Challenging the Standard of Care in Hodgkin Lymphoma

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Hodgkin lymphoma represents a major success in malignant hematology with a cure rate in excess of 80 percent. However, because most patients with this disease are young adults or adolescents, management of long-term toxicities and complications remains a challenge. The combination of ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) has been the standard chemotherapy regimen for many years, producing a high cure rate with acceptable toxicity. In 1992, the German Hodgkin Study Group (GHSG) developed the BEACOPP regimen (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone) to further improve the outcome of patients with advanced Hodgkin lymphoma and obtain a balance between maximal efficacy and least toxicity. However, long-term risks of the BEACOPP regimen include the development of secondary leukemia or myelodysplastic syndrome. Thus, long-term follow-up and monitoring for toxicities in BEACOPP-treated patients is critical.

Dr. Sandra Horning, a well-recognized expert in the field and chair of the Hodgkin Lymphoma Education Session, focused on the use of biologic prognostic factors and PET imaging in diagnosis. The clinically relevant prognostic scoring system, International Prognostic Score (IPS), assigns one point for each of seven independent risk factors: abnormal albumin, hemoglobin, WBC, lymphocyte count, stage IV disease, male sex, and age. Each identified risk reduces five-year survival by 7 percent below the 80 percent five-year survival for those with no risk factors. In those with high-risk disease (those with four to seven risk factors, in whom overall survival is reduced) controversy over the best approach remains. The use of newer imaging tools, for example, fluorodeoxyglucose-positron emission tomography (PET) imaging, may improve detection of those with bulky or residual disease who may potentially benefit from consolidation treatment.

The improvement in overall survival in Hodgkin lymphoma with newer treatment regimens, i.e. those including BEACOPP, does not come without a cost. In addition to hematologic toxicity, secondary leukemias are higher than with standard ABVD, and sterility in young adults is anticipated. Approaches to the evaluation of these therapy-related risks were reviewed by the second speaker, Dr. Lois Travis.

In the last talk, Dr. Richard Ambinder elaborated on the potential role of novel therapeutic approaches based on the biology of Hodgkin lymphoma. For example, Radiopharmaceutical-based techniques such as single photon emission CT or PET may promote the identification of EBV-positive lymphomas through induction of EBV tyrosine kinase expression. Animal studies have suggested the potential role of demethylation in reversing epigenetic silencing of tumor suppressor genes. Other studies suggest the potential for inhibition of EBV lymphomagenesis by targeting EBV cytidine deaminase or polymerase-eta expression.

Today in the Simultaneous Sessions, Dr. Engert Andreas from the GHSG will be presenting the results of the 10-year follow-up of the international randomized study HD9 trial. More than 1,180 patients were randomized to receive one of three chemotherapy regimens: 8 cycles of COPP (cyclophosphamide, vincristine, procarbazine, and prednisone) alternating with ABVD, 8 cycles of standard-dose BEACOPP, or 8 cycles of escalated-dose BEACOPP. The dose-escalated BEACOPP regimen showed superior rates of freedom from treatment failure (FFTF) and overall survival (OS). Death due to Hodgkin lymphoma was lower in the escalated-dose BEACOPP arm. Although the incidence of secondary acute myeloid leukemia was higher in the escalated-dose BEACOPP arm, there was no increase in the incidence of non-Hodgkin lymphoma and solid tumors.

The outcome of patients with all stages of Hodgkin lymphoma has improved dramatically over the past few decades. This is mainly due to the use of risk-adapted therapies using intensive poly-chemotherapeutic regimens in combination with other modalities. The excellent results obtained with the BEACOPP trials challenge the seemingly global consensus that ABVD is the gold-standard treatment strategy for advanced-stage Hodgkin lymphoma. The main challenge in the near future will be the development of strategies that decrease late morbidity and mortality but retain the same efficacy of current regimens.