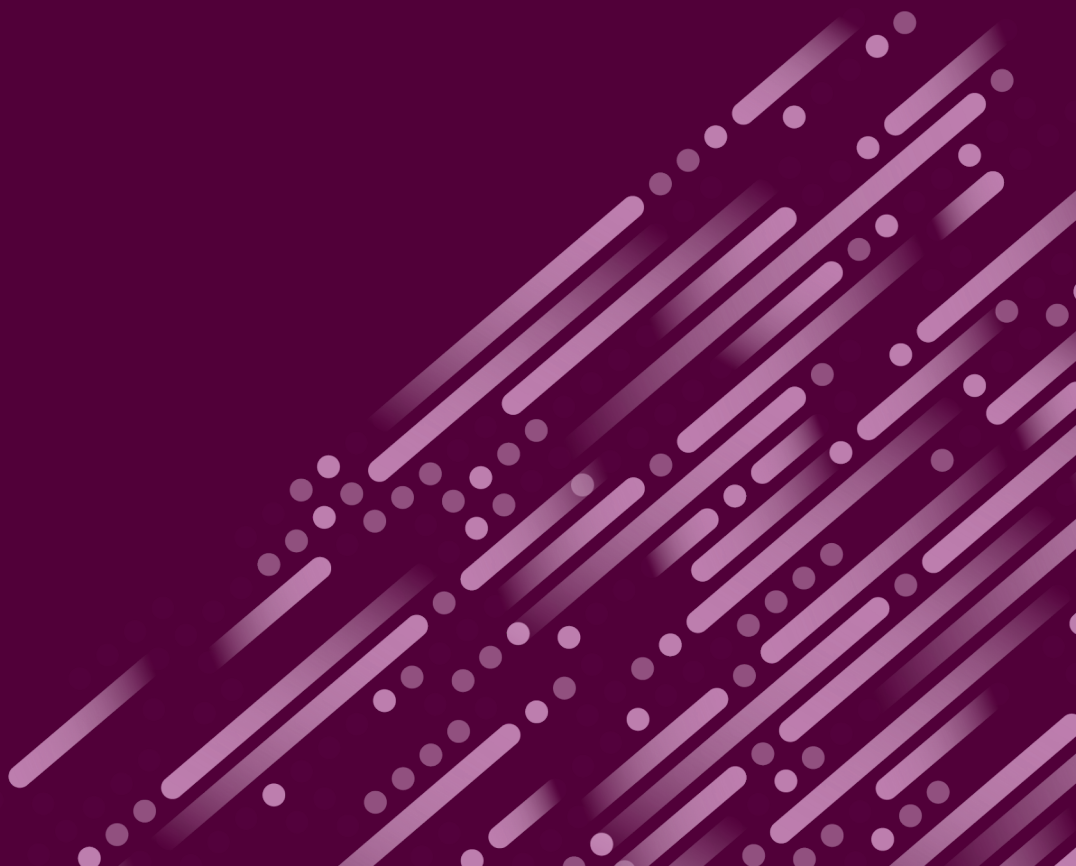
Pharma Intelligence
Informa

The 2021 American Academy of Dermatology (AAD) Conference



2021 AAD Conference

Day 2 Update - Saturday April 24, 2021

The second day of the 2021 AAD VMX meeting included On Demand presentations with live Q&A sessions, although technical difficulties were still present, with no ePosters yet available. Various highlights included the release of several late breaking presentations including, but not limited to, a presentation on results from deucravacitinib's Phase III POETYK PSO-1 study, results from the BE RADIANT trial comparing bimekizumab against secukinumab in psoriasis, and results from a Phase 2b trial in atopic dermatitis evaluating the pan-JAK inhibitor delgocitinib.

Select highlights from our team of analysts are below:

2021 AAD Conference

Day 2 Update - Saturday April 24, 2021

S0 ot Topics: What s ne in atopic dermatitis 0

Dr. Emma uttman-Yassky Icahn School of Medicine at Mount Sinai gave an encouraging presentation discussing the various treatments that may soon become available for dermatologists to add to their armamentarium to fight atopic dermatitis.

Atopic dermatitis is the most common inflammatory skin disease that affects of adults in the S and 1 of children. Similar to psoriasis, 20- 0 of patients have moderate-to-severe disease. ntil recently, there was a huge unmet need for better treatment, particularly for chronic use, so long-term disease control as treatments, such as cyclosporin, methotre ate, and azathioprine, have safety concerns. Such drugs are not specific, targeting several cytokines, T cell, and B cells, resulting in unfavorable side effects. More research has led to more specific treatments either approved or in trials for atopic dermatitis.

The Th2 immune a is is the main pathway in the pathogenesis of atopic dermatitis. Dupi ent targets the I - and I -1 cytokines through its action on anti-I - receptor alpha. The SO O-1 and SO O-2 studies evaluating Dupi ent in adults shows EASI rate of 0 with Dupi ent with dosing every 2 weeks. The RONOS

study reveals the long-term safety, including the con unctivitis signal and now some other signals, such as psoriasiform rashes, and some e acerbations of rashes on the face. Overall, however, Dupi ent is very safe for long term use. Importantly, use of Dupi ent doesn't increase infections and, in fact, there is a trend towards fewer skin infections with Dupi ent use. The IBERTY AD PEDS study in children ages to 11 years with severe atopic dermatitis showed that Dupi ent and topical corticosteroids T S achieved results similar to those seen in adults, or even better. Dupi ent is now approved in this age group as well as adolescents.

Recent studies evaluating I -1 inhibition as monotherapy, with tralokinumab and lebrikizumab, are starting to show that controlling the I -1 cytokine alone, without I - , is important in the treatment of atopic dermatitis. Three pivotal E TRA studies conducted with tralokinumab, two without T S and one simulating a real-life situation with T S, showed significance at week 1 on I A 0 1 and EASI- . or safety, there is a hint of con unctivitis, although this appears to be smaller than what is seen with Dupi ent. Similar trends appear to be true for lebrikizumab.

Nemolizumab targets the so-called itch cytokine, or I - 1. A Phase IIb allowing T S shows the efficacy on the disease is modest, with about a 1 difference between nemolizumab and placebo at 2 weeks. nfortunately, the 0mg dose fared better than the 0mg dose, thereby not showing a clear and desired dose response. As e pected, nemolizumab does well on measures of peak pruritus NRS, but the lesser effect on EASI may hinder its potential use. Safety from the Phase IIb study showed some peripheral edema, as well as some asthma events which, as a fre uent comorbid condition, will need to be monitored in Phase III.

Another interesting area of development entails the OX 0 antagonists, BR 0 and K K 0 , which involve regulatory T cells and have the potential to change the way dermatologists' approach atopic dermatitis with disease modifying potential. lenmark's BR 0 has completed a Phase IIa study, in only 2 patients, who only received 2 infusions at day 1 and day 20. The primary endpoint, unusually evaluating change in biomarkers, was achieved. Another study from Japan evaluated Kyowa's K K 0 showing a ma or reduction in EASI after ust three doses, however this study was not placebo controlled.

A press release revealed success in Phase II, with a very early signal of potential disease modification, but more results are needed.

JAK inhibitors generate a lot of e citement because atopic dermatitis is a heterogenous disease and JAK inhibitors target several key cytokines in the disease. Among the various oral candidates, JAK1 2 inhibitor baricitinib, Pfizer's JAK1 abrocitinib, and AbbVie's JAK1 upadacitinib, AbbVie's drug has uite impressive results with EASI 0 responses over 0 on highest dose. hile safety concerns need to be considered, oral JAK inhibitors are regarded with eagerness and cautious optimism by dermatologists for the treatment of atopic dermatitis. Topical JAK1 2 inhibitor ru olitinib also shows favorable data, though use of the topical will be limited in patients with high BSA involvement. urther data on systemic absorption may also be important for dermatologists to decide on the use of topical ru olitinib, particularly in pediatric patients.

S033 Late Breaker: Bimekizumab efficacy and safety versus secukinumab in patients ith moderate to severe pla ue psoriasis: Results from a multicenter randomized double blinded active comparator controlled phase 3b trial BE R DI T

irst author Kristian Reich niversity Medical enter amburg, ermany presented the first Phase III data in which bimekizumab, an I -1 A inhibitory antibody, is compared directly to an I -1 A secukinumab.

Both I -1 A and are overe pressed in psoriasis and there is increasing evidence that they both have an inflammatory role. As such, optimizing treatment would entail blocking both pathways, fully, in order to ma imize disease control in psoriasis. It has been shown that cytokines I -1 A and I -1 work together as dimers, forming an I -1 A I -1 A homodimer, an I -1 A I -1 heterodimer, or an I -1 homodimer. hile currently available I -1 A inhibitors, osenty and Taltz, can block the I -1 A homodimer and the I -1 A heterodimer to an e tent, by nature they don't block the latter I -1 homodimer.

Thus, B began investigation of the I -1 A antibody, bimekizumab, in psoriasis. BE RADIANT is one of several Phase III

trials, including many head-to-head studies, but is incredibly relevant as it provides evidence that I -1 A inhibition is indeed better than I -1 A inhibition in the treatment of psoriasis. The ob ective of the study was to compare the clinical benefit for patients with psoriasis of bimekizumab versus osenty . The primary endpoint looked at complete disease clearance, or PASI100, at week 1 , but involved measures of safety and efficacy out to week . Secondary endpoints look at the rapidity and durability of response with PASI at week , after ust one dose of bimekizumab, as well as complete disease clearance PASI100 at week .

Bimekizumab 20 mg every weeks was used for the first 1 weeks and then was continued as maintenance dosing either remaining at every or e tending the dosing to every weeks. This option for less fre uent dosing provides a point of differentiation from the currently available I -1 inhibitors, dosed at least once monthly.

The study enrolled patients. 2 of patients treated with bimekizumab achieved the primary endpoint of PASI100 at week 1 compared with of osenty -treated patients, showing an almost 1 difference from this current care option while

reaching statistical significance. At week , the difference in this gap widens to 20 difference between the two drugs, in favor of bimekizumab. Additionally, there doesn't appear to be a ma or difference between maintenance dosing every weeks and the e tended -week dosing. Similar responses were seen with PASI 0 and vI A 0 1.

Bimekizumab also appears to have a much faster onset of action, showing a PASI response rate of 1 at week , after ust a single in ection, compared to with osenty at this time. As for safety, no new safety signals emerged from the BE RADIANT trial. As e pected, bimekizumab showed a higher candida rate compared to osenty . This was mainly true for oral candidiasis, and more than of these oral cases, were mild to moderate and did not lead to treatment interruption. In conversations at the meeting, dermatologists agreed that these results were spectacular and that the need to address candida in 1 of every -10 patients would not limit their prescribing of this drug.

S033 Late Breaker: Visible Light ctivated Topical ypericin intment in CTCL: L S Study Results

DIn a late breaker presentation, Dr. Ellen Kim Penn Medicine presented results from the Phase III AS study. urrent treatment regimens for cutaneous T-cell lymphoma T include topical corticosteroids, topical retinoids, topical chemotherapy, immunotherapy, phototherapy and local radiation. A high unmet need e ists within this indication as there are few large randomized controlled trials comparing these therapeutic agents, and current skin directed therapies have short and long-term adverse effects which limit their use. There is a need therefore, for additional safe and effective therapies that are approved for T .

ypericin is a synthetic version of plant-derived ypericum and has previously been investigated systemically via intravenous and oral routes as well as topical use. The drug as a 0.2 ointment is activated by visible light in the 00- 0 nm spectrum. Once activated, reactive o ygen species are generated leading to localized and directed cellular to icity and subse uent apoptosis. The mechanism of action is non-mutagenic which may help for long-term safety.

MIn the Phase multicenter, randomized, double-blind, placebo-controlled AS study, topical ypericin along with subse uent bulb-light irradiation was evaluated for the treatment of T . The trial enrolled 1 previously treated patients 1 years of age or older with Stage IA, IB, or IIA T , and three inde lesions were treated twice weekly for three cycles weeks on, 2 weeks off . The primary endpoint was an inde lesion response greater than or e ual to 0 decrease in modified omposite Assessment Inde for esion Severity, m AI S, score. After one cycle of treatment, the primary endpoint was met with a statistically significant Inde esion Response Rate m AI S favoring the treatment arm versus placebo 1 vs. , p 0.0 1 . ollowing two cycles, the response rate increased to 0 in the treatment arm and following an optional third cycle, the treatment response rate increased further to . In a cross-trial comparison, Dr. Kim demonstrated that ypericin treatment response rates were similar to topical be arotene gel and mechlorethamine ointment although she also noted that those trials were note placebo-controlled and AI S was utilized as an endpoint.

Safety of ypericin was found to be e cellent with a 2. rate of serious adverse events in the treatment arm and none of them related to ypericin. Study discontinuations due to adverse events in the treatment are were low 1. .

During the Q&A session, Dr. Kim indicated that potential future directions and studies for ypericin include studies evaluating generalized application instead of a specified number of lesions, and assessment of duration of response. Prior to the OVID-1 pandemic, developers planned for this potential treatment to be administered in office, however, post-pandemic there is the possibility of a home light unit for patient self-administration.

S033 Late Breaker: The topical pan inhibitor delgocitinib in a cream formulation is efficacious ith a favorable safety profile: results from an eek phase b dose ranging trial in atopic dermatitis

Professor Jonathan Silverberg eorge ashington niversity presented results from a Phase IIb study evaluating twice daily dosing of 1, , , and 10 mg g of eo Pharma's pan-JAK delgocitinib cream in patients with atopic dermatitis. The primary ob ective was to establish a dose-response relationship and the primary endpoint used was the change in EASI score to week . Key secondary endpoints included vI A-AD treatment success and EASI at week . nderstanding that itch is the most common and burdensome symptom of atopic dermatitis,

patient reported outcomes included itch NRS as recorded in ADSD.

The study only included adults with atopic dermatitis covering between and 0 of treatable BSA at screening and baseline. Overall, 2 1 patients were enrolled who were generally not new to the disease, with a baseline duration of atopic dermatitis of almost 20 years, and had 10 of their BSA affected by the disease.

The change in EASI score showed a separation of all doses from placebo, which occurred fairly early on and lasted through week . The highest dose stood out as having the greatest efficacy on the primary endpoint, but also several other endpoints, such as vI A-AD treatment success and D QI, as well. Results from EASI show a similar separation from placebo as early as week 2. hange from baseline in itch symptom score as a weekly average was significantly lower across delgocitinib doses. Interestingly, the itch daily score shows separation as early as day 2 for the higher doses of delgocitinib.

Delgocitinib was well tolerated, with a safety profile comparable to vehicle. No local or systemic safety signals were identified. The lowest rates of withdrawal from the trial due to adverse events occurred in the high dose 20mg delgocitinib arm.

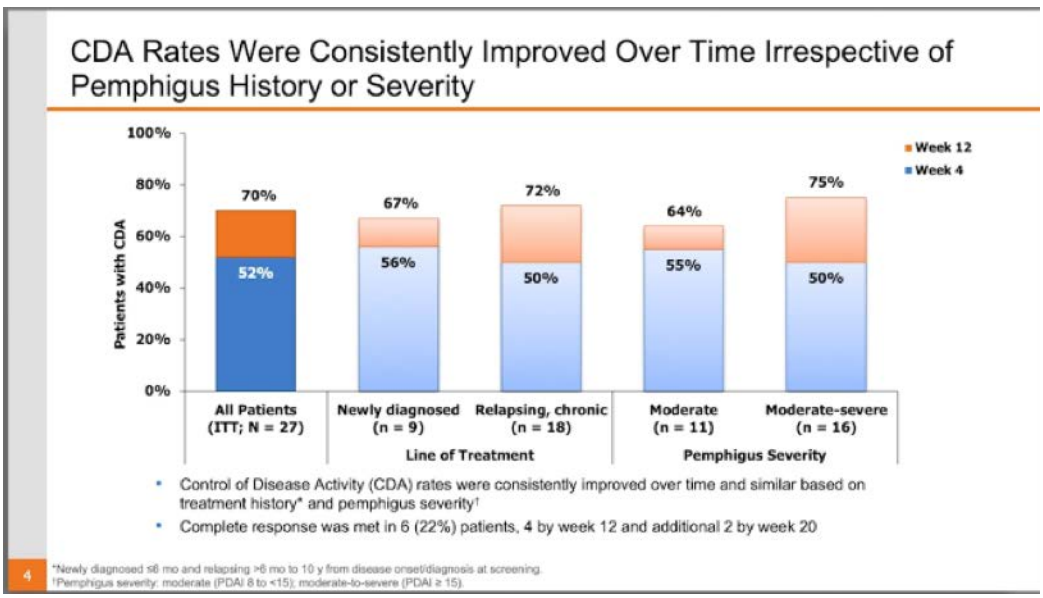
S033 Late Breaker: Treatment With Rilzabrutinib Results in Rapid and Significant Decrease in Steroid Use and Improved Quality of Life in Patients With Chronic Relapsing Pemphigus: BELIEVE Phase II Study

Dr. Dedee Murrell of St. eorge ospital Australia presented positive data from Part A of the open-label proof-of-concept BE IEVE Phase II study evaluating the oral Bruton Tyrosine Kinase BTK inhibitor, rilzabrutinib, in 2 patients with newly diagnosed and chronic relapsing pemphigus vulgaris. This represents the first time a BTK inhibitor has been evaluated in patients with pemphigus and these data provide support for the ongoing Phase PE AS S pivotal study which has completed enrollment.

Patients received 00- 00mg rilzabrutinib twice daily along with or without the use of corticosteroids. The primary endpoint of the study was ontrol of Disease Activity DA at

four weeks while secondary endpoints included omplete Response R rates and Pemphigus Disease Area Inde PDAI after 12 weeks.

The primary endpoint was met at four weeks with 2 of patients achieving DA which improved over time to 0 after 12 weeks of treatment. Improvements were observed regardless of line of treatment or severity of disease. R was met in 22 of patients, four of which achieved R by week 12 followed by an additional 2 patients by week 20.



rom baseline to week 12, the mean PDAI severity scores decreased in both newly diagnosed and relapsing patients, and these improved PDAI scores were also accompanied by reductions in corticosteroid use. urther, clinically meaningful improvements in Quality of ife ABQO scores around points were seen through week 12 with a stabilization of ABQO during the off-treatment period at week 2 , suggesting reduced disease severity.

In terms of safety, the ma ority of treatment-related adverse events TEAEs were low grade 1 2 consisting of nausea and upper abdominal pain events, and rilzabrutinib was generally well tolerated. One patient had treatment-related grade cellulitis that was resolved with treatment and the patient completed the study.

S033 Late Breaker: A Multicenter, Randomized, Open-Label, Phase 3 Long-Term Safety Study of Topically Applied Sofpironium Bromide Gel, 5% and 15%, in Subjects with Axillary Hyperhidrosis

Dr. Stacy Smith (California Dermatology and Clinical Research Institute) presented long-term data from an open-label Phase 3 study evaluating 5% and 15% topical sofpironium bromide (SB) gel, an anticholinergic agent, for patients 9 years of age and older with axillary hyperhidrosis. Although the drug has not yet been FDA approved, it is currently approved in Japan for this indication.

Primary axillary hyperhidrosis is a chronic condition that affects over 10 million individuals in the US alone and 75% of hyperhidrosis patients indicate that the disease has a profoundly negative impact on their social life, wellbeing, emotional and mental health. Unmet needs in this indication

that the disease has a profoundly negative impact on their social life, wellbeing, emotional and mental health. Unmet needs in this indication exist since acute therapies do not address the chronic nature of the disease, nor are they a cure. As a potential long-term treatment, therefore, the main objective of this study was to evaluate the long-term safety and efficacy of sofpironium bromide gel over the course of one year. Of note, this was not a rollover study so patients who were enrolled were naïve to the treatment.

299 patients completed the study and 37 patients discontinued due to adverse events. Overall, 190 patients completed the full 52 weeks of the trial. During the live Q&A session Dr. Smith elaborated that the majority of non-adverse event dropouts in the “other” category were due to patient changes to work schedules or trial site changes for which the patient could no longer participate. In the SB 5% arm, treatment-related adverse events (TEAE) occurred in 22.5% of patients with the majority of them being mild-to-moderate. With the higher percentage formulation (15%) 50.8% of patients experienced TEAEs with the majority being mild to moderate in severity. Serious adverse events occurred at a rate of 1% and 2% in the SB gel 5% arm and SB gel 15% arm, respectively. Investigators found that the incidence of subjects with any TEAEs in both treatment arms decreased over time which was expected given enrolled patients were initially treatment naïve. In the SB 15% arm, the incidence of discontinuations due to TEAEs decreased over time, however discontinuations in the SB 5% arm increased from 6-12 weeks before decreasing.

Anticholinergic adverse events were mostly mild or moderate in severity and transient in nature, and occurred in 15.7% and 28.4% of patients in the SB 5% and SB 15% arms, respectively. The most common of these included blurred vision and dry mouth. The incidence of discontinuations due to anticholinergic TEAEs also trended towards decreasing over time as patients acclimated to treatment.

Efficacy measurements were found to be clinically meaningful with significant reductions in sweat severity as measured by the Hyperhidrosis Disease Severity Measure scale (HDSM-Ax) which improved over time. Of note, over 80% of patients experienced a clinically meaningful improvement over 48-week time period.

During Q&A, Dr. Smith indicated that compared to Botox, SB gel would be a better solution for patients who are risk-averse to injections, and that he expects market access and reimbursement to favor SB gel over Botox. Stepwise measures are likely to be implemented, however, due to this drug being the 2nd potential anticholinergic on the market.