Modifications to the "Classical" Autologous Hematopoietic Stem Cell Transplantation in Multiple Sclerosis: Efficacy and Safety Study of a Less Toxic Approach Which Improves the Neurological Condition. a Mexican Perspective

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Abstract

Background: In an effort to reset the immune system, patients with multiple sclerosis (MS) have been autografted with stem cells; we have shown that these grafts can be performed on an outpatient basis with non-frozen peripheral blood hematopoietic stem cells (PBSC) and a conditioning regimen of cyclophosphamide (Cy) and rituximab, the so-called "Mexican method".

Material and methods: Since 2015, all consecutive patients with MS were autografted in two centers in Mexico, following the "Mexican method" (*ClinicalTrials.gov* identifier NCT02674217), on an outpatient basis and employing PBSC. Mobilization was accomplished with Cy and filgrastim (G-CSF); cumulative dose of Cy was 200 mg/kg. Cy doses were delivered in two separate blocks nine days apart, with the initial aim of mobilizing PBSC and purging lymphoid cells, while the second further purged lymphoid cells and conditioned the graft. After granulocyte recovery, patients were administered rituximab (375 mg/m2) and again (100 mg) every two months, over a 12-mo. period. The extended disability status scale (EDSS) score was assessed every 3 mos. after transplant.

Results: 392 patients were autografted; median age was 47 years; time to neutrophil recovery > 0.5 $x10^9$/L was 7 days (0-12). The outpatient procedure was completed in 382 patients (97.4%); 10 patients were admitted to the hospital due to neutropenic fever (2), persistent nausea / vomiting (2), iatrogenic pneumothorax (4) and dehydration (2). Transplant related mortality was zero. The 12-mo. progression-free survival was 75%. Improvement or stabilization of the EDSS score at 12 mos. was observed in 75, 72 and 60% of patients with relapsing remitting (RR), secondary progressive (SP) or primary progressive (PP) forms of MS. In patients with a response, EDSS values decreased significantly from 4.83 ± 0.21 to 3.49 ± 0.24 three mo. after grafting ($p = 0.007$) and from 4.39 ± 0.49 to 3.32 ± 0.50 twelve mo. after grafting ($p = 0.05$).

Conclusions: The Mexican autograft method in MS carries a very low morbidity and no mortality, induces neurological responses in MS, even in variants in which other autograft protocols have not proven useful, such as SP-MS and PP-MS. Additional information and follow-up is needed to further support these observations.

Disclosures Gomez-Almaguer: *Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Bristol:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees.

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