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Therapeutic Stem Cells and Their Utilization in Multiple Sclerosis Clinical Trials: A Mini Review

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Abstract

In the last two decades, stem cell therapy has been developed rapidly. Stem cells have now emerged as a new treatment for many major disorders including neurodegenerative diseases such multiple sclerosis (MS). Recently, the attention of researchers working on MS have been attracted to cell therapy using therapeutic stem cells (TSCs). In this brief narrative review we explore the application of TSCs in last 5 years registered clinical trials. At the end, we will discuss the challenges and hopes ahead of therapeutic stem cells in treating MS patients.

Keywords: Stem Cell, Cell Therapy, Therapeutic Stem Cell, Multiple Sclerosis, Clinical Trial

1. Therapeutic Stem Cell and Clinical Trials on Multiple Sclerosis Patients

Stem cells (SCs) are a type of cells that are capable of continuous production of new cells (1). These cells exist in embryos as well as adults, in living multicellular organisms including human beings (2). Cell therapy (CT) has long been recognized as a new method for treating various diseases (3-7). Stem cells are usually classified in a variety of ways based on their source and potential capacity (8, 9). Embryonic stem cells (ESCs), mesenchymal stem cells (MSCs), hematopoietic stem cells (HSCs), bone marrow stem cells (BMSCs), adult stem cells (ASCs) and genetically produced induced pluripotent stem cells (iPSCs) are the major types of cells that have been used in CT for various diseases (10). In this article we address these cells as therapeutic stem cells (TSCs). TSCs can be used either by direct transplantation into the patient or by using as a vehicles to transport the genes of interest as a tool for gene therapy (11). iPSCs as patient-specific models also were tested for exogenous gene delivery to the patients (12). Recently, novel genome editing tools including CRISPR has been widely used for gene therapy using TSCs (13).

Multiple sclerosis is a chronic demyelinating disease of the central nervous system, which the progressive degeneration of oligodendrocytes, followed by neural loss is its major remark (14). Many drugs have been proposed for this disease, but they all eliminate the symptoms rather than treating the disease (15). Over the past few years, Gene therapy and CT studies have been used to prevent, reverse and also treat the disease using TSCs which many of them are still in progress (16-22). There are about 58 clinical trials registered that using cells for MS treatment. Table 1 chronologically summarizes the most recent (last 5 years) trials, the type of TSCs used, their degree of progress and some additional information's (23).

2. The Hopes and Challenges Ahead of TSCs to Treat Neurodegenerative Diseases

TSC therapy has not reached its full potential and maturity, yet. Research in this area is still faced with several discrete challenges. The difficulty in the precise and accurate transplantation in distributed sites of lesions, predicting the precise number of the stem cells for effective transplantation without unexpected side effects to ensure the highest efficiency, accurate timing and choosing the best transplantation approach are among the most important challenges that need to be addressed (24). Other problems that we are likely to encounter after successful transplantation are: Probability of producing cancerous masses, epilepsy and immunity (25). Despite all these challenges, the scientific and clinical community are committed to advancing this therapeutic approach. They believe that this therapeu-

tic approach will have a beneficial and major role in the future treatments of this disease.

Footnotes

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Table 1. Last 5 Years Clinical Trials Using TSCs on MS Patients (23)

Study Title	Phase	TSCs	Number Enrolled	Start Date	Location(s)	Status
Intrathecal administration of autologous mesenchymal stem cell-derived neural progenitors (MSC-NP) in progressive multiple sclerosis	Phase 2	MSCs	50	September 2018	United States	Recruiting
Rct comparing autologous hematopoietic stem cell transplantation versus alemtuzumab in multiple sclerosis	Phase 3	HSCs	100	March 2018	Denmark, Netherlands, Norway, (and 5 more...)	Recruiting
Maximizing outcome of multiple sclerosis transplantation	Phase 3	HSCs	200	November 2017	United States	Recruiting
Allogenic mesenchymal stem cells and physical therapy for ms treatment	Phase 1, Phase 2	MSCs	60	September 2017	Jordan	Recruiting
Safety study of human neural stem cells injections for secondary progressive multiple sclerosis patients	Phase 1	ASCs	24	September 2017	Italy, Switzerland	Active, not recruiting
Neural stem cell transplantation in multiple sclerosis patients	Phase 1	ASCs	4	May 2017	Italy	Enrolling by invitation
Autologous bone marrow derived stem cells for the treatment of multiple sclerosis	Phase 1	BMSCs	50	July 2016	Jordan	Active, not recruiting
Safety and efficacy of intravenous autologous mesenchymal stem cells for ms: A phase 2 proof of concept study	Phase 2	MSCs	40	June 2015	Canada	Recruiting
Reduced-intensity immunoablation and autologous hematopoietic stem cell transplantation (AHSCT) for multiple sclerosis	Phase 1	HSCs	15	May 2015	Philippines	Recruiting
Autologous mesenchymal stromal cells for multiple sclerosis	Phase 1, Phase 2	MSCs	8	May 2015	Spain	Active, not recruiting
A Study of allogeneic human UC-MSC and Liberation Therapy (When associated with CCSVI) in patients with RRMS	Phase 1, Phase 2	MSCs	69	February 2015	Trinidad and Tobago	Terminated
Mesenchymal stem cells for multiple sclerosis	Phase 1, Phase 2	MSCs	1	February 2015	France	Terminated
Optimal administration mode of autologous mesenchymal bone marrow stem cells in active and progressive multiple sclerosis	Phase 2	MSCs	36	January 2015	Occupied Palestine (Israel)	Unknown
Multi-center study safety of adipose derived mesenchymal stem cells for the treatment of multiple sclerosis	Phase 1	MSCs	2	November 2014	Cayman Islands	Terminated

Safety and efficacy of bmmnc in multiple sclerosis	Phase 1, Phase 2	BMSCs	15	June 2014	India	Unknown
Outcomes data of adipose stem cells to treat multiple sclerosis	Phase 1	MSCs	221	May 2014	United States	Active, not recruiting
Intrathecal administration of autologous mesenchymal stem cell-derived neural progenitors (MSC-NP) in patients with multiple sclerosis	Phase 1	MSCs	20	April 2014	United States	Completed
Assessment of bone marrow-derived cellular therapy in progressive multiple sclerosis (ACTiMuS)	Phase 2	BMSCs	80	January 2014	United Kingdom	Recruiting
Feasibility study of human umbilical cord tissue-derived mesenchymal stem cells in patients with multiple sclerosis	Phase 1, Phase 2	MSCs	20	January 2014	Panama	Completed