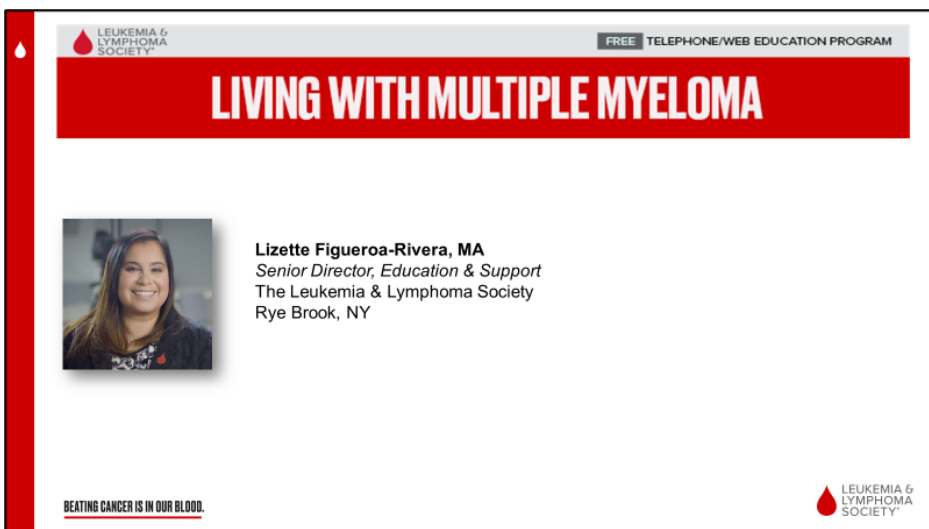


WELCOME AND INTRODUCTION



Lizette Figueroa-Rivera, MA



Hello everyone. On behalf of The Leukemia & Lymphoma Society (LLS), a warm welcome to all of you. Special thanks to Dr. Noa Biran for volunteering her time and expertise with us today. We have over 2,300 people participating in today's program from across the United States as well as other countries, including Canada, Colombia, and Iraq.

We would like to acknowledge and thank Bristol Myers Squibb, Genentech & Biogen, GlaxoSmithKline, Janssen Biotech, and Oncopeptides for their support of today's program. Following the presentation, we will take questions from the audience.

The Leukemia & Lymphoma Society is a champion for myeloma patients, caregivers, survivors, and families. Together with our volunteers, patients, researchers, healthcare professionals, and supporters, we are determined to change the future of myeloma treatment and care.

TRANSCRIPT

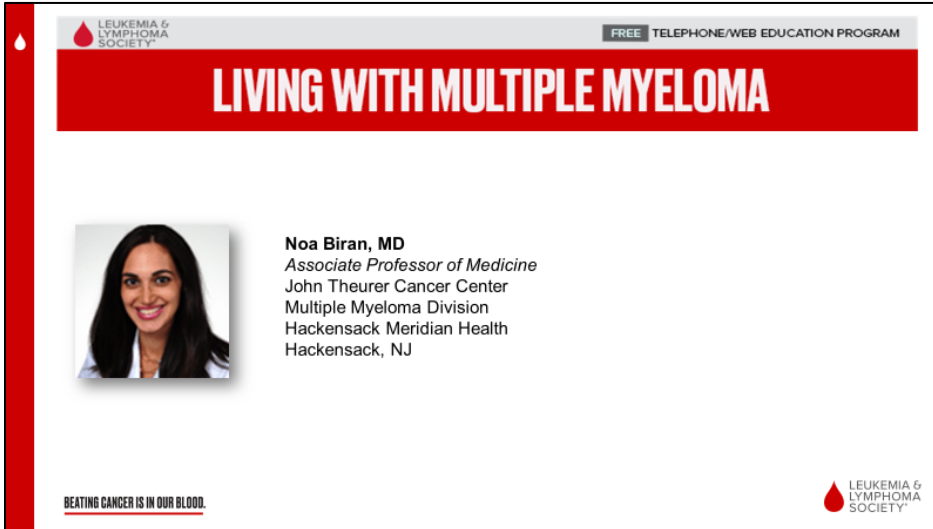
Our vision centers are driving new breakthroughs and cures, helping all myeloma patients access the care they need to survive and thrive, and addressing healthcare disparities that disproportionately impacts underserved populations.

I was speaking with a myeloma patient recently, and he raised a good point that I have not spoken about in a while. LLS knows how a blood cancer diagnosis can take a financial and emotional toll on you. The patient I was speaking to is a veteran, and when he was diagnosed with myeloma, he was not aware of some of the additional assistance myeloma patients can receive from certain funds. I wanted to highlight that veterans who were exposed to Agent Orange while serving in Vietnam, can get help from the United States Department of Veteran Affairs by calling them or emailing them. I'll have their information on the transcript of this program, and their information is also in our myeloma booklet.

Also, there's a fund that includes myeloma from the World Trade Center survivors, and I'll also have their information in this transcript as well as our myeloma booklet. And we also have our financial assistance programs, and you can always visit [LLS.org/Finances](https://www.lls.org/Finances) for more information.

PRESENTATION

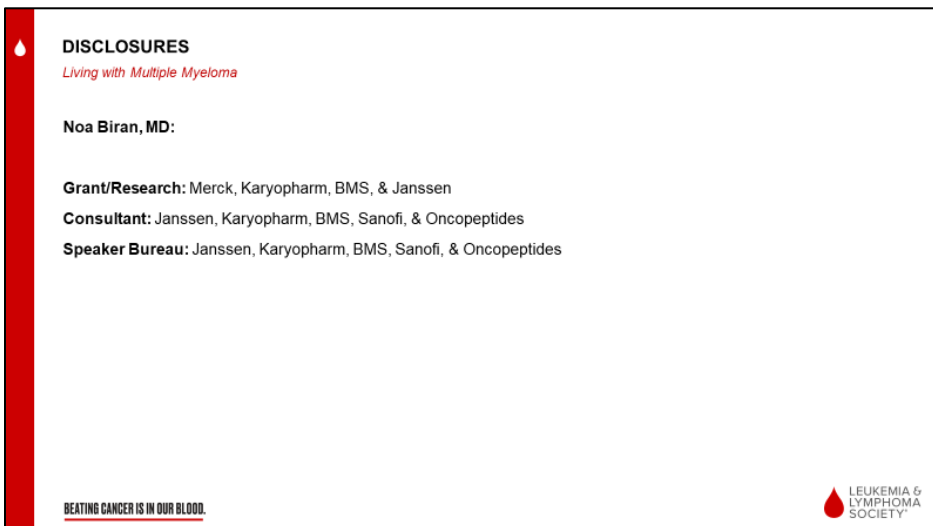
Lizette Figueroa-Rivera, MA



I am now pleased to introduce Dr. Noa Biran, Assistant Professor of Medicine at the John Theurer Cancer Center in the Multiple Myeloma Division at Hackensack Meridian Health in Hackensack, New Jersey. Dr. Biran, I'm now privileged to turn the program over to you.

Noa Biran, MD

Thank you very much. It's an honor to be speaking on behalf of The Leukemia & Lymphoma Society. You guys are a wonderful organization that really has patients at the forefront, and I appreciate having the opportunity to get to teach and educate so many myeloma patients and their caregivers, especially because this disease has so many new therapeutic options; and we're learning how to navigate this ever-changing myeloma world.

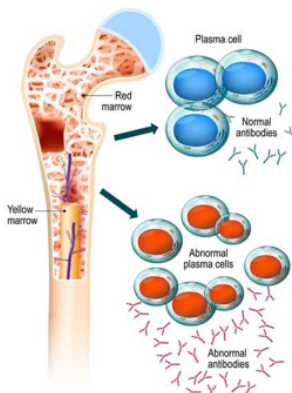


TRANSCRIPT

So, with that, I'll tell you I do have some disclosures, research, consultant, and speaker bureau support; and we'll get started.

What is Multiple Myeloma?

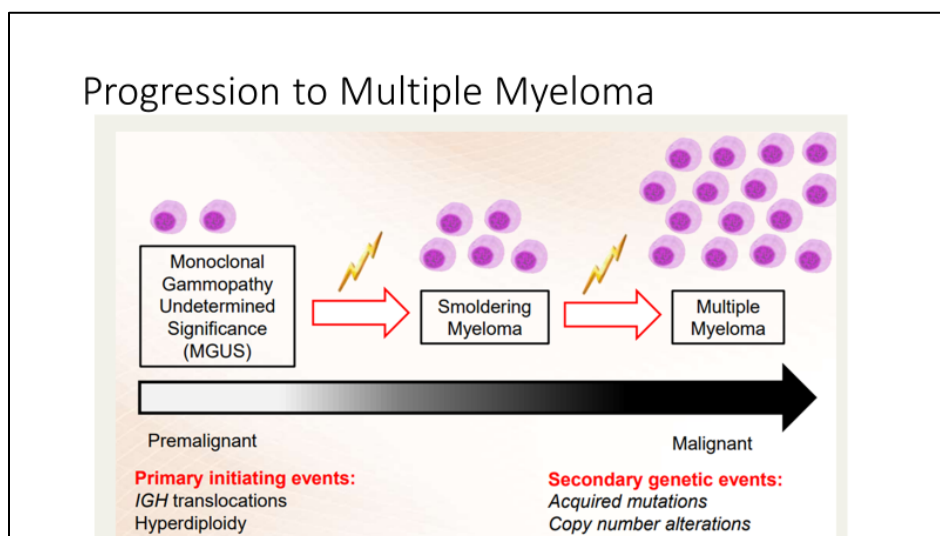
- Blood cancer that develops in bone marrow, where blood cells are produced
- Plasma cells, a type of white blood cell, become malignant
 - Plasma cells, produce infection fighting antibodies called immunoglobulins
- Malignant plasma cells (myeloma cells)
 - Produce large quantities of abnormal antibodies: monoclonal or M proteins, light chains (Bence-Jones)
 - Crowd out and inhibit production of normal blood cells and antibodies



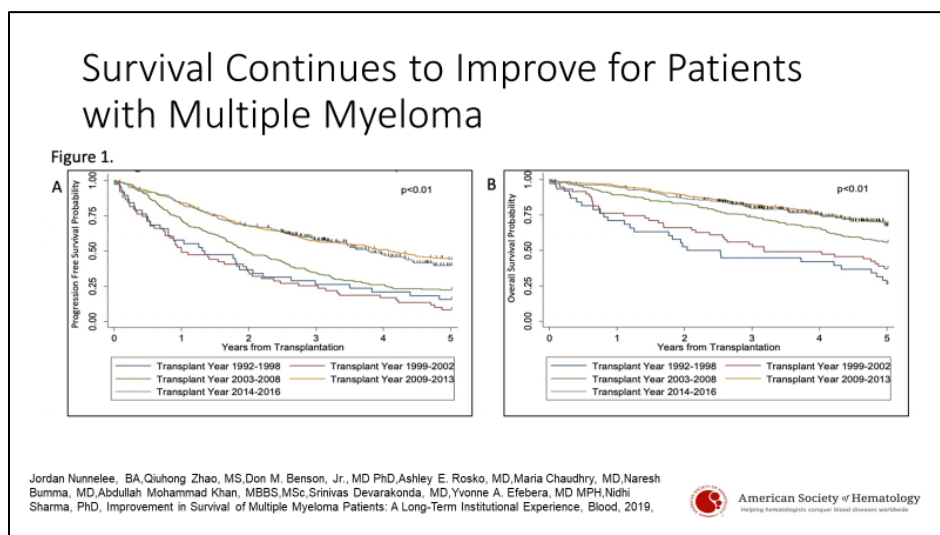
So, what is multiple myeloma? Myeloma is a plasma cell or a bone marrow malignancy. It's a cancer that begins from a type of white blood cell called a plasma cell, and those plasma cells originate from the bone marrow, which is your factory of immune cells.

So, normally plasma cells make antibodies or immunoglobulins is another way to say antibodies. And what happens when you have a cancerous plasma cell is they make dysfunctional antibodies or proteins, and those antibodies cause harm in the body. And not only do they cause harm, but you're left with an abnormal immune system because your healthy plasma cells are outnumbered, and they're unable to make normal healthy plasma cells or antibodies.

So, we see a large amount of protein that is in the blood, and that protein from the antibodies can cause problems with high calcium, with kidney failure or kidney problems or protein in the urine. It can cause anemia because the bone marrow gets crowded out by unhealthy plasma cells, and there's no room to make healthy red blood cells. And we also see bone lesions. So, we see lytic lesions or holes in the bones from disruption of the normal bones. And we also see frequent infection. So, sometimes patients can have three or more antibiotic requiring infections per year or an abnormal amount of colds, and that's from a dysregulated immune system.



So, myeloma often progresses from a quiet or inactive cancer called MGUS, monoclonal gammopathy of undetermined significance. Some patients, we find the MGUS; and some patients, we never know about it, and we just see the multiple myeloma. But in retrospect, you know, that protein may have been there not causing harm to the body for a number of years. And the cancer cells, if they are inactive, acquire mutations that make them more aggressive and more likely to proliferate; and that's how the disease goes from an inactive to an active form.



So, fortunately, we are seeing a significant improvement in survival for our patients with multiple myeloma. Every decade we're seeing more and more treatments, and that's translating into a survival benefit. And it used to be a lot of our patients who we see now were told in the beginning that they would have three to five years to live, and they're living decades. You know, we have patients more than 20 years, 15 years out. And so that's what I usually tell my newly diagnosed patients. I say, "The prognosis today is measured in decades." And there are exceptions to that, but for many of our patients and most of our patients, it's become a chronic disease.

Triple Class Refractory Multiple Myeloma

- Disease progression while on or within 60 days of a

Proteasome inhibitor

- Bortezomib
- Carfilzomib
- Ixazomib

Immunomodulator

- Thalidomide
- Lenalidomide
- Pomalidomide

Anti-CD38 Monoclonal Antibody

- Daratumumab
- Isatuximab

So, where do we need to improve? Because patients do live a very long time. There's a lot of good treatments, but there is a subset of patients that have a little bit of a harder time in terms of responding to treatments, and this is where the majority of new treatments are being targeted. And this is the triple-class refractory multiple myeloma patient. And this group of patients is defined as having myeloma that no longer responds to the three most common classes of drugs, and those include proteasome inhibitors, which are bortezomib, carfilzomib, ixazomib; immunomodulating agents, so thalidomide, lenalidomide, and pomalidomide; and our anti-CD38 monoclonal antibodies, daratumumab and isatuximab.

Triple-Class Refractory: When All Else Fails FDA Approved

Chemotherapy	BCMA-Directed	XPO1-inhibitor	Mono-Abs	HDAC-inhibitor	Peptide drug conjugate
KD-PACE/VDP-PACE/VDR-PACE	Belantamab mafodotin	Selinexor	Isatuximab	Panobinostat	Melflufen
Cyclophosphamide	Ide-cel		Elotuzumab	Vorinostat*	
Melphalan					
Bendamustine*					

*Not FDA approved for MM

So, once all three of those drugs have stopped working, we call this type of myeloma triple-class refractory therapy; and there are now, thankfully, many, many FDA (U.S. Food and Drug Administration) approved drugs and treatments to target this type of myeloma. And you can see from this table there's a list of many of them. So, we can put them into many categories, traditional chemotherapy, and part of that is your melphalan or your transplant-based therapy. There's four-day infusions such as VDP-PACE. Then we have BCMA (B-cell maturation antigen)-directed therapies.

TRANSCRIPT

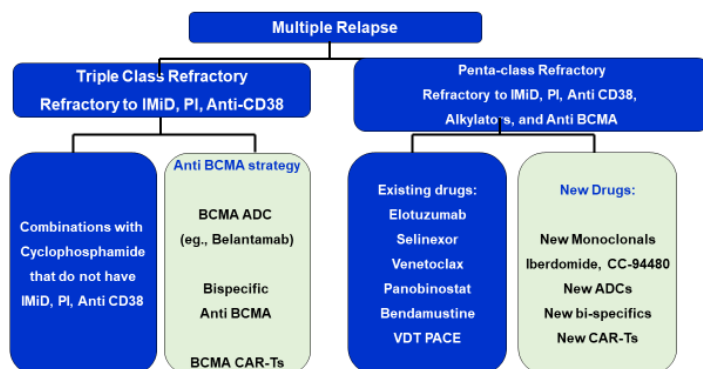
BCMA is a protein expressed on myeloma cells. I'll get into it a little more in detail, but we have belantamab, and we have Ide-cel. Ide-cel is a CAR (chimeric antigen receptor) T-cell therapy directed against the BCMA protein. We have an XPO1 (Exportin 1) inhibitor which is a drug called selinexor, and this drug works by prohibiting transport of cells, of proteins out of the myeloma cell. We have monoclonal antibodies. One of them is isatuximab and elotuzumab. We have HDAC (histone deacetylase) inhibitors, which target the DNA (deoxyribonucleic acid) of the cell. Those drugs are panobinostat and vorinostat. Vorinostat is not FDA approved for myeloma, but it can be used sometimes in this setting. And then we have a peptide drug conjugate, melflufen.

Triple Class Refractory: When All Else Fails Ongoing Clinical Trials

Monoclonal Antibodies and ADCs	CELMoDs/small molecule inhibitors	BiSpecifics	Cellular Therapies
TAK-079 (high-affinity CD38)	Iberdomide (cereblon E3 ligase) CCC-92480 (cereblon E3 ligase) Venetoclax (bcl-2)	BCMA x CD3: AMG-701 Teclistimab CC-93269 REGN5458 Elranatamab	Cilta-cel Orva-cel LCAR-B38M Lummicar-2 ALLO-715 Descartes-011 and -018
TAK-169 (CD38 fused with shiga-like toxin payload)			
TAK-573 (CD38 fused with IFN γ 2b)		GPRC5D x CD3 Talquetamab	

So, here are some not just FDA approved therapies for triple-class refractory myeloma, but we also have ongoing clinical trials; and these are very exciting drugs that are, some are in early phase development. Some are already in phase 2 and 3 trials, so closer to getting FDA approval. But we have newer monoclonal antibodies and antibody drug conjugates. We have CELMoDs (cereblon E3 ligase modulator), which are kind of the new class of immunomodulating drugs. We have bispecific antibodies which are drugs that bring the myeloma cell into close proximity of your natural, or your own body's, T cell or immune system cell to allow killing of the myeloma cell and stimulating of the immune system. And then we have newer cellular therapies or CAR T cell is an example of a cellular therapy that are being developed. So, we have newer CAR T cells, and we have CAR T cells with different targets, not just BCMA. And we're looking at some donor-derived CAR T cells, so we'll get into some of these.

Proposed Treatment Algorithm

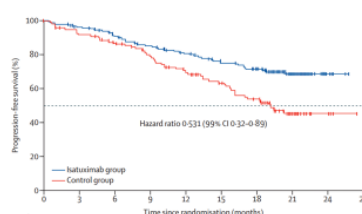
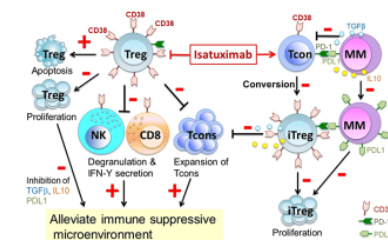


Rajkumar SV © 2020

So, right now there really is no specific treatment algorithm. There isn't an exact sequence of therapies that have to be followed. Once a patient has triple-class refractory myeloma, it really, the treatments are many-fold; and the decision of which treatment to use when, is based really on what patients have responded to in the past, what side effects those treatments give and what would be more likely to cause harm in that patient, and certain lifestyle things that we need to consider. So, it's a very difficult decision once somebody is triple-class refractory which treatment to use. But we are lucky that we have a lot of therapies at our disposal, and many patients with myeloma will end up using all of these drugs at some point in their life.

IKEMA – Isatuximab/car/dex vs car/dex

- Patients had 1-3 prior therapies
- Median 2 prior lines, 93% prior PI, 76% prior len, 20% refractory to IMiD and PI.
- Median PFS NR v 19.15 months, HR = 0.53, median f/u 20.7



Moreau P, et al. Lancet, 2021.

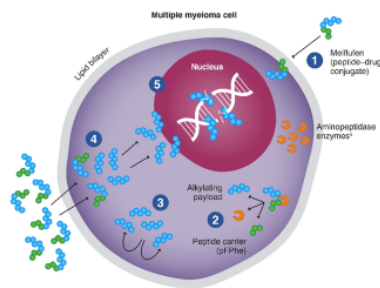
So, now we'll get into some of the therapies that are approved and that are being used, some of the newer therapies. So, this is a trial that was recently presented called IKEMA, and the IKEMA study used a drug called isatuximab, which is an anti-CD38 monoclonal antibody, similar to daratumumab, in combination with carfilzomib and dexamethasone. And half the patients received that combination, and half the patients received carfilzomib and dexamethasone alone. And we see that in patients who had only one to three prior treatments, the response rate was very good, and the patients' response

TRANSCRIPT

lasted a very long time. So, the triplet combination gave them a median progression-free survival of not reached, meaning in the follow-up period, which was about 20.7 months, half the patients still had not progressed, compared to half in the carfilzomib and dexamethasone arm. So, patients who received the carfilzomib and dexamethasone doublet in the median follow-up time of 20.7 months, the median progression-free survival was 19.5 months in the carfilzomib arm. So, the triplet combination had a much longer duration of response compared to the doublet.

OCEAN Study – Melphalan flufenamide +dex versus pom/dex

- 2-4 prior therapies, planned 495 patients, ongoing
- 16% v 12% triple class refractory, 51% and 48% previous ASCT



Median PFS

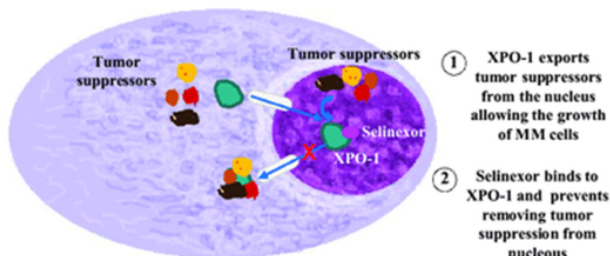
6.8 vs 4.9 months HR 0.79, p=0.03
No prior ASCT, 9.3 v 4.6 months HR 0.59, p<0.001.
In PRIOR ASCT, no difference in median PFS

Schjesvold, et al. IMW 2021, Abstract OAB50

This is another study, the OCEAN study that looked at melflufen plus dex versus pom and dex alone. This is a peptide drug conjugate. Recently, and just actually a few days ago, this drug was actually pulled. The drug company pulled it off the market because of a lack of overall survival benefit. So, this is brand new; we're going to skip this slide for now.

BOSTON Study – Selinexor/bortezomib/dex vs bortezomib/dex

- 1-3 prior therapies, N=402, 13 triple-class exposed, 6 triple-class refractory
- Median PFS 13.9 vs 9.5 months, HR 0.70



Groscki et al, Lancet 2020

But the next study I wanted to discuss was the BOSTON study which used the combination of selinexor, which is the XPO1 inhibitor in combination with bortezomib and dex – bortezomib is Velcade® – compared to bortezomib and dex alone. And you can see that we're also seeing much

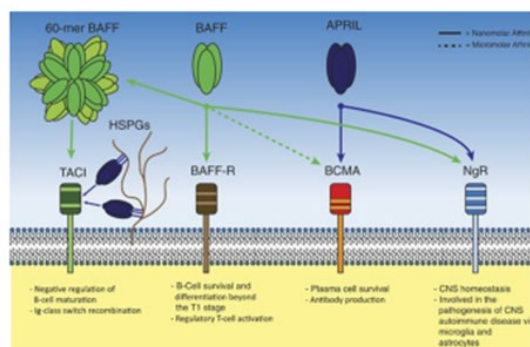
TRANSCRIPT

more durable responses, and this includes six triple-class refractory patients, so a much more heavily pretreated patient population had significantly longer duration of response compared to the doublet alone. And this seems to be the theme with multiple myeloma. When you use three drugs, you tend to have a longer duration of response and a deeper response compared to when you use two drugs alone.

Antibody Drug Conjugates

So, now we'll talk a little bit about a newer class of drugs. Many of them are being explored in clinical trials, called antibody drug conjugates.

BCMA – B-cell Maturation Antigen



Hengeveld et al *Bl Cancer J* 2015 ; Maus, June, *Clin Can Res* 2013

- Receptor for BAFF and APRIL
- Expressed on mature B cell subsets, plasma cells and plasmacytoid DCs
- Maintains plasma cell homeostasis.

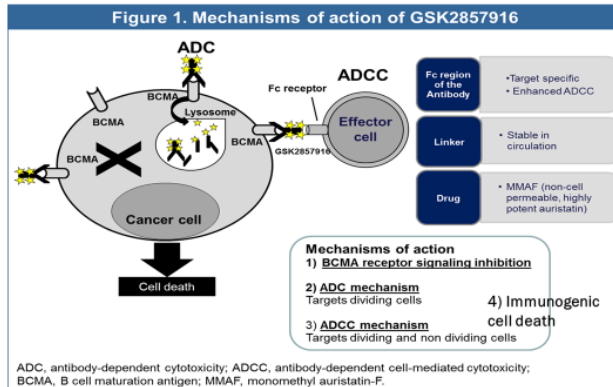
So, antibody drug conjugates have two pieces. The drug has two pieces. One of them attaches to the myeloma cells, and the other part injects a toxin into the myeloma cell, and that's how most of the antibody drug conjugates work.

So, one of them attacks myeloma through the BCMA protein, and you'll hear this a lot because a lot of the new therapies are directed against BCMA or B-cell maturation antigen. So more than 90% of myeloma cells express B-cell maturation antigen or this protein on the surface of the myeloma cell.

TRANSCRIPT

And what happens when one of these antibodies binds to BCMA, it triggers a cascade of protein signal to occur inside the cell; and it can cause cell death. And another thing that a lot of these antibodies do is recruit local T cells or local immune cells to flock to the area to help and destroy more cancer cells.

Belantamab Mafodotin

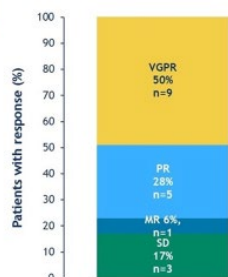


Anderson et al, AACR 2016, #CT034

So, belantamab mafodotin is a FDA-approved therapy. It's an infusion that's administered every three weeks. And what it does is it attaches to the myeloma cell through that BCMA protein, and then it injects a toxin into the cell. So, you get both direct cell killing and, as I said, it also recruits through a process called ADCC, antigen dependent cell-mediated cytotoxicity, other immune cells to the area and causes cell death.

Belantamab + bortezomib + dex DREAMM-6

Belamaf 2.5 mg/kg SINGLE + BorDex (n=18) [Part 1 + Part 2] preliminary best confirmed response data



In patients with ≥ 1 prior line of therapy, B-Vd treatment had an ORR of 78% (95% CI 52.4-93.6)

CBR was 83% (95% CI 58.6-96.4)

All patients had an evaluable response

50% of patients experienced VGPR

DoR is not yet reached

In patients with ≥ 1 prior line of therapy, Vd treatment demonstrated an ORR of 50%-63%¹⁻³

Nooka A, et al, ASCO, 2020.

And so, this drug has already been studied in many trials. One of them is called, actually almost all the studies that involve belantamab are called DREAMM, and they all have different numbers, 1, 2, 3, 4, 5, 6, depending on which combination it's studied with. So, this particular study was presented at a recent meeting, and it used the combination of belantamab with bortezomib or Velcade and

TRANSCRIPT

dexamethasone in patients that had more than one prior treatment. And you can see that it worked 78% of the time. That's what overall response rate means. It means how often does this combination work. And you can see that 50% of patients had what's called a VGPR (very good partial response), which is defined as a 90% reduction in tumor burden. And so, this was very impressive, and this is a drug combination that will likely be used.

DREAMM-5 Belantamab in combination with 5 different novel agents

Sub-study 1: Belamaf and Anti-OX40 GSK3174998
GSK3174998 is a humanized wild-type immunoglobulin G (IgG1) anti-OX40 agonistic monoclonal antibody (mAb) that binds to the co-stimulatory OX40 receptor, expressed primarily on activated CD4⁺ and CD8⁺ T cells. OX40 signalling promotes effector T-cell proliferation and survival, while blocking the suppressive function of T_{reg} cells, inducing a T-cell mediated immune response against cancer cells.
Combining belamaf with OX40 could increase anti-tumor activity via increased infiltration and activation of intra-tumor DCs, antigen-presenting T cells, and induce hallmarks of immunogenic cell death (ICD)¹ potentially leading to an adaptive immune response. This sub-study is now closed to accrual.

Sub-study 2: Belamaf and Feladlimab
Feladlimab (GSK3359609) is a humanized anti-ICOS IgG4 mAb selected for its nanomolar binding to, and agonist activity in, ICOS-expressing CD4⁺ and CD8⁺ effector T cells.²

Figure 3. Feladlimab mechanism of action

Holkova B A, et al, IMW 2021, Abstract ID 1072757.

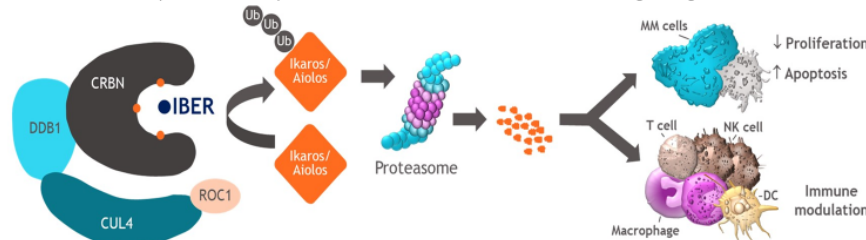
This is another study that was presented at another recent meeting, and basically the DREAMM-5 study is looking at combining belantamab with five different novel agents; and these are agents that have not yet been FDA approved. So, the point is that once you have a new drug approved and available, there's a myriad of combinations that can result in better efficacy and improve both survival and duration of remission.

CELMoDS and Small Molecule Inhibitors

The next category of drugs that are very exciting are the CELMoDS; and also, I'll talk about small molecule inhibitors.

Iberdomide

- Oral, potent novel CRBN E3 ligase modulator compound that co-opts Cereblon to enable enhanced degradation of target proteins including Ikaros and Aiolos
- In preclinical models, induces potent direct antimyeloma and immune-stimulatory activity
- Active in len- and pom-resistant myeloma cell lines and enhances cell mediated killing through immune stimulation.

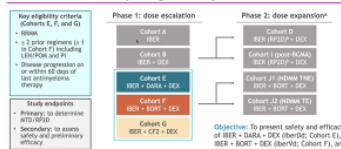


Matyskiela ME et al, J Med Chem 2018; 61:535-42.
Bjorklund CC, et al., Leukemia. 2020;34:1197-1201.

So, CELMoDS, there's a drug called iberdomide which is a pill; and it blocks a protein called cereblon, and this protein is involved in degrading protein. And we saw in laboratory studies that it really can very forcefully kill myeloma cells and also stimulate the immune system. And this works even in cells that were already resistant to lenalidomide, which is Revlimid® and pomalidomide or Pomalyst®. So, we know that it's a very potent mechanism of cell death and perhaps has activity in our triple-refractory patient.

Iberdomide in combination with daratumumab, bortezomib and carfilzomib

CC-220-MM-001: study design and objective



Prior therapies and refractory status

Characteristic	IberDd (N=43)	IberVd (N=25)	IberKd (N=9)
Prior therapies, median (range), n	4 (2-13)	5 (1-14)	4 (2-8)
ASCT, n (%)	34 (79.1)	22 (88.0) ^a	9 (100) ^a
IMiD agent, n (%)	43 (100)	25 (100)	9 (100)
POM	28 (65.1)	19 (76.0)	8 (88.9)
PI, n (%)	43 (100)	25 (100)	9 (100)
BORT	41 (95.3)	24 (96.0)	9 (100)
Anti-CD38 mAb, n (%)	21 (48.8)	23 (92.0)	9 (100)
IMiD-refractory, n (%)	41 (95.3)	20 (80.0)	8 (88.9)
POM	28 (65.1)	14 (56.0)	5 (55.6)
PI-refractory, n (%)	37 (86.0)	17 (68.0)	6 (66.7)
BORT	37 (86.0)	17 (68.0)	6 (66.7)
CFZ	25 (58.1)	9 (36.0)	5 (55.6)
Ixazomib	13 (30.2)	4 (16.0)	0
Anti-CD38 mAb-refractory, n (%)	16 (37.2)	20 (80.0)	7 (77.8)
Triple-class refractory, n (%)	14 (32.6)	12 (48.0)	5 (55.6)

More than one-third of patients in all 3 cohorts were triple-class refractory

	IberDd (N=43)	IberVd (N=25)	IberKd (N=9)
ORR	45.9%	56%	50%
Median DOR	NR	35.7 weeks	NR

RP2D 1.6 mg in IberDd cohort
Dose evaluation continues in IberVd and IberKd cohorts.

Lonial et al, IMW 2021. Abstract 1087033.

And so, iberdomide is now being examined in clinical studies in various combinations, and that is the theme here that you're going to see. Once you have an effective drug, then the next step is, "Well with which drugs does it work the best?" And that's called synergy. So, you can see when iberdomide was combined with daratumumab in patients that had multiple prior treatments, so fairly refractory patients, the response rate was 45.9%; and this is a small study, so this data is going to change as these trials enter phase 3. But, you know, we're seeing with dara there's a signal, with bortezomib there's a signal, 56% of them responded, and with carfilzomib there's a signal. And that again, very small number of patients; but when you first look at a drug, you have to look at more refractory

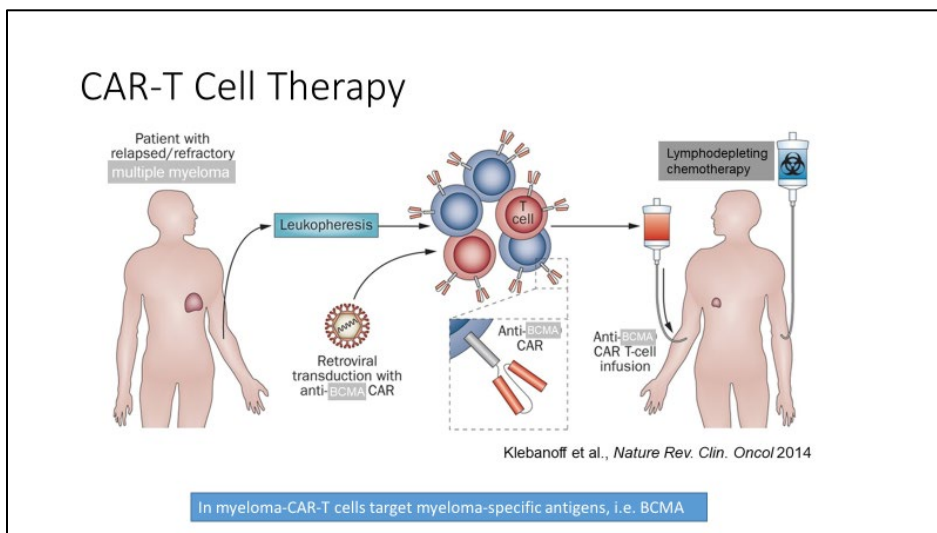
TRANSCRIPT

patients, more heavily pretreated patients to see if there's a signal. And once you see that there is good efficacy, then generally the drug is examined in earlier lines of therapy; and it often produces much more robust responses in earlier lines of therapy.

Cellular Therapies

So, next class that we'll talk about is the cellular therapy. Cellular therapies are treatments where they use either peripheral blood stem cells, so stem cells are your primitive cells that can differentiate into any immune cell or your mature T cells which are already cells that are in the blood, that have already matured into a T cell.

And the CAR T cells are part of that category. They're cellular therapies.

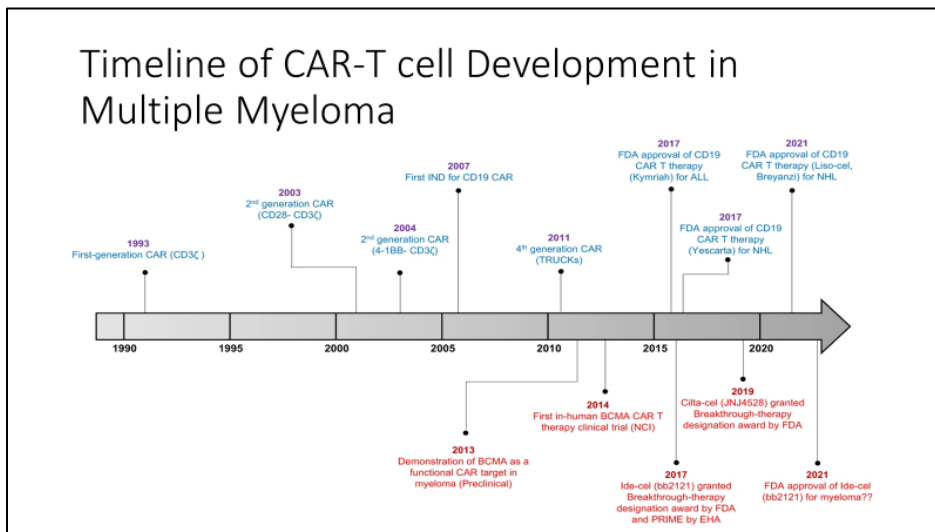


And I'm sure you've heard a lot about CAR T cells. They were originally approved for acute lymphocytic leukemia, ALL, in children. And then CAR T cells were later approved for lymphoma, non-Hodgkin's lymphoma. And this year we had our first CAR T-cell therapy approved for multiple myeloma. And the way the CAR T cells work is, the first step is a patient with myeloma, and right now

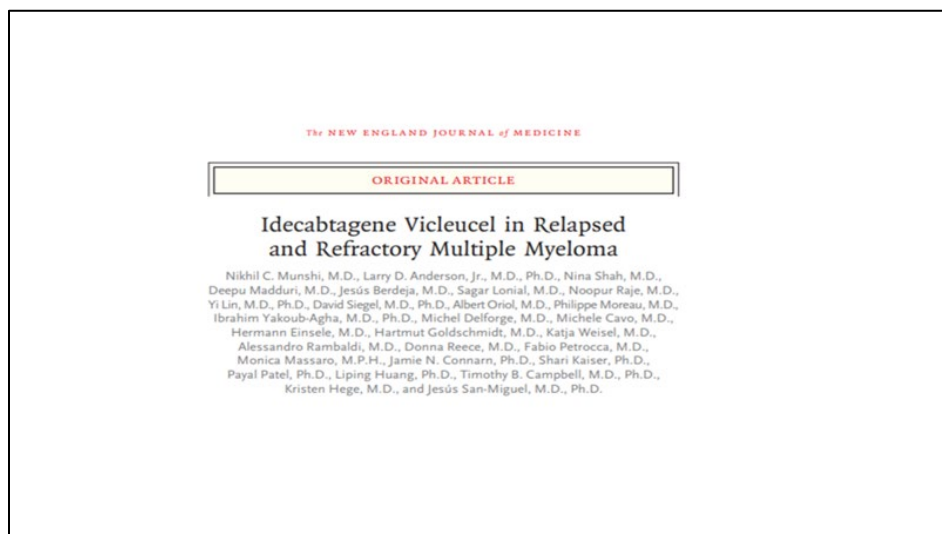
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it's approved for patients with relapsed-refractory myeloma that have failed four prior therapies. The patient's own T cells are pheresed, are removed from the body. They're harvested, and they are sent over to a laboratory where they are worked on for quite some time. And what happens is they put in a retroviral vector. They put in a virus that can't infect, but it can integrate into the DNA of the cell. And those CAR T cells, through that vector, will become chimeric antigen receptor expressing T cells. So, they will express a protein that will attack BCMA, and we talked about that before. BCMA is the receptor that lives on the myeloma cell. And now you have these CAR T cells, these genetically modified and engineered T cells, that will express an antibody that will hone directly to the myeloma cell.

And that process can take some time, generally three to four weeks, depending on which construct is used. And then once those cells are grown, they get reinfused into the patient; and generally, the patient will be in the hospital while those CAR T cells are infused for observation. And while those T cells are growing, most of the time patients have to be on some kind of myeloma-directed therapy called bridging therapy.

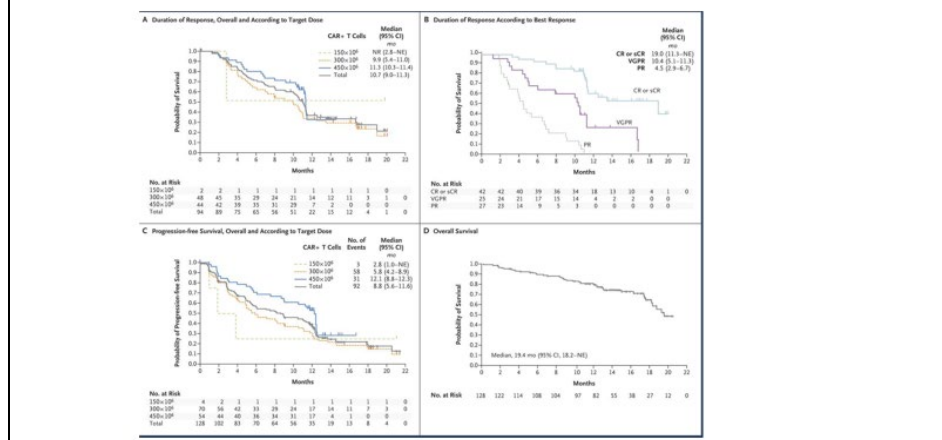


So, this is the timeline of CAR T-cell development in myeloma. In 1993 the first-generation CAR T cells were developed, and many centers have been developing them independently; and so, the trials continued until the FDA approval of ide-cel, and it's called bb2121, and that was this year in March.



So, this is *The New England Journal of Medicine* paper that resulted in FDA approval of this drug.

Ide-Cel – Median PFS 11.3 mos.



And you can see that this treatment in patients that had four or more prior therapies, so patients have really had very, very limited treatment options, at least at the time of this study. The median progression-free survival was 11.3 months, meaning the time in which the disease remains in remission before it returns was 11.3 months from infusion of CAR T.

Now patients who achieve a very deep remission at month 1, so patients who have a CR or complete remission right away can have a much longer progression-free survival. But this includes all patients with median PFS (progression-free survival).

2021 ASCO ANNUAL MEETING

8005. CILTACABTAGENE AUTOLEUCEL, A B-CELL MATURATION ANTIGEN-DIRECTED CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED RESULTS FROM CARTITUDE-1

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Primary Objectives:
Phase 1b: Safety and RP2D
Phase 2: Efficacy

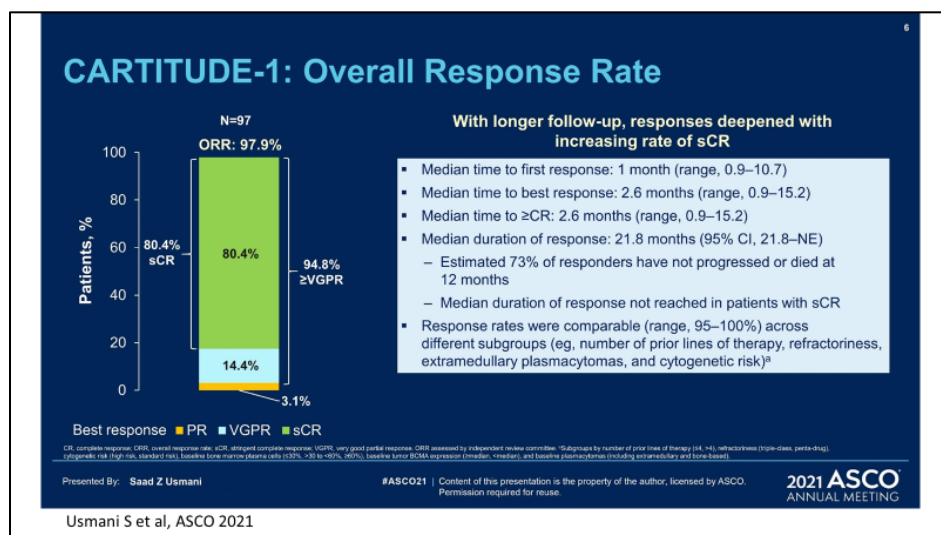
Key Eligibility:

- Progressive MM per IMWG criteria
- 3 or more prior lines of therapy OR double refractory
- Prior PI, IMiD, and anti-CD38
- ECOG PS 1 or better

Usmani S et al, ASCO 2021

Study Design:

So, this study, this is another CAR T cell that is, it's still in trials, and it's pretty much going to go for, hopefully, FDA approval in the very short term. This is called cilta-cel. It's another BCMA-directed CAR T cell, and this particular study looked at both safety, what is the right dose to give. And the second phase of the study looked at how efficacy is; how effective is the drug. And this included patients who had three or more lines of therapy or were double refractory.



And you can see that in this study, the overall response rate among 97 patients, was 97.9%. So, we don't know if this particular CAR T cell is going to be better than the ida-cel. We don't know because both trials involved two different patient populations. We can't compare apples to oranges. You know, the patients on this trial may have been less heavily pretreated, but in general we're seeing excellent rates of response. The rate of VGPR or a 90% reduction in disease burden was 14.4%. The median time for the patients to respond was one month, so we're seeing quick responses, and the median duration of response was 21.8 months.

Ide-Cel versus Cilta-Cel

CART	Ide-Cel	Cilta-Cel
Study Design	KarMMa-2 (phase 2)	CARTITUDE-1 (phase 1b/2)
Target	BCMA	BCMA
Patients, median age	n= 128, 61	n= 97, 61
Median prior lines	6 (3-6)	6 (3-8)
Triple-class/penta refractory	84%/26%	87.6%/42.3%
Tumor BCMA expression (≥50%)	85%	91.9%
CART target dose	150 – 450 × 10 ⁶ CAR T-cells	0.75 × 10 ⁶ CAR T-cells/kg
ORR at therapeutic dose	81% (450 × 10 ⁶)	97.9% (0.75 × 10 ⁶)
≥VGPR/≥CR/MRD rates	65%/39%/28%	94.8%/80.4%/57.7%
PFS/DOR	12.1 (8.8 -12.3)/11.3 (10.3 -11.4)	18-month PFS - 66%/DOR - 21.8 m
OS	19.4 mo (95% CI, 18.2–NE)	18-month OS - 80.9%
CRS (any Grade/≥Grade 3)	96%/6%	94.8%/5.4%
Median time to onset/duration of CRS	1 day (1-12)/5 days (1-63)	7 days (1-12)/4 days (1-97)
Neurotoxicity (any Grade/≥Grade 3)	18%/3%	20.6%/10.3%
Neutropenia (any Grade/≥Grade 3)	91%/89%	95.9%/94.8%
Anemia (any Grade/≥Grade 3)	70%/60%	81.4%/68%
Thrombocytopenia (any Grade/≥Grade 3)	63%/52%	79.4%/59.8%
Hypocalcemia	27%/8%	32%/3.1%
Hypophosphatemia (any Grade/≥Grade 3)	30%/16%	30.9%/7.2%

Nooka A, ASCO 2021.

So, again, it's hard to compare the two CAR T cells, but at least we can look at some of the similarities between the two trials so we can see that in both the ide-cel, that's the one that's already FDA approved, and the cilta-cell, that's the one that we'll have soon, hopefully, FDA approval. Similar rates of triple-class refractory myeloma, and then pent-up refractory means their disease has already become resistant to five different classes of drugs. So, the cilta-cel trial did have a higher number of penta-refractory patients, 42% compared to 26%.

It turns out that it doesn't matter if your myeloma highly expresses the BCMA protein. These treatments work regardless of BCMA expression, which is interesting. In the beginning, we didn't know when we first started doing these trials.

I want to also talk about something called CRS, cytokine release syndrome. Cytokine release syndrome is when those CAR T cells go a little bit haywire and activate the immune system a little bit too much, and then we can see some side effects like difficulty breathing, confusion, low blood pressure, high fevers, these types of events.

Sometimes they can be severe, and sometimes they're very, very mild. You can see that the severe CAR T cytokine release syndrome, which means grade 3 or above, occurred in 6% of patients who received ida-cel and 5.4% of patients who received cilta-cel. We do have ways to treat cytokine release syndrome, and those include a medication called tocilizumab which kind of dampers that immune response; and also, sometimes we will use dexamethasone, which is a steroid, to reduce that immune response. So, that's why patients have to be monitored in the hospital for about 14 days when getting their CAR T cells infused.

Novel CAR-T Cell Approaches

Trial Name	Sponsor	Phase	Antigen	Co-Signaling Domain	Transfer Method	Cell Source	Response
NCT03455972	Soochow University	1-2	CD19+ BCMA	OX40/CD28+ EGFRt	Lentiviral	autologous	ORR 100%
NCT04613557	Celyad	1	BCMA	NA	NA	Allogeneic - shRNA based elimination of TCR	NA
NCT04093596	Allogene	1	BCMA	NA	N/A	Allogeneic	ORR 60% at Dose-level 3

So, we know that the CAR T cells are effective, but as we saw, the disease does tend to come back in about one year. Usually depending on which trial, it's anywhere from 8 to 12 months on average. Some people can have much longer remission. Some people have shorter. But either way, we are trying to come up with new approaches of how to prolong remission time with these types of therapies.

So, we have a number of clinical trials that are ongoing. One of them involves not just targeting BCMA but another antigen called CD19. And then other trials are looking at using donor T cells, not the myeloma patient's T cells to see if we're going to get a more robust response and longer duration of remission.

Incremental Cost-effectiveness Thresholds for Coverage

Ide-Cel Cost Effective Analysis Key Findings: Incremental cost-effectiveness

- Between \$50,000 and \$150,000 per QALY is generally considered to be cost-effective in the US
 - Societal willingness to pay (~1-3x per capita GDP)
 - Individual WTP (~2x annual salary)
- UK: ~\$30,000/QALY
- Sweden: ~\$50,000/QALY
- Ide-cel
 - List Price: \$419,500 per infusion
 - Total cost: \$646,000
 - Life years gained: 1.5
 - Incremental cost-effectiveness ratio: \$319,000/QALY
 - Probabilistic sensitivity analysis
 - < \$50,000 / QALY: <1%
 - < \$100,000 / QALY: <1%
 - < \$150,000 / QALY: 3%

CONCLUSIONS:

- Ide-cel provides net clinical benefit over historical treatment, though uncertainty is large
- The therapy is **NOT** cost effective at current prices
 - Cost/QALY >> \$150,000
- Discounts from the list price of at least 37% are needed to approach reasonable willingness to pay thresholds in the US

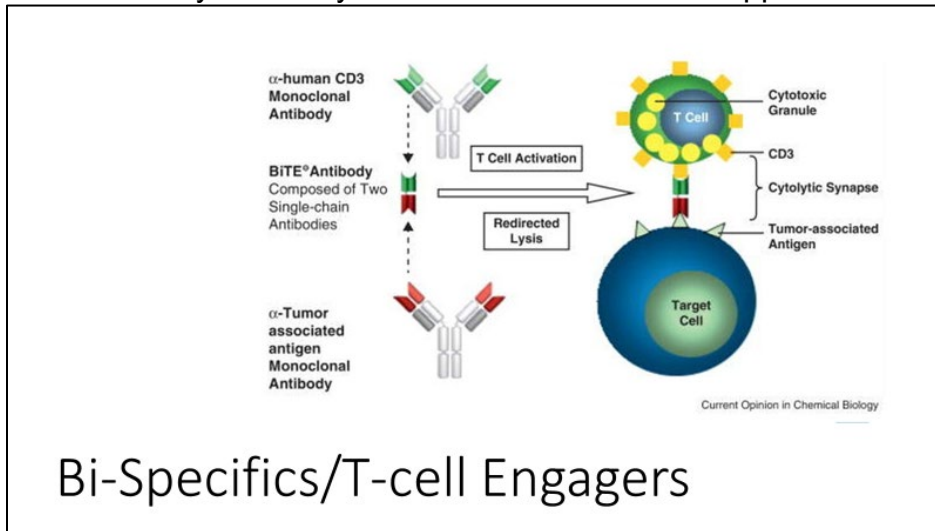
Tice JA. ASCO 2021.

So, the other thing that we have to think about, and myeloma, thankfully, I think this is a good thing, is the most expensive disease to treat because there's so many new drugs. That's a good thing. But at the end of the day, we do have some limitations; and we have to think about are these therapies cost effective? You know, are they providing a substantial benefit, not only in duration of life, living longer, but in terms of quality. And that's why we are looking at quality of life assessment and incremental

TRANSCRIPT

cost effectiveness thresholds, and there's ways of looking at this to see if these treatments are cost effective.

So, this particular study that was presented at ASCO (American Society of Clinical Oncology) showed that at the current time and at the current cost, this therapy may not be as cost effective as we think. And that's why we always have to have alternative approaches and newer ideas.



And that's what brings us to the bispecific T-cell engagers. And these work similarly to CAR T cells, except they are what we call off the shelf, ready-to-go therapy. You don't need to have T cells collected. You don't have to have your T cell growing in a lab and genetically modified in a lab. This is a treatment that can be prescribed and given right away. These drugs are not FDA approved. They're in clinical studies, and the way they work is similarly to the CAR T cells, they target a protein. Many of them target BCMA, and then they engage or bring into close proximity the patient's T cell so that the T cell can become activated and kill the myeloma cell.

BiTEs have potential advantages over CAR-T

- Off the shelf v time consuming production
- Precise dosing vs drug variability
- Broad range of specifics
- Improved tolerability with diminished rate of CRS/ICANS/hematotoxicity.
- Retreatment has been successful
- Deepest remission after 1- 3months (CAR -T >2 months for optimal response)

TRANSCRIPT

And there are some advantages of these BiTEs (bispecific T-cell engagers) over CAR T cells. So, as I said, it's a quick turnaround in terms of giving the drug. No production is required. The dose can be much more precise because with CAR T cells, sometimes after patients have had a lot, a lot of treatment, we are unable to manufacture the correct dose of CAR T cells because the T cells don't grow because they've had a lot of chemo. So much easier to dose this type of drug.

There's a very broad range of targets or specifics for these CAR T cells. Some of them have a reduced risk of cytokine release syndrome, which is the CRS. ICANS (immune effector cell-associated neurotoxicity syndrome) means the neurologic toxicity or the confusion-type side effects that we sometimes see with CAR T cells. Also, these drugs have shown that if you re-treat somebody after CAR T cell or after a BiTE, there can be success. And we see very quick remission, many of them, after one to three months. Whereas with CAR T, it may take a little bit longer to achieve an optimal deep response.

Bispecific Antibodies Summary

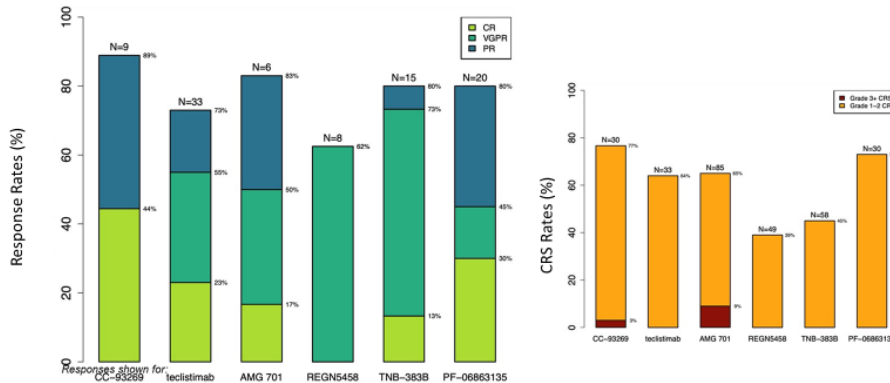
Bispecific	Teclistamab	Elranatamab	Talquetamab	AMG-701	CC-93269	REGN5458
Target	BCMA	BCMA	GPRC5D	BCMA	BCMA	BCMA
Treatment	Weekly SC	Weekly SC	Weekly SC	Weekly IV	Weekly IV	Weekly IV
Patients (N)	73	30	82	85	30	49
Prior lines	5	8	6	6	6	5
Triple-class refractory	79%	87%	99%	62%	90%	100%
ORR at therapeutic dose	65% (≥VGPR 58%)	83.3% (≥VGPR 66.7%)	70% (≥VGPR 60%)	83% (≥VGPR 50%)	88.9%	62.5%
Duration of Response	Median f/u 9 months – 80% continuing treatment	Not reached at 13 months	Not reached (7.2mos)	NR (6.5 months)	NR	6 months
CRS (Grade 1/2)	60%/15%	83.3%/16.7%	67%	27/28/9	76.7	39
ADA (immunogenicity)	1%	10.7%	12%			

So certainly, it's chronic therapy, so that's the downside of bispecifics compared to CAR T cell. CAR T cell can be one and done, and then some patients have a very long treatment-free period whereas bispecifics, you have to keep dosing them.

And there's so many that are being looked at. This table is showing us six different compounds. Many of them are subcutaneous or injection. Many of them are intravenous.

And you can see that these studies still have a small number of patients, some more than others, but some have only treated 30. Some up to 82, 85. Most of the patients enrolled on these trials are triple-class refractory, meaning they've already exhausted the three most common classes of drugs. And despite that, we're seeing substantial rates of response, so anywhere between 65 and 88.9% response rates at the therapeutic dose. Median duration of response, where it says not reached, that means patients are still responding. So, and then cytokine release syndrome, we're seeing a lower rate. So, grade 1 and 2 means mild, 60% all the way to 80%.

Promising Responses in Triple-Class Exposed Disease

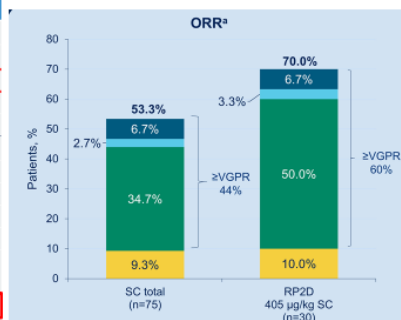


So, there are definitely promising responses for these molecules in patients who have triple-class refractory disease. You can see that this bar graph shows the response rate of all of the different molecules, and the cytokine release syndrome rate. So, we're seeing anywhere from above 65 to 89, 90% response rates.

Talquetemab: GPRC5D x CD3 Bispecific

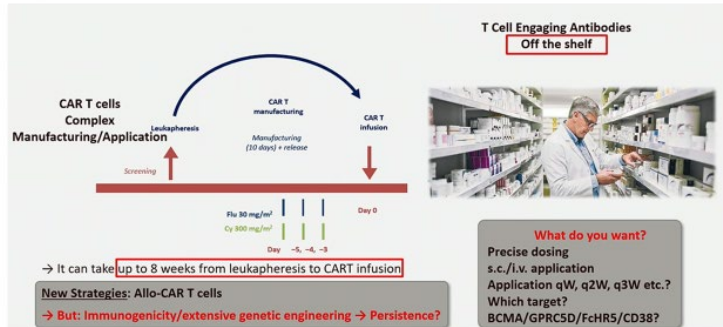
Characteristic	SC Total n=82	RP2D (405 µg/kg SC QW) ^a n=30
Prior lines of therapy, n, median (range)	6.0 (2–17)	6.0 (2–14)
Exposure status, n (%)		
Prior BCMA therapy ^a	20 (24)	8 (27)
Triple-class ^f	81 (99)	30 (100)
Penta-drug ^g	64 (78)	24 (80)
Refractory status, n (%)		
PI ^h	69 (84)	25 (83)
Carfilzomib	54 (66)	19 (63)
IMiD ⁱ	76 (93)	28 (93)
Pomalidomide	67 (82)	26 (87)
Anti-CD38 mAb ^j	77 (94)	30 (100)
BCMA ^e	14 (17)	5 (16)
Triple-class ^f	62 (76)	23 (77)
Penta-drug ^g	23 (28)	6 (20)
To last line of therapy	69 (84)	26 (87)

Berdeja J, et al, ASCO 2021.



This is one of the BiTES or bispecific T-cell engagers, talquetemab, and this one targets a protein, not BCMA, a different protein. It has a very long name. It's called the GPRC5D, and CD3 is the T cell receptor. So, it brings that GPRC5D protein, which is located on the myeloma cell next to the T cell and allows for cell killing. And so, this study is showing that 24% of patients or 27% in the patients who had the therapeutic dose had already had a BCMA therapy. And despite that, we're seeing an overall response rate on this bar graph of 70.9% in the patients who received the therapeutic dose. So, we're seeing a very promising treatment.

BiTes versus CAR-T



Einsele H, IMW 2021.

And, again, looking at BiTE versus the CAR T cell, the CAR T cells do take a while to manufacture. However, once you receive them, you have a long treatment-free period. The BiTE, you can give them right away, but then you're getting weekly or every two- to three-week treatment.

BiTes versus CAR-T

Efficacy/Toxicity

	CAR T	Bispecifics
ORR	80 - 100 %	>60 - 83 %
CR	40 - 85 %	13 - 50 %
PFS	> 1 - 1,5 yrs	> 6 mo.
CRS Gr. 3	3 - 6 %	0 - 3 %
ICANS Gr. 3	3 - 10 %	0 - 1 %

Following CAR T Cell Therapy grade 3 cytopenia can last for of 2-3 months !!

→ Hematotoxicity clearly less frequent/less severe/shorter after BiTEs vs CART cells

Munshi N et al. NEJM 2012; Madduri D et al. ASH 2020 #177; Garfall AL et al. ASH 2020 #180; Lesokhin AM et al. ASH 2020 #3206; Madduri D et al. ASH 2020 #291; Rodriguez et al. ASH 2020 #293; Chari A et al. ASH 2020 #290; Cohen AD et al. ASH 2020 #292; Harrison S et al. ASH 2020 #181; Costello C et al. ASH 2020 #134; Kumar et al. ASH 2020 #133; Piasecki et al. ASH 2020 #2350; Colonna et al. ASH 2020 #2358.

And then this is comparing among the CAR T and the bispecifics the response rate. So, the CAR T cells may be a little bit more effective, 80 to 100% rate of response compared to 60 to 83. Rates of complete remission tend to be a little bit higher. Again, the bispecifics are still early, early in clinical trials, so things can change as we get more advanced clinical trials and more data on a higher number of patients. And then cytokine release syndrome appears severe. Grade 3 means severe. Cytokine release syndrome, 3 to 6% with CAR T cells and 0 to 3% in bispecifics. And ICANS means neurologic cytokine release syndrome. Severe 3 to 10% with CAR T versus 0 to 1% with bispecifics.

Goals for Treatment for Triple Refractory Myeloma

- Improve symptoms
- Obtain a deep response
- Use your best therapy rather than reserve for later
- Consider Clinical Trials

So, to summarize our goals for patients with triple-refractory myeloma, the goal, you know, obviously, we want to first improve systems for our patients that may have bone disease or beyond dialysis, have impending kidney failure or have anemia that's making them short of breath. The first goal is get the disease burden down to improve symptoms. The deeper the response we can achieve, the more disease we can get rid of, the better. Usually that translates into a longer duration of response. And the philosophy really is use the best therapy earlier on, not save the best for later. Use your best treatments early on, get at those heterogeneous clones, and I always tell patients consider clinical trials, even in the earlier lines of therapy because the FDA-approved treatment you can get at any time. Clinical trials, you have to be in good shape, have good organ function, have a slower relapse, and that may not be the case later on in the disease course. If there's a good clinical trial that is potentially a possibility, even in earlier lines of therapy, it's a good idea to consider it.

So, we're going to change our focus for a few minutes and talk about the COVID-19 (coronavirus disease 2019) vaccination in patients with multiple myeloma.

COVID19 and MM Vaccination

From the Blood Journals | Multiple Myeloma | News | Written in Blood

Older Patients With Myeloma May Have Suboptimal Response to COVID-19 Vaccination

TUESDAY, JUNE 1, 2021

The present study shows that patients with MM seem to mount a less effective immune response to vaccination against COVID-19.

Terpos E, Trougakos IP, Gavriatopoulou M, et al. Low neutralizing antibody responses against SARS-CoV-2 in elderly myeloma patients after the first BNT162b2 vaccine dose [published online ahead of print, 2021 Apr 16] *Blood*. doi: 10.1182/blood.2021011904.

TRANSCRIPT

So, in general we know that patients with myeloma have trouble developing or mounting an immune response to all vaccines, and this has also been observed with the COVID vaccine. In particular, older patients who are on certain types of chemotherapy may have a suboptimal response to the COVID vaccine. And we've seen that antibody titers decrease month after month in our myeloma patients.

COVID 19 Vaccination in Patients with Multiple Myeloma

Should I get the COVID-19 vaccine?

The IMF strongly recommends that patients with multiple myeloma (MM), smoldering multiple myeloma (SMM), or monoclonal gammopathy of undetermined significance (MGUS) receive a COVID-19 vaccination with the Pfizer or MODERNA vaccines, whichever is available. These vaccines offer excellent benefits, and in general, have very limited and brief side effects or toxicities. As of now, the efficacy of these vaccines far outweighs any toxicity concerns.

*The IMF is very pleased to note the full approval of the Pfizer-BioNTech COVID-19 vaccine. This reflects what has been both remarkable efficacy plus and an excellent safety profile. This full approval versus the prior Emergency Use Authorization (EUA) will encourage those with vaccine hesitancy to proceed with vaccination. In addition, doctors now have flexibility to prescribe booster shots as appropriate. In the workplace, many more vaccine mandates are now anticipated which can definitely improve safety overall.

How should I make a decision about getting the vaccine?

The decision to take the COVID-19 vaccine is best made with your doctor. PLEASE discuss the planning for vaccination with your doctor. It is possible your doctor may have additional questions or concerns depending upon your exact situation.

Do I have to get the same vaccine for both shots?

Generally speaking, most people will indeed receive the planned two-step dosing for their vaccination with the Pfizer or MODERNA vaccines. If it is feasible to take the same brand of the vaccine for both doses, then do so. If not, a slight delay to wait for the same brand of vaccine for your second dose is acceptable. Finally, the use of alternate brand of vaccine can be considered if availability is an issue, but please discuss this with your doctor.

International Myeloma Foundation, <https://www.myeloma.org/covid-19-vaccination-myeloma-patients>, Sept 29, 2021.

Certain monoclonal antibody therapy can impair the ability of patients to make antibodies.

So, everybody with multiple myeloma should get the vaccine. Unless there is a particular contraindication or allergy to the vaccine, the recommendation is please proceed with the vaccine; and that includes the third booster shot.

International Myeloma Society COVID-19 and MM Data

- Patients with multiple myeloma are at increased risk of severe infection and higher mortality.
- All patients with myeloma or precursor disease (MGUS and smoldering myeloma) and AL amyloid should be candidates for COVID-19 vaccine and booster.
- Vaccine induced immune response may decrease infection rate and decrease severity of illness.

So, the International Myeloma Society is recommending all patients with MGUS, as well as smoldering, to receive the COVID-19 vaccine and booster, and AL amyloid patients. Even if antibody

TRANSCRIPT

response is not achieved, there is still some evidence that we see a T-cell response, and that offers some protection against severe COVID infection.

Timing of Vaccine

- If patient's myeloma is stable, and holding therapy is not a concern, then the vaccine should be administered between the courses of therapy.
- An ideal situation would be to hold treatment 7 days before 1st dose to 7 days after 2nd dose. This would mean holding MM therapy for around 5-6 weeks, depending upon type of vaccine and the interval between doses.
- Keeping importance of maintaining MM therapy in mind, when such long pause is not possible, consider giving 1st dose of the vaccine 2-7 days after the last dose of MM therapy and up to 10 days before restarting MM therapy, with 2nd vaccination given at the appropriate interval.
- Wait 3 months after auto-SCT.
- Ideal antibody testing is 7-21 days after 2nd vaccination.

WWW.Myeloma.Org

So, timing of vaccine is really a patient-by-patient decision. Ideally, therapy should not be given as close as possible to the vaccine. You want to be as far away from your chemotherapy as possible. That's not always possible, and in that situation the discussion should be held between the physician and the patient. So, after transplant, ideally, patients should wait three months; and then when to check antibodies, ideally, it should be checked 7 to 21 days after the second vaccine.

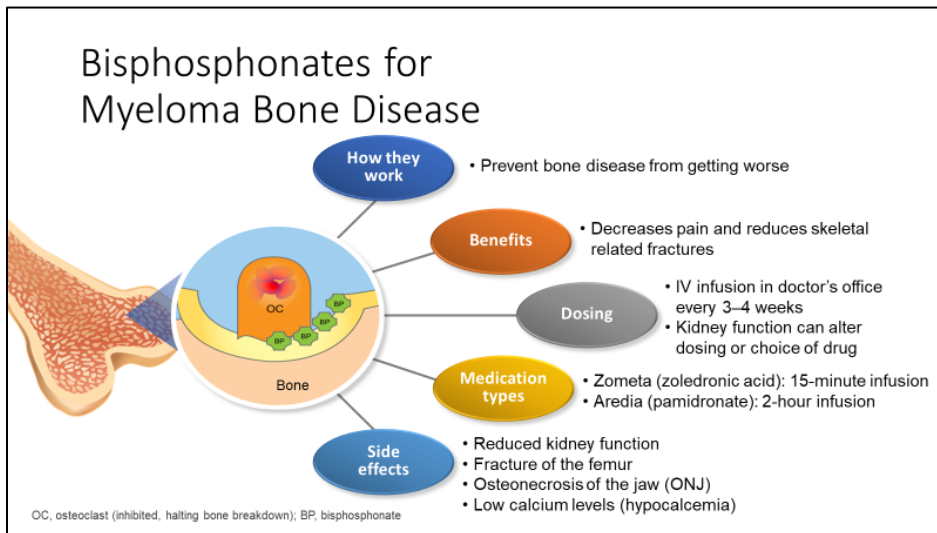
Supportive Care/Quality of Life

Okay, we're going to switch to our last section, and in myeloma, quality of life is so important because patients are on some kind of chemotherapy for most of their life. And since we are not a disease, like some diseases, for example, non-Hodgkin's lymphoma where you get your four to six months of chemo and you're done, that's not the case in myeloma. In myeloma, treatment is continuous, really forever. And so, we need to find regimens that are going to work with our life, not that are going to

TRANSCRIPT

make life not worth living. Quality of life is very, very important. Otherwise, why are we even doing the treatment?

The goal of treatment is not to make the M (monoclonal) spike low, to make the free kappa low. It's to make the patient feel better and live a good life and a long life.



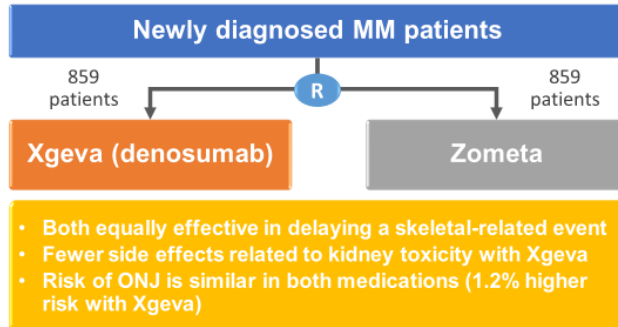
And so, I really encourage you to bring up all of these concerns to your physician because all treatment can be adjusted in order to prevent issues with quality of life and help life be a little more pleasant.

So, the first and most important piece of treating myeloma is bone, bone-strengthening medication. Myeloma, before we had bisphosphonates, was a very difficult disease to treat because patients really had poor quality of life. They would fracture bones very, very easily. They were not able to participate in many, many things.

So, any patient who has osteopenia or osteoporosis, even without lytic lesions, should be on bone-supportive care. And certainly, anyone who's had a lytic lesion or a plasmacytoma should be on bone support, and those include zoledronic acid more commonly and Aredia (pamidronate disodium), which are your bisphosphonates, and then we have a new drug which is a drug that inhibits a protein called RANK (receptor activator of nuclear factor- κ B) ligands, and that's called denosumab or Xgeva® (denosumab). The major risks of these drugs are osteonecrosis of the jaw, and that is basically when you can have an infection in the jaw that doesn't heal. And if somebody has poor dentition or needs to get an extraction, the risk of osteonecrosis increases. So, we encourage patients to have regular dental follow-up.

Patients should also have vitamin D and calcium levels checked prior to administration of these drugs because they can lower the calcium level in the blood and cause some side effects from that.

Newly Approved Xgeva (denosumab) for Bone Loss



Raje NS et al. *J Clin Oncol*. 2017;35: Abstract 8005.
Terpos E et al. *Haematologica*. 2017;102: Abstract 5782.

And these drugs are given continuously on a monthly or every three-month basis, depending on which one you're getting.

So, this is the new, it's not new anymore, but in 2017, this drug was approved for multiple myeloma, denosumab. It's an injection, and this study compared newly diagnosed myeloma patients. Half got Xgeva, half received Zometa® (zoledronic acid), and it looked like both were equally effective in delaying a skeletal-related event. The Xgeva though did have less kidney-related side effects. So, anyone who has high levels of protein in the urine or kidney dysfunction really should be receiving denosumab. The risk of osteonecrosis of the jaw was similar, maybe slightly higher in the Xgeva arm.

Reducing the Risk of ONJ: Oral Health Recommendations

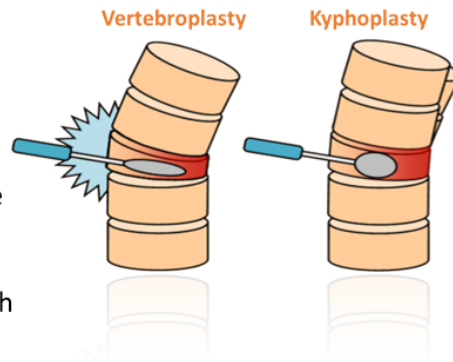
- Complete major dental work before beginning bisphosphonate therapy
- Practice good oral hygiene
- Schedule regular dental visits
- Let your dentist know that you are receiving bisphosphonates
- Keep your doctor informed of dental issues/need for dental work
- Be attentive! ONJ seems to be related to the length of time patients are on bisphosphonates



So how do we reduce risk of osteonecrosis? Always go to the dentist regularly. Your dental provider should be communicating with your oncologist if there's any invasive dental work that needs to be done. If something has to be extracted, a tooth has to be extracted, in general, it should be extracted if there's an abscess; but the patient's physician and dentist need to have a conversation.

Orthopedic Procedures to Stabilize the Spine

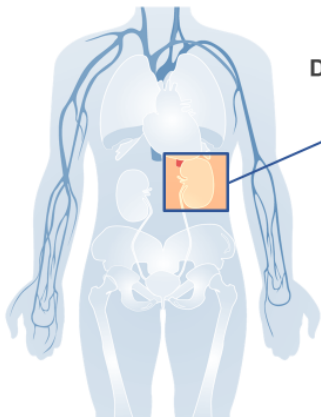
- Minimally invasive procedures
- Can be performed without hospitalization
- Small incision
- Cement filler stabilizes bone
- Potential for relatively rapid symptom relief (approximately 1 month with kyphoplasty)



Other ways of including quality of life, a lot of our myeloma patients have vertebral compression fractures, meaning the bones in the spine become so weak that they collapse on one another. And that can be extremely painful. Sometimes a patient can have a pain radiating from the back all the way to the front, and there's a procedure that's minimally invasive. It's a routine procedure. Usually, it doesn't require an overnight stay in the hospital. It's called kyphoplasty, and what they do is they inject cement into the vertebral space to open up those vertebrae, allow the nerves to have some relief, and often patients feel instant relief maybe shortly thereafter. So that's a very important option for patients with pain.

Effects of Myeloma:

Decreased Kidney Function




- Detection
 - Decreased amount of urine
 - Increase in creatinine and other proteins
- Other causes beside myeloma
 - Hypertension
 - Diabetes
 - Some medications
 - Dehydration
- Treatment
 - Fluids
 - Avoid nonsteroidal anti-inflammatory drugs such as Aleve, Advil/Motrin
 - Plasmapheresis
 - Treat other causes
 - Dialysis (severe)

What about kidneys? As we said in the very beginning, patients with myeloma always are at risk for developing problems with kidney function, so the myeloma provider should be checking regularly a 24-hour urine, so checks for protein. Even if you don't have protein in the beginning, you could develop it later in the course of disease. So, we should always be screening for myeloma-related kidney disease. All the other causes of kidney disease should be controlled as much as possible – high blood pressure, diabetes should be under control as much as possible. Avoid medications that

TRANSCRIPT

can exacerbate kidney function, such as NSAIDs, Motrin®, Aleve®, Advil®, ibuprofen; and, you know, always drink a lot of water. Patients should not receive intravenous contrast if they're having a CAT (computed axial tomography test) scan or, if they need it, it should at least be a conversation between the doctor ordering the test and the myeloma doctor.

Side Effects of Commonly Used Treatments: Velcade



Don't forget to discuss side effects with your provider!

Peripheral Neuropathy

Potential causes

- Monoclonal protein deposits on nerves
- Previous use of: Velcade, Thalidomide, Vincristine, melphalan
- Vitamin deficiency

Signs/Symptoms

- Weakness
- Numbness/tingling
- Burning
- Muscle cramping


Treatment

- Proper foot care/support
- Treat underlying cause
- Medications: oral and topical
- Physical therapy
- Potential neurology consult for further evaluation and treatment
- Dose schedule modifications!

And then we also have to think about our own treatments and what side effects they prevent. So peripheral neuropathy, numbness, and tingling. Sometimes it can exacerbate into burning, pain, muscle cramping. Sometimes it's worse at night. These types of side effects do require dose modifications or dose reductions in treatments. Some treatments need to be completely held or discontinued if you develop these symptoms.

There are treatments to help control neuropathy, but usually those treatments are temporizing. They're not solving the problem. They're just kind of subduing or making those symptoms better. There's medications. Physical therapy also tends to help, foot massage, proper shoes; so, this is a discussion that needs to be held.

Side Effects of Commonly Used Treatments: Lenalidomide (Revlimid)

Fatigue	Diarrhea	Muscle cramps	Rash
 <ul style="list-style-type: none"> • Stay active: exercise, exercise, exercise! • Healthy, well-balanced diet • Stay hydrated • Healthy sleep habits 	 <ul style="list-style-type: none"> • Increase fluids • Fiber-binding agents: Metamucil • Anti-diarrheal medications: Imodium, Cholestyramine • Diet management 	 <ul style="list-style-type: none"> • Tonic water • Increase hydration • Stretching/massage • Assess for other causes (electrolytes, low calcium) • Decrease dose 	 <ul style="list-style-type: none"> • Antihistamines: loratadine, cetirizine, Benadryl • Over-the-counter anti-itch creams – hydrocortisone or Benadryl • Potential referral to dermatology

Don't forget to discuss side effects with your provider!


TRANSCRIPT

And then lenalidomide is a common drug that we use. It's one of our backbones of therapy for myeloma. Some people are on it long term for maintenance. And this drug can have a lot of side effects. Fatigue is a very common side effect, and this is the type of fatigue that does not improve with rest. So, patients really should be staying active. Natural sunlight can help with the fatigue. Routine exercise, getting outside, eating a well-balanced diet. Diarrhea can occur. A lot of patients will get diarrhea, and this usually occurs after the sixth, seventh, eighth month. Muscle cramps, so please drink a lot of water, and a rash is a common side effect; and that can be managed with antihistamines, creams sometimes. Revlimid® does have to be stopped with the rash.

Side Effects of Commonly Used Treatments: Carfilzomib (Kyprolis)


- Common side effects**
 - Fatigue
 - In minority of patients: trouble breathing or shortness of breath, drop in blood counts
- Infrequently observed but potentially serious side effects**
 - Concerns: heart and lung toxicities
 - Side effects: reversible and manageable
- Signs to watch for**
 - Shortness of breath, difficulty breathing
 - Chest pain
 - Elevated blood pressure
 - Headache
- Treatment**
 - Manage blood pressure: low sodium diet, BP control
 - Heart evaluation: EKG and echocardiogram
 - Lung evaluation: Pulmonary function testing
 - Dose changes

Don't forget to discuss side effects with your provider!



Another common therapy is carfilzomib or Kyprolis®. Some patients can have shortness of breath or a high blood pressure with this drug, so we should always be checking a baseline echocardiogram, which is a heart test, before the therapy is initiated. And if anybody has shortness of breath, that really has to be evaluated; and the blood pressure has to be carefully managed throughout treatment.

Side Effects of Commonly Used Treatments: Daratumumab (Darzalex)








- Infusion-related reactions
- Fatigue
- Nausea
- Back pain
- Fever
- Changes in blood counts (anemia, thrombocytopenia, neutropenia)

TRANSCRIPT

Daratumumab is another commonly used therapy. It's given now most commonly as an injection, but we have to watch for infusion-related reaction; and that usually involves high or low blood pressure, itchy skin, shortness of breath. Could have a fever, and it usually happens within the first infusion or injection and often with the second. But after that, it's much less common. Also, this therapy can cause a higher frequency of fatigue and upper respiratory infections.

Side Effects of Commonly Used Treatments: Steroids (Dexamethasone)

Insomnia	Fluid retention	Mood changes	Dyspepsia–heartburn	Elevation in glucose
				
<ul style="list-style-type: none">• Healthy sleep habits• Timing• Medication to assist with sleeping as needed	<ul style="list-style-type: none">• Monitor for swelling of extremities and “puffy” face• Monitor weight changes/gain• Reduce dose	<ul style="list-style-type: none">• Irritable, anxiety, difficulty concentrating• Severe cases → depression, euphoria	<ul style="list-style-type: none">• Dietary modifications (spicy, acidic foods)• Avoid NSAIDs• Acid-blocking medications• Take steroid with food; use enteric-coated aspirin with food	<ul style="list-style-type: none">• Monitor glucose and refer/treat as needed

So, it's important that patients stay hydrated, get good sleep, monitor for mood because all of the treatments that we use often include dexamethasone (dex), which is a steroid. And that drug can have the most irritable and annoying short-term side effects and also long-term side effects. So, short-term side effects include irritability, weight gain, insomnia. Then you get very, very tired on your withdrawal days. So, for two days, you may have an elevation in mood and energy, and then two days after that a crash. And then long-term side effects of dex include high blood sugar, diabetes, weight gain, muscle shrinking, so atrophy of muscles. So, it's very important to keep exercising, keep active, try to get good sleep when you can. Warn your family that you may have some mood symptoms.

Lifestyle Enhancements

- Eat a well-balanced diet
- Get more exercise
- Regular sleep/rest periods
- Decrease alcohol consumption
- Give up tobacco
- Minimize or eliminate stress
- Take care of your emotional/mental well-being as well as your physical health!



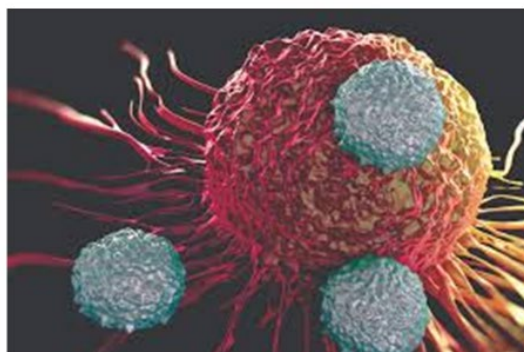
OPTIMISTIC OUTLOOK!

TRANSCRIPT

And in general, myeloma patients really need to take good care of their bodies – eat healthy, sleep, reduce alcohol. It's dehydrating, and it can affect the kidney function. Stop smoking, reduce stress. Say no when you can't do something, and really care for yourself emotionally and mentally. And it's also important to have an optimistic outlook and to have hope because really, we have a lot, a lot of new therapies. We have a lot of ways of controlling for side effects and managing side effects, and we really aim to have our patients live very long and very good quality lives.

Thank you!

Questions??



And with that I will leave you. I'm sure there's going to be a lot of questions, so I'll turn it back to our moderator. Thank you.

QUESTION-AND-ANSWER SESSION

Lizette Figueroa-Rivera, MA

Thank you so much, Dr. Biran, for volunteering your time with us today to update us on the treatments for myeloma. It's now time for our Question-and-Answer portion of our program. For everyone's benefit, please keep your questions general in nature without many personal details so Dr. Biran can provide answers that are general in nature.

Lizette Figueroa-Rivera, MA

Thank you. We'll take the first question from our web audience. Dr. Tom asks, "Can you please clarify what triple refractory myeloma is? Just because someone is on a third or a fourth line of chemotherapy, does that mean they are triple refractory?"

Noa Biran, MD

That's a great question. The answer is no, not necessarily. Triple refractory means that their myeloma progressed while on or within very close proximity to all three of those classes of drugs. So, if you've been on, for example, the combination of Velcade-Rev[limid]-dex and then your tumor markers went up while you were on it, and then you went on a combination of dara[tumumab]-pom[alidomide]-dex, and your tumor markers went up on that, then, yes, you are triple refractory because we know that both Velcade stopped working, Revlimid (lenalidomide) stopped working and dara stopped working. So, it really depends on which treatments you were on and when the myeloma markers started to go up or when you met the criteria for progression of disease. You know, just because you've had four prior therapies doesn't mean that your triple class refractory.

Lizette Figueroa-Rivera, MA

Thank you. And our next question comes from Taylor. Taylor is asking, "If you have failed a treatment using a combination with daratumumab, can you use a new treatment plan that still includes dara?"

Noa Biran, MD

Absolutely. And that's what we call synergy. If daratumumab stops working and then, for example, dara-Rev-dex stops working, sometimes if you switch it to dara-car-dex or, hopefully, with one of these novel agents, dara-belantamab-dex or dara-selinexor-dex, you can still have a response. So, drugs can still work when you change the partner.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from our phone audience, please.

Operator

Your first question is from Donna in Arizona.

Donna in Arizona

Yes. Hi doctor.

Noa Biran, MD

Hi.

Donna from Arizona

I'm getting ready to start Blenrep (belantamab mafodotin-blmf), and I just wanted to get your comments on the experience with that medication and if you have any tips for patients starting that drug.

Noa Biran, MD

Yeah. So certainly, the efficacy has been proven, so I think there's a good rate of response, a good chance that it's going to work. In our experience, the side effects are what we call keratopathy, which means eye issues. You can have dry eyes, irritable eyes. Sometimes cysts are found inside of the eye and so it's required by the law for you to have eye exams prior to each dose of treatment. Usually, that may not happen within the first one or two doses of the drug, but almost everybody by the third dose does have some ocular toxicity. And so, I would just encourage you to let your doctors know if you're experiencing any of those symptoms.

The other thing we may see is the platelet count can drop, and your treatment team will be monitoring for low platelets. So, just be careful. Let us know, let your treatment team know if you have any bleeding or bruising or anything like that. But otherwise, patients tend to feel well on the drug.

Lizette Figueroa-Rivera, MA

Thank you. And our next question comes from Willard. Willard asks, "I've been on maintenance Revlimid for about 18 months. Does Revlimid suppress the immune system?"

Noa Biran, MD

So certainly, it can in many ways. Revlimid does cause what we call bone marrow suppression, which means that it lowers your white count, your red cells, and your platelets. Sometimes it lowers your white count to a dangerous level. In particular, the neutrophil count is what we look at and those neutrophils really should be above one. If they're not, then the dose of Revlimid may have to be adjusted. Every patient who is on Revlimid should be careful of infection. Avoid large crowds, avoid shaking hands. Now, in the COVID era, that's even more pronounced than kind of our myeloma patients have been taking COVID precautions even before COVID. So, yes, you have to be careful with a suppressed immune system. You are predisposed to getting infections.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from our telephone audience, please.

Operator

Your next question is from Mike in Maine.

Mike in Maine

Yes. My question is the presentation said to reduce alcoholic consumption, and I've heard that multiple times. What I don't understand is like, the past year, I probably only had a couple servings of alcohol and I'm trying to figure out is it possible to, you know, is there an issue with adding maybe one or two drinks per week or something?

Noa Biran, MD

Yeah. That's a great point, and I think that a lot of people are thinking that, so thank you for asking. To me, and it depends on every patient is individual and it depends on what treatment you're on, but what I tell my patient is the problem with alcohol is twofold. The most important one is that it dehydrates you. Dehydration is very serious in multiple myeloma, number one, because your kidneys are always at risk of having dysfunction and you don't want the kidneys to receive any injury that they don't need. Also, a lot of the treatments can cause something called orthostatic hypotension, which is dizziness. So, if you're dehydrated on top of getting dizzy from the drugs that we're giving you, then you can fall and break a bone. Your bones are at risk of fracture. The other issue is that a lot of the drugs that we give are digested or eliminated from the body through the liver. The liver is very, very important, and we can see liver injury. You don't want to cause anymore burden on your liver, and you don't want to overwhelm your liver.

Now there's other things that can cause injury to the liver when someone has myeloma. Dexamethasone causes increased sugar retention, and fat and sugar in the liver is another possible injury to the liver, the drugs. And then if there's any way to avoid injury to the liver, then I would recommend it. A lot of times we check our patients' liver tests on a regular basis, and we do see some subtle elevations in the liver enzymes. And sometimes, oh it's just a few points off the norm, no big deal, but it can be a big deal because if that happens over ten years, 15 years, then you can get scarring in the liver and cirrhosis. And I'm not saying you're going to get cirrhosis if you're having two drinks a week, but you want to decrease the risk. You want to take care of your body as much as you can. So certainly, we want you to have a good quality of life and have a good quality, but you have to do risk benefit. And if there's a way to minimize dehydration and liver toxicity, then I would reinforce that.

Lizette Figueroa-Rivera, MA

Thank you so much for that question and answer, doctor. The next question comes from Jack. Jack asks, "Isatuximab works well but except in cases where daratumumab no longer is effective."

Noa Biran, MD

That's a very good question. So isatuximab targets the same protein as does daratumumab. There really isn't enough information out there or trial data out there to show that it works in patients who have progressed after dara. Or if daratumumab has stopped working, we don't know yet if there's a benefit in switching to isatuximab. We do know in some studies that patients with high-risk disease may benefit from isatuximab, so that's a conversation you can have with your physician. And also, in certain combinations, there may be an advantage to using it.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from our telephone audience, please. Operator, can we have the next question from our telephone audience, please.

Operator

Your next question is from Tracy in New York.

Tracy in New York

Good morning. Thanks for taking my question. In the media today, there is discussion on a potential need for a fourth booster vaccine primarily for patients who are immunocompromised six months after their third booster. For patients who have had a pretty good antibody response to previous vaccines and boosters, in your knowledge, do you see this as an ongoing schedule of boosters for patients who are immunocompromised?

Noa Biran, MD

Wow, you are really up to date. This was just like five hours ago. Yes. The CDC (Centers for Disease Control) is saying that, yes, we may need a fourth dose. There hasn't been a final announcement on that. My suspicion – and that's from checking antibodies on people on a regular basis, which are going down, and not just immunocompromised patients; everybody has decline in antibody titers month after month – is that depending on the prevalence of COVID in your location, we're probably going to be getting boosters. Personally, I see very little downside in getting a fourth booster. Obviously, the safety has to be evaluated and the FDA has to put a stamp on it, but my guess is, especially for immunocompromised patients with declining antibody titers, a fourth booster is probably in our future and maybe even more than that. Let's wait and see. If you want to know your antibody titer, you can ask your doctor to check it.

Tracy in New York

Yes, thank you.

Lizette Figueroa-Rivera, MA

Yeah, thank you. And our next question from Wayne asks, "Will my bones ever heal completely?"

Noa Biran, MD

Yeah. So, the bones definitely do heal. We see even on scans, on x-rays or even CAT scans or sometimes MRIs (magnetic resonance imaging) that the bones become what's called sclerotic instead of lytic, and that indicates healing bone. Will they heal 100% to normal? They may, but the risk of developing new lytic lesions is always there. And that's why I tell patients, "Don't abuse your bones." We usually tell patients not to do skiing or high-risk sports because the bones are always at risk of fracture. And once we stop the bone support, the bones can go back to their degenerative state, so that's even more reason to continue on the bone support indefinitely. Certainly, we can spread it out in certain cases, but bone support should be continued.

Lizette Figueroa-Rivera, MA

Thank you. That was actually the next question. Elizabeth was asking what kind of physical activity can she do without fear of breaking bones?

Noa Biran, MD

It depends on your particular case, and I say something different for every patient. But I tell almost everybody, "Avoid high-risk sports like skiing." Horseback riding may not be a great one. But it depends. We have patients who say, "My life isn't worth living if I can't go skiing." And then we deal with it. It's risk benefit. And it also depends on what fractures you've had in the past and how long you've been on bone support and what your bone density is. So, it's important to continue walking. We say 30 minutes of exercise a day. Stationary biking is very good. It also helps prevent not only bone loss, but muscle atrophy. And dexamethasone in particular causes atrophy or shrinkage of the muscles of the thigh or what we call the proximal muscles, so the upper arm and the thigh. So those, you know, doing exercises that can promote muscle strengthening of those areas are important and also to promote bone strength. So walking, stationary biking, light weights are good. And I love physical therapy. I think it's great. Really everyone can benefit from it.

Lizette Figueroa-Rivera, MA

Definitely. And I do want to thank you for letting our participants really know that it is important to have these quality-of-life conversations with their doctors and their treatment teams because there is something that you as a doctor can do to help with quality of life.

Noa Biran, MD

Yeah. And I know that a lot of visits are very short and they're very focused on the numbers, the number of the disease response, the free light chains. And it's not really about the number. You have to integrate these responses with how you feel. And to me that's even more important.

Lizette Figueroa-Rivera, MA

Sure. And we'll take the next question from our telephone audience, please.

Operator

Your next question is from Dawn in Michigan.

Noa Biran, MD

Hi, Dawn.

Dawn in Michigan

Hi. Hi. I am at the very beginning. I am 53 and I was diagnosed with plasmacytoma extramedullary, and I also have multiple myeloma. So right now, we're doing the Velcade, the dexamethasone and the Revlimid. And so, I guess I'm wondering should I talk to him about a clinical trial or adding something to strengthen the bone because the plasmacytoma completely ate away that bone.

Noa Biran, MD

Absolutely. You need a bone strengthener. I would talk to him about, or her about a bone strengthener and then what's the long-term plan because the Velcade-Revlimid-dex is certainly a good regimen in terms of getting your disease into remission but is there a plan for an autologous stem cell transplant or what's the big picture here? So, I would bring up that question.

Dawn in Michigan

Yeah. And that is what he said. After we get done with that, then I will have to do the bone marrow transplant.

Noa Biran, MD

Yes, good. That's good.

Dawn in Michigan

Okay. So, I just wanted to make sure he was kind of going along, you know, the protocols that everyone else is saying to use.

Noa Biran, MD

Absolutely. It sounds like it. Absolutely.

Dawn in Michigan

Okay. I appreciate it. Thanks.

Noa Biran, MD

No problem. Sure.

Lizette Figueroa-Rivera, MA

Thank you for the question. And the next question comes from John. John's asking, "Regarding remission status, when is MRD (minimal residual disease) tested? What level of M (monoclonal) spike should be consideration for MRD testing?"

Noa Biran, MD

Sure. So, there's different levels of remission. The best possible remission, so a PR (partial remission) means 50% reduction, at least a 50% reduction. A VGPR, or very good partial remission, means at least a 90% reduction in tumor burden. A CR, a complete remission, means that the M spike is negative, zero in the blood; the serum immunofixation and the urine immunofixation are both negative and the bone marrow has less than 5% plasma cells, so you do need a bone marrow test to confirm a complete remission. And then the last level of remission is called a stringent complete remission with minimal residual disease negativity. And that means that not only is the criteria for complete remission met, meaning M spike zero, serum immunofixation negative, urine immunofixation negative, kappa lambda ratio normal, bone marrow without plasma cells but we have a much more sensitive test called minimal residual disease. There's two ways to do that test. One is by a test called flow cytometry, which is often done at the center. And the other one is called next generation sequencing, which is often sent out. And if those tests are negative, meaning they can't detect one in a million or sometimes even more myeloma cells, then that's a very, very good prognosis. If your disease is minimal residual disease negative, then that means that the remission will probably last a very long time.

The time points at which it should be done are usually if you're going to use the next generation sequencing method, then it should be done at diagnosis because that's how they look for the exact clone for later on to test for. And then the second time you do it, it should be usually at when the M spike reaches zero or negative or at least as close to zero as possible and the serum immunofixation is negative because to me the minimal residual disease test is not as relevant if you're not even achieving a complete remission in the blood and the urine. So, first step is achieving that complete remission in blood and urine. The next step is to confirm it with the bone marrow and to do the minimal residual disease test.

Not all the centers have the ability to do it and right now there isn't any data that will tell us that you have to change the treatment based on the minimal residual disease negativity test. So, the way we are using it now is really for prognosis, not as much for management. Some doctors are using it for management in terms of, you know, if somebody is on maintenance therapy, maybe if they're MRD negative, they can stop maintenance therapy but that's not really proven. So not everybody is using that data as a treatment changing point. It's often really just prognostic.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from our telephone audience, please.

Operator

Your next question is from Joel in Colorado.

Joel in Colorado

Hi, doc.

Noa Biran, MD

Hey there.

Joel in Colorado

I know you're tired of talking about COVID and all that, but I have another question regarding that. Revlimid apparently renders the vaccines less effective or ineffective. And what's the story with throwing in some Regeneron or monoclonal antibodies on top of the vaccine?

Noa Biran, MD

So, if you do get infected, then you can certainly receive the Regeneron monoclonal antibody and most of our patients do meet the criteria. There's very strict criteria for who is and who isn't eligible. And often, there are specific centers that administer that.

Joel in Colorado

So, are you saying it's not a preventative?

Noa Biran, MD

No.

Joel in Colorado

It's for treatment.

Noa Biran, MD

It's treatment.

Joel in Colorado

Okay. Well, that answers that, and thanks for all you're doing.

Noa Biran, MD

Sure. You got it.

Lizette Figueroa-Rivera, MA

And thank you for the question. Dr. Jeffrey is asking, "Why are African American men more susceptible to multiple myeloma than others?"

Noa Biran, MD

Yes. Certainly, we don't know the answer to that question. We know that myeloma is more prevalent in African Americans as well as in patients, people of Mediterranean origin. It's slightly more prevalent in men compared to women. Why that is, we don't know. We know there are certain environmental predispositions, so people who are, for example, exposed to Agent Orange usually through the military have higher risk. People who work with flooring or dyes or construction or hair dyes, those types of chemicals can predispose. People who were present at the 9/11, you know, the jet fuel can increase risk. We know things that are associated with increased risk of myeloma, but, unfortunately, we don't have data as to why. And there is research that's ongoing trying to answer a lot of those questions. The FDA is now looking at, you know, they're requiring a certain percentage of African Americans patients or Mediterranean patients to be part of clinical trials in order to further characterize these disparities.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from our telephone audience, please.

Operator

Your next question is from Joseph in Maryland.

Joseph in Maryland

I'd like to know is there a way you could take, let's say, a prostate cancer cell, which is slow growing, and somehow use that cell to fight the multiple myeloma cells? I don't know exactly how, maybe surround it, maybe stop one of the steps in its metabolism, but could something like that be done?

Noa Biran, MD

Well, it's a good question. There is a lot of ongoing research looking at the immune-related effects of perhaps having another cancer in the body and how it affects the myeloma. And it's interesting, but sometimes we find patients who have two cancer diagnoses at once. And what we see, one of the patterns that we've observed is that when one cancer is active, it tends to suppress the other cancer. And why that is we don't know, but we think it's because the immune system is so hyperactive that it suppresses the other cancer, so we see this. Sometimes we have, for example, a CLL (chronic lymphocytic lymphoma), which is kind of a quiet lymphoma, and myeloma. And when we treat the myeloma, the CLL goes up. Then we treat the CLL, it goes down, the myeloma goes up. And we see

TRANSCRIPT

that also with prostate cancer. We have a lot of patients who have both prostate cancer and myeloma. So, there is something – you make a very good point that there is something about that prostate cancer and the immune response to it that can be simultaneously suppressing or treating the myeloma.

Joseph from Maryland

Thank you.

Lizette Figueroa-Rivera, MA

Thank you. That is very interesting.

Noa Biran, MD

Yeah. It is. It is. Yeah.

Lizette Figueroa-Rivera, MA

And our next question comes from Anorah. She asks, "What types of secondary cancers should patients be on the lookout for, and what's the best way of managing this aspect of a treatment?"

Noa Biran, MD

Yeah. So, you know, all. The answer is all types of secondary cancers. And the reason is there's a lot of reasons. So, if you just take a myeloma patient, they have a higher risk of secondary cancers. No treatment. Even without treatment. And that's something about the way, maybe their body has been exposed to some environmental trigger, that's increasing the DNA breakage and predisposition to cancer. So that may be number one. That may be a reason in itself. On top of that, we're giving this patient chemotherapy and Revlimid maintenance, meaning use of Revlimid at a low chronic dose directly after transplant can double the risk of secondary cancers and that includes myelodysplastic syndrome, solid tumors, skin cancers. It includes all cancers. So, we know Revlimid does it, but we also know that other treatments do it, including transplant itself, probably alkylating agents like Cytoxan® (cyclophosphamide). And that's because it increases breakage of DNA in cells and that increases risk of cancer. So, treatment increases risk of cancer and having myeloma increases risk of other cancers.

What can we do to mitigate that? I would say just there's not really preventatively to give, but you should stay on top of age-appropriate cancer screenings – Pap (Papanicolaou) smears, mammograms, PSA (prostate-specific antigen) checks if that's warranted, colonoscopies, skin checks. If you've had a squamous cell carcinoma, you need to go regularly for skin checks. So do that and then reduce risk of cancer by taking care of your body – drinking a lot of water, eating healthy fruits and vegetables, exercising. We know that diabetes and high sugar, high fat can increase risk of certain cancers, so reduce all the modifiable factors. You can't control everything, but if you can control somethings, then that will overall reduce risk of other cancers.

Lizette Figueroa-Rivera, MA

Thank you so much, doctor. That was our last question. Do you have anything, doctor, that you're really excited about that will be discussed in upcoming meetings in regards to myeloma?

Noa Biran, MD

I think that a lot of things are changing in myeloma. I think that we're moving more towards using combination therapies and then giving people a treatment-free period, you know, and moving a little bit away from the maintenance therapy. And then I'm excited for all the new CAR T cells and the BiTEs and all of the immune therapies and various combinations. And I think we're going to end up having a much longer life for our patients and make this really a chronic disease.

Lizette Figueroa-Rivera, MA

Thank you so much. That's really great to hear at this point in time. And thank you so much for your continued dedication to your patients, Dr. Biran.

Noa Biran, MD

You're welcome. My pleasure. I hope everyone has a great day.

Lizette Figueroa-Rivera, MA

Thank you.

CLOSING REMARKS

Lizette Figueroa-Rivera, MA

LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:

To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

- Call:** (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
- Chat live online:** www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
- Email:** www.LLS.org/ContactUs
All email messages are answered within one business day.



CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process. www.LLS.org/Navigation



NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email. www.LLS.org/Consult

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LEUKEMIA & LYMPHOMA SOCIETY

And if we weren't able to get to your question today, you can call a Leukemia & Lymphoma Society Information Specialist at 1-800-955-4572. Information Specialists are available to speak with you from 9 AM to 9 PM Eastern Time or you can reach us by email at LLS.org/ContactUs. Also, patients as well as caregivers can schedule a free personalized nutrition consult with our dietitians at LLS.org/Consult.


LLS EDUCATION & SUPPORT RESOURCES

Online Chats
Online Chats are free, live sessions, **moderated by oncology social workers**.



Banding Together Fridays Online Chat is specifically addressing questions and concerns about living with a blood cancer during COVID-19. Register now at www.LLS.org/Chat

Education Videos
View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit www.LLS.org/EducationVideos.



Patient Podcast
The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit www.TheBloodline.org.



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And LLS offers a variety of education and support resources, including online chats which are free live forums that are moderated by oncology social workers. We also offer free educational videos and podcasts.

LLS EDUCATION & SUPPORT RESOURCES




The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancer: www.LLS.org/Finances



To order free materials: www.LLS.org/Booklets

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The Leukemia & Lymphoma Society offers programs to help individuals with blood cancer. For more information, you can visit LLS.org/Finances. And to order free materials, visit LLS.org/Booklets.

Please note that continuing education credits is not being offered for this program.



THANK YOU

We have one goal: A world without blood cancers



Again, we would like to acknowledge and thank Bristol Myers Squibb, Genentech & Biogen, GlaxoSmithKline, Janssen Biotech and Oncoceptides for their support for this program. And thank you, Dr. Biran, for sharing your knowledge with us today.

To all the patients, caregivers and professionals participating in today's program, on behalf of The Leukemia & Lymphoma Society, thank you for sharing your time with us. Good-bye, and we wish you well.