and etanercept, whereas second-generation biologics encompass inhibitors of IL-12/IL-23 and IL-17, including ustekinumab (an anti–IL-12/IL-23 p40 antibody); guselkumab, risankizumab, and tildrakizumab (anti–IL-23 p19 antibodies); secukinumab and ixekizumab (anti–IL-17A antibodies); and brodalumab (an anti–IL-17 receptor antibody).

However, some data suggest that metabolic syndrome may be associated with a lower response, as defined by the psoriasis area and severity index (PASI), to certain types of biologics (eg, TNFα and IL-17 inhibitors). Pooled data from 3 phase 3 studies (FIXTURE [NCT01358578], ERASURE [NCT01365455], and CLEAR [NCT02074982]) stratified patients into responder groups based on response to secukinumab, ustekinumab, or etanercept at week 16. Metabolic syndrome was associated with a diminished response to all of these treatments, and mean body weight was lower in higher response groups of secukinumab- and etanercept-treated patients. The Outcome of Psoriatic Patients Switched to Adalimumab study, which retrospectively analyzed patients with psoriasis (with or without psoriatic arthritis) given adalimumab after conventional or biologic therapy, showed that the absence of metabolic syndrome was associated with achievement of a 50% reduction in PASI (PASI 50) and a 75% reduction (PASI 75) at 3 months, and a 90% reduction (PASI 90) after 6 months, of adalimumab therapy. However, this reduced response in patients with metabolic syndrome was not observed with tildrakizumab, as a post hoc analysis of the phase 3 trials resURFACE 1 (NCT01722331) and resURFACE 2 (NCT01729754) showed that PASI 75, PASI 90, and a 100% reduction in PASI (PASI 100) were similar between tildrakizumab-treated patients with and without metabolic syndrome at weeks 52, 100, and 148.

Stakeholder Insights

The effects of psoriasis on the patient are multifaceted given the systemic nature of the disease, and advancements in the understanding of the relationship between psoriasis and metabolic syndrome are important to identify optimal therapy for individual patients, according to Robert Groves, MD, executive vice president and chief medical officer for Banner Health | Aetna in Phoenix, Arizona. “This is a disease that has a very broad impact, and so the costs of not treating the disease are going to be relatively high,” said Groves. “The treatment options that...
are available in biologics are very expensive, so understanding which biologics should be applied to which individual patients becomes key. We don’t want to spend time on drugs that aren’t going to be effective and end up switching multiple times to find something that is effective.”

Lebwohl said that he discusses diet and exercise interventions and the implications for cardiovascular disease with overweight patients with psoriasis, because the response to many therapies is blunted in patients with obesity. He noted that the newer therapies (such as the IL-23 inhibitors) that have weight-independent effectiveness may be particularly important to consider in patients with overweight. Groves added that diet and exercise interventions for weight loss can be particularly difficult to initiate in patients with psoriasis, who are often uncomfortable with their skin condition; therefore, having a psoriasis therapy that is effective independent of body weight can be useful. “Dietary and exercise therapies are notoriously difficult to implement long-term, so having a therapy that works regardless of what’s going on with weight makes a huge difference,” he said.

Shah stated that there is often a disconnect between providers treating patients for psoriasis and those managing comorbidities that arise from metabolic syndrome; further, better education of providers and payers on optimal treatment for patients who have psoriasis and metabolic syndrome is important. Lebwohl added that effectively treating the inflammation associated with psoriasis is likely to reduce inflammation-mediated cardiovascular events, such as atherosclerotic disease and myocardial infarction. Although the newer IL-17 and IL-23 inhibitors do not have enough long-term data to demonstrate these outcomes, he suggested that “any drug that works well for psoriasis and thereby reduces those inflammatory cytokines that contribute to a heart attack will ultimately prolong the lives of our patients by eliminating the number 1 cause of death, which is heart attack.”

INNOVATIVE REAL-WORLD EVIDENCE EFFORTS TO SUPPORT PERSONALIZED CARE IN PLAQUE PSORIASIS

Haumschild and his colleagues at Emory University performed a claims analysis to evaluate the potential for reductions in total cost of care for patients with psoriasis and metabolic syndrome with tildrakizumab. They found that initiation of tildrakizumab sooner is likely to lead to better overall outcomes in patients who have both psoriasis and metabolic syndrome, which may lead to less frequent switching of medications and a decrease in total costs of care.

The investigators evaluated specialty pharmacy data to identify patients with plaque psoriasis who were taking a biologic and used data from EMRs to flag patients with an International Classification of Diseases, Tenth Revision (ICD-10) code for metabolic syndrome, with outcome measures including reductions in care, control of disease and comorbidities, and changes in quality of life. “Through that probe, we were able to identify that there is a higher cost of care in patients who have metabolic syndrome as a comorbidity with plaque psoriasis,” said Haumschild. “How do we focus in on creating care pathways so we’re able to get the right medication to that patient sooner, instead of having them step through different therapies or reinstitute several different therapies upon failure to finally get there? How do we create a pathway for that medication to see, in the real world, if we’re creating better access to this drug earlier on in therapy? Are we seeing a reduction in care? Are we seeing better control of disease? Are we seeing better control of some of these comorbidities with some of this quality-of-life data in terms of arthritis and [other comorbidities]?” Haumschild added that “those are the things that we’re trying to think through, [along with] how we evaluate a unique pathway on the payer arm [and] also protocols on the health care side that would align together to improve overall care for the patient population.”

Haumschild suggested that taking a personalized approach to therapy selection while considering that cost is likely to be at the forefront of future research and patient treatment. For patients with metabolic syndrome and plaque psoriasis, this may involve having a prequalifier for earlier access to certain therapies for patients with ICD-10 codes for
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these 2 conditions. However, Groves noted that a “knowledge management problem” exists, in which many stakeholders outside of physicians specializing in psoriasis care do not know which medication is most appropriate for a given patient. He attributed this discrepancy to a level of evidence that does not exist in a reproducible manner. Patients with equal access to biologics—patients who have access to multiple therapies in a shorter time frame.

CLOSING REMARKS

Lebwohl concluded that the multiple available therapies for psoriasis have enabled patients to live their lives as close to normally as possible, which also benefits employers by having employees who live longer and are more productive. Shah added that the use of real-world evidence to show how therapies can be optimized for patients and lower the cost of care should be the future goal. Groves noted that with the use of real-world “practice-based evidence” to personalize the approach to individual patients with psoriasis, there is reason to be optimistic about the future.

REFERENCES

12. Lebwohl MG, Leonard CI, Mehta NN, et al. Tildrakizumab efficacy, drug survival, and safety in patients with psoriasis: pooled data from the reSURFACE 1 and reSURFACE 2 trials of tildrakizumab showed that for patients who had a PASI 50 or 90 at week 16, at which point she had a dramatic response. Lebwohl remarked that for the majority of drugs, 12 to 16 weeks is a good time frame in which to assess whether a patient is responding. A post hoc analysis of pooled data from the reSURFACE 1 and reSURFACE 2 trials of tildrakizumab showed that for patients who had a PASI 50 or greater at week 4 of treatment (achieved by 41% of those treated with tildrakizumab), the probability of achieving a PASI 75 or PASI 90 at week 28 was 87.0% and 66.7%, respectively.44

Although IDNs such as Shah’s have access to a plethora of data on outcomes and costs of care for specific patient populations, they continue to have challenges in using these data to make actionable decisions and identify optimal treatments for patients with psoriasis and associated comorbidities (eg, diabetes, hypertension, hyperlipidemia). Patients with psoriasis and comorbidities tend to have complex and associated comorbidities (eg, diabetes, hypertension, hyperlipidemia). Patients with psoriasis and comorbidities tend to have complex needs for management; Shah said that taking a multidisciplinary approach that includes primary-care elements (eg, diet, exercise, diabetes control) in addition to biologic therapy is important: “Using all the tools at the IDN level and the population health level to drive some of the changes, using the data and academic detailing, can bring more value to the entire model,” he stated.

As for support services to improve adherence and thus optimize outcomes, Lebwohl said that tools such as text reminders to take medications and phone call reminders for follow-up visits can help with adherence to medications. He added that artificial intelligence can be a useful tool to evaluate total costs of care over the longer term (ie, 10-20 years), whereas insurance companies tend to view costs over a shorter time frame. “If you take a patient at year 1 and look at that same patient 10 years later, the chance he still has the same insurance is pretty low,” said Lebwohl. “[The insurance company is] looking at their costs for a few years from now. And they really are looking at those costs that year, because they know they have that patient that year but not necessarily the year after.”
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