**Genetically corrected autologous keratinocyte epidermal grafts improve wound healing and patient reported outcomes in patients with recessive dystrophic epidermolysis bullosa (RDEB)**

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**Introduction**

**Recessive Dystrophic Epidermolysis Bullosa**

- RDEB is an inherited blistering skin disorder caused by mutations in the COL7A1 gene encoding type VII collagen (C7) and is characterized by extremely fragile skin, chronic wounds, corneal abrasions, esophageal stenosis, pseudosyndactyly, significant pain and itch, and aggressive squamous cell carcinomas (SCCs).

- Despite advances in the molecular diagnosis of RDEB, current therapy is limited to supportive palliation.

- To date, no therapies have been approved by the FDA for RDEB.

- Seven adult RDEB participants (mean age 28.7 years) were enrolled in this Phase 1/2a study.

- Participants were followed for 2-5 years post-grafting to evaluate safety parameters, wound healing, and patient-reported outcomes.

- Primary endpoint: wound healing as assessed by both Investigator Global Assessment (IGA) and with Canfield Vectra 3D photography system.

- Secondary endpoint: evaluation of molecular correction of C7 and patient-reported outcomes at 3, 6, and 12 months post-grafting.

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**Methods**

- Participants were 18 years or older and were confirmed to have RDEB by genetic testing (GeneDx).

- Immunofluorescence (IF) and electron microscopy (EM) was performed to determine eligibility.

- Patients expressing the NC1 terminal of type VII collagen were eligible to enroll, as NC1 is believed to be the most antigenic portion of the C7 molecule.

- Patients who were negative for anti-C7 antibodies by IF were eligible to enroll.

- Grafting was performed and graft sites were immobilized from 2-8 days (mean 5.9 days).

- An induced wound was created and grafted for participants 1-4.

- An untreated control wound was identified and followed for participants 5-7.

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**Results**

- The large majority of participants' grafts demonstrated ≥50% healing at 3 and 6 months, with gradual decline over time.

- The percentage of wound healing based on Investigator Global Assessment (IGA).

- Clinical Improvement of grafted sites was observed.

- Gene corrected autografts showed improved healing compared to control wounds.

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**Discussion**

- Long-term follow up data from this phase 1/2a trial of 7 RDEB participants suggests that grafting wounds with gene-corrected autografts is safe and may be the first durable treatment for RDEB chronic wounds.

- Older wounds, large wounds, and those grafted on anatomical sites difficult to immobilize or prone to friction (e.g. back) healed less well than other sites.

- Limitations:

  - Small sample size.

  - Participants were able to choose the wounds they wanted grafted during Phase 1/2a (i.e. wounds not randomized).

- Next steps:

  - This treatment was granted breakthrough therapy designation by the FDA in 2017; a Phase 3 trial will begin mid-2019.

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**References**


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