Safety and Complications Reporting Update on the Re-Implantation of Culture-Expanded Mesenchymal Stem Cells Using Autologous Platelet Lysate Technique

Abstract: Mesenchymal stem cells (MSCs) hold great promise as therapeutic agents in regenerative medicine. Numerous animal studies have documented the multipotency of MSCs, showing their capabilities for differentiating into orthopedic tissues such as muscle, bone, cartilage, and tendon. However, the safety of culture expanded MSC’s for human use has only just begun to be reported.1

Methods: Between 2006 and 2010, two groups of patients were treated for various orthopedic conditions with culture-expanded, autologous, bone marrow-derived MSCs (group 1: n=50; group 2: n=290-one patient in both groups). Cells were cultured in monolayer culture flasks using an autologous platelet lysate technique and re-injected into peripheral joints or into intervertebral disc spaces with use of c-arm fluoroscopy. While both groups had prospective surveillance for complications, Group 1 additionally underwent 3.0T MRI tracking of the re-implant sites.

Results Section: The mean age of patients treated was 53 +/- 13.85 years; 214 were males and 125 females with mean follow-up time from any procedure being 435 days +/- 261 days. Number of contacts initiated based on time from first procedure was 482 at 3 months, 433 at 6 months, 316 contacts at 12 months, 110 contacts at 24 months, and 22 contacts at 36 months. For Group 1, 50 patients underwent 210 MRI surveillance procedures at 3 months, 6 months, 1 year and 2 years which failed to demonstrate any tumor formation at the re-implant sites. Formal disease surveillance for adverse events based on HHS criteria documented significantly less morbidity than is commonly reported for more invasive surgical procedures, all of which were either self-limited or were remedied with therapeutic measures. Two patients were diagnosed with cancer out of 339 patients treated since study inception; however, this was almost certainly unrelated to the MSC therapy and the neoplasm rate in similar to that seen in the U.S. Caucasian population. Knee outcome data was collected on a subset of patients. Here, >75% improvement was reported in 41.4% while decreasing the improvement threshold to >50% improvement, 63.2% reported an improvement. At an average reporting time of 11.3 months from first procedure average reported relief in the knee sample equaled 53.1% (n=133 reporting).

Discussion: Using both intensive high field MRI tracking and complications surveillance in 339 patients, no neoplastic complications were detected at any stem cell re-implantation site. These findings are consistent with our prior publication and other published reports that also show no evidence of malignant transformation in vivo, following implantation of MSCs for orthopedic use.

Significance: This present research supports the continuing trend that illustrates minimal complications reporting of culture expanded MSC’s with autologous platelet lysate technique. This information provides groundwork for a critical step forward in educating patients in the risks involved. Furthermore, this study promotes discussion of this procedure as a verifiable consideration among patients seeking alternative orthopedic treatments.

Acknowledgements: Christopher Centeno and John Schultz performed the MSC re-implant procedures, Centeno also prepared the primary manuscript and reviewed and compiled data. Michelle Cheever performed the cell culture and supervised the laboratory that was involved in cell culture. Stephen Faulkner and Jennifer Passerelli assisted in the analysis of the data and review of the manuscript. Brent Robinson and Ron Hanson assisted in manuscript review.

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