Source: American Academy of Dermatology Annual Meeting held February 16-20, 2018, in San Diego, California

OVERVIEW

Steven R. Feldman, MD, PhD, and Alan Menter, MD, as well as principal investigators, describe and provide their perspectives on key posters presented at the American Academy of Dermatology annual meeting on the management of patients with moderate-to-severe psoriasis.

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CME INFO

Target Audience
This activity was developed for dermatologists and other health care professionals who have an interest in moderate-to-severe psoriasis.

Learning Objectives
At the conclusion of this activity, participants should be better able to:

- Summarize the latest research developments in the treatment of psoriasis
- Incorporate evidence-based research into clinical practice

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Secukinumab Demonstrates Significant Improvement of Disease Activity and Health Related Quality of Life in Canadian Psoriasis Patients in a Real World Setting (#7506)
Authors: Poulin Y, et al.

Analysis by:
Alan Menter, MD

Hello, this is Dr. Alan Menter. I'm the chairman of the Department of Dermatology at Baylor University Medical Center in Dallas. I'll be discussing "Secukinumab Demonstrates Significant Improvement of Disease Activity and Health Related Quality of Life in Canadian Psoriasis Patients in a Real World Setting." This poster was presented by Dr. Poulin and colleagues at the 76th Annual Meeting of the American Academy of Dermatology, February 16 to 20, 2018, held in San Diego, California.

Summary

This real-world trial involved patients with moderate-to-severe psoriasis treated with secukinumab who enrolled in a patient support program in Canada. The majority of patients were biologic-naïve or had received only 1 biologic. Treatment with secukinumab demonstrated significant disease reduction and improved quality of life.

Importance

This real-world trial in Canada confirmed efficacy and quality of life improvements with secukinumab that was also reported in clinical trials.

Study's highlights from the lead author's perspective, Dr. Poulin

What are the most important highlights or findings of the study?

- From Real World Evidence (RWE), secukinumab appears to be among the best treatments for psoriasis in the majority of patients as they are either biologic naïve or are switching from 1 previous biologic.
- Irrespective of line of therapy, initial PASI response observed in this cohort demonstrates that secukinumab significantly reduces disease activity with up to 83.8% of bionaive patients reaching PASI < 3.
- Secukinumab significantly improves quality of life as 92% of patients reach DLQI score reduction ≥5 or DLQI 0/1 following secukinumab treatment in a real world setting.

What is the anticipated impact of the study findings on the care of patients?

- Demonstrating RWE of secukinumab efficacy, in line with phase 3 trials
- Demonstrating benefits of early treatment as bionaive patients reach better outcomes compared to biologic experienced patients

Methods

Trial participants were those enrolled in a patient support program for the treatment of moderate-to-severe psoriasis. The program provided reimbursement support, access to educational tools, injection training, and supplies. Data were collected from patients who provided consent and received at least 1 dose of secukinumab. The post-secukinumab Psoriasis Area and Severity Index, in other words, the PASI data, and the Dermatology Life Quality Index, the DLQI, were limited to those whose scores were collected 12 to 51 weeks

post treatment initiation. If multiple scores were available, the ones close to the secukinumab start date were to be used.

Key findings in this study

Two thousand two hundred sixteen patients were included, with an average age of 50.3 years, with a range from 18 to 92 years. 42.6% were females. 35.2% were biologic naïve, 29.6% had received only 1 biologic agent previously and 18.8% had received 2 biologics previously. For the 1435 patients who received 1 biologic previously, 38.3% received secukinumab, 30.0% adalimumab, 18.3% etanercept, and 8.1% infliximab.

Post secukinumab PASI data were available for 108 patients. The treatment history was similar to the overall cohort of the original 2216 patients. From a mean baseline score of 18.2, the PASI score decreased to 3.0 following treatment with secukinumab. A PASI less than 3% was achieved in less than 68.5% of the patients overall. A PASI less than 3 was achieved at 83.8% of biologic naïve and 60.6% of patients who had prior biologics.

Pre- and post-secukinumab DLQI data were available for 236 patients. The Dermatology Life Quality Index score changed from a mean of 19.1% at baseline to 3.6 following secukinumab treatment. 92.4% of patients achieved a DLQI reduction greater than 5, or a DLQI of 0 to 1.

Here are my thoughts and analysis of this study

I think it's an important study because it's real-world data. I think this study allows us, in clinical practice—all of us dermatologists—to try to assess quality of life issues in our psoriasis patients. It's not something that is frequently done in clinical practice. It's done in clinical trials, DLQI, and whereas DLQI may not necessarily be specific for psoriasis, it's the one Dermatology Life Quality Index that's been used in all of our clinical studies, and was used in this study. We'll be getting new quality of life indices for us to use in clinical practice, whether it's Psoriasis Symptom Index, where we take 8 symptoms: stinging, burning, etc, and ask the patient to rate them on a 0 to 4 basis. So the maximum will be 32. We've done a study internationally, with our international psoriasis counsel group, to show that this is a validated new index that we can share with our patients.

So how does the study, again, the results of the study, impact the future state of patient management for us in clinical practice? I do believe that studies like this real-world study of over 2000 patients will allow patients with moderate-to-severe psoriasis to feel more comfortable with understanding the nature of their psoriasis, as well as improving the relationship with their dermatologist. So many of our patients will say to us, "Doctor, you treat us with a drug that's going to suppress my immune system, cause cancer, cause infections." And I always say to them, "With drugs like secukinumab that we're using, we're no longer suppressing your immune system. We are modulating it." I give them a little card that says "Modulate means bring back to normal." So we are taking out one single, I use the term chemical (instead of cytokine) IL-17, out of your immune system that is increased and bringing it back too normal and leaving the rest of your immune system intact. This allows us as dermatologist to reassure our patients that the results from clinical studies, like this, allow patients to feel more comfortable with initiating a drug like secukinumab. Thank you very much.

Apremilast, an Oral Phosphodiesterase-4 Inhibitor, in the Treatment of Palmoplantar Psoriasis. Our Experience in Real Clinical Practice (#6086)

Authors: Madera P, et al

Analysis by:
Alan Menter, MD

Hello, this is Dr. Alan Menter. I'm the chairman of the Department of Dermatology at Baylor University Medical Center in Dallas. I'll be discussing "Apremilast, an Oral Phosphodiesterase-4 Inhibitor, in the Treatment of Palmoplantar Psoriasis. Our Experience in Real Clinical Practice." This poster was presented by Dr. Medera and colleagues at the 76th Annual Meeting of the American Academy of Dermatology, February 16-20. It was held in San Diego, California.

Summary

In this cohort of 4 patients, apremilast treatment over 6 to 14 months resulted in clear or almost clear palms and soles at 16 weeks in 2 patients.

Importance

Palmoplantar psoriasis, as you all know, causes considerable patient morbidity and is highly difficult to treat either with topicals, phototherapy, or systemic therapy. Further investigation of apremilast, in patients with palmoplantar psoriasis, I do believe is warranted, because it is such a difficult condition to treat.

Study's highlights from the lead author's perspective, Dr. Maders

What are the most important highlights or findings of the study?

- Early effectiveness in real clinical practice (50% of patients achieved clear or almost clear palms and soles at 16 weeks)
- Clear benefit in young patients (23-57 year) who are of working age and have a poor QoL due to their disease (palmoplantar psoriasis occurs in up to 40% of plaque psoriasis patients and is often associated with pain, functional limitations, a severe impact on patients' QoL and resistance to treatment. Patients suffer from more physical disability and discomfort than patients with psoriasis on other parts of the body). Positive impact on their social/ family and work life.
- Only 1/4 patient interrupted treatment because of loss of efficacy at 7 months. The rest (3/4; 75%), on April 2018, is still in treatment (treatment initiation: 05/2016; 09/2016 and 02/2017), meaning a drug persistency between 14- 24 months.
- Regarding tolerability, no AEs were reported other than diarrhea (mild to moderate in 2 patients) that did not require any treatment.

What is the anticipated impact of the study findings on the care of patients?

As stated above, palmoplantar psoriasis occurs in up to 40% of plaque psoriasis patients and is often associated with pain, functional limitations, a severe impact on patients' QoL and resistance to treatment. Patients suffer from more physical disability and discomfort than patients with psoriasis on other parts of the body. Therefore, offering them a new treatment option to improve the course of their disease will have an important impact on their lives.

The results of this study show that Apremilast may be considered as a new treatment option for this difficult-to-treat and rarely studied population of palmoplantar psoriasis, providing a relevant clinical benefit in these patients with a good efficacy-safety balance.

Description of the study

Four patients were diagnosed with moderate-to-severe palmoplantar psoriasis, and treated by apremilast 30 mg twice daily for 6 to 14 months.

Key finding in the study

The key findings in the study on the 4 patients: Three men and 1 woman, with ages between 23 and 57 years, comprised the cohort. Two patients had received multiple treatment lines, including biologic therapy. Two patients received clear or almost clear palms and soles at 16 weeks with apremilast. The average palmoplantar pustular psoriasis area and severity index (PASI) improved 68%. That's significant! One patient failed—due to lack of efficacy—at 6 months; and at the start of the treatment, 2 patients had mild-to-moderate diarrhea with the use of apremilast, that disappeared after 2 weeks of treatment, as we often see when this drug is used in ordinary psoriasis.

Here are my thoughts and analysis of the study

Admittedly, this was a small study, only 4 patients. But the very fact that 2 patients with clear or almost clear at 16 weeks is extremely important because palmoplantar psoriasis is one of the most recalcitrant, stubborn forms of psoriasis to treat, be it the plaque type or the pustular type. We all recognize that, in clinical practice, topical therapies, phototherapies, topical PUVA, XTRAC lasers, etc, and all our systemic therapies, seldom clear a patient completely, and the mere fact that we have a small study with 2 out of 4 patients showing clear or almost clear palms within 4 months of initiating apremilast treatment to me is highly important. I do believe that this is a study that is worth taking, as I said earlier, to a bigger study, to see really and truly how well apremilast works in palmoplantar psoriasis, and is the improvement maintained. You know what patients fear most with palmoplantar psoriasis? It is struggling with it for years, getting clear, and then us allowing them to flare back up again. We have to maintain long-term control. Thank you.

Retreatment With Brodalumab Results in High Response Rates in Patients With Psoriasis After Treatment Interruption (#6841)

Authors: Armstrong A, et al.

Analysis by:
Alan Menter, MD

Hello, this is Dr. Alan Menter. I'm the chairman at the Department of Dermatology at Baylor University Medical Center in Dallas. I will be discussing “Retreatment With Brodalumab Results in High Response Rates in Patients With Psoriasis After Treatment Interruption.” This poster was presented by Dr. Armstrong and her colleagues at the 76th Annual Meeting of the American Academy of Dermatology, February 16-20, 2018, in San Diego, California.

Summary

The trial involved patients with moderate-to-severe psoriasis who achieved a good initial response with brodalumab. Following treatment withdrawal and subsequent re-initiation of brodalumab, the vast majority of patients returned to their previous stable response within 16 weeks.

Importance

The importance of the study is, I believe, these results are very relevant in real-life practice because it is not uncommon for patients to stop

and restart their medications for multiple different reasons.

Methods

I'd now like to describe the study. First of all, the methodology. Patients with moderate-to-severe psoriasis were randomized with brodalumab either 140 mg or 210 mg or placebo every 2 weeks during a 12-week induction phase. At week 12, patients receiving brodalumab who achieved a static Physician Global Assessment, the sPGA score, of 0 or 1, were re-randomized to their induction dose of brodalumab or placebo. Beginning at week 16, all re-randomized patients who experienced return of the disease, which was ranked on an sPGA of 3 or greater than 3, qualified for re-treatment. In these patients, brodalumab was re-initiated at the induction dose of 140 mg or 210 mg every 2 weeks.

Key findings in the study

So now, let's talk about the key findings in this interesting study. Seventy nine of 84 patients, which is 94%, randomized to brodalumab 210 mg every 2 weeks in the induction phase and re-randomized to placebo in the withdrawal phase, experienced return of disease. The mean and median time to return of disease was 74.7 days and 56.0 days, respectively. Most patients with psoriasis who experienced a return of disease following brodalumab withdrawal returned to their previous state of response 16 weeks following re-initiation of brodalumab.

Of the patients who exhibited a PASI score—Psoriasis Area and Severity Index score—of 75 prior to brodalumab withdrawal at week 12, 92.1% achieved a PASI 75 by week 16, following re-initiation. Of the patients experiencing PASI 90, prior to brodalumab withdrawal, 91.2% reached a PASI 90 by week 16, following re-initiation. And finally, the patients exhibiting a PASI 100 prior to brodalumab withdrawal, 90.5%, reached the same PASI 100 score by week 16, following re-initiation.

Here are my thoughts and analysis of the study

I'd like to give a short commentary on what I believe is important in this study. From a protocol consideration, patients who either discontinued the biologic drug or who lost the proper insurance reimbursement, which happens to all of us all the time in clinical practice, the vast majority, which is 90%, will regain the initial exit response. That's important because we have other studies and other drugs over the years where patients did not respond as well after re-initiating therapy, and here we have 90% who do.

What about the results of the study? How does this impact the future management of patients in the field of psoriasis? If we were able to determine remissions with our psoriasis therapy, which we currently cannot, it may be possible for us as dermatologists to temper patients' therapies. In other words, even discontinue therapy for a period of time. We don't yet have biomarkers that can predict what we call "remission," or predict a reoccurrence of psoriasis. Yet all patients ask all of us, "Doctor, I'm clear. Why do I need to continue my treatment?" And I do tell them, "Because we cannot predict when you're going to flare." And here we have a drug that in 90% plus of patients in this study showed they regain their clinical response in a very, very positive manner after discontinuing therapy. And so many times patients lose their insurance or go away on vacation, forget to take their drug with them, and they have to restart it at a later stage. This is important data for brodalumab.

Efficacy of Tildrakizumab in Etanercept Partial or Nonresponders (#7636)
Authors: Crowley J, et al.

Analysis by:
Steve Feldman, MD

Hello, this is Dr. Steven Feldman. I'm Professor of Dermatology, Pathology, and Public Health Sciences at Wake Forest School of Medicine in Winston Salem, North Carolina. I'll be discussing "Efficacy of Tildrakizumab in Etanercept Partial or Nonresponders." The poster was presented by Dr. Crowley and colleagues at the 76th Annual Meeting of the American Academy of Dermatology on February 16–20, 2018, in San Diego, California.

Summary
This post hoc analysis assessed the safety and efficacy of tildrakizumab in patients with moderate-to-severe psoriasis who were partial or nonresponders to etanercept. After 20 weeks of treatment with tildrakizumab, three-quarters of partial responders and half of nonresponders to etanercept achieved a 75% improvement in the Psoriasis Area and Severity Index or PASI score.

Slightly more than half achieved a Physician Global Assessment score of 0 or 1, which is clear or almost clear. Adverse events were similar to those who received 52 weeks of treatment with tildrakizumab.

Importance
Tildrakizumab may be a reasonable option for patients with moderate-to-severe psoriasis who did not achieve an adequate response to etanercept.

Methods
This is a post hoc analysis of etanercept partial or nonresponders in the reSURFACE 2 trial. Adults with moderate-to-severe psoriasis with body surface area involvement greater than or equal to 10%, Physician Global Assessment score, PGA, greater than equal to 3, and a Psoriasis Area and Severity Index, or PASI score, greater than or equal to 12, were included in the trial.

In reSURFACE 2, patients were randomized to tildrakizumab 100 mg or 200 mg on weeks 0, 4, and 16 or to etanercept 50 mg twice weekly through week 12, then once weekly through week 28 or to placebo. At week 12, placebo patients were rerandomized to tildrakizumab 100 mg or 200 mg. At week 28, patients who were partial or nonresponders to etanercept were rerandomized to tildrakizumab 200 mg. A partial response was defined as a PASI improvement between 50% and 75%. Nonresponse was defined as less than 50% improvement in the PASI score.

Key findings in the study
Of patients randomized to etanercept to complete 28 weeks of treatment, 39 were nonresponders and 83 were partial responders. At 52 weeks, a PASI 75 score was achieved by 74.7% of partial responders and 53.8% of nonresponders. A PASI 90 score was achieved by 33.7% of partial responders and 30.8% of the nonresponders. A PASI 100 score was achieved by 14.5% of partial responders and 10.3% of nonresponders. A PGA score of 0 or 1, clear or almost clear, was achieved by 57.8% of the partial responders and 56.4% of nonresponders.

Adverse events were similar in patients switched from etanercept to tildrakizumab at week 28 compared with patients maintained on tildrakizumab for the 52 weeks. Nasopharyngitis was the most common adverse event, occurring in 12% vs 21%, respectively.

Here are my thoughts and analysis of this study

It's exciting to see data on yet another drug approved for psoriasis. Tildrakizumab is an interleukin-23 antagonist. Blocking the interleukin-23/interleukin-17 pathway seems to be the sweet spot for psoriasis management.

How do the results of this study impact the current state of patient management? Tildrakizumab was compared to etanercept in these studies. While etanercept was the first and revolutionary biologic for psoriasis, it's also one of the least effective of the tools that we now have. The data presented here tell us that tildrakizumab works when etanercept doesn't. But that doesn't change things for us so much as we already have a lot of drugs to use after etanercept. And given the efficacy and safety of those drugs, we often use them even before etanercept.

How do the results of this study impact the future state of patient management? These results add to our understanding of blocking interleukin-23 and the interleukin-23/interleukin-17 pathway. It's another block in the wall showing us that this pathway is critical in psoriasis and that blocking it is an effective and apparently a very safe way to manage psoriasis.

What questions remain? Cost of treatment is still, as far as I can tell, unknown for this drug. Moreover, we still don't know how tildrakizumab compares to all the other highly effective psoriasis treatments. It's nice to have options. With the limited data, it can be hard to decide which drug to start with. But the bottom line, I think, is that a lot of these options are all very good. We probably don't go too far wrong with our choice of any one of these new treatments.

Long-term Efficacy and Safety of Ixekizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis Sustained for 3 Years: Results of a Randomized, Controlled Phase 3 Study (UNCOVER-3) (#6581)

Authors: Leonardi C, et al.

Analysis by:
Steve Feldman, MD

Hello, this is Dr. Steven Feldman. I'm Professor of Dermatology, Pathology, and Public Health Sciences at Wake Forest School of Medicine. I'll be discussing “Long-term Efficacy and Safety of Ixekizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis Sustained for 3 Years: Results of a Randomized, Controlled Phase 3 Study (UNCOVER-3).” The poster was presented by Dr. Leonardi and colleagues at the 76th Annual Meeting of the American Academy of Dermatology on February 16-20, 2018, in San Diego, California.

Summary

This efficacy and safety of ixekizumab in patients with moderate-to-severe psoriasis has been demonstrated previously over 2 years. This trial, which utilized the label treatment schedule of ixekizumab, demonstrated sustained efficacy over 3 years, while maintaining a favorable safety profile.

Importance

These results provide reassurance as to the long-term efficacy and safety of ixekizumab in the majority of patients with moderate-to-severe psoriasis.

Methods

The trial included adults with the Psoriasis Area and Severity Index, or PASI, score, greater than or equal to 12; affected body surface area, or BSA, greater than or equal to 10%; and static Physician Global Assessment, an sPGA, greater

than or equal to 3 at both screening and baseline visits.

Prior treatment with etanercept was not allowed at week 0, and through week 12, patients were randomized 2:2:2:1 to receive ixekizumab 160 mg loading dose, then 80 mg every 2 weeks; or ixekizumab 160 mg loading dose, then 80 mg every 4 weeks; or etanercept 50 milligrams twice weekly; or placebo.

After week 12, all patients received ixekizumab 80 mg every 4 weeks to week 156. After week 60, the dose could be adjusted to ixekizumab at 80 mg every 2 weeks at the investigator's discretion.

Key findings in the study

1346 adults with a mean age of 46 years, approximately 70% men, were included. At baseline, the body surface area ranged from 28% to 28.6% of the body covered with psoriasis; PASI score range from 20.7 to 21.2; the sPGA score ranged from 3.5 to 3.6; and the Dermatology Life Quality Index score across the different groups ranged from 11.5 to 12.7.

At week 156, a PASI 75 score was achieved in 93.7% of observed cases. PASI 90 in 81.1% and PASI 100 in 56.1%. An sPGA score of 0 or 1 was achieved in 80.4% of the observed cases, an sPGA of 0 were clear in 56.5%.

86.4% to 88.5% of patients had greater than or equal to 1 treatment-emergent adverse event. 43.1% to 50.0% were of moderate severity. A serious adverse event occurred in 10.8% to 19.1%. Infections remain the most commonly observed adverse event and viral upper respiratory tract infection was the most common occurring in 25.3% to 29%. Grade greater than or equal to 3 neutropenia was observed in 0 to 1.1% across the groups.

Here are my thoughts and analysis of this study

I am old enough to remember when TNF inhibitors were approved. They were revolutionary. I thought I'd never see another quantum leap forward like that. Then, the IL-17 drugs came along and they are so effective, and they seem to come with very minimal safety baggage. Those of us who care for patients with psoriasis are blessed and spoiled!

How did the results of this study impact the current state of patient management? Based on the mechanism of action of IL-17 inhibition, we don't expect major safety issues. Perhaps we might expect an increased risk of candidiasis. Each year of additional safety data gives me more and more confidence that we do fully understand the safety profile of these drugs and it looks terrific.

How do the results of this study impact the future state of patient management? Clearly, IL-17 antagonists will play a major role in the management of patients with a moderate-to-severe psoriasis.

What questions remain unanswered? Longer follow-up will still be nice to have. I feel very confident after 3 years of follow-up, but I'll be more totally confident after we see the 5-year outcomes. The other issue is how well IL-17 antagonism compares to IL-23 blockade. Both seem very effective. Right now, IL-23 blockade seems to require fewer shots and may have less risk of exacerbating bowel disease. But, IL-23 blockers are so new, it's hard to say with any level of certainty the full side effect profile would be.

Adverse Medical Conditions in Patients with Psoriasis treated with Biologic versus Conventional Systemic Therapy: A United States Claims-Based Analysis (#6706)
Authors: Wu J, et al.

Analysis by:
Alan Menter, MD

Hello, this is Dr. Alan Menter. I am chairman of the Department of Dermatology at Baylor University Medical Center in Dallas. I will be discussing "Adverse Medical Conditions in Patients with Psoriasis treated with Biologic versus Conventional Systemic Therapy: A United States Claims-Based Analysis." The poster was presented by Dr. Wu and colleagues at the 76th Annual Meeting of the American Academy of Dermatology, held February 16-20, 2018, in San Diego, California.

Summary

In summary, this was a retrospective analysis of data from the Truven Health Analytics Market Scan Commercial Claims and Encounters database. The purpose was to compare the risk of developing adverse medical conditions among biologic-naïve patients vs patients treated subsequently with a biologic in a real-world setting. The analysis showed that biologic therapies were associated with similar or lower risk of adverse medical conditions compared to conventional systemic therapies or topical therapies amongst biologic-naïve adult patients with psoriasis.

Importance

Biologic therapies are associated with superior symptom management in patients with moderate-to-severe psoriasis compared to other conventional systemic therapies. Previous real-world studies have assessed the risk of biologics, but in a limited number of adverse medical conditions, in heterogeneous populations. This real-world analysis assessed the risk of developing adverse medical conditions described in product labeling in biologic naïve patients with psoriasis.

Study's highlights from the lead author's perspective, Dr. Wu

What are the most important highlights or findings of the study?

- Among studied adverse medical conditions (AMC), infection was most common: 28.7% to 41.8% patients had infection across cohorts
- This was followed by mental disorder (9.3% to 18.3%) and abnormal laboratory test result (6.0% to 10.8%).
- Biologic therapies were associated with a risk of AMCs similar to or lower than conventional systemic therapy/topical therapies among biologic-naïve patients, with fewer infections being the most notable finding.

What impact do you think this study will have on the management of patients with moderate-to-severe atopic dermatitis?

- Not sure, but clinicians should still be vigilant for infections despite the findings in this study.

Description of the study

Patients were adults with psoriasis diagnosed on 2 or more dates, one of which is by a dermatologist. All of these patients were biologic-naïve at the index date. The index date was a date in which the first biologic therapy or conventional systemic therapy or topical therapy was initiated. Two mutually exclusive cohorts were created based on receiving either biologic or conventional systemic therapy or topical therapy. The biologic cohort was stratified into 4 cohorts: Adalimumab,

etanercept, ustekinumab, or other biologics. In other words, a combination of etanercept, ustekinumab, and infliximab. Patients were followed until the first occurrence of one of the following: initiation of a systemic therapy for psoriasis other than the index treatment, 60 days after the index treatment discontinuation, and thirdly, the end of data availability or continuous health plan enrollment.

Studied adverse medical conditions were selected on FDA product labeling and post marketing surveillance registries. Only incident events based on ICD-9-CM diagnosis code were analyzed. Multivariate Cox proportional hazard regression models were used to compare the risk of developing an adverse medical condition between the different cohorts.

Key findings in the study

Forty-two thousand nine hundred eighty-one biologic-naïve patients met the inclusion criteria, which included enrollment in the health care plan for over 12 months prior to, and over 1 month after, the index date. Five thousand one hundred ninety-seven patients were treated with adalimumab; 3,311 with etanercept, 1,370 with ustekinumab and 187 patients with infliximab. Nineteen thousand six hundred sixty-six patients were treated with topical therapy and 13,250 with conventional systemic therapy, which included phototherapy, methotrexate, acitretin, or isotretinoin.

The median age in the cohorts was: adalimumab 46 years, etanercept 46 years, ustekinumab 47 years, and conventional systemic therapy or topical therapy 50 years. The proportion of females was slightly less than 50% of the biologic cohorts and significantly lower than in the conventional systemic therapy/topical cohort, 53.1%.

The median period study duration was significantly longer for biologic cohorts than conventional systemic or topical therapy, ranging from 5.3 to 7.9 months vs 3.3 months, respectively.

What about the adverse medical conditions? Infections occurred in 28.7% to 41.8%; mental disorder in 9.3% to 18.3%; abnormal laboratory test in 6.0% to 10.8%; cardiovascular disease in 3.3% to 5.5%; malignancy 2.1% to 2.6%; respiratory disease 1.9%to 3.7%.

The risk of an adverse medical condition was similar or lower in patients treated with a biologic vs conventional systemic therapy. Those that were significantly lower with biologic therapy compared to conventional systemic or topical therapy included: 1) the risk of infection with adalimumab, etanercept, and ustekinumab with a hazard ratio 0.86 to 0.93; 2) the risk of malignancy with adalimumab hazard ratio of 0.71; and 3) risk of respiratory disease with etanercept in which the hazard ratio was 0.80.

The risks of adverse medical conditions were similar between adalimumab and the combination of etanercept, ustekinumab, and infliximab.

What about limitations of the study? This included a limited follow-up period. Statistical power may have been limited due to the low incidence of some adverse medical conditions that were observed, and disease severity may be a potential confounding factor since biologic therapies may be prescribed for patients with more severe psoriasis compared to conventional systemic therapy or topical therapies. Only adverse medical conditions for which patients sought medical care were analyzed.

Here are my thoughts and analysis of the study

Number one: biologic agents are commonly now used in the field of psoriasis. But on the other hand, they're not as commonly used as

we used to use systemic therapy. In fact, in the United States, currently, less than 1 out of 5 patients who are eligible for systemic or biologic therapy are receiving biologic or systemic therapy. So that's an important aspect that I think we all need to recognize.

How do the results of the study impact the current state of medical management? I do believe that we can assure both our dermatology colleagues and patients that we have long-term safety data for biologic agents in comparison to traditional systemic drugs. Admittedly, we've had methotrexate for over 40 years. We've only had biologic drugs for over 20 years, but the numbers and the long-term side effects database, I do believe, allows us to assure both our colleagues in dermatology, and patients, about the long-term safety. I use the term, personally, "long-term safe control." I really do believe that's important for our patients.

What about the results about the study? How does it impact the future state of patient management? Hopefully, as I said earlier, we can slowly increase the number of patients who have moderate-to-severe psoriasis who can receive appropriate systemic or biologic agents. As I said, we have approximately 7 and a half million psoriasis patients in the US currently. Twenty percent of them have moderate-to-severe psoriasis. That's 1.5 million. Currently, less than 25% of that 1.5 million patients with moderate-to-severe psoriasis are being treated with appropriate biologics and systemic therapy. I do believe that the analysis of this study allows us to feel much more comfortable utilizing these drugs.

An Open-Label, Observational Study Evaluating Calcipotriene 0.005%/Betamethasone Diproprionate 0.074% Foam in Psoriasis Patients Being Treated With Biologic Agents (#6239)

Authors: Bagel J, et al.

Analysis by:
Steve Feldman, MD

Hello, this is Dr. Steven Feldman. I'm Professor of Dermatology, Pathology and Public Health Sciences at Wake Forest University School of Medicine. I'll be discussing "An Open-Label, Observational Study Evaluating Calcipotriene 0.005%/Betamethasone Diproprionate 0.074% Foam in Psoriasis Patients Being Treated With Biologic Agents." The poster was presented by Dr. Bagel and colleagues at the 76th Annual Meeting of the American Academy of Dermatology on February 16-20, 2018, in San Diego, California.

Summary

This open-label, single-arm, real-world trial assessed the efficacy and safety of adding topical calcipotriene betamethasone dipropionate in patients with moderate-to-severe psoriasis with significant disease activity despite stable biologic therapy. At weeks 4 and 16, topical calcipotriene/betamethasone was associated with significant improvement in every measure of disease activity. The treat-to-target goal of body surface area less than or equal to 1% with disease activity was achieved by 76% at week 4 and 68% at week 16. There were no treatment-related adverse events.

Importance

The addition of topical calcipotriene/betamethasone to biologic therapy my prevent or delay switching [to a different biologic agent] in patients with significant disease activity despite stable biologic therapy.

Study's highlights from the lead author's perspective, Dr. Bagel

What are the most important highlights or findings of the study?

- Many moderate to severe psoriatic patients even on state of the art biologic therapy for at least 24 weeks still have significant disease activity that warrants either adding therapy or switching to a different biologic agent or escalating dose.
- Adding topical therapy with Cal/BD foam (once daily) was associated with a significant improvement of every measure of disease activity at Week 4 and maintained with twice a week application through Week 16.
- The treat-to-target goal (BSA ≤1%) was achieved by 3/4 of patients at Week 4 and 2/3 of patients at Week 16

What is the anticipated impact of the study findings on the care of patients?

- Cal/BD foam is an effective, well-tolerated topical agent that significantly improves psoriasis disease management in patients on stable biologic therapy, and as add-on, provides disease control that may prevent or delay switch in patients on stable biologic therapy for moderate to severe psoriasis.

Methods

Let's go over the methods first. The trial utilized an open-label, single-blind, observational real-world design. It involved adults with psoriasis covering less than or equal to 5% of their body surface area despite being treated with biologic agents for greater than or equal to 24 weeks.

All patients received the calcipotriene/betamethasone foam once daily for 4 weeks, followed by calcipotriene/betamethasone foam on 2 consecutive days every week for an additional 12 weeks. Calcipotriene/betamethasone foam consists of calcipotriene 0.005% in combination with betamethasone dipropionate 0.064%.

Key findings in the study

Twenty-five patients were included, 18 men and 7 women, with a mean age of 53 years. 84% were Caucasian. On average, patients had a 24-year history of psoriasis. At baseline, 52% were being treated with ustekinumab, 20% with adalimumab, 20% with secukinumab, and 8% other biologics.

At weeks 4 and 16, average improvements were 63% and 49%, respectively, for Physician Global Assessment or PGA; 59% and 40%, respectively, for BSA; 77% and 59%, respectively, for the PGA times the BSA. Total clearance of psoriasis occurred by week 4 in 28%. At baseline, 12% of patients met the treatment to target goal of BSA less than or equal to 1%. At weeks 4 and 16, this increased to 76% and 68%, respectively. At baseline, 4% of patients had a PGA score of less than or equal to 1. At weeks 4 and 16, this increased 76% and 68%, respectively. The Dermatology Life Quality Index improved from 3 at baseline to 1 at both weeks 4 and 16. Other measures of treatment satisfaction also improved. There were no treatment-related adverse events or any serious adverse events.

Here are my thoughts and analysis of this study

Biologics are very effective, but a lot of the time, even the most effective biologic does not completely clear the patient of psoriasis. The low DLQI of 3 showed that patients had a great response, from their perspective, even before the topical was added. The latest guideline says

the goal should be to get the psoriasis down to less than 1% body surface area affected. Adding a topical may give a way to do that in patients who are on a biologic and who are almost there.

The glass is more than half full. In just 4 weeks, 3 of 4 patients get to less than 1% body surface area involved. On the other hand, 1 of 4 doesn't, and 1 in 3 doesn't by week 16.

How do the results of this study impact the current state of patient management? Topicals may be old-fashioned, but they're still useful for helping people on biologics get more fully clear of their psoriasis.

How do the results of the study impact the future state of patient management? New biologics keep coming and they seem to have higher and higher clearance rates. But despite that, patients often have some residual disease for which topicals will be appropriate.

What questions remain unanswered? We have to pay close attention to patients' adherence to treatment. I think the reason this study did not observe continued improvement between week 4 and week 16 is that patients may have become less adherent to their topical treatment over that time.

The other thing is this study only tested one particular topical treatment. Which one is best is not known. I suspect there might not be one best [topical] for everyone. Perhaps, the best one is the one that your particular patient wants to use!

Impact of Withdrawal and Retreatment on Immunogenicity of Gueslkumab in Patients With Moderate-to-Severe Plaque Psoriasis (#6644)

Authors: Zhu Y, et al.

Analysis by:
Steve Feldman, MD

Hello, this is Dr. Steven Feldman. I am Professor of Dermatology, Pathology, and Public Health Sciences at Wake Forest School of Medicine. I'll be discussing "Impact of Withdrawal and Retreatment on Immunogenicity of Gueslkumab in Patients With Moderate-to-Severe Plaque Psoriasis." The poster was presented by Dr. Zhu and colleagues at the 76th Annual Meeting of the American Academy of Dermatology on February 16-20, 2018, in San Diego, California.

Summary

To summarize, previous analysis of the VOYAGE 1 and 2 trials demonstrated that the incidence of antidrug antibodies to guselkumab was 6% up to week 48 with no impact on guselkumab exposure, treatment efficacy, or development of injection site reactions.

The present analysis, which involves patients from VOYAGE 2, found antidrug antibodies were detected in 10.2% of patients who were withdrawn and retreated with guselkumab compared with 6.8% of patients who continued with guselkumab throughout week 100. Systemic exposure to guselkumab and efficacy were regained after retreatment with guselkumab with no observed clinically important injection site or hypersensitivity reactions.

Importance

The findings of this trial provide reassurance as to the continued efficacy and safety— including the development of antidrug antibodies—of guselkumab, despite withdrawal and

subsequent retreatment, which is often encountered in clinical practice.

Methods

Patients with moderate-to-severe psoriasis were randomized, 2:1:1 to one of 3 groups. Group number one got guselkumab 100 mg at weeks 0, 4, 12, and 20. Group number 2 received placebo at weeks 0, 4, and 12, followed by guselkumab 100 mg at weeks 16 and 20. And group number 3 received adalimumab 80 mg at week 0, 40 mg at week 1, then 40 mg every 2 weeks through week 23.

At week 28, Psoriasis Area and Severity Index (PASI) 90 responders in group 1 were re-randomized 1:1 to either continue guselkumab every 8 weeks or withdraw from guselkumab. Withdrawal patients were retreated with guselkumab upon loss of greater than 50% of the PASI improvement they had achieved at week 28.

PASI 90 responders in groups 2 and 3 were withdrawn from guselkumab or adalimumab. Upon loss of greater than 50% of the PASI improvement they had achieved at week 28, guselkumab was started or restarted. PASI 90, nonresponders in all groups continued or started guselkumab. From week 76 to week 100, all patients received open-label guselkumab 100 mg every 8 weeks.

Key findings in the study

Key findings of the study, of the 992 patients in VOYAGE 2, 947 received guselkumab at some point in the trial and had serum samples that were evaluable for antidrug antibodies. The overall incidence of antidrug antibodies was 8.6%. Titers were less than or equal to 1 in 160 in 76.5% and less than or equal to 1 in 320 in 90.1%. The overall incidence in neutralizing antibodies was 0.4%. The incidence of antidrug antibodies occurring after exposure to guselkumab was 10.2% in those who were withdrawn and retreated with guselkumab compared with 6.8% of those who continued guselkumab.

There was no impact of antidrug antibodies on systemic exposure of guselkumab between patients who were positive for antidrug antibodies and those who were negative for antidrug antibodies; and between and after development of antidrug antibodies within a patient. Among the 32 patients withdrawn and retreated with guselkumab who were positive for antidrug antibodies, the trough serum concentration in guselkumab recovered to the level achieved prior to withdrawal; 100% achieved an IGA, an Investigator Global Assessment score, of 0 or 1; 93.8% achieved PASI 90; 2 injections were associated with a mild injection site reaction; and there was no anaphylactic or sickness-like reactions to guselkumab reported.

Here are my thoughts and analysis of this study

Let's highlight the main points of the study. First, titers of antibodies to drugs doesn't mean much to me. Every company has their own assay. What numbers we get are just numbers, we can't compare across drugs and the percent of patients who have a positive antibody response may depend totally on how much antibody was considered to be a positive result.

I pretty much ignore these antibody rates. What matters to me is the efficacy and safety of the drug. And when at least 9 out of 10 patients are having a great response, the antidrug antibody must not be that important.

How do the results of this study impact the current state of patient management? This study showed that even when there was detectable antibody, it didn't seem to make any difference to the efficacy of the drug. And when patients stop and restart, the drug should still

work. Now, we may not tell patients they need to stop and restart, but they may do it anyway. But perhaps because of a lapse in insurance, perhaps because they just wanted to see what would happen if they stopped treatment, it's reassuring to know the drug will still work.

How do the results of this study impact the future state of patient management? With 2 years of great efficacy and safety data, guselkumab is clearly among our really good psoriasis treatments. I'm looking forward to seeing us have more of this IL-23 blocker choices.

What questions remain unanswered? Two years of data is very good. I'm looking forward to when we have 5 years of efficacy and safety data. I anticipate it will be solid, but we won't know with certainty until we see it.