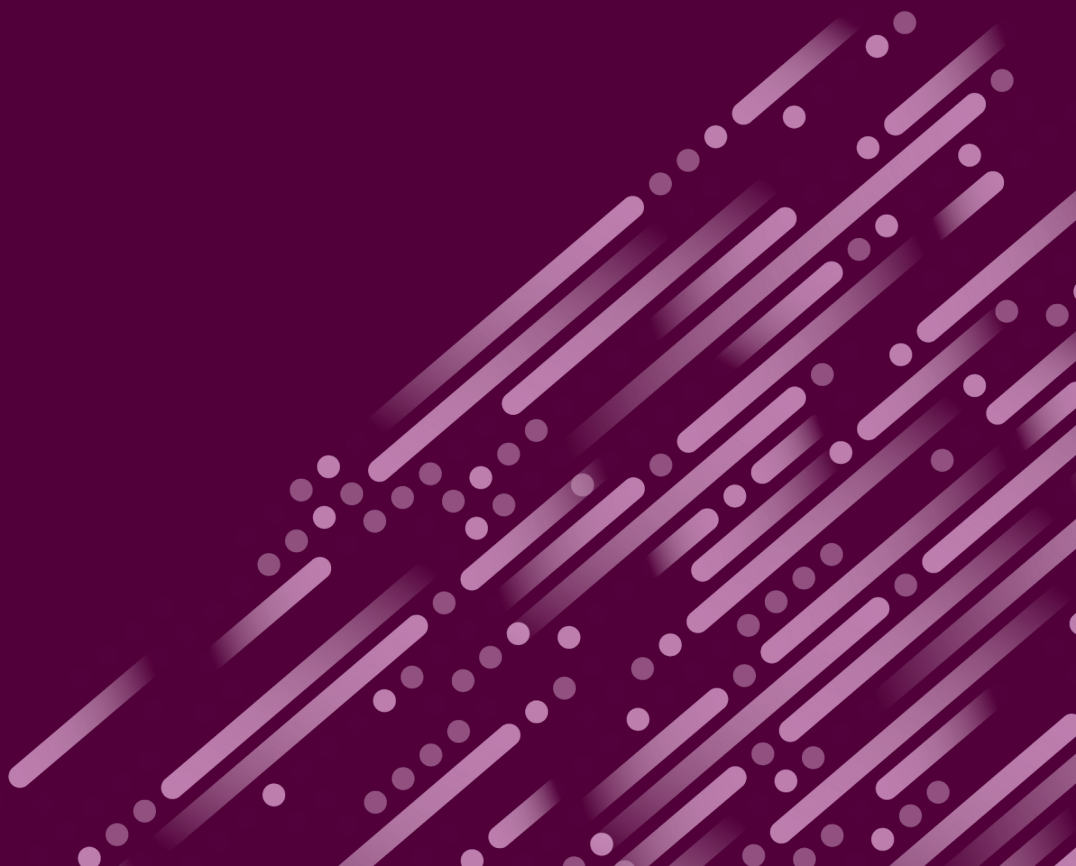
Pharma Intelligence
Informa

The 2021 American Academy of Dermatology (AAD) Conference

Post-Conference Recap



2021 AAD Conference

Post-Conference Recap

The 2021 American Academy of Dermatology (AAD) VMX Conference was held virtually online on April 23rd - April 25th, due to the COVID-19 pandemic. Numerous clinical data readouts were presented, and we summarize some exciting updates and trends from the meeting for several dermatological indications.

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S027 Hot topics in biologics for psoriasis

Dr. Mark Lebwohl (Icahn School of Medicine at Mount Sinai) presented recent results on psoriasis biologics in the S027 session on Hot Topics. Highlights from each drug have been bulleted below.

- etanercept
  - oldest biologic we have for psoriasis
  - longest and most data on its use in children
  - well tolerated by children
- adalimumab
  - also has excellent pediatric data
  - 4 and .8 mg doses are both superb for pediatrics
- infliximab
  - several biosimilars in widespread use
  - comparable efficacy and side effects to originator in most studies
- certolizumab
  - main advantage is it doesn't cross the placenta
  - growing out longer periods of time
  - most recently approved anti-TNF for psoriasis, but one of the most effective anti-TNFs

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- ustekinumab
  - has the best drug survival among the older drugs
  - also approved for pediatric psoriasis ages 6+
- secukinumab
  - new data reveals better efficacy with more frequent use every 2 weeks (approved for use every 4 weeks)
- ixekizumab
  - approved in pediatrics, efficacy in pediatrics mirrors efficacy in adults
  - side effects of interest include candida and IBD
  - fast for treatment onset
- brodalumab
  - remains the fastest drug for rapid psoriasis treatment
  - remains very effective over 5 years, showing sustained improvement
  - there is a REMS program for suicide, but in the 2 years on the market there have been no suicides, so the black box warning might one day be removed
- guselkumab
  - exciting new data is its use for psoriatic arthritis, respectable ACR20 scores but more importantly, is the signal for significant preservation from joint damage seen via X-ray

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- tildrakizumab
  - has one of the longest durations of remission after stopping treatment
  - similar to other anti-IL-23s, remains effective through five years
  - beats Enbrel substantially, and data shows early treatment in the disease course (<5 years diagnosis) is important
- risankizumab
  - this is one of the most effective drugs we have for psoriasis
  - substantial PASI90 and PASI 100 are maintained through 172 weeks of follow up
- mirikizumab
  - anti-IL-23 not yet on the market
  - similar efficacy to Cosentyx at week 16, but more so at one year (anti-IL-23s are somewhat slow, but eventually get there)
  - cross-trial comparisons show that mirikizumab should fare well compared to the other IL-23 blockers
- bimekizumab
  - one of the most exciting new drugs coming out
  - not only blocks IL-17A but also IL-17F for substantially better responses in both PASI and ACR
  - dramatically effective drug for psoriatic arthritis (ACR70 of 45.9%)

- spesolimab and imsidolimab
  - target IL-36
  - identified as playing a major role in pustular psoriasis
  - spesolimab, by week 1, after the first IV infusion, almost 2/3rds of patients are clear or almost clear, by week 4, its 100%
  - imsidolimab has less data, but showed 60% reduction in BSA by day 8 and 94% by day 29

JAKs

26237: Baricitinib, an Oral, Reversible Janus Kinase-1 and -2 Inhibitor, for Atopic Dermatitis: Head and Neck Response from BREEZE-AD5

This post-hoc analysis of the BREEZE-AD5 study evaluated the efficacy of baricitinib in treating atopic dermatitis with head/neck involvement. At baseline, 93.0% of patients had head/neck involvement. At week 2, EASI head/neck mean percent change from baseline was –37.1% baricitinib 2-mg and – 15.0% placebo (P=.0014). At weeks 2 and 16, EASI50 head/neck region response rates were higher with baricitinib 2-mg (39.7%, 29.5%) vs. placebo (22.4%, 12.9%; P=.0017 and P=.0008, respectively). At weeks 2 and 16, EASI50 head/neck erythema

score response rates were higher with baricitinib 2-mg (26.7%, 25.3%) compared to placebo (15.0%, 7.5%; P=.0145 and P<.0001, respectively). Baricitinib responded in head/neck with the same order of magnitude as whole body areas.

26884: Ruxolitinib Cream Rapidly Decreases Pruritus in Atopic Dermatitis: Pooled Results From Two Phase 3 Studies

Ruxolitinib cream is a JAK1/JAK2 inhibitor in development for atopic dermatitis. Pooled results from the identically designed TRuE-AD1 and TRuE-AD2 (N=1249 in both studies combined; mean itch NRS score, 5.1). Significantly greater itch reductions were observed by itch NRS within 12 hours of the first ruxolitinib application (mean change from baseline, –0.4 and –0.5 for 0.75% ruxolitinib and 1.5% ruxolitinib, respectively) vs vehicle (–0.1; all P<0.02). Among patients with baseline itch NRS ≥4, clinically meaningful (≥4-point) reduction in itch was achieved by significantly more patients who applied 1.5% ruxolitinib vs vehicle ~36 hours after first application (11.2% vs 2.1%; P<0.01); higher rates were observed at Week 8 (51.5% vs 15.8%; P<0.0001).

28194: Patient-Reported Outcomes of Ruxolitinib Cream for the Treatment of Atopic Dermatitis: Pooled Results From Two Phase 3 Studies

Pooled PRO results from the TRuE-AD1 andTRuE-AD2 studies were evaluated. Patients on ruxolitinib reported significant mean change from baseline at week 8 in the POEM (–10.5 for 0.75% ruxolitinib, –11.0 for 1.5% ruxolitinib, and –4.2 for vehicle; both P<0.0001), DLQI (–7.2/–7.1 for 0.75%/1.5% ruxolitinib; vehicle, –3.1; both P<0.0001) and children's DLQI (–5.3 for 0.75% ruxolitinib, –6.0 for 1.5% ruxolitinib, and –2.3 for vehicle; both P<0.01). Significantly greater reductions in skin pain NRS score were observed within 12 hours of the first application of ruxolitinib (P<0.05), with further reductions at week 8 (mean change from baseline, –2.5/–2.6 for 0.75%/1.5% ruxolitinib) vs vehicle (–1.3; both P<0.0001). Significantly more patients on ruxolitinib reported much or very much improvement in their Patient Global Impression of Change at week 8 (80.0%/84.9% for 0.75%/1.5% ruxolitinib; vehicle, 41.3%; both P<0.0001).

27620: Effects of Ruxolitinib Cream in Patients With Atopic Dermatitis With Baseline Body Surface Area =10% and Eczema Area and Severity Index Score =16: Pooled Results From Two Phase 3 Studies

Efficacy and safety of ruxolitinib cream was investigated in the TRuE-AD1 and TRuE-AD2 trials. Pooled data from these studies in a subpopulation of patients with BSA ≥10% and EASI ≥16 at baseline (n=81) shows higher response rates were with ruxolitinib vs vehicle for IGA-treatment success (50.0%/59.4% vs 0%), ≥75% improvement in EASI from baseline (75.0%/71.9% vs 7.7%), and a ≥4-point reduction in itch NRS score (50.0%/61.1% vs 27.3%).

Biologics

26880: Long-Term Efficacy and Safety Data for Dupilumab in a Phase 3, Open-Label Extension Trial (LIBERTY AD PED-OLE) in Patients Aged =6 to <12 Years With Uncontrolled, Moderate-to-Severe Atopic Dermatitis (AD)

Patients aged ≥6 months to <18 years with moderate-to-severe atopic dermatitis who had participated in a previous dupilumab

study were enrolled in the ongoing, long-term LIBERTY AD PED-OLE trial. Looking at IGA score of 0/1 at OLE baseline, one month, and one year showed rates of 18%, 24.6%, and 44.1%, respectively. At OLE baseline, 41.2% of patients achieved ≥75% reduction in EASI relative to parent study baseline, increasing to 54.4% at one month, and 79.4% at a year. The most common treatment-emergent adverse events were atopic dermatitis exacerbation (15.5%), and nasopharyngitis (13.0%), with 2.5% of patients having had a serious AE.

270138: Efficacy of Guselkumab Using Composite Endpoints in Patients With Active Psoriatic Arthritis: Domain-Specific Efficacy From DISCOVER-1 and DISCOVER-2 Phase 3 Trials

The efficacy of guselkumab in patients with active PsA was evaluated through week 24 utilizing in the DISCOVER-1 and DISCOVER-2 studies. DISCOVER-1 (N=381) entry required ≥3 swollen and ≥3 tender joints and CRP ≥0.3 mg/dL; DISCOVER-2 (N=739) required ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL. Across studies, differences between guselkumab and placebo were observed as early as Week 8 and continued to increase over time when response was assessed using joint-

focused Modified Psoriatic Arthritis Responder Criteria (mPsARC) or Disease Activity Index for Psoriatic Arthritis (DAPSA) Low Disease Activity remission composite endpoints. Further, response rates determined by omitting CRP in calculating clinical DAPSA (determined by excluding CRP) were similar to DAPSA results. Higher proportions of patients treated with guselkumab monthly or every other month as compared to placebo-treated patients also achieved Psoriasis Disease Activity Score (PASDAS) (28% and 30% vs 9%), Minimal Disease Activity (MDA) (23% and 24% vs 8%), Very Low Disease Activity (VLDA) (6% and 4% vs 1%), and remission determined using either DAPSA (10% and 8% vs 2%) or cDAPSA (13% and 9% vs 3%).

27434: Early Trends of Disease Improvement in Adult Patients With Atopic Dermatitis Treated With Dupilumab: Real-World Data From the PROSE Registry

Early trends of the initial six months of real-world dupilumab treatment from an interim analysis of patients in the US/ Canadian PROSE registry were released. 315 patients were enrolled (data cutoff: July 2019). At baseline, mean EASI was 16.9, which decreased to 4.4 by month 6.

Baseline mean body surface area affected by AD of 26.8% decreased to 7.2%. Baseline mean POEM was 18.5, which decreased to 6.9. Baseline mean peak pruritus NRS score of 6.9, decreased to 2.5. Mean DLQI decreased from 12.7 at baseline to 4.4 month 6.

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27533: Comparative Efficacy and Safety of Systemic Therapies Used in Adult and Adolescent Moderate-to-Severe Atopic Dermatitis (AD): A Systematic Literature Review (SLR) and Network Meta-Analysis (NMA)

Considering the lack of head-to-head trials of systemic therapies in atopic dermatitis, this Pfizer-sponsored network meta-analysis looked at systemic therapy in published research for atopic dermatitis. This analysis of 19 published Phase II or III randomized controlled trials conducted through October 24, 2019 involved abrocitinib, baricitinib, dupilumab, lebrikizumab, nemolizumab, tralokinumab, and upadacitinib. In monotherapy use, once-daily 30 mg upadacitinib was associated with the numerically highest rate of treatment efficacy (51.6% achieving EASI 90; once-daily 15 mg upadacitinib was 34.5%), followed by once-daily 200 mg abrocitinib (39.2%; once-daily 100 mg abrocitinib was 22.2%), and biweekly 200 mg dupilumab (27.6%). For combination therapy use, the abrocitinib regimen was associated with a 48.7% rate of EASI 90. Other efficacious combinations included dupilumab (41.7%) and once-daily 100 mg abrocitinib (37.9%).

To conclude, abrocitinib, dupilumab, and upadacitinib were consistently the most effective systemic therapies in adults and adolescents with atopic dermatitis. Abrocitinib and dupilumab

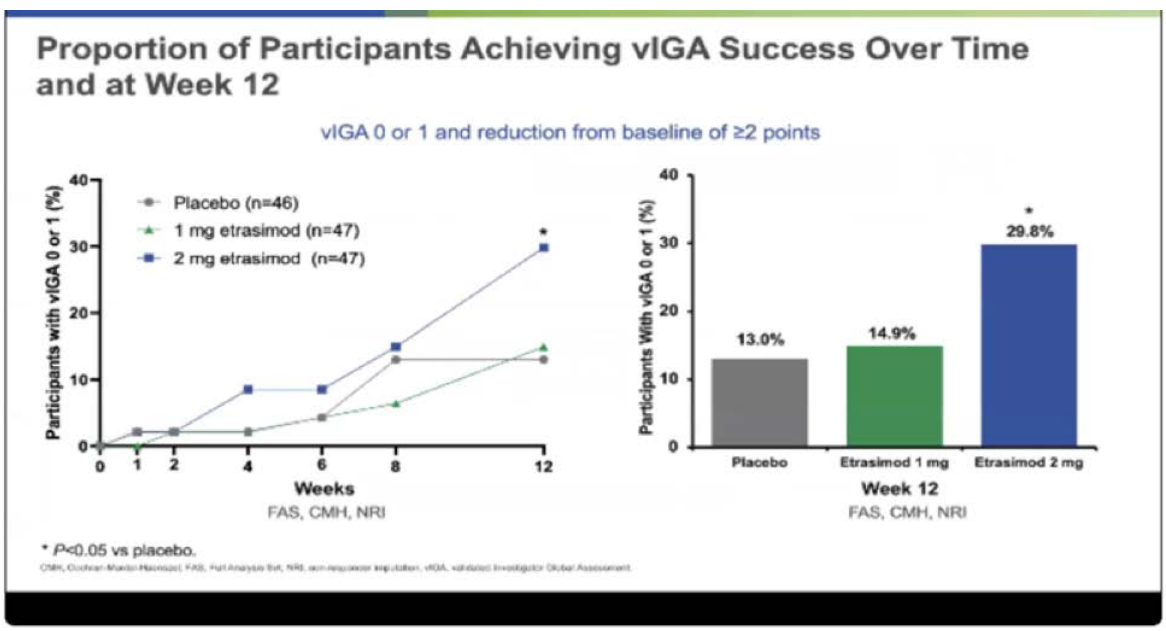
combination therapy demonstrated the greatest efficacy, and there was no significant difference in treatment-emergent adverse events in these short-term randomized controlled trials, although there were some numerical increases observed.

S033 Late breaking abstract: Etrasimod, a novel, oral, selective sphingosine 1-phosphate receptor modulator, improves patient and clinician reported outcomes in adults with moderate-to-severe atopic dermatitis in a randomized, double-blind, placebo-controlled phase 2 study (ADVISE)

Dr. Emma Guttman-Yassky (Icahn School of Medicine at Mount Sinai) reported on secondary endpoint results from the Phase II ADVISE study evaluating once daily oral S1P receptor modulator, etrasimod, in atopic dermatitis. S1P1 modulation with etrasimod may interrupt multiple pathways that mediate acute and chronic disease phases of atopic dermatitis. According to preclinical data, etrasimod disrupts immune cell trafficking, including reducing the migration of lymphocytes like T cells, B cells, and eosinophils, to the skin, thus reducing inflammation.

The Phase II ADVISE study of etrasimod was the first to evaluate S1P receptor modulation as a potential mechanism for

treatment of patients with moderate-to-severe atopic dermatitis. ADVISE was a 12-week study randomizing patients to 1mg, 2mg etrasimod or placebo. Patients could be enrolled in an open label extension. The primary endpoint was percent change in EASI from baseline to week 12. Baseline characteristics show that patient demographics were well balanced across the arms in the 140 patient study. The break down also shows that the majority of patients had moderate, rather than severe, disease.



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Results show that at week 12, 29.8% of patients who received etrasimod 2 mg achieved vIGA 0/0, while 14.9% for etrasimod 1 mg and 13.0% for placebo. On improvements of ≥4 points in peak pruritis NRS, 42.1% and 32.5% achieved this endpoint on the high and low dose etrasimod, compared to 27.0% on placebo. For DLQI, 85.7% and 82.9% improvements were seen on etrasimod 2 mg and 1 mg, compared to 64.1% on placebo and for POEM, the 2 mg group reported improvements in 73% compared to 80.6% on 1 mg and 43.6% on placebo.