A randomized trial to determine the efficacy and safety of FCX-007 in the treatment of recessive dystrophic epidermolysis bullosa (DEFI-RDEB)

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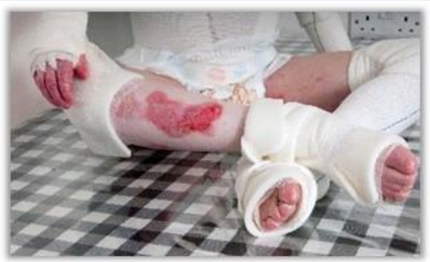
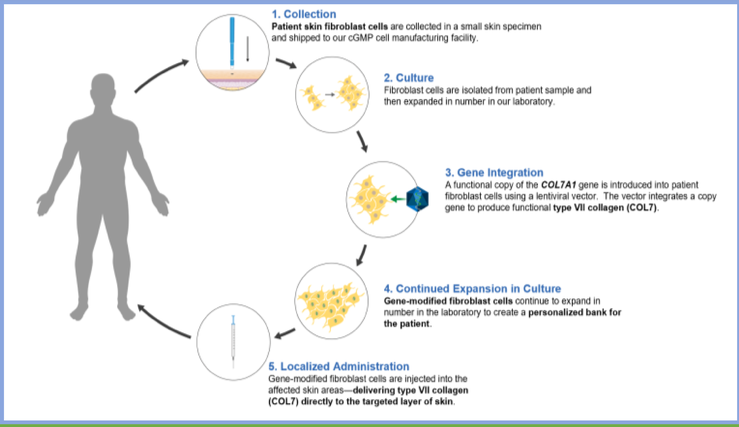
INTRODUCTION and BACKGROUND

Recessive dystrophic epidermolysis bullosa (RDEB) is a debilitating genetic disorder caused by mutations of the type VII collagen gene, COL7A1. Mutations of this gene result in a reduction or absence of a functional collagen VII (COL7) protein, the primary component of anchoring fibrils (AFs) in the basement membrane zone between the dermis and epidermis. Absent or reduced AFs results in separation of the epidermis from the dermis in response to minor skin trauma resulting in mechanical fragility of the skin and recurrent blister formation.



COL7A1 GENE-CORRECTED AUTOLOGOUS FIBROBLASTS: PRODUCTION OF FCX-007



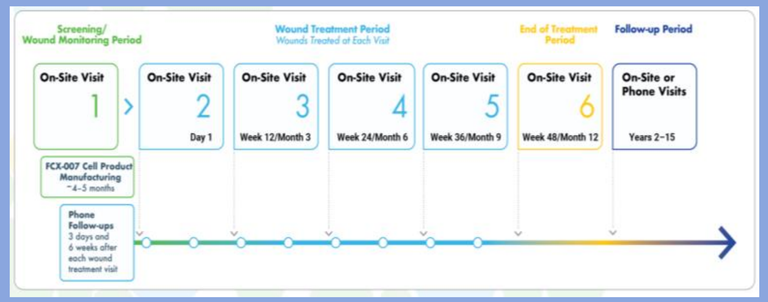
CLINICAL STUDY OVERVIEW

DEFI-RDEB is a multi-center, randomized, controlled open label Phase 3 study designed to evaluate the safety and efficacy of FCX-007 (also known as D-Fi) for the treatment of RDEB wounds.

After screening and verification of genetic mutation of COL7A1, fibroblasts are isolated from the subjects' skin biopsies, transduced with a third-generation self-inactivating lentiviral vector encoding the wildtype COL7A1 gene and expanded for local injection. Following a 12-week observation period to characterize the wounds, confirming their persistence and duration, investigators identify up to 3 pairs of wounds ranging from 10-50 cm2. One wound in each pair will serve as a target wound for treatment, while the other serves as an untreated control. Autologous gene-corrected, collagen VII-expressing fibroblasts (FCX-007) are injected intradermally in the randomly assigned target wounds on Day 1 and Week 12. Injections are repeated at Weeks 24 and 36 at the investigator's discretion.

Subjects who have received at least one treatment injection will continue in the long-term safety follow-up period through 15 years.

CLINICAL STUDY SCHEMA



ENDPOINTS and ANALYSIS

Efficacy assessments will include evaluation of complete wound closure by a blinded assessor (primary endpoint is serial assessments of first wound pair at Weeks 22 and 24), durability of response, change in wound surface area and pain level (via Wong-Baker FACES® Pain Rating Scale).COL7 expression in selected treated wounds will be assessed by immunofluorescence (IF) and immunoelectron microscopy (IEM) in a subset of subjects. Safety assessments include adverse events (including the presence of neoplasms), replication-competent lentivirus (RCL), COL7 antibody and clinical laboratory testing.

The overall study design and selected endpoints were chosen after considering results from an earlier Phase1/2 study demonstrating complete wound healing in 80% of the evaluated subjects. While no serious adverse reactions were reported in that study, the current study is of longer duration which will allow a more complete analysis of long-term benefits and risks.

CONCLUSION

RDEB is a serious and debilitating disorder which currently has no FDA-approved treatment. Using a gene therapy approach which replaces the mutated COL7A1 gene with the wild type, the Phase 1/2 study conducted previously provides efficacy and safety data that needs to be confirmed and expanded in duration. This current study was designed for that purpose. Following completion, it is hoped that the preliminary efficacy results and benefit-risk profile will warrant consideration of this approach for specific RDEB patients. (NCT04213261).

The authors are grateful to each of the patients participating in this clinical study.

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