Original research

Autologous haematopoietic stem cell transplantation compared with alemtuzumab for relapsing–remitting multiple sclerosis: an observational study

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ABSTRACT

Objective To compare outcomes after treatment with autologous haematopoietic stem cell transplantation (AHSCST) and alemtuzumab (ALZ) in patients with relapsing–remitting multiple sclerosis.

Methods Patients treated with AHSCST (n=69) received a conditioning regimen of cyclophosphamide (200 mg/kg) and rabbit anti-thymocyte globulin (6.0 mg/kg). Patients treated with ALZ (n=75) received a dose of 60 mg over 5 days, a repeated dose of 36 mg over 3 days after 1 year and then as needed. Follow-up visits with assessment of the expanded disability status scale score, adverse events and MR investigations were made at least yearly.

Results The Kaplan-Meier estimates of the primary outcome measure ‘no evidence of disease activity’ was 88% for AHSCST and 37% for ALZ at 3 years, p=0.0001. The secondary endpoint of annualised relapse rate was 0.04 for AHSCST and 0.1 for ALZ, p=0.03. At last follow-up, the proportions of patients who improved, were stable or worsened were 57%/41%/1% (AHSCST) and 45%/43%/12% (ALZ), p=0.06. Adverse events grade three or higher were present in 48/69 patients treated with AHSCST and 0/75 treated with ALZ in the first 100 days after treatment initiation. The most common long-term adverse event was thyroid disease with Kaplan-Meier estimates at 3 years of 21% for AHSCST and 46% for ALZ, p=0.005.

Conclusions In this observational cohort study, treatment with AHSCST was associated with a higher likelihood of maintaining ‘no evidence of disease activity’. Adverse events were more frequent with AHSCST in the first 100 days, but thereafter more common in patients treated with ALZ.

INTRODUCTION

Autologous haematopoietic stem cell transplantation (AHSCST) has been used as a therapeutic intervention for multiple sclerosis (MS) since more than twenty years.1 Early reports were encouraging,2,3 and followed by uncontrolled clinical trials.4,5 Some years ago, the report of a phase II randomised controlled trial comparing AHSCST with mitoxantrone was published (ASTIMS),6 suggesting that treatment with AHSCST led to fewer MRI lesions than treatment with mitoxantrone. This was followed by the report of a phase III trial (MIST)7 comparing AHSCST with disease-modifying drugs (DMD) approved by the U.S. Food and Drug Administration (FDA). In the MIST trial, treatment with AHSCST prolonged time to disease progression and increased the likelihood of improvement in disability. One shortcoming of this trial was that only a minority of patients in the control arm were treated with a second generation, highly effective DMD, such as natalizumab. Furthermore, other highly efficacious DMDs, such as alemtuzumab (ALZ) or ocrelizumab, were not available to patients in the control arm. Taken together, current evidence supports AHSCST as a treatment option for patients with relapsing–remitting MS (RRMS) with high clinical and MRI inflammatory disease activity despite the use of one or more approved DMDs.8

ALZ is a highly effective DMD, which was approved by the European Medicines Agency for treatment of RRMS in 2013 and by the FDA the following year. It is superior to treatment with interferon β–1a, with a reduction in relapse rates and reduction of sustained accumulation of disability in the pivotal trials.9,10 Although some concerns regarding safety has limited the use of ALZ, it is still considered one of the most efficacious DMDs presently available for treatment of RRMS. In a recent comprehensive systematic review of all available DMDs, made on the behalf of the American Academy of Neurologists, ALZ came out on top for prevention of relapses as well as disability progression.11

Real-world evidence is generated using data derived from the experience of patients outside of conventional clinical trials and is being increasingly recognised as a complement to randomised controlled trials.12 In this observational study, electronic health records and the Swedish Multiple Sclerosis Register (SMSreg)13 were used to compare efficacy and safety of AHSCST and ALZ using prospectively collected data from two large MS centres employing different treatment algorithms for patients with active RRMS.

METHODS

Study design, setting, and data sources

This was an observational cohort study comparing the outcome and safety of patients with RRMS treated with AHSCST using a cyclophosphamide-based conditioning regimen or ALZ. All patients...
receiving treatment for MS at Uppsala University Hospital or Sahlgrenska University Hospital are recorded in the SMSreg. Patients treated with AHSTC or ALZ from 1 January 2011 to 31 December 2018 were identified through a register search and asked to participate. Patients were followed up at least yearly with expanded disability status scale (EDSS) assessment and MRI. The presence of adverse events was sought at each follow-up visit. Health related data were continuously collected at each follow-up visit and deposited in SMSreg. Data were extracted from SMSreg 30 June 2019 and electronic health records were then scrutinised for accuracy of data and adverse events.

Procedures
AHSTC
Autologous haematopoietic stem cells were mobilised with a single dose of 2g/m² cyclophosphamide followed by filgrastim 5–10 µg/kg/day for 6–7 days and then harvested approximately 10 days after the start of the mobilisation regimen. No ex-vivo graft manipulation was performed. Patients were conditioned with a combination of cyclophosphamide and rabbit antithymocyte globulin (cyclophosphamide 200 mg/kg; rATG 6 mg/kg). Prophylaxis for fungal, viral and bacterial infection was administered during neutropenia. Prophylaxis for herpes viruses and *Pneumocystis jiroveci* continued for a minimum of 3 months.

Alemtuzumab
Patients treated with ALZ received a dose of 60 mg over 5 days and a repeated dose of 36 mg over 3 days after 1 year. New courses of 36 mg were administered if clinical relapses and/or new MRI lesions occurred. An intravenous infusion of 1000 mg methylprednisolone was administered on days 1–3. Aciclovir was given as prophylaxis against herpes virus infection for 1 month after the last ALZ infusion.

Study endpoints
Definition of data points
* A **clinical relapse** was defined as a period of acute worsening of neurological function lasting ≥24 hours not attributable to an external cause such as increased body temperature or acute infection. The **annualised relapse rate** (ARR) was defined as the number of relapses occurring during a time period divided by the number of years in that time period. **Confirmed disability improvement (CDI)** was defined as a decrease in EDSS score with at least one point from baseline sustained between two follow-up visits separated in time by no less than 6 months (0.5 points if the baseline EDSS ≥6). **Confirmed disability worsening (CDW)** was defined as an increase in EDSS score with at least one point from baseline sustained between two follow-up visits separated in time by no less than 6 months (1.5 points if EDSS at baseline was 0, 0.5 points if the baseline EDSS ≥5.5). An **MRI event** was defined as the appearance of any T2 lesion >3 mm or gadolinium enhancing lesion in the brain or spinal cord not present on the baseline scan. The baseline scan was the last MRI scan made before treatment commenced. **No evidence of disease activity (NEDA-3)** was defined as absence of clinical relapses, CDW and MRI events.

Primary endpoint
The primary endpoint was the Kaplan-Meier estimate of NEDA-3 at 3 years from the day of haematopoietic stem cell infusion or the day of the first infusion of ALZ.

Secondary endpoints
Secondary endpoints were (1) the Kaplan-Meier estimate of freedom from MRI events, (2) the Kaplan-Meier estimate of freedom from clinical relapses, (3) the Kaplan-Meier estimate of freedom from CDW, (4) the ARR after treatment, (5) the proportion of patients (EDSS ≥2) with CDI/stability/CDW, (6) the EDSS change between baseline and follow-up at one, two and 3 years, (7) adverse events of grade 3 or higher according to Common Terminology Criteria for Adverse Events (CTCAE), V.5.012 within the first 100 days after treatment (expected adverse events from AHSTC, such as neutropenia were excluded from this analysis) and (8) late adverse events after treatment, defined as autoimmune or infectious adverse events grade 2 or higher, or any adverse events grade 3 or higher present at 100 days from treatment or occurring thereafter.

Exploratory analyses
A new baseline was set 1 year after treatment initiation. Then, the Kaplan-Meier estimates of NEDA-3, freedom from MRI events, relapses and CDW at 3 years from the new baseline were used as exploratory endpoints.

Statistical analysis
Statistical analyses were performed with R V.3.5.3 (using the packages: ggplot2, survival, fBasics, ggpubr, moments, survminer, plotrix, grid, gridExtra, lattice and devtools). Data were summarised using frequencies for categorical variables, medians (IQR) for discrete variables and means (±SD) for continuous variables. To determine statistically significant differences between two groups, the χ² test, Student’s t test and the Mann-Whitney tests were used. Survival was estimated using Kaplan-Meier plots (95% CI) and the log-rank test was used.

### Table 1 Demographical and clinical data at baseline

<table>
<thead>
<tr>
<th>Centre (n)</th>
<th>AHSTC (n=69)</th>
<th>ALZ (n=75)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uppsala/Sahlgrenska</td>
<td>60/9</td>
<td>4/71</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Sex (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men/women</td>
<td>20/49</td>
<td>33/42</td>
<td>0.09***</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30 (IQR 26–37)</td>
<td>35 (IQR 30–41)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>6.4 (±5.7)</td>
<td>7.0 (±5.4)</td>
<td>0.5*</td>
</tr>
<tr>
<td>Number of previous treatments (n)</td>
<td>2 (IQR 1–3)</td>
<td>2 (IQR 1–3)</td>
<td>0.8**</td>
</tr>
<tr>
<td>Treatment naive</td>
<td>8</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Dimethylfumarate</td>
<td>8</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Glatiramer acetate</td>
<td>13</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Interferon beta</td>
<td>37</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>IVIG</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Teriflunomide</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Cladribine</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fingolimod</td>
<td>15</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Natalizumab</td>
<td>33</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>17</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ARR 1 year prior to treatment</td>
<td>1.4 (±1.2)</td>
<td>0.54 (±0.81)</td>
<td>&lt;0.0001 *</td>
</tr>
<tr>
<td>Baseline EDSS</td>
<td>3 (IQR 2–4)</td>
<td>2 (IQR 1–2.5)</td>
<td>&lt;0.0001**</td>
</tr>
<tr>
<td>Baseline ARMSS</td>
<td>6.1 (IQR 4.2–7.3)</td>
<td>4.1 (2.0–5.5)</td>
<td>&lt;0.0001**</td>
</tr>
</tbody>
</table>

*Student’s t-test, **Mann-Whitney’s test, ***χ² test.
AHSTC, autologous haematopoietic stem cell transplantation; ALZ, alemtuzumab; ARMSS, age-related multiple sclerosis severity score; ARR, annualised relapse rate.
to establish statistically significant differences between survival curves. A p value of <0.05 was considered significant.

RESULTS
Patient characteristics
In total, 147 patients were considered for the study. One patient did not meet the inclusion criteria, since he was treated with AHSCT using an alternative conditioning regimen, another patient was lost to follow-up, the remaining 145 were included, their characteristics summarised in table 1. A summary of events occurring after therapeutic intervention is shown in figure 1. Patients treated with AHSCT received 19 (IQR 18–20) days of inpatient care. Engraftment occurred on day +12 (IQR 10–13). All ALZ treated patients received at least one dose, 72 received two doses and 17 received three or more doses of ALZ. During follow-up, four patients treated with AHSCT (5.8%) and six patients treated with ALZ (8.0%) switched to rituximab; three patients treated with ALZ (4.0%) switched to AHSCT; and one patient (1.4%) treated with AHSCT switched to dimethyl fumarate. A summary of treatments given prior to treatment with AHSCT and ALZ are shown in Table 1 and online supplemental figure 1.

Primary endpoint
The Kaplan-Meier estimate of NEDA-3 at 3 years was 88% (95% CI 80% to 97%) for AHSCT and 37% (95% CI 26% to 52%) for ALZ, p<0.0001 (figure 2A, table 2).

Secondary endpoints
Efficacy
The Kaplan-Meier estimates for MRI event free survival, relapse-free survival and freedom from CDW are shown in figure 2B-D and table 2. The ARR post-AHSCT was 0.04±0.2 and 0.1±0.3 after initiation of ALZ. At last follow-up, the proportions of patients with CDI/stability/CDW were 58%/40%/1% in patients treated with AHSCT and 45%/43%/12% in patients treated with ALZ, p=0.06. The median EDSS changes at 1, 2 and 3 years after treatment initiation are shown in table 2.

Early adverse events
During the first 100 days after therapeutic intervention, none of the patients treated with ALZ developed CTCAE grade 3 or higher. In the AHSCT treated group, 48/69 patients developed grade 3 adverse events or higher. Febrile neutropenia was by far the most common grade three adverse event (58%) and was managed with intravenous antibiotics, antipyretics and fluid therapy without any long-term morbidity. Two patients had a grade 4 adverse event. One developed septic febrile neutropenia with hypotonia and EBV reactivation and was observed in the intensive care unit <24 hours but did not require vasopressor treatment nor treatment for EBV reactivation. The other patient developed fever with altered mental status and septic febrile neutropenia requiring intravenous steroids, antipyretics and fluid therapy without any long-term morbidity. Twelve patients had a grade 4 adverse event. Two patients were treated with furosemide during conditioning. Two patients experienced cardiac adverse events; one with atrial fibrillation and one case of pericarditis following cyclophosphamide conditioning. Notably, there was no case of invasive fungal infection, haemorrhagic cystitis or haemophagocytic lymphohistiocytosis. Furthermore, no CMV or EBV reactivation requiring intervention. For a full account of the acute adverse events, see online supplemental table 1.

Late adverse events
Grade 3 adverse events occurred in five patients (6.7%) in the ALZ group and in one patient (1.4%) in the AHSCT group. The most common grade 3 adverse event was immune mediated thrombocytopenia (n=4, ALZ). Other grade 3 adverse events were breast cancer (n=1, ALZ) and Lyme neuroborreliosis (n=1, AHSCT). Autoimmune adverse events occurred in 35 patients (47%) in the ALZ group and in 14 patients (20%) in the AHSCT group. The most common autoimmune adverse event in both groups was thyroid disease; in total, 31 cases (41%) in the ALZ group and 13 cases (19%) in the AHSCT group. The Kaplan-Meier estimates of thyroid disease at 3 years were 21% for AHSCT and 46% for ALZ, p=0.005 (figure 3). The most prevalent late infection was herpes zoster, occurring in five patients (6.7%) in the ALZ group and in four patients (5.8%) in the AHSCT group. There was no early or late mortality in either group. For a full account of late adverse events, see online supplemental table 2.

Exploratory analyses
After rebaseline, the Kaplan-Meier estimates of NEDA, relapse-free survival and freedom from CDW at 3 years were still higher.
with AHSCT than ALZ, whereas the Kaplan-Meier estimates of MRI event-free survival were similar between the groups (online supplemental figure 2 and table 2).

**DISCUSSION**

In this observational cohort study, we compared how two different treatment strategies for patients with RRMS affected outcome. Patients treated with AHSCT were more likely to achieve 'no evidence of disease activity' than patients treated with ALZ. As expected, the number of adverse events during the first 100 days after treatment initiation was high in the AHSCT group. These adverse events were manageable and did not result in any recorded long-term morbidity. In contrast, patients treated with ALZ had no serious adverse events related to the infusion of ALZ, but long-term adverse events were about twice as common.

In the study, we exploited differences in local treatment traditions at two major MS centres. At Uppsala University Hospital, AHSCT was predominantly used for active and aggressive MS, whereas ALZ was only used when AHSCT was considered to be inappropriate (eg, allergy to rabbit proteins) or at the specific request of patients. At Sahlgrenska University Hospital opposite conditions prevailed. Thus, treatment selection was mainly influenced by geographical location and not disease characteristics of the patients, minimising channelling bias. Nevertheless, some disparities between the groups were identified. AHSCT treated patients were on average younger, had more relapses, higher EDSS and age-related MS severity score at baseline, consistent with a more advanced and active disease. Highly active disease was associated with a lower probability of remaining in NEDA-3 despite treatment with natalizumab in the AFFIRM trial and daclizumab in the SELECT trial, whereas no such association could be demonstrated after treatment with cladribine in the CLARITY trial. Such baseline variation may have led to a slight underestimation in the magnitude of the difference in NEDA-3 in the present study. The use of prospectively entered register data and electronic health records ensured the veracity of data, although the analysis was made retrospectively.

NEDA-3 was 37% at 3years in the ALZ group, similar to the 32%–39% at 2years that was reported in the CARE-MS I and II trials. The rate of progression was also comparable to the CARE-MS trials. The ARR was 0.12 in the ALZ group, arguably a little lower than the 0.18–0.26 in CARE-MS I and II and the 0.16–0.21 in years 3–5 in the extension studies of CARE-MS I and II. However, the baseline ARR was also lower in the present study than in the CARE-MS studies and the relative decrease in ARR was quite similar. A larger proportion of patients improved in EDSS after ALZ treatment than in CARE-MS II (29%/54%/16%) and the follow-up extension study over 3years (25%/52%/23%), perhaps reflecting the presence of a run-in period when ALZ is used in clinical practice. The proportion of patients with NEDA-3 after AHSCT (88%) at

Table 2 Follow-up data

<table>
<thead>
<tr>
<th></th>
<th>AHSCT (n=69)</th>
<th>ALZ (n=75)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of follow-up years</td>
<td>195</td>
<td>217</td>
<td></td>
</tr>
<tr>
<td>Follow-up time per patient (years)</td>
<td>2.8 (±1.6)</td>
<td>2.9 (±1.1)</td>
<td>0.8*</td>
</tr>
<tr>
<td>ARR post-treatment</td>
<td>0.04 (±0.2)</td>
<td>0.1 (±0.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>ΔEDSS after treatment</td>
<td>-1 (IQR: -1.5 to 0)</td>
<td>0 (IQR: -0.5 to 1.3)</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td>Kaplan-Meier estimates at 3 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEDA-3</td>
<td>88% (95% CI 80% to 97%)</td>
<td>37% (95% CI 26% to 52%)</td>
<td>&lt;0.0001****</td>
</tr>
<tr>
<td>Freedom from MRI events</td>
<td>93% (95% CI 86% to 99%)</td>
<td>55% (95% CI 44% to 69%)</td>
<td>&lt;0.0001****</td>
</tr>
<tr>
<td>Freedom from clinical relapses</td>
<td>93% (95% CI 86% to 100%)</td>
<td>70% (95% CI 59% to 83%)</td>
<td>0.005****</td>
</tr>
<tr>
<td>Freedom from CDW</td>
<td>97% (95% CI 93% to 100%)</td>
<td>82% (95% CI 73% to 92%)</td>
<td>0.02****</td>
</tr>
<tr>
<td>Kaplan-Meier estimates after rebaseline</td>
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<td></td>
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<tr>
<td>NEDA-3</td>
<td>77% (95% CI 61% to 98%)</td>
<td>49% (95% CI 32% to 75%)</td>
<td>0.003****</td>
</tr>
<tr>
<td>Freedom from MRI events</td>
<td>78% (95% CI 62% to 98%)</td>
<td>78% (95% CI 65% to 93%)</td>
<td>0.5****</td>
</tr>
<tr>
<td>Freedom from clinical relapses</td>
<td>96% (95% CI 90% to 100%)</td>
<td>70% (95% CI 53% to 94%)</td>
<td>0.04****</td>
</tr>
<tr>
<td>Freedom from CDW</td>
<td>100% (95% CI 100% to 100%)</td>
<td>83% (95% CI 71% to 97%)</td>
<td>0.006****</td>
</tr>
</tbody>
</table>

*Student’s t-test, **Mann-Whitney’s test, ***χ² test, ****Log-rank test.

AHSCT, autologous haematopoietic stem cell transplantation; ALZ, alemtuzumab; ARR, annualised relapse rate; CDW, confirmed disability worsening; EDSS, expanded disability status scale; NEDA, no evidence of disease activity.

**Figure 3** Thyroid disease. Patients treated with alemtuzumab (ALZ) were more likely to develop thyroid disease than patients treated with autologous haematopoietic stem cell transplantation (AHSCT; log rank test, p=0.0055).
3 years) was comparable to what has been reported previously in the HALT-MS trial, 83% at 2 years and 60% at 5 years; in a Swedish survey, 78% at 2 years and 68% at 5 years; and in the MIST trial, 93% at 2 years and 79% at 5 years. The ARR of 0.04 post-AHSCT was very similar to the 0.03 that was reported in the Swedish survey. The proportion of patients with improvement/stable disease/worsening after AHSCT was also similar to the 67%/29%/4% reported in the MIST study.

Recently, the results of a real-life single-centre study comparing the outcome of patients treated with AHSCT or ALZ was reported. Although different conditioning regimen was used (consisting of BCNU, etoposide, cytosine-arabinoside, melphalan and rATG), the results were comparable to those in the present study, with a Kaplan-Meier estimate of NEDA-3 of 75% for AHSCT and 56% for ALZ, an ARR of 0.05 for AHSCT and 0.35 for ALZ after treatment initiation and an association with improved outcome in EDSS for AHSCT.

In recognition of the fact that full effect of ALZ treatment may take up to 1 year, an ancillary analysis of the primary endpoint and some of the secondary endpoints was made after a new baseline was set, 1 year after the initiation of treatment. After rebaseline, the Kaplan-Meier estimate of NEDA-3 for ALZ increased from 37% to 57% and for AHSCT decreased somewhat from 88% to 77%, but the difference between AHSCT and ALZ remained substantial and statistically significant. Patient-reported outcome measures, such as quality of life, would have been a valuable addition to the study, but these had not been collected systematically.

In this study, there were no late adverse events of grade 4 (life-threatening conditions in need of urgent intervention) or grade 5 (death). Early toxicity after AHSCT occurred to the expected degree and was manageable with standard medical care. No serious or unexpected adverse events of ALZ infusions were recorded. Late adverse events of ALZ and AHSCT have been described after treatment of MS, including both infectious and autoimmune complications as well as treatment-related mortality. Late adverse events of grade 3 or higher were uncommon in both cohorts. Nearly half of the patients treated with ALZ had an autoimmune adverse event, compared with 20% in the AHSCT group; this constitutes the major difference in the late adverse events between the groups. The frequency and distribution of thyroid malfunctions following ALZ is well in line with previous reports, although somewhat higher than in a recent systematic review, with a pooled prevalence of 33% after a median follow-up of 57 months. The frequency of thyroid disease following AHSCT (19%) was significantly lower than after treatment with ALZ, but higher than the 4.0%–17% described previously. The use of different conditioning regimens and differences in DMD treatment prior to AHSCT could affect the occurrence of secondary autoimmunity and methodological differences in identifying and classifying adverse events could also contribute to the discrepancies between different studies. Very few late infections were recorded. Minor infections were most likely under-reported by the patients, despite being interrogated about adverse events at each follow-up visit. The only grade 3 infection was one case of Lyme neuroborreliosis in one AHSCT-treated patient. Herpes zoster occurred to a minor extent with both treatments, as previously described.

A commonly used caveat of AHSCT is the lack of controlled studies. The ASTIMS trial demonstrated that AHSCT was superior to mitoxantrone in preventing new T2 lesions and relapses, but included only two patients with RRMS in the transplant arm. In the MIST trial, several comparators were used to increase the feasibility of the study, making the comparison between AHSCT and a single DMD precarious. ALZ is widely considered to be one of the most efficacious treatments for RRMS and has been highlighted for both reduction of relapses and prevention of disability progression. The present study adds to the existing body of evidence on efficacy and safety of AHSCT and suggests that treatment with AHSCT is associated with a higher probability of attaining disease control in comparison with ALZ. Adverse events were more common with AHSCT in the first 3 months after therapeutic intervention, but after that initial period, adverse events were more common with ALZ, in particular thyroid disease.

The main limitation of this study is the non-randomised intervention. Therefore, the findings should be confirmed in a randomised controlled trial and at least one is presently underway (ClinicalTrials.gov Id: NCT03477500). Meanwhile, patients who are willing to accept the predictable side effects of AHSCT and the increased risk of short-term adverse events in a one-time procedure might be better off with AHSCT, while patients who prefer a more convenient treatment that can be administered in an outpatient setting are probably better served by ALZ.
Multiple sclerosis


