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 3 Questions**

During the Community of Practice session that took place on July 16, 2026, 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 1: Does anyone have a practice regarding intravenous immunoglobulin (IVIG)? Are you just giving it monthly? What's the number that you target? Any experiences or rules of thumb?

Faculty response: The guidelines state that you should start IVIG when the level of immunoglobulin G (IgG) is lower than 400 mg/dL. This is the recommendation from the guidelines, but now we have data saying that the earlier you start, the less infection the patient will have (Banerjee R, et al. *Blood Adv.* 2025;9:4720-26). I try to request prior authorization at the same time I start the bispecific, so I don't get push back from the patient's insurance company. Sometimes it works and I start as early as possible. I prefer not to wait for the patient to be below 400 mg/dL and obviously prefer not to wait for the patient to get an infection. For patients who are not below 400 mg/dL and do have an infection, I push back if the insurance company denies coverage because the patient is not in the threshold below 400 mg/dL. I would then explain there is an indication because the patient is on bispecific therapy, the patient's IgG level is going to decrease, and the patient is already symptomatic and needs IVIG. Sometimes you need to call the insurance company and give a peer-to-peer explanation.

There is the possibility to give either IVIG or subcutaneous immunoglobulin (SCIG). There is some benefit to giving SCIG to patients because it is given weekly or every 2 weeks and the coverage is better. There are some data suggesting the patient may have less infection when it's given subcutaneously. Patients can administer it at home, which might be more convenient for them (Lingman-Framme J, et al. *Drugs*. 2013;73:1307-19). In general, you administer it when they come in for the bispecific antibody. If you're treating patients who received CAR T-cell therapy, then hypogammaglobulinemia is also potentially a long-term side effect. Instead of having them coming in only for the IVIG, you can also put them on SCIG. The half-life is also shorter for SCIG, so I give it weekly.

QUESTION 2: How do you explain the side effects of talquetamab? How do you help patients manage dry mouth/dysgeusia? How do you support patients when they tell you they don't know how long they can take the side effects even though you know it's working so well on the myeloma?

Faculty response: Talquetamab is a bispecific antibody targeting CD3 and GPRC5D. The side effects from bispecifics are related to their therapeutic class. The common side effects, which we have discussed in the prior sessions, are initially cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), cytopenias, and infection. They occur because basically the bispecific is activating the T cells and is making them target the myeloma cells. The immune system is not working normally and is overactivated, so CRS, ICANS, and infections are occurring. The additional side effects are based on the target of the bispecific. If BCMA is the target, which is a marker that is mainly expressed by plasma cells and B cells, the patients are going to experience humoral immunosuppression because they will have no more plasma cells or B cells. This is why with BCMA-targeting agents, patients have infections and hypogammaglobulinemia. This is why IVIG or SCIG is so important.

For talquetamab, the target is GPRC5D, which is a protein that was completely unknown before this drug was developed, but was found to be highly expressed in myeloma cells. The problem is that it is also expressed on the skin, the mucosa, and in some parts of the brain, so there are off-target side effects. The toxicities are mainly cutaneous and mucosal, as well as neurologic to some extent. Based on my experiences, the off-target toxicity from talquetamab tends to be worse in the first 3 months, when the drug is given weekly or every 2 weeks. Once the injection is spaced out to every month, the toxicities usually get better.

The mouth toxicity occurs because of the involvement of the mucosa. Patients are going to have dysgeusia, oral toxicity, taste problems, and very dry mouths, and it will be difficult for them to eat well. They need to see a dietitian or nutritionist. That's what we do in our clinic. You also need to give them steroid mouthwash and saliva stimulants.

For the skin toxicities, some patients will present with complete redness, which might require systemic steroids when it is a grade 3 rash. When patients experience dry skin or xerosis, it's very important for them to use topical moisturizers and emollient cream at least 2 times a day.

Antihistamines can also be useful when the patient has a lot of itching. Additionally, patients may have nail toxicity and some ulceration around the nails. Again, emollient cream and topical moisturizer are very helpful. Sometimes patients may need topical steroids. The hardest part is when patients first start the treatment, but the toxicities eventually improve.

QUESTION 3: Based on the current literature, can you outline what to recommend for a patient with newly diagnosed multiple myeloma and stage 2 disease who still has good quality of life, but has mild bone pain, immunoglobulin M (IgM) and IgG spikes, high B2 microglobulin, and genetic adverse prognostic signs? Do you stratify what you would use for first-line therapy? It's been a dilemma considering transplant for early stage patients and now less so with the availability of bispecific antibodies.

Faculty response: The first comment I would make is there is a difference between Europe and the US. More patients in Europe will go to transplant than in the US. Historically, many of the stem cell transplant (SCT) trials have been done in Europe, and they have less access to the new treatments. We don't know yet how having access to CAR T-cell therapies and to bispecific antibodies in the second line is going to change the outcome for all our patients.

That being said, when you have a newly diagnosed myeloma patient, in general you have 3 clinical scenarios: a fit, younger patient; an older but still fit patient; and an older frail patient. If you are in the first 2 categories, which means you are fit according to your age, the standard of care right now is to give you a quadruplet regimen as an induction therapy. If you are fit enough, and especially if you have high-risk cytogenetics, the recommendation would be to discuss consolidation with SCT with the patient. If the patient achieves a complete response during the induction, which means after 4 to 6 cycles of quadruplet therapy, then the benefit of SCT in that situation is less clear (Perrot A, et al. *N Engl J Med*. 2025;393:425-37). We will have the answer at some point. I think SCT might still prolong the progression-free survival (PFS) for the patients for the time being, but the benefit of this strategy is unclear if you're high risk. If you are able to test for minimal residual disease (MRD) and the patient is not MRD-negative, then that is the case where I push for transplant. If you're not high risk, have a complete response, and are MRD-negative, I think it is reasonable to delay SCT as a last option, knowing that you will have access to other therapies and probably will never need SCT.

For older patients, there is no benefit for doing SCT. The treatment is too intense, and it's going to be deleterious. For the non-frail older patient, I usually try to start with a quadruplet therapy, hoping that the patient will be able to tolerate it. I also often decrease the dose (Usmani SZ, et al. *Nat Med*. 2025;31:1195-202; Facon T, et al. *N Engl J Med*. 2024;391:1597-609; Leleu X, et al. *Nat Med*. 2024;30:2235-41). For example, I would give only 15 mg of lenalidomide, and sometimes I would do 14 days instead of 21 days. The dose of dexamethasone is also reduced. After a certain number of cycles, depending on tolerance of the patient, I transition to a doublet (usually daratumumab-lenalidomide [dara-len]), then go to a maintenance regimen. For patients who are high risk, I try to do 8 cycles of quadruplet, but the goal is to achieve the best possible hematologic response. For the older/frail patients, I usually try to give a doublet therapy with daratumumab based treatment combined with lenalidomide according to the MAIA trial with steroids or without steroids (Manier S, et al. *Lancet Oncol*. 2025;26:1323-33) or sometimes with bortezomib (DVd regimen) and transition to maintenance with a single agent (dara or len) after achieving a plateau, usually after 6 to 8 cycles based on tolerance.

Regarding how long we treat these patients, we are starting to see some good data from clinical trials. For non–high-risk patients, I think at least 2 years of treatment is probably the best. If it's possible, ideally you should stop when your patient achieves complete response or is MRD-negative. If the patient is not in that situation, I think that continuing with single-agent lenalidomide or daratumumab or both is appropriate. For high-risk patients, unfortunately, we don't have data yet to support stopping treatment. Although with access to CAR T-cell therapy and bispecifics, you could stop treatment. In the case of progression, you can give those new treatment options.

QUESTION 4: How do you feel about fixed-duration bispecifics?

Faculty response: Fixed duration is the future for bispecifics. We cannot give those medications forever. It's not possible, and in real life, we don't. We stop for most of our patients, whether it's because they have a bad infection, as you have seen in patients, or because they are in complete response for many months or even years. The benefit-risk, at some point, is in favor of stopping, in my opinion. Clinical trials are ongoing about fixed duration, especially in elderly patients, and when bispecifics are used in frontline settings. I think it's going to be the next important step.

QUESTION 5: If we were to have the same program a year from now, how would you introduce it based on your expectations [for multiple myeloma treatment]?

Faculty response: Which bispecific is the best frontline? What is the impact of giving the bispecifics frontline for patients who are going to be candidates for CAR T-cell therapy? So the sequencing is still going to be very important. Are we sure that bispecifics are the best option for all patients? Because right now, we say quadruplet is the best option for all patients.

QUESTION 6: I'm seeing a lot of teclistamab-daratumumab (tec-dara) used. Is anyone else using it and what are your experiences? Are you seeing a lot of infections?

Faculty response: Tec-dara was approved by the FDA very recently as a second-line treatment. Sometimes providers are hesitant to move forward with CAR T-cell therapy for various reasons, so they prefer to give tec-dara, which is a very efficient regimen, but is also associated with infections. IVIG is needed even if tec-dara is given as a fixed-duration therapy because sometimes the hypogammaglobinemia can last for years, even if the teclistamab is stopped. You need to make sure your patient is aware of that as well. Tec-dara is clearly becoming one of the most popular second-line treatment options.

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