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Managing Toxicities Associated With Anti-CD30 Targeted Therapy in Pediatric and Adolescent Patients

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Dr. Kelly:
Welcome to this program on Managing Toxicities Associated with Anti-CD30 Targeted Therapy in Pediatric and Adolescent Patients with Hodgkin Lymphoma. I'm Dr. Kara Kelly, Pediatric Oncologist at Roswell Park in Buffalo, New York.

We're going to focus today on the use of brentuximab vedotin, which does have specific toxicities, especially febrile neutropenia and risk of sepsis, as well as peripheral neuropathy. What's highlighted here are the rates that were observed in the recently reported AHOD1331 trial. A couple of take-home points from this. One is that the rates of these toxicities were no difference compared to the standard chemotherapy regimen, ABVE-PC. And then also importantly, the rates of neutropenia were pretty similar to what were observed in adults, maybe a little bit higher; yet, peripheral neuropathy seemed to be less common in the pediatric patients compared to the adults.

So peripheral neuropathy is one of the most important toxicities for providers to be aware of. It's primarily sensory, and most patients report some tingling, numbness of the tips of the fingers or toes. Importantly, the pediatric assessment is with the Balis scale rather than the CTCAE, which is more common in adults. Also, we see very good concordance between clinician and patient, or parent-reported assessments. So that is also reassuring to see.

From a management standpoint, most important thing is refer to the protocol. In the AHOD1331 study, we wish to maintain the dose density of the brentuximab vedotin, so the vincristine was held or reduced first. And there are specific guidelines that are in the treatment protocol. Fortunately, most peripheral neuropathy reserves following completion of treatment. We don't yet have long-term data on pediatric patients. But from the adult ECHELON trial, less than 6% continued to have grade 2 or more neuropathy.

Neutropenia and sepsis is another concern with use of brentuximab vedotin. Most important point is that you should use granulocyte colony-stimulating factor primary prophylaxis with its regimen. With this, rates of serious sepsis are quite rare. And it's important to monitor CBC, and know that delays in starting the next cycle of treatment are rare.

Infusion reactions are another concern with this regimen. This can present with, you know, typical chills, fever, nausea, anaphylaxis, though it is fortunately rare. Most times they occur with the first two cycles of treatment. Importantly, we actually did not observe any infusion reactions with the brentuximab AVE-PC in the AHOD1331 trial, but as it has been reported, it's important for providers to be aware. There are standard management guidelines. Also important is that you should discontinue the brentuximab for any anaphylaxis or for any grade 4 reactions.

There are also a number of rare toxicities with the use of brentuximab vedotin that’s important to be aware of. We didn't observe any of these in the AHOD1331 trial. But again, these have been reported. The most serious of which is PML, progressive multifocal

leukoencephalopathy. Important to be aware, it can be somewhat insidious, and so keep it in mind especially if patients are developing neurologic deficits, and get neurology involved early on for assistance with the workup. Pancreatitis is also quite rare, but do consider it especially in patients that have severe abdominal pain. But routine monitoring of amylase and lipase is not recommended. And additionally, pulmonary toxicity had been a concern in some of the adult trials. We have not observed it to be so in the pediatric studies to date, but do you consider this as a potential etiology of pulmonary symptoms, especially when no infectious etiology is identified.

So in summary, febrile neutropenia is observed and about 30% of pediatric patients receiving brentuximab, although sepsis is rare. Peripheral neuropathy seems to be a little less common than in adults. But it's important to keep an eye on and use the protocol-specific guidelines for dose modification.

Although we're still learning about the use of brentuximab in this younger population, most importantly, in our trials, no deaths have been associated with the treatment to date.

So thank you for listening to today's presentation. Hope you've learned something and hope this will help you as you manage your patients with the use of brentuximab vedotin for treatment of Hodgkin lymphoma.

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