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Treatment goals associated with stem cell transplant

Hello. My name is Sergio Giralt and I am the service chief of the Adult Bone Marrow Transplant Service at Memorial Sloan-Kettering Cancer Center in New York City. Today, I want to speak about stem cell transplant and the goals associated with the treatment, particularly in the context of patients with multiple myeloma.

It has been now more than 30 years since high-dose melphalan has been shown to be effective in patients with relapsed and refractory myeloma. In that initial paper from Dr. McElwain, et al., patients had significant myelosuppression that led to infectious or bleeding deaths. Dr. Barlogie then went on to give high-dose melphalan but supported with bone marrow, and that was the beginning of the field of bone marrow transplantation for multiple myeloma. The first observation that was made is that patients with active disease who had failed all prior therapies were able to achieve remission, some of them long-lived. Because of the good results in refractory relapse, the treatment went on to become part of frontline therapy.

From the periods of 1990 to the beginning of 2000, multiple randomized trials were performed, primarily in Europe. Most of these trials showed that high-dose melphalan in autologous transplant was associated with higher response rates, with complete remission rates of 20% to 30% which had never been seen in myeloma therapy before, and a fraction of patients not having to deal with their disease for more than 5 years.

Bone marrow transplant was rapidly replaced by stem cell transplantation with the advent of growth factors where we could see that the bone marrow stem cell could be mobilized in the peripheral blood and large quantities of them could be collected and cryopreserved. We now currently perform approximately 6,000 to 7,000 autologous transplants for myeloma in North America today every year. Why do we do these? We do these because, once again, high-dose melphalan is the single most effective way of achieving a complete remission in patients with multiple myeloma, and autologous stem cell transplant is a way of supporting patients through the myelosuppression of high-dose melphalan. The treatment is not the transplant. The treatment is the high-dose chemotherapy which can eliminate resistant plasma cells. To be able to give this high-dose melphalan, we have to support the patients with autologous stem cells that will recover the patient from the myelosuppressive effect from melphalan in probably 10 to 14 days.

What are the other goals of transplantation? So the main goal of transplantation is to achieve long-term disease control. We now have also learned that autologous transplant by itself may not be sufficient or optimal to achieve long-term disease control in most patients. Studies from both Dr. Attal and Dr. McCarthy have shown that when we give lenalidomide daily to patients who have undergone autologous transplant, the chances of relapse decrease significantly and the remissions' durations increase from an average of 24 months to more than 40 months. Lenalidomide therapy post transplant is associated with a small but significant increased risk of second primary cancers and, therefore, these patients need to be followed carefully and the risks and benefits of lenalidomide maintenance need to be discussed in detail.