ADDITIONAL RESOURCES

TURNING the TIDE

Applying Science to Patient Care in Treating Psoriasis, Psoriatic Arthritis, and Atopic Dermatitis

28

Monday,
January 28, 2019
6:00AM -7:15AM

Haleakala Ballroom
Grand Wailea
Wailea, Hawaii

ACTIVITY DESCRIPTION

Fast-paced and focused on emerging science and treatment techniques, *Turning the Tide* is an interactive activity designed to sharpen participants' understanding of psoriasis, psoriatic arthritis (PsA), and atopic dermatitis (AD) and equip them with forward-thinking patient-centered communication strategies. Through a combination of medical animation, TED Talks-style presentations, a clinical case study, and a discussion of patient-provider shared decision making, learners will explore disease pathophysiology, mechanisms of action (MOAs) of targeted therapies, evidence-based treatment recommendations, and use of decision aids. Learners will be provided access to slides and additional resources.

For valuable resources related to this activity, please visit ***forefrontcollabactivities.com/TurningTheTide***

This educational activity is held in conjunction with
the 15th Annual Maui Derm for Dermatologists 2019 Conference.

This activity is supported by an educational grant from Lilly.
For further information concerning Lilly grant funding, visit www.lillygrantoffice.com.

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LEARNING OBJECTIVES

As a result of participation in this educational activity, participants should increase their ability to:

1. **Describe** current models explaining pathophysiology of psoriasis and atopic dermatitis.
2. **Identify** mechanisms of action and effectiveness of existing and emerging targeted treatments for psoriasis and atopic dermatitis.
3. **Discuss** evolving treatment strategies and safety of treatments for psoriasis, psoriatic arthritis, and atopic dermatitis.
4. **Engage** patients with psoriatic disease or atopic dermatitis in shared decision making regarding goals of treatment, development of treatment plan, and treatment modification.

FEATURED FACULTY

Bruce E. Strober, MD, PhD

Professor,
Department of Dermatology
University of Connecticut Health Center
Farmington, Connecticut

Bruce Strober, MD, PhD is Professor and Director of the Clinical Trials Unit at the University of Connecticut Health Center's Department of Dermatology, in Farmington, Connecticut. He received his medical and graduate degrees from the Columbia University College of Physicians and Surgeons in New York, New York, and completed his postgraduate training in dermatology at New York University in New York, New York.

Dr. Strober is board-certified by the American Board of Dermatology and a Fellow of the American Academy of Dermatology. He has been a section editor at the *British Journal of Dermatology*, has authored numerous journal articles, and has spoken extensively to both physician and patient audiences in the field of dermatology.

Dr. Strober also sees patients at the University of Connecticut, where he specializes in complex medical dermatology.

Richard Martin, MD, MA

Professor of Medicine and Rheumatology,
Michigan State University
College of Human Medicine
East Lansing, Michigan

Richard Martin, MD, MA, earned his Bachelor of Science degree at the University of Michigan in Ann Arbor and his medical degree at the Michigan State University College of Human Medicine in East Lansing. He completed an internship at Butterworth Hospital in Grand Rapids, Michigan; a residency in Primary Care and Internal Medicine at the University of Rochester in New York; and a fellowship in Rheumatology at the Mayo Clinic in Rochester, Minnesota. Dr. Martin earned his master's degree in Educational Psychology and Instructional Design at Michigan State University, where he also completed a postdoctoral fellowship in Clinical Epidemiology. He founded West Michigan Rheumatology in 1991. Dr. Martin's research has focused on evaluating emerging therapies for rheumatoid arthritis, Raynaud's disease, and scleroderma, as well as developing decision aids for patients considering biologics.

DISCLOSURE AND CONFLICT OF INTEREST RESOLUTION

Educational activities provided by Forefront Collaborative must demonstrate balance, independence, and scientific rigor. All those in a position to control the content of an activity must disclose all relevant financial relationship(s) with commercial interest(s)*. For this educational activity, all conflicts of interest have been resolved through peer review and revisions to ensure independence, evidence base, fair balance, and absence of commercial bias. Disclosures appear below.

*The ACCME defines a **commercial interest** as any entity producing, marketing, reselling, or distributing healthcare goods or services consumed by or used on patients. The ACCME does not consider providers of clinical service directly to patients to be commercial interests.

The following individuals have indicated that neither they nor their spouses/partners have had, in the past 12 months, financial relationship(s) with commercial interests relative to the content of this CME activity:

PLANNERS (Forefront Collaborative)

- Christine Tebben
- Marianna Shershneva, MD, PhD

The following individuals have disclosed that they and/or their spouse/partner has had a financial relationship in the past 12 months:

FACULTY

Bruce Strober, MD, PhD

- Consultant (honoraria): AbbVie, Almirall, Amgen, Arena, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, GlaxoSmithKline, Janssen, LEO Pharma, Lilly, Medac, Meiji Seika Pharma, Menlo Therapeutics, Novartis, Ortho Dermatologics/Valeant, Pfizer, Regeneron, Sanofi Genzyme, Sebela Pharmaceuticals, Sitris, Sun Pharma, UCB
- Investigator (no direct payments made to Bruce Strober, MD, PhD): AbbVie, Boehringer Ingelheim, Celgene, Galderma, GlaxoSmithKline, Janssen, Lilly, Merck, Pfizer, Sienna Biopharmaceuticals
- Scientific Director (consulting fee): Corrona/National Psoriasis Foundation Psoriasis Registry
- Grant support for Fellowship Program (payments to the University of Connecticut): AbbVie, Janssen, National Psoriasis Foundation

Richard Martin, MD, MA

- Contracted research: AbbVie, Amgen, AstraZeneca, Lilly, and Cytori

PLANNER (Faculty)

April W. Armstrong, MD, MPH

- Consultant: Novartis, Sanofi, Regeneron, Pfizer, Celgene, Modernizing Medicine, AbbVie, Lilly, Merck, and Janssen
- Speaker and researcher: Lilly, AbbVie, and Janssen

TARGET AUDIENCE

The target audience is dermatologists. Other healthcare professionals, including rheumatologists, physician assistants, and nurse practitioners who treat patients with psoriasis, PsA, and AD, may benefit from participation in this educational activity.

CME CONTENT REVIEW

The content of this activity was independently peer reviewed by two reviewers. The reviewers of this activity have no relevant financial relationships to disclose.

This continuing medical education activity may include reference(s) to unlabeled or unapproved uses of drugs.

The views and opinions expressed in this activity are those of the faculty and do not necessarily reflect the views or recommendations of Forefront Collaborative.

ACCREDITATION STATEMENT

Forefront Collaborative is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Forefront Collaborative designates this live activity for a maximum of 1.25 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Posttest With Explanations

QUESTION 1

A 23-year-old woman presents with >95% of her body involved with an erythematous, highly pruritic, lightly hyperkeratotic dermatitis. A skin biopsy performed a week earlier by another dermatologist revealed a spongiotic dermatitis with edema and a mixed inflammatory cell infiltrate in the dermis. Which of the therapies below most likely would immediately result in rapid improvement of her skin and could be obtained that same day?

A. Apremilast 30 mg twice daily

B. Cyclosporine 5 mg/kg per day divided into AM and PM doses

C. Dupilumab 300 mg every other week

D. Etanercept 50 mg twice weekly

E. Secukinumab 300 mg every week for 5 weeks

CORRECT ANSWER: B

Explanation: Cyclosporine has well-known rapid efficacy for spongiotic/eczematous dermatitis and likely could be obtained at the patient's pharmacy that day. While dupilumab also could be very effective in this setting, the ability to obtain this drug for the patient on the same day of presentation is questionable. The other three choices represent psoriasis-specific drugs that are much less likely to be effective in this setting. Renal toxicity and hypertension appear insidiously over long-term continuous therapy with cyclosporine. Regular monitoring of the serum creatinine and blood pressure are required.

American Academy of Dermatology. Available at https://www.aad.org/practicecenter/quality/clinical-guidelines/atopic-dermatitis. Accessed Dec 4, 2018.

Simpson EL, Bruin-Weller M, Flohr C, et al. When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. *J Am Acad Dermatol*. 2017;77(4):623-633.

Posttest With Explanations

QUESTION 2

A 35-year-old man presents with discrete erythematous hyperkeratotic plaques covering approximately 15% of his body surface area, involving the scalp, trunk, and upper and lower extremities. He also displays onychodystrophy characterized by pitting and distal onycholysis. He complains of arthritis and joint stiffness in the morning lasting 30-45 minutes. His father has psoriasis. Which of the following biologics do not directly inhibit IL-23 and would be appropriate in his care?

A. Dupilumab

B. Guselkumab

C. Ixekizumab

D. Risankizumab

E. Tildrakizumab

CORRECT ANSWER: C

Explanation: Ixekizumab directly binds to IL-17, not IL-23. Ixekizumab has established rapid and potent efficacy for the treatment of psoriasis. Tildrakizumab, guselkumab, and risankizumab directly block IL-23. In the case of dupilumab, the signaling through both IL-4 and IL-13 pathways is blocked, and the drug has no known efficacy for the treatment of psoriasis.

Blauvelt A, Papp KA, Griffiths CE, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. *J Am Acad Dermatol*. 2017;76(3):405-417.

Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet*. 2018;392(10148):650-661.

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Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.

Posttest With Explanations

QUESTION 3

A 26-year-old man presents with ill-defined erythematous and lichenified lightly hyperkeratotic patches covering approximately 20% of his body surface area involving the face, trunk, and upper and lower extremities. Some patches are excoriated and others are oozing. He had mild "eczema" and asthma as a child. Which of the following medications would be most appropriate for his care?

A. Azathioprine

B. Dupilumab

C. Prednisone

D. Secukinumab

E. Tildrakizumab

CORRECT ANSWER: B

Explanation: Dupilumab is FDA-approved for the treatment of moderate to severe adult atopic dermatitis and works by blocking signaling through both the IL-4 and IL-13 pathways. Tildrakizumab directly blocks IL-23 and secukinumab directly blocks IL-17, and neither drug has demonstrated efficacy in atopic dermatitis. Azathioprine might be effective for this patient, but likely would have a lower chance of success and would involve a greater risk of toxicity. Prednisone is a poor choice for therapy for moderate to severe chronic inflammatory dermatitis, be it either atopic dermatitis or psoriasis.

Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.

Simpson EL, Bruin-Weller M, Flohr C, et al. When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. *J Am Acad Dermatol*. 2017;77(4):623-633.

Posttest With Explanations

QUESTION 4

A 21-year-old woman presents with multiple discrete and pruritic erythematous and heavily hyperkeratotic plaques covering approximately 25% of her body surface area involving the scalp, trunk, and upper and lower extremities. She denies arthritis/enthesitis. Which of the following cytokines is likely highly elevated in her serum and would be reduced by effective therapy?

A. IL-4

B. IL-13

C. IL-19

D. IL-31

E. IL-33

CORRECT ANSWER: C

Explanation: IL-19 recently has been shown to be a biomarker cytokine that correlates with disease activity in patients with psoriasis. All the other choices are cytokines associated with the pathophysiology of atopic dermatitis.

Brunner PM, Guttman-Yassky E, Leung DY. The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. *J Allergy Clin Immunol*. 2017;139(4s):S65-S76.

Nickoloff BJ, Higgs R, Rodgers G, et al. Novel immunoassay for serum IL-19 as a predictive biomarker to improve management of psoriasis patients, OP05.04. Presented at: 27th European Academy of Dermatology and Venereology (EADV) Congress. September 12-16, 2018; Paris, France. 2018.

Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.

Posttest With Explanations

QUESTION 5

A 27-year-old woman presents with new symptoms of psoriasis affecting 1% of her body surface area as well as lower extremity predominant oligoarthritis. There is swelling of the left knee and right ankle and pain with palpation of the left Achilles tendon. Which option for initial treatment of psoriatic arthritis is most appropriate for this patient?

A. Meloxicam 15 mg/day

B. Prednisone 40 mg/day

C. Injection of betamethasone into the Achilles bursa

D. Leflunomide 20 mg/day

E. Certolizumab 400 mg/ monthly

CORRECT ANSWER: A

Explanation: All of the options listed may be used in psoriatic arthritis. The correct answer is meloxicam. This patient has mild psoriasis which effects < 3% BSA. In patients with arthritis dominant PsA, EULAR guidelines encourage the use of NSAIDs to relieve musculoskeletal signs and symptoms. Prednisone may be used as an adjunctive, but a chronic dose of 40 mg/day would cause unacceptable side effects. Typically, prednisone 2.5 to 7.5 mg/day is used as a bridging agent while awaiting the onset of effect of a DMARD. Intra-articular injection with an intermediate acting steroid like betamethasone may also be helpful.

In patients with active enthesitis and/or dactylitis and insufficient response to NSAIDs, local injections may be considered, though injection of the Achilles enthesal region has a significant risk of localized soft tissue injury, ie, tendon rupture or for the plantar fascia fat pad atrophy. Thus, injections of enthesal regions are reserved for patients with disease resistant to optimized medical therapy.

In patients with peripheral arthritis, particularly in those with many swollen joints, structural damage in the presence of inflammation, and/or clinically relevant extra-articular manifestations, conventional DMARDs (sulfasalazine, methotrexate, and leflunomide) should be considered early in treatment. Leflunomide has a significant risk of fetal teratogenesis and is contra-indicated in women of childbearing potential. EULAR guidelines favor methotrexate for patients with significant skin involvement. They suggest patients with peripheral arthritis and an inadequate response to at least one conventional DMARD move to a biologic DMARD, usually a TNF inhibitor.

An exception to these recommendations are patients with predominantly axial disease that have insufficient response to NSAID. Axial disease does not respond to conventional DMARDs, thus therapy with a biologic DMARD should be considered, typically a TNF inhibitor as the first DMARD.

Coates LC, Kavanaugh A, Mease PJ, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis. *Arthritis Rheumatol*. 2016;68:1060–1071.

Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75:499–510.

Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis [Epub ahead of print]. *Arthritis Rheumatol*. 2018. doi: 10.1002/art.40726.

Posttest With Explanations

QUESTION 6

Good decision aids are designed to accomplish all of the listed features EXCEPT:

A. Help clinician to explain to patient why a particular option is the best for the patient

B. Provide specific probabilities about outcomes to aid comparison of options

C. Encourage and structure patient reflection on options after office visit with support persons

D. Gives a consistent script for the care team to reinforce patient education content

E. Create a standard operating procedure that reduces documentation to clicking an EMR macro

CORRECT ANSWER: A

Explanation: The correct answer is A. Decision aids are tools intended to structure and support a dialogue, not to persuade the use of a particular option. Shared decision making is useful in equipoise—when there is more than one medically reasonable option. In that case the patient's preference for one or more drug attribute, ie, route of administration, avoidance of certain risks, desire for maximum potency, etc, would motivate the patient to find a particular treatment most desirable. In complex medication dialogues there can be an overload of information. Patients often have limited ability and motivation to sustain attention and deliberation. Reduced health literacy, age and general health-related cognitive impairment, risk aversion, and non-native language skill all reduce patients' ability to participate in decision making. This emphasizes the need to simplify complex concepts and risk propositions to patient's level. Decision aids can lengthen the time of deliberation beyond the office visit and increase the involvement of support persons. The goal of increasing patient engagement is to reduce going for the default option, "whatever you recommend doctor."

Posttest With Explanations

QUESTION 7

How confident are you discussing the options, medication attributes, benefits, and harms with the patient who may start a new biologic?

A. Not at all confident

B. Little confidence

C. Neutral

D. Somewhat confident

E. Very confident

THERE IS NO RIGHT OR WRONG ANSWER

Explanation: Self-efficacy is a term coined by Stanford social psychologist Albert Bandura when he tried to explain the causal pathways of the benefits of the Arthritis Self-Help Course. It is an individual's belief in their ability to perform a specific behavior. Self-efficacy also influences whether a physician will be able to implement a behavior and how long effort will be sustained. Both patients and physicians who have high self-efficacy will exert effort to achieve goals. In today's program we have used skills mastery (breaking the shared decision making dialogue into small manageable tasks), modeling and social persuasion to help increase your self-efficacy to conduct a complete shared decision making dialogue.

Bandura A. Self-efficacy mechanism in human agency. *American Psychologist*. 1982;37(2):122-147.

Lorig K. Patient Education: A Practical Approach. 3rd ed. 2000. Sage Publishing. Thousand Oaks, CA.

FDA-Approved Biologic and New Small Molecule Systemic Therapies for Psoriasis, Psoriatic Arthritis, and Atopic Dermatitis

APPROVED MEDICATION	APPROVED FOR PSORIASIS	APPROVED FOR PsA	APPROVED FOR AD
TNFi			
adalimumab	Yes	Yes	
certolizumab		Yes	
etanercept	Yes	Yes	
golimumab		Yes	
infliximab	Yes	Yes	
PDE4i			
apremilast, small molecule	Yes	Yes	
IL-4			
dupilumab			Yes
IL-12/23i			
ustekinumab	Yes	Yes	
IL-23i			
guselkumab	Yes		
tildrakizumab	Yes		
IL-17i			
ixekizumab	Yes	Yes	
secukinumab	Yes	Yes	
brodalumab	Yes		
CTLA4			
abatacept		Yes	
Jak2/3i			
tofacitinib, small molecule		Yes	

Note:

1. Crisaborole, an FDA-approved, small-molecule, PDE4 inhibitor for treatment of atopic dermatitis, is not included in the chart because it is a topical medication.
2. FDA-approved conventional systemic pharmacotherapies include: acitretin, cyclosporine, and methotrexate for psoriasis; leflunomide, methotrexate, and sulfasalazine for psoriatic arthritis; and systemic corticosteroids for atopic dermatitis.
3. Systemic immunomodulatory agents—cyclosporine, methotrexate, mycophenolate mofetil, azathioprine, and interferon gamma—although not approved in the United States for the treatment of atopic dermatitis, are used for cases with severe, difficult-to-manage symptoms.

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