Hematopoietic stem cell transplantation for Multiple Sclerosis

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What it is

• a one time treatment

• an attempt to fix the underlying problem

• very effective against inflammation in MS

• leads to stabilization of disease in about 2/3 of patients with RRMS
What it is not

- not a miracle cure
- not very good for SPMS or PPMS
- not without risk
How many have tried this therapy?

- in Sweden about 100 patients
- in the transplant registries 700 patients
- in the world an estimated 1500 patients
Hematopoietic Stem cell Transplant
Adverse events

• **Acute toxicity**
  – loss of hair, nausea, mucositis
  – may need supportive blood products
  – infections

• **Late adverse events**
  – decreased fecundity
  – infections
  – secondary autoimmunity
  – secondary malignity
Mortality

• Mortality is dependent on
  – center experience
  – age of patient
  – intensity of conditioning

• Overall mortality rates have decreased

• No mortality (so far) with a low intensity conditioning regimen in RRMS patients
No evidence of disease activity
NEDA

- no development of disability (progression)
- no new symptoms (relapses)
- Now new MRI lesions
NEDA CLIMB (2014)

The graph shows the proportion of disease-free patients over time for different measures:

- Progression
- Timed walk
- Relapse
- MRI
- Relapse and progression
- NEDA

The x-axis represents the years (0 to 7), and the y-axis represents the proportion of disease-free patients (0 to 1). The graph illustrates how these measures change over the years.
### Table 3. NEDA in Clinical Studies

<table>
<thead>
<tr>
<th>Clinical Study</th>
<th>Study Duration, y</th>
<th>Patients With NEDA Status, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVANCE</td>
<td>1</td>
<td>Placebo, 15%; pegylated interferon beta-1a every 2 weeks, 34%</td>
</tr>
<tr>
<td>AFFIRM</td>
<td>1</td>
<td>Placebo, 15%; natalizumab, 47%</td>
</tr>
<tr>
<td>SELECT</td>
<td>1</td>
<td>Placebo, 11%; daclizumab, 39%</td>
</tr>
<tr>
<td>AFFIRM</td>
<td>2</td>
<td>Placebo, 7%; natalizumab, 37%</td>
</tr>
<tr>
<td>CARE-MS I</td>
<td>2</td>
<td>SC interferon beta-1a, 27%; alemtuzumab, 39%</td>
</tr>
<tr>
<td>CARE-MS II</td>
<td>2</td>
<td>SC interferon beta-1a, 13%; alemtuzumab, 32%</td>
</tr>
<tr>
<td>CLARITY</td>
<td>2</td>
<td>Placebo, 16%; cladribine, 46%</td>
</tr>
<tr>
<td>CLIMB</td>
<td>2</td>
<td>Early MS, 24%; established MS, 31%</td>
</tr>
<tr>
<td>FREEDOMS</td>
<td>2</td>
<td>Placebo, 13%; fingolimod, 33%</td>
</tr>
<tr>
<td>DEFINE</td>
<td>2</td>
<td>Placebo, 15%; dimethyl fumarate, 28%</td>
</tr>
<tr>
<td>CombiRx</td>
<td>3</td>
<td>IM interferon beta-1a alone, 21%; glatiramer acetate alone, 19%; glatiramer acetate and IM interferon beta-1a, 33%</td>
</tr>
<tr>
<td>CLIMB</td>
<td>7</td>
<td>Early MS, 6%; established MS, 10%</td>
</tr>
</tbody>
</table>
NEDA

The Swedish Experience & Chicago data

Disease activity-free survival

Disease activity-free survival

Time after HSCT (months)

Disease free survival (%)
RESEARCH PAPER

Autologous haematopoietic stem cell transplantation for aggressive multiple sclerosis: the Swedish experience

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ABSTRACT

Background Autologous haematopoietic stem cell transplantation (HSCT) is a viable option for treatment of aggressive multiple sclerosis (MS). No randomised controlled trial has been performed, and thus, experiences from systematic and sustained follow-up of treated patients constitute important information about that long-term remission, and maybe even cure, can be achieved.5–8

The goal of this therapy is to achieve long-term remission through short-lasting ablation of the immune system. The mode of action is not yet fully understood, and several mechanisms probably contribute to the effect. We know that HSCT causes a

HSCT for MS
The Swedish Experience

Time after HSCT (months)

Disease free survival (%)

Gd+

Gd-

79 %

vs

46 %
HSCT for MS
Chicago data & The Swedish Experience

![Graph showing Mean EDSS Score over Time (y)]

<table>
<thead>
<tr>
<th></th>
<th>Pre-HSCT</th>
<th>At HSCT</th>
<th>Post-HSCT</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Lowest EDSS</td>
<td>Highest EDSS</td>
<td>EDSS</td>
</tr>
<tr>
<td>RRMS</td>
<td>2.5 (0-6.5)</td>
<td>6 (3.5-9)</td>
<td>5.5 (1.5-8.5)</td>
</tr>
<tr>
<td>PRMS</td>
<td>6.5 (5-7.5)</td>
<td>6.5 (6-8)</td>
<td>6.5 (6-8)</td>
</tr>
</tbody>
</table>
HSCT for MS
The Swedish Experience

• no deaths were recorded
• no patient required ICU care

• eight patients (17%) developed shingles up to three years after HSCT
• four patients developed thyreoid disease (8.3%)
Conclusion

• HSCT is the most effective treatment of RRMS

• HSCT can reverse disability to some extent

• HSCT can be performed safely in experienced hands