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Integrating Targeted Therapy Into Frontline Management of High-Risk Pediatric Hodgkin Lymphoma

Announcer:
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Dr. Kelly:
Welcome to this program on Integrating Targeted Therapy into Frontline Management of High-Risk Pediatric Hodgkin Lymphoma. I'm Dr. Kara Kelly, Pediatric Oncologist at Roswell Park in Buffalo, New York, and I'm the Senior committee member for the AHOD1331 trial.

There have been a lot of interest in introducing targeted therapies into the management of high-risk pediatric Hodgkin lymphoma. And the two main drugs of interest are the CD30 antibody drug conjugate brentuximab vedotin, as well as the immune checkpoint inhibitors, targeting PD-1, particularly nivolumab and pembrolizumab. Today we're going to focus on brentuximab vedotin, as that has been the agent that has been first looked at in the frontline setting in pediatric Hodgkin lymphoma.

The first trial reported of using brentuximab vedotin in the high-risk pediatric group is a study that came out of the Pediatric Hodgkin Lymphoma Consortium, which is coordinated at St. Jude's. This was a single arm multicenter trial enrolled 77 patients. The treatment regimen is one that brentuximab vedotin replace the vincristine in the European OEPA/COPDac. Radiation was used for patients that weren't in a complete response after PET/CT interim evaluation. As you can see from the Kaplan-Meier curve, both event-free survival and overall survival were outstanding.

This was then followed up on a more definitive trial that was run by the NCI sponsored Children's Oncology Group, AHOD1331. In this trial, a new regimen that that brentuximab vedotin replaced bleomycin as well as day 1 vincristine, which we call the Bv-AVE-PC, was compared with the standard ABVE-PC, which has been used in multiple trials run through the Children's Oncology Group. Patients got two cycles of chemotherapy, underwent an interim PET/CT evaluation, then received three cycles of chemotherapy. Radiation was administered to patients with a bulky mediastinal mass or to slow early responding sites on the basis of that interim PET scan.

And as you can see, here, the survival was outstanding the 3-year event-free survival is 92.1%, almost a 10% improvement over the standard regimen. In addition, if you look at the relapses, there was a much earlier plateauing of relapse in the brentuximab arm compared to standard. The results of this study were published in the New England Journal of Medicine in November, and most importantly, led to the first pediatric approval of brentuximab vedotin for patients with high-risk disease, ages 2 and up.

The benefit of brentuximab extended across multiple prognostic factors. As you can see, across all these upfront, you know, prognostic factors, brentuximab was beneficial. The only two where we didn't observe a benefit was patients with stage IVB disease, or patients with bone marrow involvement, so this requires further study.

Also, really important was that brentuximab seemed to obviate the importance of that interim PET assessment. If you look at the standard arm, that's the curves that are in blue, there remained a significant difference between patients with a rapid early response

compared to slow response. But in the brentuximab arm, the red curves, the outcome was similar, no different. So it does, for the first time, show that the prognostic effect of a PET scan can be overcome with the use of a brentuximab-containing regimen.

As we look to the future, the Children's Oncology Group has been collaborating with the Adult Collaborative Group, SWOG, and another very large randomized phase 3 trial, the SWOG1826, which is comparing the brentuximab arm, this time with AVD, to nivolumab with AVD. This study has completed accrual, and we anticipate results will be coming soon. So stay tuned to see, you know what this shows.

So in summary, for pediatric patients with newly diagnosed high-risk classic Hodgkin lymphoma, BV or brentuximab vedotin with chemotherapy, improves event-free survival. It's observed across almost all subgroups, including patients with a positive interim PET scan. However, some new strategies are needed for patients with stage iVB disease, as well as opportunities to further decrease the use of radiotherapy.

Thank you for listening to today's presentation, and hopefully you've learned something, and as you look to incorporate the use of brentuximab vedotin for your patients with high-risk pediatric Hodgkin lymphoma.

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