# Stem Cell Therapy for Chronic Lumbar Disc Disease: Phase 2 Clinical Safety and Feasibility Data of Intradiscal Injections of Hypoxic Cultured Mesenchymal Stem Cells

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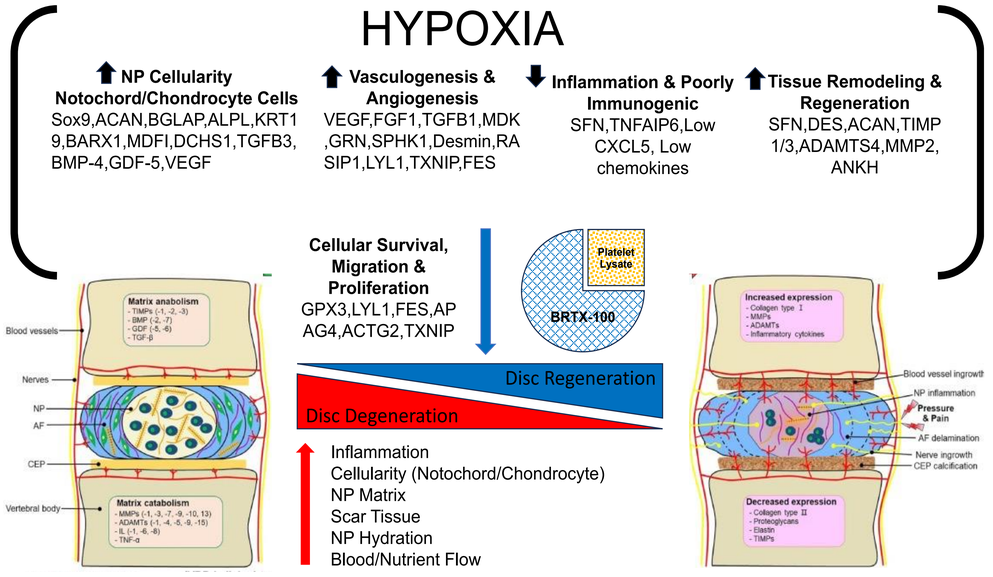
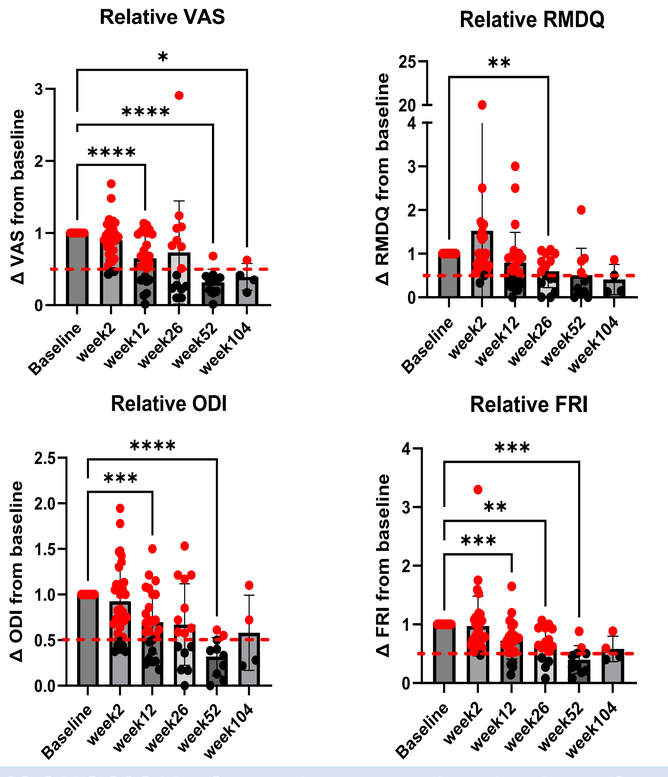
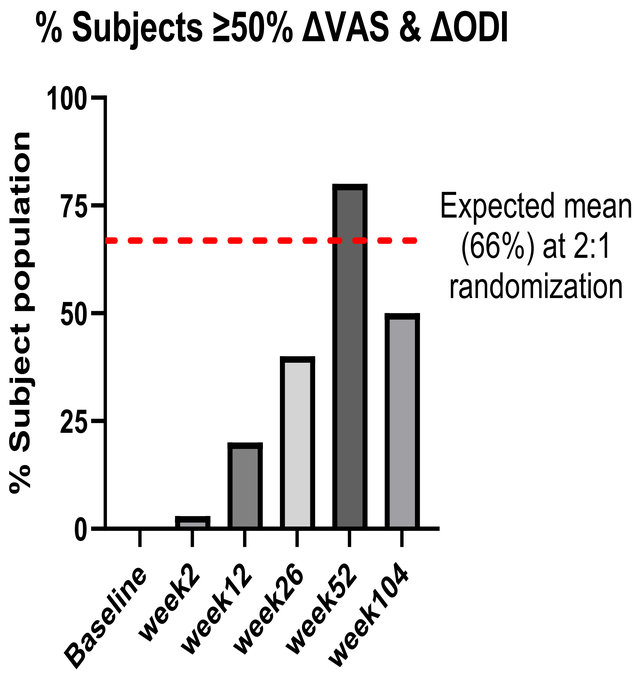
Disclosure: Francisco Silva, Jason Lipetz own equity in BioRestorative Therapies

**INTRODUCTION**: Chronic lumbar disc disease (cLDD) is a common, often confounding problem for patients and physicians. In the United States (U.S.), at least 80% of adults experience at least one episode of lower back pain during their lifetime. Low back pain is the most common cause of disability among Americans between 45 and 65 years of age and imposes the highest economic burden on the U.S. healthcare system. The standard of care for treating cLDD involves conservative non-surgical approaches or surgical interventions that target symptomatic relief and musculoskeletal stabilization. Currently, there is no clinical therapy targeting the reversal of disc degeneration or that addresses intervertebral disc cell homeostasis. Hypoxic culturing of mesenchymal stem cells (MSCs) produces many desirable biological effects that may impact the therapeutic activity of the MSCs post-transplant into the limited nutrient, low oxygen tension microenvironment of the degenerative disc. The use of this cell-based biologic for treating cLDD is a promising therapeutic strategy, due to their *ex vivo* hypoxic engineering and known orthobiologic, immuno-modulatory and anti-inflammatory properties. Here we report early blinded clinical safety and feasibility data in subjects (n=4) treated as part of the safety run-in cohort in a Phase 2 trial to targeting cLDD (NCT04042844).

**METHODS**: An ongoing Phase 2, double-blind randomized, saline-controlled, multicenter study designed to evaluate the safety and efficacy of a single intradiscal injection of autologous hypoxic cultured mesenchymal stem cells (hMSCs) combined with autologous platelet lysate in subjects with single disc chronic lumbar disc disease (cLDD) with 12-month safety and efficacy and 24-month long-term safety endpoints. Approximately 99 subjects will be randomized 2:1 to the treatment or control arm. Once it was determined that the subject met all inclusion and exclusion criteria, bone marrow and blood were collected. Hypoxic cultured mesenchymal stem cells were expanded and formulated with autologous platelet lysate. The mesenchymal stem cells were cryopreserved and shipped to the clinical sites using a temperature controlled shipper for injection. An intradiscal injection of 40 $\times$ $10^6$ cells was performed in 36 subjects. Follow up was performed on all subjects at week 2, week 12, week 26, week 52 and week 104. At each follow up visit physical examinations, laboratory values and reported AEs/SAEs to determine if there were any dose limiting toxicities (DLTs), pain and function scales used; Visual Analog Scale (VAS), Oswestry Disability Index (ODI), Short Form Survey (SF-12), Roland Morris Disability Questionnaire (RMDQ), and Functional Rating Index (FRI). This study is sponsored and funded by BioRestorative Therapies and conducted under an FDA Investigational New Drug application and IRB approved.




**DISCUSSION**: Our primary end point is safety and our secondary end point is at least a 30% improvement in **both** VAS and ODI at week 52. This blinded data of 36 subjects in our ongoing Phase 2 clinical trial using autologous hypoxic cultured MSCs formulated with autologous platelet lysate demonstrated for the first time that a cell dose of 40 $\times$ $10^6$ did not result in AEs/SAEs that were related to dose limiting toxicity and appears to be trending towards demonstrating efficacy.

**RESULTS:** All 36 subjects underwent successful dosing of either a 40 $\times$ $10^6$ cell dose of hMSCs or a sham injection at a 2:1 randomization ratio. At 26 weeks 46.672% of patients report > 50% improvement **VAS score** (n=15). At 52 weeks 90% of patients report > 50% Improvement **VAS score** (n=10) At 104 weeks 75% of patients report > 50% Improvement **VAS score** (n=4).12 week avg. improvement > 50% = 73.82%, 26 week avg. improvement > 50% = 76.94%, 52 week avg. improvement > 50% = 72.35%, 104 week avg. improvement > 50% = 68.54%. At 26 weeks 40% of patients report > 50% improvement **ODI score** (n=15). At 52 weeks 80% of patients report > 50% Improvement **ODI score** (n=10). At 104 weeks 50% of patients report > 50% Improvement **ODI score** (n=4). 12 week avg improvement > 50% = 67.57%, 26 week avg improvement > 50% = 74.04%, 52 week avg improvement > 50% = 74.63%, 104 week avg improvement > 50% = 75.13%. **Patients with ≥ 50% improvement (RMDQ)** Baseline = 0/36 (0%), week 2 = 3/34 (8.8%) week 12 = 9/25 (36%), week 26 = 7/15 (46.67%), week 52 = 6/10 (60%) week 104 =3/4 (75%). **Patients with ≥ 50% improvement (FRI) ,** Baseline = 0/36 (0%), week 2 = 1/34 (2.94%), week 12 = 4/25 (16%), week 26 = 4/15 (26.67%), week 52 = 8/10 (80%), week 104 =2/4 (50%). There were AEs/SAEs related to dose limiting toxicities of a 40 $\times$ $10^6$ cell dose. **Patients with ≥ 50% improvement in both VAS and ODI** Baseline = 0/36 (0%), week 2 = 1/34 (2.94%), week 12 = 5/25 (20%), week 26 = 6/15 (40%), week 52 = 8/10 (80%), week 104 =2/4 (50%)