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MEDICAL EDUCATION



HANDLING THE HARD QUESTIONS:

WHAT OUR MULTIPLE MYELOMA PATIENTS ARE ASKING US ABOUT BISPECIFIC ANTIBODIES

THE PURPOSE OF THIS DOCUMENT

Patients with relapsed or refractory multiple myeloma (RRMM) often ask questions about novel treatment options, including bispecific antibodies (bsAbs). Hematologists/oncologists and other clinicians involved in the management of RRMM must properly and effectively communicate appropriate responses to these questions.

This pocket guide includes a brief summary of evidence surrounding some of the most common—and challenging—questions healthcare providers face involving bsAbs. We hope you find this guide useful for your professional development.

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WHAT OUR MULTIPLE MYELOMA PATIENTS ARE ASKING US ABOUT BISPECIFIC ANTIBODIES

HOW DO I KNOW IF I AM A CANDIDATE FOR USE OF A BISPECIFIC ANTIBODY?

Bispecific antibodies (bsAbs) are a type of immunotherapy that use your own immune system to treat your multiple myeloma. To do this, bsAbs attach to both T-cells and myeloma cells, bringing them close together so that your T-cell is able to kill the myeloma cell **(see Figure 1)**.[1]

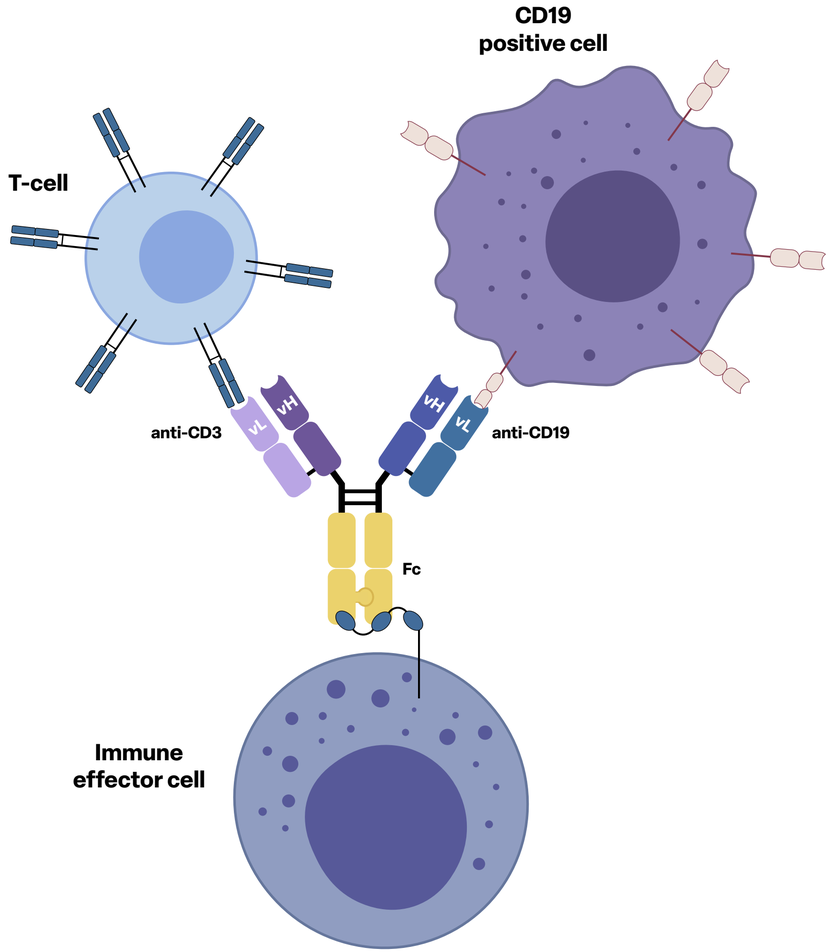


Figure 1 : How Bispecific Antibodies Work[10]

Like CAR T-cells, bispecific antibodies redirect T-cell effector functions towards cells that express target cancer-specific epitopes, but they also retain the Fc receptor, which enables them to induce a broader immune response by other immune effector cells as well. The larger size of bispecific antibodies also makes them less prone to renal excretion, helping patients avoid the need for a continuous infusion.

HOW DO I KNOW IF I AM A CANDIDATE FOR USE OF A BISPECIFIC ANTIBODY?

BsAbs are approved by the U.S. Food and Drug Administration (FDA) for the treatment of relapsed or refractory multiple myeloma (RRMM).[1-4] The type and number of therapies that you have previously received and how your disease responded to those therapies helps to inform us if bsAb treatment is right for you.[5]

The bsAbs currently approved by the FDA (as of March 2025) require that you have had at least 4 prior lines of therapy and have received 3 other classes of drugs before receiving treatment. These drug classes include proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies.[2-4] As long as you have received those treatments, there are no other contraindications to use of a bsAb. Even if you are elderly or have comorbidities, you may still be considered for treatment with a bsAb. Age alone is not a determinant of eligibility, and patients with RRMM in their 80s have received treatment with bsAbs.[1,5-9]

Our team will carefully look at your unique circumstances, including your organ function, prior therapies, home situation, and overall quality of life to determine if you are a suitable candidate for a bsAb.[1,5,6] This decision will be made collaboratively, taking into account your preferences and treatment goals. Our team will discuss the potential benefits and risks of a bsAb with you, and we will work together to develop a plan that aligns with your specific needs and circumstances.

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ARE THERE ANY SCREENING TESTS I'LL NEED TO TAKE BEFORE BEING CONSIDERED FOR USE OF A BISPECIFIC ANTIBODY?

While there are no specific screening tests to determine eligibility for bsAb therapy, there are several factors that will be considered. These include the therapies you have had in the past, your current disease status, other health conditions such diabetes or high blood pressure, your performance status, and your organ function.[1-4]

Therefore, tests designed to give a picture of your overall health and disease status will be conducted. These include blood tests to evaluate your general blood cell counts, immune system function, and liver and kidney function. Other tests may include evaluation of potential infections since bsAbs can weaken the immune system and reactivate dormant infections, as well as measurement of immunoglobulin levels, imaging studies, and cardiac tests.[1,5]

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WHAT ARE THE DIFFERENCES BETWEEN THE CURRENTLY APPROVED BISPECIFIC ANTIBODIES?

As of March 2025, there are 3 bsAbs that are FDA-approved for the treatment of RRMM: elranatamab, teclistamab, and talquetamab **(see Table 1)**. Elranatamab and teclistamab target a protein found on the outside of myeloma cells called B-cell maturation antigen, or BCMA. Talquetamab targets a protein called G protein-coupled receptor, class C, group 5, member D (GPRC5D).[1-4] All three bsAbs are administered subcutaneously, but there is some variability between the dose and dose schedule of each agent.

Table 1: Targets and Administration Route for Bispecific Antibodies Approved for the Treatment of RRMM

Bispecific Antibody	Target on T-cell	Target on Myeloma Cell	Administration route
Elranatamab	CD3	BCMA	Subcutaneous injection
Teclistamab	CD3	BCMA	Subcutaneous injection
Talquetamab	CD3	GPRC5D	Subcutaneous injection

WHAT ARE THE DIFFERENCES BETWEEN THE CURRENTLY APPROVED BISPECIFIC ANTIBODIES?

BsAbs require a “step-up” dosing phase. This involves a gradual increase in the dose, eventually leading to full-treatment dose. This is necessary to reduce the risk of certain side effects involving the immune system. The dosing schedules of elranatamab, teclistamab, and talquetamab, including the step-up phase, are included in Table 2.[1-5] Currently, bsAbs are used to treat multiple myeloma patients who have received at least four lines of previous therapy. The optimal sequencing of bsAbs with other therapies is an area of ongoing study. Various factors influence sequencing decisions, including disease factors, current fitness/frailty, and treatment availability.[1,5]

Compared with bsAbs, chimeric antigen receptor (CAR) T-cell therapies have indications in the earlier-relapse setting of multiple myeloma.[1-4,6,7] There is some evidence that suggests CAR T-cell therapy may be more effective when administered before treatment with a bsAb, particularly BCMA-targeted therapies such as elranatamab and teclistamab. This is because prior exposure to other treatments that target BCMA may reduce the potential efficacy of CAR T-cells; however, more research is needed to determine this definitively.[5] Ultimately, the decision to sequence bsAbs and other agents such as CAR T-cell therapy should be individualized based on personal factors and your disease characteristics.

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Table 2: Dosing Schedules for Bispecific Antibodies Approved for the Treatment of RRMM

Bispecific Antibody	Phase		Day	Dose
Elranatamab	**Step-up**	Step-up dose 1	1	12 mg
		Step-up dose 2	4	32 mg
		1st treatment dose	8	76 mg
	Weekly treatment	1-wk after 1st treatment dose and weekly after		76 mg
	Biweekly treatment	Wk 25 and every 2 wks after		76 mg
Teclistamab	**Step-up**	Step-up dose 1	1	0.06 mg/kg
		Step-up dose 2	4	0.3 mg/kg
		1st treatment dose	7	1.5 mg/kg
	Weekly treatment	1-wk after 1st treatment dose and weekly after		1.5 mg/kg
	Biweekly treatment	If ≥CR for ≥6 mo, frequency may be decreased to every 2 wks		1.5 mg/kg
Talquetamab *(Weekly dosing schedule)*	**Step-up**	Step-up dose 1	1	0.01 mg/kg
		Step-up dose 2	4	0.06 mg/kg
		First treatment dose	7	0.4 mg/kg
	Weekly treatment	1-wk after 1st treatment dose and weekly after		0.4 mg/kg
Talquetamab *(Biweekly dosing schedule)*	**Step-up**	Step-up dose 1	1	0.01 mg/kg
		Step-up dose 2	4	0.06 mg/kg
		Step-up dose 3	7	0.4 mg/kg
		First treatment dose	10	0.8 mg/kg
	Biweekly treatment	2-wks after 1st treatment dose and every 2 wks after		0.8 mg/kg

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HOW WORRIED SHOULD I BE ABOUT AN INFECTION? IS THERE ANYTHING I CAN DO BEFORE STARTING ON A BISPECIFIC ANTIBODY TO HELP PREVENT AN INFECTION?

When you are undergoing treatment with a bsAb, you are at increased risk of infection.[1-4] While bsAbs are designed to activate certain immune cells and target cancer cells, they can also suppress other parts of the immune system, which may increase the risk of bacterial, viral, and fungal infections.[5,6]

One effective strategy to reduce infection risk is the use of monthly **intravenous immunoglobulin** (IVIG) replacement therapy. IVIG infusions help restore antibody levels, which are critical for fighting infections, especially respiratory infections. This is particularly important for patients who experience low levels of antibodies as a result of bsAb therapy. Multiple studies have shown that utilization of IVIG among patients treated with a bsAb results in a significant decrease in the incidence of infection severity.[5-8]

Other prophylactic medications can also help prevent infections. These may include **antiviral drugs** to prevent shingles, **antibiotics** to guard against bacterial infections, and, in some cases, **antifungal medications**. The exact recommended medications will be tailored to your specific health and disease needs.[5-7]

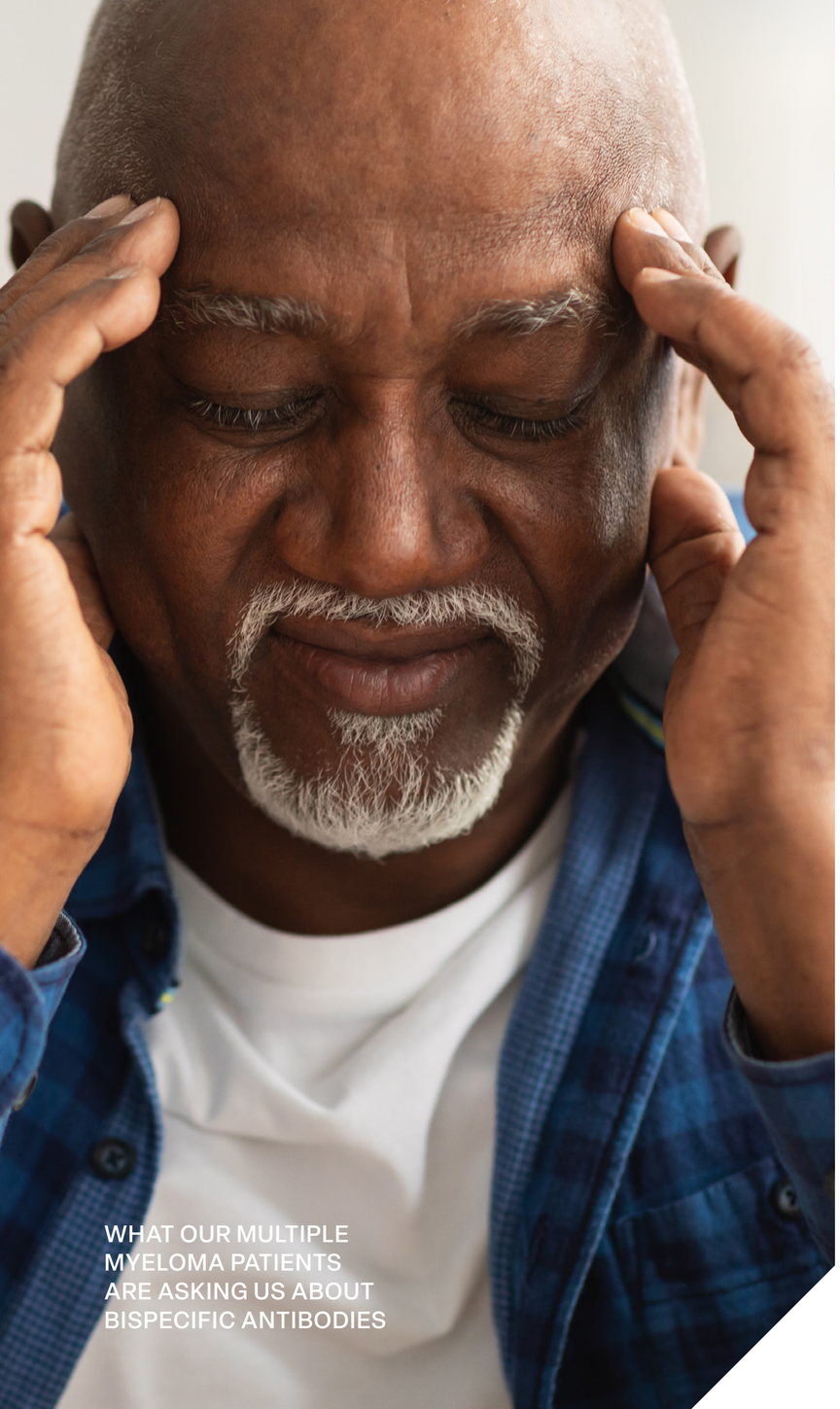
Vaccinations also play a vital role in the prevention of infection and are especially important when you are being treated with a bsAb. We want to make sure you are up to date on routine vaccinations, including the annual flu vaccine, pneumococcal vaccine, respiratory syncytial virus, and COVID- 19 vaccine with appropriate boosters. If possible, you should try to complete your needed vaccines before beginning treatment with a bsAb as vaccines may be less effective when you are undergoing active treatment.[5-7]

HOW WORRIED SHOULD I BE ABOUT AN INFECTION? IS THERE ANYTHING I CAN DO BEFORE STARTING ON A BISPECIFIC ANTIBODY TO HELP PREVENT AN INFECTION?

We will also regularly monitor your blood counts and other laboratory parameters to identify any signs of immunosuppression or infection so we can provide prompt intervention as needed. If you develop symptoms such as fever, cough, or unusual fatigue, we want to know right away since early intervention can prevent more severe complications.[5-7]

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WHAT ARE SOME OF THE OTHER COMMON SIDE EFFECTS RELATED TO USE OF A BISPECIFIC ANTIBODY?

Like all treatments for cancer, bsAb treatment will cause side effects. One of the most common side effects is cytokine release syndrome (CRS).[1-5] This occurs when the immune system becomes overly activated. CRS can develop with all of the available bsAbs and can vary in severity. CRS generally develops during the step-up dosing phase of bsAb treatment.[1-5] Its symptoms include fever, low blood pressure, and difficulty breathing. CRS is typically managed through administration of a drug called tocilizumab, and, in some cases, corticosteroids. The management course will depend on the severity of the reaction.[6] At some healthcare centers, tocilizumab is given prophylactically prior to initiation of a bsAb. Our team will closely monitor you during treatment to promptly address any signs of CRS.

Neurologic complications can also occur with bsAb treatment, although the incidence is less than CRS and cases are generally mild.[2-5] Symptoms may include headache, confusion, and difficulty concentrating. In more severe instances, delirium and seizures can occur. Peripheral neuropathy is also possible, especially if you have a history of this issue. Management of bsAb-related neurologic toxicity includes supportive care measures and corticosteroids. In some cases, anti-seizure medications may be prescribed.[1,6]

When undergoing treatment with a bsAb, you may experience low blood counts, sometimes referred to as cytopenias. These include neutropenia (low levels of neutrophils), thrombocytopenia (low platelet levels), and anemia (low levels of

WHAT ARE SOME OF THE OTHER COMMON SIDE EFFECTS RELATED TO USE OF A BISPECIFIC ANTIBODY?

healthy red blood cells).[2-5] We will monitor your blood counts regularly and provide supportive care as needed. In some cases, we may recommend delaying your next dose to allow your cells time to recover.[6]

Agents such as talquetamab that target GPRC5D are associated with a set of side effects distinct from BCMA-targeted bsAbs.[7,8] When undergoing treatment with talquetamab, you may experience rash, dry skin, itching, and redness, as well as swelling, nail peeling/splitting, and tenderness or pain in the palms of the hands and soles of your feet.[6-8] We recommend keeping your skin clean, dry, and well moisturized. Using emollients and sunscreen can also help prevent skin toxicity. Rash occurring with your first talquetamab cycle or treatment is generally managed with topical corticosteroids. Heavy creams and topical ammonium lactate creams can help to prevent or manage foot and hand peeling. Nail soaks, topical moisturizers, and topical corticosteroids can help with nail issues. We may ask you to work with a dermatologist if your issues become serious.[6-8]

Potential oral symptoms associated with talquetamab include changes in taste, trouble swallowing or feeling like food gets stuck when you eat or drink, and dry mouth. To mitigate and manage these issues, we recommend increasing your hydration, oral rinses, saliva substitutes, and gum.

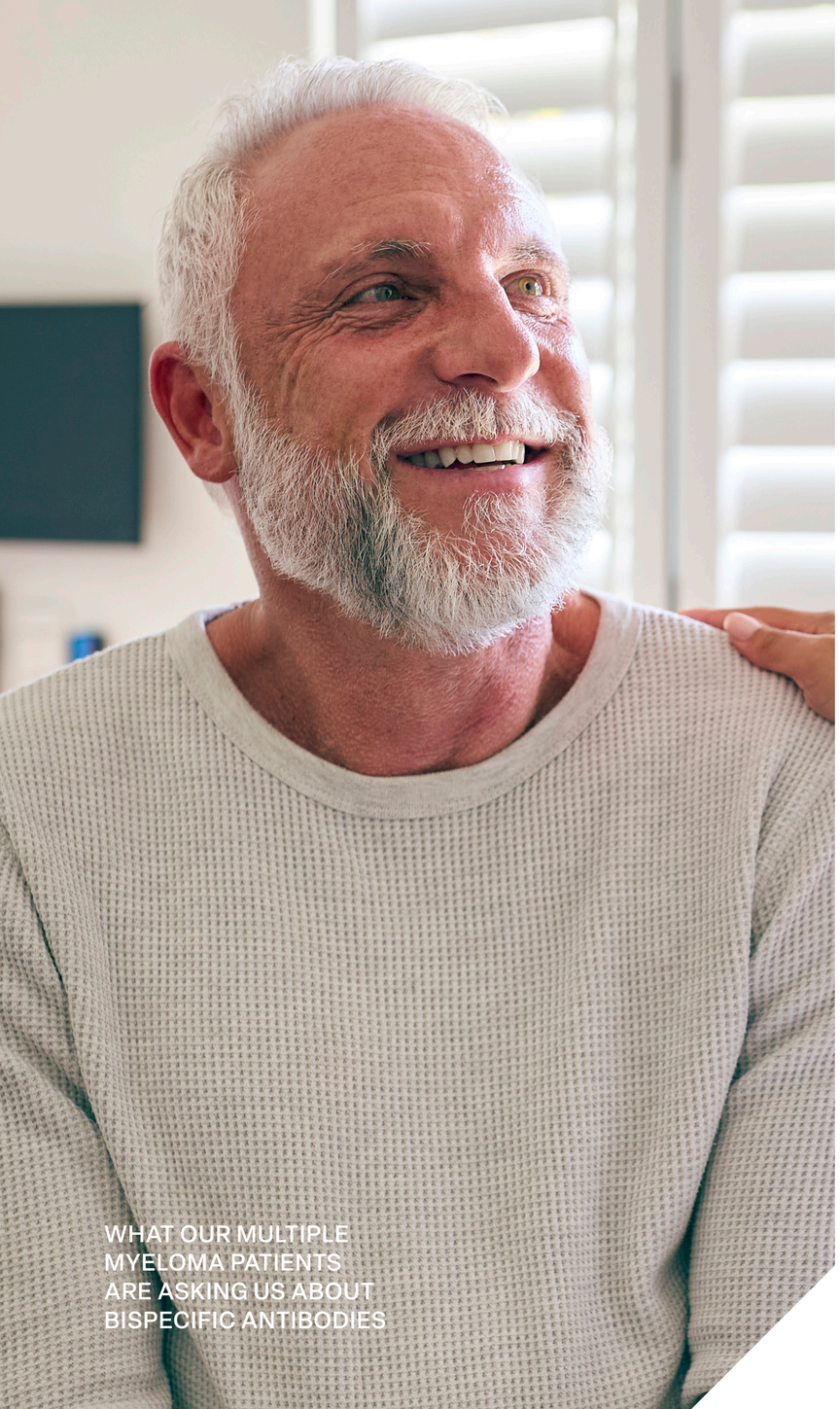
While these side effects may sound scary, rest assured that our team will do our best to lessen their impact on your quality of life and help you stay on treatment. If your symptoms become severe, we may withhold therapy and/or adjust the dose or schedule of your medication.[6-8]

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HOW LONG WILL IT TAKE UNTIL I START FEELING BETTER ON A BISPECIFIC ANTIBODY? HOW LONG IS MY RESPONSE GOING TO LAST?

While it is not possible to predict with certainty, many multiple myeloma patients begin to see improvements in their symptoms after the second full dose of bsAb therapy. The exact timeline will vary depending on disease and individual factors. In clinical trials, the time to response after initiation of bsAB therapy ranged from weeks to several months. Factors that may influence the timing of response include disease characteristics, disease burden, and your prior treatments.[1-6] Our team will work with you to set realistic expectations and closely monitor your progress.

The duration of response to bsAb therapy also varies from one individual to the next. In clinical trials, the duration of responses ranged from a few months to several years.[1-6] The duration of your response will depend on a number of things, including the type of response you have (sometimes referred to as the depth of response), your specific disease characteristics, your prior treatments, your overall health status, and how well you tolerate the treatment.[1-7]

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AM I GOING TO NEED TO BE HOSPITALIZED TO RECEIVE A BISPECIFIC ANTIBODY?

Whether or not hospitalization is required, as well as the potential duration of hospitalization associated with bsAb administration, depends on several factors, including which agent is being used, the burden of your disease, your overall health, and the healthcare center's protocols. The current prescribing information for elranatamab, teclistamab, and talquetamab recommend hospitalization for 24-48 hours after each dose (depending on the drug) during the step-up dosing phase to aid in early recognition and management of CRS.[1-3] However, many institutions have developed or are developing systems that support administration in an outpatient clinic.

That said, some patients, such as those with advanced age, significant comorbidities, or high disease burden, may still need to be hospitalized after each dose during the step-up phase so they can be closely observed.[5]

We will work with you to determine the best plan that takes into account your safety and comfort. Whether or not you receive your initial treatments in the hospital or in an outpatient clinic, we will spend a lot of time discussing potential side effects and what you and your caregivers will need to do should they occur.

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IF I FAIL TO RESPOND TO ONE BISPECIFIC ANTIBODY, WHAT COMES NEXT?

There are some patients who do not respond to their bsAb, and others where the bsAb stops working.[1-4] If this happens, we will run a variety of tests to evaluate the status of your disease and work with you to select your next therapy. Factors that influence which subsequent treatment we might select depend on your preferences, comorbidities, disease status, prior treatments, and tolerability to prior therapies.[5]

Your next treatment option might include a different bsAb. For example, if you received a BCMA-targeted bsAb, we might recommend a GPRC5D-targeted bsAb as an option. Other options, such as CAR T-cell therapy, may be considered if you have not already undergone the treatment. Combination therapy is also an option. Finally, there are a variety of clinical trials enrolling patients that are investigating novel therapies – we can help provide you with options if that is something that interests you.[5,6]

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