Phase 3, randomized, intrapatient-controlled trial of an investigational collagen type VII gene–corrected autologous cell therapy, EB-101, for the treatment of recessive dystrophic epidermolysis bullosa (RDEB)

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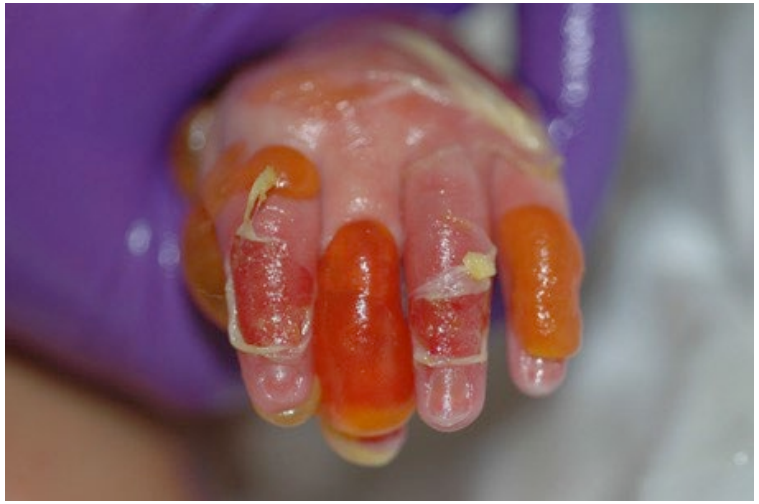
Individuals With RDEB Lack the *COL7A1* Gene That Encodes Type VII Collagen



Gene Mutated[1]: *COL7A1*

Molecular defect[2]: No anchoring fibrils, dermal-epidermal weakness

Rare Disease[3]: 1:750,000

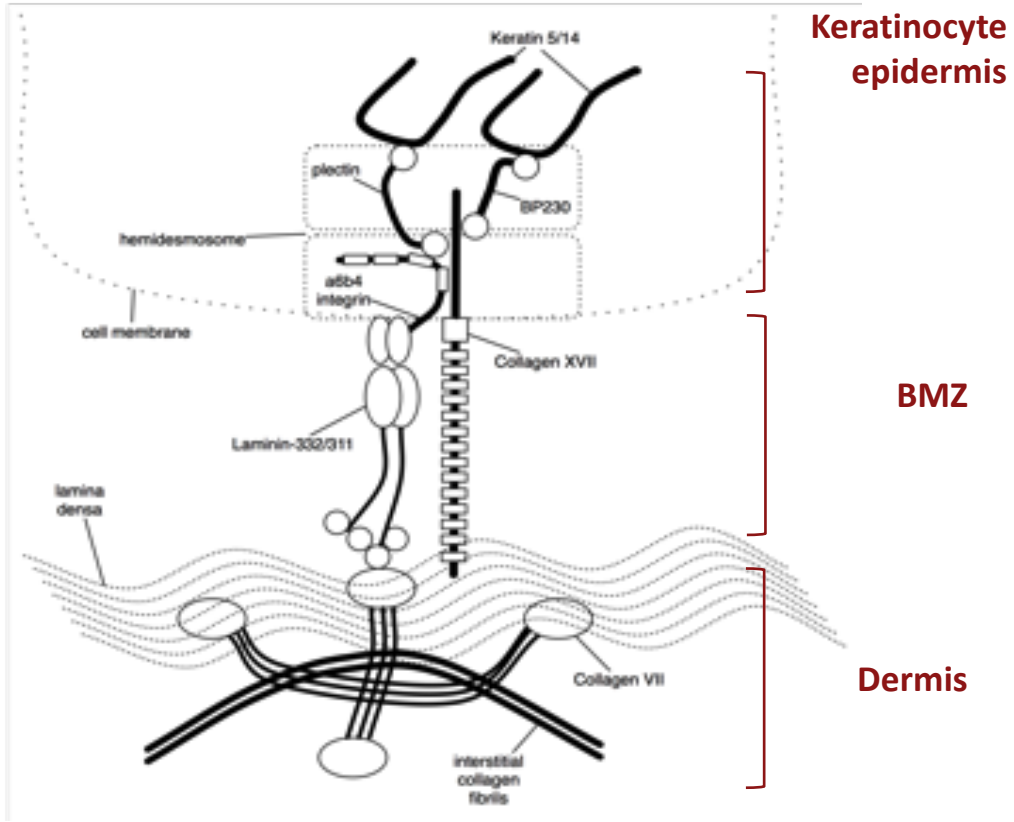


Figure from Stanford Medicine Dermatology, What is EB? https://med.stanford.edu/dermatology/research/research.html. Accessed April 30, 2023.
BMZ, basement membrane zone; RDEB, recessive dystrophic epidermolysis bullosa.

1. Horn HM, Tidman, MJ. *Br J Dermatol.* 2002;146(2):267-274. 2. Vahidnezhad H, et al. *Matrix Biol.* 2019;81:91-106. 3. Eichstadt S, et al. *Clin Cosmet Investig Dermatol.* 2019;12:933-942.

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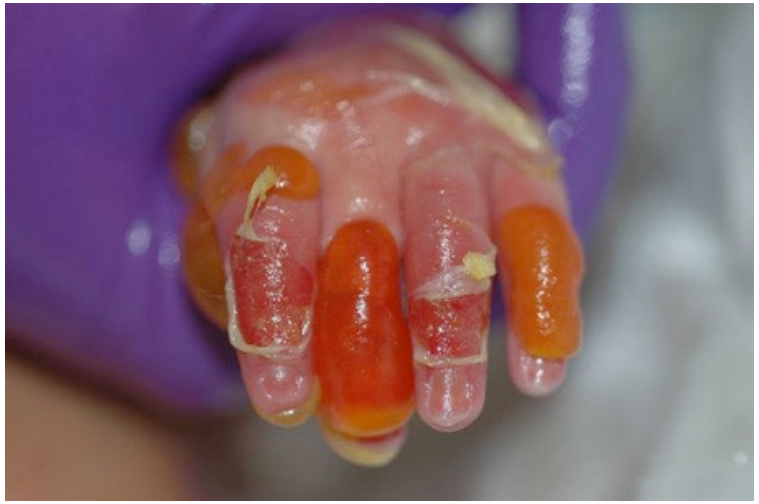


Gene Mutated[1]: *COL7A1*

Molecular defect[2]: No anchoring fibrils, dermal-epidermal weakness

Rare Disease[3]: 1:750,000

Clinical Problem[4]:

Blisters > Wounds >

Pain, Itch, Infection,

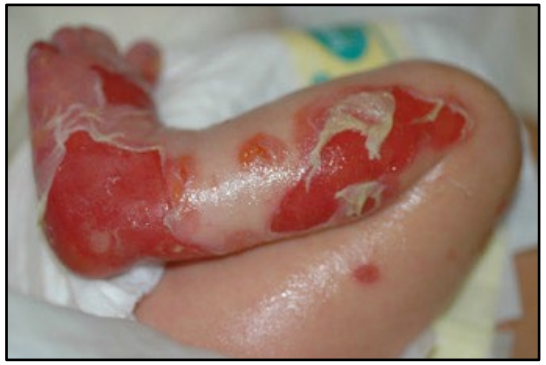
Anemia, SCC, early death

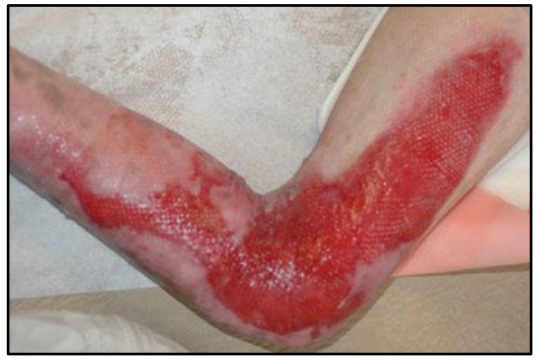
Standard of Care[5]:

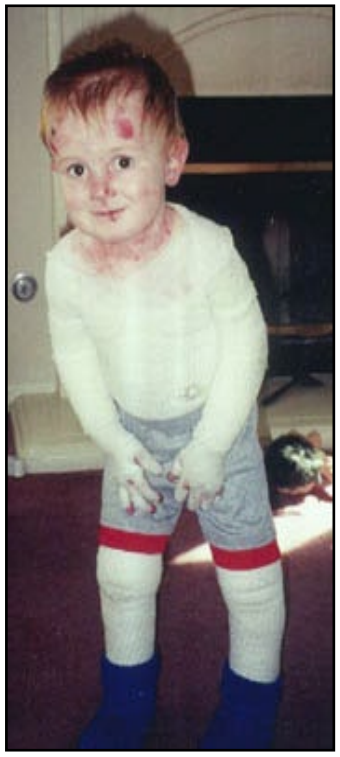
- Bandages
- Dressing
- Antibiotics

Goal:

Heal large chronic open wounds by restoring type VII collagen







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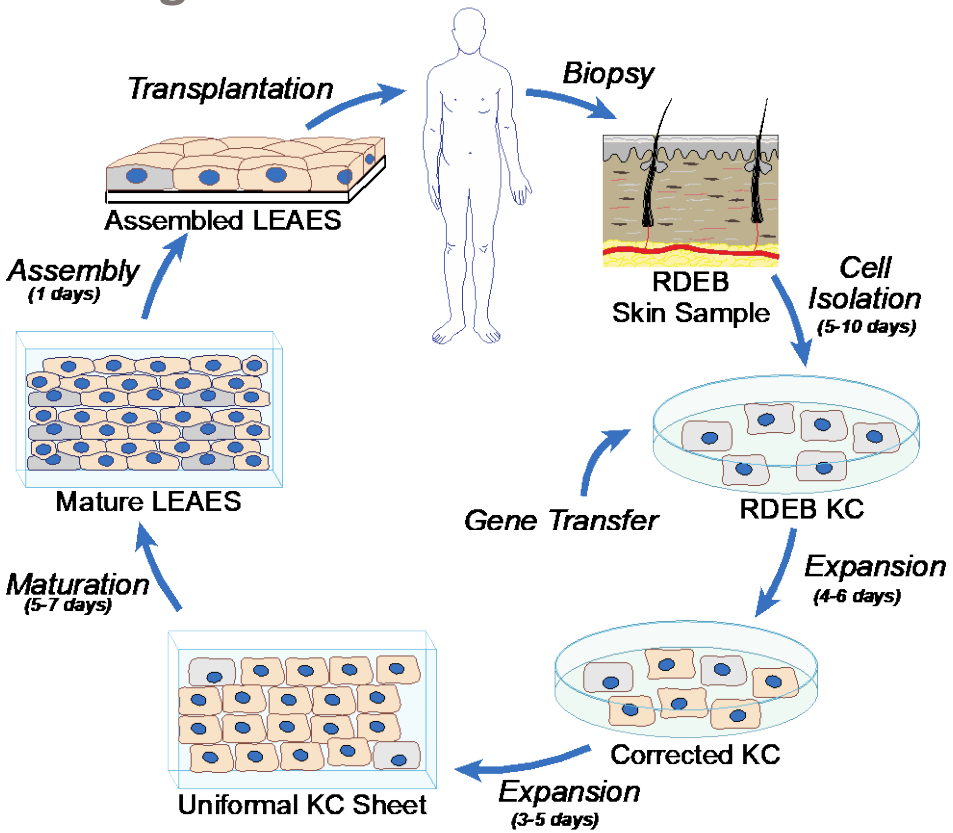
BMZ, basement membrane zone; RDEB, recessive dystrophic epidermolysis bullosa; SCC, squamous cell carcinoma.

1. Horn HM, Tidman MJ. *Br J Dermatol 2002;*146(2):267-274. 2. Vahidnezhad H, et al. *Matrix Biol* 2019;81:91-106. 3. Eichstadt S, et al. *Clin Cosmet Investig Dermatol.* 2019: 933-942. 4. Tang JY, et al. *Orphanet J Rare Dis.* 2021;16(1):175. 5. Pope E, et al. *J Am Acad Dermatol.* 2012;67(5):904-917.

Investigational Product: EB-101

~25 days to manufacture 40 cm^2 sheets (5.5 cm x 7.5 cm) utilizing retrovirus expressing the *COL7A1* gene[1-2]



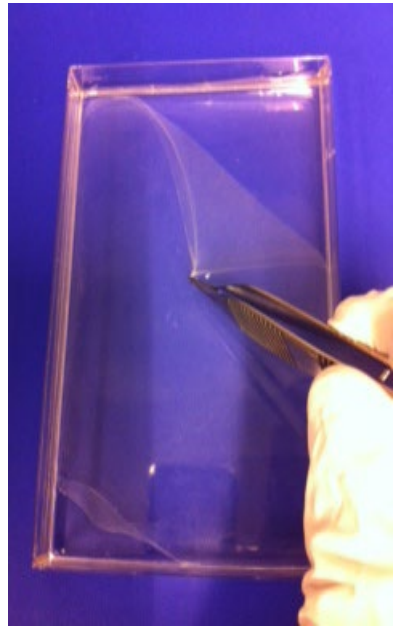


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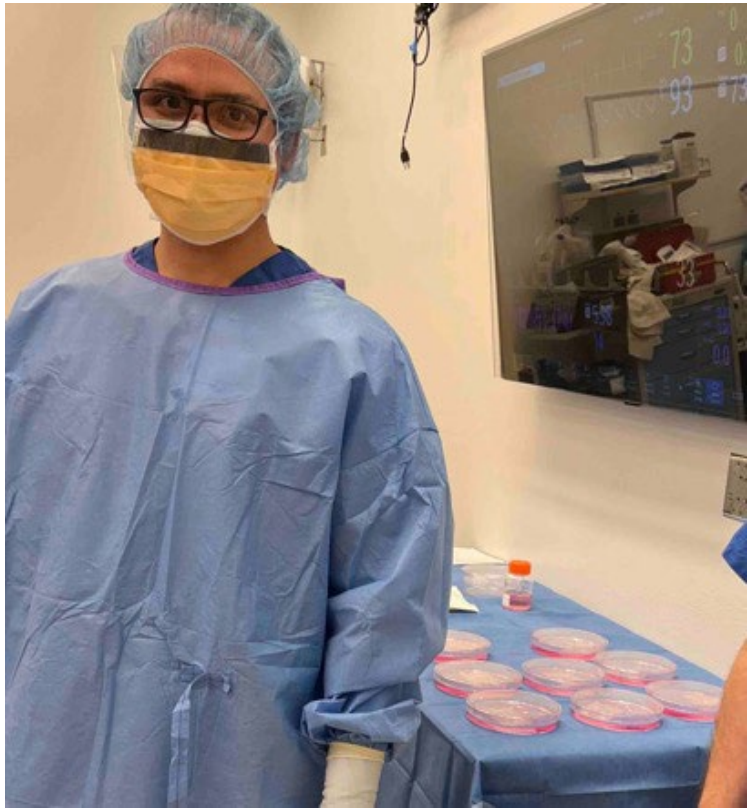
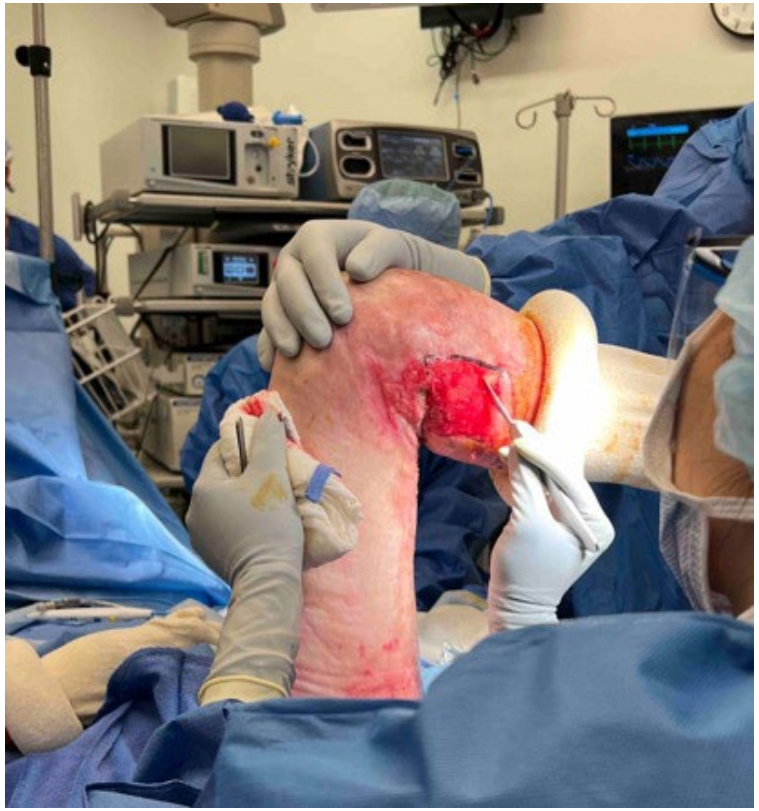
Figure from Stanford Medicine Dermatology, Prior Clinical Studies. https://med.stanford.edu/dermatology/research/research/research.html. Accessed April 30, 2023.
Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

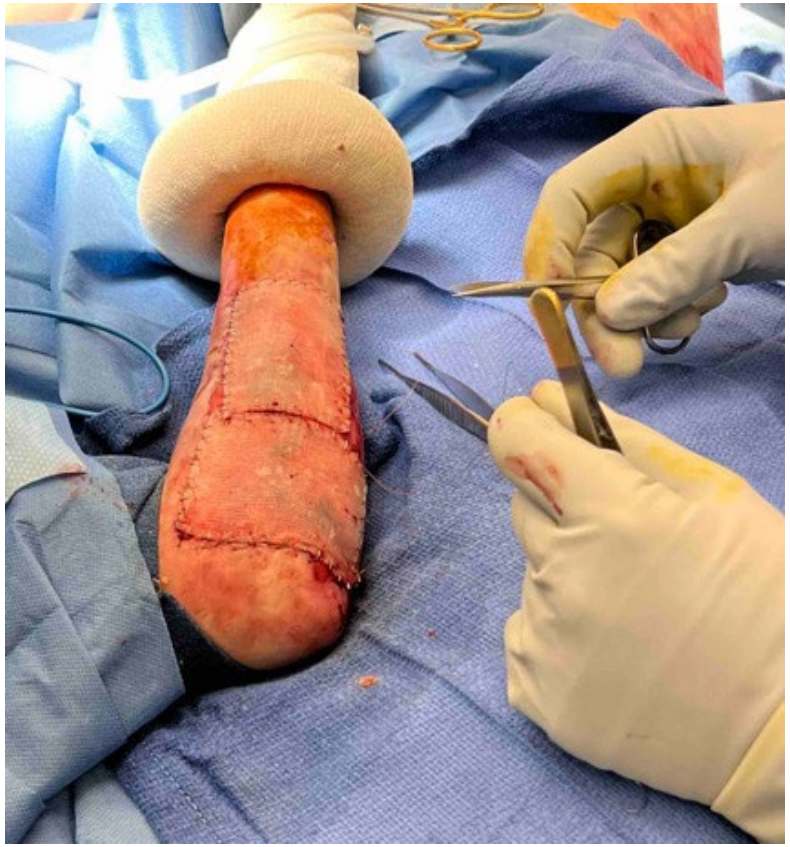
Surgical Procedure



Hand-carried from Abeona GMP facility



General anesthesia, debridement of wounds



Surgical application of up to 6 EB-101 sheets (240 cm^2)

GMP, good manufacturing practice.

Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

VIITAL: Study Design[1,2]

Phase 3, randomized, intrapatient controlled trial conducted at 2 institutions (Stanford, Univ of Mass) in the United States.

Eligibility:

- Age ≥6 years with confirmed RDEB
- ≥2 matched large, chronic[a] wounds per patient
- No evidence or history of SCC in the area that would undergo EB-101 application

Patients enrolled
N=11

Randomized wound pairs
EB-101 & Control (n=43)

Nonrandomized wounds[b]
EB-101 treated, not included in primary analysis (n=14)

Co-primary Endpoints:

- ≥50% wound healing at week 24[c]
- Pain reduction at week 24

Secondary Endpoint:

- Complete wound healing at weeks 12 and 24[c]

Select Exploratory Endpoints:

- ≥75% wound healing at weeks 12 and 24[c]
- ≥50% wound healing at week 12
- Pain reduction at week 12
- Pain reduction over time (at-home diary)
- Change in itch severity at week 24
- CrGI-Pain and PGIC-Blistering scores at week 24

Sample Size

A sample size of a minimum of 36 wound pairs in 10 to 15 participants was estimated using conservative assumptions based on wound healing and pain reduction observed in the phase 1/2a trial. Statistical power for each co-primary endpoint was initially calculated separately. **The joint statistical power for the trial was bounded by the multiplication of these 2 powers and was expected to be >80%.**

[a]Large = ≥20 cm^2 surface area; chronic = open for ≥6 months. [b]Eligible wounds based on size and chronicity that either: (a) did not have a matched wound to pair with it, or (b) were initially randomized to control, but were ultimately treated with EB-101 because their matched pair was deemed untreatable during surgery due to the patient's position. [c]Confirmed at a subsequent visit ≥2 weeks later.

CrGI, Caregiver Global Impression; PGIC, Patient Global Impression of Change; RDEB, recessive dystrophic epidermolysis bullosa; SCC, squamous cell carcinoma.

1. ClinicalTrials.gov Identifier: NCT04227106. 2. Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Demographics, Baseline Characteristics, and EB-101 Exposure

Patients With RDEB

	Total N=11
Age, median (range) — y	21.0 (6 to 40)
Sex — n (%)	
Male	4 (36.4)
Female	7 (63.6)
Race — n (%)	
White	10 (90.9)
Other (Unknown)	1 (9.1)
Ethnicity — n (%)	
Hispanic or Latino	2 (18.2)
Not Hispanic or Latino	8 (72.7)
Not reported	1 (9.1)
Wound pairs per patient median (range)	4 (2 to 5)

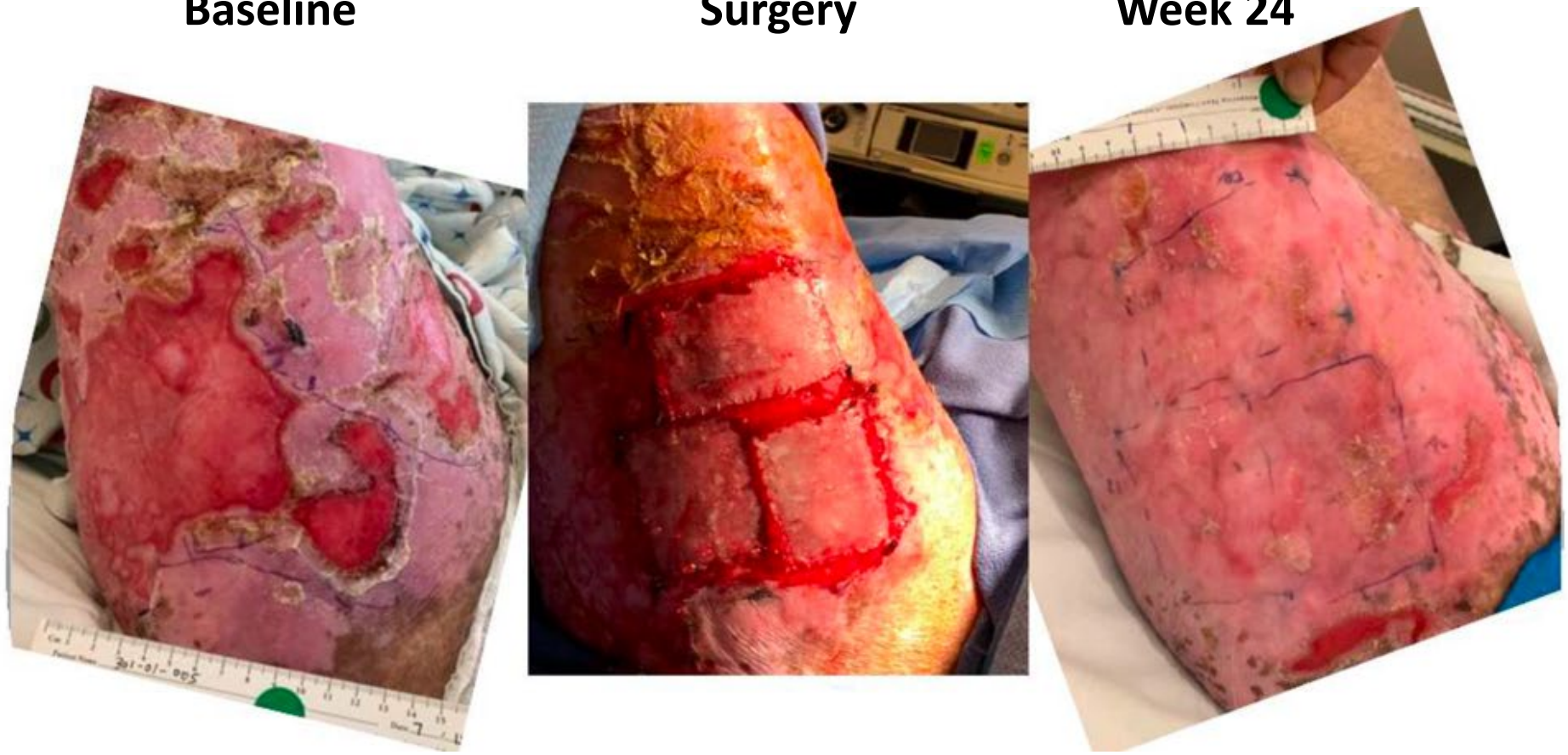
Randomized Wounds

	EB-101–Treated n=43	Control n=43
Wounds by anatomical region, n (%)		
Anterior trunk	18 (41.9)	4 (9.3)
Posterior trunk	10 (23.3)	23 (53.5)
Upper extremity	8 (18.6)	5 (11.6)
Lower extremity	7 (16.3)	11 (25.6)
Wound duration, median (range) — mo.	60 (6 to 252)	60 (6 to 252)
Pain severity, median (range)	4.0 (0 to 10)	4.0 (0 to 10)
Itch severity, median (range)	4.0 (0 to 10)	4.0 (0 to 10)
Total wound surface area covered by EB-101 per patient,[a] median (range) — cm^2	160.0 (80 to 200)	0

[a]Wound surface area was calculated after wound debridement.
Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Example of ≥75% Healing After EB-101 Treatment (upper left thigh)

Baseline **Surgery** **Week 24**

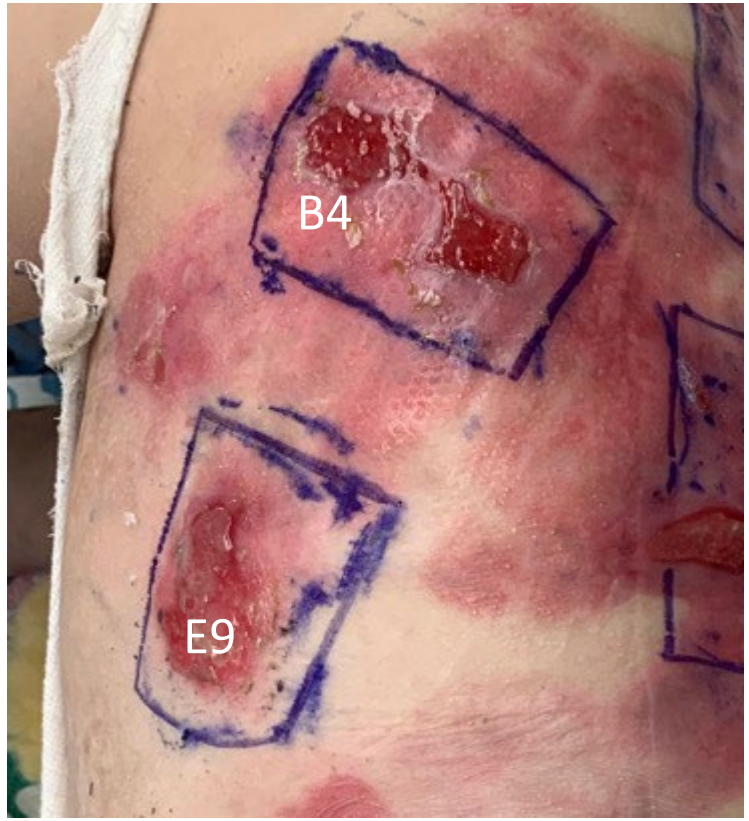


Tattooed wounds scored as >75% healed but not complete wound healing at Week 24

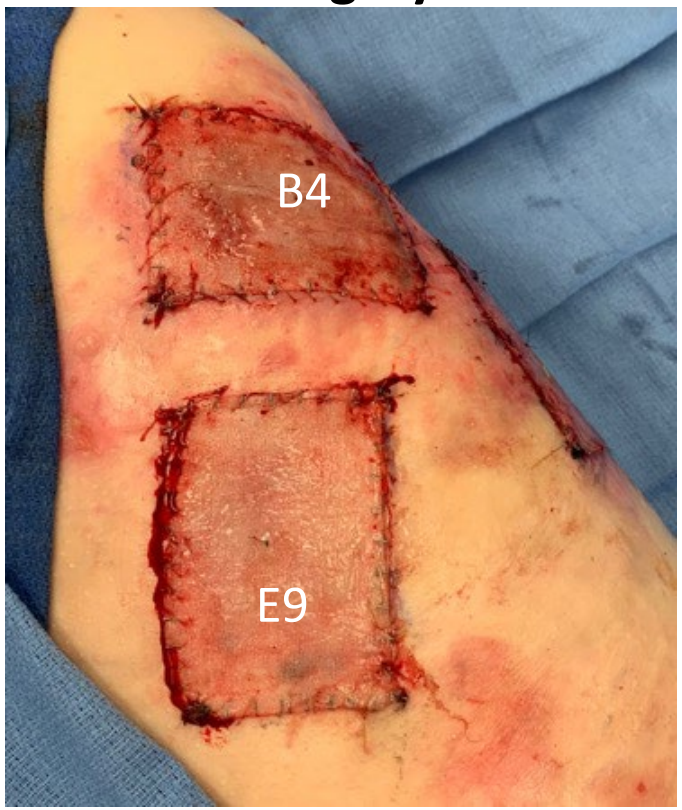
Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Examples of ≥75% and Complete Wound Healing After EB-101 Treatment (upper trunk)

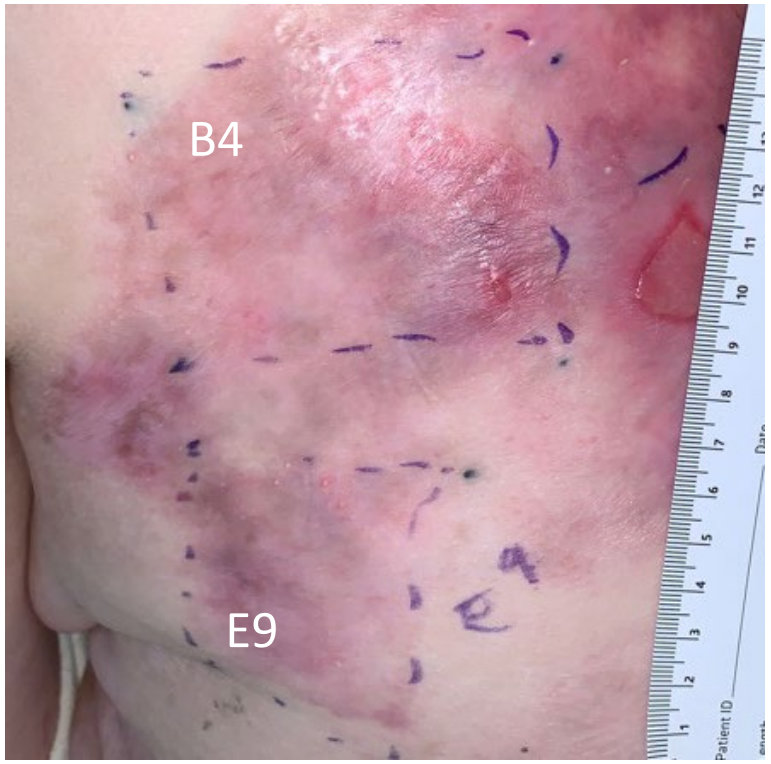
Baseline



Surgery



Week 24



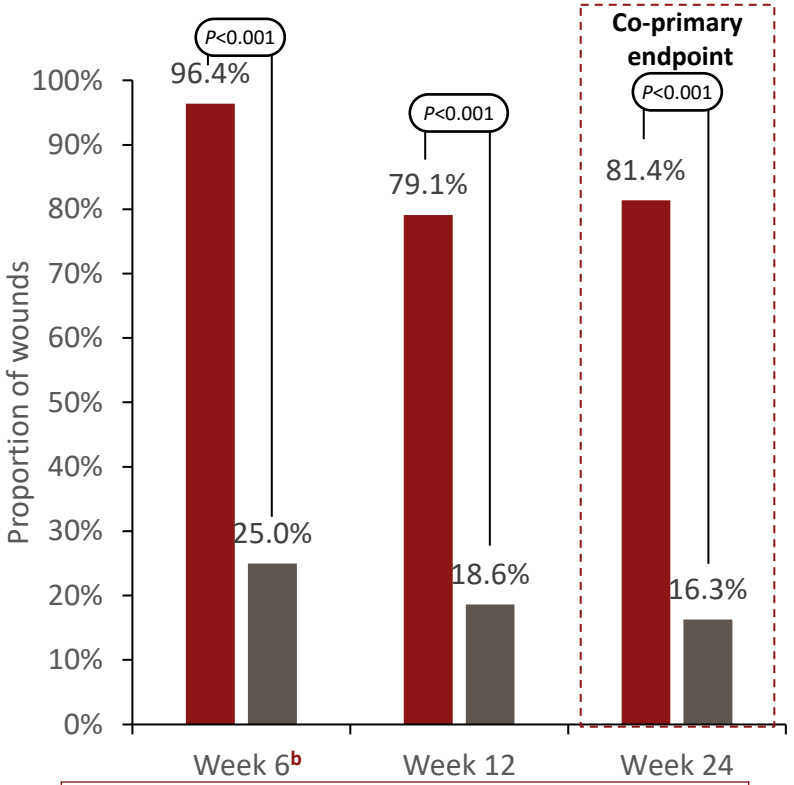
B4 scored as >75% healed at Week 24 and E9 scored as complete wound healing at Week 24

Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Wound Healing Assessments Over Time

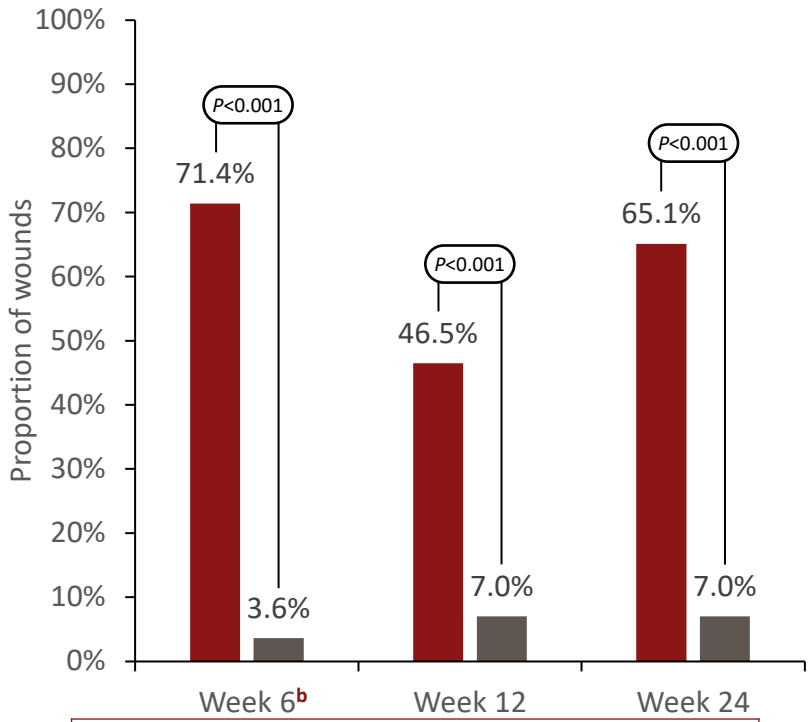
EB-101–Treated Wounds
Control Wounds

≥50% wound healing from baseline



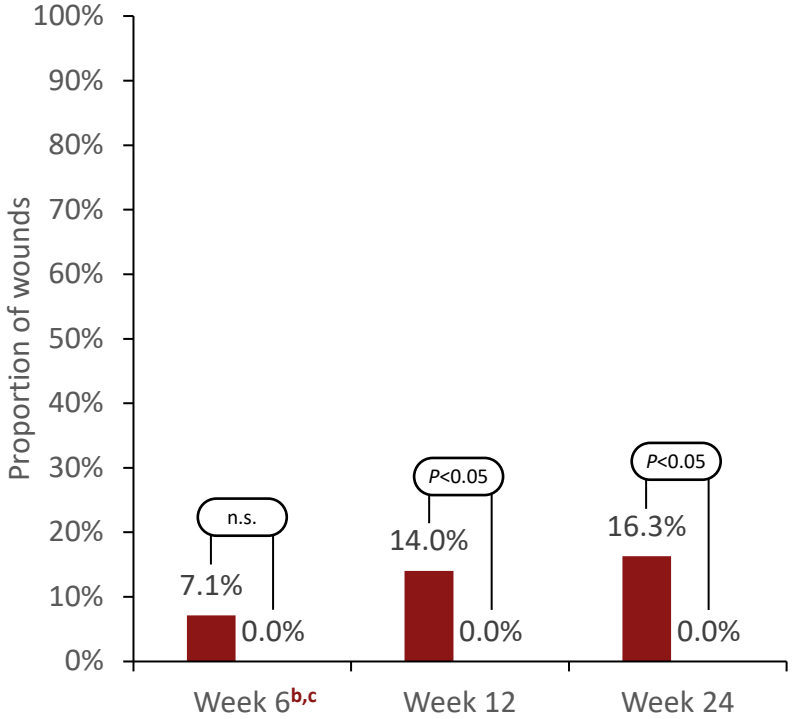
	Week 6[b]		Week 12		Week 24	
n	27	7	34	8	35	7
N	28	28	43	43	43	43

≥75% wound healing from baseline



	Week 6[b]		Week 12		Week 24	
n	20	1	20	3	28	3
N	28	28	43	43	43	43

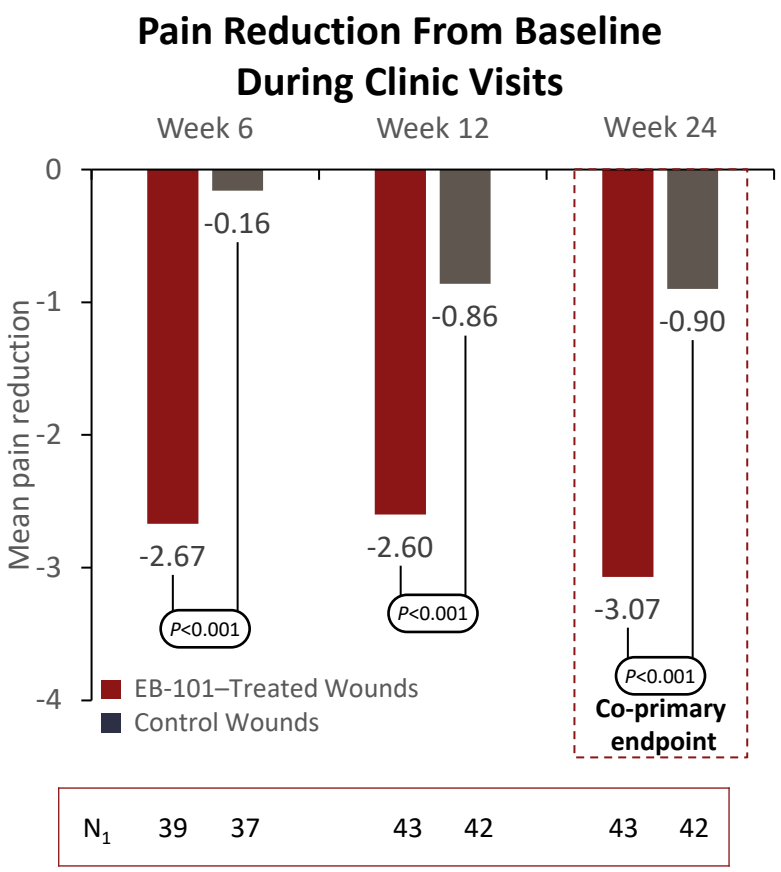
Complete wound healing from baseline[a]

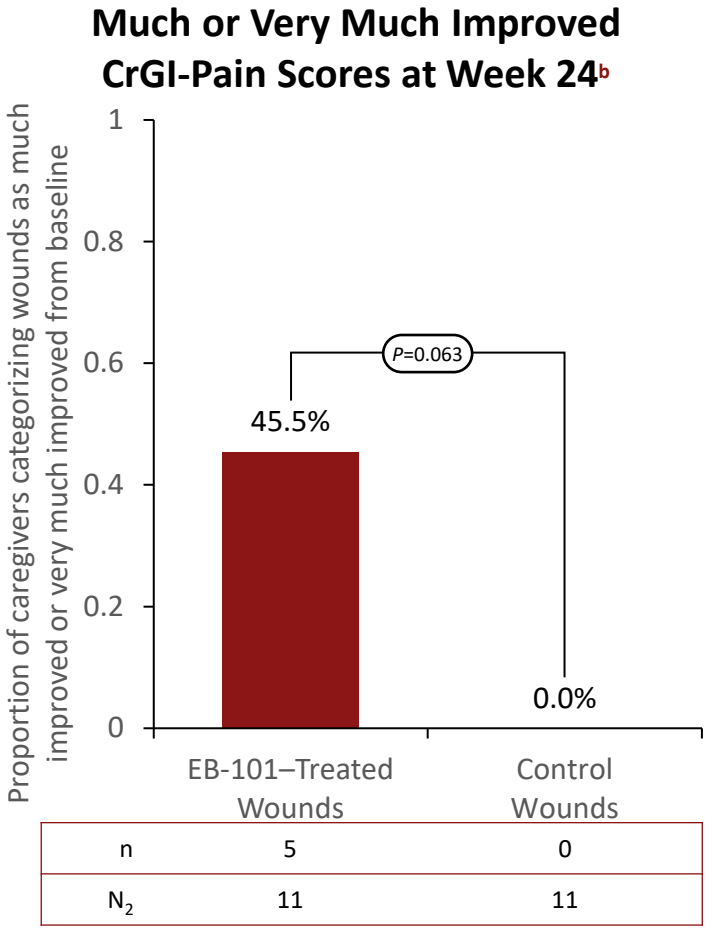


	Week 6[b,c]		Week 12		Week 24	
n	2	0	6	0	7	0
N	28	28	43	43	43	43

Wounds demonstrating a healing category at week 24 were required to be confirmed ≥2 weeks later to be included in the count.
[a]Complete wound healing was defined as re-epithelialization with no drainage or erosion and presence of only minor crusting. [b]Post hoc endpoint. [c]Missing data was not imputed; observed case only.
n, number of wounds in healing improvement category; N, number of total wounds with nonmissing healing improvement category; n.s., not significant.
Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Pain Severity Assessments[a]





Additional Pain Measures

At-home pain severity assessments using the Wong-Baker FACES scale showed statistically significant pain reduction with EB-101 treatment as early as week 3.

Pain was also assessed using PROMIS[c], with a significantly greater improvement in pain quality-sensory scores achieved with EB-101 treatment.

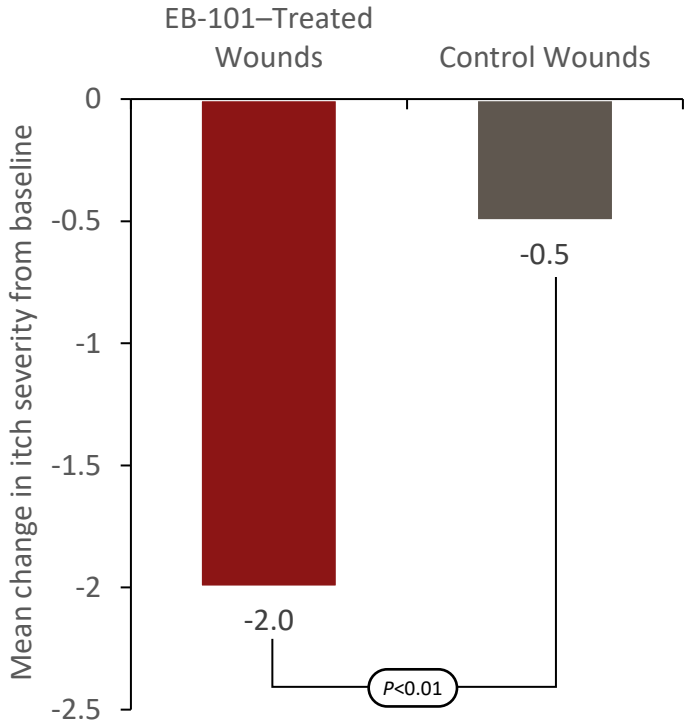
[a]Pain was assessed via the Wong-Baker FACES scale or numeric rating scale. For every post-baseline assessment, the pain reduction was calculated as baseline pain score minus the post-baseline pain score. [b]Each caregiver gave 2 responses on the CrGI-Pain, 1 for all EB-101–treated wounds (randomized and nonrandomized) and the other for all control wounds. [c]Change in pain quality and pain interference assessed using the PROMIS Pediatric Short Form 8a versions of Pain Quality (sensory and affective domains) and Pain Interference scales at week 24.

CrGI, Caregiver Global Impression; n, number of caregiver responses; N_1, total number of wounds with nonmissing pain reduction score; N_2, total number of caregiver responses at Week 24; PROMIS, Patient-Reported Outcomes Measurement Information System.

Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

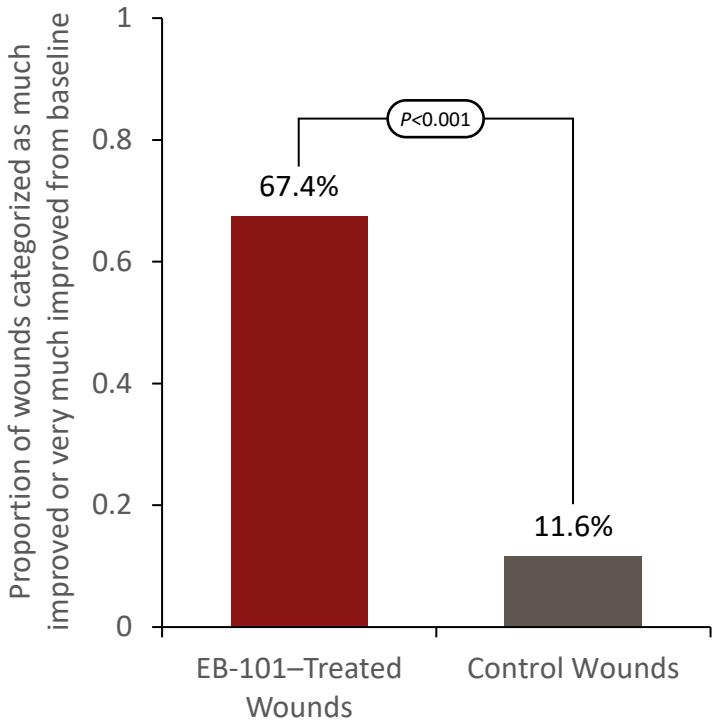
Additional Patient- and Caregiver-Reported Outcomes

Change in Itch Severity at Week 24



N_1	43	42

Much or Very Much Improved PGIC-Blistering Scores at Week 24



n	29	5
N_2	43	43

n, number of wounds in PGIC-Blistering score category; N_1, number of randomized wounds assessed; N_2, total number of wounds with nonmissing pain reduction score; PGIC, Patient Global Impression of Change.

Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Overall Summary of Wound-Specific Treatment-Emergent Adverse Events[a]

	EB-101–Treated Wounds[b]		Control Wounds	
	Patients (N=11)	Wounds (n=57)	Patients (N=11)	Wounds (n=43)
	n	n (%) E	n	n (%) E
All	7	22 (38.6) 35	4	7 (16.3) 7
Serious	0	0	0	0
Leading to new or prolonged hospitalization	0	0	0	0
Leading to trial discontinuation	0	0	0	0
Leading to death	0	0	0	0
Leading to infection	5	12 (21.1) 21	3	4 (9.3) 4
Related to EB-101	1	6 (10.5) 6	1	3 (7.0) 3

Among the EB-101–treated wounds, **20 moderate infections** and **1 mild infection** were reported, whereas among the control wounds, **3 moderate infections** and **1 mild infection** occurred.

A single participant reported moderate procedural pain at surgical sites in 6 EB-101–treated wounds and 3 control wounds.

[a]TEWAEs are defined as any study wound adverse event with an onset on or after the date of EB-101 application. [b]Results include both randomized and nonrandomized EB-101–treated wounds.
E, event.
Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.

Conclusions

Based on the results of VIITAL, a phase 3, randomized, intrapatient controlled trial, treatment of large, chronic wounds with EB-101 application demonstrated a favorable risk-benefit profile in patients with RDEB.

- **Both co-primary endpoints of VIITAL were met, with the majority (81%) of EB-101–treated wounds demonstrating ≥50% healing and a greater reduction in pain severity observed in EB-101–treated wounds compared with control wounds**
- **Even for earlier time points, the percentage of wounds demonstrating healing (≥50%, ≥75%, and complete) and the reduction in pain severity was greater for those treated with EB-101 when compared with control wounds**
- **In addition to significantly reducing pain, patient-reported outcomes related to itch and blistering showed significantly greater improvement with EB-101 treatment**
- **Caregiver-reported outcomes related to wound care and overall impression of wound pain showed consistent trends for improvement**
- **Treatment was safe and well tolerated, with no reports of patient-level or wound-specific serious EB-101–related TEAEs and only a small number of nonserious EB-101–related TEAEs, consistent with previous clinical trial experience[1-3]**

RDEB, recessive dystrophic epidermolysis bullosa; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

1. Siprashvili Z, et al. *JAMA*. 2016;316(17):1808-17. 2 .Eichstadt S, et al. *JCI Insight*. 2019;4(19):e130554. 3. So JY, et al. *Orphanet J Rare Dis*. 2022;17(1):377

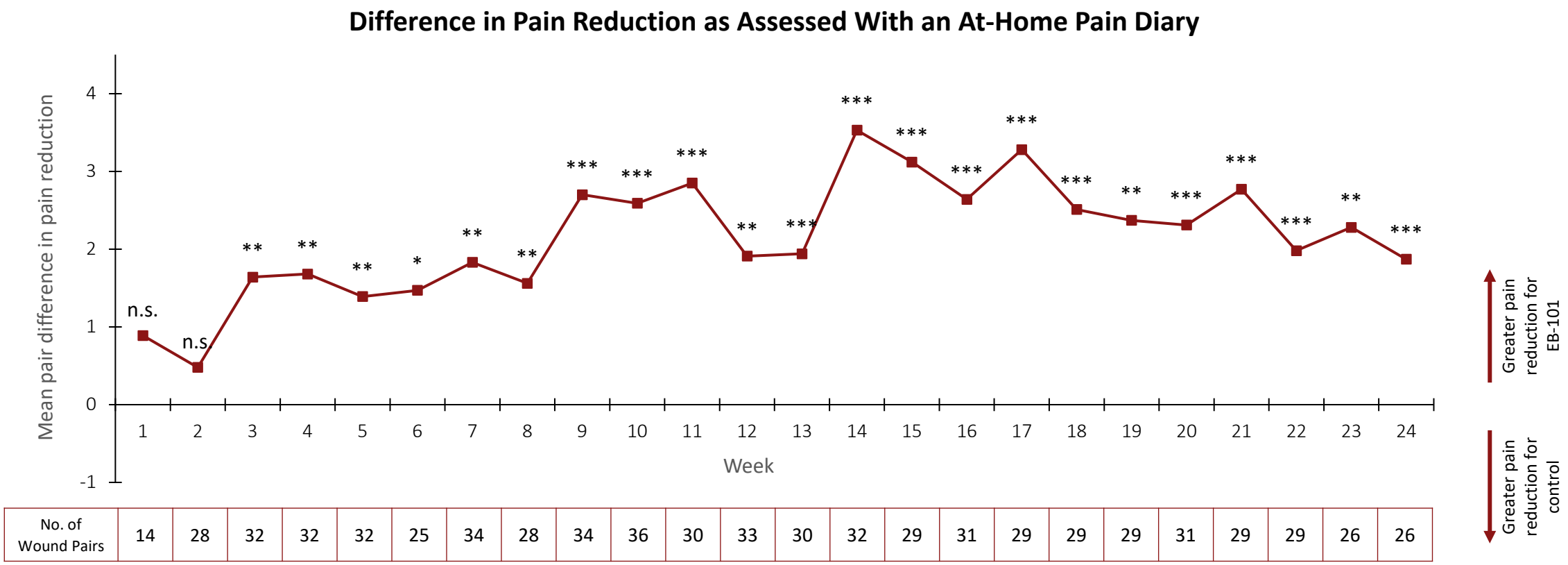
Acknowledgments

- The authors thank the participants, their caregivers, study coordinators, and support staff who contributed to this study
- We also thank Zeynep Turan, PhD, of Chameleon Communications International, for providing medical writing assistance, which was funded by Abeona Therapeutics Inc.
- This study was funded by Abeona Therapeutics Inc.

Thank you

Backup

Pain Severity Assessment Over Time[a]



No. of Wound Pairs	14	28	32	32	32	25	34	28	34	36	30	33	30	32	29	31	29	29	29	31	29	29	26	26

*P<0.05, **P<0.01, ***P<0.001.

[a]Pain was assessed via the Wong-Baker FACES scale or numeric rating scale. For every post-baseline assessment, the pain reduction was calculated as baseline pain score minus the post-baseline pain score.

Data on file. Abeona Therapeutics Inc., Cleveland, Ohio; 2023.