

SD-101 in Epidermolysis Bullosa. Presented by Amy S. Paller, MS, MD, Northwestern University Feinberg School of Medicine. The interest in SD-101 cream was initially sparked because of reports from EB families of improvement with an over-the-counter cream that had low concentrations of allantoin. Allantoin has been tested in several studies during the past 40 years and has been shown to have anti-inflammatory and anti-microbial effects; it also promotes the deposition of a wound base and helps to clear excess scale. In a preliminary study, there was evidence of an effect, so that two double-blind, randomized, vehicle-controlled were initiated. The first (a Phase 2b, 3 month study) randomized 48 patients (6 months of age or above) to either the vehicle base, a 3% SD-101 cream or a 6% SD-101 cream. Assessments were made at baseline, 14, 30, 60, and 90 days. Forty-four completed the trial, with an average age of 12 years. Most (29) had recessive dystrophic EB, 11 with EB simplex and 8 with junctional EB; these groups were evenly divided over the 3 treatment arms. In this first, small study a statistically significant difference in the proportion of the evaluable population with complete target wound closure was seen at 2 months after initiation in the 6% concentration ($p=0.04$) and, as a result, the 6% concentration was chosen for further studies. There were no serious side effects in the treatment groups thought related to the topical medication. 42 of the 44 patients these decided to continue to an extension study on the active medication. To date in this long-term follow-up, some additional reduction in body surface area affected by EB has been seen (out to month 24) and no new safety issues have emerged. The Phase 3 (ESSENCE) study has now been completed. In this trial of EB patients at least 1 month of age, 82 patients were treated with SD—101 6% cream and 87 with the vehicle base. Once again, no safety issues were seen. Unfortunately, in the entire population, there was no significant different in time to wound closure, proportion of patients with wound closure within 3 months, change in body surface area of wounds, or in patient-reported itching or pain. There were, however, some significant changes noted when analyzing subpopulations of patients, which are not being further evaluated. This was the largest double-blind, randomized, placebo-controlled study ever performed for EB. Much was learned, including some key challenges which need to be overcome in future EB trials. These include:

- i) the limited understanding of the natural history of wound healing in EB
- ii) the high vehicle control rates, which probably related to the careful physician monitoring and the daily dressing changes (more aggressive care for many patients), but in addition that the vehicle itself had many potentially ameliorative ingredients, reducing the likelihood of finding a significant difference vs. the active medication
- iii) the patient population was quite heterogenous with a range of different types of EB, severity, and demographic characteristics.

Open-label Phase 3 studies are continuing.