TRENDS-in-MEDICINE

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by Ed Susman

INFLAMMATORY SKIN DISEASE SUMMIT (ISDS): ATOPIC DERMATITIS
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SUMMARY

Early data on three topical agents to treat mild-to-moderate eczema (atopic dermatitis) were presented at the meeting, each with a different method of action. It's too early to compare them, but any agent that works would be appealing to patients.

While systemic biologic agents dominate research for treatment of atopic dermatitis (AD), most patients would rather use an effective ointment or cream to control their disease – but the key word is effective, and few of those types of treatments are available for mild-to-moderate disease.

However, researchers rolled out data at ISDS on some new topical treatments for AD that are in the early stage of development. In commenting on the studies, session co-chair Robert Bissonnette, MD, president of Innovaderm Research, a clinical research organization in Montreal, Canada, said, "What I like about these presentations…is that it shows the interest of the pharmaceutical industry in developing new topical drugs for atopic dermatitis. Right now we have nothing in Phase III development in the form of a cream or an ointment, and this is what most patients need, what most physicians prescribe, and what general practitioners prescribe…These were all early phase studies, but they all suggested efficacy, so that is good. Which one is better and which will get approved, I don't know."

NOVAN's SB-414 – a topical nitric oxide-releasing cream

Novan researchers reported that in a 48-patient, 2-week, double-blind Phase Ib trial this nitric oxide-releasing cream trended towards a benefit in reducing pruritus among patients with mild-to-moderate atopic dermatitis.

Tomoko Maeda-Chubachi, MD, PhD, vice president of medical dermatology for Novan, and colleagues planned the study after promising preclinical results. Dr. Maeda-Chubachi enrolled 14 patients who received an inactive vehicle cream, 17 patients who received SB-414 2% cream BID, and 17 patients who received SB-414 6% cream BID.

The researchers assigned the 2% cream to patients with less severe atopic dermatitis – those having a mean EASI (Eczema Area and Severity Index) score of 4.7, while the 6% cream was given to patients with a mean EASI score of 7.2.

The mean decrease in EASI score was 1.2 in the low-dose patients and 1.60 in the high-dose group. In just 2 weeks, 4 patients achieved an EASI-50, and 2 patients achieved an EASI-75 in the high-dose group. Dr. Maeda-Chubachi said, "SB-414 demonstrated trends suggestive of efficacy, and it displayed an improvement on the pruritus numeric rating scale compared to vehicle."

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Five patients – 2 in the placebo group, 2 in the high-dose SB-414 group, and 1 with low-dose SB-414 – did not complete the study. There was 1 recorded adverse event in the placebo group and 2 in the high-dose SB-414 group.

DS BIOPHARMA's DS-107 – oral and topical bioactive lipid immunomodulator

In the 8-week, 326-patient, double-blind Phase IIb ADVANTAGE trial in mild-to-moderate AD, presented in a session dedicated to topical treatments, a 5% topical formulation of DS-107, a synthetic bioactive lipid immunomodulator, outperformed placebo on the Investigator's Global Assessment (IGA). And there was a dose-dependent response. Moayed Hamza, MD, associate medical director of DS Biopharma, said this drug showed positive benefits to patients with mild-to-moderate atopic dermatitis even after the treatments had ended.

In the study, 107 patients were randomized to DS-107 5% BID, 110 patients to DS-107 1% BID, and 106 patients to a vehicle cream. After 8 weeks there was a numerical advantage to being treated with the 5% cream, with 30.3% of patients in that group achieving a ≥2-point reduction in IGA vs. 18.8% of placebo patients ($p=0.142$). However, at the 10-week assessment, two weeks after stopping treatment, 32.5% of 5% DS-107 patients achieved a ≥2-point reduction in IGA, showing that the treatment effect had not reached a plateau. In contrast, placebo patients who achieved that goal declined to 16%, and the difference was significant ($p=0.029$).

Dr. Hamza said, "Clinically meaningful improvements of atopic dermatitis scores and indexes including pruritus were recorded at each time point during this study…A Phase III study is ready to begin."

ROIVANT SCIENCES/DERMAVANT SCIENCES' cerdulatinib (RVT-502) – a topical JAK/Syk inhibitor

In a single-arm, 2-week Phase Ib trial, this topical agent, a dual Janus kinase/spleen tyrosine kinase inhibitor, appeared to reduce parameters of atopic dermatitis in 8 patients diagnosed with mild-to-severe forms of the disease. Despite the small number of patients, those treated with cerdulatinib achieved statistically significant reductions in EASI, according to Anna Tallman, PharmD, vice president of medical affairs at Dermavant.

In the study, Dr. Tallman reported that cerdulatinib produced significant changes in several important areas, including:

- Reduction of epidermal thickness at Week 2 ($p<0.05$).
- Reduction of Ki67 expression ($p<0.05$).
- Reduction of K16 gene expression ($p<0.05$).
- Reduction of IL-5 gene expression ($p<0.05$).
- Reduction of CCL13 gene expression ($p<0.001$).

There were 25 treatment-emergent adverse events in the trial, but all but one were Grade 1. There was one Grade 2 adverse event. Six of the 8 patients reported adverse events, most frequently headache. Dr. Tallman said, "These data demonstrate the potential for topical cerdulatinib as a treatment for patients with atopic dermatitis which will be further evaluated in clinical studies."