Clinical Safety & Effectiveness of Adipose Derived Stromal Cell v. Stromal Vascular Fraction Injection for Treatment of Knee Osteoarthritis: 2 Year Results of Parallel Single Arm Trials

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INTRODUCTION:

There are currently no disease modifying treatments available for knee osteoarthritis (OA), though adipose-derived cultured stromal cells (ASCs) have shown promise in experimental models. However, due to regulatory limits on use of cultured stem cells in humans, previous studies have focused primarily on the stromal vascular fraction (SVF) intraarticular injection. As a result, the therapeutic value of ASCs for knee OA remains unknown. However, the 2013 Regenerative Medicine Promoting Act on the Safety of Regenerative Medicine enacted by the Japanese government has allowed clinical administration of cells processed at government certified laboratories. The purpose of this study was to compared ASC vs. SVF intraarticular injection in patients with Kellgren Lawrence (KL) knee OA grades 2-4 in parallel single arm trials, which were approved under the Regenerative Medicine Promoting Act provisions and by our local research ethics board.

METHODS:

Eighty patients presenting at an outpatient knee clinic in Japan were enrolled with 42 (72 knees) receiving ASC and 38 (69 knees) receiving SVF intraarticular injections. Patient-reported outcome measures (PROMs) were assessed at 1, 3, 6, 12, and 24 months using the composite knee injury and osteoarthritis outcomes score (KOOS5) and pain visual analogue scale (VAS). The percentage of patients achieving minimally clinically important change (MCIC) and patient acceptable symptoms state (PASS) were also calculated. Per protocol, a subset of ASC patients received an ASC booster injection after 6 months. A repeated measures ANOVA compared results between treatment arms and by KL grade over time.

RESULTS:

PROMs improved substantially after both treatments ($p<0.05$ at all timepoints) with ASC patients more likely to achieve MCIC (50% v 24%, $p=0.01$) and PASS (45% v 24%, $p=0.04$) for Pain VAS and MCIC (43% v 16%, $p=0.02$) for KOOS5 at 12 months, though not at 24 months. The KL2/3 ASC patients had significantly superior outcomes compared to KL4 ASC patients for both KOOS5 ($p=0.01$) and Pain VAS ($p=0.03$), but no such difference was observed in SVF patients. Three ASC patients (7%; all KL grade 3) sought additional nonoperative treatment by 24 months compared to 9 SVF patients (24%, all KL grade 3; $p=0.06$). ASC booster injections conferred no additional benefit. In fact, ASC patients reported more injection-site pain and swelling after booster injection than after initial injection ($p<0.01$).

DISCUSSION AND CONCLUSION:

This represents the first head-to-head comparison of ASC to SVF for treatment of knee OA in humans. Both ASC and SVF injections substantially improved knee pain and function at all follow-up timepoints. ASC injections demonstrated significant improvements over SVF injections with regards to MCIC and PASS for Pain VAS and MCIC for KOOS5. In patients with KL2/3 knee OA, single articular injections improves outcomes to a greater degree than in patients with KL4 knee OA. There appears to be no benefit to a booster ASC injection after initial treatment. Given less donor site morbidity and equivalent to superior outcomes at 2 years, the use of ASC over SVF in the treatment of knee OA may be warranted.