HALT MS – Phase II Clinical Trial of High Dose Immunosuppressive Therapy and Autologous Hematopoietic Stem Cell Transplantation for Active Relapsing-Remitting Multiple Sclerosis

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Background

High-dose immunosuppression and autologous hematopoietic stem cell transplantation (HDIT/AHSCT) may induce sustained remissions in patients with multiple sclerosis (MS). Since degenerative changes may contribute to loss of neurological function in progressive forms of MS, this clinical trial enrolls MS patients with active disease not responding to conventional therapies.

HALT MS Trial

Phase II clinical trial of HDIT/AHSCT in poor-prognosis MS patients funded by NIH/ITN

- Conditioning using BEAM chemotherapy (Carmustine, Etoposide, Cytarabine, and Melphalan) and Thymoglobulin (rATG)
- T-cell depletion by CD-34+ selection
- Sample size 25 patients
- Primary objective: 5-year clinical/MRI disease stabilization
- Open to enrollment

BASIC ELIGIBILITY CRITERIA

- RRMS or PRMS
- Poor response to standard DMT with cumulative disability
- MS duration < 15 years
- EDSS 3.0 – 5.5
- 2 or more relapses within last 18 months with
  - EDSS increase ≥0.5 for >4 weeks

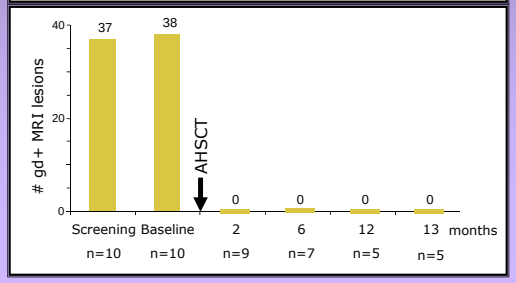
–or–

- 1 relapse within last 18 months with
  - EDSS increase ≥1 for >4 weeks and new gd+/T2 MRI lesions separated from clinical relapse

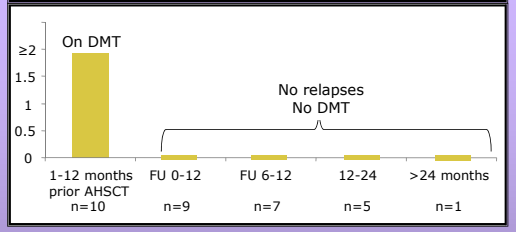
Patients

Participants	n=10	(6 female, 4 male)
Age	32.5 years	(median, range 26-46)
Baseline EDSS	4.5	(median, range 3.5-5.0)
Disease duration	3 years	(median, range 1-11)
Follow-up	12.2 months	(median, range 0-27)
CD34+ cells/kg	4.1×10^6	(median, purity 93.4%)
Engraftment	11 days post AHSCT	(median, range 11-13)

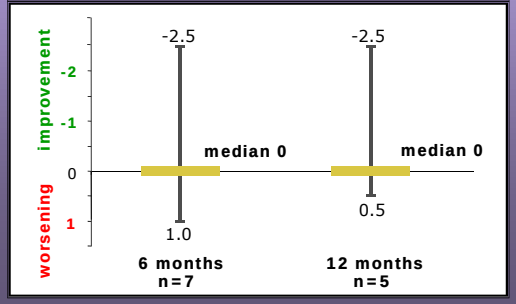
Enhancing MRI Lesions



Relapses



EDSS Change from Baseline



Post-HSCT Complications

Engraftment syndrome	n=1
Pseudo-Relapse	n=1
Pseudo-GVHD	n=1
Gallbladder obstruction	n=1
Rehospitalization for leukopenia/fatigue	n=1
Rehospitalization for iv line infection	n=1
MRSA Infection	n=1
Late leukopenia	n=1

Results

In follow-up of patients for up to 26 months (median 12) the preliminary observations are:

- No relapses since AHSCT.
- Patients have been neurological stable or improved (up to 2.5 EDSS points) with the exception of 2 patients who had some EDSS worsening compared to baseline.
- No new gadolinium enhancing lesions.
- No requirement for DMT after AHSCT.
- The observed complications were transient and toxicity appears acceptable. See above for details, no other unexpected or severe toxicities occurred.

Conclusions

The preliminary data in the first 10 patients with poorly-responsive MS to conventional MS who underwent this protocol are encouraging. Additional follow-up will be needed to confirm the stabilization of disease and neurological improvement suggested for this severely affected MS population. The trial is currently ongoing and open to enrollment.

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