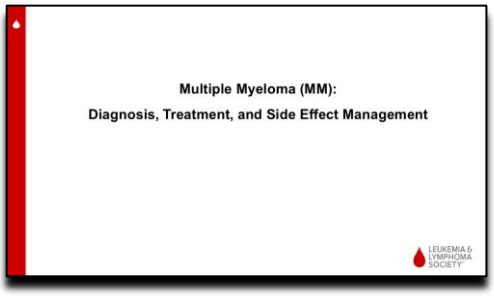
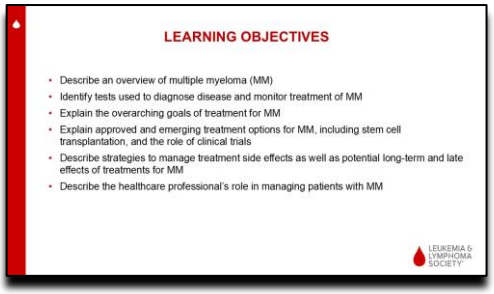


Slide 1: Multiple Myeloma (MM): Diagnosis, Treatment, and Side Effect Management

Lauren Berger: Hello everyone. On behalf of The Leukemia & Lymphoma Society thank you for sharing your time with us for this continuing education program on Multiple Myeloma: Diagnosis, Treatment, and Side Effect Management.



Slide 2: Learning Objectives

The learning objectives for this program are listed on this slide.

Slide 3: Faculty

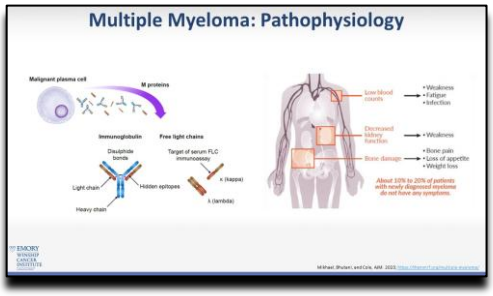
We're fortunate to have as our presenters, Dr. Sagar Lonial, a leading expert in Multiple Myeloma, and his colleague, Dr. Sara Scott, a clinical pharmacy specialist. We appreciate their dedication and their commitment to caring for patients living with blood cancer.

Dr. Lonial is Chair and Professor, Department of Hematology and Medical Oncology Anne Bernard and Gray Family Chair and Cancer, Chief Medical Officer, Winship Cancer Institute, Emory University in Atlanta, GA.

Dr. Scott is Clinical Pharmacy Specialist in Multiple Myeloma At Emory Winship Cancer Institute in Atlanta, GA.

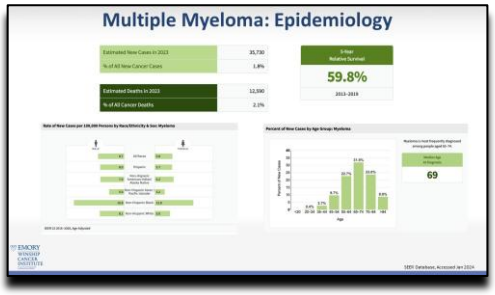
Dr. Lonial & Dr. Scott, I am now privileged to turn the program over to you.

Sagar Lonial, MD: Well, thank you very much for that kind introduction, and what we're going to do for the next few moments is really talk through the multiple aspects of myeloma, including diagnostic approach, treatment approaches, as well as side effect management; and we're going to do this in a way that really puts some of these issues and areas into real context, taking into account patient situations and cases as well.



Slide 4: Multiple Myeloma: Pathophysiology

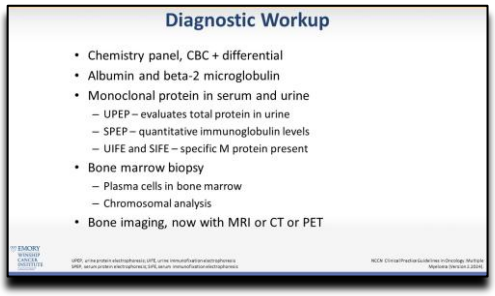
So, let's start off with a little bit of the pathophysiology of multiple myeloma. We know that it's a plasma cell disorder that results in most cases in overproduction of a monoclonal protein. That overproduction of the protein can have significant impacts on renal function as well as immunity, leading patients to have a higher risk of infections. Those increased numbers of plasma cells also seem to target bone and bone marrow, causing other potential complications, and we know that in many areas the use of some of the antimyeloma therapies can also raise the risk of thrombosis. And so, all of these factors come into play when we begin to think about how to manage patients both through their acute phases of treatment as well as the maintenance phases where our goal is to minimize toxicity and maximize quality of life and clinical benefit from the perspective of months in remission, as well as the ability to go back to their normal lifestyle.



Slide 5: Multiple Myeloma: Epidemiology

Now, when we think about the epidemiology of multiple myeloma, we know that there have been pretty dramatic changes in the last 20 years. If 20 years ago I were showing you a slide, we would describe the median survival of myeloma patients as about 2.5 to 3 years on average. Now we say that the average myeloma survival is greater than 10 years; and certainly for patients with standard risk myeloma, it may be greater than 14 to 15 years, depending upon which data set you really look at.

The median age of patients is 65, and one of the issues that I think is really important as we think about the demographics of multiple myeloma is that the incidence is almost two-fold higher among Black Americans compared to non-Black Americans. And this really is important because most of the large data sets that describe outcomes for patients with myeloma, as well as the baseline demographics and presenting features, are actually predominantly Caucasian subsets. And so, putting together access to trials, as well as demographic description, and perhaps biologic differences for patients who are African American, really is important as we move forward in the next 5 to 10 years to make sure that we understand where the diseases may be similar and where they may be dissimilar. And just as a quick example, the incidence of high-risk genetics is significantly lower among African American myeloma than it is among Caucasian myeloma, and that's just one aspect where biologically the diseases may be somewhat different. And yet we know that with differences in access to care, sometimes the outcomes are not as good as one would expect in both subsets. So, these are factors that I think everybody needs to be aware of as we get better and better drugs in the coming years.

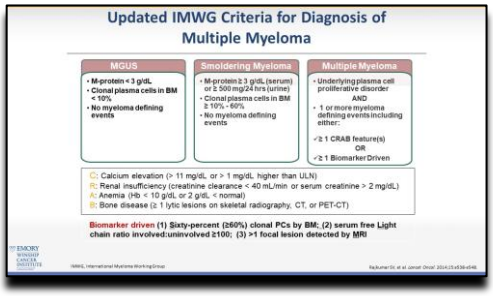


Slide 6: Diagnostic Workup

As we think about the diagnostic workup, again, it's relatively straightforward. Obviously, chemistries and blood counts are important. For staging, albumin and beta-2 microglobulin are critical. The beta-2 is most often the missing piece of laboratory data that I don't see among a number of patients. You also need good quantification methods of the protein in the urine as well as in the blood, and you need free light chain assays performed in the blood as well.

As you might expect in a bone marrow-based disease, bone marrow assessment for plasma cell numbers is important. But more importantly, the bone marrow is important for the use of cytogenetic analysis, whether that includes chromosomes, routine karyotype, FISH testing, or next-generation sequencing. These are all critical parts of how we make decisions in terms of management for patients over the long term.

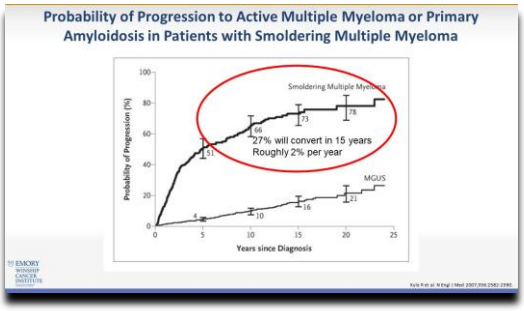
And finally, bone assessment, this is something that has really radically changed in the last decade as well. Historically, we use skeletal surveys as one way to think about imaging the bones. That has now been largely replaced by PET/CTs or MRIs, whole body MRIs, with the lowest common denominator of imaging now being whole body low-dose CT scan. If your hospitals are like mine, most of us don't have access to that technology; and so CTs and MRIs become the default methodology for imaging both at the time of diagnosis as well as subsequently in follow-up or should new symptoms arise.



Slide 7: Updated IMWG Criteria for Diagnosis of Multiple Myeloma

When we think about the updated IMWG criteria for the diagnosis of multiple myeloma, it is important to recognize that a few years ago the International Myeloma Working Group did, in fact, redefine multiple myeloma. And we did that in a way that really looks at clinical characteristics to differentiate symptomatic myeloma from MGUS and smoldering. And as you can see, MGUS on the left side is really less than 10% plasma cells, no evidence of CRAB criteria. Smoldering myeloma is more than 10% plasma cells, also with no evidence of CRAB criteria. And on the right side you see symptomatic myeloma, which in fact, doesn't matter how many plasma cells are in the marrow but really does have evidence of CRAB criteria, which includes hypercalcemia, renal insufficiency, anemia, and evidence of bone disease.

But what the biomarker-driven criteria at the bottom really demonstrate is three new criteria that we've added in, representing the fact that many of these patients may have a higher risk of progression from smoldering and so should be treated early. And these include patients with more than 60% plasma cells in the bone marrow, a serum free light chain ratio of greater than 100, or more than 1 focal lesion detected by either MRI or PET scan. These new biomarker-driven criteria have really only added about 5% to 7% to the new diagnoses category but really have allowed us to take a high-risk smoldering patient population and not allow them to develop end organ damage by early intervention and ultimately prevention.



Slide 8: Probability of Progression to Active Multiple Myeloma or Primary Amyloidosis in Patients with Smoldering Multiple Myeloma

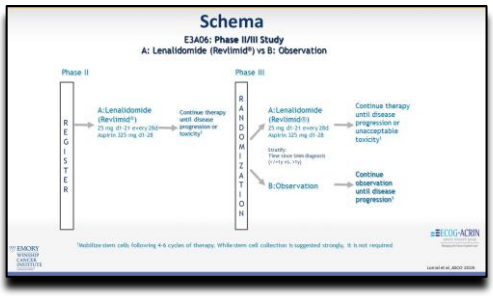
Now, the reason that smoldering is such a challenging category to deal with, really based on the fact that many patients here in this category have a variable risk of progression. And so if you look at the first part of the smoldering curve, what you'll see is about a 10% to 15% per year risk of progression. If you look at the second portion of the curve, you'll see that that's roughly a 5% per year risk of progression. And if you look at the third portion or the tail of the smoldering curve, it almost looks identical to MGUS with about a 1% to 3% risk of progression.

And so, discriminating between these three groups is really important because we are now in an era where we're talking about early intervention for high-risk smoldering. And you can see by that curve why we want to intervene in the high-risk group, but you can also see in this curve why we wouldn't want to intervene in the low-risk group, because their risk of progression is so low overall.

Slide 9: Revised Risk Stratification (20/20/20)

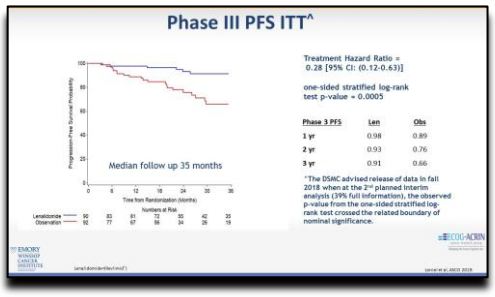
And so, risk stratification ultimately becomes an important goal as we move forward. And the 20 to 20 criteria, initially published by the Mayo Clinic, now validated in a number of other criteria, really looks at three different biomarkers to determine the risk of progression. And in a smoldering patient population, you can look at bone marrow plasma cells greater than 20%, M spike greater than 20 grams per liter or 2 grams per deciliter, or a free light chain ratio greater than 20. And if you have none of those criteria, you fall into the low-risk category with the bottom curve of progression. If you have 1 of them, you fall into the intermediate category in the middle in blue. And if you

have 2 or more, you fall into the red group, which is the highest risk group of smoldering patients.



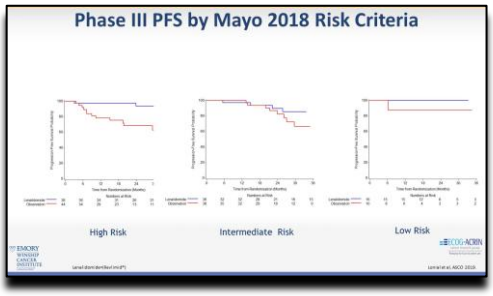
Slide 10: Schema

And this really becomes important, for instance, if you look at the most recent ECOG trial randomizing patients between lenalidomide (Revlimid®) and observation for intermediate or high-risk smoldering using an older criteria.



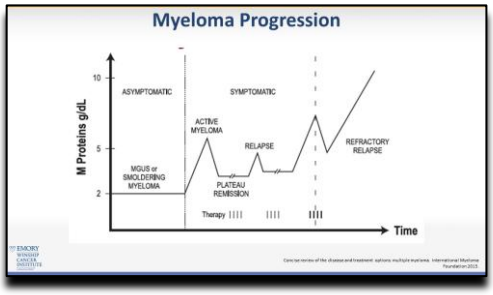
Slide 11: Phase III PFS ITT^

And what we demonstrated quite nicely was that we could show a pretty significant reduction in the risk of progression with just 2 years of single-agent lenalidomide, with almost a 70% to 80% risk reduction with just lenalidomide alone in the high-risk smoldering patient population.



Slide 12: Phase III PFS by Mayo 2018 Risk Criteria

And if you look at this by the 20 to 20 criteria, the 2018 Mayo criteria, which are the same, you'll see that the group that gained the greatest benefit was the high-risk group on the left with an over 90% risk reduction for progression, whereas the intermediate and the low risk on the right and in the middle did not appear to gain any benefit from early intervention. And so, this is the true value of risk stratification and helping us to understand where we should potentially intervene with clinical trial strategies.

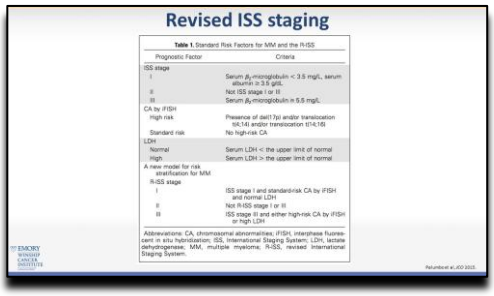


Slide 13: Myeloma Progression

So, as we begin to talk a little bit about sort of the course of a myeloma patient and how they may progress, I'm going to turn things over to Dr. Scott and have her sort of walk us through the next few slides really talking about management of early myeloma in that context.

Sara Scott, PharmD, BCOP: Thank you, Dr. Lonial. So as you can see, we always describe myeloma to our patients as a truly chronic disease state. So, this is something

that at this point in time, we do not know as curable. And with each relapse, the response time gets shorter and shorter and shorter. We've had significant progression both in the newly diagnosed setting as well as in the relapsed setting as far as our treatment algorithm.



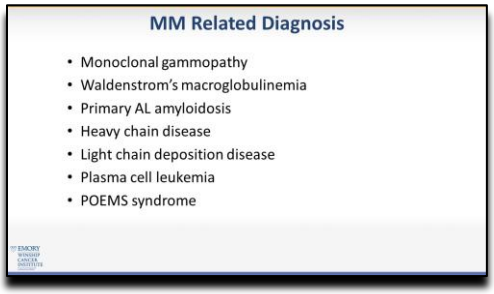
Slide 14: Revised ISS Staging

So, this describes the Revised ISS staging. This is currently even being revised again, but as you can see here, as Dr. Lonial mentioned, there's things including albumin, beta-2 microglobulin, LDH, and then the presence of high-risk cytogenetics which at this point are defined as deletion 17p, translocation 4;14, or translocation 14;16. Newer cytogenetic risks that we're including are +1q, and those will be hopefully coming in the new times. Any additions to that, Dr. Lonial?

Dr. Lonial: No, and I think you're absolutely right. And what we recognize is that the biologic implications of the genetics may be more impactful than even the historic staging approaches. And so stay tuned. As everything in myeloma changes, the definition of high risk will likely change this summer with the new IMS paper coming out, but this certainly is the current RISS staging approach.

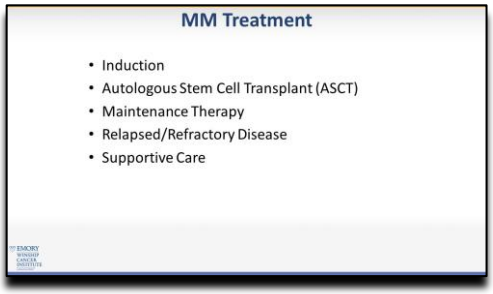
Slide 15: Risk Stratification

Dr. Scott: Perfect, thank you. And, yes, and to this point in time, we haven't really used staging to guide therapy. We primarily will fall into the risk stratification to determine maybe who's going to respond better to what and determine who gets what induction and who maybe gets what maintenance as we've progressed with more data. So, again, those high-risk cytogenetics are listed for you here. Standard risk is kind of everything else, but a couple big buckets to point out are patients with hyperdiploidy and then patients with translocation 11;14 who we think the biology and their response to therapy may be a little different, and we're continuing to learn about, and we'll talk about some therapies that may be specific for that population.



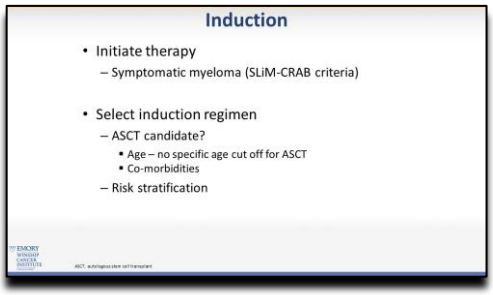
Slide 16: MM Related Diagnosis

Before we dive into therapy, I did want to point out some related diagnoses that you may hear thrown around. So monoclonal gammopathy, which may fall into the MGUS category, so unknown significance. But they may fall into something like monoclonal gammopathy of renal significance where we do know there's an impact on an organ. Waldenstrom's macroglobulinemia, which is an IgM lymphoplasmacytic lymphoma. Primary AL amyloidosis. Heavy chain disease and light chain deposition disease. Plasma cell leukemia, and then POEMS syndrome as well, which are all things that we care for in our clinic and have some overlapping therapies.



Slide 17: MM Treatment

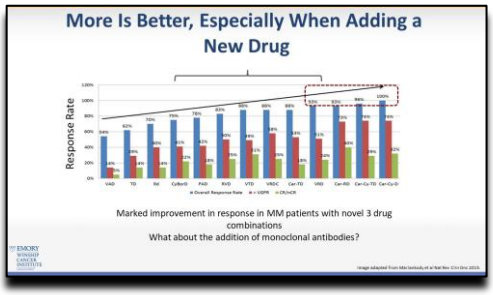
So big broad concept of treatment within myeloma that we'll step through today is induction therapy, so prior to stem cell transplant, if the patient is eligible. Maintenance therapy, whether that's post-stem cell transplant or post their induction phase. Treatment for relapsed/refractory disease, and we'll kind of talk about that in the early relapse or 1 to 3 lines of previous therapy. And then late relapse, so patients who have had 4 or more lines of previous therapy. And then finally supportive care for both complications of the disease and toxicity from the therapies we give.



Slide 18: Induction

So, starting with induction, when do we decide to initiate therapy? And this is based upon the diagnosis of symptomatic myeloma or that SLiM-CRAB criteria that Dr. Lonial walked through. As he mentioned as well, we may be initiating therapy in those high-risk smoldering patients; and that's constantly changing of what that's going to look like with ongoing data coming all the time.

The next step is when we decide to initiate therapy, what are we going to initiate? So, selecting the induction regimen really is based on two big ideas. Is this patient a candidate for stem cell transplant? So, what we're thinking about there is what is their age. We don't necessarily have an age-specific cutoff. It comes more as performance status and their comorbidities and their ability to receive this transplant. And then more recently, discussing risk stratification and what they might mean for changes with the induction regimen.

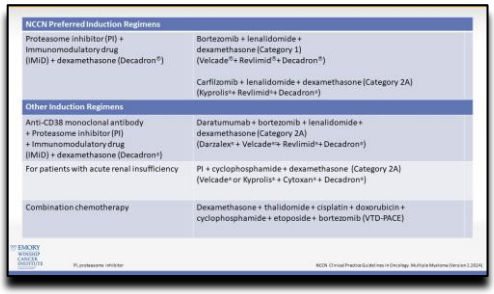


Slide 19: More Is Better, Especially When Adding a New Drug

So, this slide just kind of talks about what we've been learning over time, that more is better, so when we're adding a new drug. So, this is best evidence most recently as some slides we'll talk to with the addition of anti-CD38 monoclonal antibodies to the induction regimen. But as we can see with time, as newer and more drugs have been added to regimens, three has been better than two. Four has been better than three. And so, this is kind of displaying that overall response rate as we've been adding those novel and new regimens. And again, what happens with that addition of monoclonal antibodies, which is something we recently learned is important.

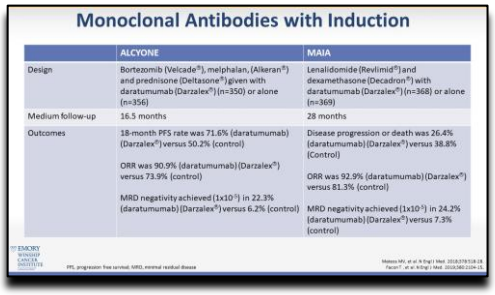
Dr. Lonial: And I think, Sara, one important differentiation between myeloma and most other cancers, particularly in the solid tumor arena, is this idea of combination therapy has really been critical to the change in outcomes for patients with myeloma.
We know that in solid tumor oncology, they'll often do combinations versus sequential single agents and look at overall survival as an endpoint to differentiate the benefit. We know that most myeloma therapy is actually based on disease biology-based targets like proteasome inhibitors, IMiDs, anti-CD38 antibodies, and corticosteroids as opposed to traditional chemotherapy.

And so, the combinability of these drugs is very different. The synergy is far more common when we combine these drugs together, and it is a completely different world than solid tumor oncology where you sort of march through. Combinations are not necessarily better because of more toxicity. We, in fact, see the exact opposite, that combinations are what has driven the improved survival and remission duration in this field overall.



Slide 20: Table

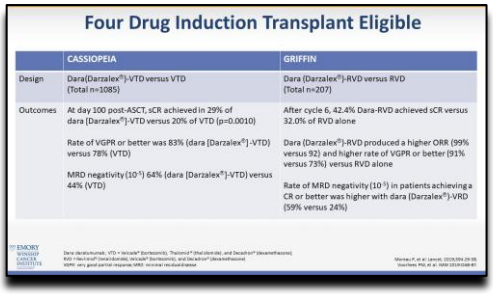
Dr. Scott: Thank you. So, this slide is just a summary for you of what the current NCCN guidelines recommend for their preferred induction regimens as well as some other induction regimens. I would not be surprised if this changes soon based on data that we got at ASH this year, but the preferred induction regimen is a triplet combination of a proteasome inhibitor, an IMiD, and dexamethasone (Decadron®). So, bortezomib or Velcade®, lenalidomide or Revlimid®, and dex. There's also the preferred regimen of putting carfilzomib (Kyprolis®), a different proteasome inhibitor, in place of bortezomib; but the category recommendation here is a little less.



Slide 21: Monoclonal Antibodies with Induction

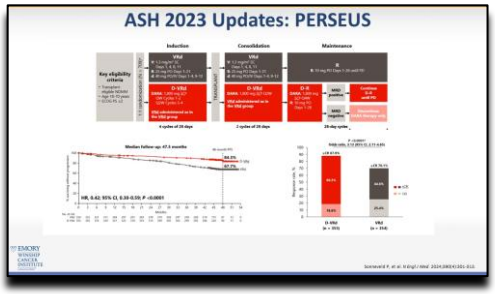
Other options, and this is our preferred, is the four-drug combination; and that is based on a few trials. And it started with the addition of these monoclonal antibodies. It was anti-CD38 monoclonal antibodies with the induction regimen. So, two of the first trials we saw are listed here for you. So, one is a quadruplet regimen of daratumumab (Darzalex®), prednisone (Deltasone®), melphalan (Alkeran®), and bortezomib. This regimen, in general, is less commonly used within the United States. We don't typically use melphalan in induction. That's the drug we're going to use for stem cell transplant. So, this is something less, but did show the benefit of the addition of daratumumab in the induction setting.

The MAIA trial was a triplet regimen which we use for patients who are not transplant eligible. So, you'll see this as a triplet regimen but again showing that significant benefit of adding that monoclonal antibody.



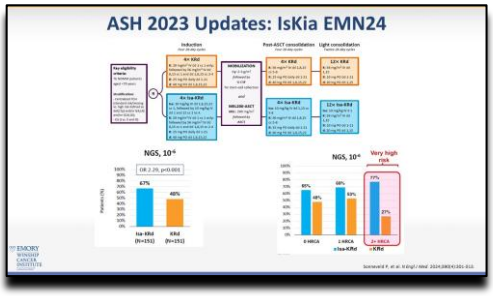
Slide 22: Four Drug Induction Transplant Eligible

We now have seen the addition of daratumumab to make a quadruplet regimen in patients who are transplant eligible. And this was initially displayed in the CASSIOPEIA and the GRIFFIN trials, so combination of daratumumab with bortezomib, dexamethasone, and then select your IMiD, thalidomide (Thalomid®)or lenalidomide. Of note, the thalidomide is not commonly used within the United States but is commonly used outside of the United States, so CASSIOPEIA was very impactful there. We'll also talk about how thalidomide may have benefit in some populations such as patients with renal dysfunction. And then the GRIFFIN trial was a Phase II trial, wasn't received as well being a Phase II trial. But most recently at ASH, we were provided with the PERSEUS trial



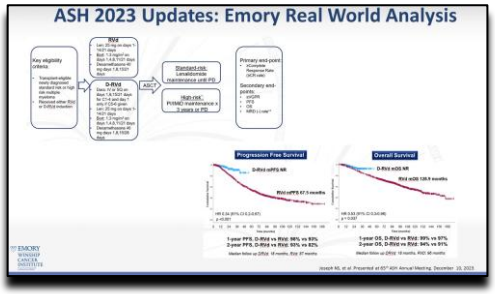
Slide 23: ASH 2023 Updates: PERSEUS

Which was the Phase III combination of daratumumab, bortezomib, lenalidomide, and dexamethasone. And as you can see here, the rates of complete response or better were 90% in patients that received this quadruplet followed by a transplant, followed by some maintenance. That was, included daratumumab within this trial. And so this was significant, and this is why I believe that the NCCN guidelines will change.



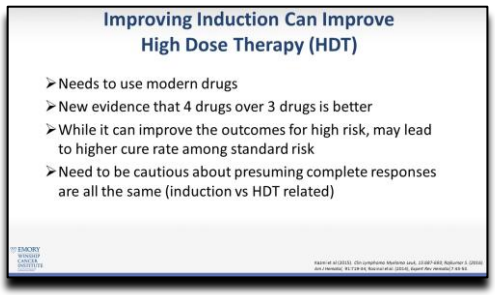
Slide 24: ASH 2023 Updates: IsKia EMN24

At ASH, we also got the other anti-CD38 monoclonal antibody isatuximab (Sarclisa®) in combination with our alternate proteasome inhibitor carfilzomib (Kyprolis®). And again, this showed significant benefit with an improvement in MRD negativity with this quadruplet regimen compared to a triplet regimen with carfilzomib, lenalidomide, and dexamethasone. This was one of our first trials where we saw MRD negativity as the primary endpoint, so something that is very interesting and I think will continue to be seen in myeloma.
And one thing I want to point out is that this was, also showed significant benefit in our very high-risk population, which as we discussed, is challenging to treat and it has shorter progression-free survival.



Slide 25: ASH 2023 Updates: Emory Real World Analysis

The last piece I just wanted to share was the Real World Analysis from our institution which showed really that this dara-Rvd combination shows within the real world and not just within this clinical trial space. So, we showed that there was significant progression-free and overall survival benefit with this quadruplet regimen compared to the triplet. This was maintained within the high-risk population and was also maintained within our African American population, which as Dr. Lonial pointed out, is often underrepresented within these populations. So, really important to display that in the real world, as well as within this underrepresented population, if we provide equivalent care, we can see equivalent outcome.



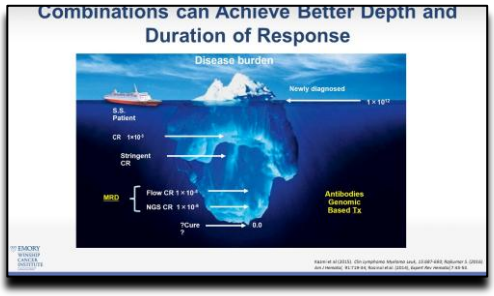
Slide 26: Improving Induction Can Improve High Dose Therapy (HDT)

Dr. Lonial: So, when we begin to think about how the impact of high-dose therapy continues to exist in the context of three- and four-drug induction regimens, it is important to recognize that most randomized trials continue to demonstrate significant benefit in terms of remission duration for patients who receive the transplant versus those who don't. And I think if you look back, even in this data set that we've just reviewed, in the PERSEUS trial, they showed 4-year progression-free survival of 84% compared to something in the 60s for the no-dara arm.

I think it's important to recognize that the median PFS in the determination study with no transplant was around the order of 4 years in general. So, every trial that we look at

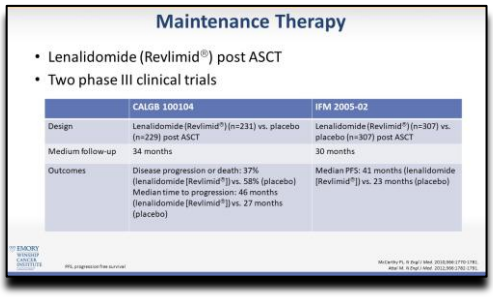
demonstrates significant improvements in remission duration by anywhere between 1 and 2 years through the addition of transplant, and this is only getting better as we use better drugs in the induction therapy context.

So, the rumors of the demise of transplant, I believe, are highly exaggerated and premature. And so, I think that is an important take-home message for both patients as well as providers to be aware that so far nothing has shown a longer remission duration than trials that include transplant as part of their treatment paradigm.



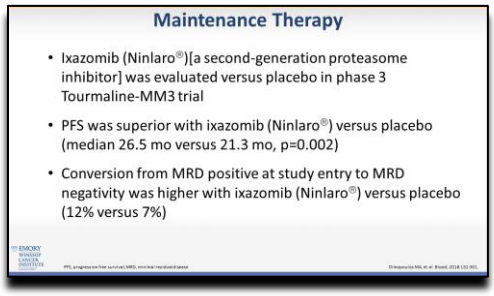
Slide 27: Combinations can Achieve Better Depth and Duration of Response

And this really translates here when we begin to think about depth of response, and I made this slide almost 15 years ago when I was trying to think of a graphical way to demonstrate the importance of MRD negativity. What you're seeing here, MRD negativity, either 10^{-5} or 10^{-6}. But we know that both of those are not necessarily surrogates for cure because we know that patients do continue to relapse even if they achieve MRD negativity at 10^{-6}. And so, what we think transplant is doing is through a different modality, achieving a deeper level of remission that is so deep that we can't even measure it right now.
And so, for instance, assessing 10^{-7} as a new methodology for MRD is currently in experimental phases; and it appears that patients who have a transplant may achieve more and deeper remissions than those who don't. And that represents the true mechanism by which transplant may continue to offer significant benefit.



Slide 28: Maintenance Therapy

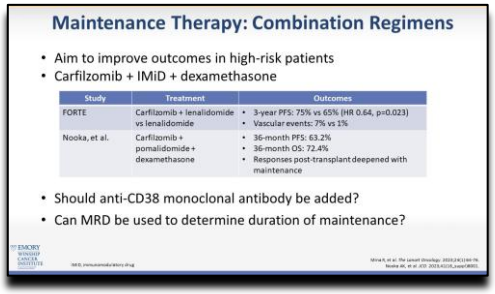
Now, as we begin to talk a little bit about maintenance therapy, I think it is important to recognize that lenalidomide maintenance post-transplant is the standard of care based on a couple of Phase III randomized clinical trials.



Slide 29: Maintenance Therapy

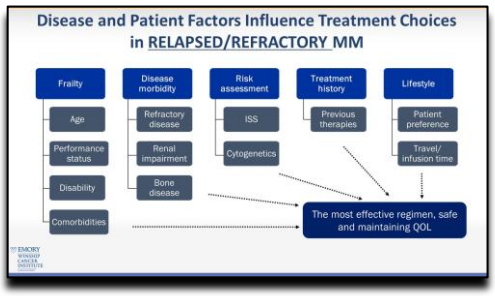
But there certainly are other areas where we're using proteasome inhibitors, and there is data from the TOURMALINE trial suggesting that ixazomib (Ninlaro®) versus placebo is superior over placebo. Whether it's actually better than lenalidomide, I think, is a little bit more of a stretch. And so, the question

about how do we position oral proteasome inhibitors like ixazomib in the context of maintenance therapy or.



Slide 30: Maintenance Therapy: Combination Regimens

Other proteasome inhibitors such as carfilzomib or bortezomib, we've seen data from the Italian group that suggests that the carfilzomib-IMiD combination is clearly superior for all patients. I think the question is, is the risk of those dual combinations worth it for the standard-risk patients given that their remission duration may be in excess of 80 months with single-agent lenalidomide? And, of course, the new questions relate to MRD-guided maintenance therapy as well as the role of anti-CD38 antibodies in the management of maintenance therapy as well.

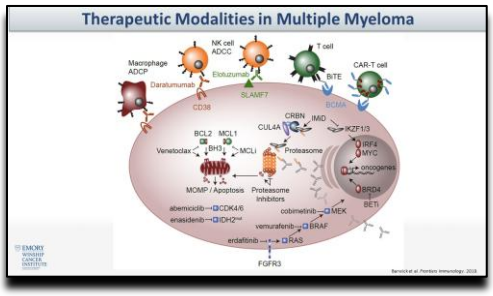


Slide 31: Disease and Patient Factors Influence Treatment Choices in Relapsed/Refractory MM

So, Sara, why don't you pick back up as we talk about sort of how we make decisions in the context of relapsed myeloma.

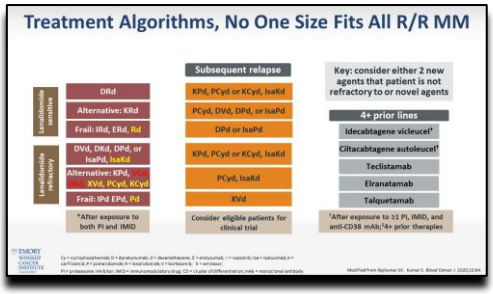
Dr. Scott: Sure. So, in the relapsed space, there is a lot that we take into account as Dr. Lonial mentioned in the last 20 years – the number of drugs that have been approved and our options in this space has significantly changed. And I think, as you mentioned, in the next month may continue to change, depending on some new approvals that are going on. So, there's a lot to take into consideration in this space. So, of course, one thing we always like to recommend is inclusion within a clinical trial. The only way we can get these approvals is by investigating these drugs within our patient. But other things to think about are the patients' frailty, disease morbidity, their risk stratification, their treatment history and how long their responses have been and their remissions have been. And then their lifestyle. A lot of our myeloma therapies are very frequent, and so are they able to come to the infusion center that often?

Taking all these things to account, this is always a multidisciplinary as well as a patient-centered discussion of what's the most effective regimen, the safest regimen, and that can maintain their quality of life.



Slide 32: Therapeutic Modalities in Multiple Myeloma

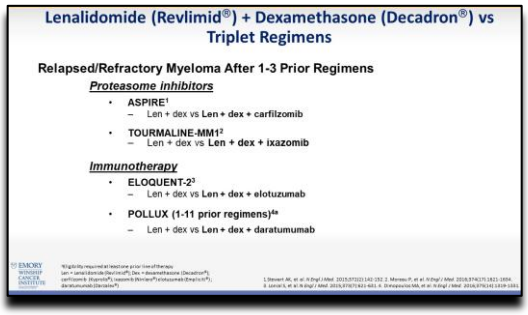
So, we have, as I said, kind of getting to the point of not unlimited, but getting there of treatment modalities within the relapsed space. So, this is kind of a summary of the complicated picture of all the options we have with our monoclonal antibodies, our oral agents, our new cellular therapy, as well as some novel things that are being studied.



Slide 33; Treatment Algorithms, No One Size Fits All R/R MM Review and Discussion

And again, this is just kind of an example of a treatment algorithm we may consider. No one size fits all relapsed patient. So, again, we have to take into account the patient as a whole and then their treatment history.

So, breaking this down, what have they received before? Are they sensitive to lenalidomide or not is one of our first considerations. And then what step of relapse are they in? So, again, are they early relapse, one to three lines of therapy, or are they in the late relapse, four plus lines, where right now is the FDA approval of our cellular therapy.

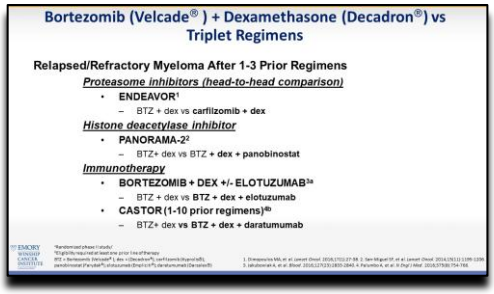


Slide 34: Lenalidomide (Revlimid®) + Dexamethasone (Decadron®) vs Triplet Regimens

Dr. Scott: So, again, this is introducing kind of the early relapsed setting. So this was one of the first trials that compared a triplet regimen to lenalidomide and dexamethasone. So, we've included lenalidomide and dexamethasone with proteasome inhibitors, with both carfilzomib and ixazomib, as well as with immunotherapy. So, elotuzumab (Empliciti®) and daratumumab. And consistently the triplet regimen outperformed the doublet regimen.

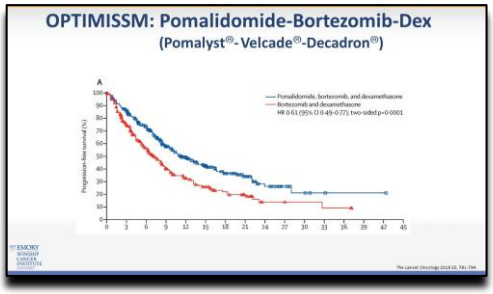
Dr. Lonial: And, and I think one of the challenges, as you're going to see in subsequent slides, is we do have lots of options; but the reality is that many patients nowadays are progressing on lenalidomide maintenance, as we described before. So, while a lot of patients gave a lot of effort to these four clinical trials, their utility in 2024 is really sort of questionable because all of these trials had len-naïve patients when they went into it. And we know being len-resistant, the likelihood of benefit from a len+ something else

combination is lower. And so, I think what Dr. Scott's going to cover in the coming slides really becomes sort of the modern paradigm of treatment approaches in 2024.



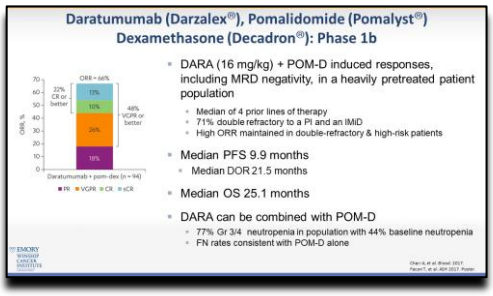
Slide 35: Bortezomib (Velcade®) + Dexamethasone (Decadron®) vs Triplet Regimens

Dr. Scott: Thank you, Dr. Lonial. So, this is really where our focus, as he said, shifted. These patients are progressing on lenalidomide, but they're really not resistant to anything else. And so proteasome inhibitors are one of our mainstays of therapy in the relapsed setting. So, their ENDEAVOR trial compared bortezomib to carfilzomib and dexamethasone, and carfilzomib in that state outperformed bortezomib. There's also been studies looking at panobinostat (Farydak®) or histone deacetylase inhibitor. This no longer carries FDA approval for multiple myeloma, so you likely will not see this used in this setting. And then again, the addition of immunotherapy with other novel therapies. So, elotuzumab in combination with bortezomib and dexamethasone and then daratumumab with bortezomib and dexamethasone. So, this really started to show the benefit of that synergy with the proteasome inhibitor and the monoclonal antibody.



Slide 36: OPTIMISSM: Pomalidomide-Bortezomib-Dex (Pomalyst®- Velcade®-Decadron®)

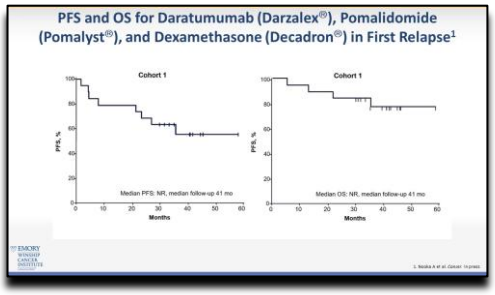
Dr. Scott: So, the OPTIMISMM trial was looking at bortezomib, dex, and pomalidomide (Pomalyst®). And what we found is that pomalidomide is effective in patients who now have resistance to lenalidomide. And so this is really our next, bringing in an IMiD combination in the relapsed setting. And as you can see here, there was a risk reduction of about 40% in the triplet versus the doublet with just bortezomib and dexamethasone alone by the addition of pomalidomide.



Slide 37: Daratumumab (Darzalex®), Pomalidomide (Paulist®) Dexamethasone (Decadron®): Phase 1b

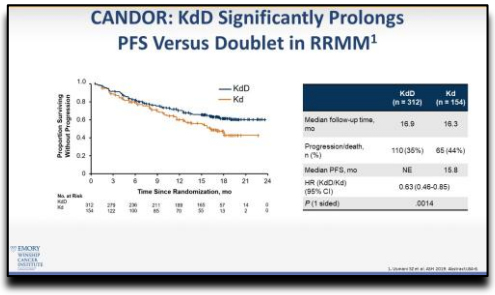
One of our most commonly used regimens in the relapsed setting is the addition of an anti-CD38 monoclonal antibody, daratumumab with pomalidomide and dexamethasone. So this trial did look at daratumumab IV, which we, most people will not be using anymore. They'll be using the subcutaneous formulation due to the improved tolerability. But as you can see here, the progression-free survival is about 10 months but an extended duration of response of about 22 months, almost 2 years, and overall survival of greater than 2 years.

Again, I want to highlight here that the addition of this monoclonal antibody did not change the toxicity profile of this regimen and did not increase when overlapping toxicities, which is one of the biggest takeaways, I think, as we add additional therapies on to these regimens.



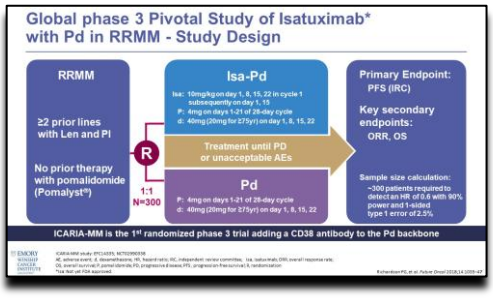
Slide 38: PFS and OS for Daratumumab (Darzalex®), Pomalidomide (Pomalyst®), and Dexamethasone (Decadron®) in First Relapse1

So, this is, again, just displaying that triplet combination. So showing in the median progression-free survival and overall survival of this dara, pom, and dex regimen.



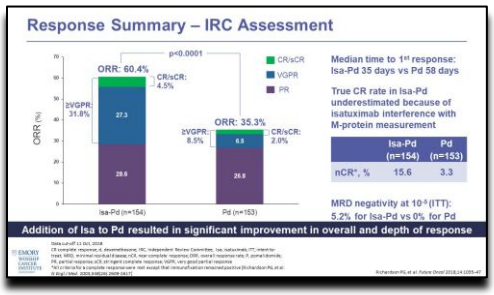
Slide 39: CANDOR: KdD Significantly Prolongs PFS Versus Doublet in RRMM[1]

The second most commonly used regimen in the first relapsed setting is daratumumab with carfilzomib and dexamethasone. Again, as Dr. Lonial said, we have a lot of options; so how do we choose between this? And what we have found and what we believe is that patients who progress earlier after transplant may benefit more from this triplet of carfilzomib with dara and dex rather than daratumumab with pomalidomide and dexamethasone.



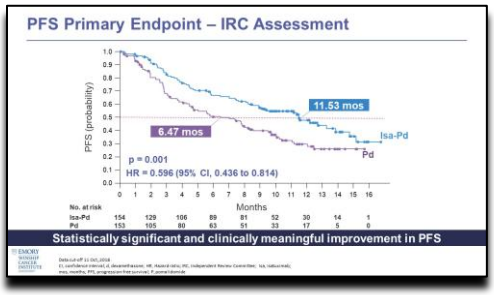
Slide 40: Global phase 3 Pivotal Study of Isatuximab* with Pd in RRMM - Study Design

There's also studies looking at the alternative anti-CD38 monoclonal antibody isatuximab. So this study was with patients who had had two prior lines of therapy, had to have an IMiD of lenalidomide and a PI. Going to be standard considering they get that in their induction regimen. And this, importantly though, patients could not have previously seen an anti-CD38. So now that we're including that in the induction regimen, this may be something that we see less in the relapsed setting.



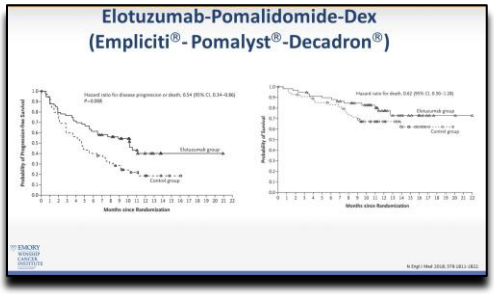
Slide 41: Response Summary – IRC Assessment

But this was the combination of isa, pom, and dex. And as you can see, a significant improvement in the overall response rate.



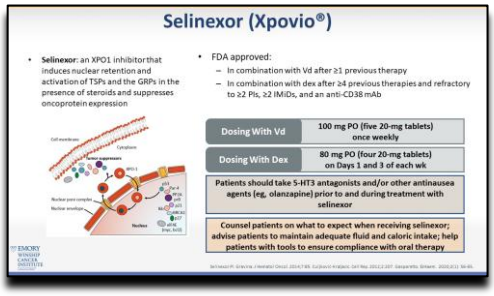
Slide 42: PFS Primary Endpoint – IRC Assessment

And important to note that the VGPR was also better. And showing here that there was about a 6- to 7-month benefit with the overall survival.



Slide 43: Elotuzumab-Pomalidomide-Dex (Empliciti®- Pomalyst®-Decadron®)

Elotuzumab is one of our alternative monoclonal antibodies, so this is a SLAMF7 inhibitor and has been studied in combination with our IMiDs and the proteasome inhibitors. One thing to really point out is elotuzumab is not effective by itself, so it really needs to be used in combination with either an immunomodulatory drug or a proteasome inhibitor. But when used in combination with these therapies does show improved progression-free survival.



Slide 44: Selinexor (Xpovio®)

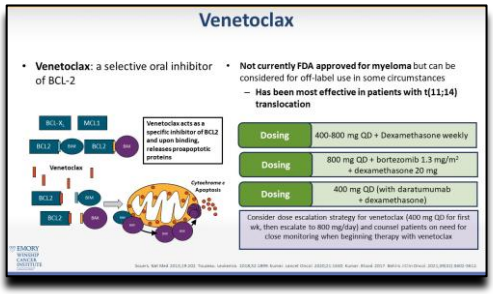
Now, I'll kind of move into some of our more novel therapies and our oral options which, like we said, when we're talking about quality of life and lifestyle, oral options are great because they can keep patients out of the infusion center.

So selinexor or Xpovio® is an XPO1 inhibitor that induces nuclear retention and activation of TSPs and GRPs and important to note in the presence of steroids. So, these have to be used alongside dexamethasone. This is currently improved in combination with proteasome inhibitors as well as just with dexamethasone. One thing to note is the doses that are FDA approved are really hard to tolerate. These patients have significant GI toxicity as well as electrolyte changes, and the myelosuppression can also impact these patients pretty

significantly. So, typically in practice you may not see this high of dosing; and often it's only done once a week instead of twice a week.

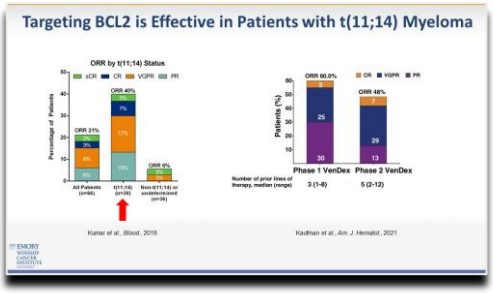
Slide 45: Selinexor Clinical Trials

This is just a summary of the clinical trials. Again, selinexor always has to be used with dexamethasone. One thing I do want to point out as well, which is a continuing theme, is that when in use with a proteasome inhibitor, the overall response rate seemed to be significantly better if we compared to just selinexor and dexamethasone alone, using caution directly comparing across trials, but they do seem to be much higher than the triplet regimen.



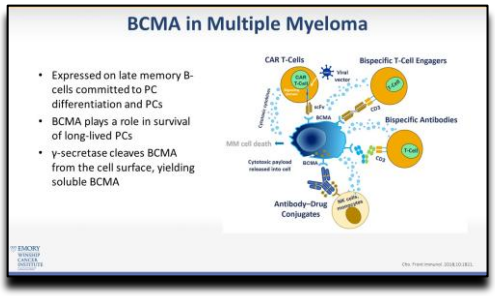
Slide 46: Venetoclax

Venetoclax (Venclexta®) is also one of the novel oral agents which is not currently FDA approved in multiple myeloma, but it has significant benefit within that patient population of the translocation 11;14 patient. So, this is a selective oral inhibitor BCL-2. Venetoclax has been around for a while in other hem disease states, but just BCL-2 binds to proapoptotic proteins; so, by inhibiting this binding, it, we can release this apoptotic protein to then go and take care of the myeloma cells.



Slide 47: Targeting BCL2 is effective in patients with t(11;14) Myeloma

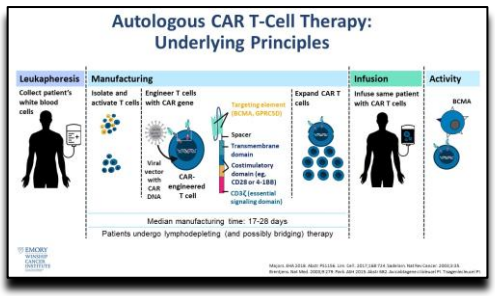
Another thing I'll point out is dosing tends to be higher with venetoclax in myeloma compared to something like AML or CLL. Here showing the overall response rate, specifically looking at those patients with translocation 11;14. So taking all-comers, the overall response rate isn't great, 20%. But when we take out just those 11;14 patients, their response rate significantly improves.



Slide 48: BCMA in Multiple Myeloma

One of our most important targets within multiple myeloma with our novel agent is BCMA or B-cell maturation antigen. So this is on plasma cells. It is exclusively on plasma cells, which really can help limit our toxicity with these therapies and create more novel targeted therapies.

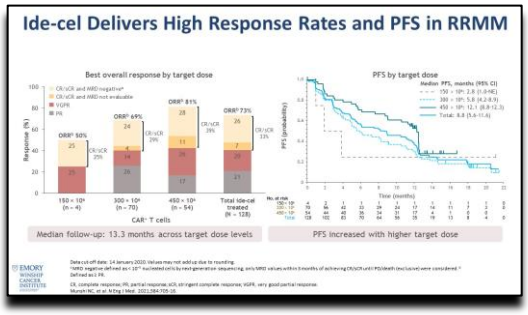
And as you can see, this is where our cellular therapies and our antibody drug conjugates can come into play. So previously had the antibody drug conjugate on the market. I don't think any of us would be surprised if that comes back to market. But that's displayed here. Bispecific T-cell engagers, which we do not have any FDA approval for, and that's primarily because the bispecific antibodies have been shown to have a much better pharmacokinetic profile. And our two CAR T-cell approved products are also targeting BCMA.



Slide 49: Autologous CAR T-Cell Therapy: Underlying Principles

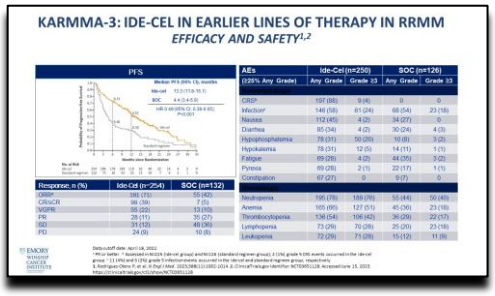
Dr. Lonial: So, let's talk a little bit about an area that is rapidly expanding not just in myeloma but in hem malignancy in general, and that's the idea of autologous CAR T-cells. And this really requires a multistep process where first the patient undergoes leukapheresis to collect T-cells. That is then shipped to the manufacturing site where viral transduction occurs to force them to overexpress a gene that allows those T-cells to target a certain protein.

In the context of ALL or diffuse large B-cell lymphoma, that's often CD19. In the case of multiple myeloma, that is often BCMA. Those cells are then expanded ex vivo, and then patients, then they are shipped back to the site where patients will receive what we call LD or lymphodepletion chemotherapy with fludarabine (Fludara®) and cyclophosphamide (Cytoxan®); and then they undergo infusion of those cells, not quite like a transplant but more like a T-cell transfusion to allow those cells to be active.
And then we wait on the, both benefit of those infusions, as well as the potential side effects of those infusions.



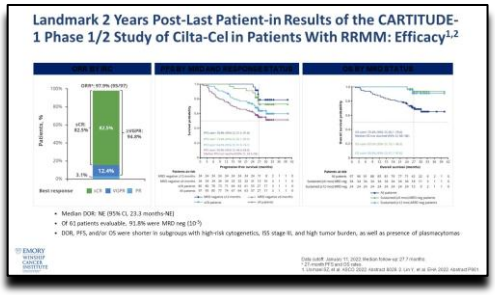
Slide 50: Ide-cel delivers high response rates and PFS in RRMM

And the side effects we'll talk about later on in terms of adverse event management, but really cytokine release syndrome and ICANS or neurologic toxicity represent the two big things that we need to watch out for. There are currently two BCMA-directed CAR T-cells that are available on the market. The first was ide-cel, and as you can see, the response rate was between 70% and 80% for ide-cel. And the median progression-free survival was around a year in a group of six or more prior lines of therapy, heavily pretreated relapsed refractory patients where very few patients had any agents that they were sensitive to in terms of bridging or other antimyeloma therapy before they went on this trial.



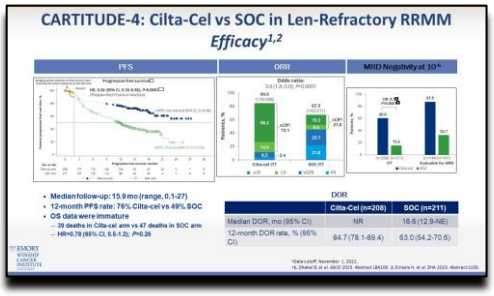
Slide 51: KarMMA-3: Ide-Cel in Earlier Lines of Therapy in RRMM Efficacy and Safety[1,2]

More recently an update of this, of an earlier line of therapy trial called the KarMMa-3 trial that compared ide-cel with best available standard of care was performed. And as you can see in this slide, significant benefit for the use of ide-cel over best available supportive care. Response rate, depth of response was clearly better for the group that received ide-cel compared to the group that did not. And we're hoping that this trial will help lead to earlier availability of CAR T-cells, not four or more prior lines of therapy which is the current label, but hopefully two or more prior lines of therapy based on data from the KarMMa-3 trial.



Slide 52: Landmark 2 Years Post-Last Patient-in Results of the CARTITUDE-1 Phase 1/2 Study of Cilta-Cel in Patients With RRMM: Efficacy[1,2]

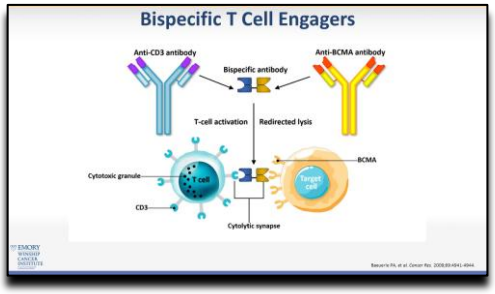
At the same time, there was another Phase I, Phase II study using a different CAR T-cell called cilta-cel where the response rate was almost 99%. The median progression-free survival is somewhere around 2-1/2 to 3 years, and again it's longer for patients that achieve deeper responses.



Slide 53: CARTITUDE-4: Cilta-Cel vs SOC in Len-Refractory RRMM Efficacy[1,2]

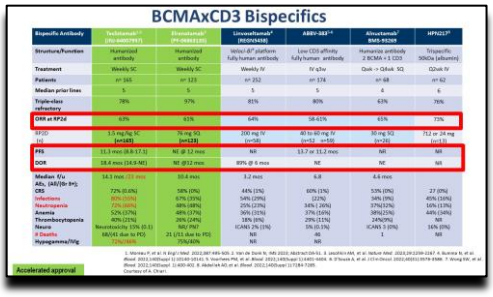
And more importantly, this was then followed up with the CARTITUDE-4 trial which was cilta-cel versus best available standard of care. And as you can see from the progression-free survival curve on the left, again, significant benefit favoring the use of a CAR T-cell with a remission duration over 2 years compared to less than 2 years for the group that received best available standard of care.

That was mimicked with overall responses and deeper rates of MRD negativity as well. So, these are really exciting therapeutic options that we are hoping will be brought earlier and earlier into the disease course, given that single agent wise they have more activity than most of our other agents that we use in myeloma.
However, it is important from both cilta-cel and ide-cel data with long follow-up is that we've not seen a plateau on that curve. So different from diffuse large B-cell lymphoma or ALL, where there is a cure curve. There's a plateau on that curve. We've not yet demonstrated that with BCMA-directed CAR T-cells in myeloma.



Slide 54: Bispecific T Cell Engagers

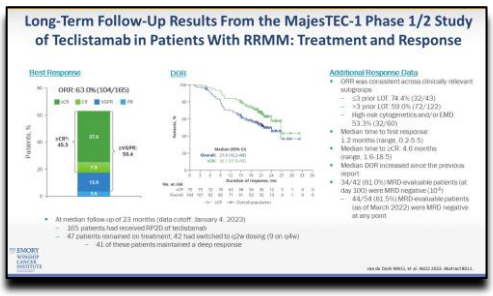
Now, the other area that Dr. Scott touched on very briefly was bispecific T-cell engagers. These are really exciting new molecules that you'll see that have both a fragment that binds CD3 or a T-cell and a fragment that binds BCMA or a myeloma cell. And it brings that T-cell in close proximity to a myeloma cell which ultimately represents, results in myeloma cell death.



Slide 55: BCMAxCD3 Bispecifics

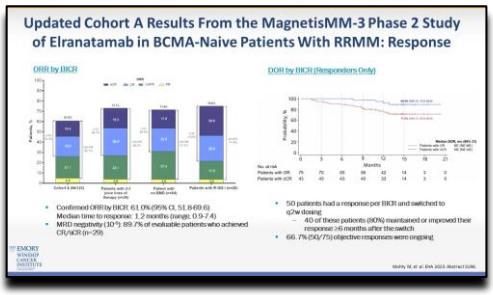
And we know that there are currently six different T-cell engagers that are in early phase development. The two on the left are in green. Those are the two FDA-approved agents. The first is teclistamab (Tecvayli®), and the second is elranatamab (Elrexfio®). And what you'll notice is that the response rates are similar. Certainly with early follow-up, the progression-free survival is similar. The incidence of cytokine release syndrome or CRS is similar, and the incidence of ICANS is similar as well. So, you do get similar adverse event profiles to CAR T-cells. They just, in general, are on average one grade lower than we see with CAR T-cells directed at BCMA. So, certainly a much more tolerable approach. It's off the shelf and is easily available for patients who need quick

access to new therapy as opposed to patients who have the ability to wait 4 to 6 weeks for manufacturing of a CAR T-cell.



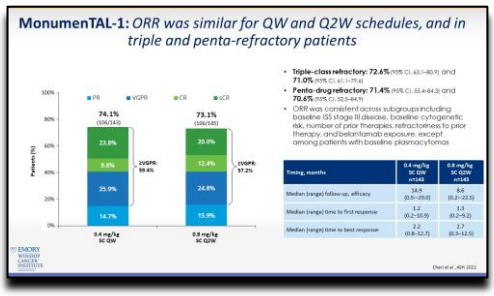
Slide 56: Long-Term Follow-Up Results From the MajesTEC-1 Phase 1/2 Study of Teclistamab in Patients With RRMM: Treatment and Response

And just to give you a flavor of some of the data, this is the MajesTEC trial that led to the approval of teclistamab. You can see the overall response rate was greater than 60%. PFS is about a year. But if you were a responder, the PFS is significantly longer, closer to 14 to 18 months in terms of duration of remission. And so, again, in a median of 6 or 7 prior lines of therapy, this sort of activity is almost unprecedented with an off-the-shelf potential treatment option.



Slide 57: Updated Cohort A Results From the MagnetisMM-3 Phase 2 Study of Elranatamab in BCMA-Naive Patients With RRMM: Response

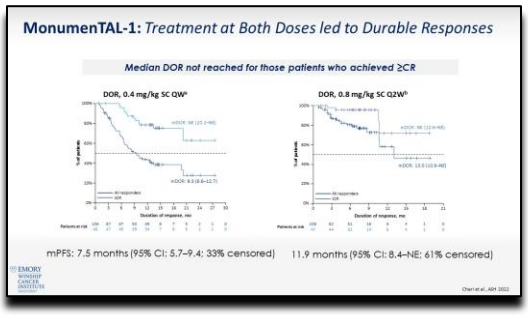
And, of course, the elranatamab is the other agent that's approved. This is data from the MagnetisMM-3 trial, a Phase II study of elranatamab. Again, median progression-free survival looks like it's over a year. Response rate again, over 60%. And what we need are long-term trials and long-term follow-up to better understand how these will all play into our sequencing and treatment algorithm for patients with late relapse. But I think between both CAR T-cells and bispecifics, we are hopeful that they will be brought earlier to bear in the treatment paradigm and likely will be partnered with many of the other drugs that we've already described in terms of the standard management of patients with relapsed myeloma.



Slide 58: MonumenTAL-1: ORR was similar for QW and Q2W schedules, and in Triple and Penta-refractory Patients

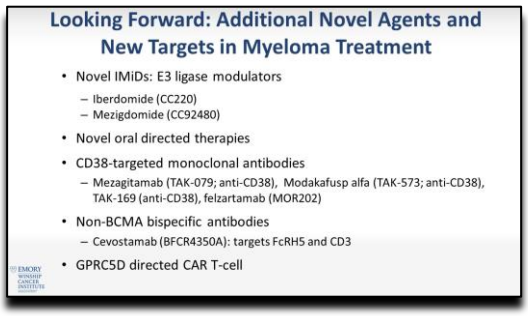
Now, the last of the bispecifics that I want to touch on is talquetamab (Talvey™), and I want to touch on talquetamab because it's a completely different target than BCMA. This is GPRC5D. So for those of you who get confused by the alphabet soup of myeloma, it's only going to get worse because GPRC5D is here to stay.

Talquetamab was approved by the FDA in the last year. Again, it has a response rate of over 70%. This is also a bispecific T-cell engager and with a different target than BCMA and clearly has significant.



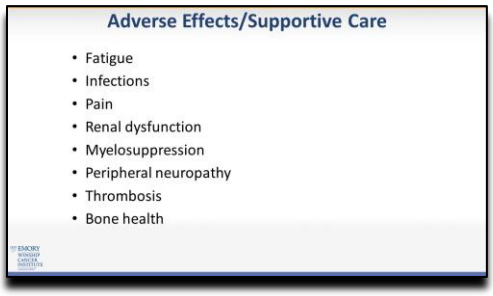
Slide 59: MonumenTAL-1: Treatment at Both Doses led to Durable Responses

Activity and significant duration of response in PFS and significant clinical benefit to patients as well.And we'll talk about differences between adverse event profiles for the BCMA-directed versus the GPRC5D-directed T-cell engagers in the next few moments. But recognize that they are different because of their binding affinity and their binding site and where we may see potential adverse events are slightly different there.



Slide 60: Looking Forward: Additional Novel Agents and New Targets in Myeloma Treatment

So, as we begin to think about additional novel agents and new targets in myeloma, I think it's important to recognize we have new drugs coming down the line. And sort of the story that I tell many of my patients who say, "Well, if I use the really good drugs early, is there going to be anything left for me later on?" And my response is to quote the Doritos commercial. "Crunch all you want. We'll make more," because I think that's really important. We always have a pipeline of new drugs coming in for patients. These are the novel IMiDs that are in development, iberdomide and mezigdomide. We have novel CD38 antibodies that are in development. We have other bispecific antibodies. We have FcRH5 as a target for a T-cell engager that's coming as well, and we have the GPRC5D-directed CAR T-cell that's in Phase II development as well. So we have many more targets coming down the road, and so using these effective drugs earlier in the treatment course really is important.

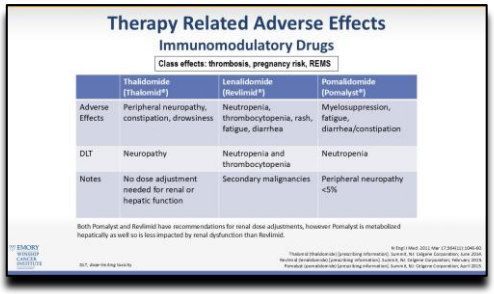


Slide 61: Adverse Effects/Supportive Care

So, I'm going to turn things back over to you, Dr. Scott, to really walk us through some of the adverse event approaches and how we manage some of these for an average patient coming through their treatment.

Dr. Scott: Okay, thank you. Yes, it is a huge part of our practice. As we said, this is a chronic disease. So, some of these things are disease-related

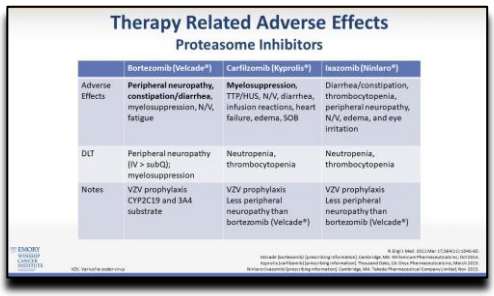
supportive care, like I mentioned, as well as direct toxicities of the therapies that we are giving. So, fatigue is, I always tell my patients, it's the disease, it's the drugs we're giving you, it's coming to treatment often. So, fatigue is pretty significant in our population. Infections, again, due to the disease, due to the therapies we're giving. Pain, renal dysfunction, myelosuppression, neuropathy, subsets of pain, thrombosis and bone health. We all hit on all of them.



Slide 62: Therapy Related Adverse Effects Immunomodulatory Drugs

So, I'll talk through the drug classes and kind of hit the highlights briefly for you. But immunomodulatory drugs are some of our original therapies. Class effects, big things, takeaways with these drugs are thrombosis. So, all patients should be on some form of anticoagulation when you're receiving these therapies. Pregnancy risk was associated with a REMS program.

And then kind of big things within each drug, thalidomide is well known for its peripheral neuropathy. Lenalidomide and pomalidomide are better known for their myelosuppression. Lenalidomide can also cause rash. I think of it as an immune-mediated rash and then diarrhea with long-term use. And then when thinking about the pharmacokinetic profile, thalidomide does not require renal or hepatic adjustment. And so, if a patient does have significant renal dysfunction, this drug may be considered over the others. But lenalidomide and pomalidomide both require that, adjustment for both.



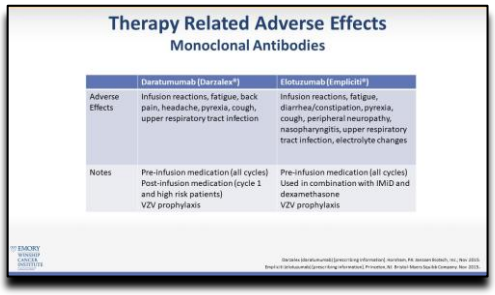
Slide 63: Therapy Related Adverse Effects Proteasome Inhibitors

Stepping into the proteasome inhibitors, again, we have three that all have slightly different binding, which makes their side effect profiles slightly different. So, bortezomib's biggest toxicity is that peripheral neuropathy; and this is something that can persist in patients for a while.

Carfilzomib, myelosuppression is the most common, so I would say the most significant that we're monitoring for are the heart failure and renal dysfunction that can occur with this drug.

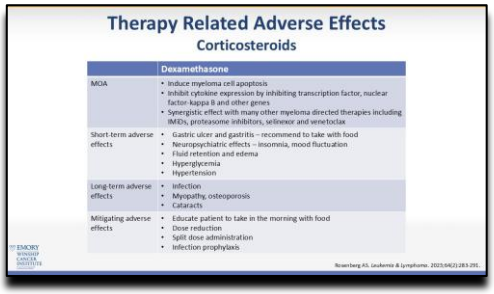
And then ixazomib is kind of somewhere in between both of these, and I would say nausea is something that I'm frequently talking to my patients about with this as well as the myelosuppression. Within the pharmacokinetic profile again, bortezomib does have significant drug interactions as well as food interactions with, you'll hear vitamin C and

green tea and grapefruit are the big three we talk about. And with all three of these drugs, these patients should be receiving VZV prophylaxis.



Slide 64: Therapy Related Adverse Effects Monoclonal Antibodies

Our monoclonal antibodies are some of our best tolerated therapies. Both daratumumab, isatuximab, and elotuzumab are all known for their infusion reaction. As I mentioned with daratumumab transition to a subcutaneous formulation, that route has really been reduced. So, we will premedicate these patients for all cycles. There's newer data coming out of our institution, as well as others, that premedication may not always be needed. And then post-infusion medications as well for some high-risk patients. As I mentioned, elotuzumab really needs to be used in combination with other therapies, whether an IMiD or a proteasome inhibitor. And again, these patients should all be on VZV prophylaxis.



Slide 65: Therapy Related Adverse Effects Corticosteroids

So dexamethasone is a backbone of myeloma therapy and it's almost always included in our multi-drug regimens because of its apoptotic activity and then synergistic effects as well. So though the mechanism of dexamethasone induced myeloma cell apoptosis is really complicated, a basic hypothesis is that it's believed to be driven by dexamethasone inhibition of nuclear factor kappa B, which then results in inhibition of the expression of cytokines and reduces cell growth and initiates apoptosis. We also have some clinical efficacy data that suggests synergistic effects of dexamethasone with other myeloma directed therapies. And this is especially relevant at the initiation of therapy.

As we're all aware, corticosteroids come with a laundry list of toxicities, some of which are listed here. So in the short term, neuropsychiatric effects are really what we see most commonly and have the greatest impact on a patient's quality of life. The insomnia and what I describe as the dex crash or the fatigue that patients feel the day after taking this medication are really our greatest challenge with this drug.

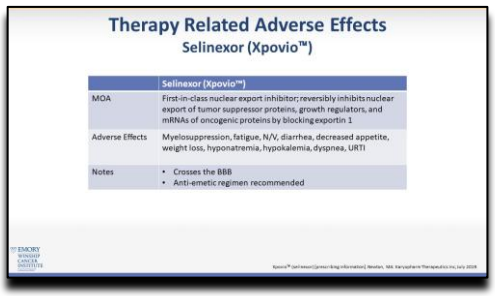
So to avoid insomnia, we do recommend that patients take dexamethasone first thing in the morning. At our institution, we give it to the patients at the infusion center, so that's not always possible. So sometimes we will then prescribe it for them to take at home if it's really impacting them. And then dex should also be taken with food to reduce the risk of gastritis.

Our institution does not routinely recommend PPIs as GI prophylaxis, but it's something that can be considered in high-risk patients.

So for example, if we have patients who we know have a history of acid reflux or a history of gastric ulcers, we may consider adding this on. Fluid retention and hyperglycemia are two other short-term challenges with this medication. And our greatest approach for mitigating these short-term side effects is dose reduction. Typically, dexamethasone is recommended once per week, but another approach we can take is splitting this total dose among different days.

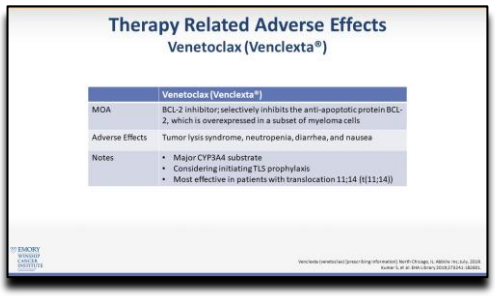
And that can help reduce some of these peak effects, which can include the neuropsychiatric changes and hyperglycemia. Long-term effects are also a concern. If you look at most clinical trials, the steroid is recommended to be continued until disease progression or intolerable toxicity, just like our other therapies. These concerns may include infection, myopathy, osteoporosis, and cataracts.

And so the practice of utilizing dexamethasone early for that disease control, those synergistic effects, but then tapering to discontinuation can really help reduce these toxicities. And this approach is becoming more and more popular.



Slide 66: Therapy Related Adverse Effects Selinexor (Xpovio™)

Selinexor I've mentioned already, but the GI toxicity is the biggest concern here. Myelosuppression as well, so this benefit of Xpovio® or selinexor, it does cross the blood-brain barrier which can be significant, not that CNS involvement is common, but something to think about. And then antiemetic regimen. So the current recommendation from the manufacturer are ondansetron (Zofran®) 30 minutes before the dose and then scheduled every 8 hours for 3 days after the dose. And then consideration of the addition of a long-acting antiemetic. I believe the most commonly used is likely olanzapine (Zyprexa®).

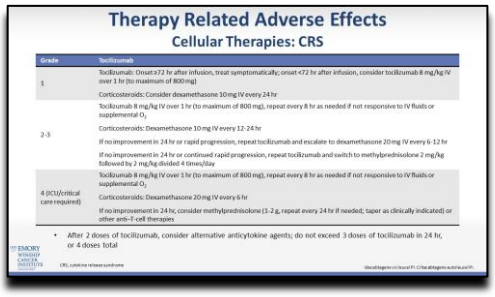


Slide 67: Therapy Related Adverse Effects Venetoclax (Venclexta®)

Venetoclax or Venclexta®, also a well-tolerated regimen in my opinion. The risk for tumor lysis syndrome within myeloma is much less than AML or CLL. We will still consider allopurinol prophylaxis for about a month in patients who have a high tumor burden. The cytopenias, neutropenia, and thrombocytopenia I would say are the most significant

here; and then the GI toxicity can really be mediated by administering this drug with food, and so the nausea and diarrhea are much less common.

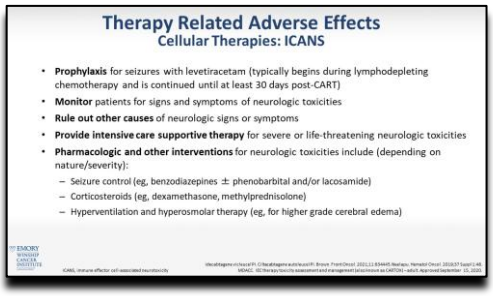
This, biggest concern with this drug is the drug interaction. So, we're fortunate that the combinations we're using with them are not as significant; but the patient's comorbidities may impact that quite a bit. And again, the translocation 11;14 should this rate or that venetoclax may be a good option.



Slide 68: Therapy Related Adverse Effects Cellular Therapies: CRS

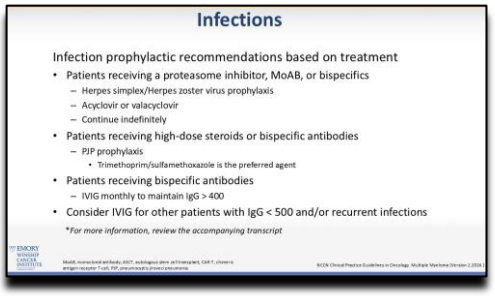
So, stepping into those toxicities with the cellular therapies that are really unique. So, CRS or cytokine release syndrome, so this is a T-cell mediated reaction that's occurring with both the CAR T and the bispecific antibody. It is most commonly treated with the anti-IL-6, and the an-, IL-6 inhibitor is tocilizumab (Actemra®) or with corticosteroids. So, historically with CAR T-cells, corticosteroids were avoided until more severe CRS due to the risk of direct cytotoxicity to those cells. More data is starting to debunk that, but it's still something that, where tocilizumab may be used sooner.

And this is something we can see with both the CAR T-cells as well as with the bispecific antibodies. But as Dr. Lonial mentioned, typically with those bispecific antibodies, it's one grade lower and sometimes less frequent. We can consider more advanced therapies, and if it becomes severe, ICU level care is required and recommended.



Slide 69: Therapy Related Adverse Effects Cellular Therapies: ICANS

ICANS is the neurotoxicity presentation that is also seen with the cellular therapies. So with CAR Ts, this can happen independently of CRS. But what we're finding with the bispecific antibodies is it's happening concurrently with CRO. All patients who receive CAR T should get prophylaxis with Keppra® (levetiracetam), and patients receiving both should be monitored for signs and symptoms of neurologic toxicities. So, there is a scoring tool that is used called the ICE score that patients are assessed with to determine the grade of ICANS. Other causes should always be ruled out, but the treatment here is somewhat similar to CRS. The only consideration that's different is that tocilizumab does not cross the blood-brain barrier well, so dexamethasone is used much earlier. And again, if it progresses, ICU level care may be needed.

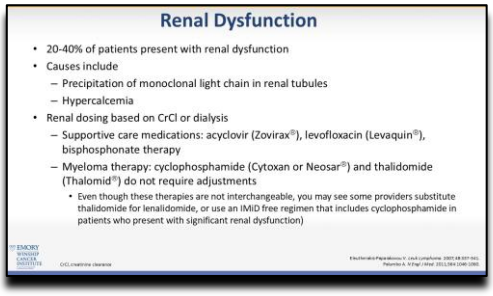


Slide 70: Infections[1]

Infections are huge within our population. As we mentioned, the disease state itself is immunosuppressive. All the therapy we're giving even more so. So, prophylaxis is really recommended based on the treatment the patient is receiving. Herpes simplex and Herpes zoster virus prophylaxis are specifically recommended for patients with a proteasome inhibitor, monoclonal antibody, bispecific, or post-transplant or post-CAR T. I will say many institutions will continue this indefinitely for the benefit of prevention.

Most commonly used are acyclovir (Zovirax®) or valacyclovir (Valtrex®). These are not different clinically; but the benefit of valacyclovir is it's once a day, so it can reduce pill burden for the patient.

PJP prophylaxis is also considered in certain populations, so high dose steroids, which we will define as dexamethasone, 20 milligrams per week or greater. And then bispecific antibodies, again, post-CAR T, post-autotransplant as well. Here, trimethoprim-sulfamethoxazole (Bactrim®) is the preferred agent, but there are alternatives for patients with an allergy or intolerance to this. IVIG is becoming very common, especially with the use of bispecific antibodies. So typically it's recommended in the guidelines that we administer IVIG to maintain an IgG greater than 400. You'll also see use of this at some institutions after CAR T-cells or in patients with recurrent infection.



Slide 71: Renal Dysfunction

Renal dysfunction, as we mentioned, is one of the CRAB criteria presentations with these patients, and some patients do not fully recover. So the causes of this can be multifactorial. We can see precipitation of the light chains within the renal tubules causing damage, and then the hypercalcemia can cause damage as well. From a pharmacy perspective, it's important to take into consideration their renal dysfunction before dosing of our therapy. So, this can include some of the supportive care medication as well as myeloma therapy. A couple to highlight that don't require renal

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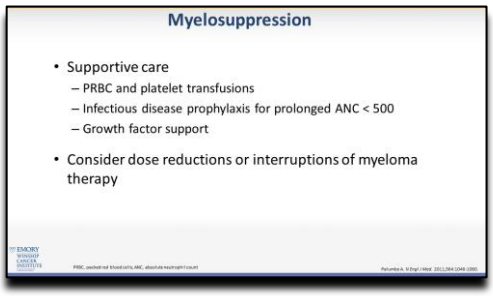
PJP prophylaxis should be considered for patients on high dose steroids. The NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections state "Risk of PJP is related to the daily dose and duration of corticosteroid therapy. Prophylaxis against PJP can be considered in patients receiving prednisone equivalent of 20 mg or more daily for 4 or more weeks." To translate this to our myeloma patients, the total weekly dose of prednisone 20 mg x 7 days would be 140 mg, which is roughly equivalent to dexamethasone 20 mg weekly. Though the NCCN guidelines on myeloma are more lenient: "For other myeloma therapy (Non CAR T-cell/BsAb: When equivalent dexamethasone dosing is >40 mg/day for 4 days per week or as clinically indicated per institutional practice," most pharmacists will recommend PJP prophylaxis for dexamethasone >/= 20 mg weekly based on the more conservative guidance. To review the NCCN Guidelines, go to www.NCCN.org

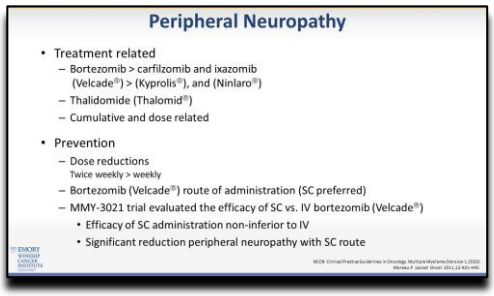
adjustment are cyclophosphamide and thalidomide, so you may see these two therapies used more frequently in patients at initial diagnosis who do present with severe renal dysfunction.



Slide 72: Myelosuppression

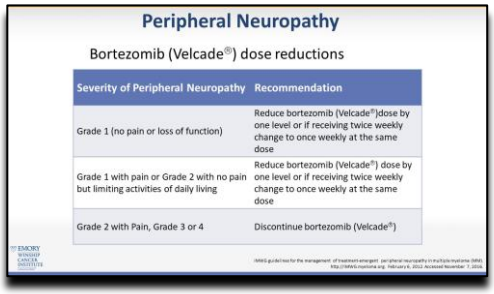
Myelosuppression is seen again, disease related, therapy related. So, a lot of supportive care here, and our goal with the supportive care is to maintain dose intensity and prevent holding of therapy. I tell my patients frequently we're here for the long game, not necessarily the strong game. The longer we can keep them on therapy the better. So, platelet transfusions or red blood cell transfusions may be needed. Infection disease prophylaxis, so if patients are severely neutropenic, in addition to the valacyclovir, we may consider addition of antibacterial and antifungal prophylaxis.

And then you'll frequently see use of short-acting growth factor. This may be used intermittently again to maintain that dose intensity and maintain these patients' neutrophils above 500 or 1,000 so that we can continue therapy safely. Ultimately though, we do have to consider dose reductions or holding therapy to allow these patients to recover.



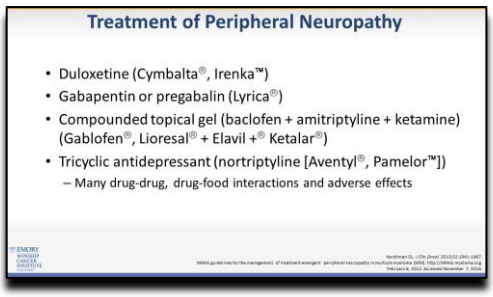
Slide 73: Peripheral Neuropathy

As we mentioned before, peripheral neuropathy is really significant with bortezomib. Within the proteasome inhibitor class, we may see this, but bortezomib is definitely the most common. Thalidomide is also peripheral, can also cause significant peripheral neuropathy. We do know that this is both cumulative with therapy and dose-related. So, there's a few ways that we can attempt to prevent peripheral neuropathy. Dose reduction is the primary one you'll see. So, a lot of institutions, instead of doing twice weekly bortezomib are moving to the weekly as it's been shown to have less peripheral neuropathy. And then you will almost never see the intravenous formulation of bortezomib as the subcutaneous formulation is noninferior and has significantly less peripheral neuropathy.



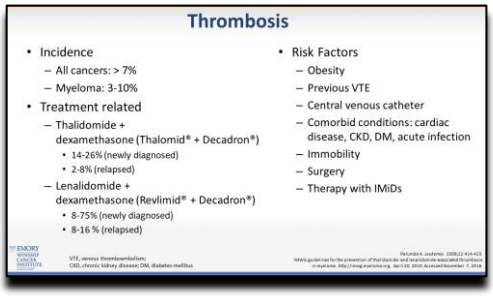
Slide 74: Peripheral Neuropathy

This is just a summary of the management of peripheral neuropathy grading. It really has to do with patients' quality of life and their ability to function with the neuropathy. We will often try to continue therapy and not discontinue, particularly in the induction setting. But as we get into the relapsed setting, quality of life does become more important to it.



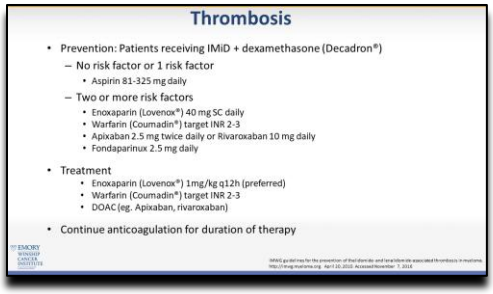
Slide 75: Treatment of Peripheral Neuropathy

Treatment here, duloxetine (Cymbalta®) and gabapentin (Neurontin®) are probably our most commonly used. We may consider pregabalin (Lyrica®) as well. And then there are some compounded topical agents we can consider. I would say tricyclic antidepressants have fallen out of favor, but you may see some patients who have been on this for a long time that they are benefitting from it. A nonpharmacologic intervention that is recently coming into favor is acupuncture, and some patients are finding benefit from this as well.



Slide 76: Thrombosis

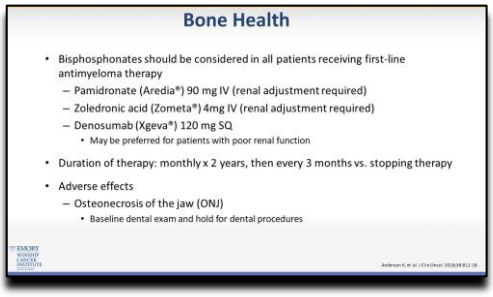
As we mentioned before, thrombosis can be a consequence of myeloma and then the addition of the immunomodulatory drugs significantly increases this risk. So within myeloma itself, up to 10% incidence of thrombosis. Risk factors are listed here for you. There are some risk scores, including the SAVED and the IMPEDE risk SCORE that you can use to more objectively quantify your patient's risk and determine what their prophylaxis should be.



Slide 77: Thrombosis

The most common prophylaxis that you'll see is aspirin. There is no difference within the dose of 81 to 325 milligrams daily. If patients have increased risk factors, we consider the use of a DOAC most commonly, but you may also see the use of enoxaparin (Lovenox®) or warfarin (Coumadin®), depending on the patient. Again, their comorbidities as well as the affordability of Lovenox® and DOACs can be quite expensive. And then treatment is just intensifying these regimens, so treatment doses of enoxaparin or DOAC. And we'll typically continue anticoagulation for

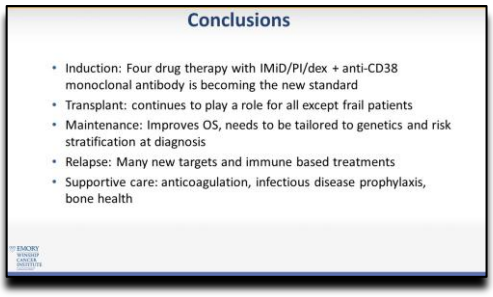
the duration of therapy and duration of the disease being present and having those risk factors from them.



Slide 78: Bone Health

Bone health is also significant within this disease state. Again, one of the CRAB criteria are presenting symptomatic myeloma presentation.
Bisphosphonates are the most commonly used, and they should be considered in all patients receiving their initial antimyeloma therapy. I would say zoledronic acid (Zometa®) is the most common, but this is formulary dependent, so you may see pamidronate (Aredia®) as well.
Bisphosphonates all require renal dose adjustments, and zoledronic acid is actually not recommended in patients with a creatinine clearance of less than 35. So, in that case, denosumab (Xgeva®) is a great alternative.

The duration of the therapy varies, but the NCCN guidelines do recommend administering it monthly for about 2 years and then every 3 months versus stopping therapy, and that's really dependent on the patient's disease status, what their bone health and disease status within their bones is, and then also provider discrepancies.
Important adverse effect to note here is the ONJ or osteonecrosis of the jaw, so all patients, if we're concerned about their dentition, should receive a baseline dental exam and then hold around the time of invasive dental procedures.

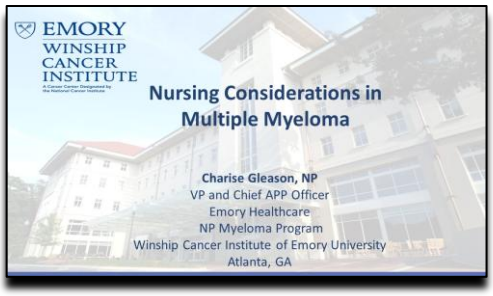


Slide 79: Conclusions

Dr. Lonial: All right, well thank you. This has, I think, been a great summary of a lot of the nuts and bolts at a high level in terms of management of patients with newly diagnosed myeloma as well as through their treatment journey. And I think really a particular focus on how counseling of patients and helping them anticipate what some of the adverse events and strategies on managing those adverse events are really important As you can see, we're now moving the armamentarium to a 4-drug regimen for induction. Transplant does continue to maintain an important role. Maintenance therapy, sequencing of therapy, and then appropriate supportive care and counseling both in terms of anticoagulation, infection prophylaxis, as well as bone health are all critical to maximizing the benefit a patient gets from overall therapy.

So, Dr. Scott and I are grateful for your joining us today and again thank you for your attention**.**

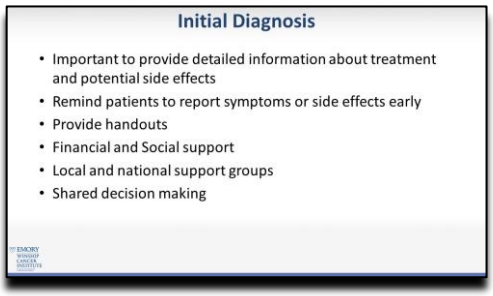
Lauren Berger: Thank you Dr. Lonial and Dr. Scott for your very clear & informative presentations.



Slide 80: Nursing Considerations in Multiple Myeloma

I now privileged to introduce Nurse Practitioner Charise Gleason to talk about the nurse's role in caring for patients with multiple myeloma. Ms. Gleason is Vice President and Chief Advanced Practice Provider officer Emory Healthcare Atlanta in Atlanta GA. Ms. Gleason.

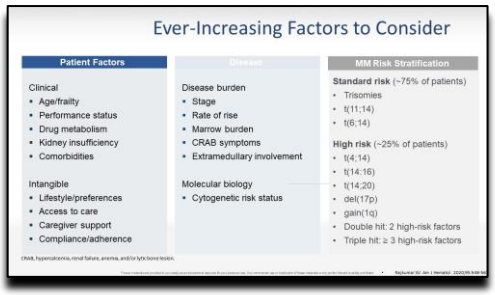
Charise Gleason, NP: Thank you. Now we're going to go through "Nursing Considerations for Myeloma.



Slide 81: Initial Diagnosis

And we'll kind of continue to think about our case study that you just discussed and how this new treatment and do, new diagnosis applies to our patient. So, you think about this initial diagnosis, and this patient is a young patient, right, active with really few symptoms. You know, went in with knee pain. So, you really want to think about, as you've got that new patient in front of you, the details that you're giving them about treatment and those potential side effects, when to report, when to reach out to you, providing handouts or however best they learn. You know, those websites, whether they need financial, social support. What are those support groups that you can lead them to as well?

And then this is really a shared decision-making moment, right? I mean we're going to make our recommendation of what's best and what we recommend for treatment and then how we get through it and manage the side effects is that relationship that we have with our patient.



Slide 82: Ever-Increasing Factors to Consider

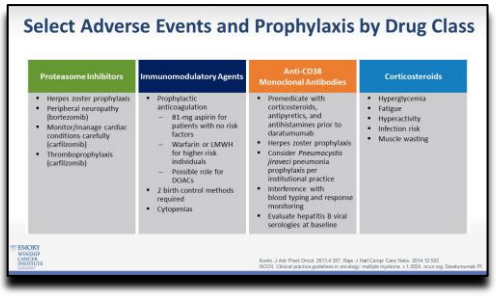
So, factors to consider, right? We look at our patient. As you've heard already from the other speakers, thinking about their age, whether they're frail or not, so that performance status. In our case, we've got a patient who has a very good performance status; but that's not always the case for our patients. You want to think about these drugs, other medications that they're on, so what side effects or interactions there might be, monitoring their kidney function, and as I said, there's other comorbidities.

We want to think about their lifestyles, so it's really important to understand our patient goal and their preferences, right? This is a young patient, a surgeon who's going to be working through induction therapy; so we're going to have to work around that, and that's going to be a big lifestyle change for this particular patient.

But our other patients, how's their access to care? Do they have a care partner to support them through this diagnosis and treatment? And then we want to think about compliance and adherence. So, if we're constantly educating our patients, updating them, speaking to them, better chance of them staying compliant with their medication, so they're reaching out, reporting to you when they're having side effects.

We've talked about the disease today, right, that disease burden, staging, thinking about how quickly is disease coming, how quickly we need to get treatment going, what other symptoms they have from myeloma. And remember, we've got patients who come in with absolutely no symptoms, right? They went to their physician for whatever reason, ended up with this diagnosis, and we're going to throw a lot of drugs at them that have side effects; and we could actually make them feel worse.

We're going to have another patient who comes in who feels terrible with their diagnosis, and we're going to give them treatment and make them feel a lot better. So, you know, different conversations, but open dialogue is so important. Discussing and reinforcing the type of myeloma they have and that risk stratification that we've already spent time talking about. In our patient's case, there are no abnormal cytogenetics, so this is a standard-risk patient who will be starting induction therapy.



Slide 83: Select Adverse Events and Prophylaxis by Drug Class

So, going through some of those adverse events, some things you want to think about from a prophylaxis standpoint, you think of proteosome inhibitors. We always want to make sure that we have Herpes zoster prophylaxis on there. We know that we can see a lot of cases in shingles in patients, both at diagnosis and throughout treatment. Peripheral neuropathy, induction therapy, these four-drug regimens, you know, does have bortezomib. We see far less cases of neuropathy since we've gone to subcutaneous, but there's still that possibility.

Managing cardiac function. If you have a patient who's getting carfilzomib, you really want to think about that. And also that thromboprophylaxis. Immunomodulatory agents, your patient has to start anticoagulation; and it really goes to do they have risk factors based on the IMWG guidelines for that. And so a patient who has no other risk factors, no history of a blood clot or a PE, an 81 milligram daily aspirin would be sufficient.

For patients who have other risk factors, you're going to look at something like a low molecular weight heparin. Warfarin though, quite honestly, you don't see us use that as much. And then the DOAC, which is oral agents that, you know, it says a possible role, but we certainly are using DOACs in most of our clinical practices.

Reminding your patients about the risk factors involved, this is a REMS program drug, and using two forms of birth control, there's also the other thing you want to think about is these drugs can be myelosuppressive; and so they can have cytopenias related to it. Again, we're putting four drugs together, so you really want to, to think about that as part of your conversation.

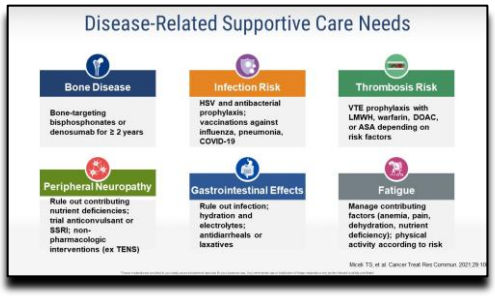
Your anti-CD38 monoclonal antibodies read typically for dose 1, we're going to premed with corticosteroids, antipyretics, and antihistamine prior to daratumumab. We give it subcutaneous now, so we see far less incidence of reactions; and the subsequent doses, really there's no issue and no prophylaxis needed.

Again, remember they get the Herpes zoster prophylaxis on there; and you might need to consider *Pneumocystis jirovecii* pneumonia, especially on a multi-drug regimen with four drugs and a higher dose of dexamethasone. Especially with that four-drug regimen, you definitely want the pneumocystis prophylaxis on there. Keep in mind that the anti-CD38 monoclonal antibodies, they can interfere with blood typing; and so we always want to send a sample to the blood bank prior to initiation of treatment.

So, isatuximab and daratumumab are IgG antibodies. So, they can interfere with your immunofixation, and so you can see circulating antibodies; and so you have to tease out whether that's myeloma or those circulating antibodies.

And then we also want to evaluate hepatitis B viral serologies, and so they're actually on our orders for dose one to send those serologies prior to initiation of treatment.

And then corticosteroids, there's a whole host of things there, and we'll talk a little bit more in depth about that, you think of hyperglycemia. So, if you had a patient who was already a diabetic, it's really important to partner with their other care team, if they have an endocrinologist or PCP because we're going to raise those blood glucose levels. And you think about fatigue, the risk of infection, muscle wasting, and those things that we'll talk about a little bit more.



Slide 84: Disease-Related Supportive Care Needs

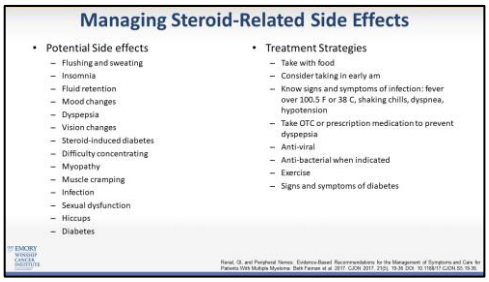
So, when we put it together and we think about those disease-related supportive care needs, we need to take care of their bones. We're going to put them on a bone agent. So, all these things happening, the diagnosis and initiation of therapy, and so you want a bone targeting agent; and typically, it's going to be in that bisphosphonate class or denosumab, and you see denosumab up front used more at renal insufficient patient. But otherwise, zoledronic acid or pamidronate.

Think about their risk for infection, so making sure they're on that antiviral. Have they had vaccines? We give the flu vaccine. Are they up to date on COVID vaccines, and when is it appropriate, as well as pneumococcal. And now we've giving the pneumococcal 20. That risk for thrombosis, making sure they're on their anticoagulation before they start therapy or as they start therapy. Monitoring throughout treatment for peripheral neuropathy, and so are there other things that can be causing it? Do they have a baseline coming in? So, that's an ongoing conversation every time you see the patient. And, you know, nurses play that role because, we might see the patient in clinic at day one of cycle, but they're coming for treatment to the infusion center throughout the cycle. And so that's a good time to ask them anything new, anything different? Are you having any of these side effects? And there are those interventions that we can do both that are pharmacologic and nonpharmacologic.

And then managing GI toxicities. It can be all over the place, right? Andy ou also want to think about is their potential for infection and not making assumptions based on the side effects. So making sure they're hydrated, making sure electrolytes are within normal ranges, and using antidiarrheals and laxatives as needed.

And then probably the biggest complaint we hear is fatigue, right? Fatigue from the treatment, fatigue from the cancer. If you're starting off a little bit more anemic, and just, it's just such a change. And the first two cycles I would say are probably the most challenging for patients as they're adjusting to all these new medications.

And so for our patient, again, this is a young patient in their 50s. this, a lot going on here, especially that neuropathy is going to be really important to a surgeon. Right, we don't want them to get any neuropathy with their treatment.



Slide 85: Managing Steroid-Related Side Effects

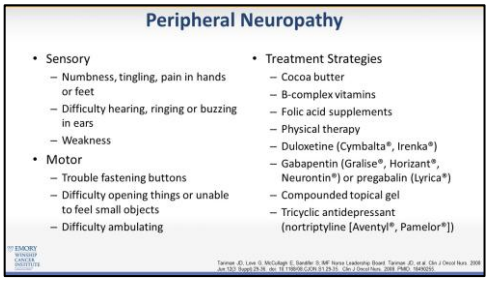
So, walking through managing some of these side effects, the first one is thinking about steroids, right? I said a whole host of side effects. And, you can rread them here, right? Flushing, sweating, insomnia, fluid retention, mood changes. You'll ask a patient how they're doing, and they're fine. And you've gota family member or a partner over there like shaking their head like, "No, not so fine on steroids." We give high doses at first, and then we tend to back down, which does help with some of these side effects.

Dyspepsia, we put people on high doses of steroids; and sometimes we forget to put them on a prescription or over the counter for that, so that reflux. So just something else to talk to the patient about and make sure that we're taking care of that.

You can get some vision changes related to steroids, so blurry eyes, so it's not unusual to see that. Watching them for steroid-induced diabetes and also if they have that baseline of diabetes, but difficulty concentrating. I mean we can just go on and on, right?

Myopathy, sexual dysfunction, and we don't always talk with patients about that, but we should. All these things are normal when you're on steroids. And so it's really helping them manage it.

So, taking with food can help. You know, most of the time we tell patients to take it in the early AM; and for a lot of patients, that works. I also have patients that would prefer to take it the first night in the evening, and then they get through the night and the next day. There's going to be that high and then that drop, and they're probably going to have, at least a night that it's very challenging to sleep. So, kind of, what works better for them. Understanding when to call us and fevers, right? Fevers over 105 Fahrenheit or 38 Celsius. Chills, , shortness of breath, hypotension, all those things, knowing that they need to call us and get seen. Our antivirals, our antibacterials, as we've discussed. Exercise. We still want our patients to exercise. And it's a little more challenging for a patient who gets diagnosed with a fracture or has a lot of pain issues, but there are still ways to get movement; and they're going to benefit from being more active. And you want to watch for those signs and symptoms of diabetes.



Slide 86: Peripheral Neuropathy

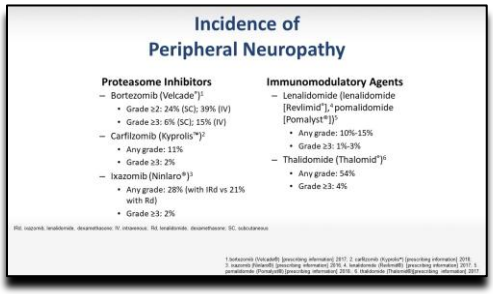
Now peripheral neuropathy, you can have it at baseline. You can have it with disease or other comorbidities, and it can come on you with treatment or sometimes even when we're going through induction treatment, no issues. But then when they go through stem cell mobilization or transplant, neuropathy can really get bothersome.

So, it's asking the right questions. And, you don't want to just say, "Do you have neuropathy?" So, again, for our case study, our patient, as a surgeon, they're going to understand what neuropathy is.

But not everybody understands, so it's something different. Your hands or feet feel different. Do you have cold sensation, tingling, buzzing? All those things you want to ask about? As it gets worse and it's more in the motor function, then they start to have trouble like buttoning or picking up a coin; and those are things that you can actually have them do. Show me how you do this. Because you want to adjust treatment. You don't want the neuropathy to get worse. You could actually cause more problems and keep them from getting a treatment or a clinical trial that they might need down the road.

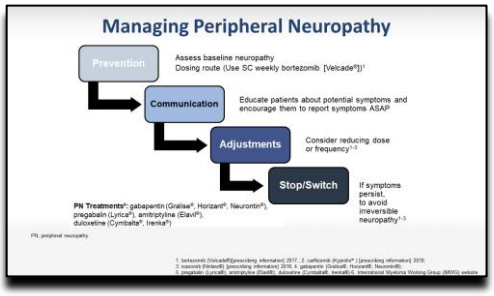
So, some of those treatment strategies, keeping the areas warm is helpful. Movement, keep them moving. Physical therapy can help with this, a squishy ball for their hands. Cocoa butter, B-complex vitamins, and these are things that the team will talk to the patient about. Nursing, you as a nurse will talk to the patient about and what are the supplements they can take?

Duloxetine, gabapentin, pregabalin, those are all prescription drugs that can help; but, of course, they come with their own set of side effects as well. So just really monitoring and, paying attention to those side effects. There are some compounded topical gels that work really well, but they can be very expensive; and not all patients can get those.



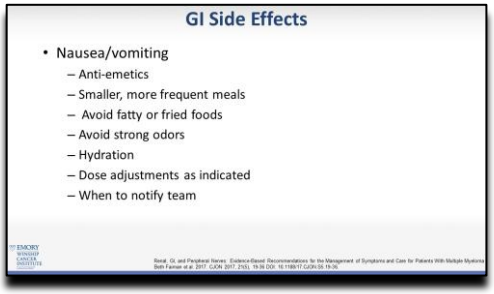
Slide 87: Incidence of Peripheral Neuropathy

So, things to, to think about, questions to ask your patients, the incidence was much higher if you look at proteosome inhibitors with bortezomib, for instance, when it was given IV. So, the incidence is much less with subcutaneous. We do still see it with carfilzomib and ixazomib. Immunomodulatory agents, you've got lenalidomide and pomalidomide, which a lower incidence but, again, it still happens. So, asking those questions is really beneficial to your patient.



Slide 88: Managing Peripheral Neuropathy

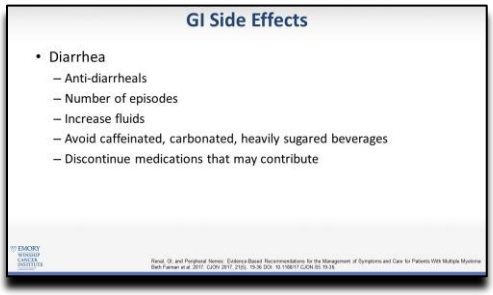
And sometimes what do we do to manage it? Sometimes we have to stop or switch, but we hope to not get to that point if we're managing it along the way. But by preventing it, constant communication about it, asking them, and then making dose adjustments as needed.



Slide 89: GI Side Effects

So, moving onto GI side effects, and this is nausea and vomiting with an induction regimen like daratumumab plus RVd, you don't usually see a lot of nausea, but it can happen. And it certainly can happen with some of our other regimens. So, you want to think about making sure the patient has an antiemetic at home to take. Smaller, more frequent meals. Avoiding fatty things, fried things; that can be a little bit more upsetting for patients. Strong odors. Right, if you think about your cancer center, the microwave has signs that say, "No popcorn, no fish." Smells like that are really bothersome for people who are undergoing treatment.

Making sure that they're well-hydrated. You can be more nauseated when you're, dehydrated and get dehydrated from being nauseated and afraid to have something to drink. And also, we might have to make dose adjustments if needed. But making sure that they know it's not normal, it's not expected for them to be miserable with that. Don't wait till your next appointment and go ahead and call us or contact us through the patient portal to let us know that you're struggling with that.

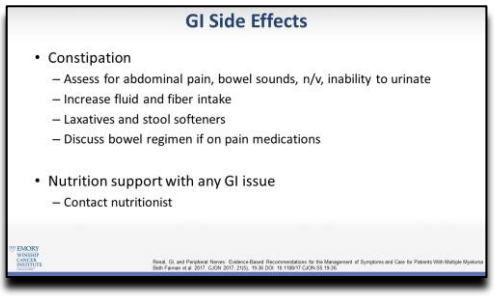


Slide 90: GI Side Effects

Now, we can also see diarrhea and/or constipation, both sometimes for some patients in the same week. So, if they're having diarrhea, antidiarrheals are fine. You just want to be careful not to go overboard with that, that we then turn into constipation. So it's kind of finding that balance. Again, fluids, you notice, central theme. Fluids are good.

You want to think about the number of episodes, especially if patient's on a clinical trial, we keep track of those things and grade them. Avoiding caffeinated, carbonated, or heavily sugared beverages can be problematic. And then you want to discontinue any medications that might be contributing to that. So, it's important to look at their med list and make sure they're not on a stool softener. Patients, some of these medications are

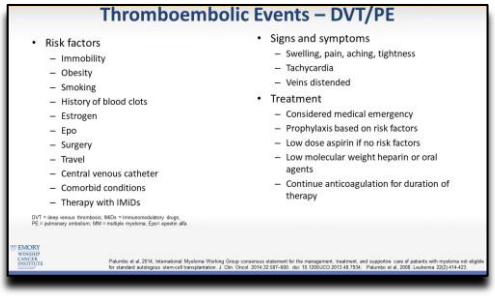
new to them, and we've got patients on a lot of medications. And so that's really important to take a look at that as well.



Slide 91: GI Side Effects

And then constipation. You want to think about bowel pain. Do they have bowel sounds? So, you know, when I'm examining a patient, I want to make sure I hear bowel sounds in all four quadrants so I know that they do at least have sounds and there is activity there.

Are they able to urinate or not is really important to know. So for constipation, you can increase fluids again. Fiber intake, laxatives, stool softeners. If they're on a pain medication, even if they're taking over-the-counter Tylenol or ibuprofen, though our patients rarely take ibuprofen, they need to consider that that can be constipating as well. If you have nutrition support, we're very fortunate in our practice that we do have a nutritionist, so she works with our patients quite a bit as well. Usually it's more on the diarrhea side, giving tips, especially with patients who are on long-term Revlimid.



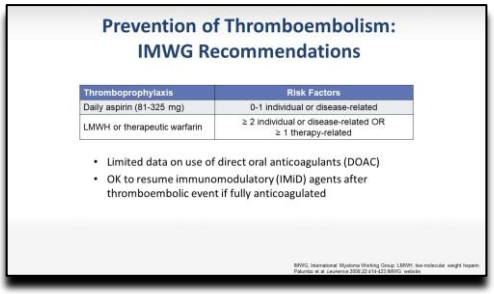
Slide 92: Thromboembolic Events – DVT/PE

And then getting back to thromboembolic events, that DVT or PE. We know that especially with the immunomodulatory agents that this is a risk. And so what makes them at a greater risk for developing a blood clot? Not moving, being obese, or smoking. If they have a history of blood clots, they're going to be on more aggressive anticoagulation when they start their regimen anyhow.

On estrogen, epo, those things that get used in a lot of other practices, we have to be really careful with our patients. If they've traveled, we've got patients who took a long flight and come back, even on an aspirin, and end up with a clot. So, talking to them about that movement and getting up, moving around, wearing compression stockings when you're traveling. A catheter in place can make you more at risk. Other comorbidities as well. But patient calls in, they're having swelling, pain, achy, tightness, and sometimes it's just distension, and it's not always red and warm. But these are things, especially if it's on one side, you want to quickly take a look at and get an ultrasound just to assess to make sure that they don't have a DVT.

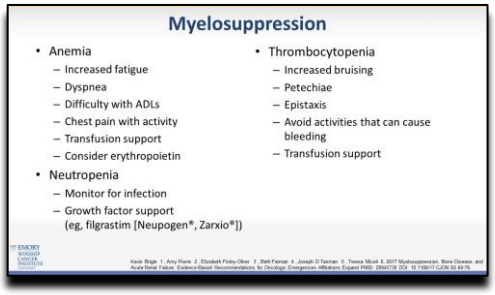
You know, PEs are a little bit different. Usually those are in the lungs. Pulmonary embolism, usually they are in the lungs. And those are more acute. You know, it's not a, "I was having pain for the last two weeks in my chest." It's like, "I got up on a Saturday, I had this terrible chest and this sense of doom." You know, that's somebody that you want assessed immediately.

So, treatment, consider it as a medical emergency. They should already be on prophylaxis, based on their risk factors; and sometimes you have to change that. But you're going to continue that anticoagulation as long as they're on therapy. And for us in our practice, if they're on an IMiD, even if they come off, we typically keep them on their anticoagulation for at least two months afterwards.



Slide 93: Prevention of Thromboembolism: IMWG Recommendations

This is the IMWG Recommendations. If you have 0 to 1 individual or disease-related risk factor, usually a daily aspirin is sufficient. And for most people, it's 81 milligrams. Now, your risk factor cannot be you previously had a blood clot or previously had a PE. Those, that puts you at a high risk category, and you're going on anticoagulation, more aggressive no matter what. If you have a 2 or more or, again, therapy related, low molecular weight heparin or therapeutic warfarin, but most of our patients are going on DOACs, those direct oral anticoagulants. Much easier for the patient and typically, even if they've had a clot, you can resume the immunomodulatory agent once you get them fully anticoagulated.



Slide 94: Myelosuppression

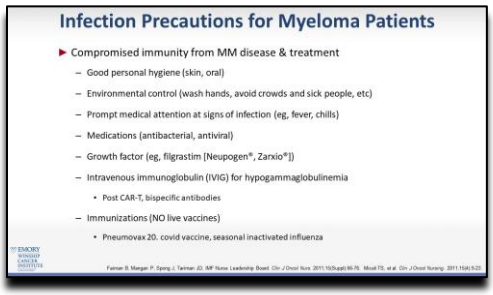
Myelosuppression, we put patients on these multiple drug regimens, and we do drop counts. So, that's why you'll see with lenalidomide and pomalidomide, if you have a patient on that, typically they take it 3 weeks on/1 week off or 2 weeks on and 1 week off, depending on what regimen they're on. And that's so they can have that week for their counts to recover.

When you add a multidrug regimen, you're going to have more myelosuppression with that. And then you also are fighting an active disease, so especially in the case of our patient who this is newly diagnosed. Their hemoglobin looked okay. But you, a lot of times somebody will start very low and so until you get disease off and then between the medication, sometimes it takes a while for that anemia to resolve.

So, paying attention to what their counts are. Is their white count dropping too low? Do you need to add growth factor support, which is very common? For anemia, looking at their fatigue, treatment causes fatigue. So, are they having more shortness of breath? Are they having any problems with their ADLs? All things that you want to talk to them about. Chest tightness, chest pain. We rarely use erythropoietin, just because that risk of thromboembolic event increases with it. The times that we do use it in a myeloma patient

is if they have renal failure or renal insufficiency, and that's in conjunction with their nephrologist. But really, it's when that hemoglobin's lower.

When they first came out, people were getting them to keep hemoglobins around 12, but we wouldn't give epo for anybody that's over a hemoglobin of 10. And then low platelets, that thrombocytopenia, you want to watch for bruising, bleeding, petechiae, and avoid activities that could cause that. Typically, in the upfront setting, we don't see as much of that, especially with induction treatment. But you can, and so you definitely see it in the relapsed/refractory patients; and so you do need to monitor for that.



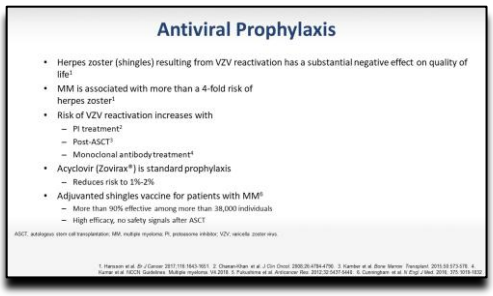
Slide 95: Infection Precautions for Myeloma Patients

We tend to treat through these things and just give them the blood support or platelet support that they need. The other thing is this is a cancer of the immune system, right? So their immune system isn't working as well. They're already more susceptible to infections, and then you put them on multiple drugs, and so you really want to think about infection and infection prophylaxis.

So, good personal hygiene, both on the skin and in the mouth. Washing hands. Avoiding people that are sick, avoiding crowds. Even prior to COVID, there were periods of times with our patients, especially in the post-transplant period, where we had them wear masks and avoid crowds. So, none of that's changed.

Prompt attention if they have infectious type symptoms, and so them reaching out, fevers, chills, but keep in mind with an older patient, they don't always have those kind of symptoms. Right, an elderly patient might just suddenly be confused. And so having that conversation with the family member or caregiver just so they recognize that you can have infection without having an actual fever. Making sure our patients are on their antivirals. Sometimes antibacterials. Are we needing to use growth factor to get those counts up? And then sometimes we need to give monthly IViG. So, patients have such low gamma globulin, so what we call hypogammaglobulinemia, that we give monthly IViG; and we do that especially in cold or flu season for patients who have had recurrent infections. But the other time with some of our newer therapies that you talked about earlier, CAR T bispecifics. They are so immunocompromised after these maneuvers that they definitely need monthly IViG for at least six months.

You want to make sure they get their Pneumovax 20. That's the latest. Their COVID vaccines as appropriate and where they are, with their platelets and where they are with treatment. And then there's seasonal influenza vaccine.



Slide 96: Antiviral Prophylaxis

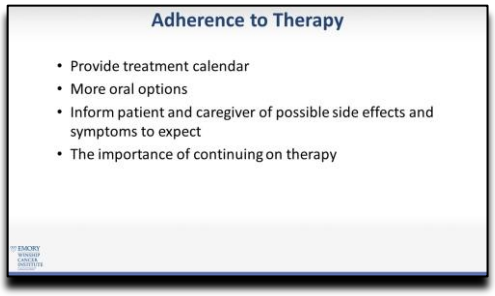
So, a little bit more about the antiviral prophylaxis. We've said we see a lot of shingles in our patients, both with myeloma and with our treatments. So making sure that they're on prophylaxis with either acyclovir or valacyclovir really reduces that risk. They can get the Shingrix vaccine, but there's no data to support whether that's sufficient for them to come off an antiviral. So we keep our patients on the antiviral prophylaxis.

Slide 97: Tools for Management of Fatigue

And fatigue is a tough one, right? People are fatigued from their cancer, they're fatigued because they're anemic, the treatment just makes them tired. So, you really want to think about the individual patient in front of you, and what are those things that you can do? And, are they having pain? Is that causing more fatigue? Are they depressed? So, asking the right questions, encouraging activity. Walking's a great activity for our patient. But if they haven't been doing anything, I mean walking to the mailbox is a good start.

Use physical therapy, if you have some kind of integrative oncology team. We're very fortunate that we have that at our cancer center that we can refer our patients into to help really give them an assessment and help them get through some of these things – so sleep, nutrition support, depression, all of those things. You want to balance the activity. it's okay to rest some. They're tired, right? But you don't want them laying in bed all day long, so you want them to think about the things they're doing.

Nutrition support. Make sure they're getting their meals. Make sure they can afford their meals, and that's where our social workers can really help us as well. And then sometimes, if they haven't slept for days because they've had steroids, sometimes we might have to give them something to help them with that.



Slide 98: Adherence to Therapy

So, thinking about adherence to therapy how do we keep our patients taking their treatments, especially when we're giving them so many things? I think it helps if we have that communication and that open relationship and we're talking about our goals of therapy, and we're really partnering with our patient, so that they do let you know if they're having side

effects and we have to hold something. What you don't want is for them not to tell you and that this month they're holding the drug and next month they're stopping their steroids. You know, we want to know about those things so we can adjust them appropriately. And then patients are more likely to stay on track.

Providing a treatment calendar. We'll do that for patients that want that. Some people would rather do it electronically for themselves. But if that's what helps you, that this is the day that I take a certain drug, getting in routines can really be helpful. And for patients and their caregivers, their care partners to understand upfront what the potential side effects are and they're not surprised by it, and we're reinforcing and asking them the right questions. It's really important for them to stay on therapy.

Myeloma is a cancer where it is going to be continuous therapy, and so our patient is going to go through induction, transplant, and then maintenance. And it's more upfront in that for newly diagnosed patients for instance. More of that commitment, more drugs.

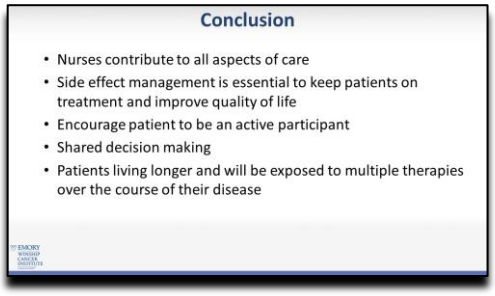
But by the time they get to that maintenance setting things are getting back to normal for them. And it's for a standard-risk patient, like our patient today, will get a single drug maintenance. You know, which is much easier at that point. So that it's really important for our patients to understand the things that they can do because this is a continuous journey of medication while they, through myeloma.

Slide 99: Strategies for Staying Well

So, what are those other strategies just to stay well? Well, balanced diet. Right, the patient gets diagnosed, and everybody comes and tells them all the different things, the supplements they need to take, the dietary changes they need to make, can't eat this, can't eat that. I tell patients just eat a balanced meal. Things in moderation. You don't have to cut out everything that you like, but you also can't only eat carbs, for instance. Or if you like a little dessert, that's fine. You can't eat nothing but sugar. So, I think understanding that you can still eat, you can still do things that feel normal to you. It's okay. It might taste a little different because of the treatment that you're on, but keeping things in balance.

Daily activity and exercise. I mean that's good for all of us, and it's good for our patients. Avoiding infection, keeping away from people that are sick, avoiding bleeding, right? But you really want patients to still do the things that make them them, right? You want them to still continue to live, and so we're going to get through this; and that's our job to partner with them to get them through this and how do we get to a place that you can manage this?

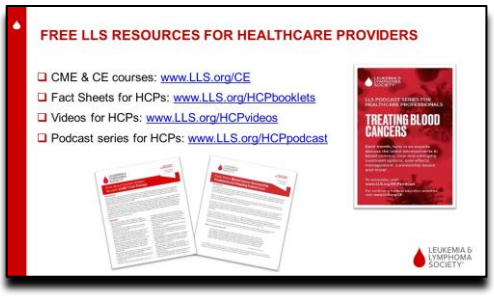
Taking advantage of available resources, and helping them to find those resources, right? Helping them to find support groups, and knowing that you're there if they need to ask for help, right? We want to encourage our patients to ask for help when needed. And ask us questions. Ask patients, tell patients, "Write down your questions when you come to clinic." These visits go quickly. You wait sometimes and have those five major things that you want to talk about that day so you make sure your issues are addressed.



Slide 100: Conclusion

Sothis is a lot today; but nurses really contribute to all aspects in care, right? They crossover at clinic, infusion, triage nursing, inpatient if they go in the hospital. So, nursing is part of all the management for your myeloma patient throughout. Side effect management is essential to keep patients on treatment and so that open communication and preserving and improving their quality of life. So, we want them to be an active participant. We think of shared decision-making. We're doing this together. We're going to give you our expert advice, but we have to have your buy-in too; and you have to understand why you're doing this.

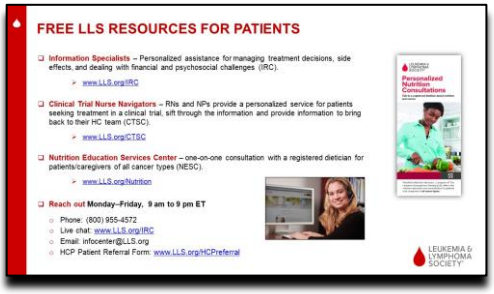
And we know that patients are living longer, and they're going to be exposed to many therapies over the course of their disease, so keeping them healthier, with less side effects is going to help them in the long run. Thank you.



Slide 101: Free LLS Resources for Healthcare Providers

Lauren Berger: Thank you Nurse Practitioner Gleason and Drs. Lonial and Scott.

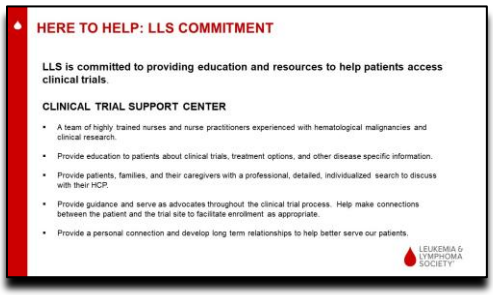
I am now pleased to share free resources. I am now pleased to share free resources for you & your patients. The Leukemia & Lymphoma Society offers free CE & CME online and in-person regional programs, as well as a podcast channel for Healthcare Professionals, where you can listen to discussions on treatment, side-effect management & more. New & interesting topics are added every few wks. Access these as well as Videos & Fact Sheets for HCPs @ www.LLS.org/CE.



Slide 102: Free LLS Resources for Patients

LLS Information Specialists are highly trained Oncology Social Workers & Nurses who provide accurate, up-to-date disease, treatment & support information, including financial. Patients can contact them directly, or you can complete a referral form. Information Specialists can also help you order free copies of booklets to give to your patients. We also offer free 1 on 1 nutrition consultation w/our Registered Dietitians by phone for patients of all Cancer Types & ages. Our Clinical Trial Support Center Nurse Navigators are RNs & NPs with expertise in blood cancers.

CTSC Nurse Navigators work 1 on 1 with patients, via telephone, to provide user friendly information, help them find appropriate clinical trials, personally assist them throughout the clinical trial process & provide information for the patient to bring back to their healthcare providers. This is unique service from LLS. I hope you will consider all of these specialists an extension of your Healthcare Team.



Slide 103: Here to Help: LLS Commitment

Here is a brief overview of the CTSC Process for Supporting Patients. The goal is not to enroll every patient into a trial, rather to increase opportunities for participation by facilitating informed decision making & minimizing logistical barriers for the patient. They work in collaboration with the patient's healthcare team to decide if a clinical trial is right for them. Ultimately, they educate, support, & empower patients to be active participants in and have control over their treatment decisions.

Slide 104: Free LLS Resources for Patients and Caregivers

LLS offers blood cancer disease specific information & support resources for patients & caregivers, including telephone & web education programs, videos, podcasts & booklets. I encourage you & your colleagues to stay up to date on the availability of LLS' Financial Assistance programs, & other resources, using links on these slides.

Slide 105: Free LLS Resources for Your Patients

Through Targeted & Culturally Appropriate programs & services, we are committed to addressing needs of minoritized communities impacted by a Blood Cancer & those facing barriers to optimal care. We are increasing resources that provide education on health equity and/or are designed to support groups that experience health disparities as well as resources for healthcare providers that serve groups that experience health disparities. Our materials are available in English & Spanish and our Information Specialists & other specialists, consult with patients in additional languages.

Slide 106: Thank You!

To all healthcare providers, I hope this information will be helpful to you, as you care for your patients. If you would like more information for yourself or support for your patients, please contact an Info Specialist at LLS at 800.955.4572 www.LLS.org/support