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What are the results from the haploidentical transplant clinical trial?

Good afternoon to the audience. My name is Astrid Pavlovsky. I am from Buenos Aires, Argentina. I am hematologist with special interest in lymphoma, and I have been asked to comment on the latest result of the haploidentical-related hematopoietic stem cell transplantation in Hodgkin lymphoma. So, we know that Hodgkin lymphoma is a curable disease. Most of our patients will have a long-term survival, but 10% to 20% will not achieve complete remission after first-line therapy, and unfortunately, 20% or 30% of these patients will eventually relapse. Most often, these patients will receive a salvage chemotherapy and will be offered autologous stem cell transplantation which can rescue about 50% of these patients, but unfortunately, there is a subgroup of that prognosis that will eventually relapse. So, an allotransplant has potential benefit with graft versus lymphoma effect, and myeloablative allogeneic transplant has been tried in these patients, but there was high non-relapse mortality. Reduced intensity condition is also an option for patients with relapsed or refractory Hodgkin lymphoma and has decreased this non-relapse mortality. However, many patients do not have HLA related or unrelated donors, so this becomes a second but very important problem. In the last years, HLA-haploidentical transplants have been an option and have shown inferior survival due to increased graft failure or graft rejection. So, to enable HLA-haploidentical transplant after non-myeloablative condition, different groups have incorporated high-dose posttransplant cyclophosphamide given early after bone marrow infusion, and this is in the purpose to kill alloreactive donor and host T-cells, reducing the incidence of graft versus host disease and graft rejection. This has shown to not affect engraftment. So, this is a new option we have for this group of patients, the publication by Dr. Burroughs (and colleagues)[1] from the Fred Hutchinson Cancer Center is a retrospective analysis comparing outcome of heavily pretreated Hodgkin lymphoma patients who received reduced intensity condition with three different donor groups, the match-related donors, the unrelated donors, and the haploidentical donors. And, we see that 2-year progression free survival was higher for the haploidentical. This was maybe due to the increase in the intensity condition or maybe the HLA disparity helping the graft versus lymphoma event. There was difference in the 2-year overall survival. The non-relapse mortality was significantly lower for the HLA-haploidentical related recipient, and this might be due to the post-transplant, (high-dose) cyclophosphamide incorporation. So, this is a good option for patients with heavily pretreated by prognosis Hodgkin lymphoma and no donor availability.

Recently, another trial has been reported from Dr. Raiola, the Genoa IAA Group,[2] and it is also a retrospective analysis of 26 relapsed/refractory Hodgkin lymphoma patients who received haploidentical transplant between 2009 and 2011. The median followup for the surviving patients is 24 months, the non-relapse mortality was extremely low, being 4% with the relapse of 31% and an overall survival of 3 years of 77%. So, this shows significantly low non-relapse mortality when using posttransplant cyclophosphamide with compared relapse rates resulting in a superior overall survival. So, for this group of patients who relapse after autologous transplantation, this is still a big problem, but haploidentical transplantation can be considered an option.

References:

1. Burroughs LM, O'Donnell PV, Sandmaier BM, et al. Comparison of outcomes of HLA-matched related, unrelated, or HLA-haploidentical related hematopoietic cell transplantation following nonmyeloablative conditioning for relapsed or refractory Hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2008;14(11):1279-1287.

2. Raiola A, Dominietto A, Varaldo R, et al. Unmanipulated haploidentical BMT following non-myeloablative conditioning and post-transplantation CY for advanced Hodgkin's lymphoma. *Bone Marrow Transplant*. 2014;49(2):190-194.