Efficacy and Safety Results From a Phase 2b Dose-ranging Study of SD-101 Cream in Patients With Epidermolysis Bullosa

Amy Paller,[1] John Browning,[2] Rummana Aslam,[3] Susan J. Bayliss,[4] Aida Lugo-Somolinos,[5] Robert Sidbury,[6] Eric Cantor,[7] Allen Reha,[7] Willistine Lenon,[8] Lindsay Reklis,[8] Ronald V. Nardi,[8] Jamie Gault,[8] Jay Barth[7]

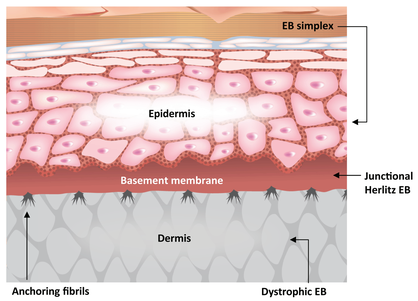
[1]Northwestern University Feinberg Medical School, Chicago, IL, USA; [2]Texas Dermatology and Laser Specialists, San Antonio, TX, USA; [3]Center for Advanced Wound Care, Hackensack University Medical Center, Hackensack, NJ, USA; [4]Dermatology Division, Washington University School of Medicine, St. Louis, MO, USA; [5]Department of Dermatology, University of North Carolina, Chapel Hill, NC, USA; [6]Seattle Children's Hospital, Seattle, WA, USA; [7]Amicus Therapeutics, Cranbury, NJ, USA; [8]Scioderm – An Amicus Therapeutics Company, Durham, NC, USA

INTRODUCTION

Epidermolysis Bullosa

- A rare group of life-threatening genetic disorders that are characterized by mechanical fragility and blistering or erosion of the skin, mucosa, or epithelial lining of other organs, in response to little or no apparent trauma[1]
- High risk of infection associated with fragile skin and the resultant shearing[1]
- Usually diagnosed in neonates; occurs in 19 per million live births in the United States[2]
- Subtypes differ by physical manifestations, genetic makeup, and prognosis (**Figure 1** and **Table 1**)[1,3]
- Symptoms of epidermolysis bullosa—blistering, scarring, disfiguration, pain—can vary in severity and lead to premature death[1,3]

Figure 1. Sites of Primary Blister Formation for Major Epidermolysis Bullosa Subtypes[4]



EB=epidermolysis bullosa.

Table 1. Epidermolysis Bullosa Types (representing ≈99% of the patient population)[1,2,4]

Subtypes	Symptoms	Frequency	Mortality Risk
Junctional	• Blistering of skin/mucosa • Severe complications, especially infection • Usually fatal early in life	≈5%	↑
Dystrophic	• Skin and mucosal blistering • Narrowing of esophagus • Higher risk of skin cancer	≈25%	
Simplex	• Superficial blistering	≈70%	

SD-101

- A topical FDA-designated breakthrough therapy for the daily treatment of wounds caused by all major types of epidermolysis bullosa[5]
  - Proprietary formulation of allantoin designed to deliver a high concentration (up to 6%) in a highly stable, soluble form[5]
  - Allantoin appears to have multiple wound-healing effects, including anti-inflammatory and antimicrobial activity and tissue formation and differentiation, specifically in stimulating development of granulations and a tendency towards epithelialization[6,7]
  - Based on the promising profile of this proprietary formulation and the unmet clinical need in epidermolysis bullosa, SD-101 3% and 6% were evaluated for efficacy and safety compared with placebo for the treatment of patients with epidermolysis bullosa in a phase 2b study (SD-003)

OBJECTIVE

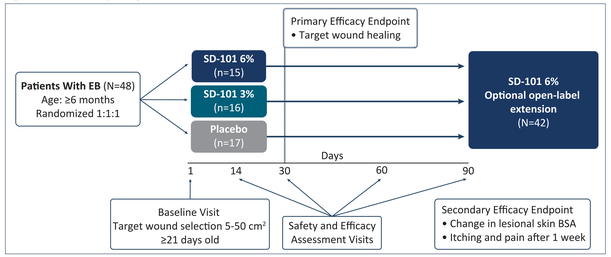
- Evaluate the safety and efficacy of SD-101 in patients with epidermolysis bullosa in a phase 2b study

METHODS

SD-003 Study Design

- SD-003 (NCT02014376) was a phase 2b multicenter, randomized, double-blind, placebo-controlled, dose-ranging 3-month study investigating the safety and efficacy of SD-101 cream (3% or 6%) applied daily to the entire body for treatment of all major forms of epidermolysis bullosa (**Figure 2**)
- Key inclusion criteria
  - Diagnosis of simplex, recessive dystrophic, or junctional non-Herlitz epidermolysis bullosa
  - Aged ≥6 months
  - Epidermolysis bullosa-related target wound ≥21 days old and between 5 and 50 cm² in size
- Key exclusion criteria
  - No clinical evidence of local infection in the selected target wound
  - Use of any investigational drug ≤30 days before enrollment
  - Use of immunotherapy or cytotoxic chemotherapy ≤60 days before enrollment
  - Use of systemic or topical steroidal therapy ≤30 days before enrollment (inhaled steroids and ophthalmic drops containing steroids are allowed)
  - Use of systemic antibiotics ≤7 days before enrollment
  - Arterial or venous disorder resulting in ulcerated lesions
- Treatment groups
  - SD-101 3% or 6% creams or placebo were applied topically once daily to the entire body as a thin layer for a period of 90 days
- Primary endpoint
  - Number of patients with complete wound closure (skin re-epithelialization without drainage) within 1 month of treatment in patients receiving SD-101 6% compared with patients receiving placebo
- Secondary endpoints:
  - Change in body surface area (BSA) of lesional skin after 3 months of treatment compared with baseline
  - Itching and pain after 1 week of treatment compared with baseline
  - Safety and tolerability monitored at each visit

Figure 2. SD-003 Study Design



RESULTS

- There were 48 patients included in the trial, and the baseline characteristics were similar between the 3 treatment groups (**Table 2**)

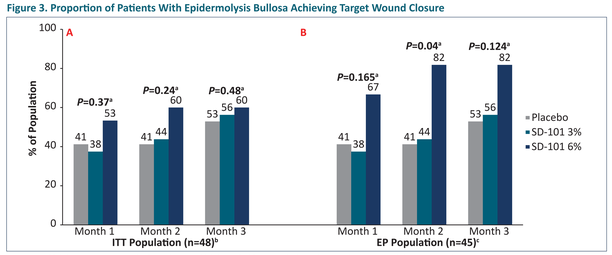
Table 2. Baseline Demographics and Characteristics[a]

Baseline	Placebo (n=17)	SD-101 3% (n=16)	SD-101 6% (n=15)
Age, years[b]	11.57 (10.40)	15.32 (15.60)	9.55 (9.20)
Target lesion size (cm²)[b]	16.74 (11.97)	13.59 (9.32)	11.31 (7.74)
Lesional BSA, %[b]	16.41 (11.03)	21.60 (12.01)	20.35 (12.29)
Epidermolysis bullosa subtype, n			
Simplex	4	4	3
Dystrophic	10	9	10
Junctional	3	3	2

[a]Baseline demographics between groups were not significantly different.
[b]Numbers reported as average (standard deviation).

- Patients in the SD-101 6% treatment group were more likely to obtain target wound closure than patients in the placebo group (**Figure 3**)

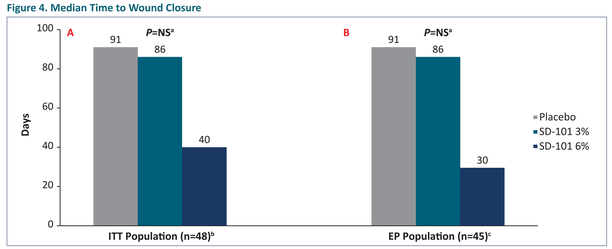
Figure 3. Proportion of Patients With Epidermolysis Bullosa Achieving Target Wound Closure



Proportion of (A) the intention-to-treat (ITT) population and (B) the evaluable patient (EP) population with target wound closure at months 1, 2, and 3.
[a]SD-101 6% vs placebo.
[b]ITT population: patients with informed consent receiving ≥1 application of treatment.
[c]EP population: ITT population excluding 1 patient due to lost follow-up and 2 patients lacking initial qualified target lesion; 1 patient was excluded from assessments at month 1 due to lack of follow-up.

- Patients in the SD-101 6% treatment group also achieved target wound closure faster than patients in the placebo group (**Figure 4**)

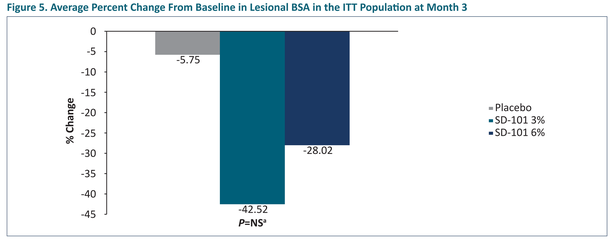
Figure 4. Median Time to Wound Closure



Median time to target wound closure in (A) the ITT population and (B) the EP population.
NS=not significant.
[a]SD-101 6% vs placebo.
[b]ITT population: patients with informed consent receiving ≥1 application of treatment.
[c]EP population: ITT population excluding 1 patient due to lost follow-up and 2 patients lacking initial qualified target lesion; 1 patient was excluded from assessments at month 1 due to lack of follow-up.

- Patients treated with SD-101 3% or 6% had a greater reduction in lesional BSA than patients given placebo (**Figure 5**)

Figure 5. Average Percent Change From Baseline in Lesional BSA in the ITT Population at Month 3



[a]SD-101 6% vs placebo.

- SD-101 3% and 6% were both well tolerated, and the frequency of treatment-emergent adverse events within each group was similar (**Table 3**)

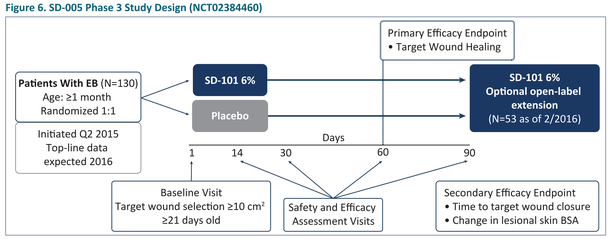
Table 3. Treatment-Emergent Adverse Events (TEAEs) of ≥10% Frequency

	Placebo (n=17)	SD-101 3% (n=16)	SD-101 6% (n=15)
Patients with TEAEs (%)	**70.6**	**81.3**	**60**
Nasopharyngitis	12	25	7
Pyrexia	12	19	33
Application-site pain	6	19	13
Pain	-	-	13
Pruritus	6	13	13
Rash	12	-	7
Rash erythematous	12	-	-
Cough	6	-	13
Oropharyngeal pain	12	-	-
Rhinorrhea	-	-	13
Vomiting	6	6	13
Headache	12	-	7

CONCLUSIONS

- Treatment with SD-101 6% cream demonstrated a higher rate of wound closure in patients with epidermolysis bullosa relative to both SD-101 3% and placebo
- SD-101 3% and 6% cream are generally well tolerated in patients with epidermolysis bullosa, and the safety profiles for all 3 treatments (placebo, SD-101 3%, and SD-101 6%) were similar
- The current ongoing phase 3 clinical trial (SD-005, NCT02384460) was designed with phase 2b results in mind, and further examine the safety and efficacy of SD-101 6% cream
  - Multicenter, randomized, double-blind, placebo-controlled study (**Figure 6**)
  - 130 patients will be randomized 1:1 to either placebo or SD-101 6%

Figure 6. SD-005 Phase 3 Study Design (NCT02384460)



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