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Abstract Submission Form

Poster Title: **Safety Results from a Phase 1 Double-blind Randomized Clinical Trial of Allogeneic Mesenchymal Stem Cells in Early RA**

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Category: **Clinical Research**

Background: This study was performed to evaluate the safety of bone-marrow derived allogeneic mesenchymal stem cells (MSCs) as therapy in early rheumatoid arthritis (RA). MSCs have immunomodulatory properties *ex vivo* and *in vivo*. MSCs as immunoregulators have been tested in multiple sclerosis, Crohn's disease, cystic fibrosis, and other disease. We hypothesized that a "window of opportunity" would exist in early RA during which immune tolerance could be restored to a "pre-RA-like" state.

Methods: We designed and conducted a Phase 1 double blind clinical trial (RDBCT) in early RA patients using a single infusion of marrow derived allogeneic MSCs. Donors were pre-screened and MSCs isolated, expanded and tested in functional suppressor assays *ex vivo*. A second bone marrow aspiration from the selected donor was performed. MSCs were expanded in the Case Comprehensive Cancer Center GMP faculty and cryopreserved. MSCs underwent purity and adventitious testing in advance and endotoxin prior to release. Studies were performed under IND # 016906 and according to the Declaration of Helsinki. Inclusion criterion included RA for less than two years and/or elevated rheumatoid factor or antibody directed against citrullinated peptides. Known DMSO sensitivity, active infection and history of disease modifying drugs (DMARDs) other than methotrexate, hydroxychloroquine and low dose prednisone were exclusionary.

Results: Of the ten patients treated, five were administered MSCs at 2 million(M)/kg and three patients at 4M/kg, and two received sham infusion. No dose limiting toxicity and no infusion reactions were observed. Two SAEs occurred that were not considered to be study related: 1) acute exacerbation of chronic low back pain; 2) hip fracture in a patient on low dose steroids. Enrollment was halted after ten patients due to stalling of enrollment exacerbated bythe pandemic. Spirometry post-infusion was discontinued with permission mid-way through the trial as no respiratory AEs occurred in conjunction with or immediately after infusion. No study related AEs related to the therapeutic agent were reported.

Conclusion: Use of "off the shelf" bone marrow derived adult "mesenchymal stem cells" appear safe using dosages up to4M/Kg. There were no dose limiting toxicities observed and patients tolerated infusion well without pre-conditioning, as is required for use of other cellular therapies. Given the safety of using MSCs, we suggest that allogeneic MSCs should be tested early in RA in a phase 2 study for their ability to induce immune quiescence and induction of host regulatory cells as well as efficacy responses.