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Step-Up Dosing of Bispecific Antibodies: The Need for Hospitalization

Announcer:
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Dr. Lonial:
This is CME on ReachMD, and I'm Dr. Sagar Lonial. And here with me today is Dr. Caitlin Costello. In this episode, we'll talk more about why patients should be admitted during the step-up dosing phase.

Dr. Costello, why is this an important measure to take for the initiation of bispecific therapy?

Dr. Costello:
Thank you. Yes, we did talk about the different schedules for different bispecific T-cell engagers and how each of them include a step-up dosing part of it. It's usually within that first week where patients are getting escalating doses. It's an opportunity to perhaps mitigate some of the toxicity we see. We know that cytokine release syndrome is seen in the majority of patients in any of these T-cell engagers. So the preemptive steps that we oftentimes take include corticosteroids, antihistamines, antipyretics, at a minimum, before each of the doses. Now we've talked a little bit about how we may start to incorporate some of our treatment opportunities like tocilizumab, for example, to help decrease the risk of it as well. But at a minimum, with the package insert, it says that these are important parts to premedicate these patients with before each of these doses in the step-up dosing. Once you get to the treatment dosing, you don't need to use those. Those patients have a much lower risk of developing CRS, but at least in the early stages of the step-up dosing, it's critical. When the risk is so high, these patients are oftentimes admitted so that they can undergo serial assessments, vital signs, heart rate, blood pressure, oxygen levels, and neurologic assessments. Just the same, remember, thinking about some of that neurotoxicity. We have ICE [immune effector cell-associated encephalopathy] scores, which are objective means of evaluating patients in terms of motor function and cognitive thinking so that we can see if there's even the subtlest finding of some of those neurotoxicity symptoms. So that's neurotoxicity. We know cytokine release syndrome is associated with those fevers or lower blood pressure or oxygenation requirements, some of which, in early phases, may be able to be observed. Many of us are kind of grabbing or reaching for our tocilizumab earlier instead of letting it escalate beyond that point, but certainly, if it begins to get to a grade 2, then absolutely intervention is necessary. With our neurotoxicity, tocilizumab is really preferred; for CRS, dexamethasone has a much more important role for neurotoxicity. As I said, I think you'd agree, same approach is don't wait. If you're starting to see some of these ICANS symptoms or any of those ICE scores starting to fall, there's no reason to wait; start to do those interventions soon.

So CRS, oftentimes first, sometimes followed by ICANS, sometimes can be completely independent. I think these are the 2 most common side effects we see in the early phases of treatment.

We've talked a little bit about cytopenias. We've seen skin and oral toxicities, specifically in those GPRC5D-targeting T-cell engagers that are unique to that target. This is kind of that on-target, off-tumor effect that we can see and lots of different approaches to look for this and know how to intervene to try and mitigate some of that risk. And don't forget the infections. Use those prophylactic antibiotics,

antiviral medicines, whatever you need, including IVIG, as a means to help prevent some of those infections, which we know can be great, particularly with our BCMA-targeted T-cell engagers.

Dr. Lonial:
Yeah, thank you very much for a great summary on that. And I think while the FDA labels suggest that everybody should be admitted, I think that our goal in the coming years is to understand is it everybody, or is it 10% or 15% of patients? I think understanding and feeling comfortable with some of these adverse events, putting the infrastructure in place to manage them as an outpatient, I think that's something we're all going to be doing more and more of, particularly as bispecifics are used not just in myeloma, but we're seeing them in acute leukemia; we're seeing them in lymphoma; I suspect we're going to start to see them in solid tumors as well. And as this becomes more and more mainstream in oncology in general, I think the push to manage these patients as an outpatient is going to come even more rapidly.

Unfortunately, our time is up. Thanks for a great discussion, Dr. Costello, and thanks to our audience for tuning in.

Announcer:
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