Introduction

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Objectives:

1. The primary objective is to determine the 5-year probability of disease stabilization in MS patients after HDIT and autologous HCT. For the purpose of this study, the 5-year probability of disease stabilization is defined as the proportion of patients who have not experienced a progressive relapse or a deterioration in EDSS score of 1.0 or more.

2. The secondary objectives of the study are to evaluate the safety and efficacy of autologous HCT, immunomodulation, and the mechanism of disease stabilization in MS patients treated with HDIT.

3. The tertiary objectives of the study are to evaluate myelin content and axonal integrity using magnetic resonance imaging (MRI) in MS patients undergoing autologous HCT.

Methods

The study is designed for MS patients, EDSS 3.0–5.5, with poor prognosis MS based on disease activity or disability as evidenced by any of the following during the 5-year period after HDIT:

- One or more relapses in 12 months or less on therapy with EDSS increase > 0.5, maintained for 6 months.
- Two or more relapses in 12 months or less on therapy with EDSS increase > 1.0, maintained for 6 months.
- Three or more relapses in 12 months or less on therapy with EDSS increase > 1.5, maintained for 6 months.
- On therapy at least 6 months before a relapse is counted to satisfy inclusion criteria #7.

Further, patients must meet the following inclusion criteria:

1. Age between 18 and 60 years, inclusive.
2. Diagnosis of MS using McDonald Criteria.
3. MS duration ≤ 15 years from diagnosis.
4. Relapsing-remitting multiple sclerosis with cumulative disability or progressive relapsing multiple sclerosis.
5. EDSS 3.0–5.5 (Appendix B) (Functional system changes in cerebral (or mental) functions and in general body sensations that may or may not be associated with motor signs or symptoms).
6. EDSS outcome 7.0 at time of transplantation.
7. a) 2 or more relapses in 12 months or less on therapy with EDSS increase > 0.5, maintained for 6 months; b) On therapy at least 6 months before a relapse is counted to satisfy inclusion criteria #7.
8. On therapy at least 6 months before a relapse is counted to satisfy inclusion criteria #7.

The study will be conducted at three sites. Subjects will be followed for 5 years after HDIT. The study is designed to include 30 patients who will be transplanted on the protocol.

Summary of SCMS2 Protocol

Case Selection:

Patients with frequent relapses and progressive disease, with EDSS scores of 6.0 to 7.0, will be included in the study. Patients with EDSS scores of 7.0 to 8.0 will be excluded from the study.

Exclusion:

1. Primary progressive MS.
2. Secondary progressive MS without relapses for > 12 months (i.e., progression without exacerbations or remissions).

Treatment:

1. Mobilization of autologous peripheral blood hematopoietic progenitor cells (HPC) with G-CSF and prednisone.
2. Selection of CD34+ hematopoietic cells using the Baxter Isolex device, and cryopreservation of the selected cells.
3. High-dose immunosuppressive therapy with BEAM + ATG mixing.
4. Repletion of the suppressed autologous CD34+ hematopoietic progenitor cell product.

Patient Assessments:

1. Intensive baseline and post-treatment evaluation of clinical and MRI imaging parameters of MS as well as immune reconstitution and mechanistic studies post-HCT.
2. The subjects will be followed monthly for the first 3 months following transplant, then every 3 months from Month 1 to Year 2, then annually until 5 years post-HCT.
3. Between visits to the transplant center, patients will be contacted monthly for the first year post-transplant, and every 3 months thereafter to inquire regarding any medical problems, and changes in neurological status or MS related medications. If the patient cannot be contacted, the appropriate health care professional will be contacted to obtain the same information and to be in contact with the patient.

Figure 1

Figure 2

Figure 3

Table


Results