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What is the role of new and emerging checkpoint inhibitors in the treatment of classical Hodgkin lymphoma?

Welcome to *Managing Hodgkin Lymphoma*. I am Dr. Stephen Ansell from Mayo Clinic in Rochester, Minnesota. I am frequently asked, “What is the role of new and emerging checkpoint inhibitors in the treatment of classical Hodgkin lymphoma?” These are agents that really have revolutionized how we think about Hodgkin lymphoma. The excellent work that was done on understanding the biology of the PDL-1/PD-1 interaction have allowed us to use this new class of agents in a very successful way in Hodgkin lymphoma patients. Studies have shown the PDL-1 expression is very high on Reed-Sternberg cells, the cancer cell or the malignant cell, in Hodgkin lymphoma, and this is driven by genetic amplifications and genetic variation at chromosome 9P24.1, resulting in very high expression of PDL-1. PDL-1 suppresses PD-1-expressing T-cells by sending a negative signal into the T-cells and suppressing their function. The role of the immune checkpoint inhibitors is to block the interaction between PDL-1 and PD-1. Initial data in the early phase 1 trials of pembrolizumab and nivolumab, two PD-1 blocking antibodies, showed very high response rates and very promising results. Subsequent phase 2 trials confirm these excellent results, and these agents have now become mainstream and utilized very commonly in patients with classical Hodgkin lymphoma. Mostly, this has been used in the post-transplant setting, but now these agents are being used earlier in the disease course and in combination with other chemotherapies and other agents.

There are trials ongoing that recently reported of combining brentuximab vedotin, an antibody drug conjugate, with an immune checkpoint inhibitor such as nivolumab or pembrolizumab, and these results have shown very high response rates in patients prior to going to autologous stem cell transplant. In fact, there is now a trial ongoing in elderly patients using brentuximab vedotin in combination with nivolumab for elderly patients who do not tolerate regular chemotherapy particularly well. That will show whether an almost chemo-free regimen could be used as the frontline treatment in patients with Hodgkin lymphoma. Furthermore, in frontline treatment, nivolumab is being used in combination with ABVD chemotherapy and being tested as initial treatment for Hodgkin lymphoma. As you can tell, the emerging data for immune checkpoint inhibitors show that this class of agent has efficacy across the spectrum, used upfront as first-line therapy and as post-transplant salvage. In fact, now even in

post-allogeneic transplant patients where there has been some concern that possibly this would be an unsafe place to use these agents, there has been efficacy demonstrated in those patients too. I think the role is one that is evolving. We are learning exactly where to use these agents, but clearly it has been shown that you can use these agents in multiple types of patients and also in combination with other treatment. Thank you very much for watching this activity.