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Preventing CRS and Neurotoxicities Related to Bispecific Antibodies

Announcer:

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

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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.

When using bispecific antibodies for patients with heavily pretreated relapsed and refractory myeloma, it's important to both recognize and effectively manage cytokine release syndrome, or CRS.

So let's go through a couple of cases and just think through how we would manage some of this in the context of what do you think about, Dr. Costello?

Dr. Costello:

Great question. So like we've said, new drugs, new toxicities. And I think we've all learned a lot about cytokine release syndrome, both with bispecific antibodies and with CAR T cells. So I think let's just touch briefly on that. Remember that this is kind of boxed warning that requires REMS programs for everyone to be educated on what to look for, what to expect in the management of CRS.

So what we know about cytokine release syndrome is that it's most commonly seen during the step-up dosing, so really during that initial exposure to therapy. Now in theory, if patients need to go through the step-up dosing again in the future, you could see those same CRS happen again.

We know that this is most common with patients who have high tumor burden, right? More killing means potentially more toxicity. And with different drugs, we know that that CRS can happen at different times. Sometimes it's with the first dose; sometimes it's with the later doses. There are very specific instructions in the package inserts about when these patients should be hospitalized, when they may be potentially discharged to the outpatient setting. So I think lots that we are learning on how to look for and be prepared to manage CRS.

What about you, Dr. Lonial? What do you do in your practice to monitor for CRS?

Dr. Lonial:

Yeah, so I think it really depends on where they're being treated. If they're in the hospital, our nurses have the criteria and the guidelines in terms of what to do. And we actually have APPs [advanced practice providers] on call at night in the hospital as well. And they understand this because they've been doing it for 4 or 5 years now, and know that at certain points, we just want to go ahead and give tocilizumab. Our nurses also have pretty clear questions that they use to assess CNS [central nervous system] toxicity over time. And then, again, there's a pretty significant educational handout that gets given to them when they're discharged. So I think that perspective is really important.

What I will tell you is that our group is actually going to preemptive tocilizumab for patients as an outpatient to allow them to be managed almost exclusively as an outpatient, except in rare situations, as you described, Dr. Costello, where there's so much tumor burden, we're worried that a single dose may not provide the coverage they need, they're frail, or perhaps they don't have the support to be able to come in if there were something to happen that we didn't expect on a regular basis.

Dr. Costello:

So you've mentioned that you do cutting-edge prophylactic tocilizumab. What do you do, let's say, for a patient who is seen in the hospital and they have a fever, and they have low blood pressure and maybe start looking like they're needing some oxygen. What would be your intervention at that point?

Dr. Lonial:

Yeah, no, I think this is the real challenge, because these are patients that are set up to have infectious complications. And you don't want to say, "Oh, this is definitely just CRS." So I think we do the standard infection prevention and prophylaxis as well. But at the same time, if the timing is right and it just makes sense, we'll give them a dose of tocilizumab pretty early. I know the criteria typically say grade 2, which means needing oxygen, as you just described; we'll likely start at grade 1.5. And the reality is there's no downside to giving tocilizumab. All it does is potentially protect patients, and if you're covering them for infectious complications, you've got some additional support during that period of time. So I think covering all your bases early on is really important.

Dr. Costello:

I think that's so important to say, "Why wait?" I think we have all been kind of trained initially, and now seeing that you're doing it prophylactically, you know, as in the outpatient setting, we do the same thing. I think at the earliest sign of the first fever, go for it; it's not going to compromise the effectiveness of the drug. So if everybody can rest a little easier, and including the doctor at night in getting to sleep because there's no fevers that you're being called about, then great. So that's the CRS management.

When it comes to ICANS, however, it's slightly different. Remember, ICANS is that neurotoxicity which oftentimes, but not always, is preceded by CRS. Symptoms, as you mentioned, can be watched for with very specific questions. These are patients that sometimes require dexamethasone in order to manage them.

Dr. Lonial:

I think you're absolutely right. And I think understanding and being comfortable with these toxicities really represents how we're going to move forward to allow this to be given to more patients.

Well, this has been a great but brief discussion. Hopefully you can put some of these tips into your own practice tomorrow. And thank you again for listening.

Announcer:

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