

Late-Stage Phase 2 Clinical Safety and Efficacy Data of Intradiscal Injections of Hypoxic Cultured Mesenchymal Stem Cells: Study Update.

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INTRODUCTION: Chronic lumbar disc disease (CLDD) is a widespread issue and the leading cause of disability worldwide. In the United States (U.S.), it's estimated that at least 80% of adults will suffer from lower back pain at some point in their lives. Lower back pain is the leading reason for disability in Americans aged 45 to 65 and is the biggest financial strain on the U.S. healthcare system. Standard of care for treating CLDD include non-invasive methods or surgery aimed at reducing pain and stabilizing the spine. Currently, there's no treatment available that can reverse disc degeneration or effectively remodel the cellular microenvironment within the intervertebral disc. Recently, orthobiologics and in particular stem cells have emerged as a promising strategy for regenerative therapy for degenerative disc disease. Hypoxic culturing of MSCs produces many desirable biological effects that increases the therapeutic activity of the MSCs post-transplant into the nutrient-poor, low oxygen 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 clinical safety and efficacy data in subjects (n=44), (33M/13F) treated as part of an ongoing Phase 2 trial targeting CLDD.

METHODS: An ongoing Phase 2, double-blind randomized, sham-controlled, multicenter study designed to evaluate the safety and efficacy of a single intradiscal injection of 40×10^6 autologous hypoxic cultured mesenchymal stem cells (hMSCs) combined with autologous platelet lysate in subjects with chronic lumbar disc disease (CLDD) with 12-month safety and efficacy and 24-month long-term safety endpoints. 99 subjects will be randomized 2:1 to the treatment or control arm. Data used for study metrics is collected at baseline, week 2, week 12, week 26, week 52, and week 104. Pain and function scales used; Visual Analog Scale (VAS), Oswestry Disability Index (ODI). Primary endpoint is safety and secondary is a clinical response, defined as at least a 30% decrease in pain as measured on the VAS scale and at least a 30% increase in function based on the ODI at Week 52 as compared to baseline. This study is sponsored and funded by BioRestorative Therapies and conducted under an FDA Investigational New Drug application and IRB approved.

RESULTS SECTION: 44 subjects underwent successful dosing of either a 40×10^6 cell dose of hMSCs or control. Subjects who completed the 52 and 104-week visit did not experience AEs/SAEs that were related to dose limiting toxicities of using 40×10^6 cells. All AEs were non-serious and related to expected increased post-procedural back pain. At 26 weeks 53.57% of patients report > 50% improvement VAS score (n=28). At 52 weeks 75% of patients report > 50% Improvement VAS score (n=12) At 104 weeks 75% of patients report > 50% Improvement VAS score (n=4). At 26 weeks 53.57% of patients report > 50% improvement ODI score (n=28). At 52 weeks 74.63% of patients report > 50% Improvement ODI score (n=12) At 104 weeks 50% of patients report > 50% Improvement ODI score (n=4). At 26 weeks 57.14% of patients report > 50% improvement RMDQ score (n=28). At 52 weeks 50% of patients report > 50% Improvement RMDQ score (n=12). At 104 weeks 75% of patients report > 50% Improvement RMDQ score (n=4). At 26 weeks 35.71% of patients report > 50% improvement FRI score (n=28). At 52 weeks 66.67% of patients report > 50% Improvement FRI score (n=12). At 104 weeks 50% of patients report > 50% Improvement FRI score (n=4)

DISCUSSION: Previous clinical studies have claimed that the harsh microenvironment of the disc could impact high cell dose viability and result in a non-efficacious or the worsening of clinical outcomes. At 52 and 104-weeks in our ongoing clinical trial AEs/SAEs reported were not related to dose limiting toxicities of using 40×10^6 cells and although this is blinded and early clinical data it is important to note that the VAS and ODI, collected during 12, 26, 52, and 104-week follow-up visits demonstrated a positive trend indicating a strong safety and efficacy signal and did not show significant worsening of pain and function.

SIGNIFICANCE/CLINICAL RELEVANCE: Results demonstrate that intradiscal injection of hMSCs represent a potential viable option using orthobiologics for the treatment of patients suffering from CLDD. Current trial data from the present study suggest that a cell dose of 40×10^6 of hMSCs are suitable for intra-discal injection of degenerated discs and not limited by the harsh microenvironment of the disc. Strong safety profile as well as positive efficacy trends demonstrate that hypoxic cultured mesenchymal stem cells may be used for treating patients suffering from CLDD.