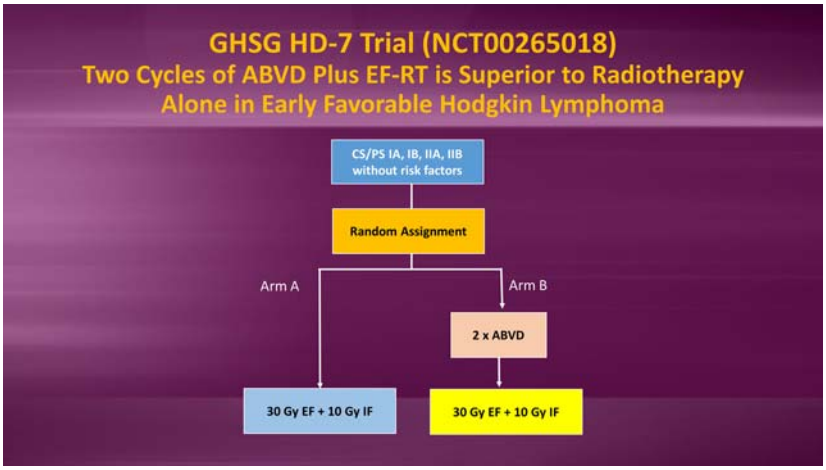
Paul Bröckelmann, MD
German Hodgkin Study Group (GHSG)
Department I of Internal Medicine
University Hospital of Cologne
Cologne, Germany

Welcome to *Managing Hodgkin Lymphoma*. My name is Dr. Paul Bröckelmann and I am working with the German Hodgkin Study Group at the University Hospital of Cologne. I am speaking live from the 10th International Symposium on Hodgkin Lymphoma. In the next few minutes, I am going to review key data presented in the following three abstracts. Which include, T010 which is long-term followup of HD7 and HD10 trials in early-stage favorable Hodgkin lymphoma, T023 which is the keynote study of pembrolizumab in relapsed/refractory Hodgkin lymphoma, and T025 which is the study and patients' preferences among German Hodgkin Study Group trial patients.

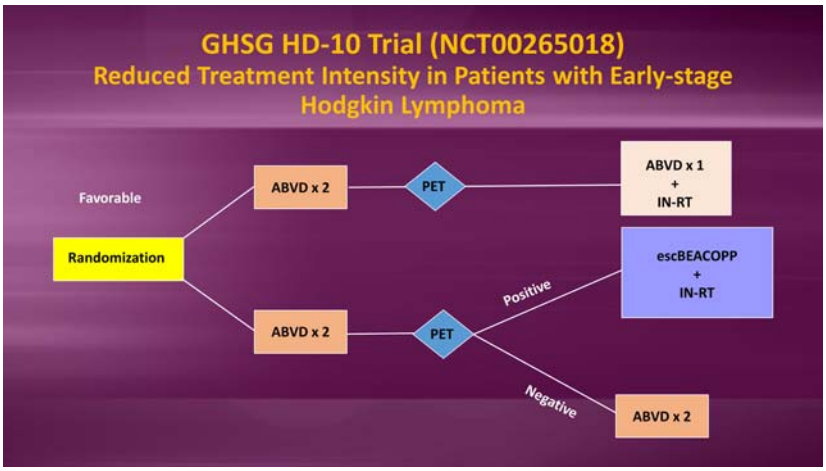
The first abstract I am covering is T010 which is long-term followup of the German Hodgkin Study Group trials HD7 and HD10 in early-stage favorable Hodgkin lymphoma. When looking back, combined modality treatment in this setting was established with the HD7 trial and treatment intensity markedly reduced with the HD10 trial.

In HD7, a total of 627 patients were enrolled and our followup analysis with 15 years of progression-free survival confirmed a significant superiority of combined modality treatment toward involved-field radiotherapy only with a difference of more than 20%.



In HD10 which enrolled 1,800 patients, we found that when looking at the four arms of varying treatment intensity either 2 or 4 cycles of ABVD followed by either 20 or 30 Gy of

radiotherapy that the non-inferiority of the least intensive arm was confirmed in comparison to the most intensive arm.

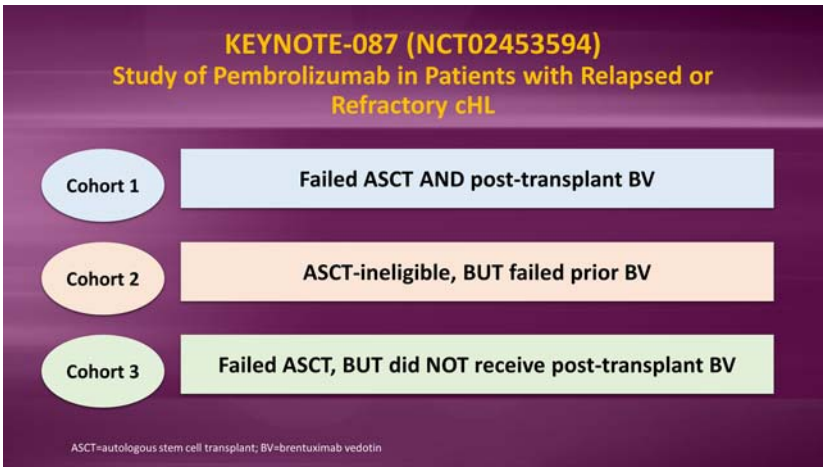


When looking at the figures for two times ABVD followed by a 20 Gy of radiotherapy, we found that the 10-year progression-free and overall survival are very favorable with the figures of 87.2% and 94.1%, respectively. In summary we did not find any statistical differences in terms of the second malignancies. Therefore, continued long-term followup is necessary to really assess the beneficial effects of treatment intensity reduction in these type of patients.

The second abstract I would like to cover is T023 which is the study of pembrolizumab in patients with relapsed or refractory Hodgkin lymphoma, KEYNOTE 087, which is investigating pembrolizumab in three different cohorts of patients with refractory Hodgkin lymphoma. In general, treatment options apart from brentuximab vedotin are rare in this setting and therefore new therapeutic options are most welcome. Many analyses pre-clinically showed that there might be genetic dependence in Hodgkin lymphoma for PD-1 and PD-1 ligand interaction for tumor survival either by genetic amplification or also EBV induced.

In this MSD sponsored phase 2 trial, the interim analysis of three cohorts, each with 30 patients enrolled, was presented. The first cohort included patients who failed both ASCT and brentuximab vedotin. The second cohort included patients who were ASCT ineligible but failed prior brentuximab vedotin. The third cohort included patients with ASCT failure who have not received brentuximab vedotin afterwards. Pembrolizumab was administered at a flat dose of 200 mg absolutely and at 3 weekly intervals, which is of interest since this is a longer treatment-free interval than with other anti-PD-1 antibodies and continued until progression or toxicity occurred. In the heavily pretreated patients

who presented with refractory disease in more than 40% of cases and more than three lines of therapy, in 60% of cases, the overall response rate across the first two cohorts was 73%, while an overall response rate of 83% was observed in cohort 3, ie, those patients who did not receive brentuximab vedotin after ASCT failure. The CR rate compared favorably to other agents investigated in the few with up to 30% of patients achieving a CR after treatment.



In general, the agent was well tolerated with grade 3 or 4 AEs rarely occurring in up to 4% of patients and no grade 5 adverse events. In summary, pembrolizumab constitutes valuable therapeutic options, but continued followup is necessary to both assess long-term efficacy but also safety of this agent.

The third abstract I would like to cover is T025 which is the study of patient's preferences among survivors of first-line therapy treated within German Hodgkin Study Group trials. When looking at treatment for Hodgkin lymphoma in the first-line setting, despite cure from Hodgkin lymphoma, showed long-term side effects of major interest, and to date, little is known regarding the patients' preferences in terms of aim of therapy and burden of respective side effects such as second malignancies or other occurrences. We therefore had a look at more than 1,000 patients who were initially treated within HD13 to HD15 and 50% of those patients, which is more than 500, returned the questionnaire. In the results, we found that the chemotherapy, irregardless of intensity, and also the duration of chemotherapy was considered a great or very great burden for more than 80% of patients. In contrast, the radiotherapy was only considered a great or very great burden by 25% to 60% of patients depending on the stage of Hodgkin lymphoma at initial diagnosis. One major side effect which was often mentioned as a burden is fatigue which was experienced by more than 90% of patients prior to treatment but consisted in more than 40% also after treatment and therefore is considered a great burden in this

population. When asked for the main goal of therapy, more than 70% of patients named the cure of Hodgkin lymphoma as the main goal of therapy, and this is in line with prior British analysis in nearly 200 patients. The risk of a second malignancy was rated equal to the relapse of Hodgkin lymphoma. This is something which could be interpreted as the general fear of another treatment for malignant disease irrespective of Hodgkin relapse or second malignancy. Along these lines, only 2% of our patients would have chosen a less intensive approach when looking back at their therapy.

In summary, cure is the main goal for our patients and therefore progression-free survival constitutes an adequate endpoint in Hodgkin lymphoma trials in the first-line setting, and the occurrence of second malignancy is rated as an equal burden than relapse of Hodgkin lymphoma. Thank you for viewing this activity, and for additional resources, please be sure to view the other educational activities on *ManagingHodgkinLymphoma.com.*