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Practical Considerations and Adverse Event Management with CD19-Directed Therapies in R/R DLBCL

Announcer:
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Dr. Caimi:
Hello, my name is Paolo Caimi. I am from Cleveland Clinic. This presentation is on the "Practical Considerations and Adverse Management with CD19-Directed Therapies in Relapse and Refractory Diffuse Large B-Cell Lymphoma". We have seen this slide before, highlighting the expression of CD19 through the maturation stages of B cells, and the corresponding B cell malignancies. This wide distribution makes CD19 an attractive target for immunotherapy in lymphoma.

There are three approved classes of agents targeting CD19: the monoclonal antibody Tafasitamab, the antibody drug conjugate, Loncastuximab, and multiple CD19-targeting chimeric antigen receptor CAR T-cells.

Starting with Tafasitamab, perhaps the most important practical consideration is the schedule and the need to coordinate the prescription of the oral Lenalidomide with infusions of Tafasitamab. One aspect to keep in mind, particularly in the few weeks of treatment, is that patients will have several visits per month to the infusion center to receive their Tafasitamab.

Although in general, Tafasitamab combined with Lenalidomide is a well-tolerated combination, hematologic toxicity, rash, and other adverse events have been observed with this combination. The main management strategies include the use of growth factors to treat the emergence of neutropenia, as well as dose modifications, particularly of Lenalidomide, for management of hematologic and non-hematologic toxicities.

Loncastuximab has a different safety profile, with hematologic toxicity in a quarter of patients, but also with elevations of gamma-glutamyl transferase and the development of fluid retention, either with peripheral edema, pleural and pericardial effusion. Management of adverse events of Loncastuximab includes growth factor support for hematologic toxicities and close monitoring of the patient's GGT levels as well as the patient's weight. So early interventions, including holding or decreasing Loncastuximab doses can be considered. The use of diuretics, including spironolactone, has been recommended for management of the fluid retention adverse events.

Important management consideration for Loncastuximab include the use of dexamethasone on the day before, the day of, and the day after the Loncastuximab infusion. Intravenous dexamethasone can be used if the patients omit the doses prior to the day of the infusion. Photosensitivity is also common with Loncastuximab and prevention of sun exposure, including physical barriers and avoiding direct sunlight are important.

CAR T-cells targeting CD19 have a very specific set of toxicities. In particular, the risk of Cytokine Release Syndrome and the risk of neurologic toxicities, which are now termed "Immune effector Cell Associated Neurotoxicity Syndrome".

Cytokine Release Syndrome manifests initially with fever but can progress to a systemic inflammatory syndrome with hypotension,

hypoxia, and multi-organ failure.

The grading of CRS is based on the presence of fever, the presence of hypotension with or without the requirement of fluid infusions as well vasopressor administration, and the presence of hypoxemia and requirements for positive pressure ventilation.

The management of CRS include supportive care measures including antibiotics for possible infections. But with moderate and severe presentations, the addition of cytokine blockade with Tocilizumab and the use of corticosteroids is important to arrest the inflammatory process. Intensive care monitoring and supportive care are important to maintain patient stable.

Neurotoxicity presents as encephalopathy, which can be mild to severe, usually with initial word finding difficulty and dysgraphia.

Monitoring for neurotoxicity is frequently done with the ICE tool, which tests for orientation, naming, command following, evaluation of writing and attention. This simple tool can be applied in the office or at bedside. The severity grading considers the ICE score as well as the level of consciousness, presence of seizures, motor findings, and the development of cerebral edema.

Management is usually supportive care for patients with mild presentations of neurotoxicity. But those patients with moderate or severe cases of neurologic complications will require treatment with systemic corticosteroids as well as intensive care unit management.

In conclusion, we have seen that CD-targeting immunotherapies have a very diverse safety profile with different logistics with regard to their administration. The management of each agent is based on the anticipated side effects. They all require certain specific logistic considerations, for example, the frequent infusion schedule for Tafasitamab, the need for pre-medication with corticosteroids for Loncastuximab, and the close monitoring, sometimes with preemptive hospitalization for patient with CAR T-cells. Thank you for your attention.

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