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Allogeneic Transplant

Impact of monoclonal antibody antiCD25 in the scenario of acute graft-versus-host disease refractory to corticoids.

Carlos Orozco Oviedo (Serviço de Hematologia e Tcth Hospital Clinicas de Porto Alegre), Alessandra Aparecida Paz* (Serviço Hematologia e TCTH Hospital de clinicas de Porto Alegre), Lisandra Rigoni (Serviço Hematologia e TCTH Hospital de clinicas de Porto Alegre), Gustavo Fischer (Serviço Hematologia e TCTH Hospital de clinicas de Porto Alegre), Lucia Mariano da Rocha Silla (Serviço Hematologia e TCTH Hospital de clinicas de Porto Alegre) e Liane Esteves Daudt (Serviço Hematologia e TCTH Hospital de clinicas de Porto Alegre)
* PRESENTER

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The acute graft-versus-host disease (aGVHD) is still the leading cause of morbidity and mortality after Hematopoietic Stem Cell Transplantation (HSCT). Approximately 50% of patients who undergo related or unrelated allogeneic transplant develop aGVHD. Of these, approximately 30% are corticoid-resistant, requiring a second-line treatment. To date, there is no literature consensus on what is the best therapeutic strategy for this severe complication of HSCT and different therapeutic strategies have been used, including monoclonal antibodies (Anti CD25 or Anti-tumor necrosis factor). Objective: To evaluate the response to monoclonal antibody antiCD25 in patients who are refractory to steroids in our center. Methods: We retrospectively evaluated the records of patients submitted to related and unrelated allogeneic HSCT from 2004 to 2010. Thirty-seven patients with aGVHD were refractory to corticosteroids and were assessed regarding the response rate to antiCD25 taking into account the frequency and degree of GVHD, overall survival (OS) and underlying disease variables, gender and age of the donor, type of conditioning, ABO mismatch, gender and age of the recipient. Results: A total of 149 patients were included in the analysis, 81 patients (54.3%) developed aGVHD and 37 patients (45.7%) were refractory to steroids and 97.3% (36 patients) used antiDC25 as second-line treatment. The complete response rate to AntiCD25 was 24.3% in 28 days. The overall survival (OS) of patients without aGVHD at 5 years was 66.6%; in patients with aGVHD grade I-II was 50.0% and grade III-IV, 12.5%. For patients who were refractory to steroids and received antiCD25 as a second-line treatment, overall survival at 5 years was 22.2%. At the multivariate analysis, the age of the donor and of the recipient were risk factors for the development of aGVHD grade IV. The causes of death were sepsis (97%) and hemorrhagic stroke (3%). Conclusion: In our population the overall survival at 5 years in corticoid-resistant patients who received therapy with antiCD25 was 22%. These results are equivalent to those found in the literature, demonstrating an extremely high mortality rate for patients who develop corticoid-resistant aGVHD. The main cause of mortality in our patients was sepsis, most probably demonstrating a poor immune reconstitution associated with the use of antiCD25. Further investigations of new strategies for early detection of aGVHD as biomarkers or therapeutic innovations are necessary to effectively improve survival in these patients.

Keywords: GVHD, antiCD25, Corticoid resistance, Hematopoietic Stem Cell Transplantation.