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AMERICAN ACADEMY OF DERMATOLOGY 77TH ANNUAL MEETING HIGHLIGHTS

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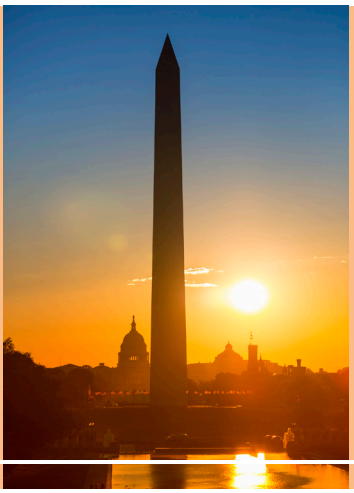
The U.S. capital hosted the 77th Annual Meeting of the American Academy of Dermatology (AAD), with more than 18,000 attendees from countries around the globe, including Brazil, Mexico, Canada, the United Kingdom, Colombia, Argentina, Spain, Pakistan, India, and Saudi Arabia.

The following selection of presentations and posters, from AAD's 77th Annual Meeting, centers on psoriasis and psoriatic arthritis.



PALMOPLANTAR PSORIASIS: A GREATER TREATMENT CHALLENGE

This presentation was given by Dr. Bruce E. Strober as part of the general program.

About 25% of patients with moderate to severe plaque psoriasis have palmoplantar psoriasis. Conversely, 20% of those who have predominantly palmoplantar psoriasis (PPP) will have psoriasis elsewhere on their body, which may be just a plaque on the knee or in the scalp.[1-3] This finding is very helpful for making a diagnosis, said Bruce E. Strober, MD, PhD, clinical professor in the Department of Dermatology at the University of Connecticut in Farmington, CT. There is a higher incidence of palmoplantar psoriasis in women and in smokers.[1-3]

Palmoplantar psoriasis has been defined as many different morphological subtypes: it can be thoroughly hyperkeratotic, with scaly red plaques; primarily pustular, which some people believe is a different entity called palmoplantar pustulosis; or a mixed texture of both hyperkeratotic plaques and pustulosis.[3] Dr. Strober said, "It could be biased toward just the hands and feet being involved, or even just the hands being involved and not the feet, or just the feet being involved and not the hands."

Very severe palmoplantar psoriasis can inhibit the ability to work or walk or complete activities of daily living, can be disfiguring, and can create emotional distress.[4] According to Dr. Strober, "All the therapies that one could use for psoriasis could be used for palmoplantar psoriasis, including topicals and phototherapy, older drugs like methotrexate, cyclosporine, acitretin, or the newer biologic or oral therapies, such as apremilast—I even have used dapsone successfully."[5] Although therapies that work for plaque psoriasis

might be effective for palmoplantar psoriasis, it is without question a greater treatment challenge than chronic plaque psoriasis, said Dr. Strober. "My rule of thumb is whatever you think the efficacy is for chronic plaque psoriasis with any given drug, divide it by 2 and you get the efficacy for palmoplantar psoriasis."

TNF Inhibitors for PPP

Tumor necrosis factor α (TNF) inhibitors are very viable, said Dr. Strober. The adalimumab randomized placebo-controlled study included 72 patients randomized 2 to 1 with a reasonable primary endpoint—a Physician Global Assessment of hands and/or feet (hfPGA) score of clear or almost clear—which was achieved in adalimumab patients about a third of the time and almost none of the placebo patients.[6] Dr. Strober noted that while adalimumab achieves a very good score of 70% to 80% in plaque psoriasis patients, it is effective in only a third of palmoplantar psoriasis patients. Infliximab and etanercept also can be effective choices.[6]

Interleukin 12/23 Inhibitors for PPP

Efficacy of ustekinumab has been demonstrated in patients with palmoplantar psoriasis (plaque and pustular types) in case reports and case series, which show 12/23 inhibition.[7,8] "I've had personal experience show me this could be the case as well," said Dr. Strober. "Thus, 12/23 inhibition in the form of ustekinumab might be successful, especially in patients with TNF-inhibitor induced palmoplantar psoriasis."

TNF-inhibitor induced palmoplantar psoriasis can occur in patients with a history of rheumatoid arthritis or Crohn's disease who receive TNF inhibitors (infliximab or adalimumab) for the treatment of those diseases. Treatments of TNF-inhibitor induced palmoplantar psoriasis range from topical corticosteroids to stopping the TNF inhibitor.[9]

Interleukin 17 Inhibitors for PPP

In post hoc subgroup analyses of patients with palmoplantar psoriasis treated with ixekizumab 80 mg every 2 weeks, 52% achieved a PPASI 100 response versus 8% of placebo at 12 weeks. Dr. Strober noted that these findings need to be taken with a grain of salt because the study included patients with moderate to severe plaque psoriasis affecting the rest of the body. Conversely, in the GESTURE study, which evaluated secukinumab in over 200 patients with palmoplantar psoriasis,[10] researchers made sure these patients had genuine palmoplantar psoriasis; they had to have some psoriasis outside the palm and soles to establish the diagnosis, said Dr. Strober. "The data were clear, at 16 weeks; a third of the patients showed a palmoplantar psoriasis Investigator's Global Assessment score of 0/1 [3 = moderate on a 5-point scale] if they had the 300-mg secukinumab dose, standard FDA-approved dose for psoriasis, and about 1 in 5 if they had the 150-mg dose, but essentially none of the placebo."

Apremilast

A study that evaluated apremilast in patients with palmoplantar psoriasis with a primary endpoint similar to that used for the secukinumab studies showed a quantitative difference, said Dr. Strober. "In fact, about 14% of patients who received apremilast achieved a Patient's Psoriasis Global Assessment (PPGA) score of 0 or 1 versus about 4% of the placebo, but this wasn't statistically significant." He added that the primary endpoint was not met in the apremilast study yet secondary endpoints were. For example, 75% reduction in Palmoplantar PASI was achieved by the apremilast patients not the placebo, a statistically significant difference, and reductions in DLQI and improvements in work productivity were seen in patients receiving apremilast versus placebo.[11] "This somewhat aligns with what I've seen in practice, that apremilast can be effective for a large number of patients having palmoplantar plaque psoriasis, though the study's primary endpoint wasn't met; therefore, this was labeled a failed study."

Summary

On the frontier of palmoplantar psoriasis management are several new treatments: the IL-23 inhibitors, for which more data are needed; the topical and systemic JAK inhibitors, one of which, XELJANZ, is approved for psoriasis and psoriatic arthritis; and perhaps an IL-36 receptor antagonist, which has been shown to be effective in generalized pustular psoriasis. "Palmoplantar psoriasis is a tough entity to treat that is much less responsive to our typical therapies for psoriasis," said Dr. Strober, "yet with patience and perhaps combination therapy, we can achieve success."

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PSORIATIC ARTHRITIS IN THE CLINICAL SETTING

This presentation, sponsored by Novartis, was given by Dr. Valerie M. Harvey at a dinner program titled "Hands On Psoriatic Disease: A Live and Augmented Reality Experience for Advancing Patient Care Despite Modern Time Constraints." The program took place on March 1, 2019, at the Renaissance Washington DC Downtown Hotel, and was independent of the AAD's Annual Meeting.

At a program that took place concurrently with the AAD's Annual Meeting, Valerie M. Harvey, MD, MPH, spoke about how to approach patients with psoriatic arthritis in the clinical setting. Dr. Harvey is co-director of the Hampton University Skin of Color Research Institute and director of the Hampton Roads Center for Dermatology in Newport News, VA. She specializes in medical dermatology with a particular interest in pigmentary disorders and skin conditions that disproportionately affect minority patient populations. She gave a highly interactive presentation, complete with a patient interview, demonstrating a practical approach in a dermatology clinic to show physicians that it's feasible to incorporate screening for psoriatic arthritis via a dermatology-centric joint exam into a busy day. She highlighted an opportunity to screen psoriasis patients with psoriatic arthritis. "I encourage dermatologists to remember the risk factors for psoriatic arthritis, including scalp disease, nail disease, and intertriginous involvement," she said.

Dr. Harvey offered words of encouragement, saying that implementing PEST (the Psoriatic Epidemiology Screening Tool) does not have to be daunting, and at her clinic, it was as simple as having a team meeting—with the entire team. "We held a staff meeting to discuss integrating the PEST screening for psoriatic arthritis," she said. "We included both the front office and the clinical staff. I took that opportunity to educate them about psoriatic arthritis and why it was important to screen for it in our patients with psoriasis."

In a recent study, "Use of a Validated Screening Tool for Psoriatic Arthritis in Dermatology Clinics," researchers from the St. George's Healthcare NHS Trust in London, UK, found that through implementing a modified PEST questionnaire, a 100% PEST completion rate was obtained for eligible patients in the final cycle compared to 0% at baseline.[1] Additionally, 5 (18.5% of the group) out of the 27 patients completed a PEST score greater than 3, and all 5 of those patients were appropriately referred to rheumatology. Therefore, "Identifying PsA early through highly sensitive tools like PEST is a recommended concept according to national guidance," the researchers said.

What questions can a patient expect when given the PEST tool? These include family history, how long they've had symptoms, and whether or not their psoriasis limits their day-to-day activities. These questions are within the norm; most patients are used to answering them on most general medical forms. After questions, a limited joint exam usually follows, and then a simple examination of the Achilles tendon and the plantar fascia. All of this was performed onstage during the presentation.

Photo courtesy of the American Academy of Dermatology

"It was nice; we had a stopwatch actually going during the physical exam," Dr. Harvey said. "We were able to show the audience that it's certainly doable and in a very reasonable amount of time. I believe it took a little bit over two minutes to complete the entire joint exam. [We were] just showing the audience that it's not too time intensive and doesn't interfere with clinic flow."

Following the demonstration, Dr. Harvey summarized her talk and highlighted that there's a certain sense of responsibility that dermatologists have to diagnose psoriatic arthritis early. "It's critically important to consider it in all of your patients who present with psoriasis," she said. "We do this by taking a good history and performing a limited joint exam when needed. It's a great opportunity to educate our patients on psoriatic arthritis, because many of them don't make the connection between their joint symptoms and their skin disease." Signs and symptoms of psoriatic arthritis include fatigue; stiffness of longer than 30 minutes after periods of inactivity; pain; swelling and tenderness of the joints; and ligament and tendon insertions into bone (entheses). Dactylitis or swelling of the digits can involve numerous digits and is usually asymmetrical. Nail dystrophy can also serve as a risk marker for subsequent development of psoriatic arthritis.[2]

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USING IMMUNOLOGY TO TREAT PSORIASIS

This presentation was given by Dr. Paul Yamauchi as part of the general program.

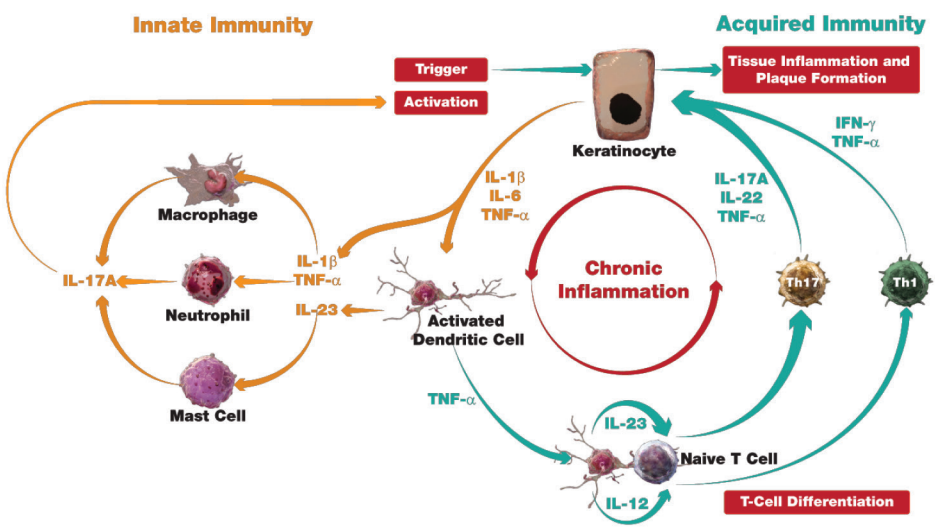
New psoriasis treatments are targeting the immunology of psoriasis to treat the signs and symptoms of the disease. These agents are referred to as biologic agents and have dramatically changed the landscape in treating psoriasis. There are also new oral agents that target the immune system to treat psoriatic disease.

Paul Yamauchi, MD, clinical assistant professor of medicine in the Division of Dermatology at the David Geffen School of Medicine at UCLA and adjunct associate professor at the John Wayne Cancer Institute in Santa Monica, presented "Immunopathogenesis of Psoriasis,"[1] which reviewed the role that immunology plays in the treatment of psoriasis.

In his presentation, Dr. Yamauchi focused on the fundamentals of the two pathways that are implicated in the pathogenesis of psoriasis: interleukin (IL)-17 and IL-23. There are six classes of IL-17 from A to F, with IL-17A and IL-17F being the ones that drive psoriasis. IL-17A is the class of IL-17 that is subject to targeting by drugs such as secukinumab and ixekizumab.

What does treating psoriasis from an immunology point of view look like? It comes down to more than just looking at symptoms and expands to which part of the immune system should be treated. The

Innate and acquired immune pathways promote keratinocyte activation and chronic inflammation



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different types of immunities affected—innate or acquired—play a key role. IL-17A, for example, is produced by both the innate and acquired immunity, and treatments depend on if you want to focus on the IL-17A cytokine or the receptors. "Secukinumab and ixekizumab target IL-17A directly, whereas brodalumab targets receptors to IL-17," Dr. Yamauchi explained. "Secukinumab was the first IL-17 inhibitor to be approved in the U.S. about 4 years ago, and with the introduction of this antibody, this therapy has really been the game-changer in treating psoriasis."

With secukinumab, it has been shown that 90% to 100% clearance can be obtained in a relatively rapid timeframe, around 12 weeks when treatment is initiated, and the same holds true with both ixekizumab and brodalumab. It's shown that these drugs are fast, effective, and durable, but they're also safe. "These drugs have been on the market for years, and according to safety data, neither secukinumab nor ixekizumab increased rates of infections, cancers, heart attack, or strokes," Dr. Yamauchi said.

In terms of the IL-23 pathway, there are currently three therapies approved: guselkumab, tildrakizumab, and risankizumab. All the IL-23 inhibitors have efficacy to treat psoriasis, Dr. Yamauchi said, with 90% to 100% clearance of the psoriasis for many patients.

This is great news for patients who have conditions in addition to psoriasis. Recent studies have shown that secukinumab has been shown to also be effective in the treatment of psoriatic arthritis.[2] A 2017 American College of Rheumatology meeting abstract[3] from Mease et al. states that secukinumab exhibits significant efficacy, with a favorable safety profile, in the treatment of psoriatic arthritis and moderate to severe psoriasis.

When treating psoriasis and psoriatic arthritis with biologic agents, there are different hierarchies of options, and they are usually fairly obvious. For example, if the patient has both psoriasis and psoriatic arthritis, then one might be inclined to go with an IL-17 inhibitor. Inflammatory bowel disease such as Crohn's disease and ulcerative colitis has been associated in a small percentage of patients with psoriasis. If the patient has psoriasis and Crohn's disease, then using an IL-23 inhibitor will be more suitable. However, if the psoriasis patient believes fastest clearance is most important, the IL-17 pathway works slightly faster than the IL-23 pathway, so that may be better suited than the IL-23.

"For patients with both psoriasis and psoriatic arthritis," said Dr. Yousef Binamer, consultant dermatologist at King Faisal Specialist Hospital and Research Center in Riyadh and assistant professor at Alfaisal University in Riyadh, "if you don't intervene early, it might lead to permanent joint damage and disabilities because psoriatic arthritis is destructive if you don't treat early." He noted that it is important when choosing a medication to be sure that the patient doesn't have arthritis and to ask him at every visit whether he has developed any symptoms. "If arthritis develops while the patient is on ustekinumab, then you need to switch him to another agent—forexample, anti-TNF or with IL-17—or to add methotrexate," Dr. Binamer said. "This is because ustekinumab may not be very effective for psoriatic arthritis, especially axial arthritis, which is common in psoriatic arthritis."[4,5]

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TAILORING TREATMENTS FOR PSORIASIS

This presentation was given by Dr. Mark B. Lebwohl as part of the general program.

When considering treatments for psoriasis, one has to take into account many different factors, including age, gender, pregnancy status, weight, and whether one or more other conditions are present. Despite the availability of several new systemic agents for psoriasis treatment, choosing the right therapy in certain patient populations can be challenging, for example, for special populations or disease states. There are few up-to-date reviews on systemic therapies for moderate to severe psoriasis in pregnant and pediatric patients and in patients with concomitant chronic infections, such as hepatitis, HIV, and latent tuberculosis.[1-4]

Mark B. Lebwohl, MD, the Waldman Professor of Dermatology at the Kimberly and Eric J. Waldman

Department of Dermatology at the Icahn School of Medicine at Mount Sinai in New York City, focused on congestive heart failure, latent TB, and HIV infection, citing an article that he co-wrote, "Which Therapy for Which Patient," published in 2019.[1,2] For advanced congestive heart failure, he said that it appears as a contraindication to remicade. "That was based on a study with a thought that infliximab would improve congestive heart failure," he said. "But in fact, the infliximab 10 mg/kg group had more hospitalizations or deaths than the placebo group in this study. At 5 mg/kg, there were not more hospitalizations and deaths, but at the 10-mg dose, there clearly were. It was 18 percent at Week 14 and 27 percent at Week 28."

Dr. Lebwohl said that based on recent research, the rate of heart attacks is dramatically reduced—by about half—when treatment is done with TNF blockers. A recent study suggested that secukinumab might have a beneficial effect on cardiac risk by demonstrating an improvement in flow-mediated dilation in patients with psoriasis.[5] "So that and all of the other IL-17 and IL-23 blockers can be used in patients with congestive heart failure," he added.

The second comorbidity was with TB, and once a patient is exposed, they will test positive for the rest of their life.[3] In patients with psoriasis who are on TNF blockers, TB is commonly extra pulmonary. How does a doctor determine if the patient has been reexposed if it doesn't show up on a chest X-ray? "All package inserts warn about TB and suggest testing for TB prior to starting those drugs. That's true for infliximab adalimumab, etanercept, and certolizumab," he said.

The package insert for etanercept, which appears to have the lowest risk of tuberculosis, does warn about TB, stating that patients need to be evaluated for latent or active TB. Tuberculin skin tests or serologic tests for TB exposure should be performed both before and during treatment. That said, there have been cases of tuberculosis that have occurred in patients on etanercept, so it is recommended that patients who have a positive TB test should be treated with prophylaxis regimens for latent TB. The recommendation is actually—in patients who are positive for latent TB or have active TB—that you should start anti-tuberculosis therapy first before you start a biologic.

"There are also patients who test negative for latent TB," Dr. Lebwohl said, "then develop active tuberculosis. The TNF blockers can be used in patients who receive TB prophylaxis."

But the downside, he added, is that if they are reexposed, or develop new TB, it is going to be much harder to find, because TB tests remain positive.

What follows are conclusions about treating psoriasis in patients with latent TB:

- It is safe to use IL-17 inhibitors and apremilast in patients with LTBI.
- TNF α inhibitors and ustekinumab can be used only after tuberculosis prophylaxis has been initiated for at least a month.
- Additional safety data are needed for IL-23 inhibitors, but these will likely be safe.
- Methotrexate and cyclosporine can be used in patients with LTBI after tuberculosis prophylaxis.
- Acitretin is safe to use in this setting.

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CANADIAN REAL-WORLD STUDY: SECUKINUMAB DEMONSTRATES SIGNIFICANT IMPROVEMENT OF DISEASE ACTIVITY AND HEALTH-RELATED QUALITY OF LIFE AT ONE YEAR IN CANADIAN PSORIASIS PATIENTS

This poster presentation was given by Dr. Howard Yanofsky and colleagues.

A new real-world study of Canadian psoriasis patients taking secukinumab—a human anti-IL-17A monoclonal antibody—finds the biologic significantly reduced disease activity and improved patient quality of life after one year of use.[1]

Considering quality of life is very important when a patient reports, for example, being depressed, that they are single, or that they are not involved in society, said Dr. Yousef Binamer, consultant dermatologist at King Faisal Specialist Hospital and Research Center in Riyadh and assistant professor at Alfaisal

University in Riyadh. "Once the disease is affecting quality of life and has a big impact, you need to act more promptly to achieve high quality of life, especially in certain patients, such as women, teenagers, and university students," he said.

Health Canada approved secukinumab in February 2015 as the first anti-IL-17A for treating moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

The study, presented as a research poster, assessed for the first time the one-year real-world effectiveness of secukinumab in Canadian patients by collecting information on demographics, treatment patterns, and impact on disease.

"The real takeaway of this research is that secukinumab has a quite high retention rate, and that people maintain their effective response over time," said lead researcher Howard Yanofsky, MD, in the Division of Dermatology, Faculty of Medicine at McGill University in Montreal, QC, Canada.

Retention and sustained effectiveness are important parameters, he noted, because of the complication in changing therapies.

Dr. Yanofsky and the research team examined the effects of secukinumab in the real-world setting using the Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) measures. PASI scores were provided by the treating physician; DLQI scores were either provided by the treating physician or collected through phone interviews between patients and nurses.

The ultimate goal of therapy is an improvement of 90% or better (PASI90 response).

Effectiveness Parameters

In the Canadian study, the mean baseline PASI score of patients was 17.4 (n = 119). The mean follow-up PASI dropped to 1.9, and 78% of patients had reached PASI < 3. Among the biologic naïve patients (n = 60), 83.3% had reached PASI < 3 and 75.0% had achieved PASI90. For biologic experienced patients (n = 59), 72.9% reached PASI < 3 and 57.6% achieved PASI90.

"If secukinumab was their first medication, and you look at the end after a year, you see that roughly 84% of the people are still doing very, very well," Dr. Yanofsky said.

Quality of Life

Saudi doctors have seen similar results. Dr. Afaf Al Sheikh, head of the Dermatology Division at King Abdulaziz Medical City National Guard Hospital and assistant professor at King Saud Bin Abdulaziz University for Health Sciences in Riyadh, said she has been treating psoriasis patients for a long time.

"This condition has a major and profound effect on the patient's everyday quality of life," she said. "And this quality of life now is being recognized as an important outcome measurement for our patients. The clinical measurement tools don't always correlate directly with the real impact of the disease burden. As physicians we always address this issue of quality of life, and from real clinical practice, I can say that secukinumab, as shown in the study, provides a great improvement in quality of life for our patients."

Overall, the mean baseline DLQI score was 18.8 (n = 159). The mean follow-up DLQI was 3.1, with 94.3% of patients reaching DLQI reduction ≥ 5 or DLQI score of 0-1.

"Many times, the high level of severity of the PASI doesn't correlate with the disease's interference with quality of life," explained Dr. Yanofsky. "Sometimes you have a patient who, in your mind, has a severity index that's reasonably low and yet, their quality of life index, or the diminution of their quality of life, is quite high."

High Retention

The study also found the overall secukinumab retention rate was 75.7% (n = 1677/2216) at 52 weeks. For biologic naïve patients the rate was higher at 84.2%, compared with biologic experienced patients at 71.3%. Retention rates are presented as the proportion of patients still on a drug 52 weeks post-initiation.

"It's always better if you have a high retention rate," Dr. Yanofsky said. "It just makes everybody's life simpler. It makes the doctor's life simpler, it makes the patient's life simpler. The importance of this poster was to show that indeed, there's a high retention rate."

In real-life practice in Canada, secukinumab is prescribed as an early biologic treatment with the majority of patients being either biologic naïve or first biologic switch, the study noted. Despite the small sample size, one-year PASI response observed in this cohort demonstrates that secukinumab significantly

reduces disease activity in a real-world setting irrespective of line of therapy, the study said.

Dr. Yanofsky points out that if a patient switches among therapies, the retention rate falls. "This is in keeping with our understanding that when you do start to fail with one of these classes of drugs, it's much harder to achieve a good result with a different biologic of a different class," Dr. Yanofsky said. "There's great value for those that maintain their effectiveness."

Dr. Al Sheikh underscored the important role that sustained efficacy plays in choosing an agent. "A higher retention rate is always an advantage, and it will reflect directly on the quality of life as well as decrease the patient's need for another biologic," she said. "When the patient starts to fail an agent, it's too hard for him to get a good result with another agent. So he has to maintain the effectiveness over time, which is really important for both the patient and the physician."

The poster also noted that the safety and efficacy of secukinumab 300 mg has been well established in an extensive clinical program. Among the findings, the poster indicated that secukinumab demonstrates superiority compared to etanercept and ustekinumab; provides sustained and long-lasting high levels of efficacy maintained over 5 years; and has a favorable safety and tolerability profile over 5 years.

The sustained effect is very important, said Dr. Issam Hamadah, chairman of the Dermatology Department at the King Faisal Specialist Hospital and Research Center in Riyadh and an adjunct clinical professor at the Alfaisal University in Riyadh. "Because psoriasis is a chronic disease, we need to have something that works for a long time. That's more important than having it work fast."

Dr. Hamadah also noted that psoriasis is an unstable disease. "So, all factors that contribute to the disease fluctuation also contribute to the treatment response, whether it's stress, sickness, whatever."

Getting patients stabilized on one therapy is important, he added. "We need to have patients as normalized as possible," Dr. Hamadah said. "Whatever makes them do this and [makes them] happier and disease free is definitely my choice in finding what to give the patients. Secukinumab is superior to ustekinumab in our experience."

Dr. Yanofsky praised the effectiveness of IL-17s biologics compared with other products, including the new IL-23s. In addition to psoriasis, the IL-17s are approved for treatment of psoriatic arthritis, which gives the physician the opportunity of treating two different conditions or two aspects of the same condition with one therapy, whereas the IL-23s to date have not been approved for psoriatic arthritis, he noted.

Reference

1. Yanofsky H, Siddha S, Adam DN, Wang CA, Xu J, Tian H, Rihakova L, Parent S. Secukinumab Demonstrates Significant Improvement of Disease Activity and Health Related Quality of Life At 1 Year in Canadian Psoriasis Patients in a Real World Setting. Poster presented at: American Academy of Dermatology Annual Meeting; March 1-5, 2019; Washington, DC.

This poster presentation was given by Dr. Jerry Bagel and colleagues.

The psoriasis therapy secukinumab "is superior to ustekinumab in clearing skin and improving quality of life in patients with moderate to severe plaque psoriasis," according to a CLARITY head-to-head randomized, controlled Phase 3b clinical trial.

The research, presented as a poster, showed results of the study.[1] It compared efficacy based on co-primary objectives of 90% or more improvement from Baseline Psoriasis Area and Severity Index (PASI90) and a score of 0/1 (clear/almost clear) on the 5-point modified Investigator's Global Assessment (IGA mod 2011 0/1). The study also reported 16-week Dermatology Life Quality Index (DLQI) results.

This is the second head-to-head trial comparing secukinumab with ustekinumab. PASI90 responses were greater with secukinumab compared with ustekinumab from Week 4 (16.7% vs. 4.0%) out to Week 16 (76.6% vs. 54.2%). Similarly, IGA mod 2011 0/1 findings were greater with secukinumab at Week 4 (26.9% vs. 7.8%) and at Week 16 (78.6% vs. 59.1%). Response rates measuring DLQI 0/1 (i.e., no impact of skin disease on patients' quality of life) were greater with secukinumab compared to ustekinumab at Weeks 4, 12, and 16 (33.9% vs. 18%, 64% vs. 51.7%, and 68.4% vs. 55.9%, respectively).

These two therapies vary slightly based on their mechanism of action, explained study co-author John Nia, MD, a dermatology resident at the Icahn School of Medicine at Mount Sinai in New York City. Secukinumab is a blocker of Interleukin 17a, which is one of the drivers for psoriasis, while ustekinumab is a blocker of the p40 subunit of IL-12 and IL-23.

"You're honing in tightly on the exact driver of psoriasis," he said of the two biologics in the study. "Because these drugs for psoriasis have been getting so good over the last 20 years, where doctors used to be happy with only some clearance, now people are looking at 100% clearance."

Nia acknowledged that practitioners are fortunate to have therapies that work so well on psoriasis, and that the field is getting highly focused on the final PASI. Dr. Issam Hamadah, chairman of the Dermatology Department at the King Faisal Specialist Hospital and Research Center in Riyadh and an adjunct clinical professor at the Alfaisal University in Riyadh, said he has seen good maintenance response for the various therapies. "I've seen good results with secukinumab, and the maintenance was longer than ustekinumab," he said.

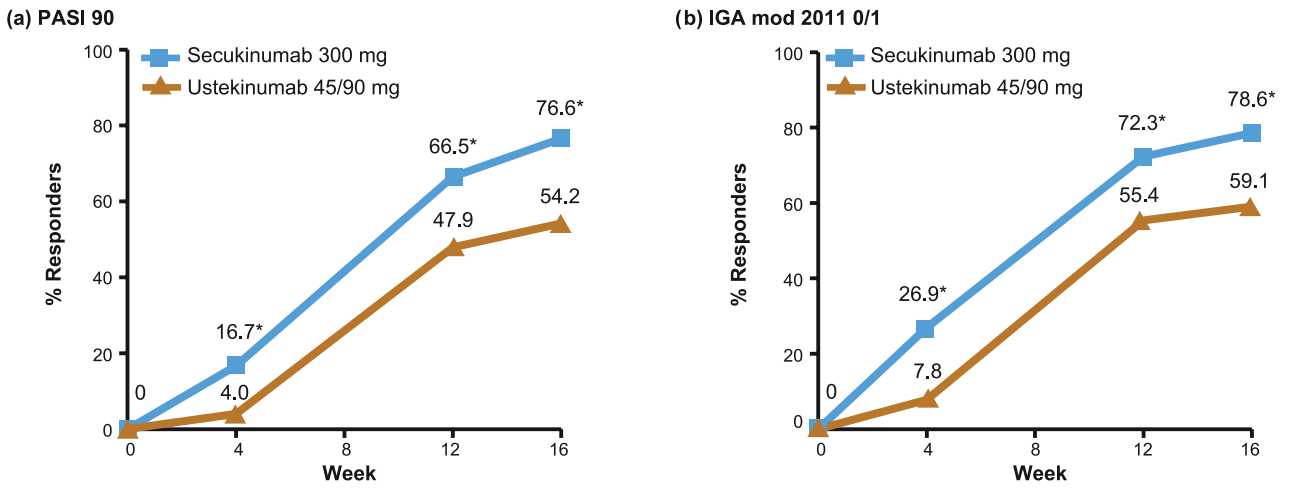
Dr. Yousef Binamer, consultant dermatologist at King Faisal Specialist Hospital and Research Center in Riyadh and assistant professor at Alfaisal University in Riyadh, said "the efficacy of secukinumab is higher as well as the durability, if you consider the labeled doses."

Together with previous data from the CLEAR study, these findings provide further evidence demonstrating the superior efficacy of secukinumab compared to ustekinumab, the poster concluded. In the CLARITY study, a total of 1,102 patients were randomized to either secukinumab 300 mg (n = 550) or ustekinumab 45/90 mg (n = 552).

Reference

1. Bagel J, Nia J, Hashim P, Patekar M, Hugot S, Sheng K, Xia S, Gilloteau I, Blauvelt A, Lebwohl M. Secukinumab Is Superior to Ustekinumab in Clearing Skin and Improving Quality of Life in Patients with Moderate to Severe Plaque Psoriasis: CLARITY, a Randomized, Controlled, Phase 3b Trial. Poster presented at: American Academy of Dermatology Annual Meeting; March 1-5, 2019; Washington, DC.

(a) PASI 90 and (b) IGA mod 2011 0/1 responses up to Week 16



Missing values handled by multiple imputation
*$P < 0.0001$
IGA mod 2011 0/1, Investigator's Global Assessment, 2011 modification, clear (0) or almost clear (1) score; PASI 90, Psoriasis Area and Severity Index 90% improvement vs. Baseline

ANALYSIS OF PHASE 3 TRIALS FINDS SECUKINUMAB RESPONSE IS SUSTAINED IN MAJORITY OF PATIENTS

This poster presentation was given by Dr. Matthias Augustin and colleagues.

Loss of efficacy in patients taking the psoriasis treatment secukinumab was low over time, according to recently published data.[1]

A high proportion of patients treated with secukinumab achieved a 90% reduction in the Psoriasis Area and Severity Index (PASI90) within 16 weeks. Data from patients treated over 5 years in a similar SCULPTURE study show that high levels of efficacy are sustained, researchers noted.[2]

The research poster examined efficacy of secukinumab over time.

"Basically, what this poster is saying is that secukinumab had a good maintenance response," said Paul S. Yamauchi, MD, PhD, clinical assistant professor of medicine in the Division of Dermatology at the David Geffen School of Medicine at UCLA and adjunct associate professor at the John Wayne Cancer Institute in Santa Monica.

Secukinumab is a fully human monoclonal antibody that selectively neutralizes IL-17A, a cornerstone cytokine in the development of psoriasis. The study

compared patients who received secukinumab 300 mg to those who received the therapies etanercept 50 mg or ustekinumab 45/90 mg over 52 weeks. Reductions in efficacy were defined as shifts from higher to lower response categories between 2 consecutive visits maintained for a third consecutive visit.

Median time to first loss of efficacy was not reached for secukinumab in the FIXTURE trial, but was 54.1 weeks for etanercept. In the CLEAR trial, median time to loss of efficacy was again not reached for secukinumab, but was 52.6 weeks for ustekinumab. Continued treatment with secukinumab resulted in a regaining of efficacy in a high proportion of patients who experienced a reduction of efficacy, and persistent reduction of response was uncommon, the study found.

"The data show that secukinumab has better stable efficacy without reduction of efficacy," Dr. Yamauchi said of the findings. "Psoriasis is a condition that waxes and wanes. So despite being on therapy, some patients will flare. But if you continue to treat with secukinumab, that partial loss response will then go away, and then patients will be able to regain efficacy."

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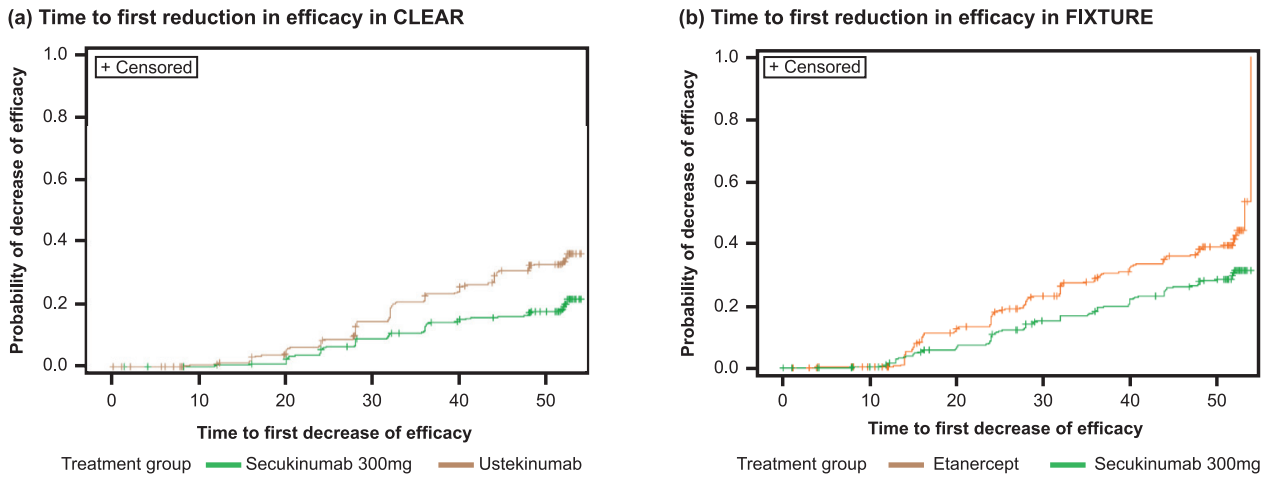
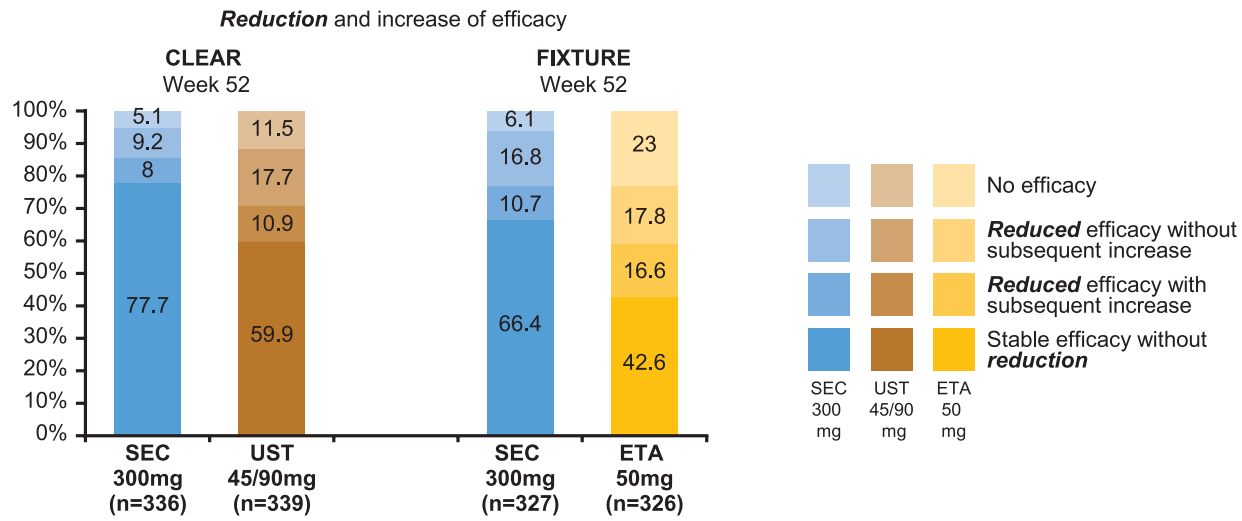
1. Augustin M, Thaci D, Eyerich K, Pinter A, Radtke M, Lauffer F, et al. Persistent Reduction of Response to Secukinumab Is Uncommon in Plaque Psoriasis Patients: A Pooled Analysis of FIXTURE and CLEAR. Poster presented at: American Academy of Dermatology Annual Meeting; March 1-5, 2019; Washington, DC.
2. Bissonnette R, et al. *J Eur Acad Dermatol Venereol.* 2018 Sep;32(9):1507-1514. doi: 10.1111/jdv.14878. Epub 2018 Mar 22.

Time to first reduction in efficacy with secukinumab and ustekinumab (CLEAR, a) or etanercept (FIXTURE, b)



Reduction in response (PASI<75 as insufficient response) in CLEAR and FIXTURE



STUDY FINDS LOWER IMMUNOGENICITY POTENTIAL IN SECUKINUMAB THAN IXEKIZUMAB

This poster presentation was given by Dr. Sebastian Spindeldreher and colleagues.

Data from a recent study show the psoriasis therapy secukinumab has lower *in vitro* immunogenicity potential compared with the biologic therapy ixekizumab, which could be a factor in maintaining the efficacy of secukinumab.[1]

What this poster shows is that secukinumab has less immunogenicity, or less propensity to form antibodies against the therapy, compared with ixekizumab, based on the assays performed, said Paul S. Yamauchi, MD, PhD, clinical assistant professor of dermatology at the David Geffen School of Medicine at UCLA, Division of Dermatology, and an adjunct associate professor at the John Wayne Cancer Institute in Santa Monica.

When a patient receives a biologic agent, over time his or her body produces a set of antibodies against the biologic agent, called neutralizing antibodies, said Dr. Yamauchi, who was not one of the study authors.

"We're basically immunizing ourselves against the therapy that is being used to treat us," he explained. "And when that happens, then the therapy stops working, because you're neutralizing it with the antibody formation. This is not a good thing, because once that happens you've got to try something else."

Dr. Afaf Al Sheikh, head of the Dermatology Division at King Abdulaziz Medical City National Guard Hospital and assistant professor at King Saud Bin Abdulaziz University for Health Sciences in Riyadh, said that doctors cannot ignore the immunogenicity role when they use biologic medication in general.

"The less the immunogenicity, the better maintenance of the response and the more adherence to the treatment," she said. "The formation of neutralizing antibody against biological agents definitely will affect the efficacy and the durability of the therapy. And gradually, the patient and the treating physician also will notice that this agent doesn't work anymore or doesn't work as well as it used to."

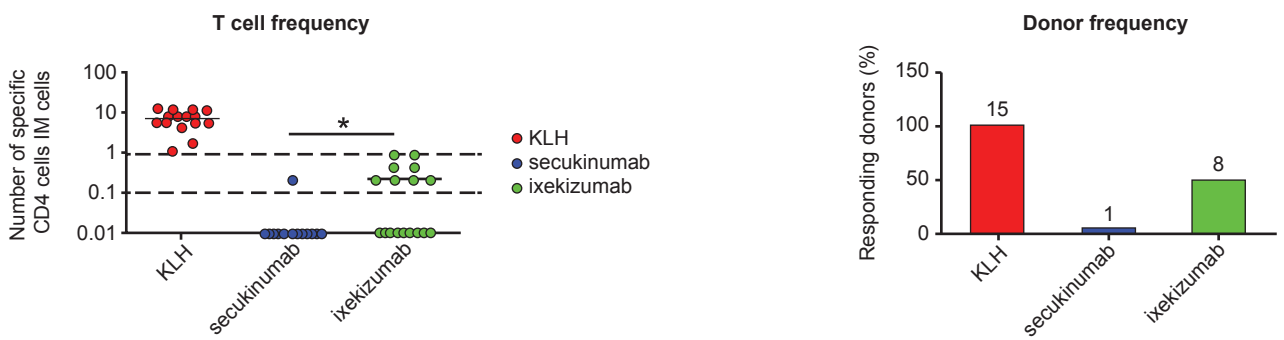
Dr. Al Sheikh described how sometimes the doctor needs to switch the patient to another agent. "That tells me how much immunogenicity is important, and plays a major role in using biologics," she continued. "You do not want to do that. If you have a medication with the least immunogenicity, this makes it less likely for the patient to lose response in the long term."

Dr. Yousef Binamer, consultant dermatologist at King Faisal Specialist Hospital and Research Center in Riyadh, noted that the correlation between antidrug antibodies formation and drug efficacy is important. "The presence of neutralizing antibodies will decrease the efficacy of the medication; thus, it will require dose adjustment—increasing the dose or shortening the interval—or you need to switch to another biologic agent," he said. "We see this issue more with anti-TNF agents and not with the interleukin inhibitors."

Secukinumab has been shown to be highly efficacious in the treatment of moderate to severe plaque psoriasis, with early, sustained effect and a favorable safety profile in Phase 3 studies.[2,3]

The biologic has previously shown lower *in vitro* immunogenicity potential compared with other therapies used to treat psoriasis, and a significantly

T cell and donor frequencies



Wilcoxon matched-pairs signed rank test:*: p<0.05

lower T-cell precursor frequency as compared with ixekizumab. T-cells play a central role in regulating cell immunity. The study included an analysis of secukinumab and ixekizumab in an *in vitro* CD4 T-cell assay, and the frequency of specific CD4 T-cells present in the blood of the healthy blood donors was evaluated for each antibody.

"What these data show is that because secukinumab has less immunogenicity, then in theory it should have better durability and maintenance of response," Dr. Yamauchi said.

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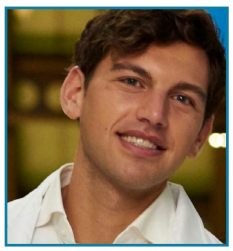

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Special thanks to Courtney Schneider