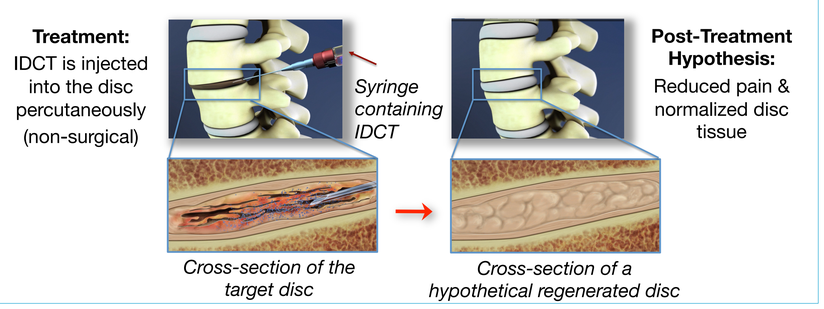
Clinical Study to Evaluate the Safety and Preliminary Efficacy of IDCT, a Cell Therapy to Treat Moderate, Symptomatic Lumbar Degenerative Disc Disease

Lara I. Silverman PhD[1,2], Domagoj Coric MD[3], Kevin T Foley MD[1,2,4]
[1]DiscGenics, Salt Lake City UT, [2]Departments of Neurosurgery, Orthopedic Surgery, & Biomedical Engineering, University of Tennessee Health Science Center, Memphis TN, [3]Carolina Neurosurgery & Spine Associates, [4]Semmes-Murphey Clinic

Introduction

- In this first-in-human clinical study, a novel allogeneic cell therapy known as IDCT is being evaluated for safety and preliminary efficacy in 11 clinical sites across the US (clinicaltrials.gov NCT03347708).
- Previously, mode of action studies demonstrated two potential therapeutic effects of the active ingredient, known as discogenic cells, which include both a directly regenerative capacity to create new intervertebral disc tissue, as well as an anti-inflammatory effect (**Figure 1**). Preclinical evaluation of IDCT in mouse, rabbit, dog and pig models have shown promising therapeutic potential, specifically via improvement of disc height and normalization of tissue architecture, without safety concerns.
- Based on these findings, under supervision by the CBER branch of the FDA utilizing an IND, this first-in-human clinical trial is evaluating safety and efficacy of two doses of IDCT compared to controls.

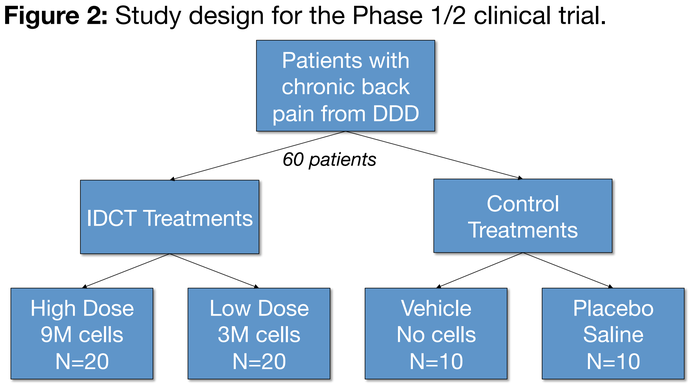
Figure 1: Clinical mode of delivery and hypothesized outcomes after treatment with investigational product IDCT



Methods

- Five lots of discogenic cells were generated from adult disc tissue over the course of 4-6 weeks in a clean room according to cGMP.
- When complete, the allogeneic cells were frozen and stored in the vapor phase of liquid nitrogen for testing at two doses.
- For lot release, the potency, identity, purity (endotoxin, residual impurities), and safety (sterility, mycoplasma and virus testing) were evaluated and required to meet preset specifications.
- For the clinical trial, FDA allowed the trial through an IND application, and now the protocol is being approved by IRBs associated with clinical sites.
- Men and women age 18-75 are being considered with a modified Pfirrmann grade 3-7 in the target disc, and randomized into four cohorts (**Figure 2**). Patients may not have involvement of more than 1 symptomatic disc, persistent nerve pain, full thickness annular tears, grade 2 or higher spondylolisthesis, lumbar spondylitis or other undifferentiated spondyloarthropathy, or Type III Modic changes around the target disc, amongst other criteria. Upon consent, suitable patients are being randomized into the clinical study.

Figure 2: Study design for the Phase 1/2 clinical trial.



Key Study Features:

- Prospective study design
- Single injection
- Double-blind, vehicle and saline control
- Two doses; Low & High
- Multicenter
- Outcomes: Safety and preliminary efficacy
- 1 year primary, 1 year extension

Methods Continued

- After 1, 3, 6, 12, 18 and 24 months, the patients are being evaluated for pain via Visual Analog Scale, disability using the Oswestry Disability Index, quality of life using EQ-5D, use of pain medication, time to subsequent spine intervention, and mobility via the TUG test (Timed Up and Go), amongst other measures, which are compared to baseline. Additionally, radiographic evaluations are being performed (x-ray, MRI) to evaluate disc height, disc volume, disc hydration, angular motion, and other relevant parameters.
- A grouped sequential design is employed. After 6 patients are enrolled, a Data Safety Monitoring Committee (DSMB) will review the unblinded safety data to determine if the study can continue. Stopping points again occur after 30 and 36 patients.

Results

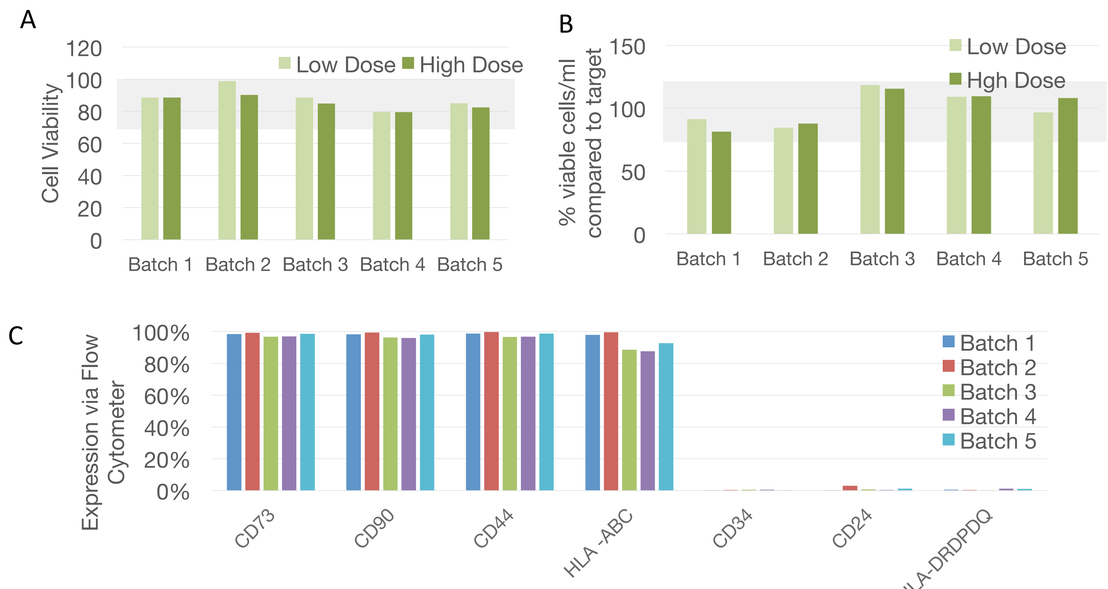


Figure 3: (A) Viability measured via trypan blue exclusion assay, must be >70%. (B) Viable cell density must be +/- 20% of target dose. (C) Surface marker expression profile must be positive for first 4 markers and negative for last 3 markers.

- All 5 cGMP batches of IDCT successfully met the criteria.
- Sterility, endotoxin, mycoplasma and virus testing all passed the requirements.
- The cell viability was 88.6% ± 7.0% for low dose and 85.2 ± 4.4% for high dose (**Figure 3A**). The viable cell recovery compared to the target cell concentration was 100% ± 13.7% for low dose and 100.5% ± 15% (**Figure 3B**).
- Surface marker expression was consistent across the batches, as shown in **Figure 3C**.
- After the first 6 patients, the DSMB reviewed the unblinded safety data, and allowed the study to continue.

Conclusions

- We generated 5 cGMP lots that met the release specifications. Batch 3 and 4 are being used in the clinic.
- Clinical use of the cells is ongoing. To date, 10 patients have been included in the clinical trial.
- No serious, investigational product-related adverse events have been reported at the time of this publication (January, 2019), with the longest follow-up being 6 months. Given the blinded nature of the study, no efficacy data will be available until all patients are enrolled and complete 1 year of follow-up.

This product is under clinical investigation and has not been approved for use by the FDA or PMDA.

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