MARCH 2022

A report from the Annual Meeting of the American Academy of Dermatology

By Grace Hile, MD

SUMMARIZING SESSIONS WITH A FOCUS ON PSORIASIS
INTRODUCTION

The 2022 American Academy of Dermatology (AAD) Annual Meeting was held Thursday, March 24 – Tuesday, March 29 in Boston, Massachusetts. This program was packed with over 900 world-renowned speakers and 300 scientific sessions and showcased the latest innovations in dermatology and venereology. Grace Hile, MD, has written the congress report below, summarizing the eleven most important presentations with a focus on psoriasis.

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How to Select a Systematic Psoriasis Treatment for your Patient that Makes Sense
Craig L. Leonardi, MD, IPC President
Saint Louis University, St. Louis, Missouri, United States

Given the growing armamentarium for the treatment of psoriasis, choosing the right treatment for your patient can be a challenge. Dr. Leonardi reviewed guidelines for psoriasis treatment and evidence-based conclusions in the settings of comorbidities and lifestyle factors. A high-yield summary is shown in Figure 1 below.

Figure 1. Optimal treatment recommendations for psoriasis based on comorbidities and patient factors. Table based on Mentor et al. JAAD;2011
Take away:

- TNF inhibitors, IL-12/IL23, IL-23 inhibitors, and IL-17 antagonists are considered safe in pregnancy (category B). Acitretin and methotrexate are contraindicated.
- Ustekinumab and adalimumab should be used with caution or avoided in patients with a history of skin cancer. NB-UVB should be discontinued.
- Acitretin, cyclosporine, and methotrexate should be avoided in settings of moderate alcohol use, given the increased risk of hepatotoxicity.
- Cyclosporine has many drug-drug interactions.
- Psoriasis patients have an increased risk of myocardial infarction that correlates with disease activity.\cite{2,3}
- Treatment with TNF blockers decreases cardiovascular risk-adjusted hazard ratio (0.46, 95% CI 0.25-0.85)\cite{4} and risk reduction correlates with cumulative use.\cite{5}
- Clinicians should consider the number needed to treat (NNT; #patients treated to achieve one additional outcome) when considering therapies for patients. (Figure 2)

![Figure 2](image.png)

**Figure 2.** NNT for various psoriasis therapeutics.
References


Innovations in Topical Treatment for Psoriasis
Charles W. Lynde, MD, FRCPC, DABD, FCDA, IPC Councilor
The University of Toronto, Toronto, Canada

Topical therapy in the treatment of psoriasis is important. Most patients are amenable to topical therapy and may be more hesitant to systemic therapies. Additionally, biologics may not achieve complete clearance, and topicals can be used as adjunctive therapy. A 2018 National Psoriasis Foundation Survey revealed only 14% of patients were “very satisfied” or “extremely satisfied,” with 75% noting that lack of efficacy was the reason why. 54% of patients said they would have continued using a topical if it was effective.

An ideal topical treatment is effective, safe, non-irritating, cosmetically elegant (non-greasy), non-steroid, can be used long term for maintenance, and can be used on multiple sites (scalp, face, genitals, body).

Emerging topical therapies

Fixed combination:
- Halobetasol Propionate and Tazarotene Lotion (2-grade IGA improvement from baseline and “clear” or “almost clear” at week 8), Figure 3.

![Figure 3. Percentage of patients achieving primary endpoint from Stein Gold et al, J Am Acad Dermatol 2018.](image-url)
- Calcipotriene and betamethasone dipropionate cream or Talconex suspension with PAD technology (PGA treatment success in 50.7% of Talconex)

**New Molecules:**
- Tapinarof Cream 1% (significant PGA response at Week 12 vs vehicle \(P<0.0001\))^2
- Roflumilast Foam
  - DERMIS-1: IGA success at week 8 in 42.4% vs 6.1% \((p<0.001)\), PASI 75 by week 8 in 41.6% vs. 7.6% \(P<0.0001\), PASI 90 by week 8 in 22.4% vs. 2.3% \((p<0.0001)\)
  - DERMIS-2: IGA success at week 8 in 37.5% vs. 6.9% \((p<0.001)\) and PASI 75 by week 8 in 39% vs. 5.3% \((p<0.001)\) and PASI 90 in 17% vs. 2.3% \((p<0.0001)\)

**Key points:**
- Topical treatments continue to be a mainstay in the treatment of psoriasis.
- Topicals are often used in combination treatment with systemics or biologics.
- There are new formulations, fixed combinations, and molecules in the pipeline that are safe, effective, and improve the quality of life for psoriasis patients.

**References:**
As the immunopathogenesis of psoriasis is evolving, new targeted therapies are being developed and show a high safety margin and improved efficacy.

Take away from recent Bimekizumab trials:
- Bimekizumab (IL-17A/F) is superior to adalimumab over 52 weeks (PASI75/90/100/IGA 0/1, phase 3).
- Bimekizumab is superior to ustekinumab over 52 weeks (PASI75/90/100/IGA 0/1, phase 3).
- Bimekizumab is superior to secukinumab over 52 to weeks (PASI75/90/100/IGA 0/1, phase 3).
- Bimekizumab improves psoriatic arthritis (ACR 20, week 12, phase 2b).
- Safety/possible safety signals for:
  - Mucocutaneous candidiasis is common (15%), with most cases being mild to moderate and manageable (reported with other IL-17 blockers).
  - Inflammatory bowel disease is rare (reported with other IL-17 blockers),
- Data for up to 2 years have revealed no new safety concerns and is durable over two years.

Take away from recent Deucravatcitibinib trials:
- Deucravatcitibinib is superior to apremilast (PASI 75, week 16, phase 3)
- Good efficacy (less than most biologics) but better than oral drugs currently on the market
- Safety improved from other JAK inhibitors, except for a slight increase in herpes zoster
- Convenience: once-daily oral drug

Interesting innovations in systemic treatment for psoriasis in earlier stages:
- Sonelokimab (IL-17A/F nanobody) improves psoriasis over 24 weeks (phase 2b).
- Spesolimab (IL-26R antibody) improves generalized pustular psoriasis (phase 2), and can likely be used to abort/prevent flares (not for continued use).

References

5. Armstrong A. *AAD Annual Meeting*, 2021


Psoriasis Basic and Translational Research: Best Papers from the Past Year
Andrew Blauvelt, MD, MBA, IPC Board Member
Oregon Medical Research Center, Portland, Oregon

As the immunopathogenesis of psoriasis is being uncovered, novel therapeutics are emerging. Dr. Blauvelt summarized significant advances in translational science with a focus on therapeutics.

New dual IL-17A/F inhibitors have exceptional efficacy and durable response in plaque psoriasis. Phase 3 trial data show bimekizumab (IL-17A/F) to be superior to the placebos, ustekinumab (IL-12/23), adalimumab (TNFa), and secukinumab (IL-17A only). Notably, Bimekizumab resulted in PASI 100 response to week 52 (Figure 4). Phase 2b data shows sonelokimab (nanobody anti-IL-17A/F) having an IGA 0,1 response in up to 85% of patients.

![Figure 4](image.png)

Figure 4. PASI 100 response to week 52. PASI 100= 100% improvement from baseline in Psoriasis Area and Severity Index. Taken from Reich et al. Lancet 2021
In a recent proof-of-concept clinical trial, spesolimab (anti-IL-36 RA) showed rapid clearance of guttate pustular psoriasis (GPP) and downregulation of key inflammatory pathways.

Tapinarof is a novel topical therapeutic aryl hydrocarbon receptor (AhR)-modulating agent that downregulates IL-17 and promotes skin barrier normalization with antioxidant activity. Phase 3 trials have shown efficacy and tolerability of tapinarof in plaque psoriasis, representing an important advance in the development of topical medicine.

Galectin-7 is an anti-inflammatory protein that abrogates IL-17-mediated inflammation in keratinocytes and is decreased in psoriasis lesions. Interestingly, fluvastatin and simvastatin increase galectin-7 production and decrease psoriasis-like disease in mice, suggesting statin medications may be useful in psoriasis treatment.

The use of biologics in psoriasis patients diagnosed with COVID-19 has been intensely debated. Recently, the main COVID-19 receptor, ACE2, was shown to be overexpressed in psoriasis lesions and associated with IL-17 mediated inflammation. Secukinumab treatment lowered ACE2 expression, suggesting untreated inflammatory disease might lead to increased risk or severity of the COVID-19 infection.

The durability of response is an important unmet need in psoriasis management. A negative but important trial was recently published in JAMA Dermatol, showing that costimulatory CD28/B7 signaling with abatacept did not suppress the psoriasis molecular signature or prevent psoriasis relapse after ustekinumab withdrawal. This data suggests clinical relapse may involve other T cell activation pathways.

Key points:
- Dual IL-17A/F inhibition shows superiority in the treatment of plaque psoriasis compared to IL-17A alone, IL-12/23, and TNFa-inhibitors.
- Tapinarof is a novel topical AhR-modulating agent that is safe and efficacious in plaque psoriasis.
- Untreated psoriasis may increase the risk of COVID-19 severity

References:


New Developments in Psoriasis Comorbidity and COVID-19
Joel M. Gelfand, MD, MSCE, IPC Board Member
The University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania, United States

An increasing number of risk factors for psoriasis comorbidities are being reported. A recent study showed skin activity correlates with psoriatic arthritis (PsA) risk (for every 1% BSA, there is a 2% risk of PsA). Multiple studies are being published that aim to answer whether biologic treatment of psoriasis can reduce risk, yet results vary, and RCT is needed.1,2,3

There is a long-standing belief that patients with psoriasis are more prone to liver disease, yet direct evidence supporting this was lacking. A recent study large population-based study revealed psoriasis and PsA influence liver disease, independent of other major risk factors.4

Cardiovascular (CV) disease is an important comorbidity in psoriasis and PsA. In a recent meta-analysis, authors show a strong reduction in blood-based cardiometabolic risk biomarkers with adalimumab (improved CRP, TNF-a, IL-6, and GlycA) and phototherapy (improved CRP and IL-6). Only ustekinumab improved aortic vascular inflammation.5 Other studies suggest biologic treatment of psoriasis is associated with a reduction in coronary inflammation6 and improvement of coronary plaques.7

There have been recent initiatives aimed to increase dermatologists’ participation in CV prevention in psoriasis patients. Work is ongoing to develop a centralized care model to improve patient outcomes.

Guidelines for care of psoriasis patients on systemic nonbiologic therapies8 and CVD9 are referenced below.

The latest COVID-19 data in clinical decision making for psoriasis patients summarized below:10
- Patients who are not infected with SARS-CoV-2 or receiving mRNA vaccine/booster should continue their biologic or oral therapy for psoriasis and/or PsA in most cases.
- Untreated psoriatic disease is associated with a serious impact on health and can lead to permanent joint damage and disability.
- Consider holding methotrexate x2 weeks post booster.

References:


Updates on Topical Therapies for Psoriasis
April W. Armstrong, MD, MPH, IPC Councilor
Keck School of Medicine, USC, Studio City, California, United States

Topical therapies are the most used agents to treat patients with mild to moderate psoriasis and are important adjuncts to phototherapy, systemic, or biologic agents in moderate to severe disease.

A recent phase 3 trial demonstrated proactive management with a combination of calcipotriene/betamethasone dipropionate foam twice weekly, proving superior efficacy and an additional 41 days in disease remission when compared to reactive therapy.¹

Fixed-dose combinations of topical therapeutic agents may optimize efficacy and minimize safety and tolerability concerns. Halobetasol propionate 0.01%/tazarotene 0.045% lotion applied twice daily was superior to a vehicle with 45% of patients showing clinical improvement at week 8.² Another combination of calcipotriene/betamethasone dipropionate foam once daily was well tolerated and resulted in 54% success at week 4.³

Combination agents are often limited by pH incompatibility. New vehicles utilizing PAD™ technology, a new method of mixing oil and water using low levels of surfactant, allow for solubilization and stabilization of active compounds with less irritation (Figure 5). A phase 3 trial of CAL/BDP-cream is superior vs. active control, with 43% of patients on combination achieving a clear or almost clear endpoint and a 2-point reduction in PGA score.⁴ Head-to-head study of CAL/BDP PAD-cream vs CAL/BDP topical suspension showed cream offers improved quality of life and treatment satisfaction for patients.³

Figure 5. Schematic of PAD-Technology in oil-in-water droplet taken from Armstrong et al. JEADV 2022
Systemic oral phosphodiesterase type 4 (PDE-4) inhibitors have been effective in the treatment of psoriasis. In the phase 3 study, topical PDE-4 inhibitor roflumilast 0.3% cream was superior to a vehicle, with 42% of patients achieving the primary endpoint of clear or almost clear by week 8.4

Key points:
- Proactive topical treatment increases efficacy and disease remission compared to reactive therapy.
- Fixed-dose combinations may optimize efficacy and minimize safety and tolerability concerns.
- New vehicles, including PAD, allow increased solubilization and pH stabilization and result in improved treatment satisfaction for patients.

References:
Psoriasis: Biologics
Jashin J. Wu, MD, IPC Councilor
Dermatology Research and Education Foundation, Irvine, California, United States

IL-17 inhibitors:
- Secukinumab (IL-17A) is approved for moderate to severe plaque psoriasis and psoriatic arthritis (PsA). In 2021 it was approved for patients >6 yo with weight-based dosing. Phase 3b trial shows efficacy in treating palmoplantar pustular psoriasis with a 75% reduction in palmoplantar pustular psoriasis area severity index (ppPASI75) at week 16.¹
- Ixekizumab (IL-17A) is approved for moderate to severe plaque psoriasis and PsA. It was recently approved for moderate to severe plaque psoriasis in children 6-17. A 24-week head-to-head comparison showed ixekizumab was non-inferior to guselkumab (50% vs. 52%, difference -23%), with no difference in PASI100.²
- Brodalumab (IL-17RA) is approved for moderate to severe plaque psoriasis and is the only biologic where patients need to have failed other systemic therapies.³ There is a black box warning about suicidal ideation and behavior.
- Bimekizumab (IL-17A/F) is an upcoming therapy not yet FDA approved. Head-to-head showed PASI 100 of 73.5 in bimekizumab vs. 48.3 in secukinumab (p<0.001).⁴

IL-23 inhibitors:
- Guselkumab (IL-23) is approved for moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy and PsA. 2 ongoing trials (VOYAGE 1 and VOYAGE 2) with efficacy PASI 90 in 81.8% treatment vs. 50.5 in placebo.⁵
- Tidrakizumab (IL-23) is approved for moderate to severe plaque psoriasis. 5-year pooled data from resurface 1 and reSURFACE2 showing PASI75/90/100 of 88.7/65.9/32.8.
- Risankizumab (IL-23) is approved for moderate to severe plaque psoriasis and PsA. PASI 90 of 87 in treatment vs 57 in placebo at 52 weeks (p<0.001) and PASI 100 66% in treatment vs 40%.

Which to pick?
- IL-23 inhibitors are Dr. Wu’s first-line biologics for the 70% without psoriatic arthritis.
- IL-17 inhibitors, certolizumab, or adalimumab are Dr. Wu’s first-line biologics for the 30% with psoriatic arthritis.
- Not much etanercept or infliximab (except etanercept in kids)
- Severe flare- cyclosporine at 5mg/kg/day.
- If worried about adverse events, it is recommended to use acitretin and UVB.
References


Generalized pustular psoriasis (GPP) is a rare and often life-threatening inflammatory disease characterized by episodic pustule development and systemic inflammation that occurs with or without plaque psoriasis vulgaris (PV). Stimuli for GPP flares include medications, infections, and pregnancy.

To date, there are no federally approved therapies for GPP in the United States or Europe. Cyclosporine at 3-5 mg/kg/day is a simple and effective treatment for a short duration and is often used in the setting of severe or recalcitrant disease, and is safe (category B) in pediatric and pregnant patients. Limited studies in Japan have resulted in the approval of secukinumab, ixekizumab, and guselkumab. A case series suggested infliximab is efficacious for GPP and may have sustained results for some patients.¹,²

Gene mutations in the IL-36 cytokine, such as loss-of-function mutations in the IL-36 receptor and overexpression of IL-36, have been discovered in patients with GPP.³ Overexpression of IL-36 itself may explain the subset of patients that develop both plaque and pustular disease.⁴ Innovative therapies targeting IL-36, including imsidolimab and spesolimab, are currently undergoing phase II and III clinical trials, with promising results (Figure 6).⁵,⁶

Figure 6. Response to treatment of GPP patients using IL-36 inhibition. From Bachelez et al. NEJM 2019
Key points:
- Pustular psoriasis is a potentially life-threatening condition and is distinct from plaque psoriasis vulgaris.
- IL-36 is a central cytokine in the pathogenesis of pustular psoriasis, and a mutation in IL-36 RN is present in some patients.
- Currently, there are limited biologic treatment options, including IL-17, IL-23, and TNF blockers.
- IL-36 antagonists are in development and show promising efficacy in generalized pustular psoriasis.

References
Patients with psoriasis are at increased risk for comorbid conditions. Treatment regimens for psoriasis patients should be tailored to meet specific needs based on disease severity, the impact on quality of life, the response to previous therapies, as well as the presence of comorbidities.

Dr. Lebwohl summarized the current data on psoriasis therapy by focusing on the common comorbidities of psoriatic arthritis (PsA) and obesity and provides an evidence-based insight to choose appropriate systemic treatment. The high-yield chart below is modified from his talk and Kaushik et al, *JAAD* 2019, with a focus on PsA and obesity.

### Comorbid conditions to consider when selecting systemic psoriasis treatment:

<table>
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<tr>
<th>Class of drugs</th>
<th>Drug/comorbidity</th>
<th>PsA</th>
<th>Obesity</th>
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<td>TNFα inhibitors</td>
<td>Etanercept</td>
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<td>Adalimumab</td>
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<td>Mease et al. <em>Arthritis Rheum.</em> 2005</td>
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<tr>
<td></td>
<td>Golimumab</td>
<td>++</td>
<td>+</td>
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<tr>
<td>Anti-IL-17A inhibitor</td>
<td>Secukinumab</td>
<td>++</td>
<td>++</td>
<td>McInnes et al. <em>Lancet</em> 2015</td>
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<tr>
<td>Anti-IL-17A inhibitor</td>
<td>Ixekizumab</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Anti-IL-17 receptor</td>
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<td>Methotrexate</td>
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<td>Cyclosporine</td>
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<tr>
<td></td>
<td>Acitretin</td>
<td>+/-</td>
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Note: Two plus symbols (+++) indicate preferred agents; one plus symbol (+) indicates that the agent can be used; one plus symbol and one minus symbol (+/-) indicate that the drug can be used but is controversial, one question mark (?) indicates that there are not enough data, and x indicates that a drug is contraindicated.
Psoriasis: Comorbidities
Wilson Liao, MD
University of California, San Francisco, San Francisco, California, United States

Approximately 1/3 of patients with psoriasis will develop psoriatic arthritis (PsA), and early detection and treatment are important to prevent long-term morbidity. Cardiovascular disease (CVD) is another common comorbidity in psoriasis, and the risk is independent of traditional CVD risk factors.

Many significant comorbidities are related to metabolic syndrome and, subsequently, insulin resistance. The prevalence of non-alcoholic fatty liver disease (NAFLD; driven by obesity) is 1.5-3 times higher in psoriasis. Sleep and mood disorders are also increased in prevalence in psoriasis.

The pathogenesis of these comorbidities is multifactorial. Certainly, shared cytokines or ‘cross-talk,’ mainly via TNFa, IL-17, and leptin, play a role. Patients with PsA and inflammatory bowel disease (IBD) but also CVD share similar susceptibility loci, suggesting genetics may increase the risk of both diseases. Interest in environmental triggers, including the gut microbiome, has accelerated as research shows a profile of gut flora in psoriasis is similar to IBD. The clinical implications and role of treatment in comorbid conditions are largely unknown.

Some studies suggest treatment of psoriasis reduces the risk of CVD. TNFa inhibitors and MTX have the most evidence to reduce the risk of CVD in psoriasis. Biologic therapies did not show benefit in aortic imaging studies. Anti-inflammatory medications such as colchicine may have some benefits (hazard ratio of 0.77). In patients who had an MI and elevated CRP, IL-1b inhibitor canakinumab was also shown to reduce risk.

Though psoriasis patients have increased CVD risk, many are not adequately managed. A recent survey suggests that dermatologists may be able to bridge this gap in care by providing screening and management recommendations.

Key points:
- PsA is prevalent in psoriasis patients, and prompt diagnosis is vital to prevent poor outcomes
- Pathogenesis of comorbidities in psoriasis is complex and includes shared cytokines, genetics, and environmental factors
- Treatment with MTX and certain biologics may reduce cardiovascular comorbidities
- Dermatologists can take an active role in screening and management of these comorbidities

References:


Psoriasis: Topical Therapy, Oral Therapy, and Phototherapy
George Han, MD, PhD
Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Uniondale, New York, United States

What is new in topicals?

Topicals may be helpful as monotherapy for limited BSA or for patients who cannot or wish not to go on systemic medication. Innovations in combination creams, including Halobetasol/tazarotene lotion, allow for synergistic efficacy and counteraction of concerning side effects such as irritation and skin atrophy. An additional benefit of Halobetasol/tazarotene is the elimination of HPA axis suppression, allowing for long-term use. A recent phase 2b study showed Rulumilast cream (PDE-4 inhibitor) resulting in IGA of clear or almost clear (28% on treatment, 8% placebo) at week 6 with improved tolerability compared to other topical PDE-4 inhibitors.1

What is new in oral agents?

Advances in oral therapy include new FDA indications for treating mild to moderate psoriasis with apremilast. Deucravacitinib (allosteric inhibitor of TYK2) broadens the narrow therapeutic window seen with JAK inhibition and is an exciting emerging target. Phase II trials of deucravacitinib show 3 mg BID is similar to 6 mg BID in efficacy (PASI75 69% vs 67%, respectively) with a good safety profile. Studies also indicate that deucravacitinib may be efficacious in treating psoriatic arthritis (ACR20/50/70 of a placebo, 6 mg QID, or 12 mg QD response at week 16). Piclodenison (small molecule inhibitor of Gi protein-associated A3 adenosine receptor) is on par with apremilast in phase III trial.

Other emerging therapies include oral medication LP0200, with a novel mechanism of an IL-17 homodimer that prevents interaction with its receptor. Preclinical trials are ongoing. Early phase data of EDP1815, a monoclonal strain of Prevotella histicola that affects the gut microbiome, show modest improvement with a mean PASI reduction of 16-21%. This medication is not absorbed, thus carrying little to no risk of medications, and results may be durable.

References: