Slide 1: THE FUTURE OF AML TREATMENT: WHAT'S NEXT?

Operator:

Welcome to *The Future of AML Treatment: What's Next?* telephone and web education program. It is now my pleasure to introduce your moderator, Lizette Figueroa-Rivera. Thank you, Lizette. Please begin.

Slide 2: WELCOMING REMARKS

Lizette Figueroa-Rivera:

Hello, everyone. On behalf of The Leukemia & Lymphoma Society, I'd like to welcome all of you. For many patients and families, coping with a blood cancer diagnosis can be complicated, stressful, and overwhelming. With so much information available online from so many different sources, it could be challenging to know what is accurate or up-to-date. LLS is the leader in free information and comprehensive support for blood cancer patients, families, caregivers, and healthcare professionals.

From diagnosis and treatment to remission, survivorship, and ongoing wellness, our understanding of the molecular basis for AML has dramatically improved over the past 10 years. This knowledge, along with technical improvements in new therapeutic approaches for cancer, is changing the outcomes for patients. While we have begun to chip away

at AML, there is still much work to be done. LLS has provided tremendous funding support in research, including close to 80 active academic grants, to explore every avenue to further improve outcomes for AML patients. Please continue to inform us of what you need during this time and please continue to let us be there for you.

For this program, we would like to acknowledge and thank AbbVie Inc., and Genentech, Inc. and Biogen, for their support of this program.

Slide 3: FACULTY

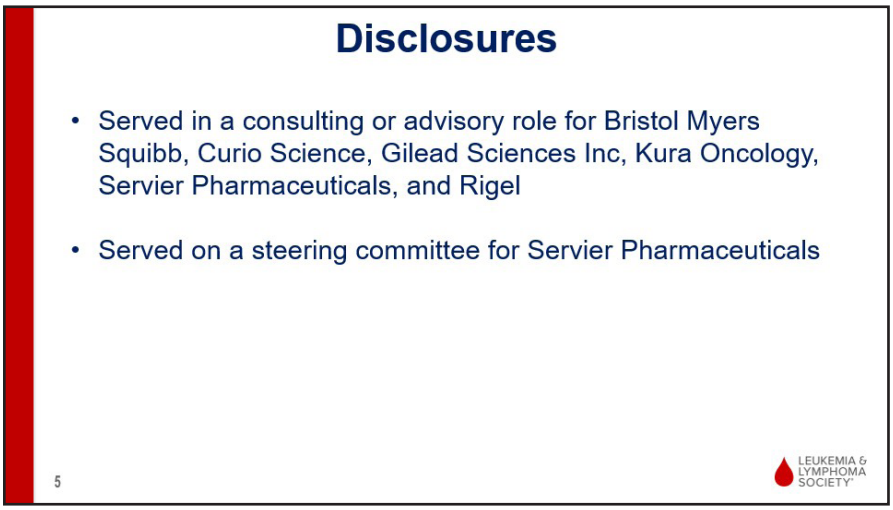
It is now my pleasure to introduce Dr. Rory Shallis, Assistant Professor at Yale Cancer Center and Smilow Cancer Hospital in New Haven, Connecticut. Dr. Shallis, I'm privileged to turn the program over to you.

Slide 4: The Future of AML Treatment: What's Next?

Dr. Rory Shallis:

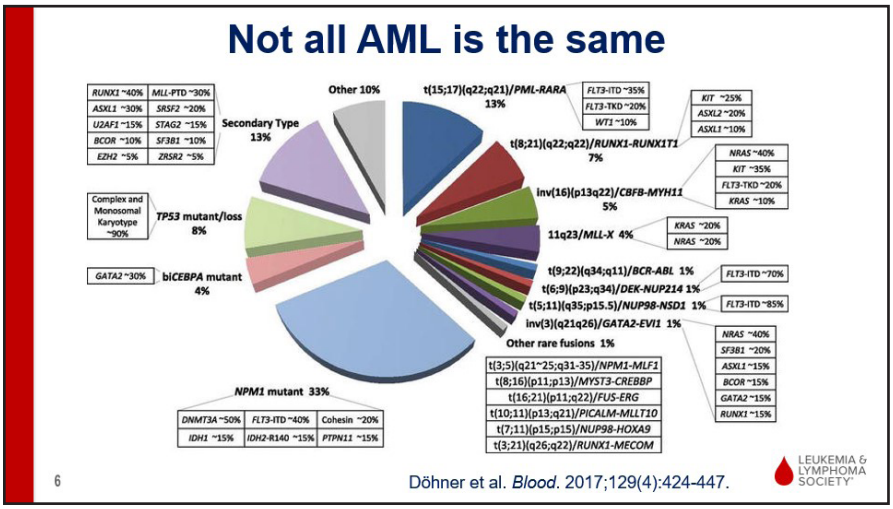
Thank you so much. It is a privilege and an honor. I was asked to talk about the future of AML treatment, as the title suggests. It is my hope that at the end of this webinar, each and every person listening, whether you are a patient, a caregiver, a loved one, or just an interested party or listener, has gained some helpful knowledge relating to the treatment of AML, as best we can do in this time frame. I was also asked to discuss a few other topics that contribute

to good care of a patient with AML. We'll certainly touch on these, as quite honestly, you can't talk about the future without knowing where current things stand and where we have room for improvement.



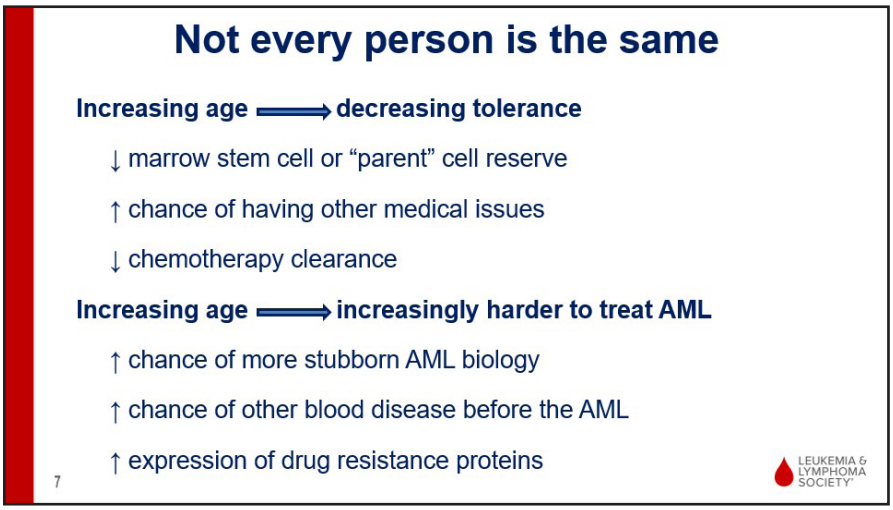
Slide 5: Disclosures

Here are my disclosures.



Slide 6: Not all AML is the same

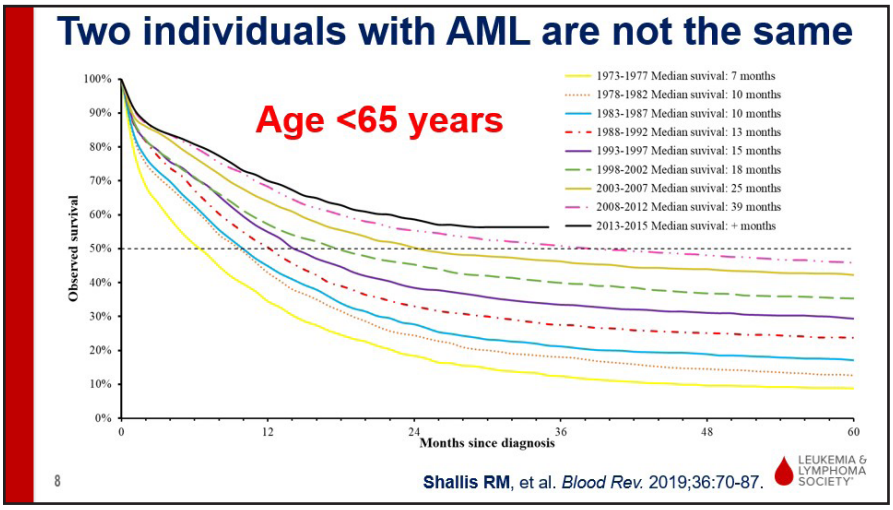
One of the first things we must recognize, especially when it comes to putting together a treatment plan, is that AML (acute myeloid leukemia) is one of the most diverse diseases we encounter in our clinic, owing to the many genetic changes that put these cells specifically on the path to becoming disease.



Slide 7: Not every person is the same

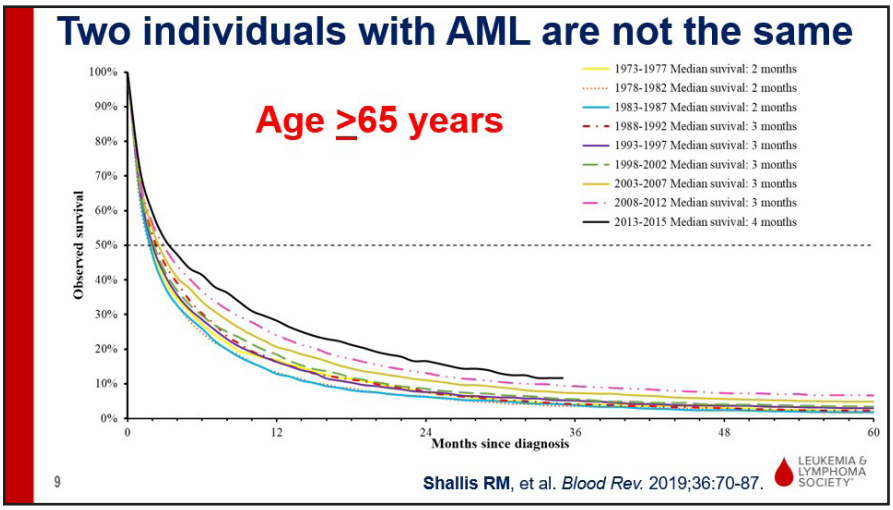
The average AML cell doesn't only have one of these abnormalities in the machinery that would otherwise keep a normal cell, but almost every AML cell will have several, almost like a hand assembled from a deck of cards. You can imagine how many combinations of these abnormalities are possible, and how certain hands are either easier or harder to play against or beat. Similarly, everybody's different, literally, every body is different. Much of these changes become apparent with age.

Given that the average age at time of diagnosis of AML is 68 years, in the United States at least, it is important to realize that with increasing age, the longer our bodies are on earth, the greater the likelihood we are to develop other medical issues, the harder it takes for the bone marrow parent cells to keep their strength, to keep producing normal cells, and make up for this injury to the bone marrow, as well as changes in metabolism that alter the way we clear particular chemotherapies. On top of that, with increasing age, the greater the chance that this poker hand, forgive the poor metaphor, this poker hand is a harder one to face.



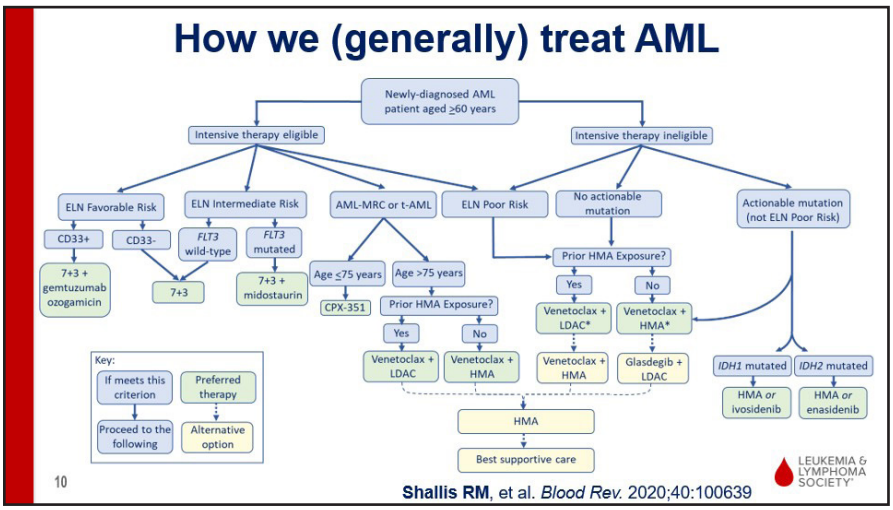
Slide 8: Two individuals with AML are not the same

Because of these issues, I show you a figure. One that illustrates how outcomes have improved over time, dating back to the 1970s to most recently, a few years ago on how these lines or these curves progressively get higher on the graph with increasing time or era. Basically, meaning a greater proportion of patients are living longer.



Slide 9: Two individuals with AML are not the same

The higher the bar, higher the curve, the better people are doing. However, this is a graph of individuals diagnosed with AML before the age of 65 years. This is how we're generally doing for individuals diagnosed at an older age. It makes the understanding of goals and decisions regarding management quite important, as you can imagine. These discussions were likely simpler no more than 10 years ago, but as we've been blessed with more effective therapies, better supportive care, antibiotics, and practice patterns, and the like, now it's gotten a bit more complicated. A welcome complication that often sparks debate even amongst leukemia specialists.



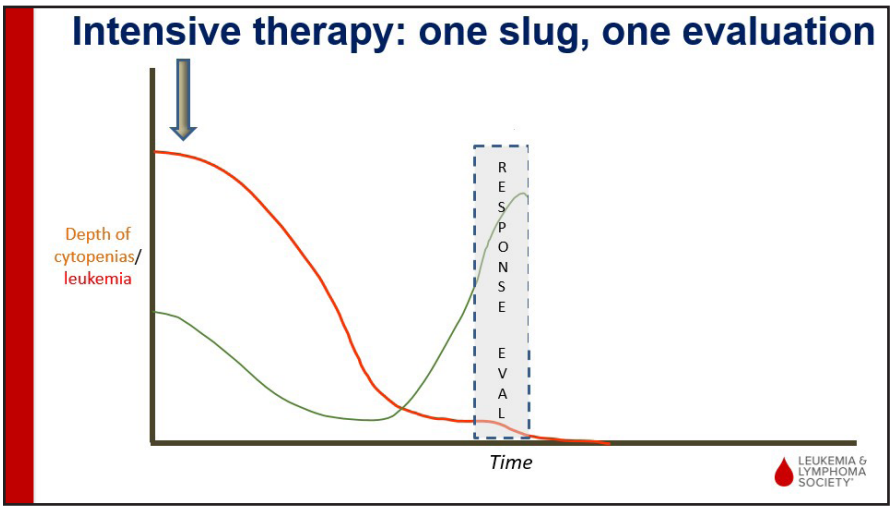
Slide 10: How we (generally) treat AML

There is no way that we can belabor this slide, or this figure, or discuss how we treat every situation that a patient with AML can encounter, but this is a figure that illustrates at least a general framework for managing AML based on the 2 main things we talked about, disease biology, the hand of cards, and the combination essentially, and the ability of a patient to accept the risks of intensive intravenous or IV chemotherapy, which goes something like this:

Slide 11: Intensive therapy: one slug, one evaluation

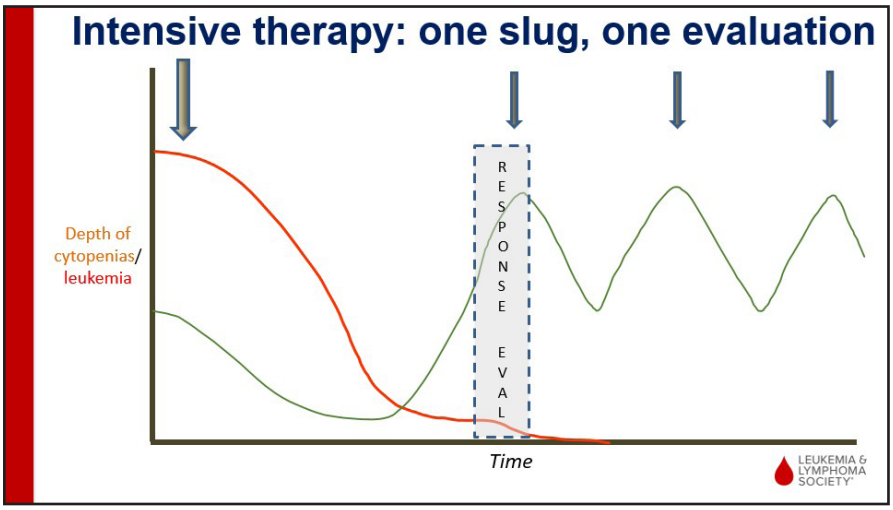
It's been the standard of care since the early 1970s for many individuals. It's generally about 2 intravenous or IV medications that are given over several days in the hospital, almost certainly in the hospital, and are strong enough to hopefully kill leukemia cells preferentially, but not sparing the normal cells in the bone marrow that can really withstand this forceful therapy in the longer term. But in the short term, on the order of four-ish weeks, can be longer, they will go low, to the point of needing red blood cell transfusions, platelet transfusions, antibiotics to prevent infection - that is quite common in up to half of patients - but who also may encounter hopefully brief injury or strain to organs like the liver, the colon, the kidney, amongst several others, and in being direct, sorry to be direct, but this is the right thing to do. The risk of dying from these complications is 10% to 20% depending on where you look, clinical trial-wise or real-world data.

When the bone marrow is able to wake up towards the end of this period, we do a bone marrow biopsy, hopefully at this point to see the state of the bone marrow, to see if we've really taken control of the bone marrow at this point.



Slide 12: Intensive therapy: one slug, one evaluation

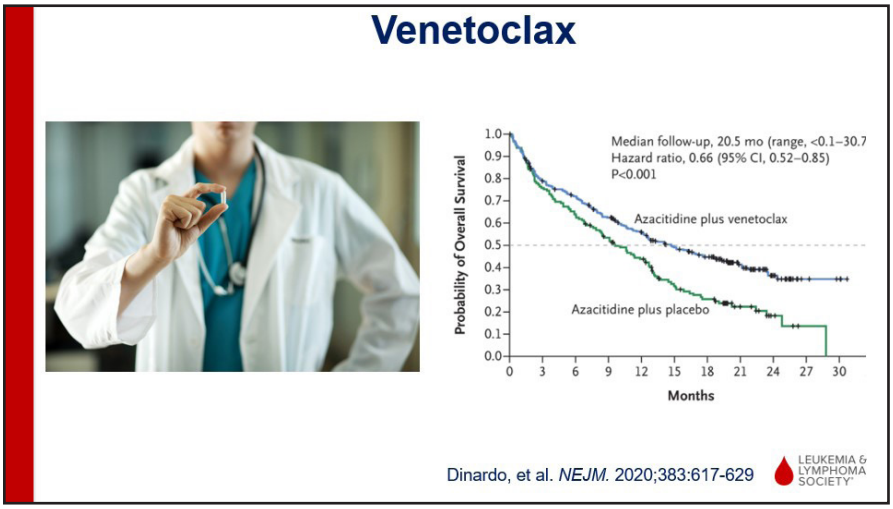
In other words, you really get a one-time shot of heavy-duty therapy, wade through the valley of low blood counts and what comes with it, and then in several weeks' time, fingers crossed, blood counts hopefully recover and come up.



Slide 13: Intensive therapy: one slug, one evaluation

This is the point at which we do the bone marrow biopsy to look for a response. Should the response be a good one, in other words - remission, using the term literally, the disease has remit. It's been pushed back. We then proceed with what is known as consolidation therapy. Forgive these terms, but they're the terms we use. This is done basically in several weeks' time. This is really just meant to build upon that response, usually 3 to 4 cycles of chemotherapy. It's still intensive, but a little bit lighter than that first slug, as I frame it here. The hope is that any lingering microscopic disease in the bone marrow or elsewhere is eventually eradicated and puts patients well on a path to cure. That is at least our hope.

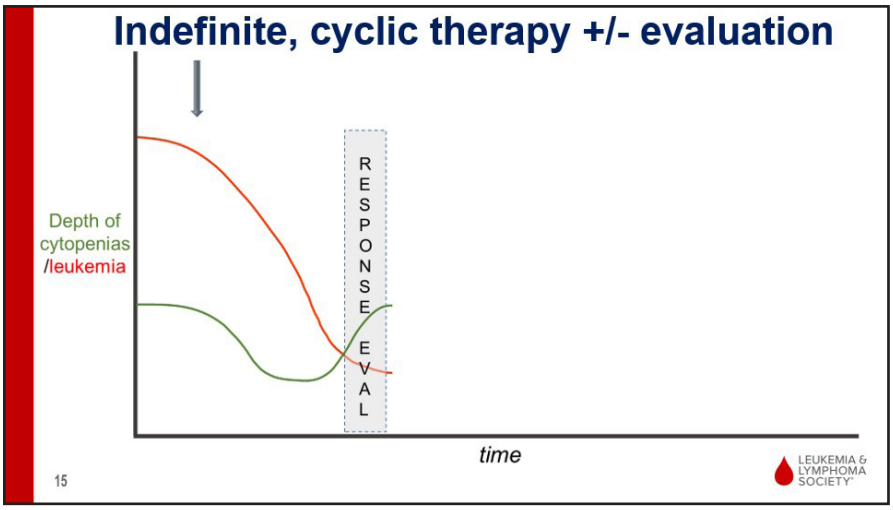
Up until 2018, patients that could or did not want to accept the risks of intensive chemotherapy here had really otherwise limited options, sorry to say. That is until the development and study of a pill that maybe many of you have heard of, and in fact maybe are receiving, this is venetoclax, the brand name being VENCLEXTA®.



Slide 14: Venetoclax

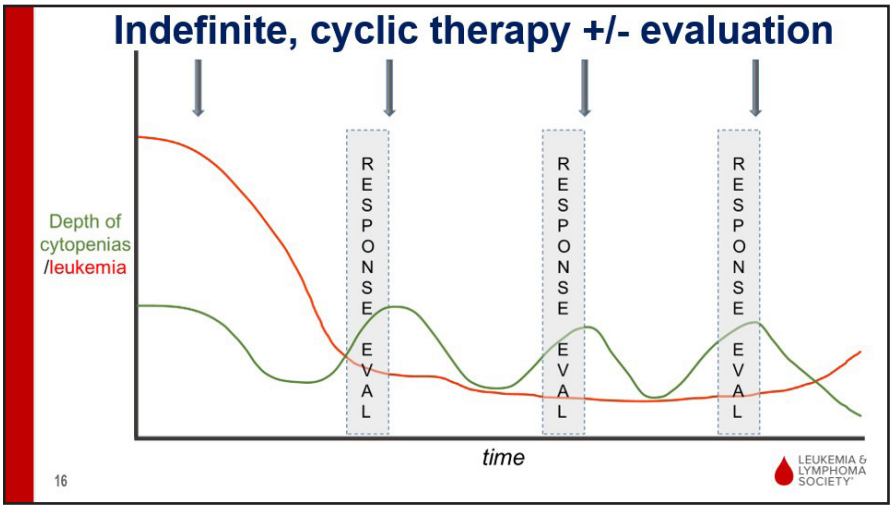
When combined with another drug known as azacitidine (Vidaza®) or AZA, showed excellent responses and better outcomes when compared with azacitidine alone, which was a reasonable standard prior to 2018 for many patients that really couldn't get intensive chemotherapy. We now use this combination regimen like water, including for many patients that actually can get intensive therapy, but for one of a few, if not several reasons, we feel this regimen best aligns with their goals.

This breakthrough has changed how we help many patients navigate their journey with AML. Instead of a one-time slug or, forgive the term again, an all-or-nothing bone marrow biopsy 4 to 6-ish weeks later, this type of therapy is given generally every 4 weeks or so. We don't really stick to every 4 weeks in most patients, with bone marrows done a bit more frequently until we get to a good response or remission. In fact, they can be done pretty often even amongst patients that are in remission.



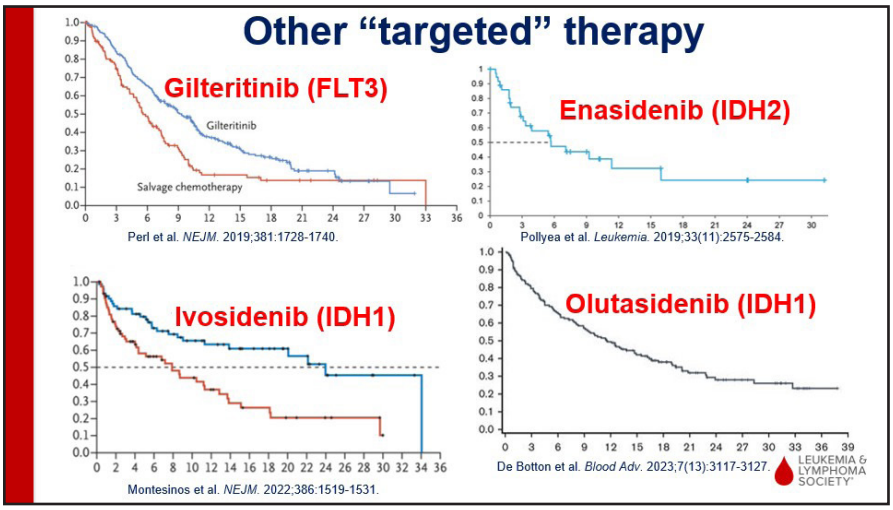
Slide 15: Indefinite, cyclic therapy +/- evaluation

Because this treatment is pretty continuous and indefinitely given, that's the term we try to use, indefinite, just because we give it as long as it's working, and patients are able to tolerate.



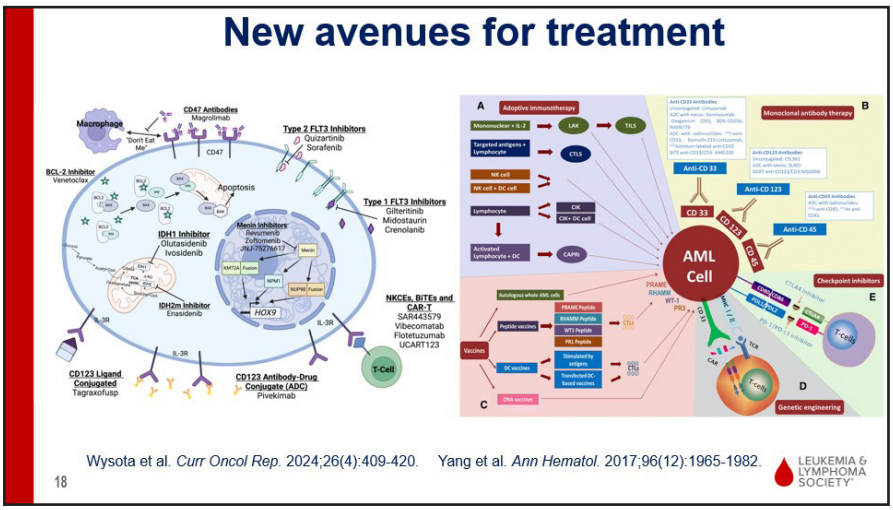
Slide 16: Indefinite, cyclic therapy +/- evaluation

Patients tend to spend more days than not with low blood counts, and the risks of infection, organ injury or strain, and maybe poor outcomes of this therapy, they're still present, but they are a bit lower. I should say quite lower when compared with intensive therapy.



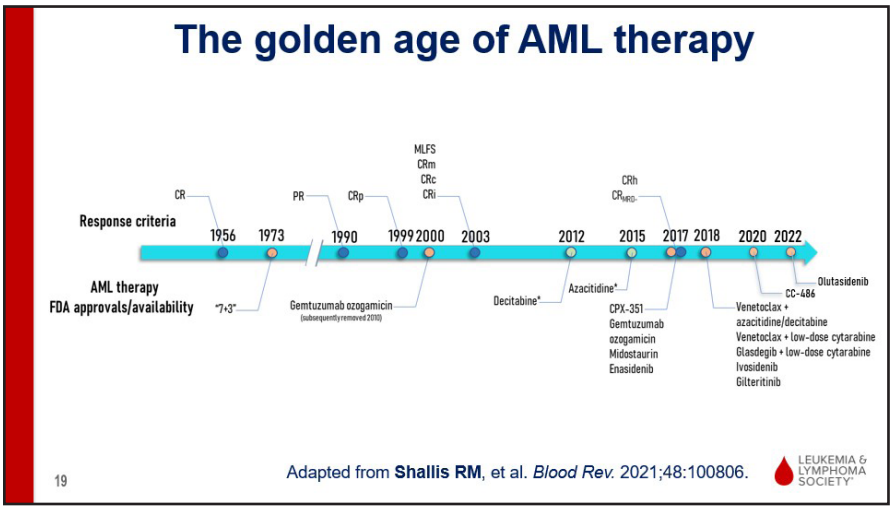
Slide 17: Other "targeted" therapy

Venetoclax is not the end of it. Since 2017, there have been a few other pills that have entered the AML arena, specifically the targeted therapies, as we call them, given their ability to target particular proteins that are either in and/or on leukemia cells, with the big ones being those that target some of which you may have already heard, like FLT3 or IDH1 or IDH2. These are a couple of them, at least--looking back to those curves I showed you before that patients getting these targeted therapies can do better compared to older standards of care. I'm actually leaving one out. Quizartinib (Vanflyta®) is another FLT3 inhibitor that was just recently approved. Our armamentarium for these targeted therapies has been improving, and we think improving the outcomes of patients along the way.



Slide 18: New avenues for treatment

It has been the result of the recognition, as we've discussed, that AML is a disease driven by many changes to the genetics and the proteins that drive these cells, but also the development of therapies against them. There's more to it than targeting proteins, as well as there have been many ongoing trials looking at things like immunotherapy, cellular therapies, and many others that may be the next venetoclax or game changer or perhaps at a minimum, the next good thing for a particular subset of AML or a particular patient with a specific form of AML. We may eventually, it's my hope at least in the next 25, 50 years, maybe ambitious, that we have a regimen for each individual hand of cards that AML plays against us. This is a busy slide, but just going to show you this is just a drop in the bucket of what is going on with regards to the development of new therapies for AML and moving the needle even further.



Slide 19: The golden age of AML therapy

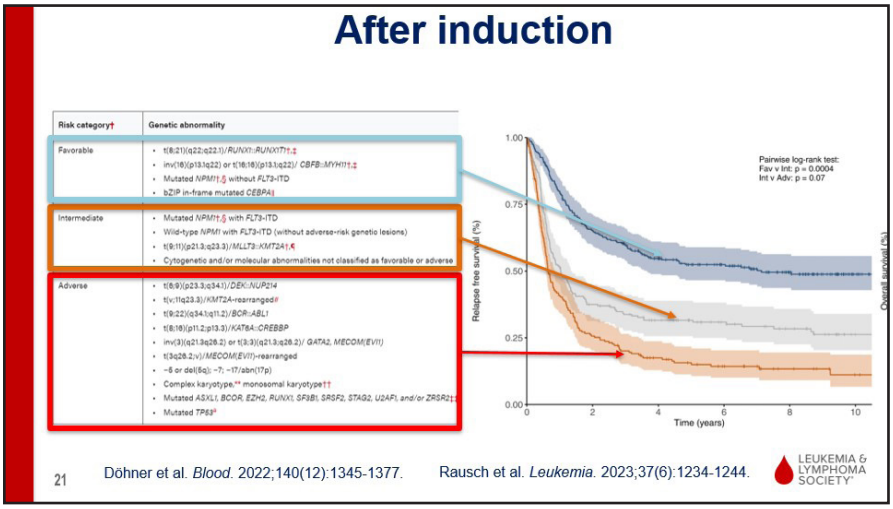
This is what the bearing of this fruit looks like in a timeline. That puts my contention that we are in the golden age of AML therapies in context. You can see here the number of names in black on the bottom. These are the names of drugs. It's basically exploded only in the last 5 years or so, and I expect this to only grow to the point where pre-2017 may soon be regarded as the Stone Age of treating AML. An exciting time for sure and for a good reason.

Slide 20: Clinical trials/research

How does this happen? Clinical research. It's my hope that every individual unfortunately diagnosed with AML is fortunately plugged into a center that has a selection of clinical trials, that for those that are newly diagnosed are almost never "guinea pig trials" as some patients often express or tell me, but rather, delivering a standard of care that we discussed, but with possibly a better drug added to hopefully improve the standard. That's really the only way we improve the standard over time. Whether you are eligible depends on a discussion with a number of providers. It's a nuanced one and they require some additional testing. Either way, it is your decision.

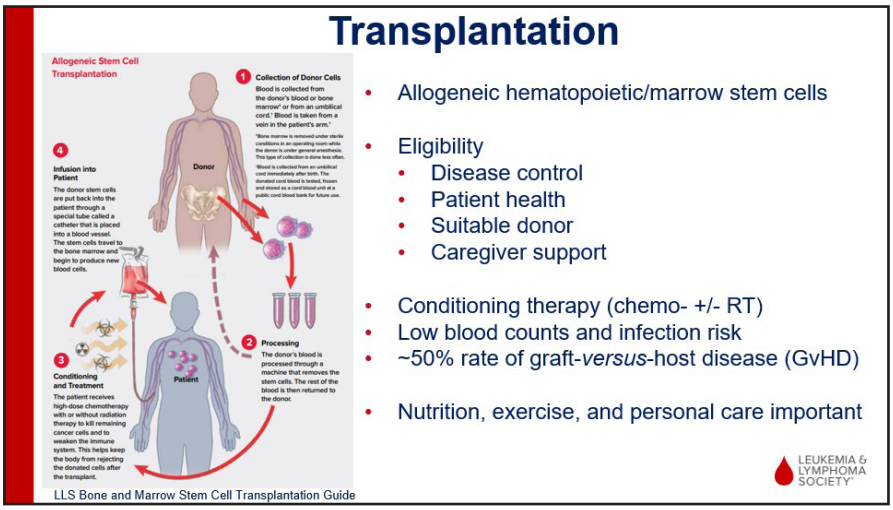
To be on trial you need to be informed of the rationale, the logistics, the expected benefits, and possible side effects of the treatment. You have to be informed of these things before you provide consent to be on a clinical trial. I will say patients ask a lot of questions when it comes to why they should even consider being on a clinical trial. There are some things that make some patients nervous. The first is this one: not all trials have a chance of the patient receiving placebo, but again, even in this case, it is also delivering a standard of care.

Another common question is cost. What does this cost me other than maybe some extra time? Are there extra tests? More of the financial incentives. Most trials, you really don't get paid. We don't get paid. Cost rates are settled by the company doing the trial and everything else that would otherwise be part of that standard of care goes through insurance as if you were not on a trial. Then of course, at any time on a trial you wish to stop or pursue an alternative and sometimes there are, but many times there are not, this is your right and it must be respected. But, we'll just ask that this again be a thorough discussion with your leukemia team before committing to stopping.



Slide 21: After induction

It doesn't stop there. Chemotherapy, whether it's intensive or less intensive as we try to call it these days, may be insufficient in putting a patient in position to have a long-term outcome, if not cure. For this reason, we need to consider other means of what we again call consolidation. For AML, based on disease biology, that hand of cards again, falls into the red box and in many cases, the orange box corresponding to the curves on the right here.



Slide 22: Transplantation

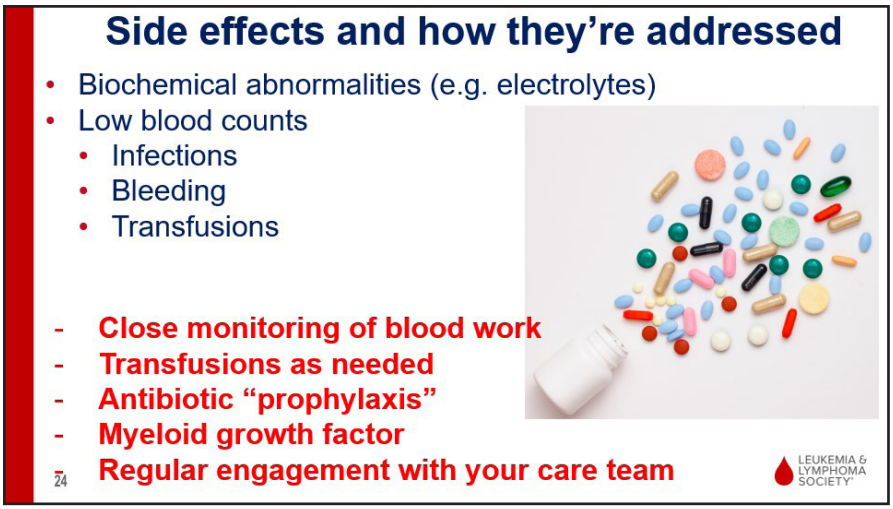
Remember, higher is better outcome. We consider another therapy once the disease, once the AML is in remission, and that is a stem cell transplantation. More specifically, and it gets a little wordy, this is an allogeneic hematopoietic stem cell transplantation, or in other words, another person's bone marrow cells. Similar to intensive therapy to get disease or AML into remission, a transplant of this nature, it's a tall order but it can be impactful.

It requires a few things. It requires disease control, or in other words, a form of remission. It requires having decent health and support to safely get through the complications that are below [on the slide] but also a suitable donor that is more likely than not, not an issue. But there are some patients, unfortunately, patients of mine that are meeting all these bars, but there's not a suitable donor to proceed and again move the needle for this individual patient.

Again, similar to intensive chemotherapy, a transplant does carry risk of low blood counts that may lead to significant infection, but also a little bit different here, what is known as graft-versus-host disease or GVHD as you might have heard it called, which is when donor cells go off target and start to injure normal tissues, organs in the recipient, in the patient. Because of these high stakes, it is important to be as healthy as your body can be, including during treatment, so nutrition and general personal care are quite helpful, if not critical, I would say.

Slide 23: You're not alone: Meet your care team

This help is not only on the patient, not only on you, or the leukemia doc, or the transplant doc, but as many of you may have guessed based on the number of people you may have met on your team, it is a large one, inclusive of nurses, other subspecialty teams, pharmacists, social workers, psychologists, nutritionists, spiritual care, and the list goes on. Should you be on a trial, a whole slew of research team members, all aligned in making your journey and care you receive on it, hopefully seamless and optimal.



Slide 24: Side effects and how they're addressed

Part of that journey may, and I should say is very likely to just be honest, come with side effects. Now, the types of side effects differ based on the type of AML therapy in which you embark, but generally, most will cause changes in blood work, most commonly lower blood counts that we already discussed may, or in many cases, will increase the risk of infection and bleeding for which we offer red blood cell transfusions, platelet transfusions, and then offer another layer of protection with oral antibiotics to hopefully prevent as many infections as possible, but they are imperfect. Many of our patients do, despite our best efforts, encounter infections that can be mild, can be serious, can be life-threatening.

We sometimes give the bone marrow a boost with what's known as a myeloid growth factor. It's an injection, usually subcutaneous or in the belly to help make more white blood cells in an effort to hopefully have enough of those cells to again prevent infection, usually on top of the antibiotics. Because of these risks, many of which can be prevented, which again is our main goal or lessened, staying in close contact with your team is critical. Too many patients, including in my experience, lose contact or alert us when small things that could have been prevented, they just keep it close to their vest. It could have been prevented and they eventually become bigger things that have more critical consequences, if not very dangerous and life-threatening. Communication early and often is key.

Slide 25: Side effects and how they're addressed

Other side effects, at least the common ones, right? We can't go through all of them for every individual regimen, like GI side effects. Nausea is a common side effect that these days can be prevented pretty darn well compared to no more than a couple of decades ago, 25, 30 years ago. Many of the regimens we use for AML inherently incorporate anti-nausea medication as you get the therapy, but you should likely be armed with a take-home medication that you can administer yourself as needed should you encounter nausea or you wish to prevent it at home, either before pills or meals, etc.

Many people here and beyond have heard of Zofran®, that's a branded medication for ondansetron, Compazine® (prochlorperazine), and these are great backbones. We have several others in several different classes of medications. Just for example, under-recognized one is Zyprexa® or olanzapine. That is increasingly being recommended earlier, including by several guideline panels.

I have to plug our palliative care colleagues that are not necessarily hospice colleagues. This is a common misconception. They are different. These are individuals whose area of expertise is helping you or your loved one manage side effects alongside your treating team as an extra layer of support, as we like to call them, and maybe they like to be called as well. They are just like other anti-nausea medications or other layers of support. They are underutilized as well.

Slide 26: Side effects and how they're addressed

Beyond nausea, another common one which can cause distress is many patients ask about hair thinning and loss, and rightfully so. The IV or intravenous chemotherapies are notorious for this, with the understanding that it does come back, sometimes a little bit different with regards to texture and thickness, rarely color. It does come back, usually in the span of days, usually several weeks.

It is noticeable, which is why many individuals expecting this effect should be counseled and actually do opt to move to a shorter haircut to hopefully make this transition at least a little bit easier. These days we do have very good wigs that in many cases are covered by insurance. Please work with your team to navigate these possibilities early.

Slide 27: Side effects and how they're addressed

This journey is often not an easy one. I'd hesitate to say that any journey for someone going through this is easy. That's just a misnomer. Some patients are stoic for any number of reasons, others are open and honest about their emotions, and I would say we welcome everything in between, even though some patients might not have any close family or friends that can be there day in and day out for support.

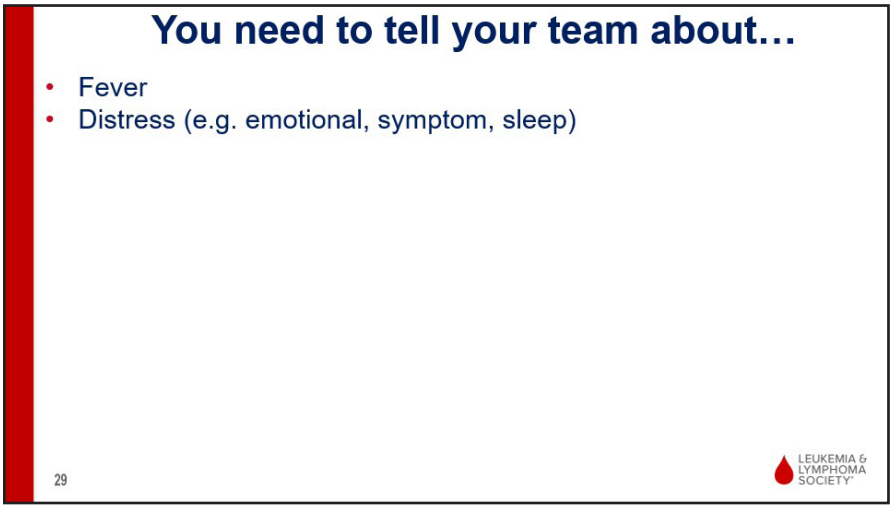
Anyway you cut it, you are not alone, and you are not the first person to go down this path. Many members of your team, even though you may not yet be introduced to them are explicitly there for this reason. We can connect you with members of the palliative care teams, the social work teams, or those that are maybe just again, more directly specialized to optimize mental health, which is important for just good medical care.

Slide 28: Side effects and how they're addressed

Again, if there's a common theme, communication. Communication is where it starts, and that's not where it ends as well. It just has to be a continuous thing. Communicate with your team members, anybody and everybody that is willing to listen, which would hopefully be everybody. I had to put this on there. The most common issues that patients experience, I would say, are sometimes the ones, in all honesty, we do not have quick fixes for. These include fatigue and loss of appetite, which in many situations are due to other medical issues.

These can be tested for by your team. There are some maneuvers before discussing and even administering or relying upon medications. These maneuvers are often inexpensive, not too time-consuming, even though yes, it does require a commitment and may be the difference maker. Protecting good quality sleep, which is easier said than done, it's often predicated upon good management of discomfort in many forms or any form and stress.

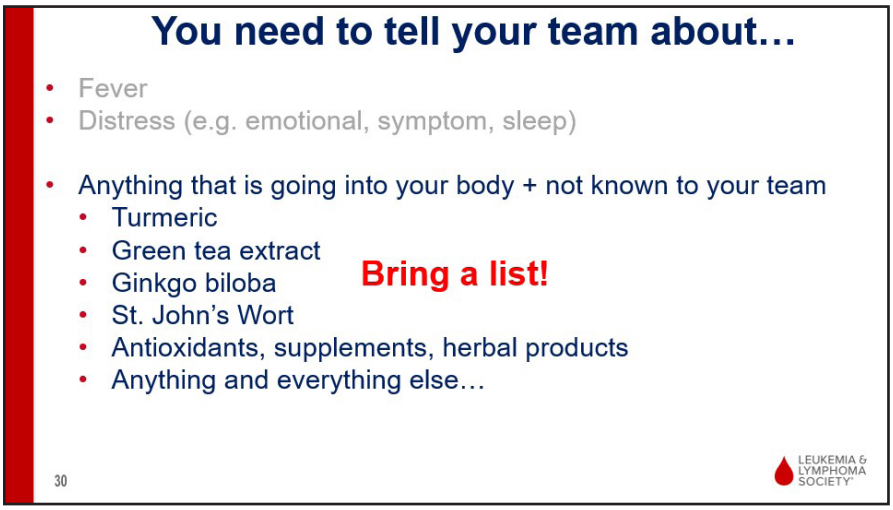
Again, if there's a common theme here, to be open and direct with your team about your concerns, or for those family members that are listening, your concerns about your loved one, this is always helpful in managing their medical care. Some of these are non-negotiable. We always want to know about these stressors that can again impact medical care and possibly outcomes as well. If that care is just a little bit less than optimal, just because communication is less than optimal, we want to know, irrespective of blood counts about fevers.



Slide 29: You need to tell your team about…

When blood counts, more specifically, white blood counts are low, a fever can be dangerous, so please call. They tend to be more dangerous when the neutrophils or the ANC (absolute neutrophil count), as you might have heard it called, is low. Many of the things we have to do can be lifesaving. Please call if there's a fever.

The definition of fever is debated. Anything that you can feel or is not a normal temperature on a digital thermometer we would regard as a fever. Worst case, it's a phone call to your team that can be navigated, maybe with just some reassurance and maybe just extra vigilance. Please, any fever, call your team members.

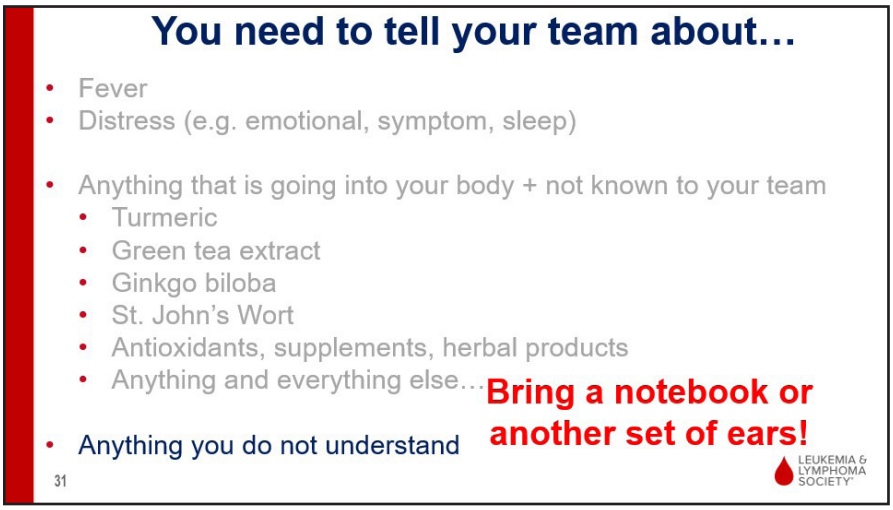


Slide 30: You need to tell your team about...

This is important in the era of newer drugs and combinations and an increase in the motivation to be healthier, a good thing for sure, I definitely commend patients for doing this. I ask you to always let your team know about medications, supplements, vitamins, powders, mixes, anything not on your medication list.

More often than not, it's not a big deal and has no appreciable impact that we can at least discern. But, there are things you may be ingesting that can increase the risk of toxicity or side effects due to an interaction with what otherwise would be a critical therapy. This may actually lead to worse outcomes.

Here are some examples that are important to note, but please alert us to anything and everything. At worst case, it's a conversation, and again, more often than not, it will be a non-issue. Again, communication is key here. I would say bring a list. I would say please alert us to anything that does not make sense or is not clear.



Slide 31: You need to tell your team about…

Some providers or team members are maybe better communicators than others and it's the duty of the team, especially as it relates to treatment, to make sure you understand what to expect. In my experience, the patients that are motivated to be this engaged in understanding tend to have the least, or let's just say a less bumpy journey.

Again, just ask for clarifications or any filling in of the gaps, reading materials, or "Hey, can you please explain that again?" This is something which I would say is a requirement for anybody sitting before you trying to explain what AML is, what the treatment looks like, some side effects, and what maybe the next step should be, communication.

Slide 32: The honest questions

I wanted to offer at least 3 questions that I think are under-asked in the clinic and are probably amongst those that have the highest yield. What if I want a second opinion?

Of course, you may get different opinions from 2 different specialists and it just happens these days with so many options, including clinical trials. If there is confusion, then very often the 2 teams can discuss so you're not confused in the middle and professionals can, I would argue, always find agreement. It is for this reason that I encourage patients to seek a second opinion, but perhaps not to the point of excess, like 4 or 5, 6, 25 opinions, as at a certain point it does make it difficult to unify a recommendation for treatment and may in the end, I would say, only cause emotional distress. On top of that, it can potentially lead to an unsafe delay in starting treatment.

This is actually a misconception that every AML is an emergency to treat. I have to be treated within 2 to 3 days or something bad is going to happen. In most cases we can delay and be more thoughtful about getting the information together, maybe additional testing. Please seek a second or third opinion, in some cases the doctor or team member before you can actually start that introduction. I just basically said there is a point at which there is an unsafe delay in treatment. What that threshold is, how much time is individualized, and it depends on your individual circumstances.

What happens if I do nothing?

In other words, what may my life look like if we forgo therapy for AML? This may mean doing everything short of embarking on treatment, still doing antibiotics, blood transfusions, etc. Some people when faced with a particular AML that is a hard hand of cards to beat, I'm a big metaphor person and pardon me if this is a bad one, based on goals, quality of life, and maybe things that we just can't account for, he or she may decide of sound mind and will to focus on comfort and this is not unreasonable in many situations.

It's a question that again is an honest one and one which can be very helpful to ask. It's an honest question to help people make the right decisions for them, and your doctor should give you an honest answer. That's just the truth of it.

Lastly, one of the questions I've grown to love as patients have seemed to ask me more commonly over the last few years is, "What haven't I asked?"

This puts the ball on the team score to make sure some of the critical questions, maybe two, the ones we have here, are asked directly informing good understanding, which, as I said before, is a requirement for good AML care. It doesn't stop here.

Slide 33: Survivorship

From the moment you or your loved one is delivered a diagnosis of AML until the day we leave earth, each patient is a survivor. Those that live longer with or without, hopefully without disease, can have longer-term effects of chemotherapy. Some of the agents we use in intensive therapy do have delay, let's just say, heart effects that just require some vigilance every time you're sitting before your team member that's hopefully doing an examination and maybe might get additional testing to look at heart health. That's just one example.

Longer-term survivorship care does include that which is related to psychosocial well-being. There are many situations in which it is emotionally and sometimes physically traumatic where some patients can develop PTSD (Post-Traumatic Stress Disorder). As I've mentioned before, we do have team members that it is their job and it's their area of expertise to help you navigate these things and hopefully be more of a long-term relationship.

I would also say that those individuals that are living longer, hopefully without disease, can still get the same things that Joe Schmo on the street without AML can still get. This is, we're maintaining a relationship with your PCP, your primary care provider, and other providers, maybe your cardiologist, maybe your nephrologist, your kidney doctor. It's still important in preventing, as best possible, other medical conditions that really can impact care and quality of life beyond the AML. I see all too often that once a patient is stamped with the diagnosis of AML, some of the other providers just kind of fade away into the background and Shallis is going to be their PCP. They're going to be the nephrologist now.

In many cases, yes, we do take on a little bit of that burden just because it is more of a subspecialty care that is required and maybe our disease sort of takes precedence. I have no shame in admitting my limitations and expertise when it comes to kidney health, heart health, and again, there's maybe a certain point where more doctors is maybe not as good, but I would say at least maintaining that relationship with your PCP. In discussion with your leukemia team, some of the providers that maybe are important to keep in your fold can still be important and really help you derive the benefits that you are destined to derive with the therapies that you're likely on, and with the team that hopefully is by your side throughout this journey, which if I haven't made the case, should hopefully be a long one.

Slide 34: THANK YOU

I thank you again for the invitation, the opportunity, and the attention. I hope, as I've said at the outset, that I've imparted some, at least some, helpful knowledge to empower patients, their loved ones, and anyone else who just is kind enough to drop by to be effective contributors to the care of patients with AML, and without a doubt, I look forward to any questions. Thank you so much again.

Slide 35: ASK A QUESTION

Lizette:

Thank you for such great information, Dr. Shallis.

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

We'll take our first question from the web audience. Doctor, Dorothy asks: What new treatments are available or being worked on for elderly AML patients who are not eligible for transplant?

Dr. Shallis:

Excellent question, Dorothy. This is an area of intense research and a lot of it is really geared towards, as best we can, slowly but hopefully moving away from having to give most, if not as many patients as possible, intensive, I would say, hardcore chemotherapy. We've been given this for 50 years now. For many types of disease this is still, as it stands right now, the best means by which some patients can achieve cure or long-term survival at least. It comes down to a particular disease biology.

Much of what is, and hopefully I've at least touched on this in the talk, is coming down to the hopeful development of pills, pills that can target specific proteins or certain aspects of the machinery in these disease cells that maybe are more specific for a particular subtype of AML. Most of these pills are pretty well tolerated. They have some risks. Venetoclax is one that's the first into the fray. It does have some toxicities that I'm sure much of the audience might already be aware of. As best we're trying, it's very likely that we might be moving away from chemotherapy as a whole, specifically to apply it to many more patients that just can't get that intensive chemotherapy.

This is a little bit ambitious, but I think we are kind of breaking the deadlock. Again, I would really just call back to what I said before. I do think this is the golden age of medication development to treat particular types of AML that may, in only a few years' time, be purely pills and pretty well tolerated.

Lizette:

We'll take the next question from our telephone audience, please.

Operator:

Our next question comes from Reema. Go ahead, Reema.

Reema:

I want to ask the doctor: My daughter is 29 years old. She's 60 days after auto transplant. We never found any match. In your opinion, what kind of chances does she have in the auto transplant on survival compared to allogeneic?

Dr. Shallis:

Hi, Reema. That's a very specific question and I'm sorry to hear of these troubles. Much of what I would kind of counsel you on is that this really depends on a lot of the nuance, a lot of the details that relate to individual circumstances. What kind of leukemia? That's a bit more detailed than what it even was 5, 10 years ago. The types of treatments that were given to get to, in this case, an autologous or auto transplant, which as you seem to be aware, is not commonly done with AML. I'm sensitive to situations in which maybe you just don't have the things available to really put a patient in the best position to derive the best benefits. Not to say you should leave anything on the table. I'm unsure how I can be helpful without knowing much of these details.

Lizette:

The next question comes from Lois. Lois is asking: Should your current oncologist recommend clinical trials not offered in their institution or do you have to find these yourself?

Dr. Shallis:

That is an excellent question. I'm embarrassed to say, I probably should have actually included that in my talk. This is important. Who does this? Is this the job of the doc that's sitting in front of me? Is there some element of bias? Or are they really going to refer me to another center? I can tell you, I've done it myself. There are some times when, based on a particular patient situation, there's a trial that just makes sense and it might just be the trial that we don't have open or available, maybe anytime soon at our center or our hospital, in which case I practice in a part of the country where it's not terribly difficult, not to minimize it, but it's not terribly difficult for patients to travel down 95 to go to another city, in which case there's a bunch of hospitals and it's a small community. We tend to know many of the leukemia specialists in the field. It's, I think, a 2-way street. It's kind of like a 2-prong approach.

Patients should be empowered to look for clinical trials. Look on the websites for neighboring centers, the names you tend to know, but look at academic site websites. I'd say, more often than not, it's pretty navigable to look at the website of my leukemia team, what trials, and you click it and it can give you a sense of the trials.

Sometimes it might be a little outdated and not up-to-date beyond a couple of months, maybe a year, hopefully not, but I would say most of your leukemia team members, and certainly the leukemia doctor, the specialist before you, should know what makes sense for you. It's both. Do some research by yourself but also ask your doctor directly. Is there a trial that makes sense for me here? If not, can I please explore somewhere closer that's not too far away?

Lizette:

Yes, and Lois, LLS does have a Clinical Trial Support Center where we guide you through finding any trials that may be appropriate for you. You can contact them at LLS.org/Navigation, or through our Information Resource Center, which I will give you that number at the end of this program.

Operator, can we take the next question from the telephone audience, please?

Operator:

Our next question comes from Thomas. Thomas, your line is open.

Thomas:

Thank you. My question is: I have chronic graft-versus-host. I'm about 2½ years post-transplant and my complication, the main complication is bronchiolitis obliterans. My lung function is at 37%. I just wondered what the doctor might know about the bronchiolitis?

Dr. Shallis:

Hi, Thomas. It's a good question and your situation is not a rare one. I would say graft-versus-host disease or GVHD affects at least half of patients depending on the data source you're looking at. Coin flip, you're going to develop some form of GVHD. Much of that is chronic GVHD, which we actually do know tends to predict a little bit better outcomes.

If you're having a touch of GVHD, the Goldilocks scenario, not too much not too little, then you're probably deriving some benefit from the graft actually working on leukemia. For someone who's 2 years out, more than 2 years out, congratulations. That is a good milestone. Long involvement by GVHD is not uncommon as well. Hopefully, it's mild and there are some medications that can be tried to alleviate some of the symptoms plus or minus some element of lung function.

I would really hope that in addition to seeing a transplant team member or team in general, that you're also plugged in with a specialty pulmonology or a lung specialty team. We often work very closely with, as I said, many subspecialty team members, and in your case it makes sense to, hopefully, be plugged in with a lung specialist that might have other tricks up his or her sleeve.

Lizette:

Our next question is from Barbara. Barbara is asking: When a patient is considered cured from AML, when should a patient start looking for solid tumors and what tests should be administered, such as MRI, CT scans, blood tests?

Dr. Shallis:

Another excellent question, I think taking it one step further from my slide, which I didn't want to provide too much detail just because it is still dynamic, these guidelines are not really ready for prime time. The first part of that question really depends upon when we consider someone cured. This itself is somewhat debated, so the rate or the distance from last time that you received chemotherapy that is increasing the chances that, hopefully the disease is gone.

Two years is a pretty good milestone. We like 5 years, we love 10 years. In that, within the first couple years of completing therapy if you're back on your feet and can otherwise tolerate the procedures that would come with getting back on track with routine cancer screening, I would argue it's standard of care. There are some situations in which maybe it's not the right time, so if maybe there's transplantation, there's maybe quite active GVHD going on.

Even if we find a small colon cancer on a colonoscopy, what would really be the right time to treat it outside of cutting it out, that gets a bit nuanced. To try to be helpful, I would say it's, again, a discussion with your team members, but getting back on track with routine cancer screening is critical, especially after transplantation which is a procedure that itself we know comes with an increased risk of secondary cancer. As soon as your team member thinks you're ready, I would say personally, without knowing the details of one situation, I would say within that first 2 years we should be back on track barring any sort of bad complications.

Lizette:

The next question comes from Ned. Ned asks: I've heard that MPN (myeloproliferative neoplasms) patients, particularly primary myelofibrosis, when they convert to AML are more difficult to treat. Why is that?

Dr. Shallis:

That's an excellent question and one which just to be totally brutally honest is one which is one of intense research. It comes down to the disease biology. Patients whose AML is arising out of a prior blood cancer and the MPN are forms of malignancy/cancers, it's more likely that this disease is going to harbor more stubborn biological features, which make our standard of care treatments not work as well.

I'm not saying they don't work, but not work as well in the frontline setting, and then after that maybe doesn't do the trick, for instance. Our second- and third-line options get a bit more difficult. Traditionally these are patients for whom a stem cell transplantation, in this case an allogeneic hematopoietic stem cell transplantation, it probably should be a strong consideration. This is an area, again, of intense research and, yes, our current therapies are insufficient. It's, again, individualized based on the disease biology that we just, in all honesty, don't fully understand at the moment, but this hopefully will change very soon.

Lizette:

We'll take the next question from our telephone audience, please.

Operator:

Our next question comes from Luann. Luann your line is now open.

Luann:

I would just like to say that I am an AML survivor 10 years out. I had an allogeneic stem cell and I had a core, and my cousin was the bridge. I wanted to know, I had a graft-versus-host disease, very bad, but I got through that. Now, I still find that, I'm sorry to say this, but I still find that I have diarrhea. That was a major problem when I had graft-versus-host disease. I'm saying: Why do I still have that 10 years later?

Dr. Shallis:

Luann, I'm very happy to hear of your success and it is definitely a success story. It sounds like your journey was not an easy one and if I've made anything clear, it's that it's the rare patient who has an "easy journey" in 10 years, good for you. Pretty good. Without knowing the specifics of your diarrhea, I would say that it could still be anything. I would hesitate to say that it still can't be GVHD, at least in some small form that, in all honesty, we do have some pretty good tricks for.

10 years after a transplant, perhaps there are some providers that would say, "Hey, you're good. You don't need to see me anymore." I'm not quite sure if that's your situation, but worst case, you still need a primary care provider. It might be a good idea to also establish care with a gastroenterologist or GI specialist because you might need some further evaluation if it's that much to bother you.

Lizette:

The next question comes from Layla. What therapies are available for AML relapse?

Dr. Shallis:

Another great question. A lot, but it's all relative. I'd say much of this is in the clinical trial realm. In the relapsed or refractory setting, I would hesitate to say there's any true standard of care. We don't know which treatments are truthfully the best, at least for all patients that might be in that particular situation, which is why we again individualize it based on maybe some of the proteins that the disease has in or on it that might lend weight to trying, "Hey, we have a pill that actually targets that."

In the relapsed setting the treatments tend not to work as well, but we still try them, especially because they generally are going to be a combination of pills, plus or minus an injection or two. Clinical trial, I would argue is the standard in

this circumstance. They might actually study the things that we have available to us now plus something else which could be the next game changer.

I can rattle off a number of pills that are going to be available to us in the next 1 or 2 years that were just investigational, only studied in clinical trial at that point. In the relapse/refractory setting, no true standard, clinical trial is the main one we know how to help these types of individuals, and I strongly encourage those in the situation to really seek that out.

Lizette:

June is asking: Are CAR T (chimeric antigen receptor T-cell therapy) treatments available for AML?

Dr. Shallis:

Another great question. The correct answer is no. They're not available. However, with a caveat, with an asterisk, they are available in clinical trials. Another common theme that trials are really how we help move the field and form the next generation of trials and maybe help folks that maybe it could be you in clinical trial, but also 10, 15 years from now. Maybe that's the new standard.

CAR T for AML has been a difficult ride with a few disappointments getting into the weeds. There's a few reasons for why that's the case, but maybe we're seeing a little or maybe we're on the precipice of some reason for optimism in identifying at least good targets for what these CAR T-cells are looking for and how they operate, how long they stay around. I think we're finally having some good clinical trial data for a couple of these products, which differ in some small ways. At the moment they are available, but only in clinical trial.

Lizette:

We'll take the next question from our telephone audience, please.

Operator:

Victoria, your line is now open.

Victoria:

Thank you so much. My husband was an AML patient. I say was because he ended up with a UTI (urinary tract infection) that we didn't know about that went septic and he passed away in January. What is the best or where is the best place for me to make donations to AML research?

Dr. Shallis:

A great question Victoria and I'm sorry for your loss. Donations definitely help. There are several places that I could direct you. The first, depending on where you want to donate to, but the first place I would ask is your team member. Often there is a whole slew of individuals that are tasked with fielding these types of requests and knowing what your goals are, what your wishes, and some of the specifics as to where you think such a gift should go. There are also many opportunities outside of your center that you could find online. I have no doubt that LLS actually has support for this as well.

Lizette:

Yes, thank you. We are sorry for your loss. Our next question doctor comes from Marie. Marie's asking: How long does transplant or chemo fatigue last after transplant? Why is it different for each patient?

Dr. Shallis:

Another great question and one which is very common. This is a symptom or side effect that has to be accepted to go through transplant. I can't think of a single person that I've met or recommended to go to a transplant that didn't have

some fatigue, at least some fatigue through transplant. Again, going back to some of the aspects of the talk, many things can cause fatigue.

Sometimes they are medical. Infection can cause fatigue. Sometimes metabolic disturbances, electrolyte abnormalities can be responsible. More often than not, however, it's not one thing. It's a couple of things and getting chemotherapy is a big reason. The time by which people can feel improvement and the pace at which they can actually feel that improvement is completely different from person to person, just because literally, again, to use something I said before, every body is different.

We have different levels of heart health, kidney health, lung health, metabolism, stamina, and everything maybe that we just can't account for. Some people just feel fatigued for a few weeks, maybe a few months. I have some patients that never get back to 100%, but we settle for 90%, 85%, depending on the lifestyle you used to have beforehand. That usually dictates how much fatigue you notice and how much of a change that you can appreciate.

There's no good answer for that question and there's a wide range. Again, I would ask you to really engage with your transplant team members because there might be something that they can evaluate that maybe is reversible or fixable to some degree or can at least be helped with some strategies for improving at least one, if not maybe several aspects of health.

Lizette:

Our next question comes from Linae. She's asking: Do I need to get all of the vaccines again after my transplant?

Dr. Shallis:

Another common question and I do think this is part of the typical spiel that a transplant provider or transplant physician would give on day one. Usually, that's a longer meeting than 30 to 60 minutes, closer to 60, where they're going through soup to nuts, everything that comes with transplant. Including the things that come after transplant, which is really where much of the risk is accepted.

Yes, after transplantation, just because of that's the transplant we're talking about here, at least. The chemotherapy that's given for the stem cells to nestle and find a home and be healthy in the longer term do actually injure the cells that were previously responsible for making antibodies. Generally, a certain time point, usually it's a year after transplantation, you get your baby vaccines again, which certainly is not a short list, but that's the time point at which I would imagine you'd be recommended to receive those vaccinations again.

Lizette:

We'll take the next question from our phone audience, please.

Operator:

Our next question comes from Stephanie. Stephanie, your line is open.

Stephanie:

I was diagnosed with AML in 2021 and I'm wondering how long do I have to continue to do chemo? I was not a candidate for bone marrow transplant.

Dr. Shallis:

Hi, Stephanie. If I think I heard your question correctly, it seems that your situation is one in which you were diagnosed with AML in 2021, was not able at that time to proceed to a stem cell transplantation, and it seems you're still on chemotherapy. It's hard for me to know which one type of therapy that is. If I had to guess, I suspect it's something known as HMA (hypomethylating agents) venetoclax or AZA (azacitidine) venetoclax, but that is purely a guess.

Again, going back to what I was saying midway through the talk is that these are the types of therapies for the vast majority of patients. I'm going to say, 95% of individuals. There's only a few reasons why you stop therapy really. One is if you're sure it's not working. For someone who's been on for 3 years, probably it's working to some degree. Probably deriving some clinical benefit, probably not without some side effects, but again, it's always a calculation and 3 years is not a short amount of time.

Two, would be if it's working, but we're encountering just a lot of side effects and we can't stay on therapy and it's too difficult to the point where quality of life is really, really hurt here. We have to consider switching to an alternative therapy. The third is use it until it stops working, which is probably the situation that you seem to be in. That's probably what I would guide you.

Lizette:

Our last question today is from Lillian. She says: I'm an 11-year stem cell transplant thriver. My AML diagnosis was in 2013. I had a stem cell transplant 3 months after diagnosis. I'm doing well. Am I considered cured? Is there ever a cure and is there a chance of reoccurrence?

Dr. Shallis:

Surviving and thriving. I agree, 13 years is nothing to sneeze at. That is a time point at which I'd feel comfortable personally, if I was on your care team, saying that you were cured of your disease, at least the AML. It still requires vigilance for other things that can come up that you're still destined to get just being a human on this planet. I would ask you to maintain good health, keep doing what you're doing because it's clearly working for now.

I'm not being a cowboy here. There are a number of studies which have shown that people that survived 10 years are almost undoubtedly cured of their original leukemia. Now, there are some situations, just to be thorough because I try to be exact in what I say, there are some situations in which that leukemia might have arisen out of another predisposition. There's another condition that led to the AML to develop and that might increase your chance of getting another AML again. That is not very common, but trying to be thorough in answering a question that's what I have to say, but 13 years, good for you. I'm going to say you're cured.

Lizette:

Thank you Lillian for that question which was our final question today. Special thanks to Dr. Shallis for volunteering his time and expertise with us today.

Slide 36: LLS EDUCATION & SUPPORT RESOURCES

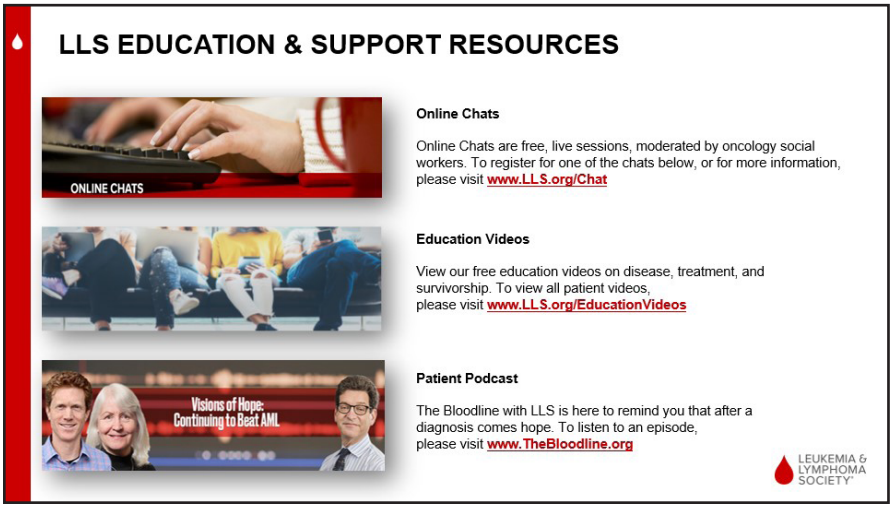
If you want more information or resources, you may speak to an LLS Information Specialist at 1-800-955-4572 from 9:00 AM to 9:00 PM Eastern Time, or you can reach us by email at LLS.org/ContactUs.

Slide 37: LLS EDUCATION & SUPPORT RESOURCES

You may also reach out to one of our Clinical Trial Nurse Navigators in our Clinical Trial Support Center by visiting LLS.org/Navigation, or you can call an Information Specialist to get in contact with them.

If you haven't already done so, please make an appointment with one of our Nutrition Educators. They are registered dieticians that can answer questions for patients and caregivers with any type of cancer.

They are free consults and you may contact them by visiting www.LLSNutrition.org, or you may call toll-free 877-467-1936.



Slide 38: LLS EDUCATION & SUPPORT RESOURCES

You can download and print the slides as well as view this program from our website at LLS.org/Programs.

Slide 39: THANK YOU

Again, we'd like to acknowledge and thank AbbVie Inc. and Genentech Inc., and Biogen for their support of this program. Dr. Shallis, thank you again for volunteering your time with us, and on behalf of The Leukemia and Lymphoma Society, thank you all for joining us. Goodbye and we wish you well.