

**INTRODUCTION:**

- RDEB is a genetic disorder leading to widespread wounds with no approved therapies.
- We conducted a literature review of clinical, humanistic and economic disease burden.

**METHODS:**

- A systematic literature search in MEDLINE and Embase through April 2, 2020 was conducted.
- An experienced reviewer independently screened all titles and abstracts for inclusion. A second reviewer performed data extraction quality assurance.
- 65 studies reporting clinical, economic and humanistic burden in English were included.

**RESULTS:**

<i>Economic Burden:</i>		
<i>Direct Costs</i>	<i>Indirect Costs</i>	<i>Impact on Families</i>
<ul style="list-style-type: none"> <li>Wound dressing up to est. \$245K/yr/pt (2012 data)</li> <li>Medications</li> <li>Hospital stays and clinic visits</li> </ul>	<ul style="list-style-type: none"> <li>Frequent, time-consuming dressing changes</li> </ul>	<ul style="list-style-type: none"> <li>50% of US patients had high/severe impact on finances</li> </ul>

<i>Humanistic Burden- Patients</i>
Patients experienced anxiety (41%) and depression (31%)
<i>Humanistic Burden- Parents</i>
Negative impact on their ability to remain physically and emotionally close to their significant other (90%)
Chose not to have more children (64%)
Relationship negatively affected (59%)
Little energy to do more than care for their child (50%)
67% of divorced parents (22%) reported RDEB as a major/primary, factor

<i>Clinical Impact: Wounds</i>
Affected ≥30% of the body in 60% of patients; 10-30% of the body in 28% of patients
Chronic and large wound- correlate with pain
A mean of 3 chronic and 11 recurrent wounds per patient, most moderate (48%) or severe (26%)
Over 80% of patients reported overall pain scores ≥ 5/10
70% of patients reported an infection within 2 years
95% of squamous cell carcinomas were on extremities and in areas of chronic wounds

<i>Clinical Impact: Particularly Bothersome Symptoms</i>
Recurrent and chronic wounds
Blistering skin lesions
Esophageal stenosis
Anemia
Malnutrition/nutritional problems
Pseudosyndactyly or musculoskeletal contractures
Microstomia
Ocular involvement
Congestive heart failure/cardiomyopathy

**CONCLUSIONS:**

- Large, chronic wounds comprise the main clinical burden in RDEB, which is well documented in literature.
- There is considerable economic and humanistic burden for patients and their families.
- New therapies that target the underlying disorder and reduce wound burden could potentially address the disease, and associated humanistic and economic burden.

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### INTRODUCTION:

- Recessive dystrophic epidermolysis bullosa (RDEB) is caused by mutations in the *COL7A1* gene, encoding for type VII collagen.
- Resulting wounds are often large, can become chronic, and are painful.
- We report long-term outcomes following EB-101 gene-corrected autologous cell therapy for chronic RDEB wounds in a phase 1/2a study.

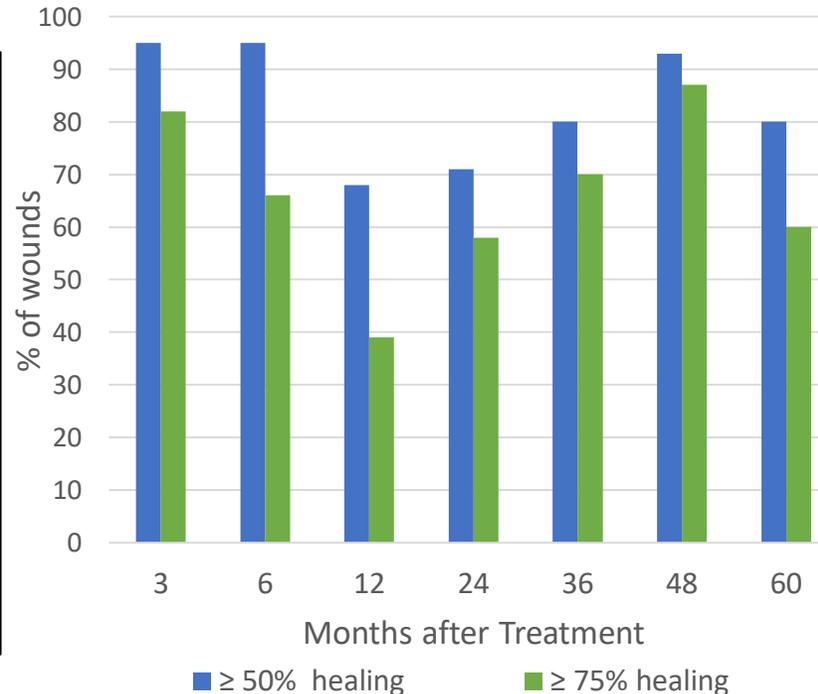
### METHODS:

- Study participants with RDEB were ≥18 years old, had two *COL7A1* genetic mutations and chronic open wounds ≥ 20 cm<sup>2</sup>, for ≥ 12 weeks.
- Autologous keratinocytes were cultured from intact skin biopsies, transduced with a retrovirus containing full-length *COL7A1* and cultured to form epidermal sheets.
- Gene-corrected sheets (EB-101) measuring 35 cm<sup>2</sup> were transplanted onto 38 chronic wound sites in 7 participants from 2013 to 2017.
- Presence of pain was assessed with clinic visits for each treated wound site.

### RESULTS:

- EB-101 treatment ~ 210 cm<sup>2</sup> chronic wound area per patient resulted in considerable reduction of wound burden: median 3- and 6-month reduction of ≥ 130 and 121 cm<sup>2</sup>, respectively (range 131-157 cm<sup>2</sup> for both), based on investigator assessment.
- This reduction was durable.

**Wounds with ≥ 50% or 75% healing**



### Pain relief was associated with EB-101 treatment:

	% Painful Wounds	% Painful Wounds with ≥50% Healing
Pre-grafting	53.0% (20/38)	---
3 months	0.0% (0/38)	0.0% (0/36)
6 months	15.7% (6/38)	11.1% (4/36)
12 months	5.3% (2/38)	0.0% (0/26)
24 months	8.1% (3/37)	3.7% (1/27)
36 months	0.0% (0/20)	0.0% (0/16)
48 months	0.0% (0/15)	0.0% (0/14)
60 months	0.0% (0/5)	0.0% (0/4)

### CONCLUSIONS:

- Treatment of large, chronic wounds with EB-101 resulted in considerable and durable reduction in wound burden.
- ≥50% wound healing was associated with long-term pain relief.
- An ongoing EB-101 Phase 3 study (VIITAL) will further characterize the relationship between healing of large RDEB wounds and pain relief.