LP-047

Characteristics of Patients With Epidermolysis Bullosa in the Phase 3 ESSENCE Study of SD-101

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INTRODUCTION

- Epidermolysis bullosa is a rare, often severe, genetic disorder 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]
  - Often diagnosed in neonates; occurs in 19 per million live births in the United States as estimated from the National Epidermolysis Bullosa Registry, a cross-sectional and longitudinal epidemiologic study of patients with epidermolysis bullosa across the continental United States[2]
  - Subtypes differ by physical manifestations, genetic makeup, and prognosis[2]
  - Symptoms (blistering, scarring, disfiguration, pain) can vary in severity and may lead to premature death as well as major morbidities, including life-threatening infections, sepsis, and squamous cell carcinoma[1,3-5]
- SD-101 is a topical treatment containing a high concentration of allantoin in a proprietary formulation, designed for the treatment of blisters and skin lesions in patients with epidermolysis bullosa[7,8]
- In 2013, SD-101 became one of the first drug candidates to receive Breakthrough Therapy designation from the US Food and Drug Administration for the treatment of patients with epidermolysis bullosa[7,8]
- The efficacy and safety of SD-101 has been investigated in SD-003, a phase 2b, multicenter, randomized, double-blind, vehicle-controlled, dose-ranging, 3-month study (NCT02014376)[4]
  - Treatment with SD-101 cream containing 6% allantoin (SD-101 6%) demonstrated a higher rate of wound closure in patients with epidermolysis bullosa relative to treatment with vehicle
  - SD-101 6% was generally safe and well tolerated in patients with epidermolysis bullosa

OBJECTIVE

- To describe the baseline characteristics of patients with epidermolysis bullosa enrolled in the ongoing ESSENCE trial as of February 2017

METHODS

- ESSENCE (SD-005; NCT02384460) is a phase 3, multicenter, randomized, double-blind, vehicle-controlled, ongoing study to assess the efficacy and safety of SD-101 6% vs vehicle (SD-101 0%) on lesions in patients with simplex, recessive dystrophic, or junctional non-Herlitz epidermolysis bullosa[9] (**Figure 1**)
  - The 2 primary endpoints are time to complete target wound closure and proportion of patients with complete target wound closure
  - Secondary endpoints include change in body surface area index (BSAi) of lesions and blisters, patient-reported itching, and patient-reported pain

Key Inclusion Criteria

- Diagnosis of simplex, recessive dystrophic, or junctional non-Herlitz epidermolysis bullosa
- Age ≥1 month
- Target wound ≥21 days old and between 10 and 50 cm^2 in size

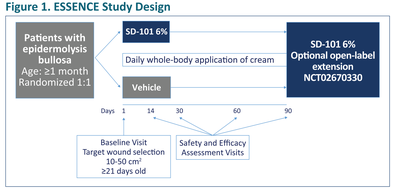
Key Exclusion Criteria

- Clinical evidence of local infection in the selected target wound
- Use of immunotherapy or cytotoxic chemotherapy ≤60 days before enrollment
- Use of any investigational drug or 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

Application

- SD-101 6% or vehicle is applied topically once daily to the entire body as a thin layer for a period of 90 days. Patients/parents are taught how to apply the cream at first visit

Figure 1. ESSENCE Study Design



ESSENCE was initiated in Q2 of 2015, and topline results are expected in Q3 of 2017.
Q=quarter.

Assessments

- During patient visits, the following evaluations are performed:
  - Baseline-selected target wound closure evaluation using ARANZ SilhouetteStar™. Complete target wound closure is defined as skin re-epithelialization without drainage
  - BSAi of lesional skin: percentage of total body coverage of epidermolysis bullosa–related lesions (blisters, erosions, ulcerations, scabbing, bullae, and eschars, as well as areas that are weeping, sloughing, oozing, crusted, and/or denuded)
  - BSAi of wound burden: percentage of total body coverage of epidermolysis bullosa wounds, defined as open areas on the skin (epidermal covering is disrupted)
  - Itch, using the Itch Man Pruritus Assessment Tool[10]
  - Pain, using the Face, Legs, Activity, Cry, Consolability (FLACC) scale for patients aged 1 month to 3 years and the Wong-Baker FACES® Pain Scale for patients aged ≥4 years. Each of the 5 categories in the FLACC scale is scored from 0 to 2, with a cumulative score ranging from 0 to 10. The Wong-Baker FACES® Pain Scale also ranges from 0 to 10. Higher scores indicate greater pain[11,12]

BASELINE RESULTS

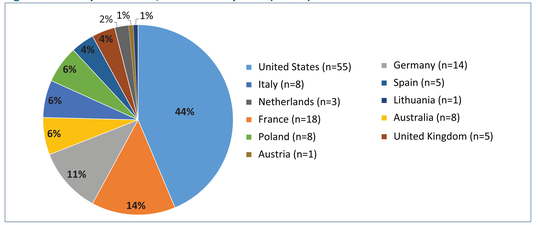
- As of February 21, 2017, ESSENCE was enrolling patients worldwide and included patients of varying ages and all major types of epidermolysis bullosa (**Table 1** and **Figure 2**)

Table 1. ESSENCE Baseline Demographics and Characteristics, as of February 2017

Baseline	Total (N=126)
Age	
All patients, years	15.1 ± 14.3 (0, 67)
0 to ≤1 month	0 (0)
>1 to ≤24 months	17 (13.5)
>24 months to ≤12 years	58 (46.0)
>12 to ≤18 years	15 (11.9)
>18 to ≤65 years	35 (27.8)
>65 years	1 (0.8)
Male	59 (46.8)
Race	
Black/African American	7 (5.6)
Asian	8 (6.3)
White	105 (83.3)
Unknown	5 (4.0)
Mixed	1 (0.8)
Epidermolysis bullosa subtype	
Simplex	14 (11.1)
Recessive dystrophic	85 (67.5)
Junctional non-Herlitz	27 (21.4)
Body mass index, kg/m^2	
All patients (n=125)	17.4 ± 4.4
Age >1 to ≤24 months (n=17)	16.5 ± 4.2
Age >24 months to ≤12 years (n=57)	15.6 ± 3.7
Age >12 to ≤18 years (n=15)	16.7 ± 3.3
Age >18 to ≤65 years (n=35)	20.9 ± 4.2
Age >65 years (n=1)	20.1 ± N/A
BSAi of lesional skin, %	
All patients (n=124)	24.4 ± 19.4
Age >1 month to <8 years (n=42)	15.6 ± 14.8
Age ≥8 years (n=82)	28.9 ± 20.0
BSAi of wound burden, %	
All patients (n=124)	10.8 ± 11.0
Age >1 month to <8 years (n=42)	8.9 ± 11.5
Age ≥8 years (n=82)	11.9 ± 10.6
Target wound size, cm^2	21.67 ± 27.5

Data reported as mean ± standard deviation (min, max) or n (%). The number of patients included in each analysis is noted if data were not available for all 126 patients.
BSAi=body surface area index; N/A=not applicable.

Figure 2. Country Enrollment, as of February 2017 (N=126)



- Patients enrolled in ESSENCE demonstrated a substantial burden of pain at baseline (**Table 2**)

Table 2. Baseline Pain Scores

Pain Assessment	n/N	Baseline
FLACC scale (age >1 month to ≤3 years)	15/22	
Mean ± standard deviation		3.9 ± 2.1
Median (min, max)		4.0 (1.0, 9.0)
Wong-Baker FACES® Pain Scale (age ≥4 years)	102/104	
Mean ± standard deviation		3.2 ± 2.7
Median (min, max)		4.0 (0.0, 10.0)

Both pain scales range from 0-10, with higher scores indicating greater pain.
FLACC=Face, Legs, Activity, Cry, Consolability; n/N=number of patients included in analysis/number of patients eligible for assessment.

- The medical history of patients enrolled in ESSENCE varied, with the most commonly recorded medical conditions at baseline being pruritus and pain (**Table 3**)

Table 3. Medical History by System Organ Class Reported in at Least 20% of Patients

System Organ Class and Medical Condition	Total (N=126)
Gastrointestinal disorders	83 (65.9)
Constipation	55 (43.7)
Gastro-oesophageal reflux disease	26 (20.6)
Skin and subcutaneous tissue disorders	79 (62.7)
Pruritus	63 (50.0)
General disorders and administration-site conditions	69 (54.8)
Pain	63 (50.0)
Infections and infestations	56 (44.4)
Surgical and medical procedures	54 (42.9)
Blood and lymphatic system disorders	50 (39.7)
Metabolism and nutrition disorders	50 (39.7)
Injuries, poisonings, and procedural complications	30 (23.8)
Eye disorders	29 (23.0)
Congenital, familial, and genetic disorders	28 (22.2)

Data reported as n (%).

CONCLUSIONS

- ESSENCE is one of the largest clinical trials of an investigational drug conducted in patients with epidermolysis bullosa
- Patients enrolled thus far have substantial pain burden and large chronic wounds, and represent a range of disease severity (both in epidermolysis bullosa subtype and extent of body coverage of epidermolysis bullosa lesions), ages, and geographic distribution
- Top-line results for the phase 3 ESSENCE study are expected in Q3 of 2017

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DISCLOSURE

Conflicts of Interest

CB serves on advisory boards for Sanofi, is a consultant for Expanscience, is an investigator (uncompensated) for Amicus Therapeutics, is a speaker for La Roche-Posay and Expanscience, and has received honoraria from Celgene and Novartis. SE and DK have no conflicts of interest to disclose. FS has been a speaker for La Roche-Posay. JB is an investigator and conducts clinical research for Amicus Therapeutics, Galderma, Valeant, Patagonia, and Regeneron, and is a speaker for Medimetriks and Promius. AP is a consultant and investigator for Amicus Therapeutics. HL, AR, RL, and JB are employees of and own stock in Amicus Therapeutics. JG, WL, LR, and RN are employees of Scioderm - An Amicus Therapeutics Company and own stock in Amicus Therapeutics.

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