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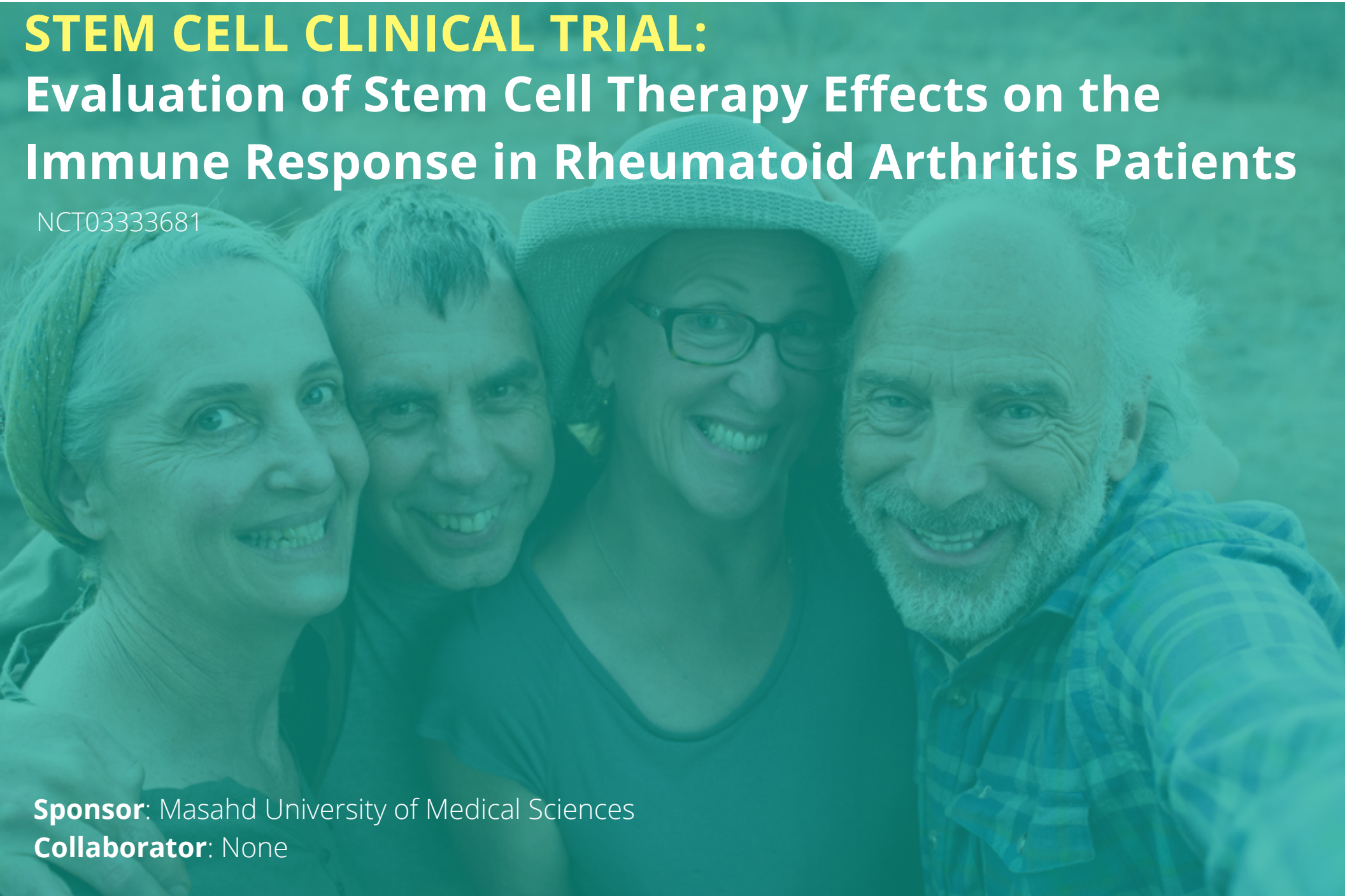
STEM CELL CLINICAL TRIAL:

Evaluation of Stem Cell Therapy Effects on the Immune Response in Rheumatoid Arthritis Patients

NCT03333681



Sponsor: Masahd University of Medical Sciences
Collaborator: None

BACKGROUND:

- Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disease leading to functional impairment.
- The exact causes of RA are still unknown, but there is supporting evidence that T cell subtypes of the immune system play a role in the disease pathogenesis.
- Cytotoxic T cells promote bone degradation through their secretion of cytokines that promote inflammation. Th17 cells act as inflammatory mediators and produce high levels of IL-17 (a pro-inflammatory cytokine).
- Regulatory T cells (T-regs) on the other hand act to suppress immune responses and promote homeostasis.
- Increased levels of Th-17 cells and IL-17 as well as decreased levels of T-reg cells have been reported in patients with RA.
- This indicates that the T-reg/Th-17 imbalance plays a pivotal role in the progression of RA.
- Mesenchymal Stem Cells (MSCs) are multipotent progenitor cells capable of differentiating into different tissue types.
- MSCs also have the capability to modulate immune cell responses of B cells, T cells, dendritic cells, and natural killer cells.
- In addition, they are involved in tissue repair processes by secreting various cytokines.
- These characteristics of MSCs make them an ideal candidate for cellular therapy for RA.

METHOD:

- 9 patients with RA who were refractory to standard therapies were enrolled in this study.
- Autologous MSCs were cultured from 50 mL of bone marrow that was aspirated from the iliac crest of each patient.
- Mononuclear cells were isolated from the marrow for culture by Ficoll density gradient centrifugation.
- Flow cytometry was performed to validate culture; cell viability was also tested.
- All enrolled patients received one intravenous transfusion of 1 million MSCs per kg with evaluations being performed at 1, 6, and 12 months.
- Evaluations included the measurement of immunological factors to include T-regs, Th17 cells, CD4+ and CD8+ cells isolated from the peripheral blood.
- In addition, Disease Activity Score-28 for RA with ESR (DAS28-ESR) and a Visual Analogue Scale (VAS) for pain were also performed.

RESULTS:

- **A significant increase was detected in T reg cell percentages 1 month following infusion.**
- **Fluorescent intensity for FOXP3 (a suppressor of T reg cells) showed a significant decrease at 6 and 12 months versus before treatment.**
- **There was also a decreasing trend in Th17 percentages following MSC treatment with a significant decrease detected at 12 months.**
- **Fluorescent intensity for IL-17 (a pro-inflammatory cytokine secreted by the Th-17 cells) also decreased at 6 and 12 months following treatment.**

RESULTS: CONTINUED

- **DAS28-ESR and VAS scores were used to evaluate disease activity and pain respectively.**
- **A significant decrease in DAS28-ESR was observed at 1 and 12 months following MSC treatment.**
- **VAS scores resulted in a significant decreasing trend for pain during the 12 month follow up period indicating an improvement in quality of life.**
- **There were no complications or reported adverse effects during the trial in any of the 9 participants.**

CONCLUSION:

- Data reported by this trial indicates that autologous bone marrow derived MSC therapy can reduce the severity of disease and increase the quality of life in refractory rheumatoid arthritis patients.
- Further studies are necessary to determine the optimal dose and injection schedule to gain more insight on the therapeutic benefits MSC therapy for RA.

ASSOCIATED PUBLICATIONS:

- https://clinicaltrials.gov/ct2/bye/rQoPWwoRrXS9-i-wudNgpQDxudhWudNzlXNiZip9Ei7ym67VZR0wSg05SKCVA6h9Ei4L3BUgWwNG0it