Advancing RRMM Care Through Communities of Practice: Educating Community-Based Hematologic/Oncologic Teams on the Use of BCMA-Directed BsAbs—A Project ECHO® Initiative

Community of Practice: **Session 1 Questions**

During the Community of Practice session that took place on December 11, 2025, Dr. Raphael Szalat addressed questions from the participants. Below are the questions asked during the discussion and Dr. Szalat's responses (based on the transcript).

QUESTION: There are 4 bispecific antibodies now available. How do we pick which bispecific to give to our patients?

Faculty response: Initially, teclistamab was the only BCMA-directed bispecific antibody that was approved, so it was easy—there was only one—and then came elranatamab. I try to select the bispecific according to the efficacy that we know from the clinical trial, and I try to see if the patient is going to be a good fit or not. Between teclistamab and elranatamab, one thing that might be more convenient (but it's not based on criteria) is it's a fixed dose for elranatamab, whereas teclistamab is based on the weight of the patient. So if you have a patient who is very overweight, it might be a little bit challenging to give teclistamab. In terms of efficacy, elranatamab might be a little bit more effective based on the data, but if you look at real-world data, it seems elranatamab and teclistamab have similar efficacy. For outpatient, sub-Q, teclistamab or elranatamab are similar. I have not identified any clear clinical difference when I'm using them. They have the same side effects and the same efficacy. Now we have linvoseltamab, which seems to be more efficient based on the clinical trial results, including with longer follow-up, but as it was more recently approved, I have not used it yet. Linvoseltamab is given IV, and the CRS happens within 15 hours, so it's a shorter time, and this needs to be taken into consideration as well. It will likely be my first choice for patients who prefer or are agreeable to receive IV treatment.

QUESTION: For patients with compromised renal function, which bispecific antibody would you choose?

Faculty response: The clinical trials excluded patients with kidney dysfunction, but we now have more data from real-world settings about using bispecific antibodies in patients with kidney dysfunction, and even in patients on hemodialysis. And we have used, so far, both teclistamab and elranatamab with no issue. Patients on dialysis are frailer and I admit them, because for patients on dialysis, having CRS might be more complicated to manage. But for a fit patient, we might even consider doing it as an outpatient. I recommend doing the injection after dialysis. Let's say your patient is on dialysis Monday, Wednesday, and Friday—I would potentially do the first injection on a Monday evening or a Tuesday morning. There is no specific dose adjustment in that setting, and the toxicity profile seems to be the same. What you need to adjust is the prophylaxis medications, and those should be renally dosed. That's very important for sulfamethoxazole/trimethoprim, which would be given less frequently.

QUESTION: Have you ever had problems with insurance access to these medications?

Faculty response: For the bispecific, I have not. I try to respect the approval, and for now, bispecifics are approved after 4 lines of treatment. But sometimes you can play a little bit with the regimen that your patients have received. So, for example, if a patient is in third-line therapy and I start him with a regimen such as DPD and the response is not great, I can add, for example, oral cyclophosphamide for 1 cycle, and then I would say, here are the 4 lines of treatment. Those are the little things that can help with the insurance to get the approval. The goal being to try to move as quickly as possible to the bispecific.

One thing that I have had a problem with is IVIG. IVIG is critical when you give bispecifics (and also when you give CAR-T) because all the patients are going to be hypogammaglobulinemic. And unfortunately, this is a life-threatening situation for our patients. I've had some pushback recently from insurance, saying that you need to wait for the gamma globulin to be lower than 400 and they would not approve the IVIG for my patient. But when I was at ASH last weekend, everybody was really recommending starting IVIG as soon as possible, to not wait for the gamma globulin

to be lower than 400. So, what you can try to do is to make sure the insurance understands, for example, if your patient has IgG myeloma. The gamma globulin that you measure includes the involved IgG plus the noninvolved IgG, so you can say the noninvolved IgG are less than 400 and the patient is indicated for IVIG. The sooner you initiate the process, the better, because you need to start IVIG as soon as possible.

QUESTION: Are you using acetaminophen and/or dexamethasone prophylactically for outpatients after BiTE administration?

Faculty response: For outpatients, we actually use it before and we don't use it after. For most of the patients, we would also add tocilizumab. I was discussing with colleagues over the weekend and I was saying it should not be universal tocilizumab for everybody, but I think in the setting of an outpatient, especially at the beginning, when you're not very well experienced, it is preferable to give it outpatient. We have done it without tocilizumab, but I think if you are planning not to give tocilizumab, you want to be 100% confident about how reliable your patient is and how to connect with him, or be sure he lives close to the hospital, if needed. Your patient might experience a little bit of fever, which will be the case for the majority of patients, and usually there is no issue. Our concern is really about grade 3 and 4, and those grade 3 and 4, obviously, are very, very uncommon. By giving tocilizumab, you're mainly preventing grade 1 and 2. And if you have a young, fit patient, or less young, but fit, and also that is reliable and has good caregivers, that's totally doable.

QUESTION: If tocilizumab is given prior to the first dose and the patient does not present with any CRS, what would you do before the second dose? Would you give a second dose of tocilizumab?

Faculty response: In myeloma, most of the events will happen after the first dose, a little bit less after the second dose, and almost none after the third dose. And the half-life of tocilizumab is relatively long—it can last for more than 10 days. So, if you did not observe any CRS or ICANS after the first dose, we usually don't give a second dose of tocilizumab, even if the patient is frail or you feel they have a higher risk.

QUESTION: Infectious complications are unfortunately very common—a patient may have cytopenia, and so you will likely delay some of the treatment. So, when you delay the treatment, what do you do in terms of preventing recurrent risk of CRS?

Faculty response: What is very important is the timing and the patient's response to treatment. Has your patient already achieved a response with the treatment? If the time between the injections is up to 3 months, the risk of having CRS or ICANS is probably close to zero. On the condition that the patient is not progressing—because if the patient is progressing, the plasma cell burden is going to be much higher, and then the risk of having a CRS is back. But otherwise, the risk is almost zero and you don't need to repeat tocilizumab.

The recommendation, officially, from the trials and from the FDA, is within 28 days. If you're beyond 28 days, you should repeat step-up dosing, but with more experience, we observed that if your patient is in good response, if you are beyond 28 days, and let's say less than 2 to 3 months, you can still just continue with the dose that the patient was getting before with no step-up dosing.

QUESTION: Can you discuss dosing intervals? Some institutions are using different intervals than what is in the package insert.

Faculty response: The dosing schedule of the bispecific is very likely to change. Basically, the bispecific's schedule is every week for 8 weeks, and then every 2 weeks for 3 months, and then once a month. But we might dose less frequently, especially in patients who are frail (eg, a frail older patient with history of severe infections prior to bispecifics), and on the condition that you observe a hematologic response. You can start as soon as partial response, but right now, people are waiting to see a VGPR, then you can start to decrease the intensity, move to 2 weeks, and even to once a month. This is based on the pharmacodynamics of the medication. You don't need to give it once a week to make sure it stays in the system. It's very intensive to give it every week at the beginning, because if you have a big tumor burden, you're going to be more efficient. But if you already see a response, you don't need to be that intensive.

QUESTION: Do you have any concerns about ICANS? How do you manage ICANS? How frequent do we see ICANS with bispecific antibodies?

Faculty response: ICANS is very uncommon, especially severe ICANS with bispecifics, but it can still happen. I have seen it in patients with very aggressive and advanced disease, in hospitalized patients with bad disease, very high tumor burden, so it's unlikely that you will see this patient in the outpatient setting. If you have a patient with high tumor burden, EMD, or high LDH levels, it is safer to administer bispecific antibodies inpatient. Make sure that your patient is not progressing very quickly. Usually, most of the ICANS are headaches, but severe ICANS can be very problematic and we treat them with steroids as first line.

QUESTION: What do you do if a patient has high fever after the first step-up dose?

Faculty response: The patient most likely has CRS grade 1 after the first dose. So, depending on the patient (eg, frailty, fitness, comorbidities), you can do symptomatic treatment, or you can give tocilizumab. The key here is to make sure that the first event is resolved before you give the second dose. Especially if you didn't give tocilizumab. So, the biological markers of inflammation are very important. When I see a patient who has CRS after the first dose, I make sure it's under control before giving the second dose, and I often even delay 1 to 2 days, just to see that the CRP and the ferritin levels are trending down. In a patient who might have a continuing CRS, and especially if the cultures are negative, I would have a low threshold to give a dose of tocilizumab. Also, ICANS happens often in the context of CRS, and not always at the same time. If a patient develops bad CRS, they are at higher risk of developing bad ICANS. I would have a low threshold to give tocilizumab.

QUESTION: Is there ever a point of bridging chemo to decrease burden prior to BiTE? Knowing that most people are already penta refractory by the time bispecific antibodies are recommended, is it a terrible idea to give bispecific antibodies with very high disease burden?

Faculty response: We talk about bridging a lot in the context of CAR-T and much less in context of bispecific antibodies. It is true that a high tumor burden is associated with more complications, CRS, ICANS, and probably less efficacy, although we don't really have good data to say high tumor burden, low tumor burden is better. In general, when we give a bispecific, there's not a lot of options for bridging, so I would not say to not do a bridging therapy, but I would say if you do without bridging therapy, in context of progressing disease and high tumor burden, I would admit the patient. In context of extramedullary disease, I combine with radiation of plasmacytoma. There is a paper that was published recently about classic chemotherapy, such as DCEP regimen, as a bridging therapy prior to bispecifics. And it seems to be working okay. There are some questions about the T-cell fitness after such chemotherapy and the past medical history of the patient (because you need T cells from the patient to be working well). If you give chemo and then the T cells are depleted, it might affect the treatment, but there is at least one publication that I know that shows that it is safe. And it's not affecting the efficacy of the bispecifics to do a bridging with a DCEP sort of regimen. So you have the option. DCEP is a very aggressive regimen; it will lead to aplasia. Often patients will be admitted, they often need a central line, so it's not very easy to do, and you would need to make sure you have the infrastructure to do so. This paper provides more information: https://pmc.ncbi.nlm.nih.gov/articles/PMC12540854/

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