Q&A

CME Outfitters

Based on a CME Outfitters Live & On Demand webcast held on May 1, 2015

Faculty Response to Questions from the Live Webcast

Coordinating Care Between Dermatologists and Rheumatologists to Improve Outcomes in Patients with Psoriatic Arthritis

Q: Can you tell me more about the latest treatments for psoriatic arthritis and how they differentiate?

A: *The results of some head-to-head studies comparing biologic agents approved for psoriasis are now available. Head-to-head studies of biologics have shown that secukinumab has superior efficacy compared to etanercept and secukinumab is also superior to ustekinumab. Infection rates were higherfor secukinumab and etanercept compared to placebo.[1]*

Overall, to differentiate these agents among psoriasis patients, it is important to account for the presence of psoriatic arthritis (TNF inhibitors have robust efficacy for PsA), patient weight (if the patient is overweight, consider a weight-based dosing medication such as ustekinumab), and dosing convenience (maintenance dosing of every week for etanercept, every other week for adalimumab, every 12 weeks for ustekinumab, every 8 weeks for infliximab, and every 4 weeks for secukinmab).

Q: You mention that patients on apremilast may lose weight, what is the mechanism for that weight loss?

A: *At the current time, there is no known mechanism that accounts for the weight loss that is observed in a small proportion of patients on apremilast. However, the weight loss does not appear to be related to the diarrhea.[2]*

Q: I am an internal medicine doctor, what is linkage between pathway and efficacy. Is there data that shows IL-17 drugs are more efficacious or fewer side effects? How do I differentiate these drugs?

A: *The IL-17 inhibitors appear to work more "downstream" in the Th17 pathway. That is, the IL-17 inhibitors block IL-17, which is predominantly generated by the Th17 cells. By inhibiting the action of IL-17, these biologic agents appear to be highly efficacious because IL-17 is now thought to play a central role in psoriasis pathogenesis by increasing chemokine production in the skin. However, IL-17 is important for responding to extracellular pathogens and induces destruction of the pathogen's cellular matrix. Therefore, one known side effect associated with IL-17 inhibitors is oral candidiasis.[1]*

Secukinumab is the currently approved IL-17 inhibitor for psoriasis. Head-to-head studies have shown that secukinumab has superior efficacy compared to etanercept and ustekinumab.[1]

Q: Can we use these newer treatments on young adults?

A: *Apremilast and IL-17 inhibitors were studied in patients 18 years or older for psoriasis, therefore, to date, it is unknown whether we can use these newer treatments in those 18 years or younger.[2]*

Q: I have not begun to integrate some of the newer medicines in my practice yet but feel that enough patients may have been exposed to these therapies that now I feel more comfortable but I am curious what are some of the most common side effects you see and are there other things I need to be careful of?

A: *For apremilast, common side effects include nausea and diarrhea. These side effects are mitigated by the titration pack during week 1 of therapy. From my clinical experience apremilast has a reassuring safety profile.[2]*

For IL-17 inhibitors such as secukinumab, common side effects include headache, nasopharyngitis, and oral candidiasis. For IL-17 inhibitors, the usual precautions that are commonly applied to biologics approved for psoriasis also apply here, such as monitor patients for active infection and avoid prescribing the medication in those who are at baseline immunosuppressed, become infected, or has a recent history of malignancy. Oral candidiasis is one condition that appears to have a dose-dependent relationship to IL-17 inhibitors.[3]

Q: Is apremilast as efficacious as the other biologics? Can you talk about the pathway and how it works in more detail please?

A: *While no head-to-head comparisons currently exist comparing apremilast with biologics. One indirect comparison study presented at the annual AAD 2015 meeting showed that the efficacy of apremilast is not different from methotrexate among those who are naïve to systemic medications but more studies need to be conducted.4*

Apremilast is an inhibitor of PDE4, which is the major enzyme class responsible for the hydrolysis of cyclic adenosine monophosphate (cAMP), an intracellular second messenger that has downstream effects on a network of pro-inflammatory and anti-inflammatory mediators. With PDE4 inhibition, and the resulting increases in cAMP levels in immune and non-immune cell types, expression of a network of pro-inflammatory mediators is muted and the production of anti-inflammatory mediators is increased.[2,5]

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Q: Here is my reality, my patients present after consulting with Dr. Google and they want to start with some of the newer treatments but I have to put them through the more traditional therapies and let them fail and suffer first. How do you mange this and how do you talk to the patient about this?

A: *Sometimes the payers may require that the patients undergo other treatments first before getting on the desired treatment initially preferred by the prescribing clinician. In these cases, I usually try to appeal any denial decisions on the prior authorization and see if we could get the patient on the desired therapy. However, often during the initial encounter with the patient (before my office staff prepares the prior authorization), I usually prepare the patient for the possibility of failure to obtain the desired drug and the need to go through step therapy. I think that, if they are prepared for potential denial before the actual denial and if they understand that you are doing your best, their response is usually quite positive.*

Q: Can you talk about drug combinations? Is there evidence to support combination therapy with a biologic and a DMARD?

A: *The article by Armstrong et al published in JAMA Dermatology 2015 addressed the topic of combination therapy with biologics and DMARDS in the psoriasis population. Of the currently FDA-approved biologics, etanercept and methotrexate combination therapy is the most-well studied, and this combination is more effective than either etanercept or methotrexate used alone. Thus, etanercept combined with methotrexate can be used when desired efficacy is not achieved with monotherapy with either medication. Gottlieb at al. showed that, at week 24, 77.3% of patients receiving combination etanercept + methotrexate therapy achieved PASI 75 compared to 60.3% of patients receiving etanercept monotherapy ($p<0.0001$). A combination of infliximab and methotrexate or a combination of adalimumab and methotrexate may result in additional efficacy beyond biologic monotherapy, but data on these particular combinations are limited.*[6,7]

Q: How long can patients be on a biologic? Are the meds taken forever or can they be stopped if there's improvement?

A: *At the current time, our understanding is that the patients may need to take biologic medications for many years and possibly indefinitely. This is partly due to the observation that the majority of patients who stop taking biologic medications tend to experience recurrence of psoriasis. Patients with psoriatic arthritis are also likely to experience recurrence of joint symptoms and progression of joint disease. Furthermore, the natural history of psoriasis is actually poorly understood, and epidemiologic data are lacking regarding the effects of taking biologics indefinitely in the psoriasis population.*

References

1. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, Puig L, Nakagawa H, Spelman L, Sigurgeirsson B, Rivas E, Tsai TF, Wasel N, Tyring S, Salko T, Hampele I, Notter M, Karpov A, Helou S, Papavassilis C; ERASURE Study Group; FIXTURE Study Group. Secukinumab in plaque psoriasis--results of two phase 3 trials. *N Engl J Med*. 2014 Jul 24;371(4):326-38. PMID: 25007392.
2. Celgene Corp. Highlights of prescribing information for Otezla® (apremilast) formulation. Drugs@FDA Website. http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205437s000lbl.pdfPublished March, 2014. Accessed July 7, 2015.
3. Novartis Pharmaceuticals. Highlights of prescribing information for Costenyx™ (secukinumab) formulation. Drugs@FDA Website. http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125504s000lbl.pdf. Published January, 2015. Accessed July 7, 2015.
4. Clinical Trials.gov. Website. Phase 3b Safety and Efficacy Study of Apremilast to Treat Moderate to Severe Plaque-plaque Psoriasis. https://clinicaltrials.gov/ct2/show/NCT01690299.
5. Schafer P. Apremilast mechanism of action and application to psoriasis and psoriatic arthritis. *Biochem Pharmacol*. 2012;83(12):1583-90. PMID: 22257911.
6. Armstrong AW, Bagel J, Van Voorhees AS, Robertson AD, Yamauchi PS. Combining biologic therapies with other systemic treatments in psoriasis: evidence-based, best-practice recommendations from the medical board of the national psoriasis foundation. *JAMA Dermatol*. 2015 Apr;151(4):432-8. PMID: 25517130.
7. Gottlieb AB, Langley RG, Strober BE, et al. A randomized, double-blind, placebo-controlled study to evaluate the addition of methotrexate to etanercept in patients with moderate to severe plaque psoriasis. *The British journal of dermatology*. Sep 2012;167(3):649-657.

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