2023 ONS Fireside Chat

April 29, 2023

Transcript

Grace Allison (MMRF): Welcome and thank you for joining us for today’s Oncology Nursing Society (ONS) Fireside Chat. My name is Grace Allison and I’m joined today by Brittany Hartman, and we are patient navigators at the Multiple Myeloma Research Foundation (MMRF). We are also pleased to be here with Daniel Verina and Elizabeth Aronson who are both nurse practitioners in multiple myeloma at The Mount Sinai Hospital in New York City.

Brittany Hartman (MMRF): Last year at ONS, there was a big focus on chimeric antigen receptor T-cell (CAR T) therapy for treatment of multiple myeloma. This year, there has been a shift to a lot of talks on bispecifics. Daniel, would you be able to tell us a little bit about what types of patients are eligible for bispecifics and, in general, what is a bispecific antibody for treatment of multiple myeloma?

Daniel Verina, NP: Absolutely. I think where we are sitting right now in myeloma is a great opportunity. I think the bispecifics really fill a nice niche for patients who may not be eligible for CAR T therapy at this point. They are for patients who have had up to four lines of therapy, including a proteasome inhibitor, immunomodulator, and one of the monoclonal antibodies. Most of the time they’ve had four or five lines prior to getting the bispecific treatments themselves. What makes bispecifics so unique is that they contain two different antibodies. One is an antibody that we call a B-cell maturation antigen (BCMA) that’s directed to attach to the myeloma. The other antibody attaches to cluster of differentiation 3 (CD3) on the T cells. Bispecifics target the myeloma cell and stimulates our own immune system to engage and go after myeloma. That’s where they have really revolutionized our new treatment for these patients.

Brittany Hartman (MMRF): Excellent. And can you tell us a little bit about the availability of bispecific antibodies as far as FDA approval?

Daniel Verina, NP: Currently, the one that is available is Tecvayli (teclistamab). There are several others still in clinical trials.

Elizabeth Aronson, NP: Talquetamab and cevostamab.

Daniel Verina, NP: Absolutely. We’re very excited about those agents coming in, but teclistamab is available now and is FDA approved.

Grace Allison (MMRF): Elizabeth, say your patient is selected to receive Tecvayli in the hospital or as an outpatient. Can you explain to us what a patient should expect?

Elizabeth Aronson, NP: Sure. Tecvayli is an off-the-shelf product, unlike CAR T Therapy, which requires manufacturing, bridging chemotherapy, and lymphodepletion chemotherapy.
Tecvayli is available without any of those procedures. It’s manufactured in the lab and it’s available off the shelf. Once it’s been prescribed, it’s really like any other process when giving conventional chemotherapy. We need to get insurance authorization and schedule admission to the hospital. In our center, we give the first dose of Tecvayli in the infusion center. It’s given subcutaneously. Then we use a step-up dosing strategy. We give a low dose to start. After that first dose, the patient is brought into the hospital. That’s considered day one. On day four, we’re going to give a little bit bigger dose and on day seven we’re going to give the final treatment dose. After the final treatment dose, the patient is observed for 48 hours and then they go home from the hospital. Unless they had a terrible reaction during that process, they’re going to be receiving the rest of their doses in the infusion center as a weekly subcutaneous injection and they’ll be going about their life.

There are some unique toxicities that we have to look out for. We’re kind of familiar with them now because they’re similar to what you experience with CAR T therapy. Those are the immune-related adverse events. The first one is called cytokine release syndrome (CRS). It sounds a little bit scary, but essentially it’s inflammation. We’re intentionally revving up the patient’s immune system by using their T cells to kill the myeloma. The byproduct of that process is inflammation. The cardinal sign is a fever, which can range from feeling a little bit like you have the flu to being sick enough that you need to go to the intensive care unit (ICU).

I will say, though, we’ve gotten really good at managing CRS. We have some good treatments available, so it’s pretty rare that patients get that sick, although it can still happen. The treatment for CRS is an intravenous (IV) medication called tocilizumab. Usually, we’re going to be giving that by the time they have a grade two CRS, which means there’s low blood pressure or low oxygen levels along with the fever. If the patient is more frail and has high fevers and the fever isn’t going down with just Tylenol, we may give it even earlier. The way that it works is it blocks and mops up one of those cytokines that’s creating so much inflammation. It’s really effective at controlling that storm without stopping the T cells from doing their work. That’s our go-to medication for CRS. There’s one other immune-related adverse effect that’s important for patients to know about and that’s called immune effector cell-associated neurotoxicity syndrome (ICANS).

This is also related to inflammation, but the inflammation is affecting the brain. It can range from a headache or feeling a little bit sleepy to being in a coma or having a seizure. We really learned how to manage this, so it’s very rare that patients will get the severe case. In most cases, what we’re looking out for is confusion and we’ll be asking the patient a ten-point set of questions called the Immune Effector Cell Encephalopathy (ICE) Score. Things like counting backwards from 100 by 10 and answering different questions. If there’s a change in the ICE Score, that will clue us in early that the brain is a bit inflamed. The first treatment that we would give is seizure prophylaxis, although some institutions start that before you get in there. The gold standard treatment is steroids, so we use a dose of dexamethasone. The CRS and ICANS associated with bispecific antibodies seems to occur at a lower incidence and lower severity than what’s seen with CAR T therapy. In general, it’s very treatable and very well tolerated.

Daniel Verina, NP: Thank you, Elizabeth. That’s absolutely great. It’s true, we’ve gotten

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much better.

Elizabeth Aronson, NP: Isn’t it great to see that patients don’t get as sick as they used to when we first started using these?

Daniel Verina, NP: Absolutely, I do agree. One of the risks is if they tolerate the full therapeutic dose up front, they’re then treated outpatient. It’s important for the outpatient team to monitor the patients for these toxicities because there are delayed CRS effects and ICANS can happen months later.

We also learned about infections from CAR T therapy. Patients are getting BCMA-directed and CAR T directed therapies, but they have profound hypogammaglobulinemia—very low immunoglobulins (IGs), which puts them at high risk for infections. Almost 50% of patients have some type of infection. Some of them can be severe. I’ll be honest, unfortunately, there have been some deaths in patients who have infections. In our institution, and in most others that are giving this therapy, we start the patient on IVIG. We give this to them to protect them on a monthly basis so that they don’t get these infections. Does it protect them 100%? The answer is no. But, more mature age patients are at higher risk. They may not respond as well to an infection. You want to make sure somebody 80 years old doesn’t get pneumonia or some opportunistic diseases. Do you agree?

Elizabeth Aronson, NP: Absolutely. We do have to be careful with this high risk for infections. Something that has come out with the clinical trials is that it’s a cumulative risk. What that means is that your risk is going up as you get more treatment. Over time, patients’ risks for very serious infections, even infections requiring hospitalization, becomes quite high. I think prescreening for hepatitis B, making sure every patient is on viral prophylaxis for prevention of a herpes reactivation, and administration of other medications are important to prevent infection.

All patients on teclistamab should also be getting their annual vaccines. Inactivated vaccines are completely safe for these patients and they should be getting an annual flu vaccine and be up to date on their COVID vaccines. We know they’re not going to respond as well as we would like, but it’s still prudent to get the vaccines.

Brittany Hartman (MMRF): So speaking about vaccines, this is a question that we get a lot as patient navigators from our patients with myeloma. Is there a certain timepoint at which you would recommend giving vaccines?

Elizabeth Aronson, NP: Absolutely. I would avoid getting vaccines or any new significant treatment during the step-up period. While you’re getting the step-up doses and that first full dose, that’s when we’re expecting to see fevers and CRS. If you’ve got a vaccine, which is very well tolerated, muddying up that picture, that can be a problem. Also, you’re getting steroids during that step-up period. I would say after those first three to four weeks, it would be safe. I just wouldn’t get it the same day as you’re getting your teclistamab treatment. But we encourage all our patients to get vaccinated.

Daniel Verina, NP: Elizabeth, brought up a very good point that the risk for infection is
cumulative. It’s different than CAR T therapy, where we use the “one and done” terminology. The patient gets this one therapy and then they’re watched and the infection rate goes down because their immune system builds itself up. They are getting continuous therapy until they have adverse events or unacceptable toxicities, or if they progress. So, there is a slight difference. Even though teclistamab is given weekly, once the patient is stabilized, if we have to give vaccines, there is a window. We have a 28-day period between each dose at full dose. You can hold it an extra week, so they can get their vaccines and then go back to the schedule. So, there is a little bit of a wiggle room to keep them on their vaccine schedules.

Elizabeth Aronson, NP: You make a great point, Daniel. The way we do things in clinical trials and the way a drug is approved is not always the way real-world experience is going to look. The approved maintenance dose for teclistamab is a 1.5 milligram per kilogram subcutaneous dose weekly until disease progression. In the real world, especially for adverse effects or just to get vaccines or for other issues, it’s pretty apparent that you can get good disease control without hitting every single one of those weekly doses. We have held doses and patients remain in a good response even if they miss some of those weekly doses.

Daniel Verina, NP: And they have very good responses, right? The patient population is heavily pretreated, even in the clinical trials. We said more than four lines, but our patients have had seven, eight, ten lines of therapy, and we’re still getting over 65% of patients having a response to teclistamab. That’s impressive. In myeloma, with single-agent drugs, usually response to therapies are about 28% to 30%. But now we’re talking about one therapy that’s giving 63%, 64% overall response, so that’s very good in that market.

Brittany Hartman (MMRF): That’s great. Patients definitely would be excited that it’s a monotherapy because multidrug regimens all come with a different onset of side effects. So this is really exciting for patients.

Elizabeth Aronson, NP: It’s a regimen that is, for the most part, without steroids, because some of our patients have received so much steroids. That’s really taxing on their mental health for a lot of patients. With this regimen, you receive steroids as a premedication in the step-up period, but after that, patients should be able to stop the steroids.

Brittany Hartman (MMRF): Great.

Grace Allison (MMRF): Do they use the steroid as a premedication before they give teclistamab, when they’re giving the step-up dose, for example?

Elizabeth Aronson, NP: Yes, they do. The patient gets dexamethasone, acetaminophen, and diphenhydramine before the subcutaneous dosing because it mitigates CRS.

Grace Allison (MMRF): Right. Daniel, you mentioned IVIG for infection prevention. I know that we’ve heard with patients on CAR T therapy that they’re also on a lot of prophylactic antibiotics and antivirals. Do you see the same usage in bispecifics?
Daniel Verina, NP: I think they're very comparable. We do use a lot of antivirals, like for herpes zoster. Some may also do pneumocystis pneumonia (PCP) prophylaxis. In CAR T, it's usually a minimum of six months until the patient's immunoglobulins reconstitute themselves, so they're on six months of IVIG. When you're talking about therapies that are continuous, these patients may be on IVIG for quite some time and it's usually not given on the same day. Like Elizabeth said, patients shouldn't receive vaccines on the same day that they're getting teclistamab. You might have to work it into their treatment schedule so they're not getting both drugs at the same time.

Elizabeth Aronson, NP: At ONS, I've had the chance to talk to people who are doing this all over the country and institutional protocols vary. That's important for patients to know. If you're talking to someone and they're on a very different infection prevention regimen, it's important that your team is being thoughtful about what is best for that particular patient and how to prevent these infections and manage them.

Daniel Verina, NP: Patients should also tell us when they don't feel well. That's the other part too. They need to be a little bit more forthcoming and very honest in saying that they have the sniffles. Nobody wants to have their nose swabbed again. We may have to hold the drug to reassess, but we have flexibility with teclistamab in that you have 28 days once they're on full dose. If you have to hold therapy for two weeks, significant responses are still observed. Having an infection puts them at risk of hospitalization and sometimes even death.

Elizabeth Aronson, NP: I want to reiterate what you just said because it's probably one of the most important points and it could also save lives. I have had patients come in for a scheduled dose and they didn't tell me that they had a fever for the past week or two because they didn't want to miss their dose. One particular patient's partner was livid that I hadn't received a phone call and that patient ended up septic and in the hospital. It's ok to miss a dose of teclistamab. You will still likely have good disease control. Infections can be life threatening. So, it's absolutely imperative that you seek care quickly, so that we can help because these are treatable infections and we want you to make all the milestones.

Grace Allison (MMRF): If you had somebody who developed a fever in the initial phase, how do you differentiate whether the fever is related to CRS or an infection?

Elizabeth Aronson, NP: Great question. Even though it's a cumulative risk that gets bigger as you go on, that doesn't mean you can't have an infection in the early period. Every patient at first fever is going to get an infection workup alongside their CRS and ICANS treatment. We need to make sure that there aren't two things happening because that will not be a good situation. So, the infection workup is going to happen in tandem with CRS treatment and management.

Daniel Verina, NP: Even in outpatients, because of that delay infection is treated first plus cytokines.
Brittany Hartman (MMRF): Right. We’ve mentioned that Tecvayli is continued weekly. At what point would you consider stopping or changing therapy? Would it ever go on a different schedule? For example, every other week. Could you explain that to us?

Daniel Verina, NP: It’s a good question. It is approved by the FDA to be given weekly. I think changing the schedule is up to the providers and how well the patient is tolerating treatment. Like many therapies, the dosing instructions say to do it on this particular schedule, but you’re also evaluating the patient’s lab work and symptoms. If they are getting frequent infections, we may have to generally modify what we give them even if they’re having a response. So, I think it’s an individual call for each person.

Brittany Hartman (MMRF): Essentially this patient would continue on therapy until they’re at the point of progression and needing to switch therapies?

Daniel Verina, NP: Absolutely. Because in myeloma we always say continuous Therapy, right? We don’t do holidays any more, even though patients want them, or they just leave us and take a holiday anyway. Continuous therapy keeps the disease away, and that’s how the FDA approved teclistamab. It’s been out and approved since February. Within a year from now, who is to say what new data we’ll have because it’s still in clinical trials. Right? Once it’s been approved, that doesn’t mean the trials stop. There are other things that we’re looking at for this therapy.

Brittany Hartman (MMRF): Grace and I have attended plenty of sessions here at ONS over these last few days. The availability of bispecific antibodies and other emerging therapies is really exciting for our patients.

Daniel Verina, NP: We’re excited.

Grace Allison (MMRF): Speaking of that availability, I know that initially the CAR T therapies had slots. That’s how they were made available to the patients. Daniel, are bispecifics on the same set up, or are they more freely available?

Daniel Verina, NP: CAR T has a product manufacturing slot issue. The CAR T cells have to be collected from the patient. Then the therapy has to be manufactured by using a virus to expand the patient’s own CAR T cells. Like Elizabeth said earlier, teclistamab is off-the-shelf. It’s just a matter of getting insurance approval. From an outpatient or even an academic center standpoint, having the bed availability is also a logistic that should be considered. The patient gets a card that says they’re going to be on a bispecific. Once we know that the hospital has an available bed, once the patients get the outpatient therapy they can be admitted into the hospital.

You don’t want to give the outpatient therapy and then the bed isn’t available for the next 48 hours. So, it’s kind of logistical streamlining. I think a lot of the centers in the United States are working on that same process. How can I streamline my patient from outpatient into inpatient? Hopefully, once we get a better understanding of the cytokine storms and CRS, maybe this therapy could be given outpatient for the first two doses and then we can see what happens. So, again, time will tell.
Brittany Hartman (MMRF): We’ve seen that different speakers from different institutions have had different processes. Some will start the first step-up dose in the hospital. Elizabeth, can you tell us approximately how long a patient would anticipate the hospital stay to be, especially during step-up dosing?

Elizabeth Aronson, NP: Typically, a 48-hour observation is required after the dose. Our institution is opting to do that whole hospitalization—get both step-up doses and the full dose, and then discharge the patient 48 hours afterward—because we’re in New York City and it’s not that easy to get in and out.

Brittany Hartman (MMRF): On average, about how long would you say you see most patients for that one hospital stay?

Elizabeth Aronson, NP: That would be a nine-day stay. There have been a few instances where the patient is continuing to have fevers or other reasons why they can’t leave the hospital. If all goes as expected, it’s a nine-day stay to complete the full series.

Brittany Hartman (MMRF): These are questions that Grace and I get when patients call in. They need to know how long they have to be off of work, who will take in the mail and take care of the pets at home, and all of these real-life considerations that our patients are really concerned about. So, it’s good to be well aware of what to expect.

Elizabeth Aronson, NP: Different institutions are probably going to proceed differently depending on their resources. Some may split up those 48-hour observations, let the patient go home for a night, and maybe have them come back the next morning. It’s really important for the patient to ask their treating team about scheduling and logistical issues because they may look different from center to center.

Grace Allison (MMRF): Daniel, we’ve heard about what it’s like as an inpatient to have that initial step-up dose. When a patient is an outpatient, what are we looking out for in terms of side effects?

Daniel Verina, NP: I think they’re exactly the same side effects that we’re looking at for the inpatient. We’re looking for that cytokine storm and ICANS because it can be delayed. Even if the patient tolerated that full dose the first time, the risk is cumulative. The patient could have another side effect even a month later. There are two things that are kind of important. The healthcare team in the inpatient and even in the outpatient setting is quite aware of different symptoms. A lot of times, we may not see the patient every day but nurses do see patients on a daily basis. They watch the patient walk by. They could see if their gait changed. We may not see it because we’re sitting down and they’re already in their chair. That’s something that they’re going to ask the caregivers, “Have you seen any changes?” Are there gait changes or is their hand shaking? One of the great tools that we use, which we learned from CAR T therapy again, is handwriting. Having the patient write the same statement. Ironically, we should be doing that or instruct their caregivers to have the patient write the same sentence even at home. If they start to see something different, have a log to record it, to show their temperature, and their eating habits because we don’t know what changes.
Once they leave us—it’s like having children, right? Once they are out of your house you don’t know what they’re doing, so it’s them reporting back. The same thing with relying on the caregiver. The patient may get insomnia. Are they not sleeping? That could be the step-up dose or the steroids that we give. Some patients still require some type of steroid even in the outpatient setting because they have minimal side effects and we don’t want them to feel uncomfortable. Steroids have many other side effects. The patient could be moody. They can have highs and they can have lows. Is it the steroid that’s causing this, or could it be a mood swing, or inflammation? So, we’re making them fill out the “count by 10”. Mood changes could also be another sign that we’re looking at.

**Elizabeth Aronson, NP:** I will say that 98% of the CRS and ICANS will occur during the step-up period. If a patient presents with a fever after that period, my first thought is infection. In tandem, I want to be considering CRS and ICANS because things happen that aren’t always within the normal range. One thing that is pretty present across the board while on teclistamab is cytopenia, which can be across all cell lines—white count, red count, platelets. There’s quite a degree of variability, so some patients are going to need a dose of Neupogen (filgrastim) now and then and that’s about it. Other patients may need a blood transfusion. These cytopenias seem to be more confined to the earlier cycles and then get better as treatment goes on.

**Grace Allison (MMRF):** Elizabeth, when patients get CAR T they’re often advised not to drive for a certain length of time, usually 30 days. Is that the same advice that they get when they’re on a bispecific?

**Elizabeth Aronson, NP:** Great question. It’s a little bit different for teclistamab. The guidance in the package insert is that patients should not drive or operate heavy machinery for 48 hours after dosing in that step-up dosing period when there is the highest risk for those adverse effects. After that, there is no driving restriction. So, it’s a little bit more liberal.

**Grace Allison (MMRF):** Yes. Thank you.

**Brittany Hartman (MMRF):** I get a lot of patients who call and they’re at a point where they’re anticipating that they’re relapsing, maybe a biochemical relapse where you’re seeing an uptick in the labs. Many times we’re in this space now with myeloma that there are so many options, but that leads patients to come to us with anxiety over “how do I know that I’m making the right choice?” Specifically, a lot of times patients come to us and ask if they can get CAR T or a bispecific, which one should they get? I’d like to hear both of your perspectives. What type of patient would you give CAR T to first over a bispecific? Do you see that patients tend to respond better if they get a CAR T or bispecific prior to the other? Daniel, we’ll start with you.

**Daniel Verina, NP:** That’s a good question. I think it is multifactorial. It’s based on how aggressive that patient’s disease is progressing or growing. There is a manufacturer time that can take from four to eight weeks to get the CAR T cells back. A patient may not have that time because their disease is growing faster. Even when giving them bridging therapy or getting them to collect the cells they may progress too quickly. I would say at that point, your bispecific might be the option because it’s off-the-shelf and you can start the therapy right away. Patients who are slowly biochemically relapsing, but have a little bit more time may be appropriate for CAR T-cell therapy.

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Because it’s “one and done.” We’ve seen very good responses in patients like that.

Also, what does the patient really want themselves? There’s no age limit. That’s something important to know, too, that eligibility for teclistamab or CAR T therapy is not age related. We’ve given CAR T therapy to 80-year-old patients. So, it is not because they’re older, give them teclistamab. What do you think, Elizabeth?

Elizabeth Aronson, NP: I totally agree with all of the points you made, and I have a few to add. I would advise a patient who is slowly or biochemically progressing on teclistamab to get every bit of mileage out of that drug before they switch. I think if you’re nervous about the numbers going up, maybe ask for monitoring a little bit more frequently, but don’t jump ship on a drug that is working for you that you know you can tolerate. One on which you already went through initial side effects and you’re doing well on. Because we know that myeloma is still relapsing, so you want to get every bit of mileage you can out of that drug.

I totally agree with Daniel that there’s no “black and white” answer that older patients should get a bispecific and younger ones should get CAR T. I don’t think that’s clear at all. It’s kind of fitting all the pieces of the puzzle together to say what is right for a patient with myeloma that has relapsed, because each relapse is going to look different and you need to figure out if you have the time to get through bridging and so forth. The response rates are different for each CAR T product. With Cilta-cel (cilta-cabtagene autoleucel; Carvykti) we’re looking at 98%. With Ide-cel (idecabtagene vicleucel), I think it’s around 72%. And with Tecvayli, it’s around 62% or 63%.

That being said, if you’re waiting for CAR T because you want the 98% response, but you’re not going to make it because your disease is progressing, if you’d do well on a bispecific, then take the bispecific. Then maybe the CAR T will be available to you down the line. It’s all very individualized, which makes our jobs interesting and exciting. Patients have to consider a lot of different factors and understand all the weighing that goes into choosing a product.

Daniel Verina, NP: CAR T therapy takes a lot of effort. There’s a lot of upfront testing and monitoring even before the cells get collected. It requires time management. It’s almost time toxicity—the amount of time the patient may have to stay in the institution before they even get their cells collected, then the bridging therapy, and then more testing on top of that. They may not be willing, or they may be living far away— not everybody lives next to your institution.

Grace Allison (MMRF): Elizabeth, based on what we learned at this year’s ONS, is there one key message you’d like our patients to know about bispecific therapy?

Elizabeth Aronson, NP: What patients need to know is that they are in a time in myeloma, and we’ve been saying this for years now, when it’s really exciting. Teclistamab is the first bispecific that’s been approved, but it’s not going to be the only one. There are a lot of other bispecific antibodies in the pipeline that are coming to us pretty soon, and they have different targets and work a little bit differently. I think this is the opportunity to really learn about this drug class, get to know it a little bit. Some of the side effects can sound a scary. They can sound a little bit like science fiction and that can be overwhelming for patients. What I would say to encourage patients is that we are
getting really good at managing them. All treatments have side effects and what’s important is that we’re able to manage them and patients are able to have a good quality of life.

Teclistamab and all the bispecifics that are coming are really going to give new hope to patients who had very limited treatment options with not great response rates. These agents are potentially going to give patients years of life and they have manageable side effects. This is a really great time to start learning about and getting familiar with them. They offer opportunity for patients who maybe wouldn’t be able to get CAR T.

Grace Allison (MMRF): Daniel, anything to add that you learned at this year’s ONS regarding bispecifics?

Daniel Verina, NP: I agree with Elizabeth. We’re in the renaissance period of myeloma. It’s a rebirth of where we stand and teclistamab, other bispecifics, and CAR T have really springboarded us even further to looking at other markers in myeloma and new therapies that treat different mutations. So our patients have a lot coming forward. We’re definitely going to be a generation of new life.

Brittany Hartman (MMRF): Thank you both for being here with us. This is really exciting. Elizabeth and Daniel from Mount Sinai Hospital, we really appreciate you taking the time to give our patients a little bit more insight into the exciting treatment options for myeloma.

Daniel Verina, NP: Thank you. I appreciate it.

Elizabeth Aronson, NP: Thanks for having us.