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### The Role of Radiotherapy in AHOD1331

#### Announcer:

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#### Dr. Hoppe:

Welcome to this education session on the Role of Radiotherapy in AHOD1331. My name is Bradford Hoppe, Professor of Radiation Oncology at Mayo Clinic in Jacksonville, Florida.

Combined modality therapy with chemotherapy and radiotherapy has played an important role in curing pediatric Hodgkin lymphoma. Unfortunately, combined modality therapy also puts survivors at significant risk. Up to 40% of patients on the Childhood Cancer Survivorship Study have grade 3 or higher late effects at 25 years. And this can include second cancers, cardiac disease, and pulmonary toxicities. While systemic therapy contributed to these toxicities, the large radiation fields and high radiation doses that were used decades ago certainly contributed significantly to these toxicities. Therefore, there was a need to reduce the radiation exposure to patients on the more contemporary Hodgkin lymphoma trials.

AHOD1331 helped reduce the overall radiation exposure for patients by limiting radiation to only sites of bulky mediastinal disease and slowly responding sites to total dose of 21 Gy. An additional 9 Gy boosts was delivered only to sites that did not achieve a complete response by the end of systemic therapy. Finally, AHOD1331 allowed the use of the most conformal radiotherapy technology including IMRT and proton therapy.

This slide shows you the significant change in radiation field size for a patient with stage IV pediatric Hodgkin lymphoma between the POG 9425 study on the left where the patient would likely get total nodal radiation, which is the field in blue, versus the smaller involved site radiotherapy field just to the bulky mediastinal mass that the patient would receive on AHOD1331. This smaller field would lead to significantly less radiotherapy dose to the breast, heart, lung, and thyroid, and subsequently reduced risk of late effects.

Involved-site radiotherapy was delivered for large mediastinal adenopathy on this trial based on earlier results from AHOD0031, in which an exploratory analysis amongst patients with large mediastinal adenopathy and anemia demonstrated a significant benefit for the addition of involved-site radiotherapy with 4-year event-free survival of 89%, versus 78% without radiotherapy.

Sites of slow early response after two cycles of systemic therapy were also included based on exploratory data suggesting that they were sites at higher risk of relapse. In the AHOD0431 low-risk study, patients with a slow early response based on a PET scan after one cycle of systemic therapy had significant improvements in progression-free survival with the addition of radiotherapy. Furthermore, the most common site of relapse for those patients who didn't get radiotherapy was in that specific slowly responding site location.

When we look at the results of AHOD1331, we can see that 317 patients received radiotherapy without any significant difference between the two arms. Patients received radiotherapy due to large mediastinal adenopathy alone in 70% of the time, slow early response only in 7% of the time, and 24% of patients due to both LMA and slow early response; 45% of patients on the trial received IMRT radiotherapy and 27% received proton therapy, with the remaining 29% receiving 3D conformal radiation.

In this slide, you can see the color wash dose distribution for an example case for 3D conformal radiation on the left, IMRT in the middle, and proton radiotherapy on the right. The orangish-red color represents the high dose of radiotherapy, the aqua color represents moderate dose, and the blue represents a low-dose radiotherapy. Proton therapy uses charged particles that go a certain distance and stop, which results in no exit dose. As you can see with 3D conformal and IMRT, there is an exit dose with photon radiation. Patients selected to receive proton therapy at significantly lower radiation doses to the heart and breast compared to IMRT and 3D conformal radiation.

In summary, radiotherapy played an important role in managing patients with bulky mediastinal disease and slowly responding sites of disease on AHOD1331. The contemporary radiation fields and technology significantly reduced the radiation exposure to critical tissue and are expected to minimize the risk of late effects amongst these survivors.

Thank you.

**Announcer:**

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