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Where does nivolumab fit in the treatment paradigm for HL?

Welcome to *Managing Hodgkin Lymphoma*. My name is Dr. Paul Bröckelmann, and I am working with the German Hodgkin Study Group at the Department I of Internal Medicine at the University Hospital of Cologne based in Germany. I am frequently asked, “Where does nivolumab fit in the treatment paradigm of Hodgkin lymphoma?” Nivolumab is working as an immune checkpoint inhibitor by blockade of the *PD-1 PD-L interaction*, thereby engaging the immune system. Impressive results have been reported in patients with advanced melanoma or lung cancer and more recently also in relapsed classical Hodgkin lymphoma leading to FDA approval in May of 2016. The pivotal phase 2 trial in 80 patients failing prior brentuximab treatment reported an overall response rate of more than 66% with few complete remissions. In contrast to other agents, the drug was very tolerable and had very durable remissions of several months or even more than a year. Even after cessation of treatment was observed. Self-reported quality of life improved while on treatment. Nivolumab hence offers a promising treatment option for patients who are either ineligible for brentuximab, for example, for causes such as neuropathy, or failing brentuximab. At the moment, various clinical trials are already underway or in preparation to evaluate the specific role of nivolumab in earlier lines of therapy or in combinatory approaches. Despite frequent PD-L1 expression by the malignant Hodgkin Reed-Sternberg cells, the detailed mechanism of anti-PD1 blockade in classical Hodgkin lymphoma today remains rather unclear. Since Hodgkin Reed-Sternberg cells commonly lack MHC 1 molecules due to mutation in beta-2 microglobulin, a direct T-cell mediated cytotoxic effect seems rather unlikely. Instead, the checkpoint blockade might remodel the originally protective microenvironment, allowing an effective antitumor immune response by the healthy immune system. Keeping in mind the distinct biology of classical Hodgkin lymphoma and its features of immune dysregulation, nivolumab and also other checkpoint blocking agents carry a strong mechanistic rationale and even today already constitute very active treatment options for patients with relapsed or refractory classical Hodgkin lymphoma. Thank you for viewing this activity. For additional resources, please view the other educational activities on *ManagingHodgkinLymphoma.com*.