Phase II Clinical Trial (HALT MS: Immune Tolerance Network) of High Dose Immunosuppressive Therapy (HDIT) and Autologus Hematopoetic Stem Cell Transplantation (AHSCT) for Active Relapsing-Remitting (RR) Multiple Sclerosis (MS): Early Results

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Objective

To determine if HDIT/AHSCT induces sustained remissions and prevents loss of neurological function in poorly-responsive RRMS.

Background

HDIT/AHSCT may induce sustained remissions in patients with autoimmune disease. In a previous clinical trial of HDIT/AHSCT for advanced progressive-type MS (median EDSS 7.0), estimated progression rate was 37% at 6 years. Since degenerative changes may contribute to loss of neurological function in progressive-type MS, HDIT/AHSCT in RRMS was studied.

Design/Methods

- Phase II clinical trial of HDIT/AHSCT with high-dose chemotherapy (BEAM) and antithymocyte globulin was conducted in RRMS (EDSS 3.0-5.5 with ≥ 2 relapses on treatment and ≥ 1.0 EDSS worsening over past year).
- Autologous hematopoietic cell graft was T-cell depleted by CD34 selection.
- Sample size was 25 patients with planned 5-year follow-up consisting of 8 required study visits
- Case reports of first three patients are presented.

Halt-MS Inclusion Criteria*

- Relapsing remitting MS with cumulative disability, or progressive relapsing MS
- Duration of MS less than 15 years from diagnosis
- EDSS 3.0-5.5 (functional system changes in cerebral/mental functions and in bowel and bladder functions not taken into consideration in determining EDSS for protocol eligibility)
- T2 abnormalities on brain MRI consistent with MS
- Two or more relapses in 12 months or less on IFN or GA, or cytotoxic therapy with EDSS increase > 0.5 maintained for > 4 weeks *OR*
at least three gadolinium-enhancing lesions on MRI, obtained 3-4 months after relapse

* Currently in the process of being modified

Case 1

27 ♀ RRMS Diagnosed: 1999

- **Confirmed exacerbations:** 3/2005, 7/2005, 9/2005, 12/2005, 3/2006, 7/2006, 8/2006
- **Multiple enhancing MRI lesions (brain):** 4/2002, 4/2005, 6/2005, 7/2005, 9/2005, 2/2006, 3/2006, 7/2006, 8/2006
- **Previous treatment:** Weekly IFNβ1a, tiw IFNβ1a, IFNβ1b, GA, methotrexate, mitoxantrone, IV methylprednisolone, plasmopheresis
- **Transplant:** 2/2007
- **EDSS:**
  9/2006 – when screened: 5.5
  2/2008 1 year S/P: 4.5
  No exacerbations; MRI = no enhancement
  Now off all MS medication

Case 2

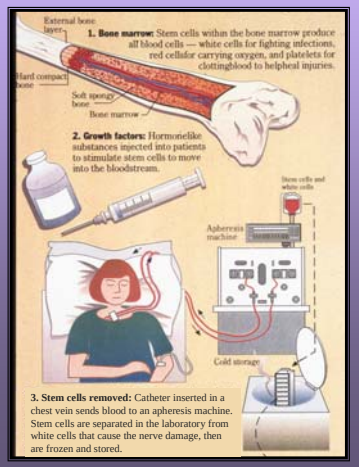
26 yo female RRMS Diagnosed: 2004

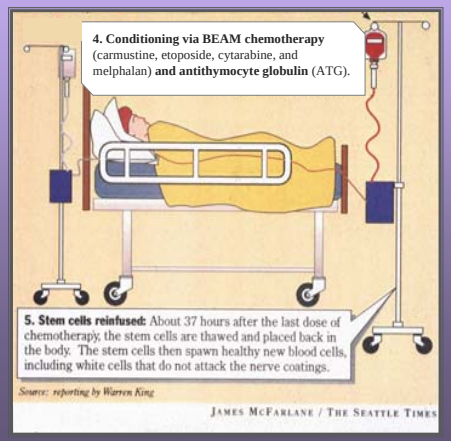
- **Confirmed exacerbations:** 7/2005, 12/2005, 6/2006
- **Multiple enhancing MRI lesions (brain, cervical and thoracic cord):** 4/2004, 3/2006, 5/2006
- **Previous treatment:** GA, IV methylprednisolone
- **Transplant:** 7/2007
- **EDSS:**
  10/2006 – when screened: 4.5
  1/2008 6mo S/P: 2.0
  No exacerbations; MRI = no enhancement
  Now off all MS medication

Case 3

46 ♀ RRMS Diagnosed: 2003

- **Confirmed exacerbations:** 11/1997, 2/1998, 1/2003, 3/2004, 11/2004, 12/2004, 2/2006, 8/2006
- **Multiple enhancing MRI lesions (brain):** 1/2003, 11/2004, 3/2006
- **Previous treatment:** GA, mitoxantrone
- **Transplant:** 7/2007
- **EDSS:**
  11/2006 – when screened: 4.5
  2/2008 7mo S/P: 4.5*
  No exacerbations
  Now off all MS medication
  - Complicated by low back pain and HNP





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References:

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