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ADC-Related Hematologic Adverse Events

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Smit:
This is CME on ReachMD, and I'm Dr. Egbert Smit from Leiden University Medical Center in the Netherlands.

I would like to review the hematological AE [adverse event] profile as reported in the DESTINY-Lung02 study. As you know, this was a study that compared 2 doses of trastuzumab deruxtecan in a randomized fashion. One dose was the 6.4 mg/kg administered every 3 weeks as an IV infusion that was tested in the DESTINY-Lung01 study where it was associated with a high response rate to patients with HER2-mutated non-small cell lung cancer but was associated with severe toxicities in the sense of ILD. And therefore, a lower dose was also tested, the 5.4-mg/kg dose, as we know that from breast cancer.

The efficacy between the 2 doses was similar in this randomized study, with response rate in excess of 50% and progression-free survivals in the order of 9 months for both arms. However, the safety profile for the 5.4-mg/kg dose was substantially better, and therefore, this dose was approved for treatment for HER2-mutated non-small cell lung cancer.

The rate of hematological toxicities in that cohort was for neutropenia 42.6%, with the incidence of grade 3 or more neutropenia was 18.8%, and anemia 36.5%, and the grade 3 or more in 10.9%, and thrombocytopenia in 27.7% with the grade 3 or more clinically relevant rate was only 5.9%.

So how do we manage these toxicities so that patients can stay on treatment safely? First and foremost, I think we should optimize the dose to ensure the most favorable safety profile, ie, for those patients with a HER2-mutated non-small cell lung cancer with treatment. And a dose of treatment should be 5.4 mg/kg given every 3 weeks as an IV infusion. We have to keep in mind that, actually, we are administering chemotherapy, so all the rules for alleviating hematological toxicities or preventing hematological toxicities should be applied to these patients. So we should identify risk factors for hematological AEs and follow the guidelines on baseline assessments and monitoring to ensure early detection of these treatment-emergent adverse events with respect to hematological toxicities.

We may manage them, the neutropenia. We do not think that primary G-CSF prophylaxis is necessary for patients starting with T-DXd therapy, but secondary prophylaxis may be administered to prevent cycle delays or dose reductions for those patients that have experienced grade 3 neutropenia, and in particular patients that experience febrile neutropenia.

For patients that have anemia, dose delays and/or dose reductions may be applied for those that have grade 3 or more anemia. And iron therapy or blood transfusions should be considered if clinically indicated.

Although very infrequent, thrombocytopenia and dose delays and reductions, again, should be considered for those that have grade 3 or more thrombocytopenia. And supportive platelet transfusions should be considered if clinically indicated.

Some of the other more investigational ADCs developed in non-small cell lung cancer are also associated with hematological toxicities.

And I think the most important one is the patritumab deruxtecan, which is associated with a grade 3 rate of neutropenia in the order of 15%, but more importantly, a grade 3 rate of thrombocytopenia of in approximately one quarter of the patients. And again, these should be managed like any patient treated with cytotoxic therapy.

Well, that's all the time we have today, and thanks for tuning in.

Announcer:
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