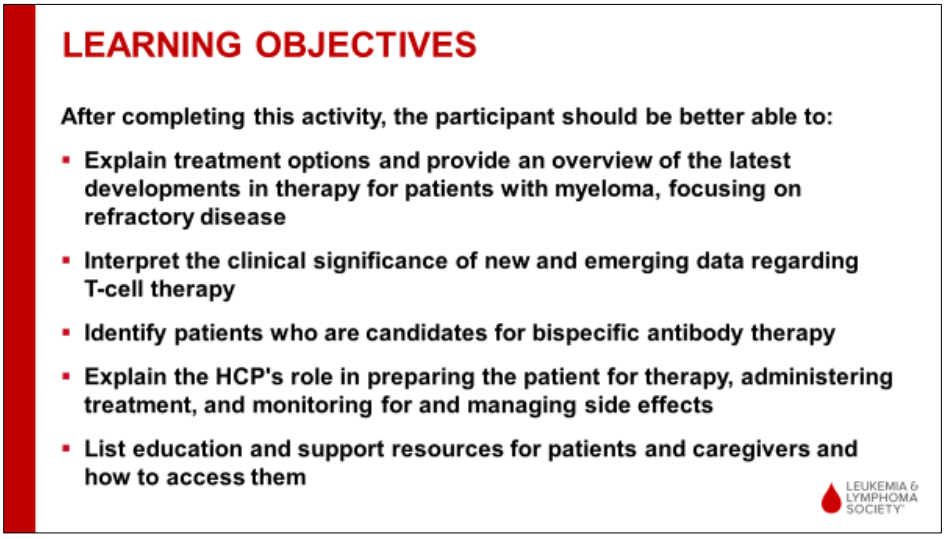
WELCOME AND INTRODUCTION

Lesley Hoerst, BSN, RN

Welcome. On behalf of The Leukemia & Lymphoma Society (LLS), thank you for joining us for "Treating Multiple Myeloma with T-cell Directed Therapy: Bispecific Antibodies." We would like to thank Janssen Oncology for their support of this webinar. LLS is committed to improving patients' quality of life through healthcare professional education, patient education, and support resources. LLS advocates for funding to accelerate the discovery and development of blood cancer therapies. Over the past 70 plus years, LLS has invested more than $1.6 billion in cutting-edge research funding nearly all of today's most promising advances. This webinar will provide the opportunity for HCPs (healthcare providers) to build their knowledge on treating multiple myeloma with T-cell-directed therapy and management of patients receiving active treatment, including monitoring for and managing side effects, and the role of the healthcare team members when treating these patients. It will include information about approved therapies and those in clinical trials. A review of resources

can be provided to your patients, as well as additional education resources for you will also be provided.

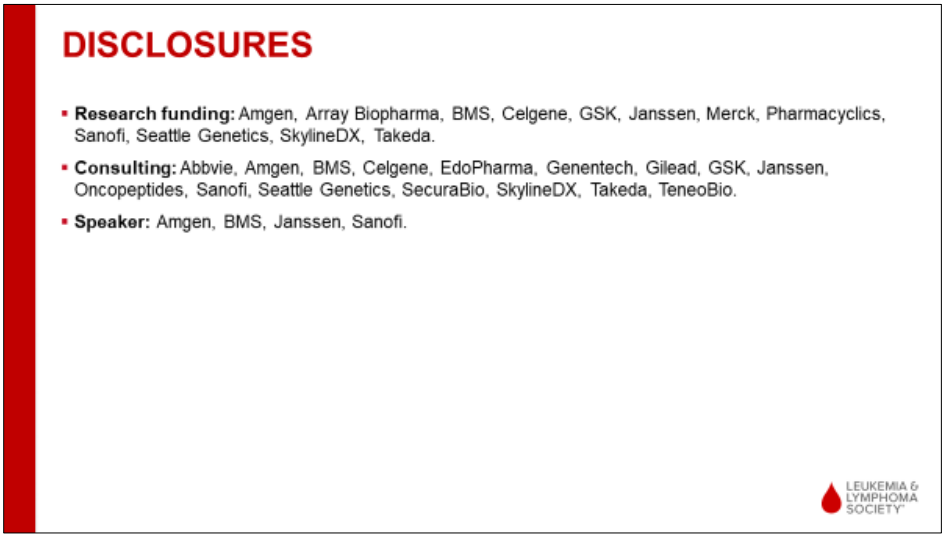
Please note continuing education (CE) credits are not being offered for this program.



The learning objectives for today's program are listed on this slide.

I am honored to introduce our speaker today. Saad Usmani is a hematologist/oncologist as well as the Chief of the Myeloma Service at Memorial Sloan Kettering Cancer Center in New York. Thank you for sharing your time and expertise with us.

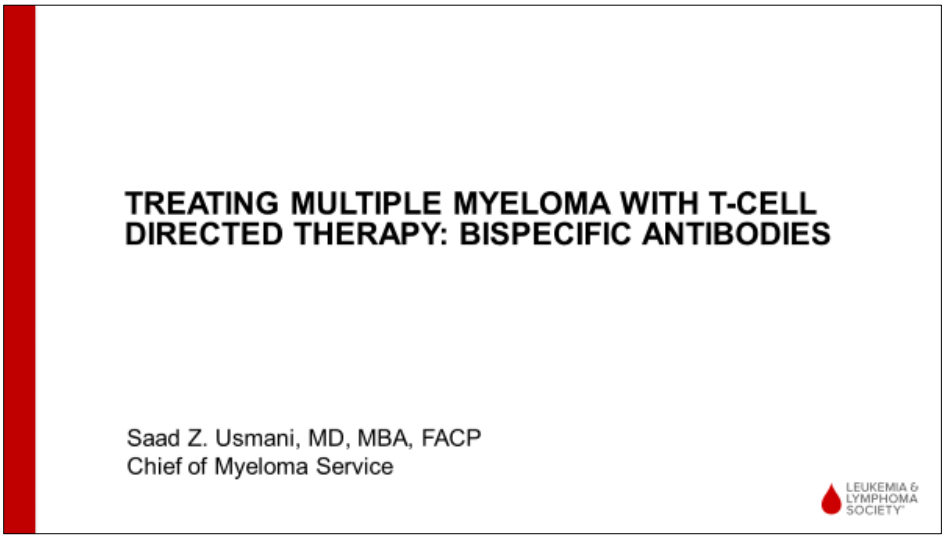
Following his presentation, I will share information about resources from The Leukemia & Lymphoma Society.



Faculty disclosures are listed here. We encourage you to submit questions to the presenter as you are listening today. Please type your question in the Ask a Question box under the speaker video window. We will answer them later in the program.

Also, please be sure to complete the evaluation at the end of this program. Your feedback is important to us to help plan future programs.

PRESENTATION

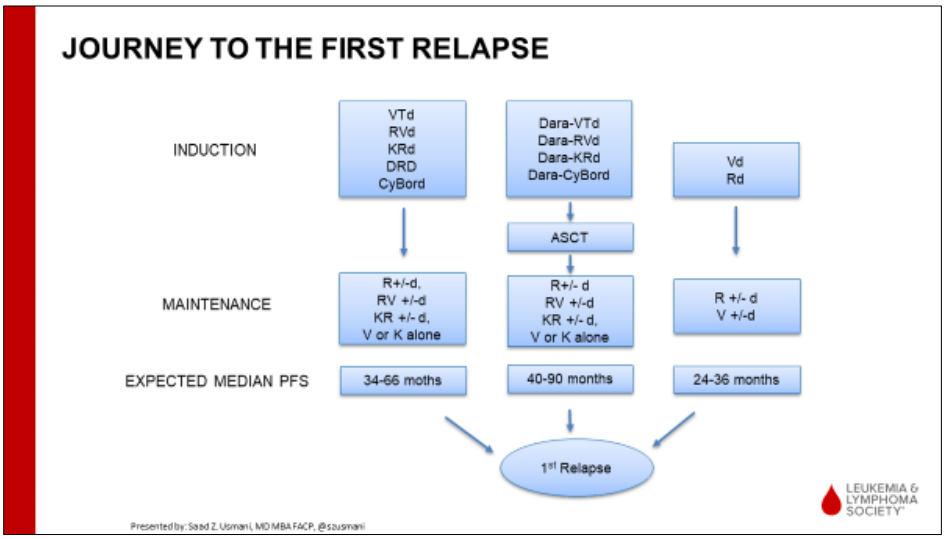


Lesley Hoerst, BSN, RN

Dr. Usmani, it is now my pleasure to turn the program over to you.

Saad Z. Usmani, MD, MBA, FACP

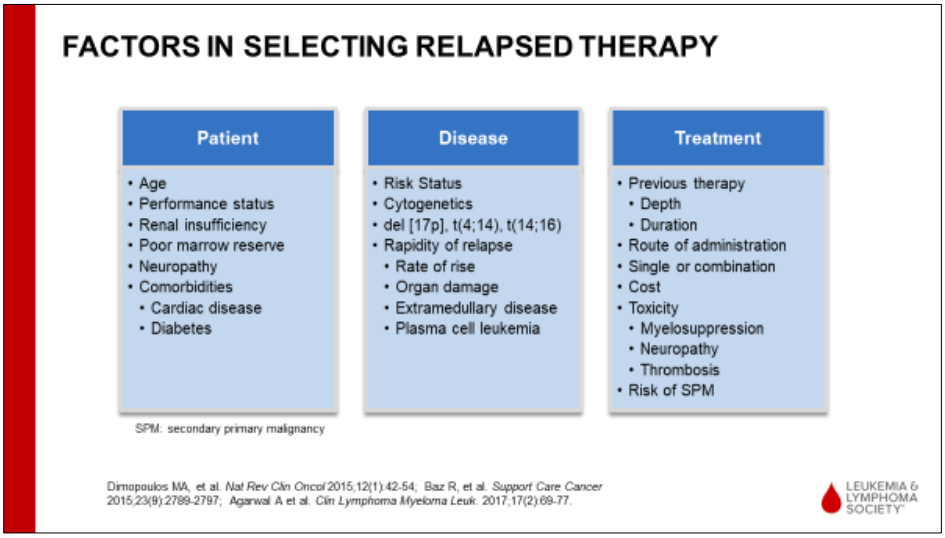
Thank you so much for the kind introduction and thank you to all attendees who've joined this webinar. It is my privilege to speak on this forum, and I'll be focusing my talk on bispecific antibodies in multiple myeloma and really trying to share not just existing data but where potentially the field may be heading in the coming years.



So, as we think about multiple myeloma and the treatment landscape, we have come quite a long way in the past 15 years. The majority of patients in the United States (U.S.) are getting either a three- or a four-drug combination as part of their initial induction therapy before being considered for an autologous stem cell transplant and then going on to maintenance. And this schema of treatment induction with or without transplant followed by maintenance is typically what we follow. I think there are some nuances to whether certain high-risk patients may receive, as part of their initial therapy or maintenance, certain drugs preferentially, but, in general, that's kind of the schema.

And then we don't have as much two-drug use in the U.S., but the reason why I shared this on the slide is there are certain parts of the world where because of access two-drug combinations are still utilized and sometimes very old, frail patients may get two-drug combinations as well.

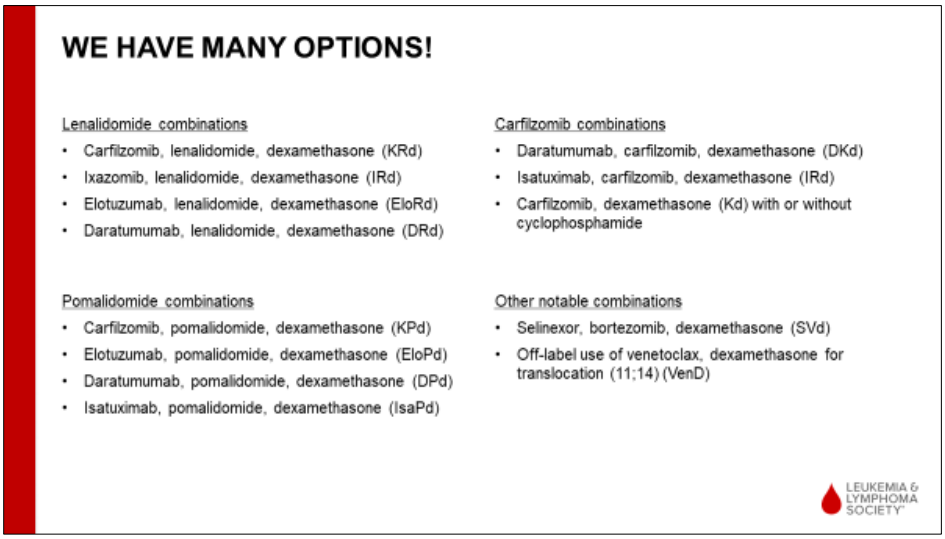
So, depending on the disease biology and the treatments patients get, the median expected progression-free survival can be variable from one patient to the other; and so that journey to first relapse is different for patients. And this is why when we are managing relapsed disease, we are paying attention to patient-specific factors, disease-specific factors, as well as treatment-specific factors.



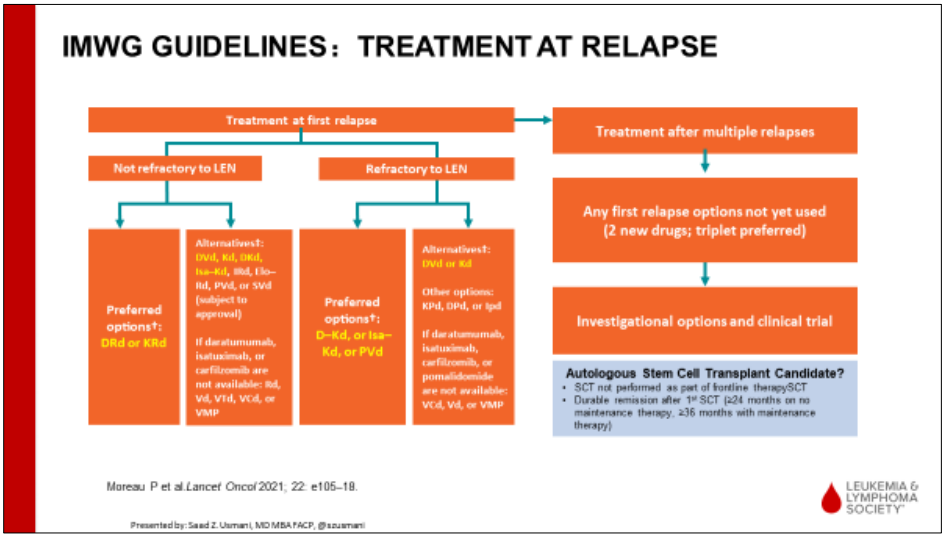
So, from the patient's perspective, their age, performance status, comorbidities, organ reserve are all very important. From a disease perspective, how the relapse is happening, whether it's fast high burden or is it slow biochemical relapse? Is the patient high risk or have they started to develop high-risk features; clinical phenotypes such as circulating plasma cells or extramedullary disease? And then in terms of previous treatments received, what was the depth and duration of response? Was it combination treatment? Were there any side effects related to it? Were there any logistic challenges that the patient may have in coming to the cancer center making the choice between an oral or less frequent-dose parenteral treatment, you know, a preference? We pay attention to all of those different things.

And my question here, as I talk about patient treatment disease-specific factors and logistic issues, you can think about the following: Which factor is not as important in selecting relapsed therapy? Is it (A) caregiver support, (B) performance status, (C) cytogenetics, or (D) previous therapies? Please feel free to pick an answer and then I'll wait for all of you to respond and then share what that answer looks like.

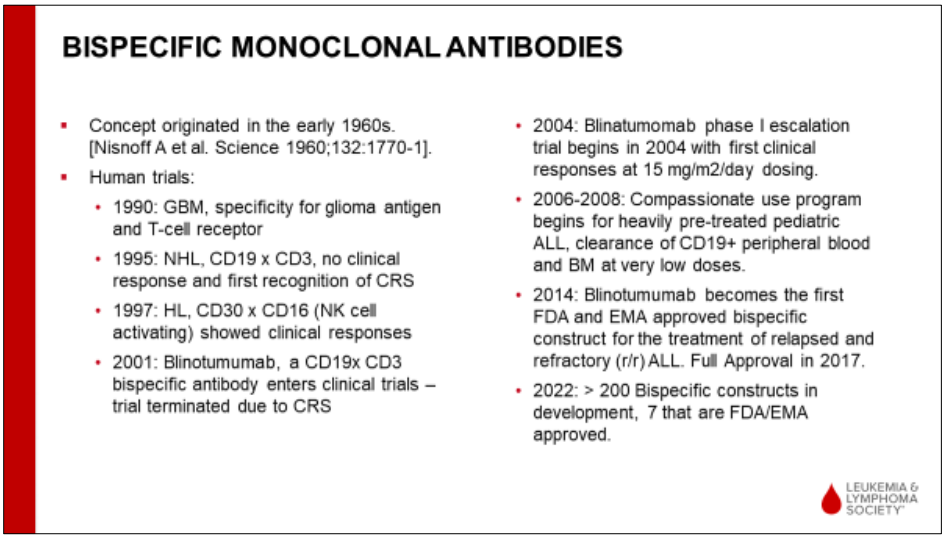
All right, so the correct answer here would be choice A as we're thinking about the various factors. Important but all of these factors are important, but this was simply a question around what is the more important factors, certainly.



The good news is we have many options for patients when the patients do have a disease relapse. We have patients who can potentially get lenalidomide (Revlimid®)-based combinations. Lenalidomide-based combinations are applicable to patients who have been off of lenalidomide. Sorry. Lenalidomide combinations are applicable to patients who have been off of lenalidomide maintenance for a while either because they were on a drug holiday, or their disease was in good control and the physicians felt that they need to be off of treatment for a little while. But many patients that we treat today in the United States are on len-maintenance. And if they are progressing, then typically we would think about, carfilzomib (Kyprolis®) or pomalidomide (Pomalyst®)-based options for those patients. And then in certain instances selinexor (Xpovio®)-based triplet with bortezomib (Velcade®) and dexamethasone (Decadron®) has been utilized. And then venetoclax (Venclexta®) with dexamethasone – it's an off-label use of this therapy for translocation (11;14) – sometimes we can get insurance approvals to use that therapy for patients. So, there are many options and, you know, that exposure or refractoriness to lenalidomide is an important step in determining what kind of options we can use for the patients who are in their first relapse.



But as patients get into subsequent relapses, we try to pick options that they have not used before, at least one or two new drugs that have not been part of the previous treatment. And, certainly, we pay attention to those drugs having had good activity. We always prefer patients to go on clinical trials if they're available, especially with the novel immunotherapies that are not currently available for earlier lines of treatment. And then if patients had a stem cell transplant and got good benefit from it on the first go around, we can use this as a second transplant. Or if someone decided not to have their stem cell transplant early on but if someone did not have a stem cell transplant as part of their initial therapy but collected stem cells, they can get the stem cell transplant as part of their therapy at the time of relapse. So, it's important to keep that option available for our patients as well.

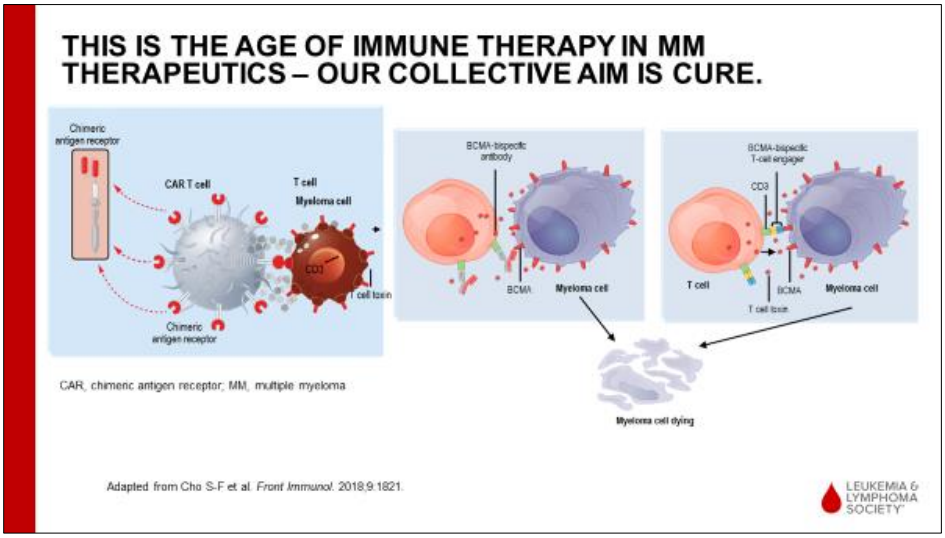


Now I'm going to turn my focus on the bispecific monoclonal antibodies. And this is not a new idea. The concept of bispecific monoclonal antibodies came about back in the early 1960s where the idea was to see if we can get antibodies to target cancer cells as well as the patient's immune cell. But it took a while to get this idea up and off the ground in human trials. Back in 1990 with GBM,

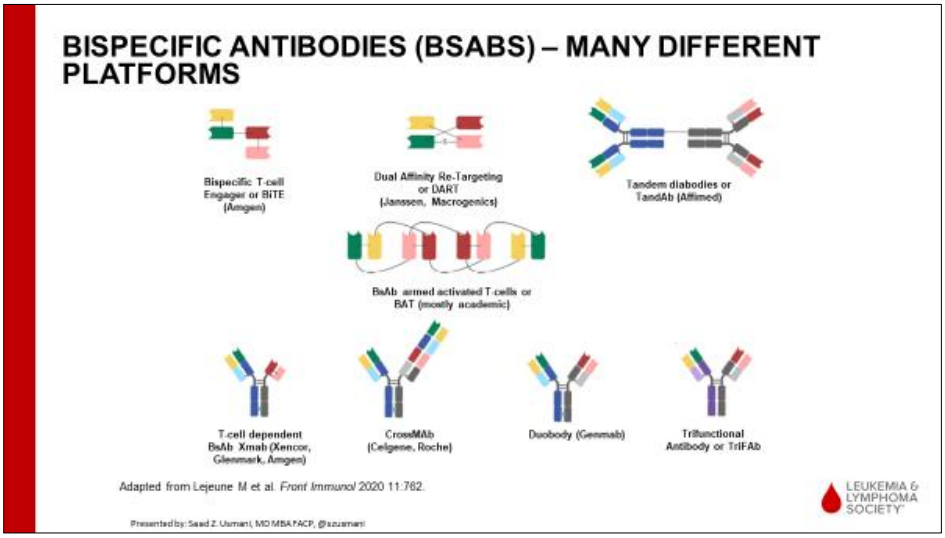
(glioblastoma multiforme), glioblastoma was one of the difficult-to-treat malignancies; there was early use of this technology there, but we did not have appreciable results.

Then in 1995 in non-Hodgkin lymphoma, there were CD19 (cluster of differentiation 19) bispecific antibody but there was no clinical response to that approach, but there was a first recognition of cytokine release syndrome (CRS). Then there was a study with Hodgkin disease or Hodgkin lymphoma where CD30 was targeted along with NK (natural killer) cell activation. So, there was some clinical responses, but, again, the technology was fairly early.

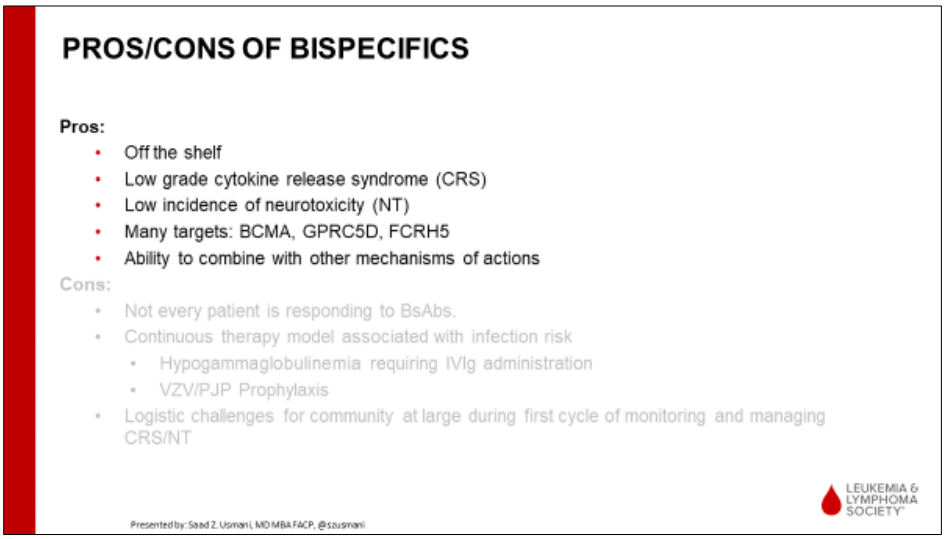
Then came the early experience with blinatumomab (Blincyto®), which is a CD19-directed bispecific entering clinical trials, but then there were serious concerns about cytokine release syndrome and the trials were terminated. But then, again, in 2004, there was a dose phase 1 escalation study with blinatumomab that began in 2004, and there were some early responses in that initial experience in more advanced pretreated pediatric ALL (acute lymphocytic leukemia). That's where the compassionate use program began showing good activity, and that really turned the tide in favor of this particular bispecific eventually getting accelerated and then full approval for relapsed/refractory ALL. And that really started the whole bispecific antibody revolution. And there are so many different constructs in clinical trials and in development, and I'm going to be focusing on myeloma here.



So, this is truly the age of immune therapy in myeloma therapeutics, and we are aiming now, you know, we are confident that we can think about curative strategies by incorporating immune therapies. We still have to prove this point, but there is a lot of conversation amongst the myeloma research community that this may be a possibility as we're ushering in this era of immune therapies into myeloma.



So, bispecific antibodies in myeloma have many different platforms and constructs, and this really depends on the structure of the antibody whether it's part – small components of the antibody that are put together or the whole antibody is modified in different ways to identify one part identifying the cancer cell and the other part identifying the immune cell, in this case for the most part being the T-cell.



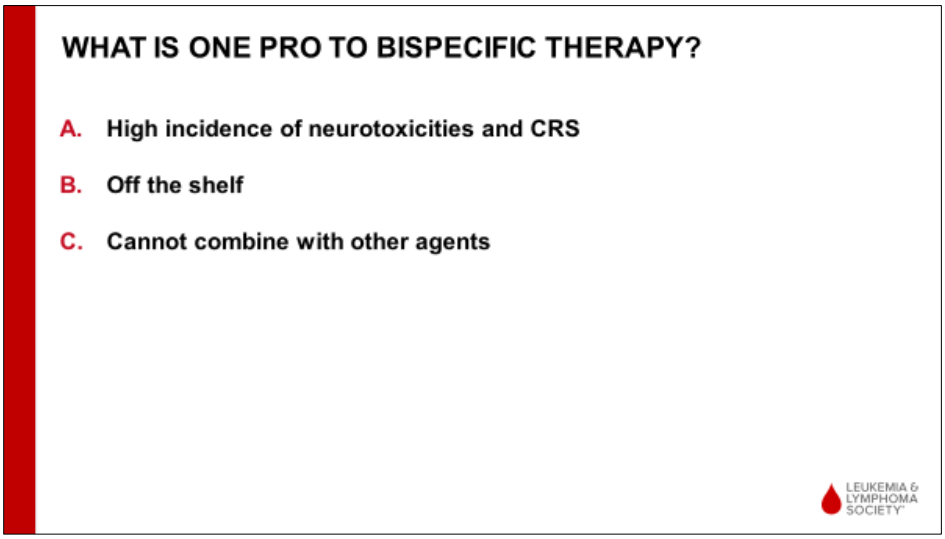
So, I'm going to share with you the pros and cons of bispecifics in myeloma and then really talk about some of the clinical data with the bispecifics that we have.

So, starting off, the big advantage of bispecifics is that they're off-the-shelf treatment. If available, you can start these treatments very quickly within a week or 10 days of figuring out the patient may be eligible for that therapy.

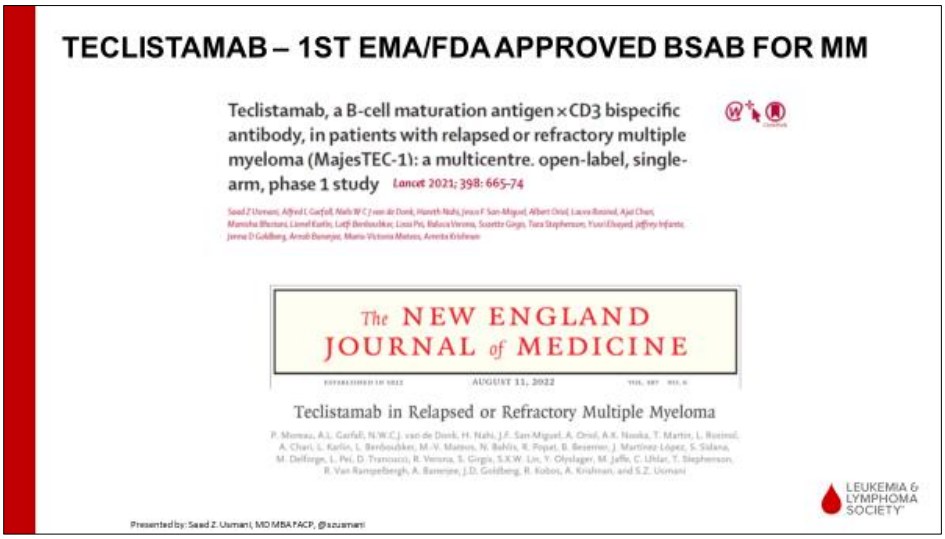
Then in terms of the cytokine release syndrome, when it happens, it happens at a low grade and it's very manageable. It only happens within the first two/three doses of treatment and then it doesn't

happen again. And then, unlike CAR (chimeric antigen receptor) T-cell therapies, the incidence of neurologic side effects during that early phase is not something that we see commonly.

And then with bispecifics we have a lot of data with B-cell maturation antigen, but there are other targets like GPRC5D (G protein-coupled receptor, class C group 5 member D) on the myeloma cells and FcRH (Fc receptor homolog) where bispecifics are being utilized, and then we can combine the bispecifics with other mechanisms of action and use those combinations together for patients. So, I think that's another big advantage of these therapies.

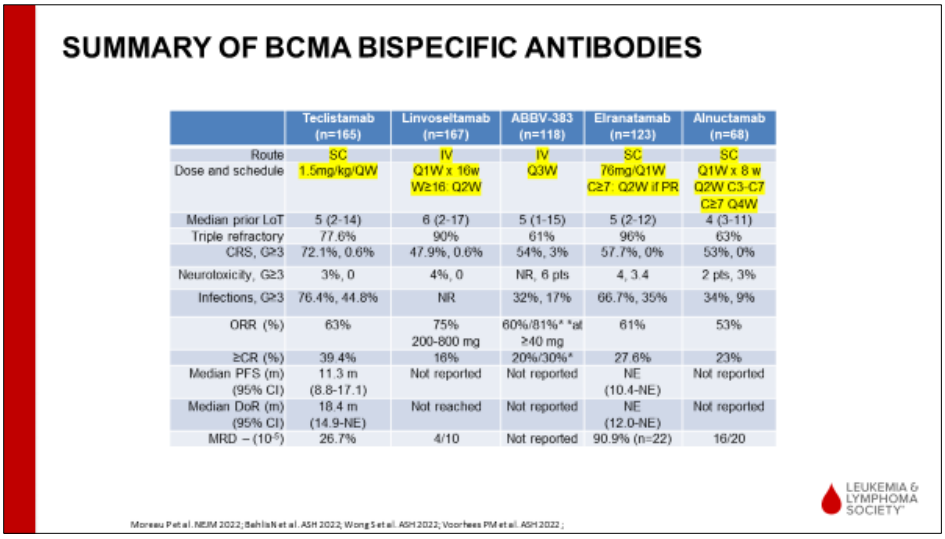


So, before I go any further, this is another question. So, what is one pro to bispecific therapy? Is it high incidence of neurotoxicities and CRS, is it being off the shelf or is it (C) cannot combine with other agents? All right, so the correct answer is (B) being off the shelf as an option.



So, with that let me just move on to that great story about teclistamab (Tecvayli®) being the first EMA/FDA (European Medicines Agency/U.S. Food & Drug Administration) approved bispecific

antibody for myeloma. And I had the privilege of helping its clinical development. And the great news is that teclistamab isn't alone in this area. We have many different bispecific antibodies now.

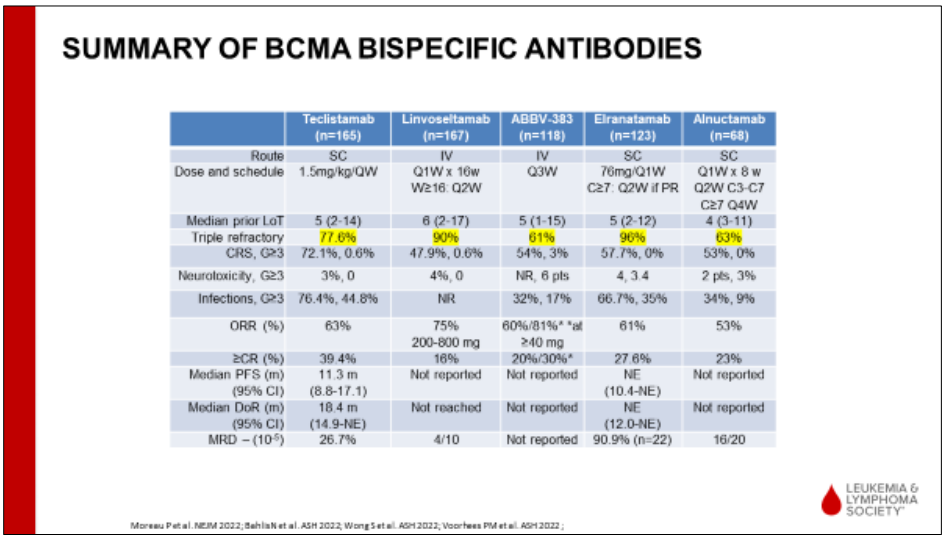


	Teclistamab (n=165)	Linvoseltamab (n=167)	ABBV-383 (n=118)	Elranatamab (n=123)	Alnuctamab (n=68)
Route	SC	IV	IV	SC	SC
Dose and schedule	1.5mg/kg/QW	Q1W x 16w W≥16: Q2W	Q3W	76mg/Q1W C≥7: Q2W if PR	Q1W x 8 w Q2W C3-C7 C≥7 Q4W
Median prior LoT	5 (2-14)	6 (2-17)	5 (1-15)	5 (2-12)	4 (3-11)
Triple refractory	77.6%	90%	61%	96%	63%
CRS, G≥3	72.1%, 0.6%	47.9%, 0.6%	54%, 3%	57.7%, 0%	53%, 0%
Neurotoxicity, G≥3	3%, 0	4%, 0	NR, 6 pts	4, 3.4	2 pts, 3%
Infections, G≥3	76.4%, 44.8%	NR	32%, 17%	66.7%, 35%	34%, 9%
ORR (%)	63%	75% 200-800 mg	60%/81%* *at ≥40 mg	61%	53%
≥CR (%)	39.4%	16%	20%/30%*	27.6%	23%
Median PFS (m) (95% CI)	11.3 m (8.8-17.1)	Not reported	Not reported	NE (10.4-NE)	Not reported
Median DoR (m) (95% CI)	18.4 m (14.9-NE)	Not reached	Not reported	NE (12.0-NE)	Not reported
MRD – (10^{-5})	26.7%	4/10	Not reported	90.9% (n=22)	16/20

Moreau P et al. NEJM 2022; Bahlis N et al. ASH 2022; Wong S et al. ASH 2022; Voorhees PM et al. ASH 2022.

These are the five that are the farthest along in terms of clinical development. I had shared that slide which showed the various platforms and structures or constructs of the bispecifics, and that's what enables some of these therapies to be given subcutaneously on different dosing schedules.

So, one thing that we are trying to understand better is how to give these therapies early on and then can we after the early response, managing the safety or cytokine release syndrome, can we then move on to less frequent dosing for our patients?

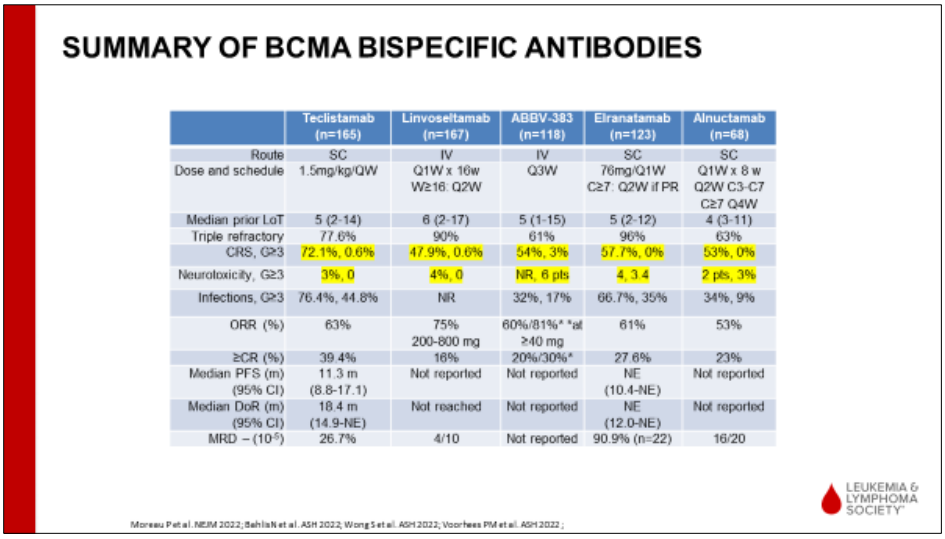


	Teclistamab (n=165)	Linvoseltamab (n=167)	ABBV-383 (n=118)	Elranatamab (n=123)	Alnuctamab (n=68)
Route	SC	IV	IV	SC	SC
Dose and schedule	1.5mg/kg/QW	Q1W x 16w W≥16: Q2W	Q3W	76mg/Q1W C≥7: Q2W if PR	Q1W x 8 w Q2W C3-C7 C≥7 Q4W
Median prior LoT	5 (2-14)	6 (2-17)	5 (1-15)	5 (2-12)	4 (3-11)
Triple refractory	77.6%	90%	61%	96%	63%
CRS, G≥3	72.1%, 0.6%	47.9%, 0.6%	54%, 3%	57.7%, 0%	53%, 0%
Neurotoxicity, G≥3	3%, 0	4%, 0	NR, 6 pts	4, 3.4	2 pts, 3%
Infections, G≥3	76.4%, 44.8%	NR	32%, 17%	66.7%, 35%	34%, 9%
ORR (%)	63%	75% 200-800 mg	60%/81%* *at ≥40 mg	61%	53%
≥CR (%)	39.4%	16%	20%/30%*	27.6%	23%
Median PFS (m) (95% CI)	11.3 m (8.8-17.1)	Not reported	Not reported	NE (10.4-NE)	Not reported
Median DoR (m) (95% CI)	18.4 m (14.9-NE)	Not reached	Not reported	NE (12.0-NE)	Not reported
MRD – (10^{-5})	26.7%	4/10	Not reported	90.9% (n=22)	16/20

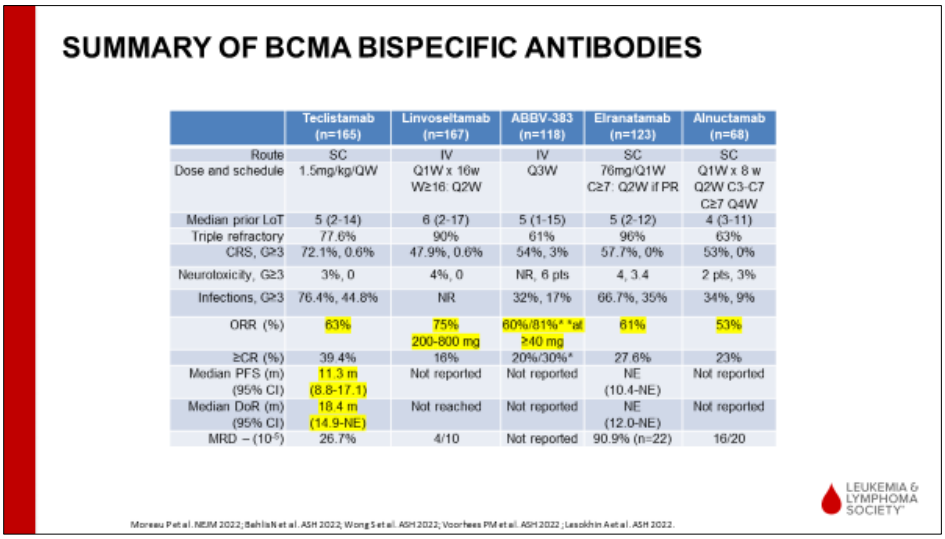
Moreau P et al. NEJM 2022; Bahlis N et al. ASH 2022; Wong S et al. ASH 2022; Voorhees PM et al. ASH 2022.

The other important thing about each of these different bispecific antibodies is the nature of patients that actually went on these trials. So, a high proportion of patients were refractory to the existing classes of drugs, the three big ones that we call the proteasome inhibitors, immunomodulatory drugs as well as the anti-CD38 monoclonal antibodies. And what you see is that vast majority of these

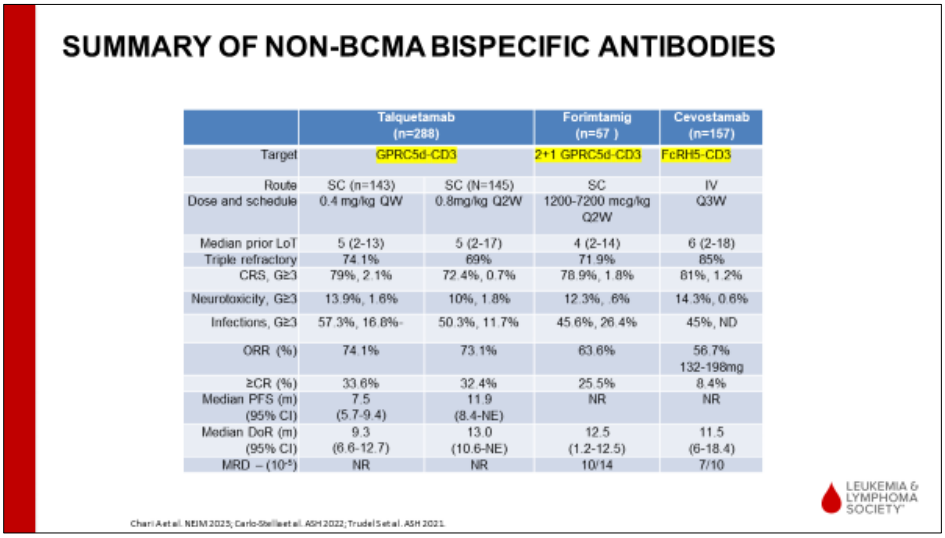
patients had refractoriness to those three classes of drugs. So, this is a very difficult-to-treat patient population in our clinics, and we typically as a standard of care don't have many options for them.



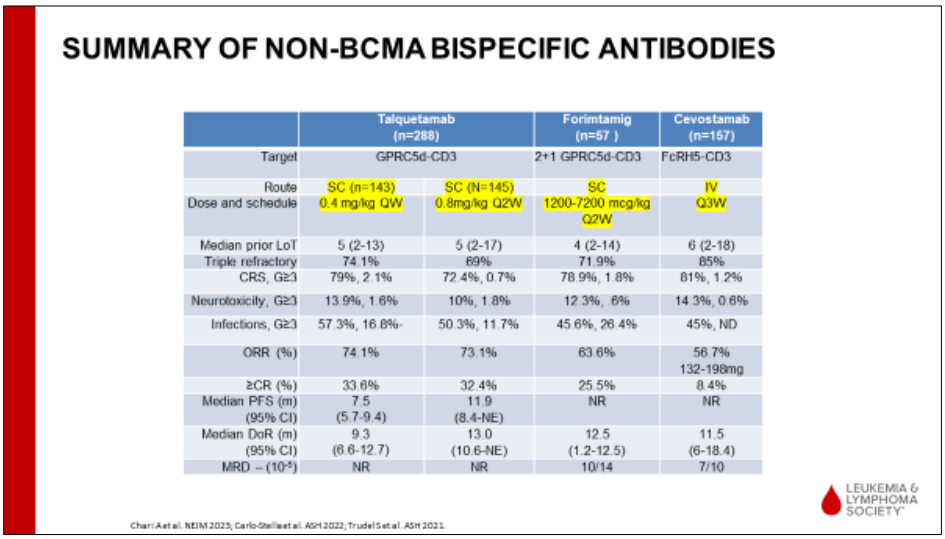
The other thing that I mentioned, you know, the cytokine release syndrome can happen with each of these constructs, but the likelihood of high-grade, Grade 3 or higher, CRS is very low. And the same is true for neurologic side effects. It happens very rarely, and, if it happens it's usually Grade 1 or 2. It's not Grade 3 or higher.



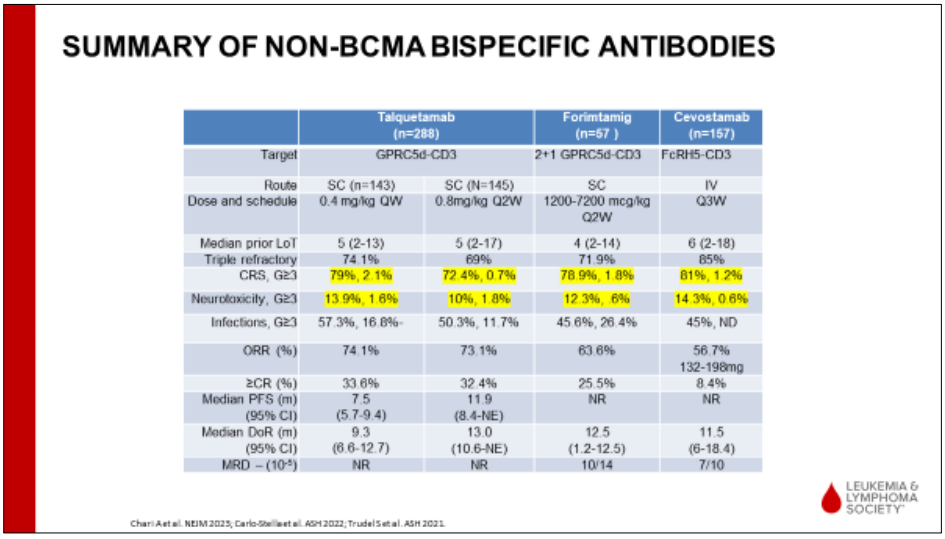
What's remarkable to see is the response rates with each of these bispecifics well over 60%. This includes the data for teclistamab which is now available for use for our patients, and we've been using this in our clinics.



What about bispecific antibodies to other non-BCMA (B-cell maturation antigen) targets? So, we have talquetamab, which is the farthest along in its clinical development targeting GPRC5D as the protein. We have forimtamig, which is also targeting GPRC5D, but we are just learning about some of this experience and data over the past few months. And then we have cevostamab, which targets FcRH5. So beyond BCMA, we have other bispecifics that are in clinical development.

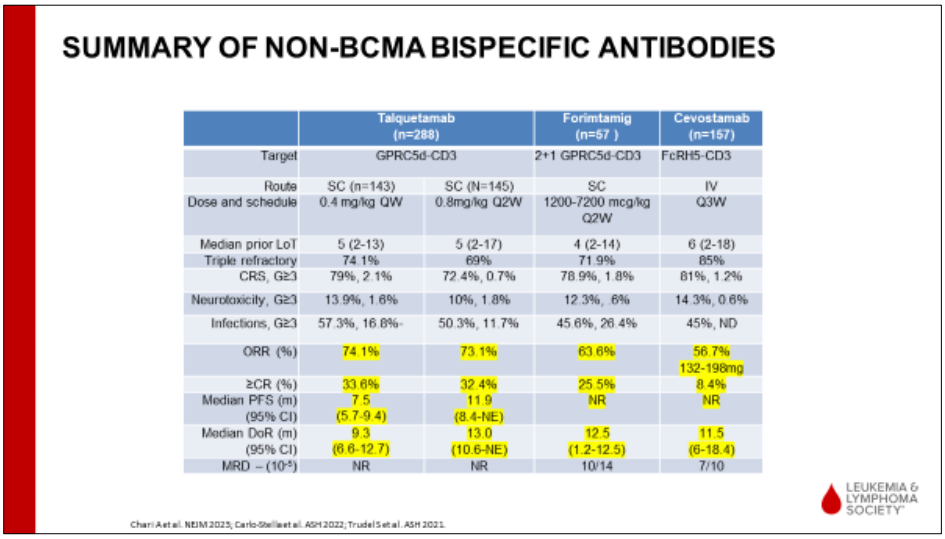


And both the GPRC5D targeting bispecifics you can see can be given under the skin, or subcutaneously, but the dosing schema and schedule is a little different for each of these. The cevostamab bispecific is given IV (intravenous), but it's given every three weeks.



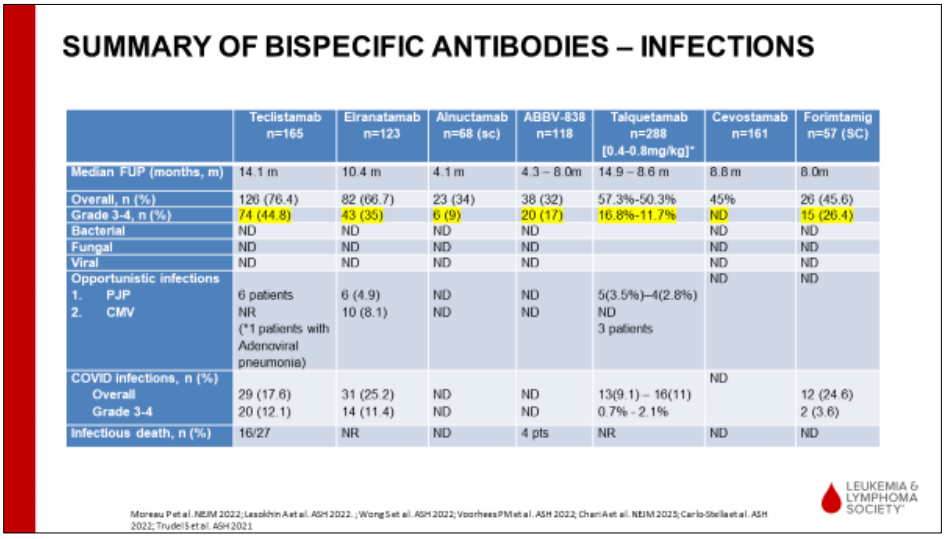
	Talquetamab (n=288)		Forimtamig (n=57)	Cevostamab (n=157)
Target	GPRC5d-CD3		2+1 GPRC5d-CD3	FcRH5-CD3
Route	SC (n=143)	SC (N=145)	SC	IV
Dose and schedule	0.4 mg/kg QW	0.8mg/kg Q2W	1200-7200 mcg/kg Q2W	Q3W
Median prior LoT	5 (2-13)	5 (2-17)	4 (2-14)	6 (2-18)
Triple refractory	74.1%	69%	71.9%	85%
CRS, G≥3	79%, 2.1%	72.4%, 0.7%	78.9%, 1.8%	81%, 1.2%
Neurotoxicity, G≥3	13.9%, 1.6%	10%, 1.8%	12.3%, .6%	14.3%, 0.6%
Infections, G≥3	57.3%, 16.8%-	50.3%, 11.7%	45.6%, 26.4%	45%, ND
ORR (%)	74.1%	73.1%	63.6%	56.7% 132-198mg
≥CR (%)	33.6%	32.4%	25.5%	8.4%
Median PFS (m) (95% CI)	7.5 (5.7-9.4)	11.9 (8.4-NE)	NR	NR
Median DoR (m) (95% CI)	9.3 (6.6-12.7)	13.0 (10.6-NE)	12.5 (1.2-12.5)	11.5 (6-18.4)
MRD – (10^{-5})	NR	NR	10/14	7/10

Again, the good news about each of these constructs is that CRS doesn't happen as high grade and neurologic side effects are not as common. They're perhaps a little bit more common than what we saw with the BCMA bispecifics, but we do see these side effects, but they too are mostly Grade 1 and 2. Very few Grade 3 or higher side effects are seen.



	Talquetamab (n=288)		Forimtamig (n=57)	Cevostamab (n=157)
Target	GPRC5d-CD3		2+1 GPRC5d-CD3	FcRH5-CD3
Route	SC (n=143)	SC (N=145)	SC	IV
Dose and schedule	0.4 mg/kg QW	0.8mg/kg Q2W	1200-7200 mcg/kg Q2W	Q3W
Median prior LoT	5 (2-13)	5 (2-17)	4 (2-14)	6 (2-18)
Triple refractory	74.1%	69%	71.9%	85%
CRS, G≥3	79%, 2.1%	72.4%, 0.7%	78.9%, 1.8%	81%, 1.2%
Neurotoxicity, G≥3	13.9%, 1.6%	10%, 1.8%	12.3%, .6%	14.3%, 0.6%
Infections, G≥3	57.3%, 16.8%-	50.3%, 11.7%	45.6%, 26.4%	45%, ND
ORR (%)	74.1%	73.1%	63.6%	56.7% 132-198mg
≥CR (%)	33.6%	32.4%	25.5%	8.4%
Median PFS (m) (95% CI)	7.5 (5.7-9.4)	11.9 (8.4-NE)	NR	NR
Median DoR (m) (95% CI)	9.3 (6.6-12.7)	13.0 (10.6-NE)	12.5 (1.2-12.5)	11.5 (6-18.4)
MRD – (10^{-5})	NR	NR	10/14	7/10

In terms of activity, you know, again, the good news is that each of these constructs gives a very high response rate, so well over 60%, 73 and 74% for talquetamab. Why is this important? It's important because our previous, you know, I'm sharing with you response rates of 60, 70% and the treatments – such as daratumumab (Darzalex®) or isatuximab (Sarclisa®), carfilzomib, pomalidomide – those treatments, when they were approved by the FDA, their single-agent response rates were between 20 to 30%. So, our bar has been raised with these immunotherapies. The bispecifics are really showing a high proportion of response.



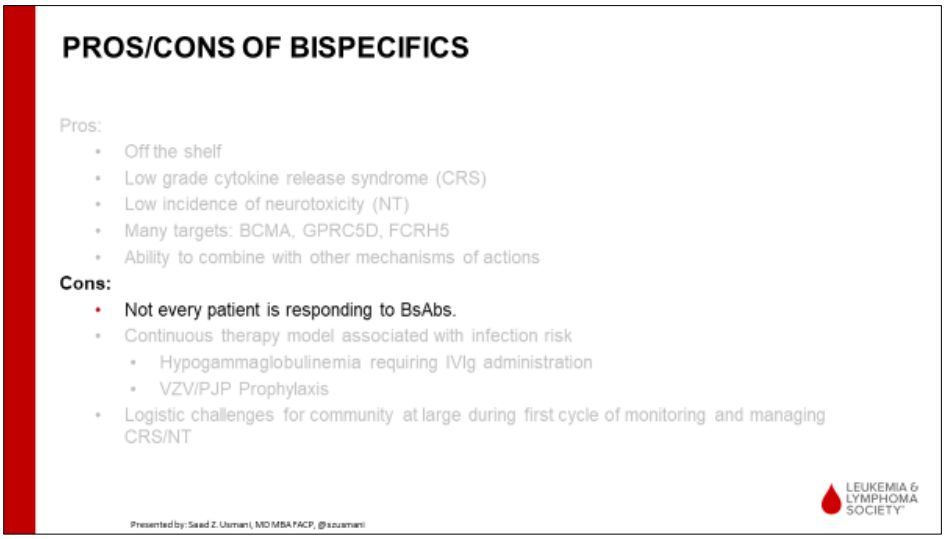
SUMMARY OF BISPECIFIC ANTIBODIES – INFECTIONS

	Teclistamab n=165	Elranatamab n=123	Alnuctamab n=68 (sc)	ABBV-838 n=118	Talquetamab n=288 [0.4-0.8mg/kg]*	Cevostamab n=161	Forimtamig n=57 (SC)
Median FUP (months, m)	14.1 m	10.4 m	4.1 m	4.3 – 8.0m	14.9 – 8.6 m	8.8 m	8.0m
Overall, n (%)	126 (76.4)	82 (66.7)	23 (34)	38 (32)	57.3%-50.3%	45%	26 (45.6)
Grade 3-4, n (%)	74 (44.8)	43 (35)	6 (9)	20 (17)	16.8%-11.7%	ND	15 (26.4)
Bacterial	ND	ND	ND	ND		ND	ND
Fungal	ND	ND	ND	ND		ND	ND
Viral	ND	ND	ND	ND		ND	ND
Opportunistic infections						ND	ND
1. PJP	6 patients	6 (4.9)	ND	ND	5(3.5%)–4(2.8%)		
2. CMV	NR (*1 patients with Adenoviral pneumonia)	10 (8.1)	ND	ND	ND 3 patients		
COVID infections, n (%)						ND	
Overall	29 (17.6)	31 (25.2)	ND	ND	13(9.1) – 16(11)		12 (24.6)
Grade 3-4	20 (12.1)	14 (11.4)	ND	ND	0.7% - 2.1%		2 (3.6)
Infectious death, n (%)	16/27	NR	ND	4 pts	NR	ND	ND

Moreau P et al. NEJM 2022; Lesokhin A et al. ASH 2022. ; Wong S et al. ASH 2022; Voorhees P M et al. ASH 2022; Chari A et al. NEJM 2023; Carlo-Stella et al. ASH 2022; Trudel S et al. ASH 2021

LEUKEMIA & LYMPHOMA SOCIETY®

And then an important thing that I want to talk about now is infections because across the board, you know, I've talked about activity, I want to talk about the main long-term concern that we have. With each of these bispecifics regardless of whether it's BCMA, GPRC5D, or FcRH5, we see a high proportion of patients getting infections and this is because we keep on giving the bispecifics until they're working. And now we're trying to figure out, can we scale back on the frequency of the dosing? And I'll be sharing some anecdotes in one of my slides because now we're getting into the potential cons of the side effects.



PROS/CONS OF BISPECIFICS

Pros:

- Off the shelf
- Low grade cytokine release syndrome (CRS)
- Low incidence of neurotoxicity (NT)
- Many targets: BCMA, GPRC5D, FCRH5
- Ability to combine with other mechanisms of actions

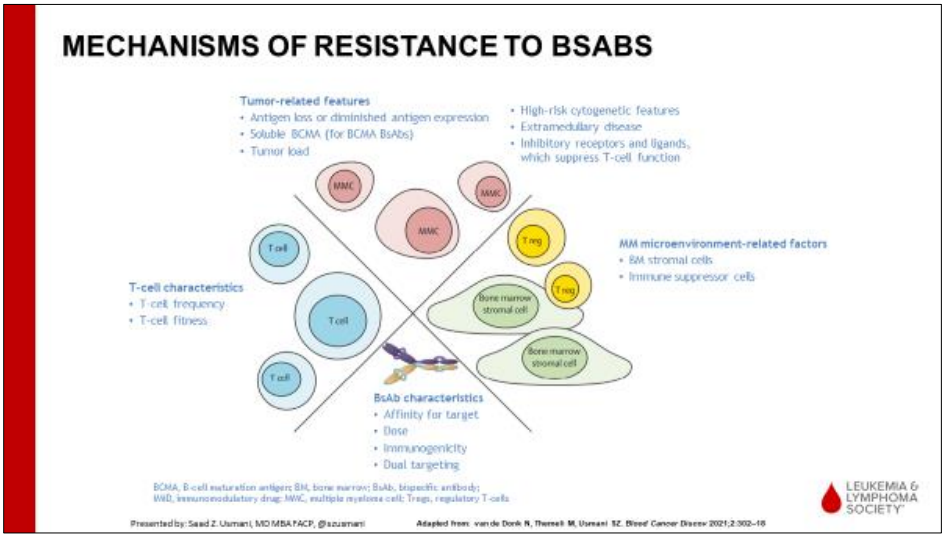
Cons:

- Not every patient is responding to BsAbs.
- Continuous therapy model associated with infection risk
  - Hypogammaglobulinemia requiring IVIg administration
  - VZV/PJP Prophylaxis
- Logistic challenges for community at large during first cycle of monitoring and managing CRS/NT

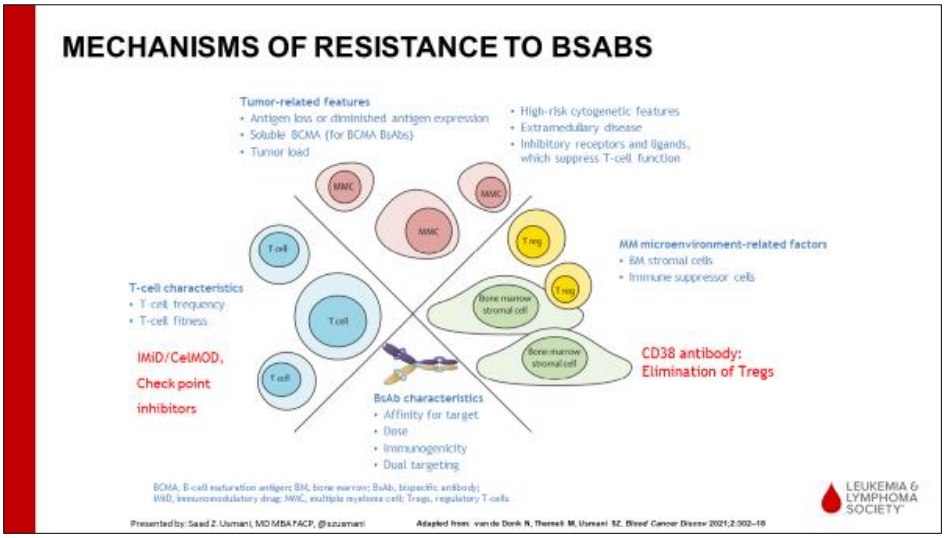
Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

LEUKEMIA & LYMPHOMA SOCIETY®

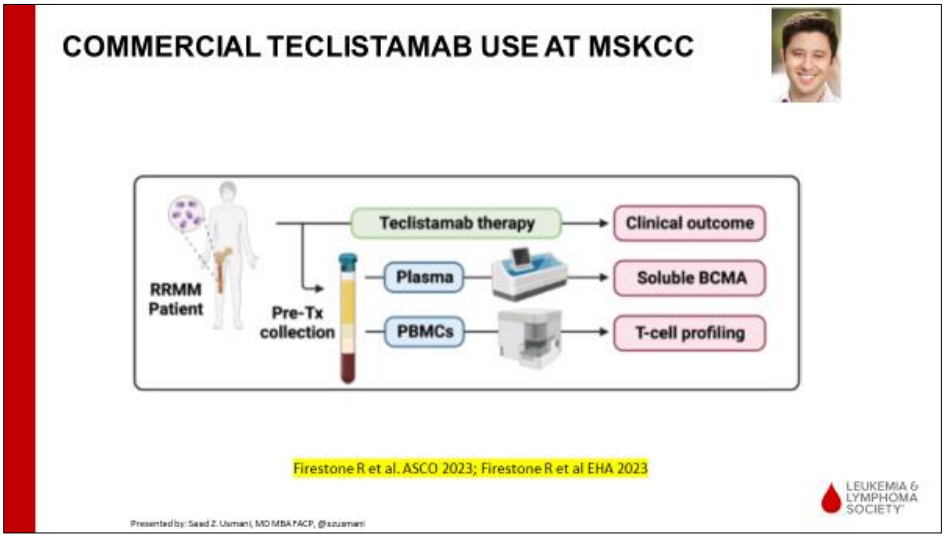
So, not every patient is responding to bispecifics. It's not 100% response, and the reason for that is many folds.



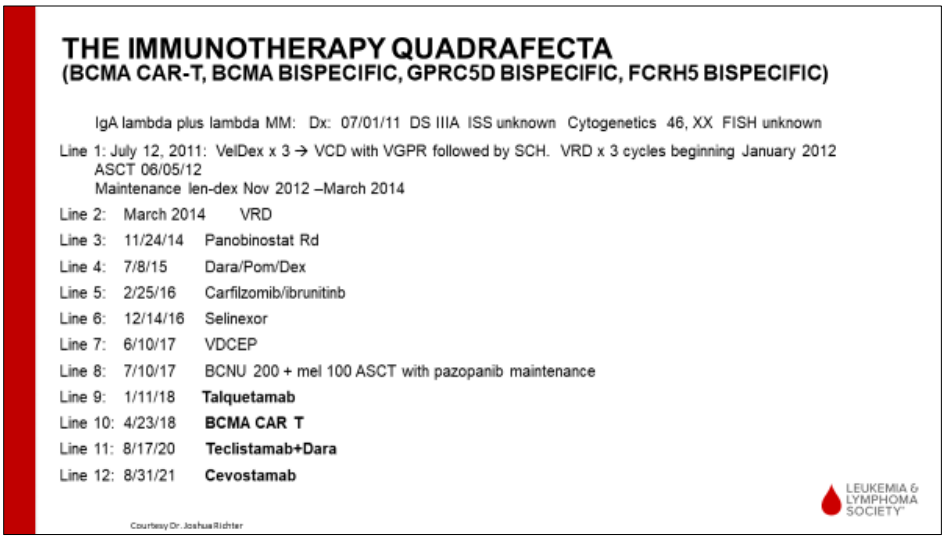
So, it has to do with the tumor-related factor, so there could be loss of antigen that we are trying to target with bispecifics or diminish antigen expression. We could also have T cells that are not as fit and active as they should be. And then depending on the bispecific antibody, its affinity for the target, immunogenicity, and the dose, you know, that can be a potential challenge. And then the disease biology and bone marrow microenvironment having immune suppressor cells that are not letting the T cells do their job. All of these are important issues.



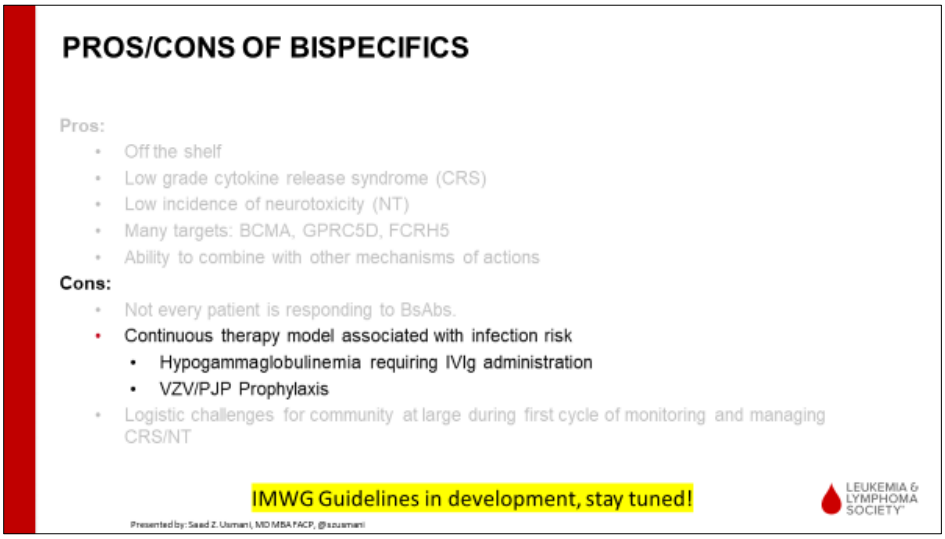
What I can share with you, and this is that there are strategies in the clinic that we are trying to see if we can overcome by combining bispecifics with immunomodulatory drugs and CELMoDs (cereblon E3 ligase modulatory drugs) and even with checkpoint inhibitors. And then there is already clinical data with bispecifics being combined with CD38 antibodies to eliminate T regs (regulatory T cells).



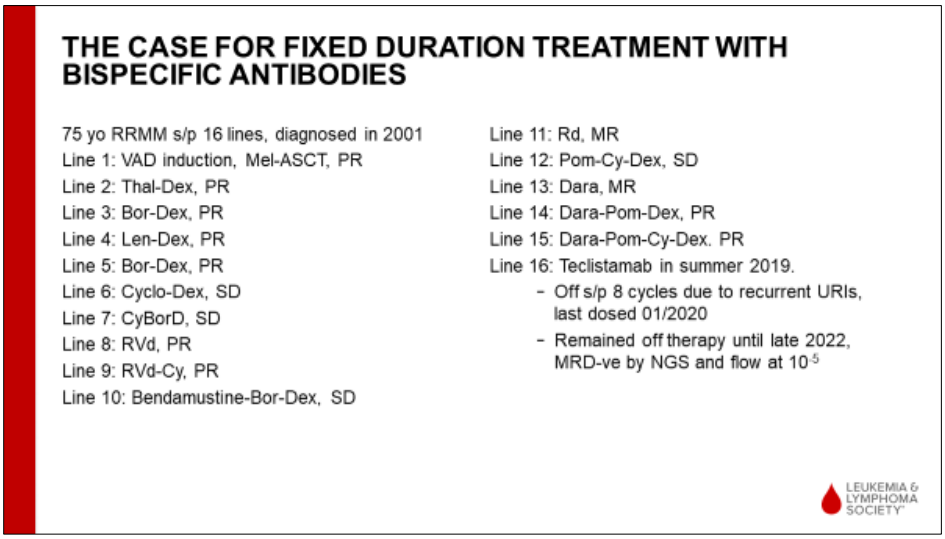
So, some of these strategies are happening; I do want to give a shout out to my fellow, Ross Firestone, who's actually presenting some of his translational data in trying to figure out are there any T-cell profiling data that can help us figure out which patients are benefiting or not benefiting from commercial teclistamab. So, he's going to be presenting this data next month at ASCO (American Society of Clinical Oncology Annual Meeting).



One of the important lessons here we're learning is that we can have, and this case is courtesy of my colleague Dr. Joshua Richter at Mt. Sinai where what he demonstrated with this particular patient's case, they got placed on this bispecific antibody talquetamab but that did not work well for them. It worked only for two or three months, but they went on to receive a BCMA CAR T-cell therapy. And that CAR T-cell therapy benefited them for over two years. But when the myeloma came back, the patient was able to get a BCMA-directed bispecific with daratumumab at that time and that benefited them for a year before they went on another bispecific, this time with cevostamab, which is an FcRH5 bispecific antibody. So, the point being that you can use different immunotherapies in patients over time and keep them going.



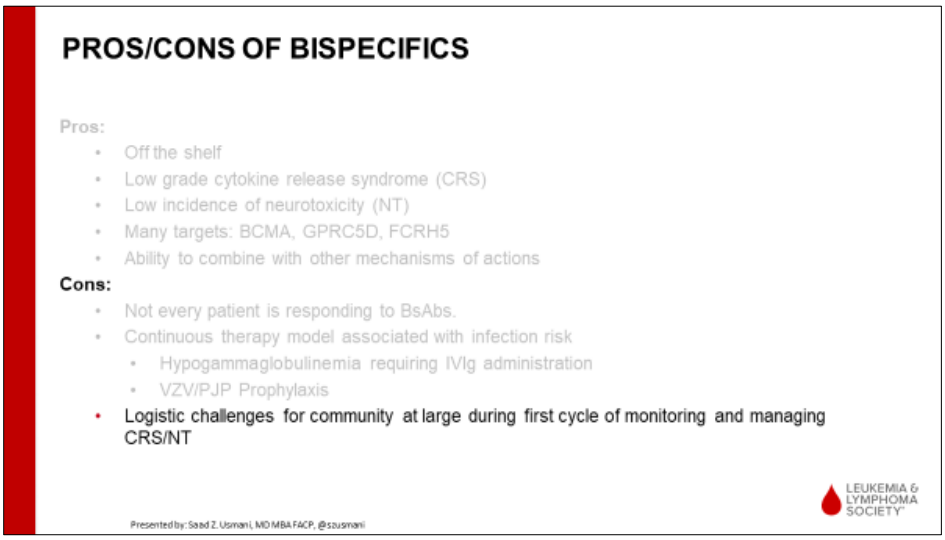
All right. So, the other important thing that I talked about the con is continuous therapy model, which is associated with infection, hypogammaglobulinemia which requires IVIG (intravenous immunoglobulin) administration, and all of our patients are on zoster and PJP (pneumocystis jirovecii pneumonia) prophylaxis while they're receiving it. Well, there are International Myeloma Working Group guidelines in development on how best to manage this scenario, so just stay tuned about those guidelines.



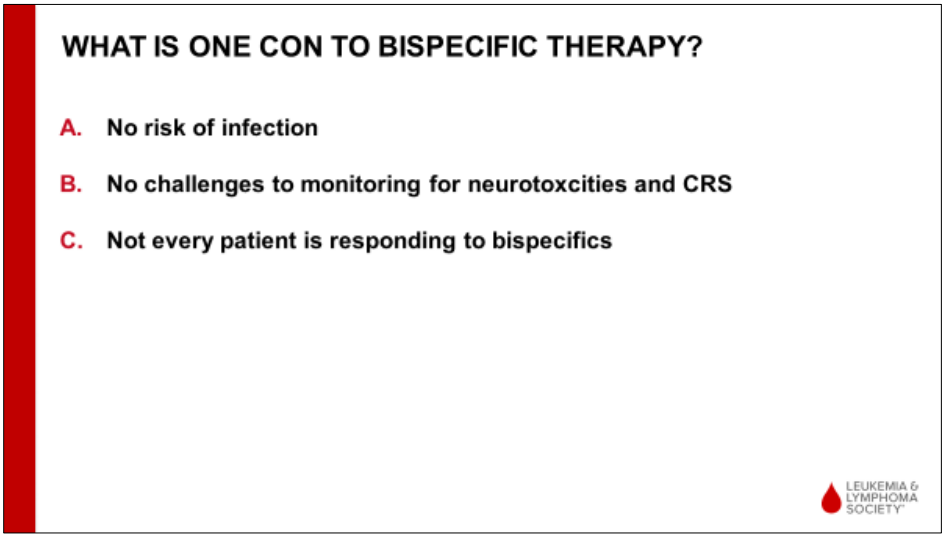
But I want to share another interesting experience or anecdote with you. So, this is one of my patients who went on teclistamab as part of MajesTEC-1 study in the summer of 2019 as their 16th line of treatment. But the patient was prone to getting upper respiratory tract infections and pneumonias off and on and that issue was part of his whole disease course previous to getting on teclistamab. But they were having these recurrent URIs (upper respiratory infections) and so they got admitted with pneumonia in January, late January. And after that admission, we decided to hold treatment and then

eventually take him off of study and just watch him because he was still recovering from that admission.

This was the first time that the patient had been—The only other time that patient had been off of treatment was after the initial stem cell transplant, but after that they had been on continuous therapy for a while. This patient went into an MRD (minimal residual disease) negative status and stayed off of therapy for almost three years. And that was quite remarkable to see that you can utilize a bispecific antibody to give that kind of deep response to patients. So, the point I want to make is that we can think about fixed duration treatment, and there are clinical trials that are going to be exploring this possibility.

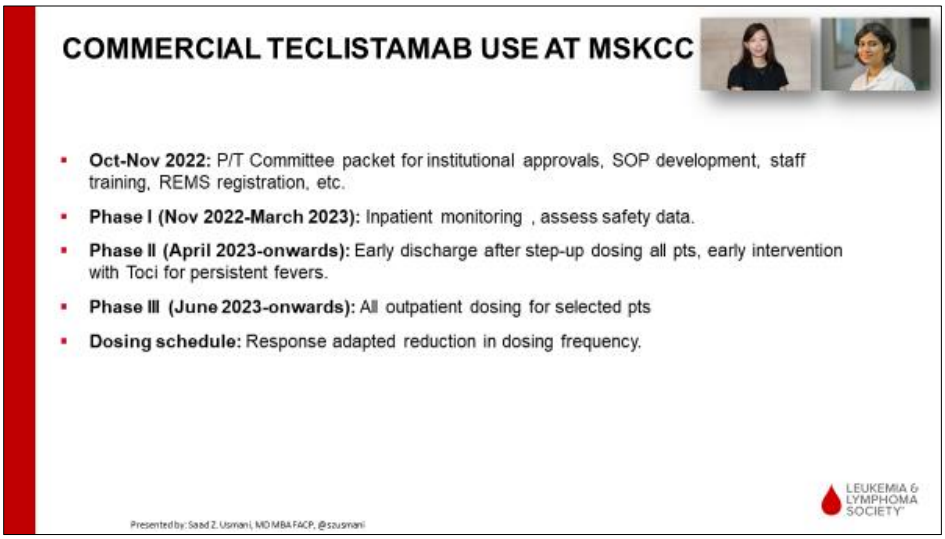


And then the last piece which is important from a con standpoint is logistic challenge for our community at large during that first cycle of monitoring and managing CRS and neurotoxicity. And I think this is going to be an important learning curve. It's doable, achievable, but I think it's going to be a learning curve for our community colleagues. And this is where we can help and facilitate things for our community colleagues to take best care of our patients.



So, a question for you guys as well here. What is the one con to bispecific therapy? No risk of infection, no challenges to monitoring for neurotoxicity and CRS, or that not every patient is responding to bispecifics. So, please feel free to answer.

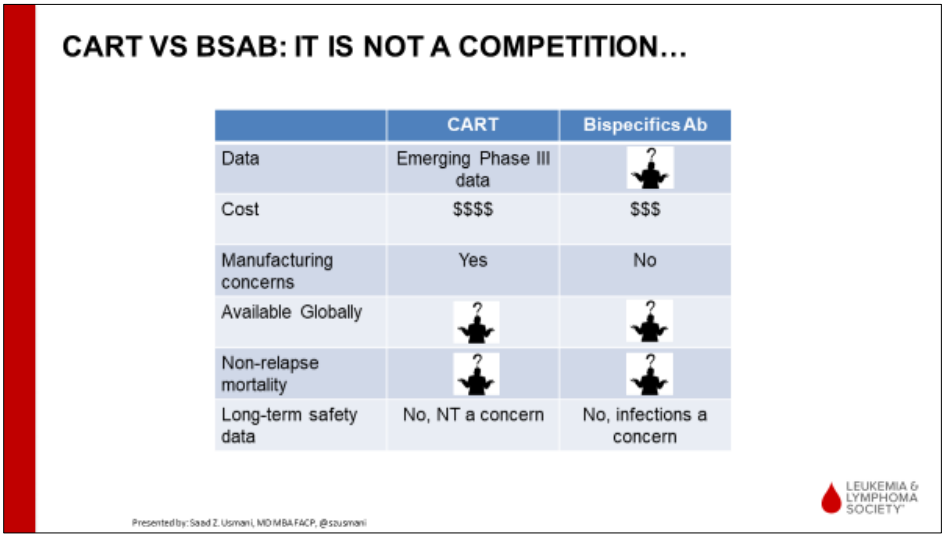
All right, so the correct answer is (C) for this particular question.



All right, so I want to share our own experience of commercial teclistamab at MSK (Memorial Sloan Kettering Cancer Center). When the label came out, it requires patients to be monitored closely during the first cycle of treatment for CRS. So, when the FDA approval came at the end of October, we were able to move swiftly to get the SOP (standard operating procedure) developed, our P&T (Pharmacy and Therapeutics) Committee to approve teclistamab for use and then get all our team members REMS (risk evaluation and mitigation strategies) registered. In the initial phase of the rollout, we admitted patients for that first week of three doses – the two step-up doses as well as the first full dose – and assessed safety data.

TRANSCRIPT

From April onwards, we started to utilize early discharge after the step-up dosing for patients and then early intervention if patients, you know, with tocilizumab (Actemra®) if they had persistent fevers. And later in the summer, we're going to do all outpatient dosing for a select group of patients. And then in terms of dosing schedule, we are developing a response-adapted reduction in dosing frequency to every two weeks and then every four weeks for our patients. So, we're trying to make this easier in terms of logistics for our patients but basing it off of really, you know, patients getting to a good response because with teclistamab being given weekly in the MajesTEC-1 trial experience, what we've seen is patients get to the best response within four months. So, using that data, we will be able to shape our clinical practice.



And then when it comes to comparisons with CAR T-cell therapies and bispecifics, I don't think it's a competition. Both of these therapies are going to be helping our patients around the world. Not every patient may be CAR eligible or have accessibility to CARs, and bispecifics have benefits of being given in the community and being combined with other things. But we do need long-term safety data. We need to think about global availability of these therapies and look at the nonrelapse mortality due to side effects as well. So, a lot of work still for us to do, but, as I mentioned, this is an exciting era of immune therapies for our patients.

With that being said, I want to give a shout out acknowledgement to the Myeloma Service at MSK as well as our transplant cellular therapy team members before I hand things back over. Thank you so much.

Lesley Hoerst, BSN, RN

Thank you so much, Dr. Usmani, for your very informative and comprehensive presentation.

I am now pleased to share free resources for you and your patients. Though this program is not offering continuing education credit, you can access LLS's professional education website where we offer free CE (continuing education) and CME (continuing medical education) online courses as well as a podcast channel where you can listen to healthcare professionals discuss treatment, side effect management, and strategies to support your patients. New and interesting topics are added every few weeks. To access these, as well as our videos and fact sheets on a variety of topics, please visit LLS.org/CE.

The Leukemia & Lymphoma Society Information specialists are highly trained oncology social workers and nurses who provide accurate, up-to-date disease, treatment, and support information, including financial information. Patients can contact them directly or you can complete a referral form.

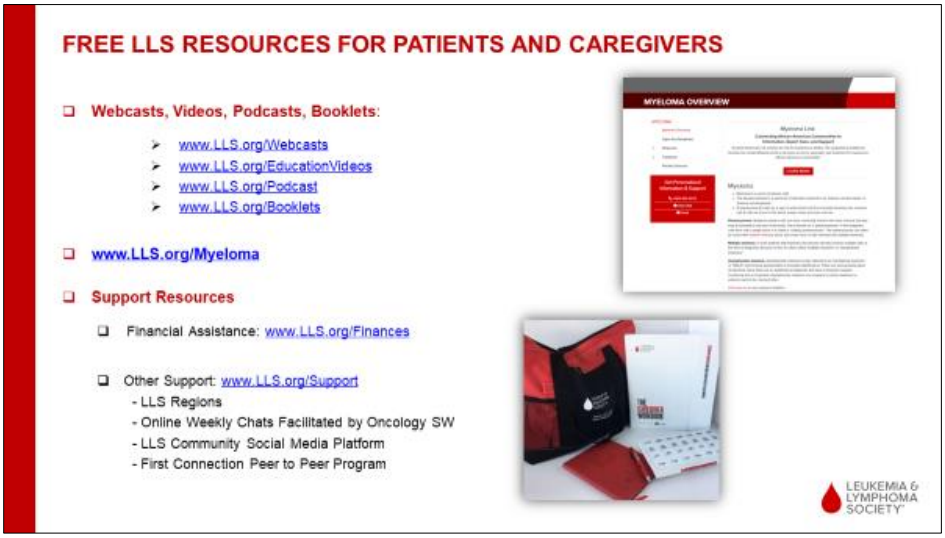
Information Specialists can also help you access or order multiple free copies of booklets to give to your patients.

Our Clinical Trial Support Center Nurse Navigators are registered nurses and nurse practitioners with expertise in blood cancers. They work one on one with patients via telephone to provide user-friendly information, help find appropriate clinical trials, personally assist them throughout the clinical trial process, and provide information for the patient to bring back to their healthcare provider. This is a unique service from LLS.

Refer your patients for a one-on-one free nutrition consultation with one of our Registered Dieticians through The Leukemia & Lymphoma Society's PearlPoint Nutrition Services®. Consultations are by phone and are available for patients of all cancer types and all ages and are available in many languages using our interpretation services.

For information or to refer or connect a patient with an Information Specialist, Clinical Trial Nurse Navigator, or Registered Dietician, please use the URLs (uniform resource locator) listed on the slide.

I hope you will consider all of these specialists as an extension of your healthcare team.



LLS offers blood cancer disease-specific information and support resources for patients and caregivers, including telephone and web education programs, videos, podcasts, and booklets.

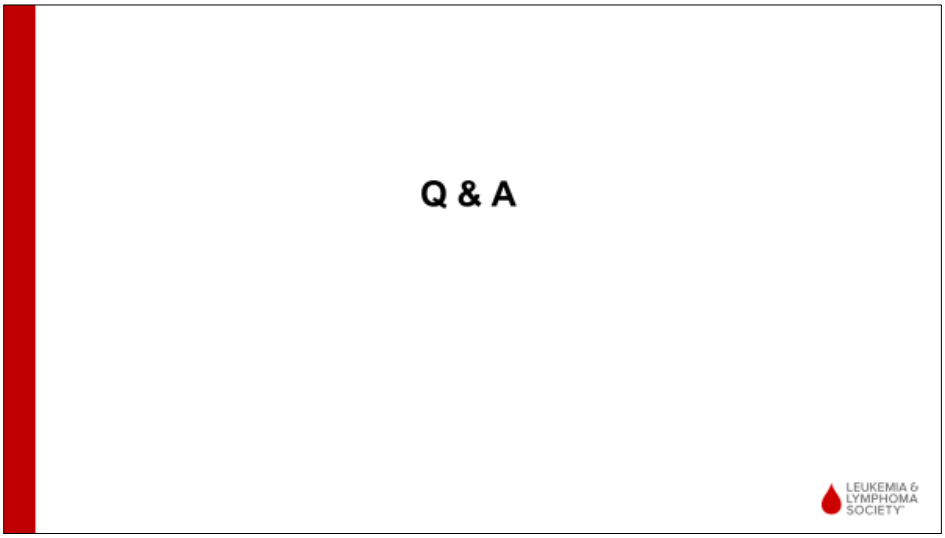
You may know about LLS's Financial Assistance Programs, and I encourage you to stay up to date on the availability of funds, as well as additional support resources using the links on this slide.

Here are some examples and informational cards you can order through LLS at no charge to give to your patients, or they can access them on the LLS website.

Through its targeted and culturally appropriate programs and services, LLS is committed to addressing the needs of underserved communities impacted by blood cancer and those facing systemic and structural barriers to optimal care. One of these initiatives is Myeloma Link, a national outreach program that raises awareness of the higher incidence of myeloma in the Black community. Visit LLS.org/Myelomalink for more information.

If you have questions on any LLS resources, please contact an Information Specialist. We know that you are the key to patient treatment, support, and helping with survivorship challenges for myeloma as well as other cancer types. We are here to support you and your patients. Please reach out to us.

QUESTION-AND-ANSWER SESSION



Lesley Hoerst, BSN, RN

It is now time for the Question-and-Answer portion of our program. Please type your question in the Ask a Question box under the speaker video window to submit your question.

Saad Z. Usmani, MD, MBA, FACP

The first question is, "How do you nutritionally optimize patients for this type of treatment?"

That is a very patient-centric thing, so, I think you have to take a look at what the patient's preferences would be and engage our dieticians in helping the patients on that end. But there is no specific or special diet or nutrition that is different from any other treatment that we're giving. It's more health and disease-specific guidance that we can give for the most part. And the only important thing that I can share, and this actually leads into the second question that I'm seeing here. So, let me read that question and then I can address the second part to it. So, with the GPRC5D bispecific antibodies, GPRC5D in addition to being present on the B cells and myeloma cells it's also present in skin and on the surface of the tongue, so patients can get skin dryness, nails becoming brittle, and taste changes with GPRC5D treatments if they're continued for longer durations of time. So, this is where less frequent dosing, dosing interruptions, and engaging the dietician to help our patients in terms of what they can eat and enjoy becomes important. But that's something that's seen with the GPRC5D bispecific antibodies and even with the CAR T-cell therapies.

Lesley Hoerst, BSN, RN

Our next question is from Patricia, "On average, how long are patients on teclistamab? You said best response is usually within four months. Do patients stop the drug after four months?"

Saad Z. Usmani, MD, MBA, FACP

No. They don't stop after four months. So, if you're responding, the duration of response is over 18 months. The point I was making is that this drug or this therapy can get patients into deep responses very quickly, so within four months. When I say, "best response," patients start responding to treatment after one cycle but then the myeloma levels continue to decline until they hit as low as they can go. So, they hit as low as they can go at an average around four months, and if that is happening, that may be a good time to say, "All right, instead of going into the clinic every week, maybe I can have my patient come back every other week to get treatment." And if that other week strategy continues to demonstrate that the myeloma is still at a low level and not rising, then maybe in a few months you can say, "All right, instead of coming every two weeks, why don't you come every four weeks." So, you can lessen the duration or increase the duration between doses for patients if patients have had a good response. That was the point I was trying to make.

So, to your original question, on an average, when patients respond to teclistamab, they stay on it for over 18 months. That's what we've seen in more advanced patients, you know, that patient population. That number may be very different for someone who is an early relapsed myeloma patient or even in the newly diagnosed setting.

Lesley Hoerst, BSN, RN

Our next question is from Zal. "With these new meds, is there some point where some centers are considering myeloma patients for solid organ or kidney transplant?"

Saad Z. Usmani, MD, MBA, FACP

That's actually a very good question. And our discussion is always on a case-to-case basis, and it depends on the kind of myeloma that patients have and the kind of response they've had to treatment and what's the expectation. It's very difficult to do this in late relapsed patients but in early relapse or newly diagnosed setting, this is certainly something that we discuss with our solid organ transplant colleagues.

Lesley Hoerst, BSN, RN

Okay. And I think we have time for one last question, and this was actually a question that was submitted ahead of time. "With the role of CAR T and BiTE (bispecific T-cell engager) technology meds fast approaching, where do you see proteasome inhibitors being used?"

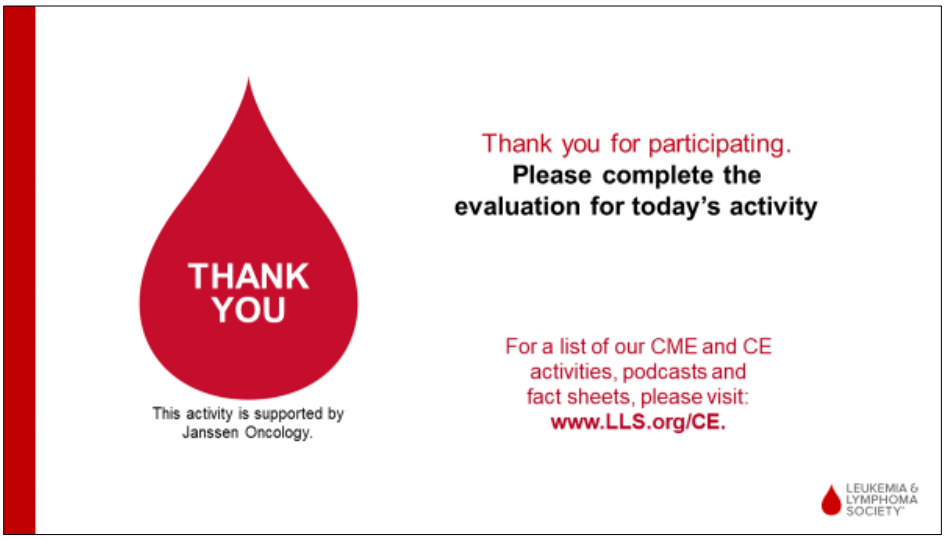
Saad Z. Usmani, MD, MBA, FACP

I think we need proteasome inhibitors in the frontline treatment being combined with—My answer is the conventional, original, small molecule drugs like proteasome inhibitors aren't going anywhere. They're part of the solution for our patients. Immunotherapies are coming and they are target specific but they're not focusing on the pathways that the myeloma cell relies on to carry on its work to proliferate, to grow. So, I think we need both of those strategies working together to eventually find the cure or answer for our patients. So, I don't think that that drug class is going anywhere. We're still going to be using it.

Lesley Hoerst, BSN, RN

Thank you for that question and thank you to the audience for all of your questions and for your participation today.

CLOSING REMARKS



Lesley Hoerst, BSN, RN

Thank you, again, Dr. Usmani, for your continued dedication to our patients and to fellow healthcare professionals.

This concludes our program. The slides for this program will be available for download on The Leukemia & Lymphoma Society web page in the coming days at LLS.org/CE. This program will also be available as a replay in the coming weeks.

Thank you all for participating. We hope the information presented will be useful in your work with families and patients. We look forward to your participation on future LLS programs.