Myelodysplastic Syndromes
Transitioning to Acute Myeloid Leukemia

LEUKEMIA & LYMPHOMA SOCIETY®

TRANSCRIPT

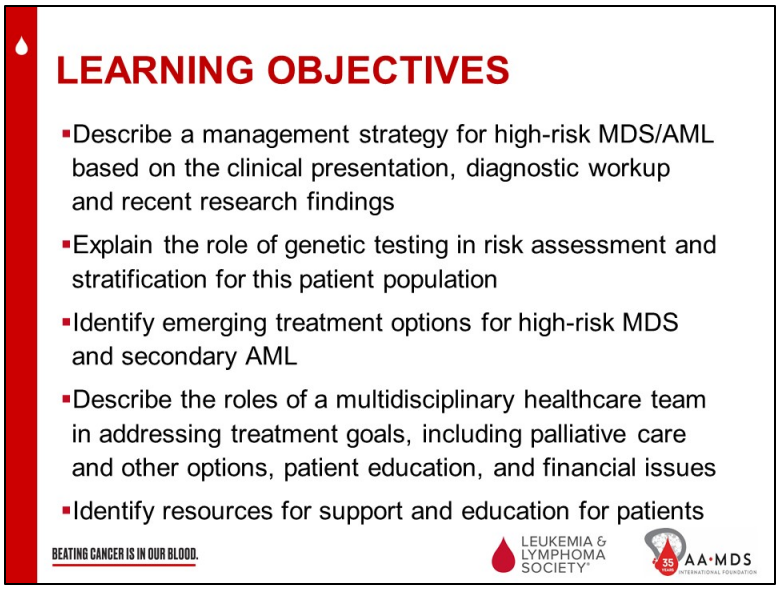
WELCOME AND INTRODUCTION

Caroline Kornhauser, MPH
Good afternoon, on behalf of The Leukemia & Lymphoma Society (LLS) and the Aplastic Anemia & MDS International Foundation (AAMDSIF), thank you all for joining us today. I'd like to take a few moments to tell you some information about the LLS and AAMDSIF. LLS is committed to improving patients' quality of life through programs and other professional and support education programs. We offer live and archived patient and professional programs for which you can earn CME, nursing, or social work credit.

The LLS advocates for funding to accelerate the discovery and development of blood cancer therapies. To date, LLS has invested more than $1.3 billion in research to advance therapies and save lives.

The Aplastic Anemia & MDS International Foundation is the world's leading nonprofit health organization dedicated to supporting patients and their families who are living with aplastic anemia (AA), myelodysplastic syndromes (MDS), paroxysmal nocturnal hemoglobinuria and related bone marrow failure diseases.

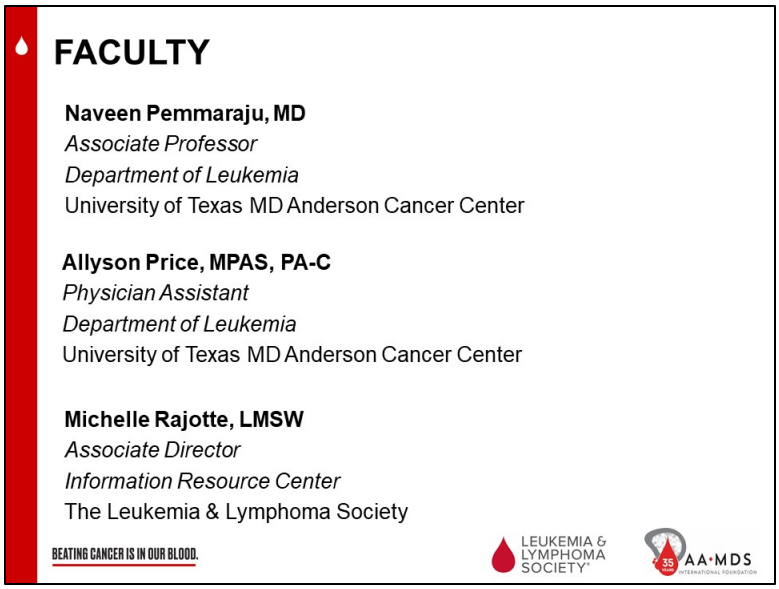
Founded in 1983, AAMDSIF provides patient education resources, professional education programs, research grants and advocacy for bone marrow failure disease research funding.



Today, our presenters will describe a management strategy for high-risk MDS/AML (acute myeloid leukemia) based on the clinical presentation, diagnostic workup, and recent research findings; explain the role of genetic testing and risk assessment and stratification for this patient population; identify emerging treatment options for high-risk MDS and secondary AML; describe the roles of a multidisciplinary healthcare team in addressing treatment goals, including palliative care and other options, patient education, and financial issues and identify resources for support in education for patients.

To receive CE credit for this program, please complete the evaluation. Your feedback is important in helping us plan future programs and is also required for you to receive continuing education credit.

A certificate of completion will be issued to you after the evaluation is submitted. The certificate will be a downloadable PDF.



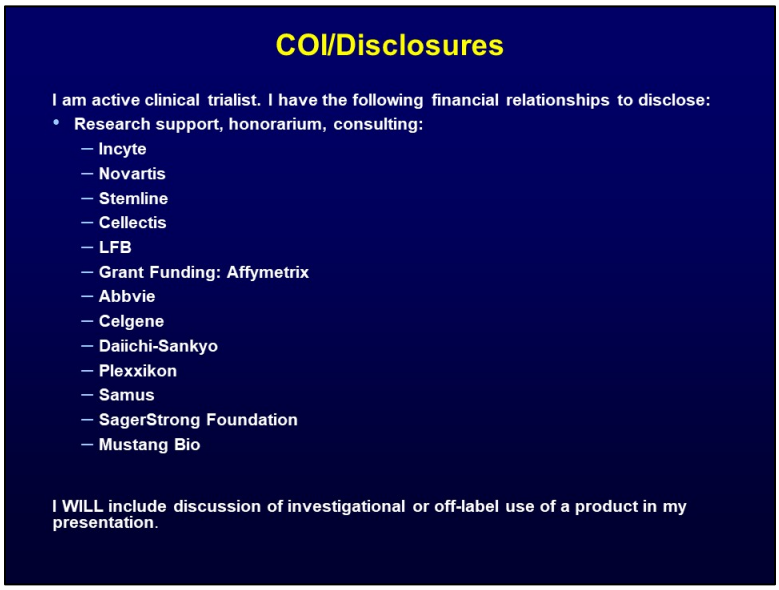
I'm now honored to introduce our speakers for today. Dr. Naveen Pemmaraju, Associate Professor and Allyson Price, physician assistant for the Department of Leukemia at The University of Texas, MD Anderson Cancer Center in Houston, Texas, as well as Michelle Rajotte, Associate Director of the Information Resource Center at The Leukemia & Lymphoma Society. Thank you all for sharing your time with us today.

It is my pleasure now to turn the program over to Dr. Pemmaraju.

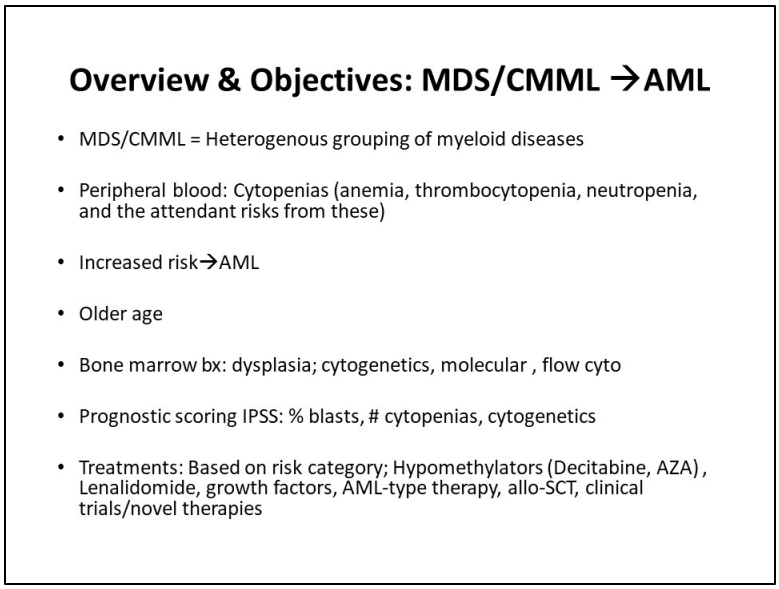
PRESENTATION

Naveen Pemmaraju, MD

Well thank you very much for that kind introduction and thank you all to the viewers/listeners out there. It's my honor to present to you an update on myelodysplastic syndrome transitioning to acute myeloid leukemia or AML.



For full disclosure, I am an active clinical trialist, and I work with multiple companies in order to bring novel therapeutics to our patients, and so this is a list of my disclosures. For sure, as with any rare leukemia or rare disease presentation, I will be discussing investigational or even off-label uses from an expert perspective. Let's begin.

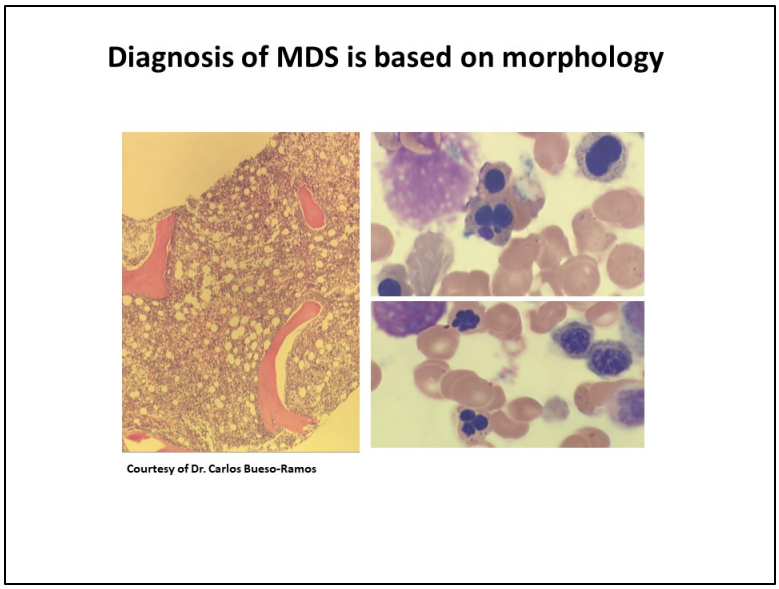


Overview and objectives for MDS, myelodysplastic syndrome, and the related CMML, chronic myelomonocytic leukemia, as it transitions to acute myeloid leukemia or AML. The first principle is that this group of diseases really represents a family of dozens, maybe hundreds, of different blood diseases or blood cancers all under one roof. The common denominator is that the bone marrow does not work properly: myelo, meaning bone marrow, dysplastic meaning cells not made appropriately.

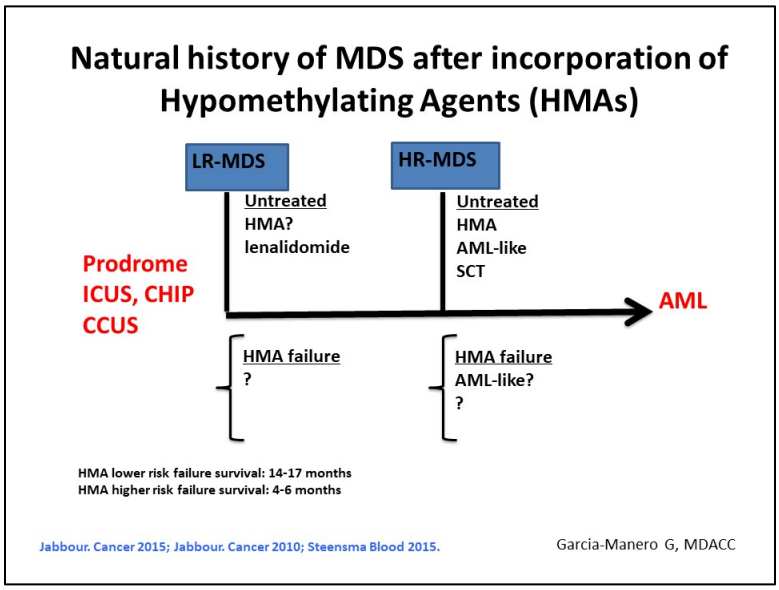
In the blood, that is the peripheral blood, we see low blood counts in most of our patients, so anemia, low red blood cells, thrombocytopenia, low platelets, neutropenia, low white cells. And, of course, the risk from these: anemia, shortness of breath, fatigue, bleeding, thrombocytopenia, bleeding, neutropenia, infections.

It is true that as we look for MDS, that it increases as we age and that the increased risk is not only age but other factors that we'll go over that lead to an increased risk of acute myeloid leukemia. Both conditions are life-threatening in and of themselves, including the now recognized phenomenon that patients can have death and dying with MDS itself before even transitioning to AML.

Over the course of this talk, we'll look at the bone marrow findings which show dysplasia, abnormal cells, the chromosomes or cytogenetics and molecular information. There are some simple, easy-to-use prognostic scoring systems which means, giving us the ability to tell how low, intermediate or high risk your disease is and then, finally, some of the treatments that are approved and those in research.

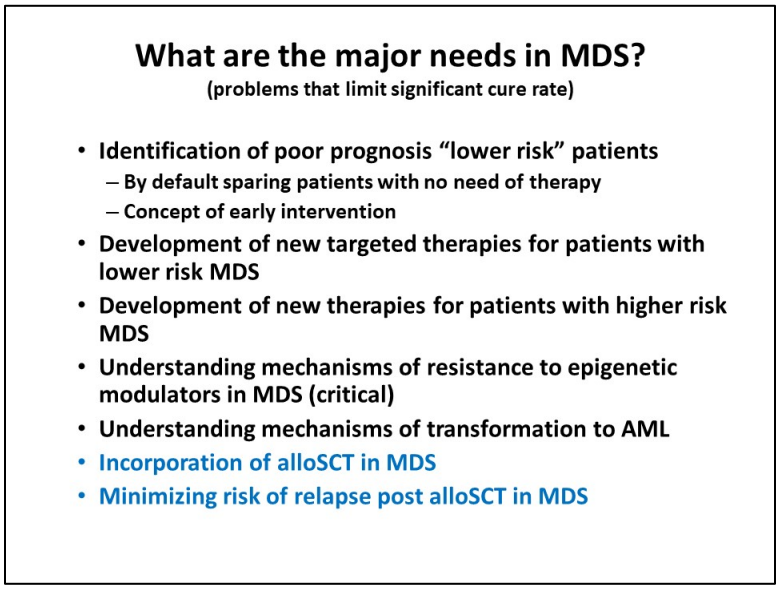


So, we begin by looking under the microscope in the pathology lab. This is actually a difficult diagnosis to make, particularly in people who are not expert or who don't see the disease often, therefore, emphasizing the importance of expert hematopathology. This is a bone marrow on the left and on the right, and what you can see here is that the cells are being made improperly. To the naked eye, it may not appear so, but there are advanced stains and expertise that's required to be able to tell this. But, basically, myelodysplastic syndrome, abnormally made cells in the bone marrow that may present into the bloodstream.



Now here on this slide the natural history of MDS kind of as a timeline. As our thinking has evolved, we now understand that there may be a prodrome or pre-MDS state known as CHIP, clonal hematopoiesis of indeterminate potential, on the associated syndromes. These are patients who do not yet have an outright cancer or malignancy but may have a predisposition to develop, and this is an emerging, evolving field.

In terms of MDS, we divided into LR, low risk, or high risk, HR. And you can see on the slide here that there are a few treatment options for each one but with several question marks, and we'll go through them. The bottom line is that there are not dozens of treatments that are FDA-approved for these diseases, and so urgent research is necessary. And when a patient is not able to respond to one of these treatments that are available, outcomes can be poor.



So, what are the major needs in a rare leukemia, rare blood disease such as MDS? Well, as I mentioned, just identifying the diagnosis and prognosis is very difficult. Even if someone scores as lower risk, patients may still do poorly, may still die, may have infections or blood transfusions.

The development of new targeted therapies has been quite difficult over the last few decades and greatly assisted by organizations such as the ones sponsoring this current program, pharmaceutical companies, and academic centers to try to figure out new pathways. I think that understanding the mechanism of how the disease works, how it resists drug therapy is critical to our development of new drugs. And as you'll see here, the available systems that are in place such as allogeneic stem cell transplant, taking the cells of one person, putting into another, are okay, but only for a small group or subset as most of our patients are older or frail or unable to go for a transplant.

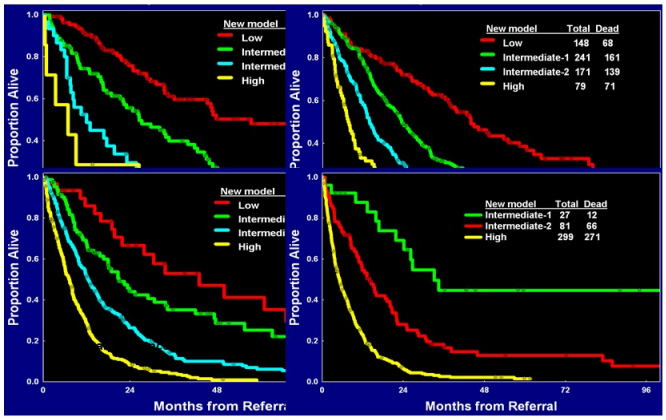
International Prognostic Scoring System: IPSS

- Greenberg et al 1997 Blood

- % BM blasts
- Cytogenetics
- Cytopenias

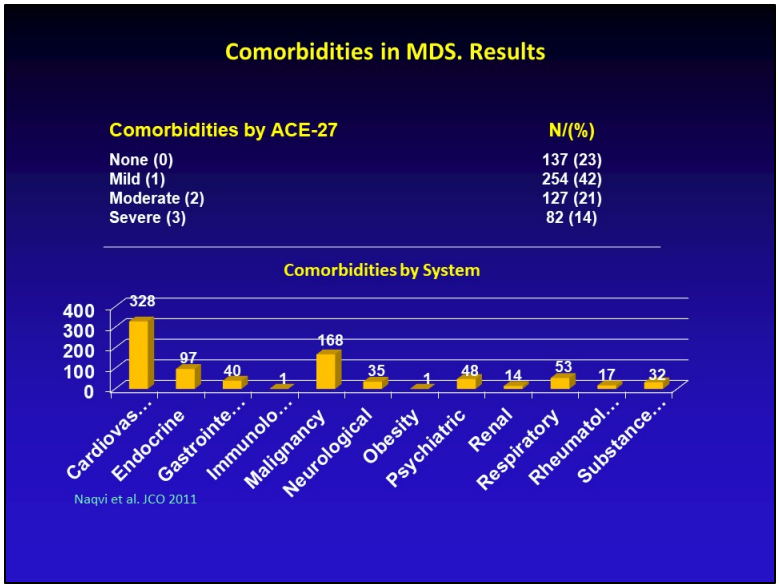
So, we begin with prognosticating. How bad is one's disease? Well, in 1997, the seminal paper that we still use came out in *Blood*, which is one of our major publications. It's called the IPSS, International Prognostic Scoring System, and the goal here is to use three simple, available tools to tell us how low or intermediate or high risk the MDS is. Number of bone marrow blasts, fairly self-explanatory. Cytogenetics means your chromosomes, and then cytopenia means the degree or number of anemia, thrombocytopenia or neutropenia. So, we put those into a quick formula, and then that allows us to tell who's who.

Survival by MDS model within IPSS Risk

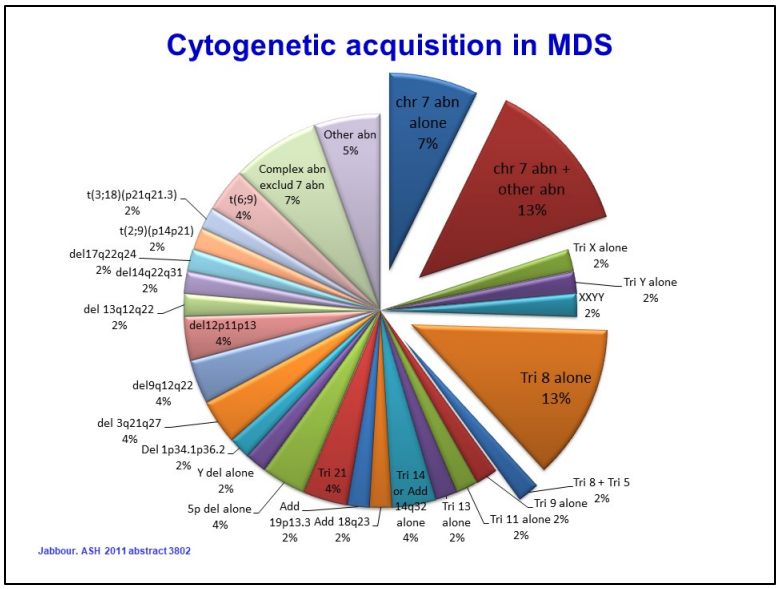


Now when we look at this model in terms of survival, how patients do in terms of their life expectancy in this risk, it separates out nicely. These are called Kaplan-Meier curves. You'll see those frequently in any field of oncology. It gives you an estimation of overall survival. The top lines here are the low risk. You expect them to do the best, and they do, followed by intermediate with the green, and then intermediate II and then high risk.

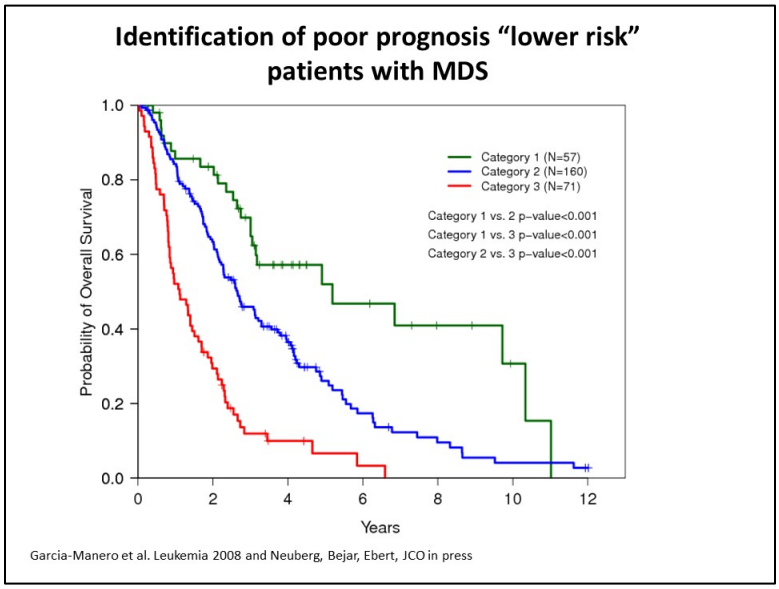
What you basically see here is that whether you have an older model or a new model of these scoring systems is that you can stratify or divide out our patients so you have a heterogeneous group of diseases and a heterogeneous grouping of outcomes, and we can start to figure out who needs therapy and who doesn't.



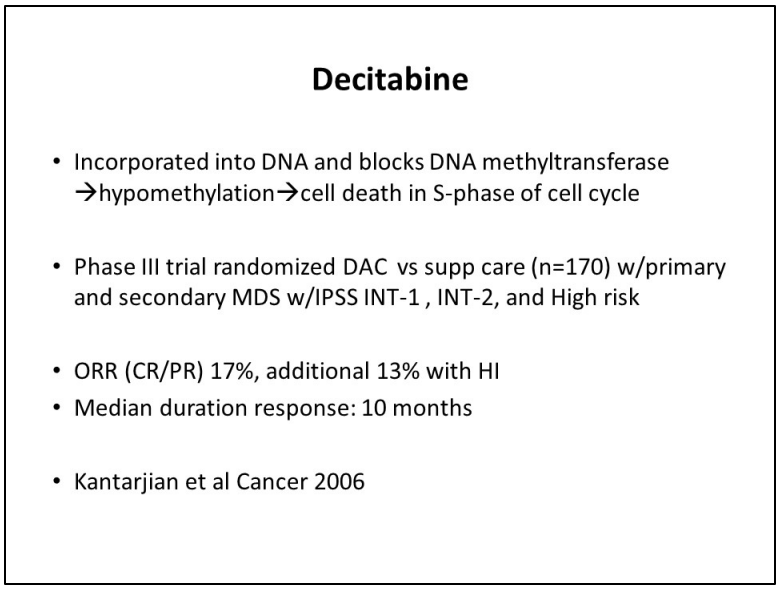
But the problem with MDS is many-fold. One is the age. A lot of our patients are older. The median age or average age is closer to older 60s, 70s and above. So, a lot of patients have comorbidities, as many of you know, anything from mild to moderate. One of our physicians, Dr. [Karin] Naqvi, did a nice study that showed that many of our patients have systems outside of the blood and bone marrow, most importantly, cardiovascular side effects, that really limit the ability to give or recommend therapies outside of the blood cancer. So, this is an important aspect for those in nursing, in social work, [and] case management who are trying to plan the overall care of the patient.



Now as we understand more about MDS, it moved from just understanding what's under the bone marrow to what are other factors. And now we check chromosomes, at least at our center at MD Anderson, on every patient who comes in the door. Well, it's important. The number of chromosomes that are abnormal versus normal, as seen on this somewhat complex chart, can really emphasize who's low, intermediate or high risk outside of those traditional features I showed you, outside of the blasts and the cytopenias.

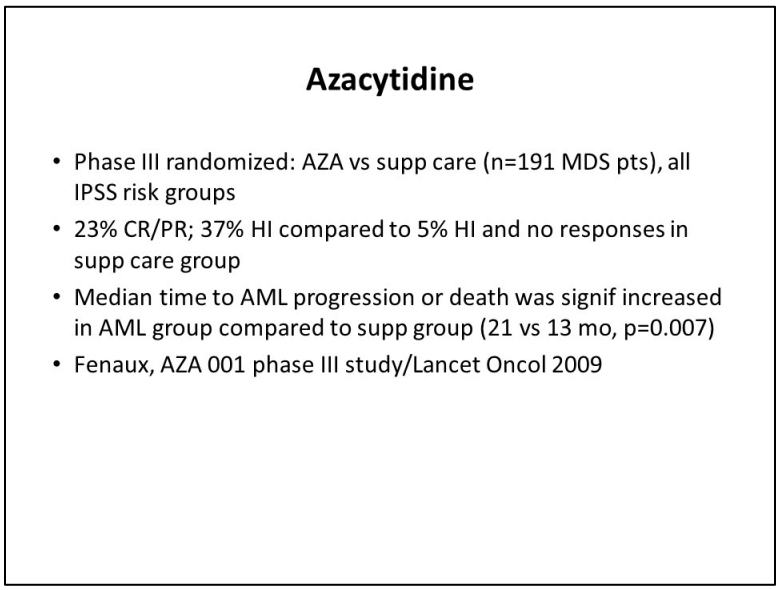


Now in addition to that, we're starting to understand that those who are low risk for MDS may not be as low risk as we thought, and the meaning there is that when you apply the new factors, chromosomes, molecular findings, you will see a subgroup of patients who can still do poorly even with quote/unquote "low risk." So even these names may not really apply to the patient in front of you. So, the key concept here is that MDS is a cancer. It is a life-threatening cancer by itself, and people can have infections, bleeding, other complications just from the disease.



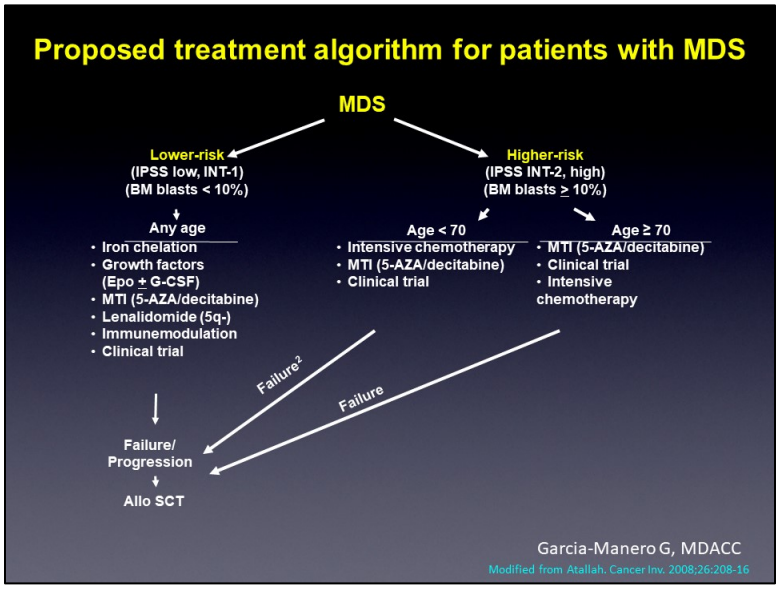
Now there's only a few FDA-approved therapies. The first one is decitabine, as shown on this slide. Decitabine is a bit different from the standard chemotherapy in that it tries to incorporate itself into the building block DNA and tries to block a specific pathway. Now this then blocks the cell cycle formation and then ultimately hoping to abrogate or stop the MDS formation.

There was a phase III, which is one of the latest possible trials that randomized decitabine against regular or available therapy in patients with MDS, and really by itself not an overwhelming amount of complete remissions as you see here; and patients were able to stay on for close to a year. The implication here is that even though you may not put patients into a remission, with repeated and long-term therapy, you may be able to stabilize the disease.



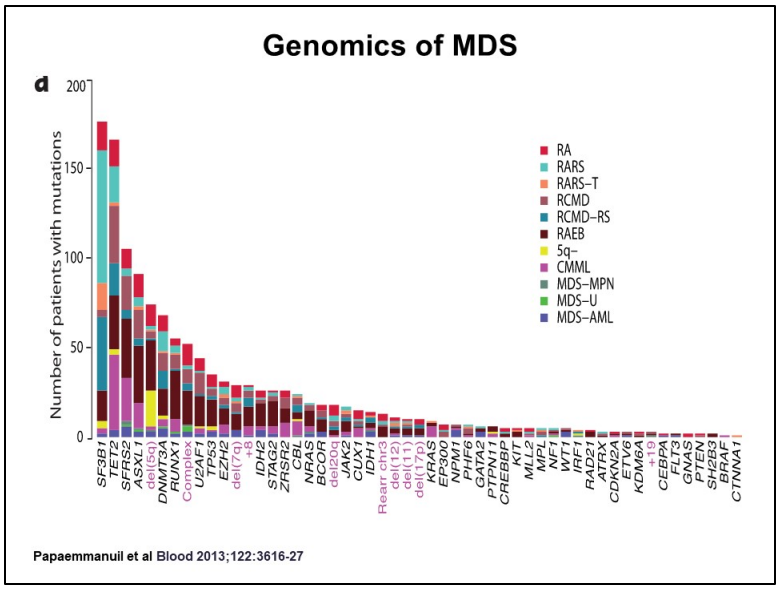
Azacitidine, the cousin drug of decitabine, is also FDA-approved for this indication, also has phase III data showing the safety and feasibility and, again, some modest responses as a single agent, including about a quarter to a fifth of these patients having a CR or PR, complete remission or partial

remission. The key is, does this treatment prolong or stop the progression to AML, and it looks like that some subgroups may have benefitted from delaying the progression to a leukemia.



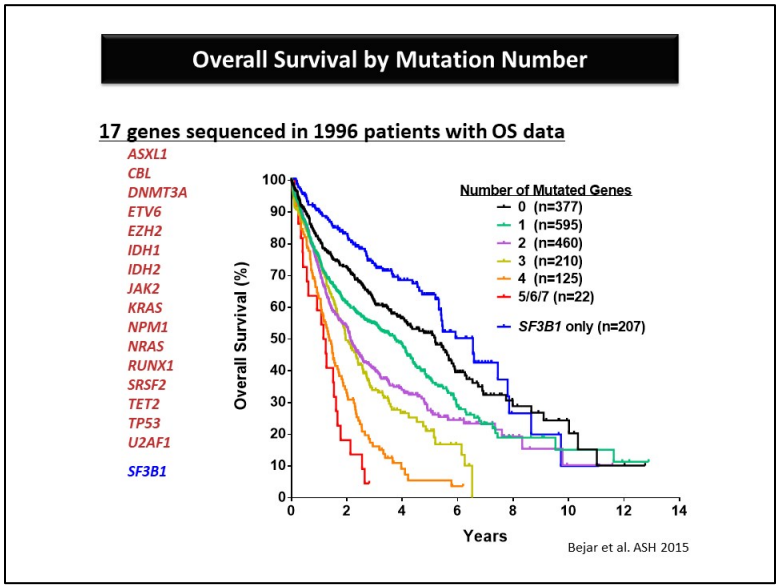
And so those are single agents. Those are what's out there. There's a third drug known as lenalidomide for a subgroup of patients known as 5q minus. And this algorithm, by my colleague and world leader Dr. Garcia-Manero, we are changing our thinking in real time. So, the lower risk I showed you on the left-hand side; some of these patients may be able to be observed. Some of them may get supportive care or growth factors and then consideration of clinical trials always at the forefront.

On the higher-risk side, we went through some of these therapies, intensive chemotherapy for maybe a small subgroup of fit patients, the so-called hypomethylating agents (HMA) I showed you, azacitidine and decitabine; and, again, I want to emphasize clinical trials. Even if your local hospital doesn't have access, contacting an organization such as LLS, the Aplastic Anemia Foundation or looking online at clinicaltrials.gov. And then if there's suboptimal response or failure to these therapies, considering the allogeneic stem cell transplant in the appropriate patient.

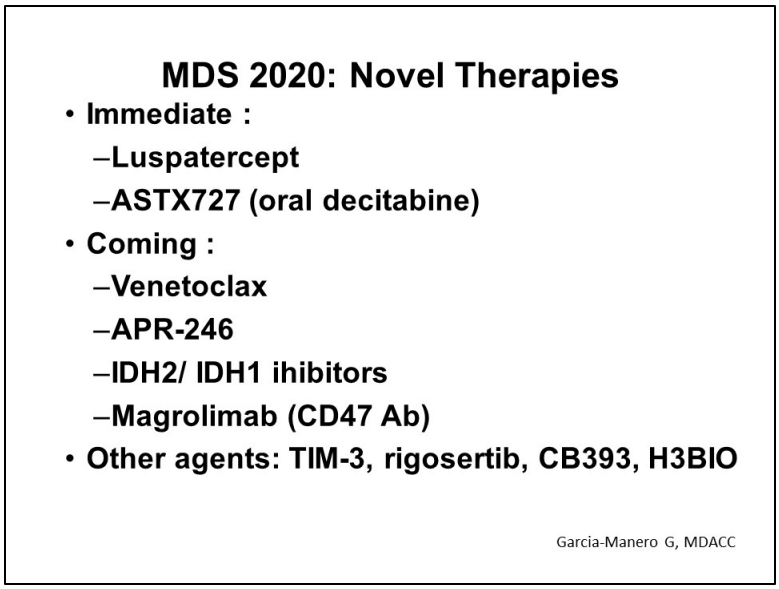


Well, so that's the state of the field now. Now in terms of future directions, what our group and others are working on around the world is can we further classify this very difficult-to-treat disease. One way to do it is look at the molecular foundation. What is the DNA doing? What are the mutations that are there? And this chart shows you that there are a number of different molecular mutations if you look deep enough in almost every patient with MDS, some more frequent than others.

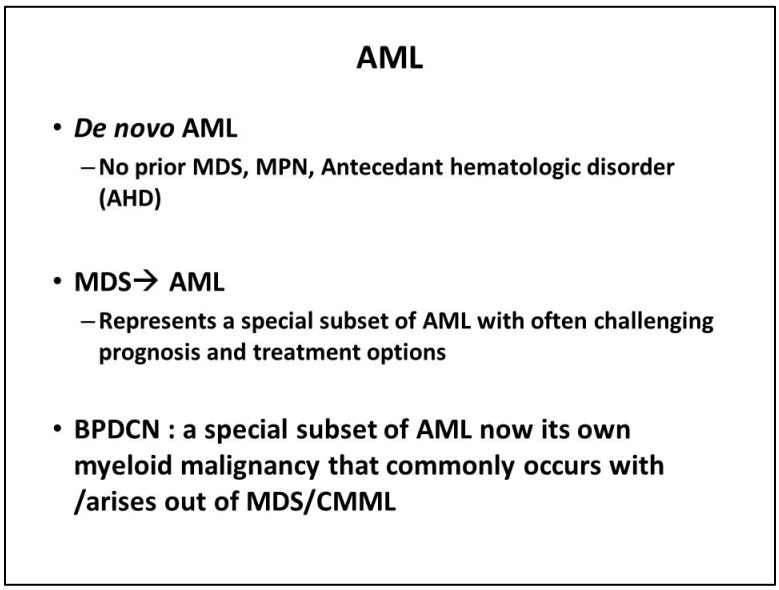
And the concept here is that the number of mutations and the type may very well prognosticate how you're going to do.



As shown on this slide, this is taking 17 gene sequence in almost 2,000 patients. And basically, again in his Kaplan-Meier overall survival curve, the number of mutations that one has, so the more that a patient has, the worse off they are, is kind of the key theme here. So how mutated is the DNA in the patient?



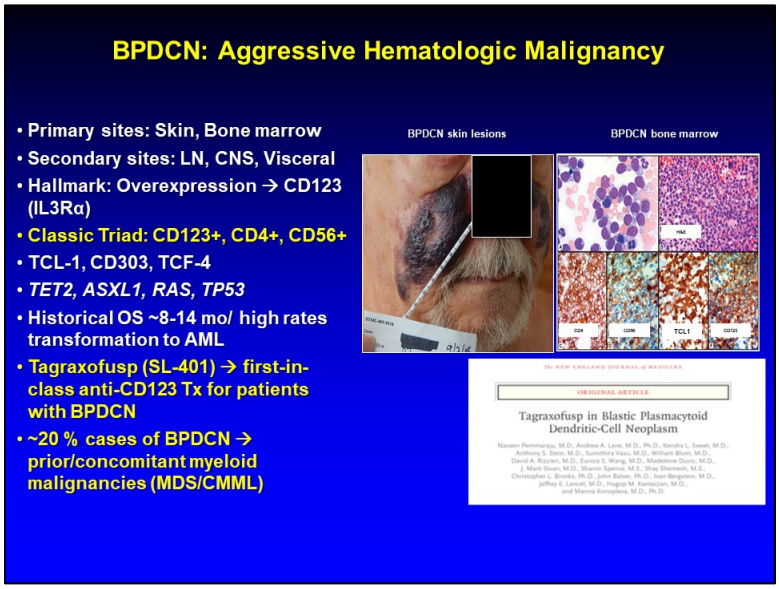
And so, the state of myelodysplastic syndrome now in 2020 and beyond is one of encouragement because even though there's only a few available therapies, there are many therapies to come. And the ones listed on this slide, including the luspatercept, venetoclax and others are already in active clinical trials or finishing late stage trials and are being put forward for FDA approval in the coming years.



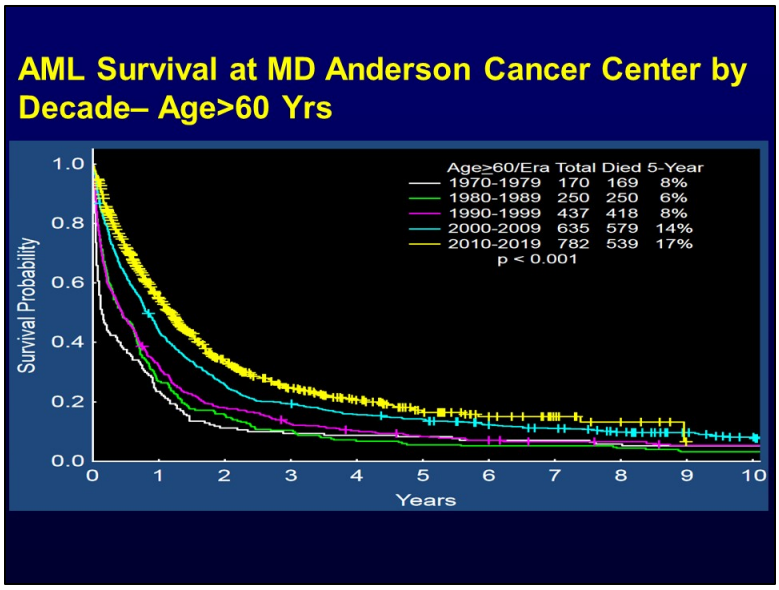
So, let's turn our attention for a few moments to AML or acute myeloid leukemia, which affects 20,000 Americans a year and 10,000 die. AML can, in fact, present on its own, de novo as we call it from scratch with no prior antecedent hematologic disorder such as MDS, MPN (myeloproliferative neoplasm) or aplastic anemia. But, very commonly, the MDS does evolve into AML, which is the subject of our talk today.

This represents a very difficult-to-treat special subset of patients that often have worse prognosis than those of other patients with AML. My group, in particular, focuses on very, very ultra-rare diagnoses,

including the entity blastic plasmacytoid dendritic cell neoplasm (BPDCN), which we have also found can co-occur with MDS or arise out of it.

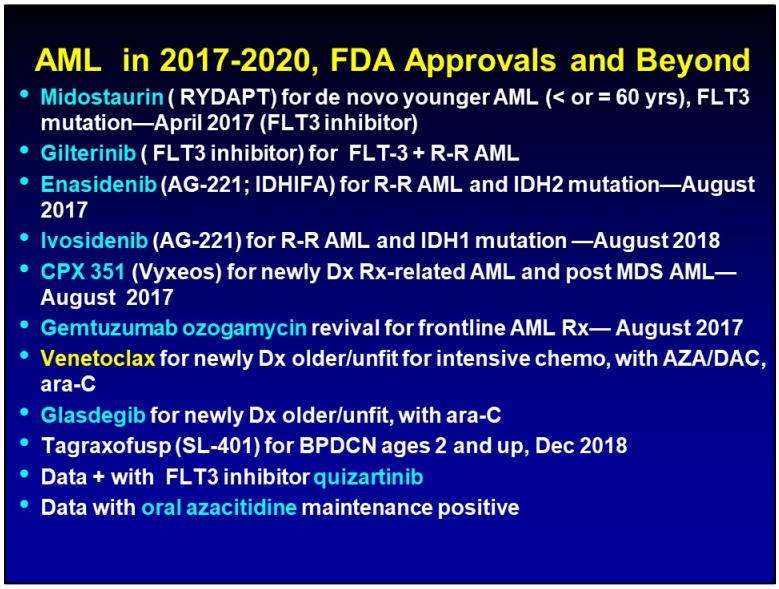


With regards to ultra-rare diseases, I mention that here because the LLS in particular has been instrumental in helping us pioneer treatment for the BPDCN. In particular, this used to be classified as an AML; but what we found is that over 20% of patients will have a CMML or MDS in the background, but this has a very different behavior from that of classic AML. And LLS was actually instrumental in helping to fund and support the early trials, and we did pioneer the first ever approved drug for this indication, published in *The New England Journal* [*of Medicine*] several months ago.



As we turn our attention to the more common AML, Dr. [Hagop] Kantarjian, our Chairman at MD Anderson, has shown that AML survival over time is actually improving. This improvement is not dramatic over time, but it does show that by era, by decade with improvements in therapies,

supportive care, transfusions, antibiotics, and other maneuvers, that we are slowly moving the progress for this rare disease.

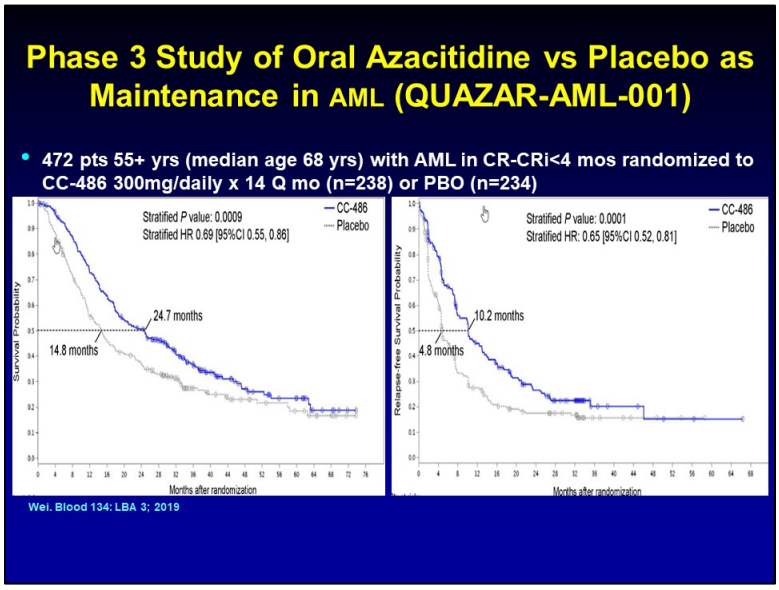


Now in terms of therapies that are available in 2017 to the present, this is a very exciting time for AML. I list here, these are the FDA-approved therapies that have just been pioneered in the last three years. Take a look at this list. The first two are FLT3 inhibitors, which target a very specific pathway, again, either in patients who had MDS, transformed to AML or AML in particular. The next two are so-called IDH (isocitrate dehydrogenase) inhibitors, so that's another pathway that AML cells use to gain proliferative advantage. The next drug, CPX-351 is specific to this talk because it's the only one approved specifically for people with MDS who have gone to AML and then several other drugs here, including the very important venetoclax, which targets BCL2. The key take-home point from this important slide is that for any caregivers in any of the allied health professions to know that AML has had an explosion, really a quadrupling, quintupling of available drugs in just the last three years.

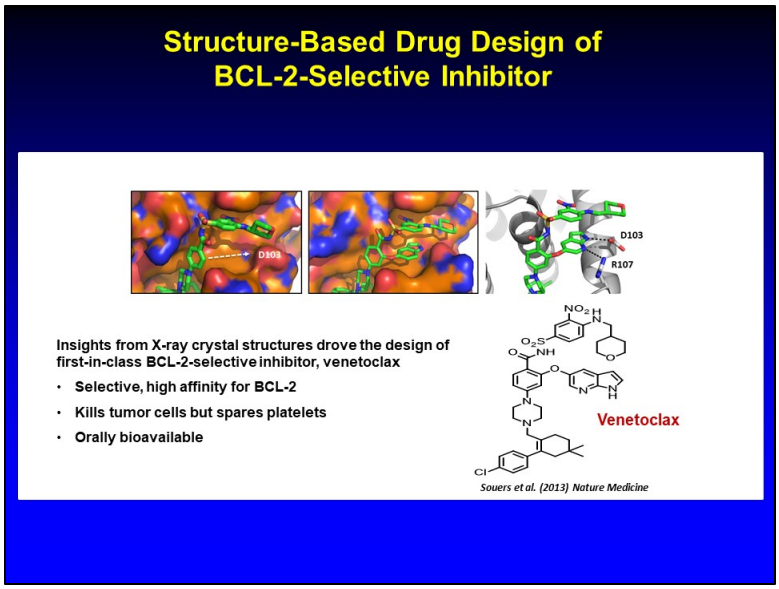
CPX-351

- CPX 351 (Vyxeos) for newly Dx Rx-related AML and post MDS AML—approved August 2017
- Fixed 5:1 liposomal formulation of 7+3
- OS benefit (statistically significant) in randomized clinical trial in t-AML/s-AML (arising out of MDS) vs 7+3

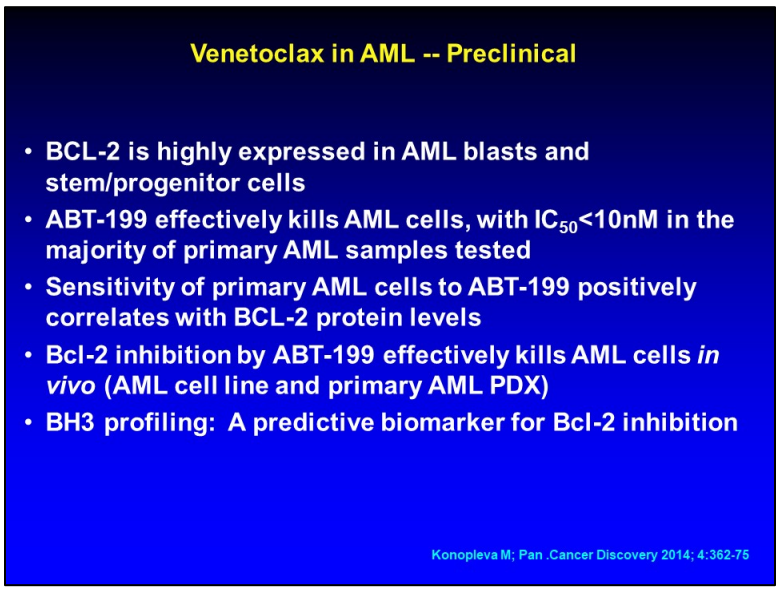
The CPX-351 in particular I mentioned, this one is the only approved drug on the list specific to therapy-related AML, that is people who had prior MDS with treatment or MDS straight to AML approved in the last three years. It's a novel drug, but it actually takes old chemo drugs, some of you have heard of 7 and 3, anthracycline and Ara-C in a fixed formulation, in a liposomal delivery. And it did show in a randomized trial a small but statistically significant overall survival benefit. And so, this drug is available, FDA approved.



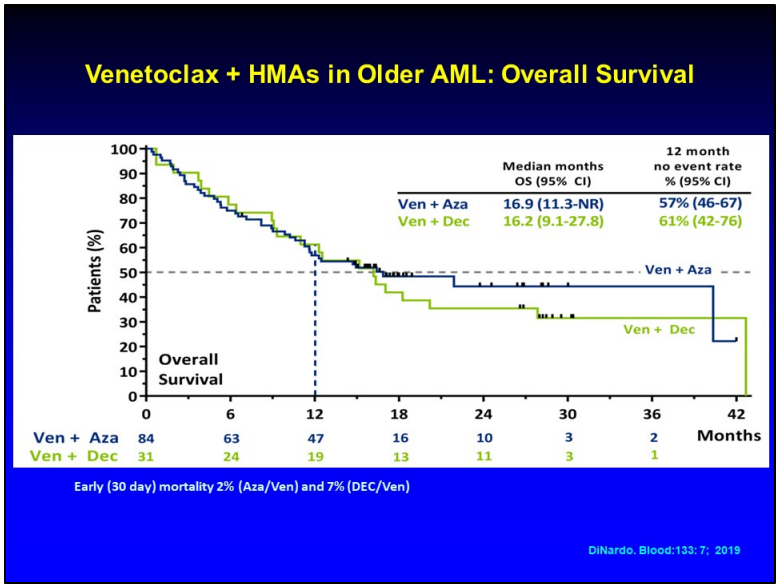
For the azacitidine, there was some excitement generated at our recent meeting at ASH (American Society of Hematology Annual Meeting) for an oral formulation. The current drug is either IV or sub-Q. This was tested in a randomized, phase III study against placebo in patients with AML for the maintenance; that means after you finish your standard therapy. And in this large study, there was statistically significant benefit for overall survival with this oral formulation. As you're seeing from this talk, that could be potentially very exciting for researchers because then this oral formulation may be able to be moved into MDS, CMML, and other precursor states.



Finally, the other last drug of importance is that of venetoclax which targets a novel pathway called BCL2. So, all of these drugs are trying to target different pathways in the cancer cell and may be very important in MDS and AML.



This unique molecule is also oral. It's given as a drug in the clinic or in the inpatient. And we and others have found that it's highly expressed in the AML blasts, so the so-called stem cell; and this will now be tested in MDS as well. It's gained FDA approval already in two leukemias, CLL leukemia, chronic lymphocytic, and then the AML, acute myeloid leukemia.



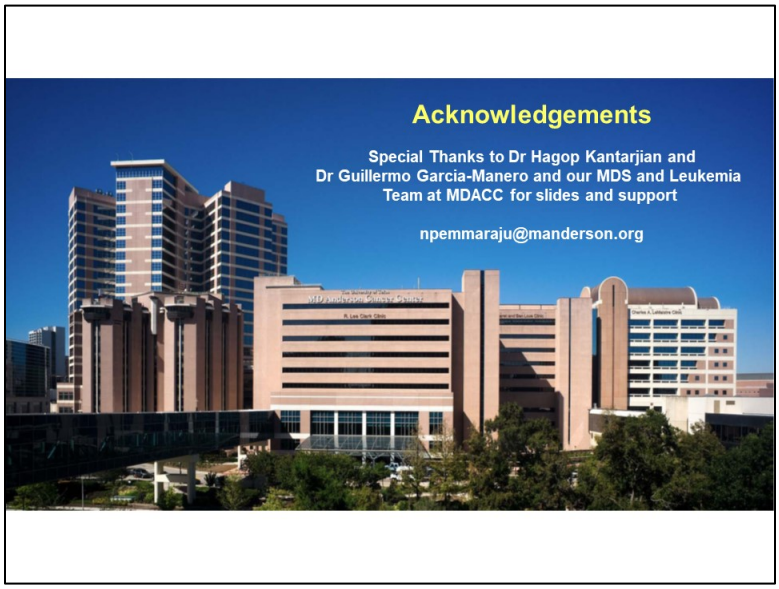
The venetoclax in particular has been able to be combined with the hypomethylating agents, decitabine and azacitidine, and that's how it got its approval in AML. Well, of course, as you're seeing from this talk, this may be very important for MDS because both of these agents have been shown to be used. The HMA's already approved in MDS, and so this is important because this type of drug combination can be delivered to patients 70s, 80-year-old and above, and so it gives us a new tool to give to our patients.

MDS/CMML transitioning to AML

- Intermediate/higher risk MDS/CMML → high rates of transformation to AML
- Prognostic scoring based on:
  - Traditional clinical factors (IPSS; clinical such as blasts/cytogenetics/cytopenias)
  - Newer techniques including high risk molecular mutations and # of mutations (ASXL1, TP53, etc)
- Can also commonly be present with/transform to BPDCN
- Represents a challenging clinical situation with several emerging therapeutic options now, but still urgent need for more clinical trial/novel approaches

Well what about this transitioning? That's the topic of today. For anyone who's involved in the care, nursing, advanced practice provider, social work, case management, on the hospital side or in the clinic, I think the take-home point is that there is a very high risk for these diseases, which used to be thought of as precursor or pre-leukemia. Now we know they are leukemia or cancer themselves to go to AML, which has an even poorer outcome.

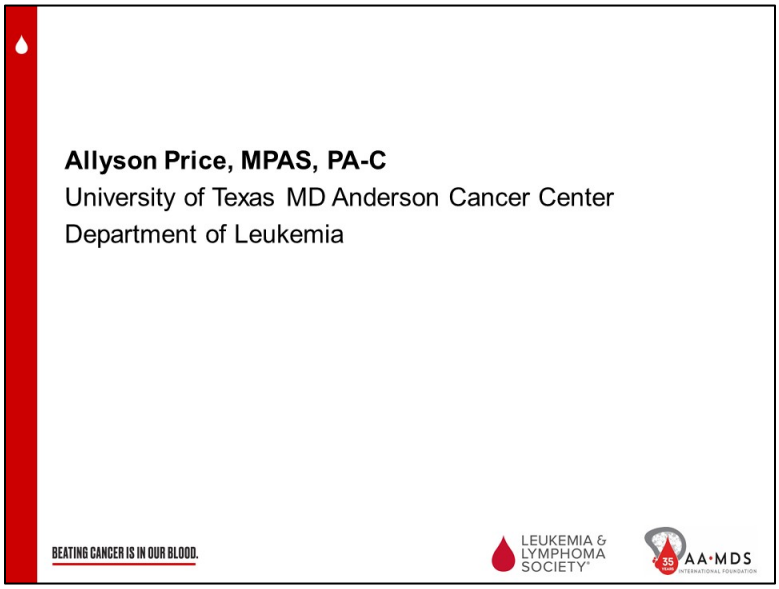
We know now that you can prognosticate, tell how someone's going to do based on traditional clinical factors readily available but also these newer techniques such as high-risk molecular mutations and that even some of the rarer blood cancers that some of us see at the academic centers or even in the community, BPDCN, aplastic anemia, the MPNs, all of these can then transform to MDS or AML. And then finally, this concept that clinical trials are more important now than ever and that research needs to be funded and needs to be carried out by multiple different entities.



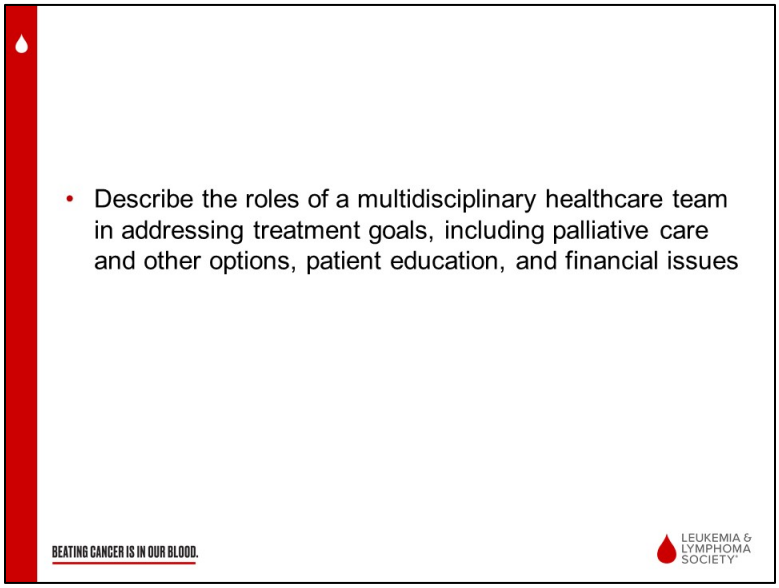
With that, I'd like to acknowledge my team here at MD Anderson Leukemia, in particular, our Chairman, Dr. Hagop Kantarjian and also our leader of MDS, Dr. Guillermo Garcia-Manero, who have generously provided their mentorship to me, their time, and, of course, for the slides and support.

With that, I'd like to turn it over to Allyson, Ally Price, who's one of our outstanding physician assistants who leads the ability for the APPs, the advance practice providers, to provide some of the critical care, especially at this large academic center. Ally, I'd like to turn it over to you.

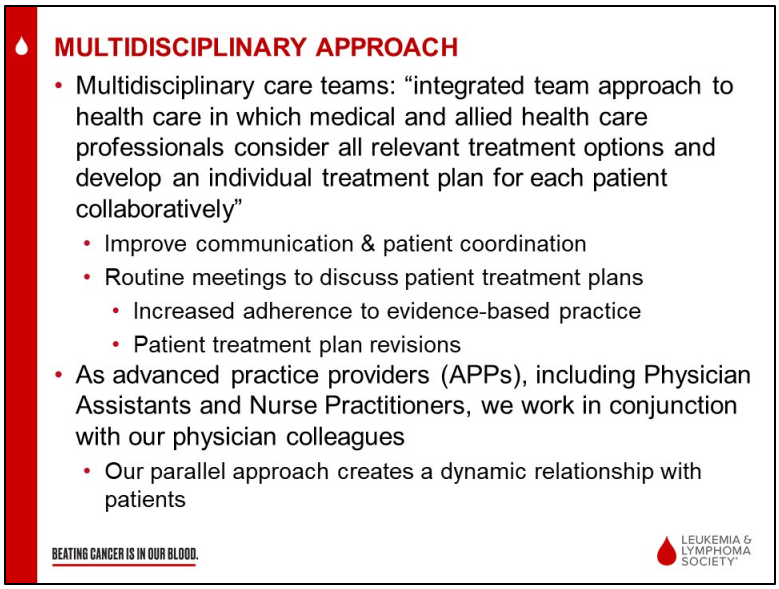
Allyson Price, MPAS, PA-C



Thank you, Dr. Pemmaraju and thank you for your presentation to us. I think it's great to have that overview.



What I would like to describe a little more in detail today is not necessarily the treatment itself but what it takes to care for these patients who have transitioned from myelodysplastic syndrome or CMML into acute myeloid leukemia. And a lot of times there's a lot of cooks in the kitchen as we would say. It takes a multidisciplinary approach, so just addressing the treatment goals since they're so individualized with all the advancements we have in technology, including palliative care, other options, patient education so they can understand what's going on and have a voice in their own treatment as well as financial issues itself.



So, as I said, the multidisciplinary approach is pretty much having a lot of cooks in the kitchen. It takes an integrated team approach which medical and allied healthcare professionals consider all relevant treatment, whether it's clinical options, whether it's FDA-approved regimens and develop an individual treatment plan for each patient collaboratively.

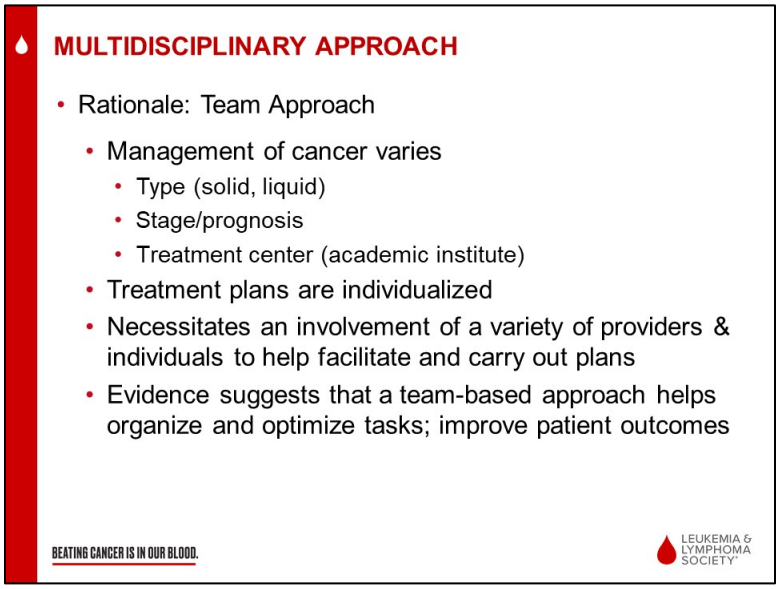
So for us, at an academic institution, we have pathologists, we have oncologists, we have advanced practice care providers, we have nursing, we have our research teams, so we have multiple meetings throughout the week where we discuss patient options based off certain features of the disease. And like Dr. Pemmaraju said, as MDS or these other types of diseases transition to AML, they may develop new changes, whether it's chromosomal abnormalities, changes in their genes, what is expressed. The treatment can get very detailed and get individualized, very specific.

And so, what it takes is for us to have these research meetings, planning meetings, grand rounds to make innovative treatment based off these features of the disease itself. This approach allows us to select the best option for patients and take other types of socioeconomic situations or logistics. Does the patient live near you? Are they out of state? Are they out of the country? Do they have a primary caregiver who's flexible? What is the logistics that it's going to take for a patient to get the treatment he or she needs, and what is also the treatment goal?

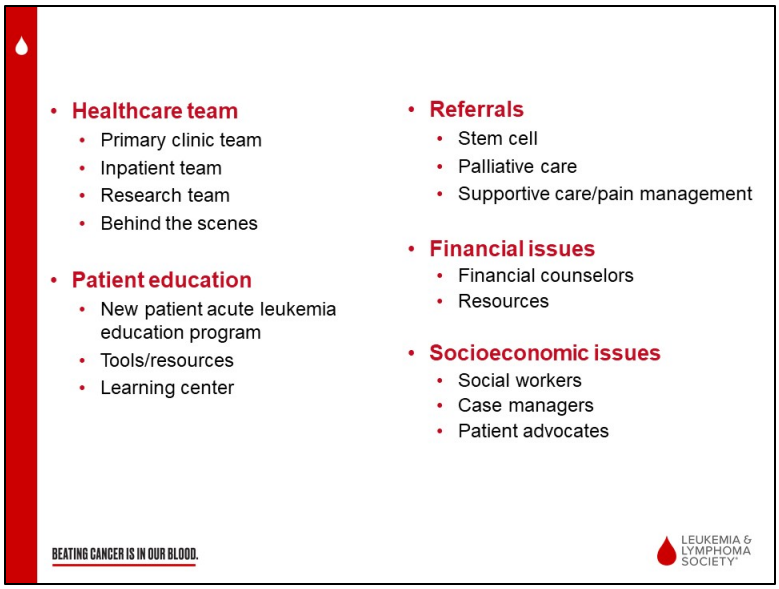
So, we look at this multidisciplinary approach. We come up with plans A through Z based off this patient's goals and their desires as well. This approach allows us to improve communication, it creates more of a trust amongst the patient provider dynamic and it also gives patients a voice in theirs.

So, like I said before, we have routine meetings weekly, whether it's on Tuesdays or Thursdays, discussing outpatient, inpatients. It also shows us that we haven't increased adherence to evidence-based practice and that we can make slight revisions in the patients' treatment based off each other's experience. This allows integration of advance practice providers such as physician assistants, nurse practitioners as we work in conjunction with our physician colleagues. We almost serve as a bridge in

this dynamic between oncologists and the patient itself. Our parallel approach creates a dynamic relationship with patients.



So, the team approach is not necessarily a new concept, but I think it's being more integrated in the oncology world. There's lots of research out about this as well. It's very unique in the liquid tumors. It helps us integrate certain stages, prognosis of the disease, and whether a patient is getting treatment locally or whether they're able to come to an academic institution like MD Anderson itself. Treatment, like I've said multiple times, is very individualized. It takes lots of eyes and ears on the patient, especially since a lot of these patients require multiple transfusions. They need frequent monitoring of adverse effects and just to make sure patients are being compliant. This evidence suggests that a team-based approach helps organize and optimize treatment and improve patient outcomes and necessitates an involvement in a variety of providers and allows everyone to have a voice at the table.



So, this is just kind of a breakdown of certain things that we look at. I wanted to really highlight patient education. So myself as well as other physician assistants here at MD Anderson have created a patient education program. So, what we have done is taken these patients who have this new diagnosis, whether it's myelodysplastic syndrome or whether they have transitioned from MDS to AML. They come to an outpatient learning center where we go over disease, we go over expectations of chemotherapy, side effects, management, what to expect when you have a fever, where to go and also just kind of integrating all the resources that are available, whether it's from the institution itself, whether it's resources like from The Leukemia & Lymphoma Society and also answer questions that they may have.

We have seen that patients who are directly admitted to the inpatient service sometimes have a bit of a learning gap because they're very flustered with the new diagnosis and everything that's going on at once. They're getting IV antibiotics; they're getting chemo and then all of a sudden, they get transitioned to outpatient where they have a little more freedom and control and they're not being monitored 24/7. So, this education program is helping to gap that and to help them understand where to go.

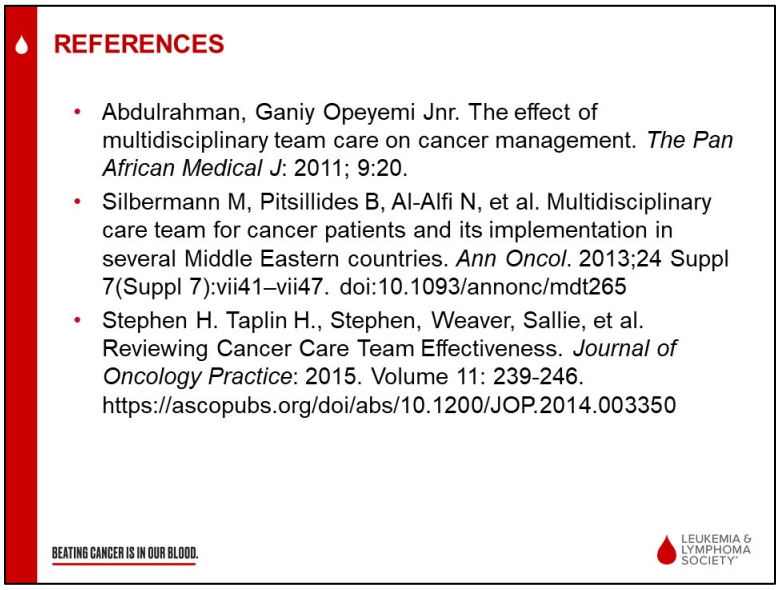
So, back up at top where we had healthcare teams, we also distinguished a big difference between the primary clinic team versus the inpatient team, just emphasizing that the clinic team has the reigns on their treatment. We're making the big decisions, we're their line of communication versus the inpatient team who maybe if they were transitioned in the inpatient into the hospital may have more voice into everyday decisions. Do they need IV fluids? Do we need to change antibiotics such as that?

If a patient is enrolled on a clinical trial, we also have the research team which MD Anderson is extra eyes, and they help manage some of the logistics of the protocol themselves. I also added in this behind the scenes because there's a lot of people behind the scenes that the patients aren't aware of, whether it's a patient scheduler, whether it's a nurse answering or a triage pathologist, there's a number of people who go into this multidisciplinary approach.

So, a lot of times we have other referral services that we're utilizing here in academic institutions, whether a patient is going to stem cell or maybe their transitioning into palliative care. We also have a great other department here, supportive care, who help manage pain, side effects of chemotherapy, as well as psychiatry type of needs that a patient may need.

For financial issues, we have a lot of people who help with that as well. We have our financial clinic, social workers, case managers, and certain resources such as LLS that we are trying to implement so this is not as financially toxic to the patient.

With that being said, I will transition over to Michelle.

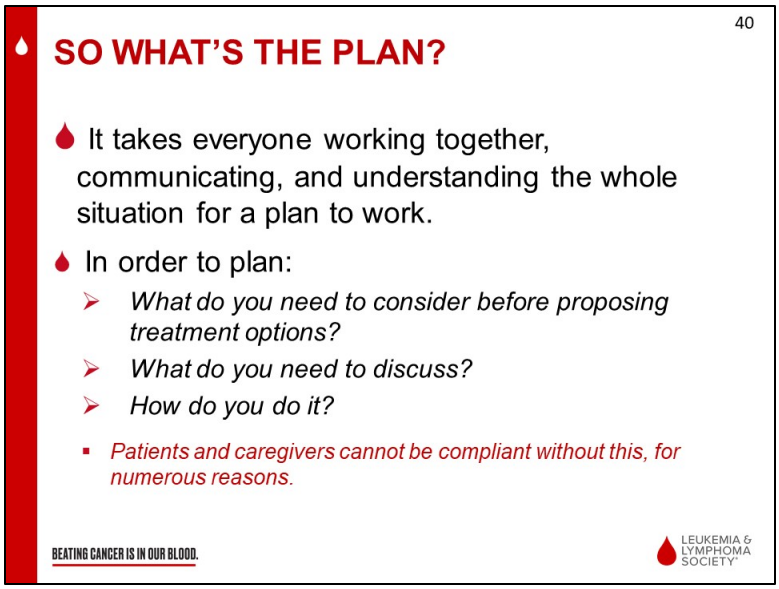


Here's some of my resources that were used in the slide presentation and thank you so much.

Michelle Rajotte, LMSW

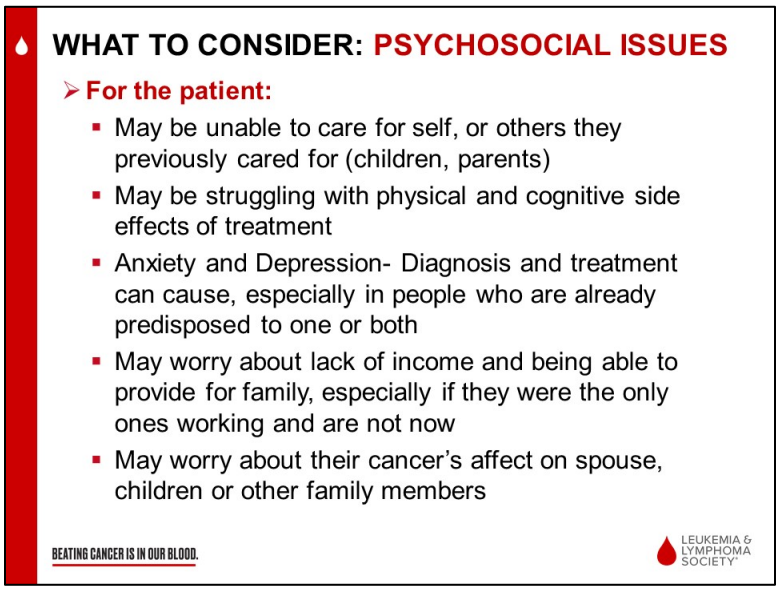
Hi, everyone. So, Allyson did a great job of just talking about how complicated all of this is and how many people are involved in one person's care, and it's really important to all be on the same page.

So, you come up with a plan, but then how do you move forward with it?



So, some of the things that you have to take into account, and some of this may seem very straight forward and common sense. But for the patients and the caregivers who you're working with, this is a whole new world for them, especially if they're newly diagnosed; and they may not know what to expect, and they may not know even what to ask or what to look for. So, it really does take everyone working together like Allyson was talking about – communicating, understanding the whole situation for it really to work and for patients and caregivers to be compliant.

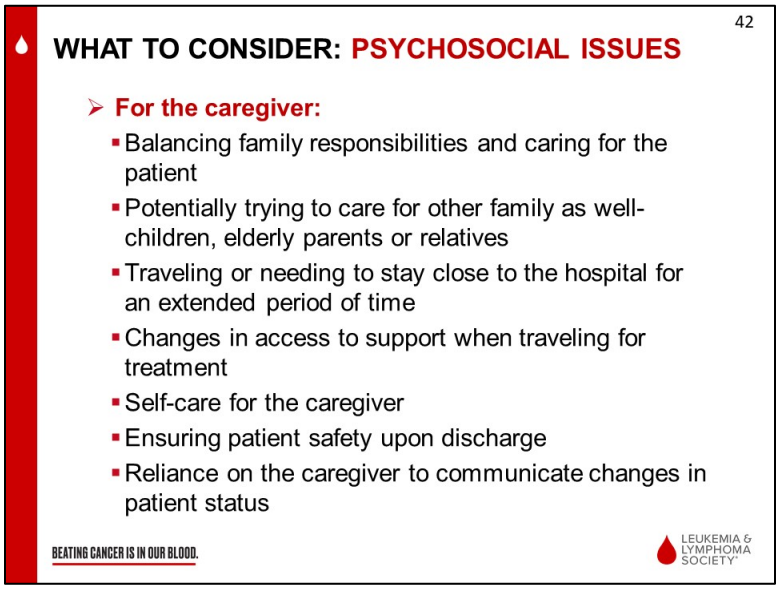
So how do you do this? What do you need to consider before proposing treatment plan options? Are some of the things realistic? So, it may look great on paper, but when you look at the situation of the patient and the caregiver, it may just not work. What do you need to discuss, and how do you do it?



So, for the patient, some of the psychosocial issues to consider, are they able to care for themselves or are they caring for others as well? So, what is their responsibility? Do they have support? Are they living on their own? Are some of the side effects to some of these treatments going to be dangerous

for them because they don't have support or they're responsible to take care of children or elderly parents or other people in their home that they are the main support. They may be struggling physically or cognitively with side effects from the treatment, so these are things that you're going to look at not only when they're first going through treatment but along the way, all the way though survival because it's going to change, depending on where they are in this process and how they're doing.

Anxiety and depression. So you have some people who may be predisposed to that before they even start, and it only is going to, unfortunately, get exacerbated by the fact that now they're going through cancer treatment. They may worry about their lack of income because maybe they're the sole provider for their family, and now they can't work, so what do they do? And that just puts a lot more pressure. And then if they have to travel long distances for treatment, is that something they even either physically or financially can afford to do? And they also may worry about their family members: their spouse, their children, how are they going to communicate with them? How are they going to talk to them about this? How do they support them as well while they're going through?

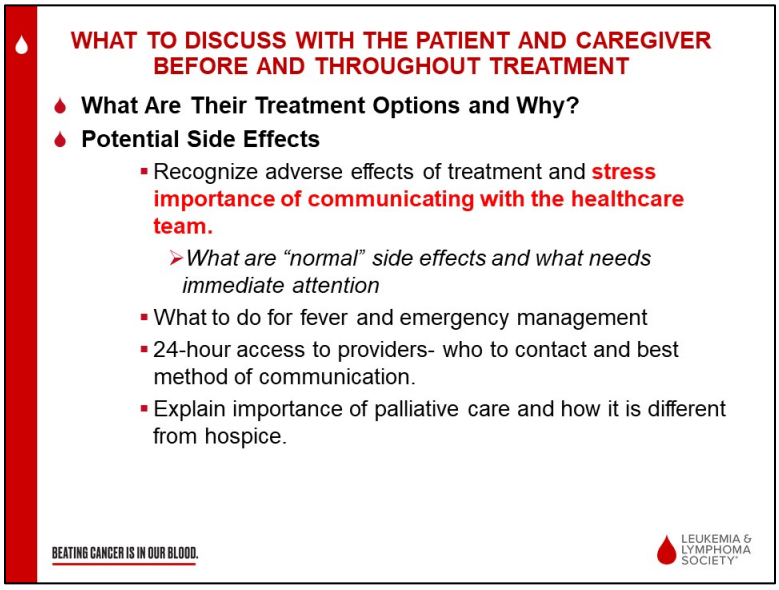


And then for caregivers, it's extremely stressful for caregivers; and a lot of times we're getting calls from people who are saying, "Yes, I'm a caregiver, but I also have cancer myself or I'm also diabetic or I have other health conditions and I just happen to be the one who's in better shape so I am now the caregiver for my husband or my sister because now they have a blood cancer.

And they're trying to balance out those family responsibilities, so how do they care for themselves and for the person who's going through treatment and maybe for the other things that are going on? Again, they may be caring for other people in the family. They have to possibly travel and get the patient back and forth to treatment. You know, how do they do that? How do they take care of themselves? And a lot of times caregivers don't do that, and if they fall apart, then everything kind of domino effects, and they're not going to be able to follow through on what that patient needs.

And a lot of times they're the primary communicator for you of what's going on with that patient, especially if they're not doing so well or they're having issues. A lot of times it's going to come from the caregiver and not necessarily a patient.

And, also, they need to know very specifically what they need to know, which sounds straightforward, but they need to know exactly what to expect. And if this happens, then do that. We get calls all the time from people, calling us, asking us questions because they don't want to bother their doctor or they think, well, they're really busy, and we always encourage them, "Call your doctor. Call the doctor's office, call the hospital. Talk to someone who knows. They can pull your record. They can give you specific guidance because it's important for you to communicate and let them know what's going on because they can't help you or really take care of you if they don't understand what's going on."

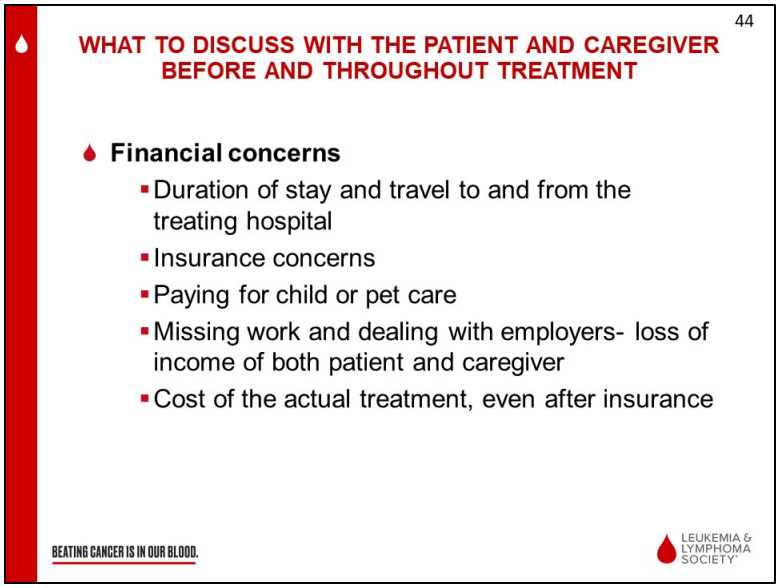


So, the other thing is while you're going through with them talking about what are their treatment options or why. So, if someone says, "I want to go for a stem cell transplant," but it's not realistic for them. What are the other options? We talked a lot about even clinical trials today. And then also the potential side effects to some of these medications. A lot of times people will read them and get scared because they think they're going to get everyone, and we explain to them you may not get everyone. But there may be some that are going to affect your quality of life or it may not be realistic for you because of your situation.

And then what are normal quote/unquote "side effects" and what are things that need immediate attention? What do you do when you go to the Emergency Room? Don't sit there with a room full of patients who may have the flu or some other communicable disease. Let them know you're going through cancer treatment. You're immunocompromised. You have to be seen sooner rather than later or at least put somewhere that you're not going to be in more danger.

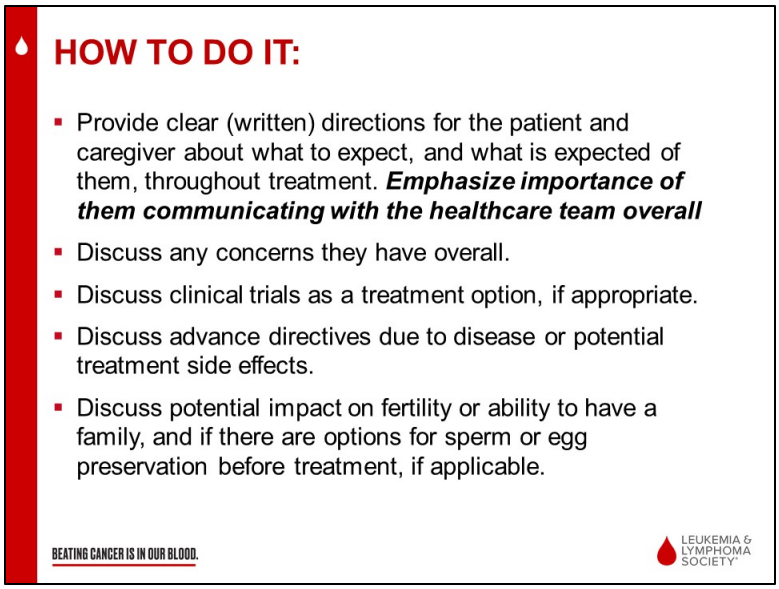
Who do they call when there's a problem? Is there a phone line? Is there a direct number they're supposed to call? How do they handle it when something comes up and they need your support?

And also, palliative care. A lot of times when we even bring it up on calls, people think it's hospice; and we try to explain, "No, it's really another support for you to be able to get through this to help you with the side effects, to help you with whatever it is that you may need just to keep you more comfortable as well."



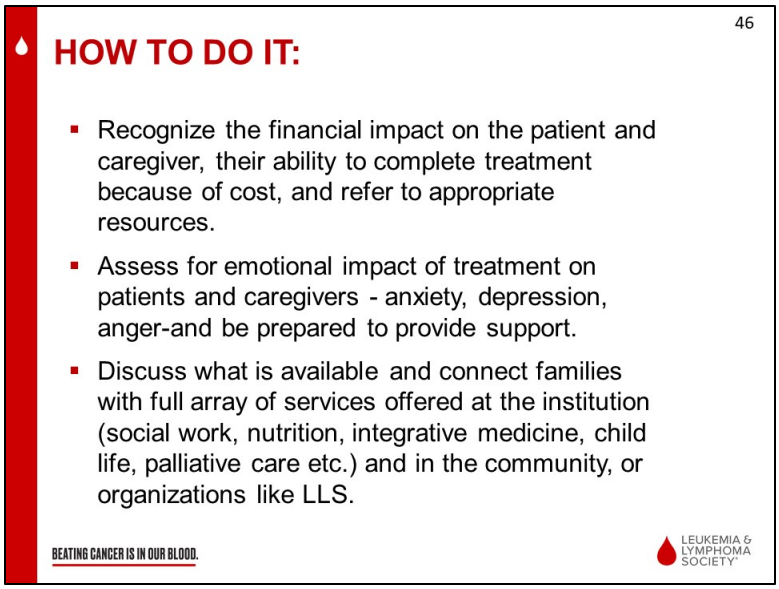
And then financial concerns. It's great that there's so much research going on right now, but we know that with the research and the new drugs comes higher prices a lot of times. And some of these patients, when they call us, "Yes, we can help them as much as we can with copay." But sometimes because they're medications that they may need to stay on for a longer amount of time, it may not be realistic for them to be able to afford the copays long term, so how do we figure that out for them?

They're also paying for other things. They may be paying for childcare. They may be paying for pet care. They're missing work. They may be traveling back and forth, so all those are things that they're trying to take into consideration to see how do I do this now. So, it just adds that extra stress on top of having that cancer diagnosis.

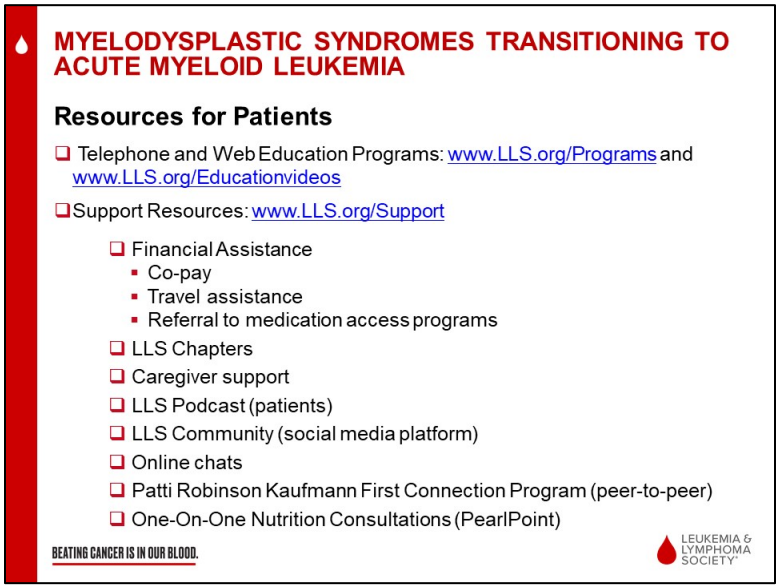


And then, again, we live in this world every day. We understand what's involved. But for a lot of people, they need that very specific direction, that step-by-step, even written down. "Oh, this is what you need to do." Because when they're going through that hard situation, having that resource is going to be key for them. And always emphasizing the importance of communication, just discussing things overall, talking again about clinical trials, especially since with MDS, AML, there's a lot going on in research but, unfortunately, with MDS, like we talked about today, there's not a lot of treatments that are available that may or may not work.

And then if it's a younger patient, which of course with MDS and AML, we don't always see that, but if it does come up and if it's applicable, talking about fertility preservation because that's a huge component for young adults; and it's something that we hear about a lot. And, again, with this population, you may not see that a lot, but it may actually happen.



And I think just overall evaluating throughout the cycle of what the patient is going through because their needs are going to change, their questions are going to change, and it's really important to make sure that they are getting the information and the support that they need. And there's a lot of different ways that you can do that. Depending on where you're coming from, there may be a lot of resources right in your institution. You know, social workers, nutritionists, integrated medicine, palliative care options. You can go into your local community or even organizations like LLS and other organizations that have those resources that can help your patients and be there to support and help them get what they need as well.



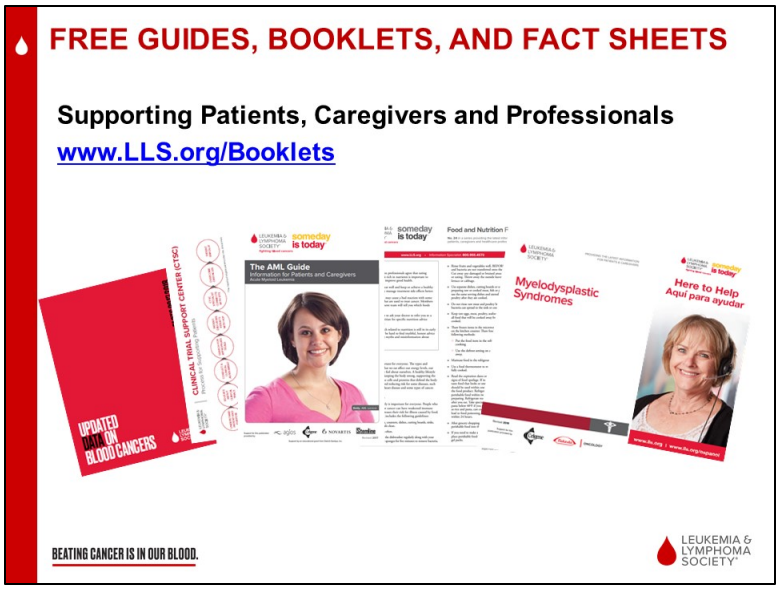
So, talking about resources, LLS has a lot of different resources, and all of these are free to patients, caregivers, healthcare professionals. We provide telephone education programs for patients. We have support resources. We have financial assistance. There's local LLS chapters within the community. There's a lot of caregiver support. We have a caregiver workbook. We have an online chat that takes place on the evenings that's moderated by a social worker that can help. There's

podcasts. There's a lot of different things. There's a program where they can talk to other patients or caregivers who are trained patient volunteers who can help them understand what it's like to go through it because they're now going through it, and they've been through it already.

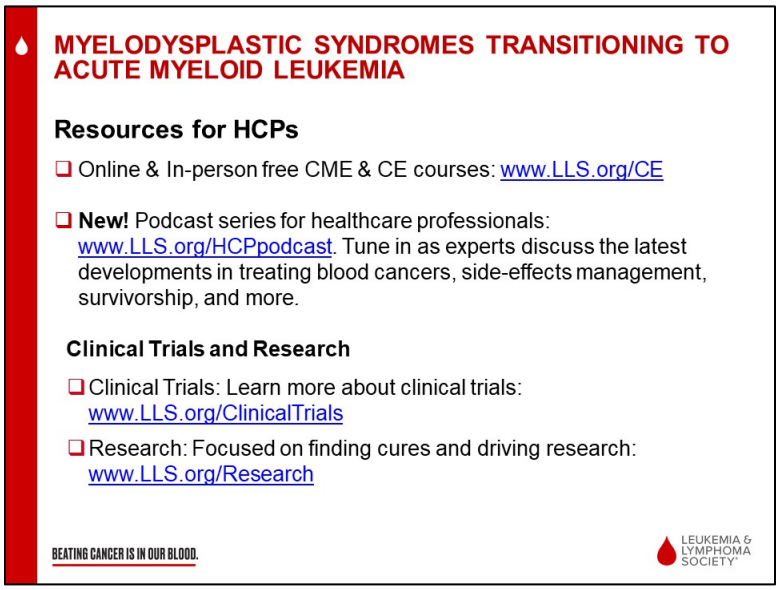
We have a nutritionist who can help out, give them some guidance about things like what do I do if things don't taste good anymore? How do I keep my calorie intake up and make sure that I'm eating what I should be eating?

And then for clinical trials, we do have a clinical trial support center which is staffed by clinical trial oncology nurses; and they're able to do one-on-one searches for patients to see what clinical trials may be out there, not that they're going to take over, but it's a way for them to help look to see what clinical trials might be available to that patient. They would then have the patient take those back to you, talk through them, see what may be appropriate, what may not be appropriate, and then help them from there if it's something that they do want to go forward with because there's a lot of obstacles sometimes to getting into clinical trials. And we want to make sure that doesn't hold somebody back from getting what they need.

We also have the Information Resource Center, where we are staffed by master's level healthcare professionals, and most of us are social workers. We do have a nurse, and we have some other master's in other health fields, and we're able to again provide information, support. We pretty much will talk to people, see where they're at, see what they need, and go from there. And, again, it's just another way to help people understand what it is that they need to know in order to make educated decisions and move forward with their treatment and care.

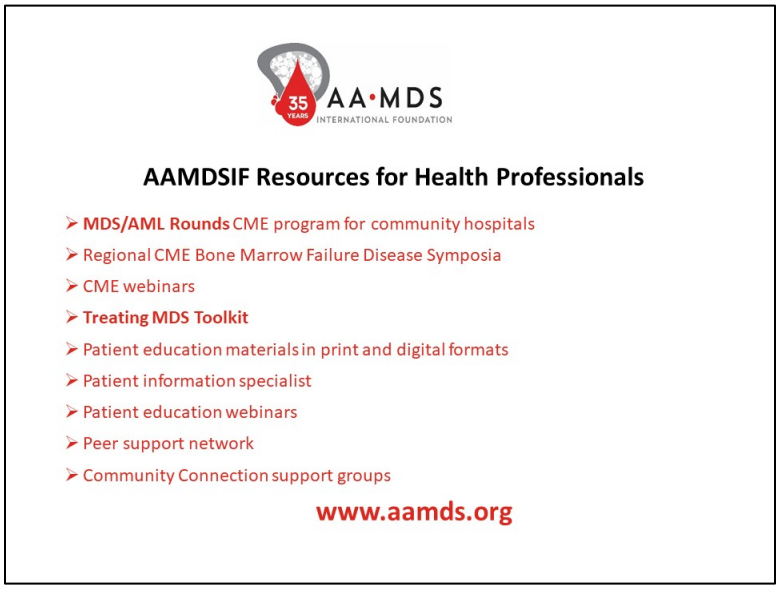


And, again, we have tons of booklets that they can order online, you can order for your patients or caregivers and be able to support them and give them out to them in your clinics.



And then there's resources for healthcare professionals as well. So, we have podcasts, we have these programs that are also archived on our website, and then we have a lot of different information that you can find right on the website as well. And now I'm going to turn it over to Alice, thank you.

Alice Houk



Thanks, Michelle. The Aplastic Anemia and MDS International Foundation also has a number of resources for health professionals and also for patients. One program that this audience may particularly be interested in, we have an MDS/AML rounds program that is an accredited program in a one-hour format that we bring to particular community hospitals. We have the speaker and all of the content available, and you would just need to contact us to schedule that program.

We also have regional educational bone marrow failure disease symposia. We have them in different parts of the country. This year we have some scheduled in Atlanta in April and Cleveland in October. We also have a number of educational webinars for health professionals available on our website. These are recorded satellite symposia from ASH or the ONS Congress meetings and some others that we've done independently. But those are available at no charge through our website.

We have a treating MDS toolkit that is currently being updated, but a lot of the content is still available on our website also. And this is a convenient patient education packet of information with one-page information sheets and other content that is helpful for patients throughout the MDS journey and for those who may transition to AML as well.

All of our patient education materials are available in both print and digital formats. We can send them to you at no charge or they can be downloaded from our website. We have a patient information specialist available every weekday via email and other messaging in nonbusiness hours for getting back to people who may call during nonbusiness hours on a regular weekly basis. She can answer a lot of questions about finding a specialist, information about their diseases, some caregiver support, patient support, all kinds of resources like that that we can connect them with.

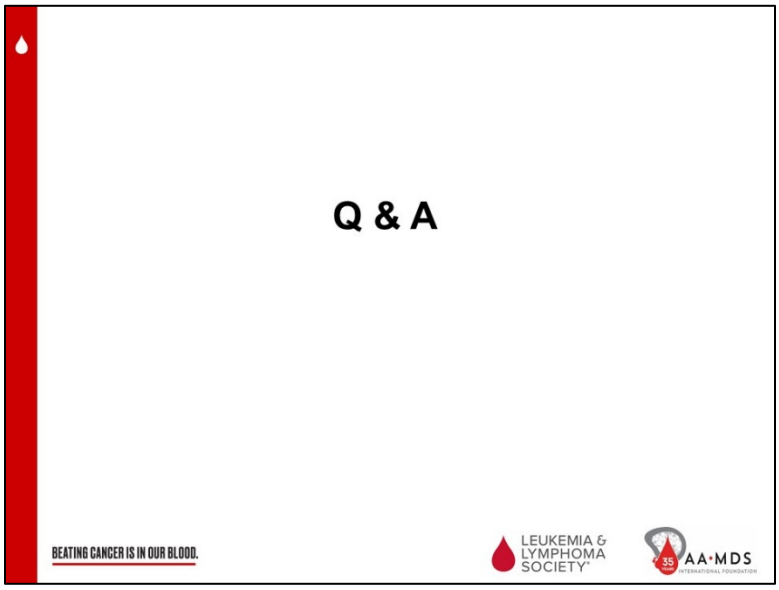
We have a number of patient education webinars that are available live and also archived. We have over 100 of those available on our website, and they cover a range of topics by disease and also quality-of-life type issues.

We also have a peer support network where we have one-on-one support, and we match patients and caregivers with others who may be in a similar situation as them; and that's available also through our patient information specialists.

And, finally, we have a number of community connection support groups in various locations around the country, and some of those are also in partnership with LLS chapters. And, again, you can contact us directly to find those; and they're also listed on our website. For all of these resources, you can find them on our website, http://www.aamds.org or, of course, by contacting us at the foundation.

QUESTION-AND-ANSWER SESSION

Caroline Kornhauser, MPH
Well thank you so much. Thank you to Dr. Pemmaraju, Allyson, and Michelle for such clear and informative presentations.



It is now time for the question-and-answer portion of our program.

Caroline Kornhauser, MPH
We will take our first question. BJ asks, “Can you speak to mixed MPN/MDS pathology and treatment options?”

Naveen Pemmaraju, MD
Thank you very much. This is Dr. Pemmaraju here. This is a very important question, and we thank you for this. So MDS/MPN, which is what our audience member is referring to, myelodysplastic syndrome overlap with the myeloproliferative neoplasm, is a unique hybrid category in between the two. Interestingly, the most common disease entity is the CMML, which Ally, and I mentioned earlier today.

So previously, CMML was considered in the MDS family of diseases, but now that and several other related diseases have been given their own bucket. It’s important because as we refine in terms of chromosomes, molecular mutations, treatment options, we’re finding that that hybrid bucket may act either as one or the other or as its own entity. In other words, it may behave more like an MDS, more like an MPN, or, in fact, a true hybrid.

So, there are no specific FDA-approved therapies for the so-called MDS/MPN unclassified. The CMML, as we mentioned, is essentially treated as MDS in the clinic; and so, this is where when people say there’s an urgent, unmet medical need, there really is. There are no targeted therapies. So, in the clinic, clinicians will often borrow from one or both of those diseases and do what’s called a combination therapy or what I would urge as referral for a clinical trial. And we and other groups have

those. But just to that point, CMML is a member of the MDS/MPN, but there are other ones that are more rare or unclassified. And those usually don't have as specific a therapy. They're borrowed from the others. Thank you.

Caroline Kornhauser, MPH
And we have a couple questions about palliative care, so I'm going to start with Orphelia. She asks, "How receptive are the transplant physicians to palliative care consultation early in treatment?"

Allyson Price, MPAS, PA-C
This is Ally Price. So, I would say that most transplant physicians are very receptive to early consultation. Since the leukemia department, transplant, and palliative care all work in parallel, we all feel that earlier exposure is better. And I know that Michelle mentioned earlier palliative care doesn't necessarily mean hospice. It just means additional eyes, resources for the patient to utilize if necessary; and I hope that answers the question, Orphelia. Thank you so much.

Caroline Kornhauser, MPH
And maybe you answered this, but as a follow-up question, Kimberly is asking, "How may palliative care be integrated into patient care from the time of diagnosis and who should make these recommendations?"

Naveen Pemmaraju, MD
Hi, this is Naveen Pemmaraju again. I really appreciate what Ally Price just said. I just want to reiterate those comments. I think this is something that in the real-world clinic, sometimes we as clinicians and patients struggle a bit. I think that our group here is one of the founding members of the so-called onco-palliative care; and what they found is that the word palliative itself can give myths and challenges to the patient because it conjures up specifically end-of-life care. But as Ally delineated, they actually changed their name to palliative and symptom control group for this very reason.

So, I think that it's a good discussion to have in the first few visits to do what's called goals of care. That's what the audience member is asking. And that's what we try to do here in our group, as Ally mentioned. So multidisciplinary care but also emphasis early on. What are the goals of care for the patient, the family? What are the expectations? What are those that are created by us and by them? And in that setting, then you can design an appropriate symptom control palliative care program.

For us, early upfront palliative care is beneficial, as Ally mentioned, because it is that extra group that's looking at the symptoms, the suffering, the pathos part of it, just the actual misery and suffering of going through some of these diseases and, of course, medication and other therapy.

So, I think to answer this question, it is really up to the oncologist and the patient to come up with a plan of goals of care and then based on that go for the referrals to palliative care, symptom control.

Towards the end of life, which is something that we also do very frequently as well, and it's our honor to do that, that's another chance to reconsult or to see them for the first time. And then, again, this reevaluation of goals of care, the determination of transition to end-of-life or hospice care, the evaluation to treat the suffering and the patient themselves rather than the disease. All of these things are benefitted by early, upfront, long-term, ongoing parallel care.

Caroline Kornhauser, MPH
Thank you, Ally, and Dr. Pemmaraju. Our next question is from Della, and she has two questions. The first is, "You mentioned chelation therapy and growth hormone for treatment. Can you explain how those therapies work to help?"

Naveen Pemmaraju, MD
Yes, right. I mentioned that, correct. So, the growth therapy, I just want to make sure that it makes sense. So, it's not growth hormone therapy. That's possibly something different. But here growth factors, very specific class of drugs that are used commonly in MDS which help to promote or stimulate hopefully healthy cells to grow. So, the classes are to help the white blood cells. There's the common injection we call a G-CSF, filgrastim, and the newer versions. The longer-acting shot that some of our patients are used to, trade name is Neulasta, pegylated filgrastim. It lasts maybe up to 14 days, two weeks. That's a growth factor shot that tries to promote the healthy white blood cells to grow.

There is another class of drugs that aims to try to help the red blood cells grow. Those are called EPO or erythropoietin stimulating agents. They have an abbreviation ESA. A lot of our MDS caregivers and patients will know that.

Again, this is an effort, it's a nonchemotherapeutic effort to try to promote healthy cells to grow. And the most challenging remains the platelets, which there's really no effective shot that can do that. There's some drugs out there. Some of our audience members will know that, some of the staff – eltrombopag, Promacta, and the related drugs.

Here's the problem with those. So, they can be used sparingly and judiciously in the low-risk MDS, so those are people that you're not giving chemotherapy to, that you're observing. But there is a theoretical concern that the growth factors may stimulate myeloblasts, so that means the leukemia or cancer cells, so they need to be given very appropriately and judiciously.

And then the second aspect of it is they may have side effects, reactions themselves. They may lead to blood clots, particularly with the ESA class, and they're not really treating the underlying cancer. So the concept here is growth factors as supportive care agents, adjunct to chemo drugs or given solely in the setting of nonchemotherapy low risk can actually be a very nice addition or tool but still requires essentially the oncologist and the appropriate staff and the multidisciplinary care to give those. So that's kind of what we were mentioning when we say, "Growth factors." Not necessarily growth hormone factors which are used in other cancers and in other disease states.

Caroline Kornhauser, MPH
Thank you. And her second question is, she is a pediatric RN, and currently has a 13-year-old male with MDS that comes in for blood transfusions. “How often do you see MDS in the pediatric population?”

Naveen Pemmaraju, MD
Yeah, I want to take that question too and be happy to see what other follow-up there is. This is very important, on purpose we didn’t mention that because it is considered to be quite rare to have myelodysplastic syndrome in the adolescent young adult population. However, having said that, there are two concepts. One is because it does occur, you have to figure out two important concepts. One is that there is a high preponderance of familial or genetic, familial or heredity genetic syndromes that can lead to young person’s having aplastic anemia and MDS, and I think this is important. So, some of them are known pretty classically, Fanconi’s anemia. Some of these kind of classic diseases that have been in medical textbooks for decades. So, patients need to be tested for that.

But the other concept with that is the formal leukemia or genetics testing. This is more common I think in solid tumors so young people with breast cancer, etc. But it turns out there are many syndromes that are known and probably a lot more that are unknown that travel with solid tumor and liquid tumors in families. So, anyone who’s, I would say, under the age of 40 actually, so AYA goes up to the age of 39 by the NCCN designation, really in our practice should have some consideration for either a genetics consultation or some thought towards that. Again, the known entities versus unknown.

The second concept of what you bring up with the teenager with MDS. Because it’s so rare and almost everything in this disease area is extrapolated from the adult experience, primarily older adults that can be quadruple or quintuple the age of the patient mentioned here, I think it’s important that that person has multidisciplinary care from the beginning. Pediatric, AYA, adult meeting together themselves, with the patient. At our center, of course, we’re blessed at having one of the major centers in the world. We have a separate AYA clinic that’s being formed to try to address this. But here, especially for the topic of this conversation, and I want to turn it over to the rest of the team, I can’t emphasize enough how important the psychosocial aspect is, so counseling with the parents, the child, the day-to-day care, how to give the transfusions.

The pediatric patients that I’ve had the honor of taking care of, a lot of interaction with the parents and making sure that the right IV tubes are given. It’s just very different from the majority of patients with MDS. So, I think that’s 1A and 1B, looking for the genetic component to this and then also paying attention to the unique needs of that vulnerable population. I want to turn it over to the rest of the team. Any other thoughts, guys, on that?

Allyson Price, MPAS, PA-C
I have a thought too, just to piggyback on that as well, Dr. Pemmaraju, is that I think there’s a huge concept of preservation of identity in the inpatients and specifically the AYA patients which the multidisciplinary team approach is better at addressing than some individual APP oncologist. And so, inpatients who are younger and patients who are older too, you’re going through the treatment, you’re getting transfusions, your life has just got flipped upside down. But what’s important to you? How can we still get you involved in some type of activity that preserves your identity because a sense of

identity that's lost, patients have a huge struggle with; and so I think you know as a provider just asking a patient, "Hey, I know that you're going through this, and you have to get transfused and you have to come to your facility now twice a week or several times throughout the month. What can I do to help you feel more like yourself?" And I think just asking that goes out of the way in these patients in preservation of their identity, psychosocial issues as well.

Michelle Rajotte, LMSW
Hi, this is Michelle too. We have a young adult chat that takes place on Tuesday evenings, and a lot of the feedback I get on there, there are some people on there who have older diseases. So, there's somebody on there who's in their 20s who has myeloma. There's another person who has a very rare disease that he's in his 20s. Really, most people don't get it until they're in their 60s and 70s.

So some of the feedback that they gave was that it's very lonely because you don't fit in pediatric, you don't fit in adult really because you're kind of in that midrange; and everybody around you who has that diagnosis is much, much older than you and doesn't understand what you're going through necessarily because you're at a totally different place in your life. So just making sure that they get that support from other young adults who are going through it, and even if they don't have the exact diagnosis, just being able to understand what it's like to go through it, especially when it's not the typical, that range of Hodgkin's lymphoma or anything that they usually get in that age range, because it can feel very isolating for them.

Caroline Kornhauser, MPH
Okay, thank you all so much. Our next question is from Jennifer, and she wants to know, "If MDS is a cancer or a blood disease." Can you expand upon that a little bit, Dr. Pemmaraju?

Naveen Pemmaraju, MD
Wow, thank you. That is really becoming one of the most important questions in the clinic. You know, a lot of these blood cancers that we treat used to actually be known as disorders or diseases, and it's built into the name. One in particular, the MPDs, myeloproliferative disorders, which the name has changed to MPN to reflect neoplasm or cancer.

So MDS, the history is very interesting. So, in the '60s and '70s, it was thought to be more of a disorder or a group of diseases and was known as quote/unquote "preleukemia." This was before the age of chromosomes, cytogenetics, molecular, and other advanced testing we have routine now. But as time went on, it was understood that it met all the definitions of what we consider a modern cancer: clonal, evolution, or basis of disease, molecular mutations, infinite or immortal growth and then, of course, clinically the concept that a person can have morbidity and mortality, which means death and dying just from the disease itself.

So, to answer this very specifically, yes, MDS by definition is a cancer. It can be life-threatening in some individuals. We can prognosticate, stratify, diagnose and treat as a cancer. And when a person needs therapy, they actually get chemotherapy which can only be given in the space of an oncology office.

The last thing I would say is I try to explain to patients and staff and other faculty and other doctors anytime we talk that the word cancer should not be stigmatized or be hidden. Let's use the word for

what it is but understand that cancer comes in so many infinite forms: indolent, slow growing, fast acting, acute, chronic, solid tumor, liquid tumor and that no two cancers are the same. Every patient is different. Every cancer is different. And even if you can't show an x-ray or a CT scan, you can still show a drawing, do a drawing, give each person where they're at, meet them where they are to explain to them what it is, even if it's a complex or rare disease. So, I think this is a very important question by our audience.

Caroline Kornhauser, MPH
Thank you so much. And our last question is from Rami, and, Michelle, you had mentioned the role of the caregiver. "Do you have any specific advice or recommendations for us to best care for our loved ones or any specific self-care tips that you had mentioned?"

Michelle Rajotte, LMSW
Yeah, it's tough as a caregiver because your needs always come last. But, yeah, it's that classic you have to put your oxygen mask on first to take care of everybody else, so how do you do that?

And we do have a lot of resources through LLS. Like I said, there's an online chat that takes place on Monday evenings. You can go on for as long as you can. A lot of times we'll have people logging on either from a hospital room because their loved one's in the hospital or they have five minutes that they can get on and just really get some support.

We have a workbook that's really very comprehensive of what they need to keep track of, but also there's a self-care part in there and how to manage stress. It really is just figuring out, even if it's just taking ten minutes a day to decompress and just breathe, because most of the time you don't think to do that because it's just what needs to get done.

And everybody's situation is different, and there's different levels of stress. And if you don't take care of yourself and take that time and really get the support you need and reach out and see who else can help, it's going to be really hard to do that long term.

Caroline Kornhauser, MPH
Well thank you for that question, Rami, and thank you to the audience for all of your questions today. Again, thank you to Dr. Pemmaraju, Allyson, and Michelle for your continued dedication to patients and fellow healthcare professionals.

CLOSING REMARKS

Caroline Kornhauser, MPH

So, this concludes our program for today. I would like to thank the Aplastic Anemia and MDS International Foundation for partnering with us today and to everyone for participating in today's program. We hope the information presented will be useful in your work with patients and families. Please complete your evaluation form.

Thank you so much everyone. Have a great day.