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Author Email:
kelly.rendon@bioxcellerator.com

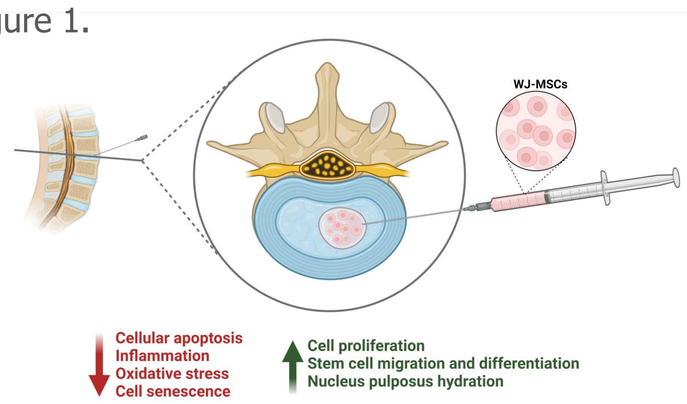
Clinical effect of intradiscal treatment with allogeneic mesenchymal stem cells derived from umbilical cord Wharton's jelly (WJ-MSC) in adults with Degenerative Disc Disease (DDD). BioXcellerator, Medellín, Colombia.

KJ Rendón-Morales[1]*, FA Barrios-Arroyave[1], LA Palacio[1], V Mesa-Pietralunga[1], N Zapata-Franco[1], J España-Peña[1], K Halpert-Correa[1], HF Ortega-Arellano[2], C Quintero-Gil[2], L Lopez-Quiceno[1].
[1] BioXcellerator, Medellín, 050021, Colombia. [2] BioXtech, Medellín, 050021, Colombia.

Introduction

Based on preclinical and clinical studies, it has been demonstrated that mesenchymal stromal cells (MSC) based therapy has the potential to contribute to intervertebral disc repair in patients suffering from Degenerative Disc Disease (DDD) by modulating the inflammatory response and promoting the natural repair process of the intervertebral disc matrix. The mechanisms of action of MSCs on the intervertebral disc are shown in Figure 1.

Figure 1.



Objective

To describe the clinical progression in DDD patients after intradiscal cell therapy with allogeneic Wharton's jelly stem cells from the umbilical cord (WJ-MSC).

Methods

A retrospective cohort observational study analyzed the effects following MSC therapy based on WJ-MSC in DDD patients. Ethical approval was obtained by an independent ethics committee (CEI-0324-07-2022).

Clinical outcomes were measured by Visual-Analog-Scale (VAS), and Oswestry-Disability-Index (ODI). Clinical assessments were performed at baseline and 3-6-12 months after intradiscal/into-facet delivery of a single dose of $10x10^6$ WJ-MSC per target disc. The application procedure is shown in Figure 2.

Figure 2.

WJ-MSCs were obtained from a clinical-grade GMP-compliant laboratory. Flow cytometry analysis of P7 cells demonstrated >84% expression of CD105, CD73, and CD90, with <2% expression of CD45, CD34, CD11b, CD19, and HLA-DR. The cells also displayed in vitro differentiation into osteoblasts, adipocytes, and chondrocytes.

Results – Sociodemographic data

- A total of 25 patients were included (November/2021-June/2022). All subjects completed 12 months of follow-up.
- Female 20% (n=5), Male 80% (n=20).
- Countries: United States 72% (n= 18).
- The mean age was 45.12 years old (SD=12.90).

Results – Clinical data

- Follow-up time: The median time from non-exposure (onset of symptoms or diagnosis of DDD to WJ-MSC therapy) was 144 months (IQR=127).
- Lumbosacral DDD (n=18, 72%), Thoracic DDD (n=7, 28%). The most common number of affected discs was 3 (n=10, 40%).
- Pre-therapy spine MRI= MODIC-1 changes (n=6, 24%), MODIC-2 changes (n=7, 28%), Pfirrmann-III (n=15, 60%), Pfirrmann-IV (n=4, 16%).
- One or more previous spinal surgeries (n=7, 28%).
- History of radiculopathy (n=14, 56%).
- Physical therapy before MSC therapy was acknowledged by 5 subjects (20%). The median minutes/week of physical therapy in the last year before intradiscal therapy was 120 (IQR=0).

References

Zhang W, Wang D, Li H, Xu G, Zhang H, Xu C and Li J (2023), Mesenchymal stem cells can improve discogenic pain in patients with intervertebral disc degeneration: a systematic review and meta-analysis. Front. Bioeng. Biotechnol. 11:1155357. doi: 10.3389/fbioe.2023.1155357

Results – Pain assessment

- Pre-therapy VAS score: 4 → VAS-12m score: 2 (*p=0.007*).
- In 76% (n=19) subjects, the VAS-12m score improved or remained the same compared to pre-therapy (*p=0.003*).
- Radiographic findings:

Figure 3 shows a representative case of a patient in which it is observed:

3A. L4-L5 Pretherapy MRI (May/2021)
3B. L5-S1 Pretherapy MRI (May/2021)

Radiology report findings: 1) MODIC type 2 changes, L4-L5 endplate irregularity, and hyperintensity. 2) Endplate edge hyperintensity and posterior bulging at L5-S1. 3) Pfirrmann grade III degeneration at L4-L5/L5-S1.4) Lumbar scoliosis of left convexity, spondylosis, osteoarthrosis, small disc complex of osteophytes at L4-L5, and minimal degenerative anterolisthesis at L5-S1 with decreased width of foramina for both roots.

Figure 3A.

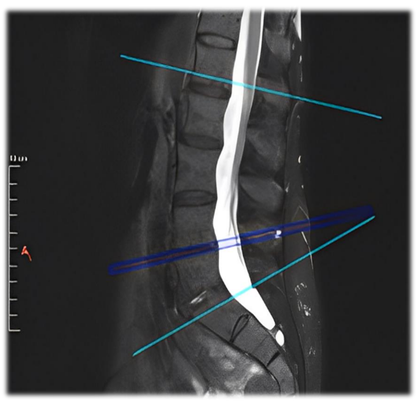
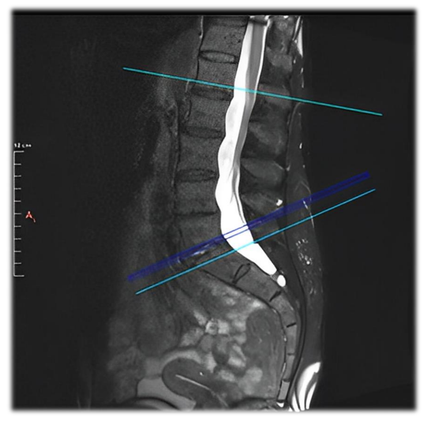


Figure 3B.



3C. L4-L5 follow-up evaluation (May/2022)
3D. L5-S1 follow-up evaluation (May/2022)

Improvement of edema in end-plates at L4-L5 and decreased bulge with changes in disc hydration at L5-S1.

Figure 3C.

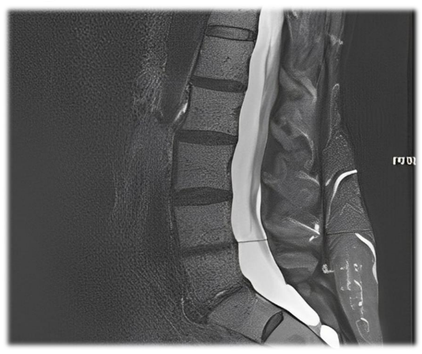
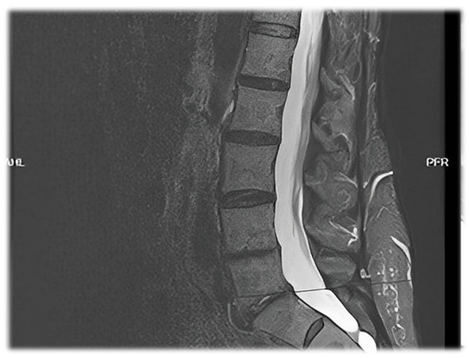


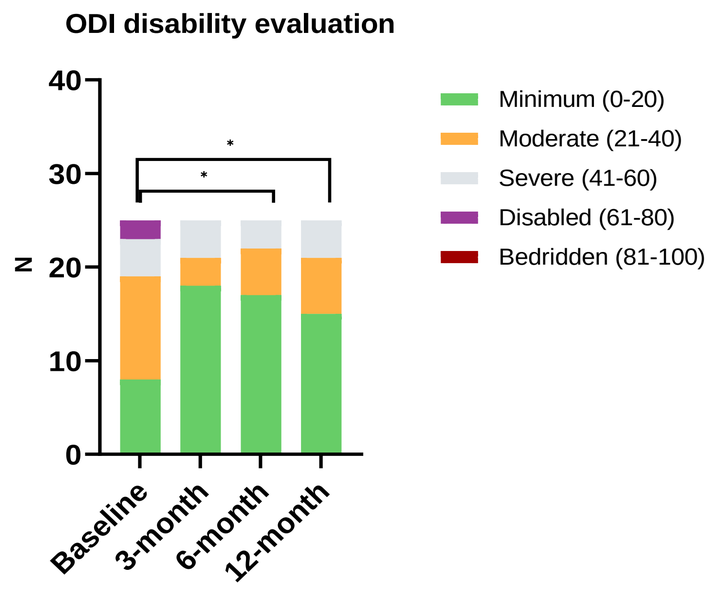
Figure 3D.



Results – Disability assessment

- Pre-therapy ODI 24% → 12 months, 16% (*p=0.130*).
- In 80% (n=20) subjects, the ODI-12m score improved or remained the same (*p=0.003*).
- Responder *patient: reduction in ODI percentage >=10%.* 8 patients responded favorably to WJ-MSC (32%).
- Variables associated with treatment response: number of affected discs (*p=0.006*), number of discs receiving WJ-MSC injections (*p=0.004*), reduction in VAS from pre-therapy to VAS-12m (worsened vs improved or remained the same) (p=0.047), MODIC-1 (*p=0.075*), MODIC-2 (*p=0.076*).
- *Cox regression*: MODIC-1 (*p=0.047*, HRa=5.38 95%CI=1.00,29.07), number of affected discs *(p=0.043*, HRa=0.26 95%CI=0.07,0.94).

Figure 4.



Conclusion

No serious adverse events were reported. Intradiscal delivery of WJ-MSCs was safe and effective in DDD patients.