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(866) 423-7849

Current Response-Based Treatment of Pediatric Hodgkin Lymphoma

Announcer:
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Dr. Hoppe:
Welcome to this education session on Current Response-Based Treatment of Pediatric Hodgkin Lymphoma. My name is Bradford Hoppe, and I work at Mayo Clinic Jacksonville, Florida.

Management of patients with pediatric Hodgkin lymphoma starts with risk stratification, where more intensive systemic therapy is used for patients at increased risk. The risk groups are broken down into the low-risk patients who have early stage disease without any risk factors, intermediate-risk patients who are early stage patients with risk factors such as bulky disease or B symptoms, and high-risk patients with stage III or IV disease, and often including patients with Stage IIB bulky as well.

In general, following combined modality therapy with systemic therapy and radiotherapy to initially involve sites, low-risk patients have excellent event-free survival. While intermediate and high-risk patients have very good event-free survival with increased intensive systemic therapies.

While the risk of recurrence has been low with combined modality therapy, the treatment has been associated with significant risk of late effects with 40% of survivors developing a significant grade 3 or higher late effect 25 years or more after treatment. These include nonmalignant and malignant second cancers, cardiac disease, and pulmonary issues. While systemic therapy contributes to these effects, the large radiation fields that were utilized 30-40 years ago, and the high radiation doses that were used back then, led to a lot of these late effects. As a result, a primary driver of research in pediatric Hodgkin lymphoma has been to reduce the use of radiotherapy.

Interim and end-of-chemotherapy imaging with CT scans and/or PET scans have been found to be strong prognostic factors for identifying patients at risk of relapse in both pediatric and adult Hodgkin lymphoma. Therefore, the cooperative groups have utilized the imaging response to help identify patients where treatment can be de-escalated, such as omitting radiotherapy, as well as patients at higher risk of relapse, where we cannot de-escalate therapy, but in some cases actually intensify therapy.

The Euronet-PHL-C1 study recently reported their response-adapted treatment approach for all three risk groups, where response assessment is used to determine who gets involved-site radiotherapy. All patients receive two cycles of OEPA chemotherapy. Patients with intermediate risk go on to receive additional two cycles of COPDAC chemotherapy, and patients with high risk get four cycles of COPDAC chemotherapy. Patients with a rapid response based on PET and CT scan after two cycles of a OEPA do not get radiotherapy, while those with a slow response received involved-site radiation after completion of systemic therapy.

In the COG, the response-adapted approach for patients with low-risk disease is an adapted adult regimen where patients get two cycles of ABVD followed by an interim PET response. If the patient has a complete response by PET scan, they receive an additional two cycles of ABVD, and no radiation. While those patients who have a partial response by PET, can intensify therapy with escalated BEACOPP and involved-site radiotherapy.

For intermediate-risk patients, the Children's Oncology Group response-adapted approach selects who will get involved-site radiotherapy based on AHOD0031. Patients receive four cycles of ABVE-PC systemic therapy, and then undergo PET/CT scan after both two and four cycles of chemotherapy. Those patients with a very good partial response after two cycles based on CT component, and a complete response after four cycles based on both PET and CT do not require involved-site radiation, while all other patients require radiation.

Finally, in high-risk patients the new COG response-adapted approach helps identify additional individual sites requiring radiotherapy. In this regimen, all patients receive brentuximab vedotin, and AVE-PC chemotherapy for five cycles, followed by involved-site radiotherapy to sites of bulky mediastinal disease. And patients with a slow early response also received radiation to those slowly responding sites based on the PET/CT scan after two cycles.

To conclude, pediatric patients with Hodgkin lymphoma have excellent outcomes with combined modality therapy; however, treatment can improve by finding safer treatment strategies with lower risk of late side effects. Encouraging results with response-adaptive strategies have helped reduce the use of radiotherapy without compromising efficacy. This is especially true with the excellent results AHOD1331 in high-risk pediatric Hodgkin lymphoma patients with the addition of brentuximab vedotin.

Thank you.

Announcer:
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