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Five-Year Outcomes of Halt-MS: High-Dose Immunosuppressive Therapy and Autologous Hematopoietic Cell Transplantation for Severe Relapsing-Remitting Multiple Sclerosis

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Preferred Presentation Method: Oral Presentation

Introduction: Most patients with relapsing-remitting multiple sclerosis (RRMS) do not achieve a sustained remission after disease-modifying therapy.

Material (or patients) and methods: A phase II clinical trial of high-dose immunosuppressive therapy (HDIT; BCNU, etoposide, ara-C, melphalan and antithymocyte globulin) and autologous hematopoietic cell transplantation (HCT) was conducted in patients with highly active RRMS who had failed conventional therapy to assess the rate of sustained remission. Eligibility required an EDSS of 3.0 (moderate disability, fully ambulatory) to 5.5 (severe disability, ambulatory only 100 meters without aids) and ≥2 relapses on therapy in previous 18 months. A primary endpoint event or treatment-failure was defined as death or evidence of MS disease activity including any of: 1) relapse 2) new MRI lesions or 3) disability increase >0.5 EDSS points during 5 years post-transplant. Adverse events (AE) were recorded according to NCI-CTCAE v3.0. In addition, the Multiple Sclerosis Impact Scale (MSIS-29), a patient-based quality of life measure, and the Multiple Sclerosis Functional Composite (MSFC), a three-part standardized assessment instrument, were used to assess MS disease activity.

Results: 25 patients with median age 37(26-52) years were treated with G-CSF and prednisone to mobilize the autograft. The autograft was CD34-selected (Baxter, Isolex). 24 patients received HDIT/HCT according to protocol. Median follow-up was 62 months (min 12, max 72). In the first 3 years after HDIT, there were 121 grade 3 and 93 grade 4 AE, mostly hematological and gastrointestinal. Between 3 and 5 years after transplant, there were 15 grade 3 and 0 grade 4 AE. 3 deaths occurred on the study, all after subjects had met another MS disease activity or disability component of the composite endpoint. One patient experienced progressive loss of neurological function and death at 32 months. Also, two patients died > 3 years post-transplant. None of the deaths were related to study treatment.

At 5 years, the probability of event-free survival according to the primary endpoint was 69.2% (90% CI: 50.2%>82.1%); progression-free and relapse-free survival were 90.9% (90% CI: 73.7%>97.1%) and 86.3% (90% CI: 68.7%>94.5%), respectively, and probability of freedom from disease activity detected by brain MRI was 88.2% (90% CI: 67%>96.2%). As reported in our interim analysis of three-year outcomes [1], in which 7 out of 24 patients who received HCT met primary endpoint, no further events occurred by the close of 5 years. Further, MS disease burden as measured by T2 weighted lesion volume on MRI was significantly reduced by 6 months as compared to baseline and was sustained for 5 years (median change: -1.208 ml; p<0.001). T1 lesion volume was increased at 5 years (median change: 0.094 ml; p=0.041). While both the MSIS-29 and the MSFC showed improvement at Year 5 with median difference from baseline of -8.5 (p=0.091) and 0.11 (p=0.303), respectively, changes were not statistically significant.

Conclusion: HDIT/HCT for highly active RRMS induced a high rate of remission of MS disease activity which was sustained at 5 years, without maintenance therapy. Most treatment-related AE were as expected, consistent with the transplant regimen.

References: 1. Nash RA, et al. *JAMA Neurol.* 2015;72(2):159-169.

Would you like to apply for the Best Young Abstract Award ?: NO

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