Acute Myeloid Leukemia: Your AML, Your Treatment, Your Decision

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Andrew Schorr:
I’m Andrew Schorr from Patient Power, and welcome to this Patient Empowerment Network program, “Acute Myeloid Leukemia: Your AML, Your Treatment, Your Decision.” Over the next hour, we’re gonna get answers from leading AML specialists – one in Houston, Texas at MD Anderson Cancer Center and one in New York City at Weill Cornell Medical Center, New York Presbyterian Hospital – and you’ll also meet a patient who’s a five-year AML survivor. I wanna thank the financial supporters who’ve made grants to the Patient Empowerment Network. That’s Celgene Corporation, Astellas, Jazz Pharmaceuticals, and Daiichi Sankyo. But remember, these outside funders have no editorial control.

We welcome your questions to aml@patientpower.info. So, let’s go around the country and meet them. First of all, I wanna go to Westchester County, New York, and I want you to meet Jerry Brennan. Jerry is a five-year survivor. Jerry, thanks for joining us.

Jerry Brennan:
Thank you for having me, Andrew. A pleasure.
Andrew Schorr:
Also, Jerry, joining us not far away in New York City is your physician, who’s an AML specialist, Dr. Pinkal Desai, at New York Presbyterian and also Weill Cornell. Dr. Desai, thanks for joining us.

Dr. Desai:
I’m very happy to be here.

Andrew Schorr:
And, I’m sure you’re very happy that Jerry is with us now, five years out, right?

Dr. Desai:
Very, very excited.

Andrew Schorr:
Okay. We’re gonna talk about what’s worked for him and what could work for other people. Now, let’s go over to Houston, Texas and MD Anderson Cancer Center, and that is Dr. Tapan Kadia, who’s been with us before, also a researcher and an AML specialist. Dr. Kadia, thanks for being with us.

Dr. Kadia:
Andrew, it’s a pleasure. Thanks for having me.

Andrew Schorr:
Jerry, I wanna start with you, all right? So, Jerry, first of all, let’s go back to your story. How were you feeling five years ago that sent you to the doctor in the first place?

Jerry Brennan:
That’s a great question. I was very fortunate from the beginning because I was feeling fine, no symptoms, went to work on a regular morning, and about an hour after getting into work, I had a weird sensation, and the best way to describe it was weak and clammy. I knew something was wrong; I just didn’t know what.

Finally, I said, “I must have a virus,” and I left work. I was gonna go home, take some Tylenol, and take a nap, and on the way home, I had remembered I had a tick on me a couple of weeks prior, and by the grace of God, I decided before I go home to stop by – I called my doctor and said, “Hey, I think I have Lyme disease. Can I come in for a Lyme test?” He said, “Sure.” Just lucky that he found some stuff, and we proceeded from there.

Andrew Schorr:
Right. Of course, at one point, you were asked to go to the emergency room, and they did more blood testing. Back to your internist, and your internist said, “I think you could have leukemia,” right? Pretty terrifying.

Jerry Brennan:
Correct. My primary doctor called me later that same afternoon. When I left his office, he said, “You probably have a virus, but I’m gonna pull some extra blood and check on a few things.” He didn’t say what. Later that afternoon, he was calling me, saying, “Hey” – he was asking me questions first, like “How are you feeling?”, and I’m like, “Great. I had a great nap, and I feel great.” The way he was asking me, I knew something was wrong, and I said, “Doc, what is it?” He said, “Your blood counts are low, and I’d like you to get up to the emergency room as soon as you can.”
Andrew Schorr:
That’s what’s happened with many AML patients. The doctor says, “Go to the emergency room now,” or somebody goes to the emergency room because they’re feeling so terrible and so worn out. Okay, so, your internist was a pretty smart person who said, “I need to connect you with a specialist,” right? That brought you to Dr. Desai in New York City.

Jerry Brennan:
Correct. I got a call, went through some more bloodwork a couple of times, and on a Saturday morning, the phlebotomist from the group had called and said, “Hey, I hate to give you the news this way, but I wanna get it because we have to get moving on this. I’m sorry to tell you, but you have leukemia.” He asked me a couple questions about how I felt about different hospitals; one of them was Weill Cornell.

I said, “Doc, I know it’s a great hospital, but other than that, I don’t know. You tell me. What’s the difference?” He said, “Well, if I go here, this is what the process is, but if I go to Weill Cornell, I’ll call you back in 10 minutes with an appointment and a doctor’s name.” True to his word, I got the call, he said, “You have an appointment at 10:00 a.m. Monday morning with Dr. Desai,” and that was my second blessing.

Andrew Schorr:
Okay. I know you think she’s an angel in your life. Here you are five years out. Dr. Desai, I wanna ask you a question. I understand that AML is not always a five-alarm fire, but sometimes, like in Jerry’s case, it can be, where you have to get on it right away. Could you describe that? People wonder with these symptoms, could they have had them for a long time, or is it like this happens, and then you have to be in the hospital right away?

Dr. Desai:
With AML, the issue is that most people will have some degree of count abnormalities for some time, and most patients feel it in the form of either they get tired, like how Jerry felt, and that’s how it’s caught. So, it’s considered acute leukemia with the concept that when – it’s not something that you live for months before it gets diagnosed. Most of the time, a few weeks of it, the counts are low enough, and something happens – either a fever or some symptoms that prompt someone to do a CBC, and thereon, go to a specialist.

Now, some patients with leukemia can present with a very high white cell count, which is always extremely dangerous, and those are the people we really are worried about because you don’t want that to linger on for too long because that can infiltrate organs, and you can have somebody really sick come into the hospital, and may have major complications, even after we start chemotherapy. So, generally, the idea is that if someone is suspecting acute leukemia and acute myeloid leukemia, the leukemia center and our specialist has to evaluate the patient right away.

So, many times, depending on the blood counts, we tell them to go to the emergency room if the white cell count is too high, but if the white cell count is somewhat decent, usually, it can wait for a couple days, but usually not more than – we don’t advocate people sitting around with low white cell counts because any infection that can happen in this setting can be dangerous. Once the suspicion is there, they need to see a leukemia doctor right away.
Andrew Schorr:
Okay. And, one of the things we’ll emphasize in this program is AML has been changing. We have two noted specialists with us. It’s really important these days – I would underscore that, and Jerry’s gonna tell you, he was in a clinical trial – things are changing that you get evaluated, at least get a second opinion or a consultation with an AML specialist because there’s a lot to keep up with – fortunately – about AML now, and subtypes that we’ll discuss along the way today. So, Jerry, you were hospitalized pretty quickly, weren’t you?

Jerry Brennan:
Yes. I went in to see Dr. Desai that Monday, and I was admitted that Friday. I had been down pretty much every day to get blood work and some bone marrow biopsies, and started the treatment on Friday.

Andrew Schorr:
Right. And, you were ultimately in the hospital for about five weeks.

Jerry Brennan:
Yes, five weeks exactly. I think the original idea was three weeks. They added me to a trial program, which added a second dose of chemo, which added a week, and my blood counts were slow to rebound, so it kept me in for five weeks.

Andrew Schorr:
We should mention that Jerry’s treatment was five years ago, so things have been changing. There’s a lot to discuss. But, Dr. Desai, related to a clinical trial, that clinical trial may well have been what helped Jerry so much, right?

Dr. Desai:
Exactly. So, the clinical trials we have with leukemia – they’re designed – things have changed over the course of time, but the exact idea is to try to improve upon the outcomes from the standard of care, and adding newer drugs or other strategies to their management in order to get into a better relation, putting more people into remission, so absolutely, clinical trials are very important, and I’m sure it had a great role in putting Jerry right into remission, and now, staying in it for five years.

Andrew Schorr:
Okay, Jerry. So, that was the kicker for you. Let’s talk to another researcher. Dr. Kadia, there you are down at MD Anderson. You, like Dr. Desai, are heavily in research, and you’ve had a lot to research over the last few years, and more coming. Not everyone’s AML is the same, right? We’re talking about almost a constellation of versions of AML, and medicines being developed for different subtypes, right?

Dr. Kadia:
Absolutely. I think what you say is spot on. I think more and more over the past couple of decades, we’ve realized that AML is very heterogeneous, not only from the type of patients we see, but among them, the type of leukemias we see. So, you can divide them in many different ways. People have divided them by age, people have divided them based on prior malignancies, prior neoplasms that occur, private development in MDS like myelodysplastic syndrome prior to AML.

And then, we talk about things like cytogenetics, which are the chromosome abnormalities which happen in AML, which help distinguish whether the AML’s gonna be a little bit more favorable an
outcome, or whether there are gonna be difficulties in getting in remission, whether the patient will require a transplant. We also do – now, the next level of heterogeneity is mutation testing. What that is is we actually will sequence the DNA of the leukemia cells.

Over the past few years, we’ve recognized that there are recurring mutations or small abnormalities within the DNA that actually have an impact, not only on the prognosis, but they can predict the response of different types of therapies. This is a whole new era where we’re really looking at different individualized AMLs in different ways, and treating them in those respective ways. We’ve realized that these genetic abnormalities not only give us an idea of the prognosis, but also the treatment course in how these patients do. So, it’s important when patients come in to really characterize this heterogeneity, identify what they’re gonna respond to, and then base the therapy on what you find.

Andrew Schorr:
So, in other words, what version of AML are you dealing with?

Dr. Kadia:
Absolutely. We talked – a few minutes ago, Dr. Desai talked about the rapidity with which we treat. Right off the bat, you can see there are patients who are older with AML and younger patients with AML. It’s a very simple way of dividing it, but many older patients with AML typically have a pre-existing condition, such as myelodysplastic syndrome, which may have gone unrecognized for months or years with some low blood counts, and then they present with low blood counts. Those patients tend to have white counts in the low range – lower than normal – and typically, you watch them for a couple of days, three days, as an outpatient.

Then, you may have de novo AML in a younger patient who has a different phenotype, or much more proliferative across the phenotype, where you need to get them in the hospital, get that white count down, make sure they’re not having organ infiltration, and start the process there. There are many different ways of looking at the heterogeneity of AML, but “different versions” is right. You really need to figure out what you have.

Andrew Schorr:
So, Dr. Desai, when someone is referred to you now, is this genomic testing usually part of the workup, if you will, to say, “What are we dealing with here?”

Dr. Desai:
Absolutely. I feel like nowadays, with the kind of leukemia treatments and drugs available, not just – like we were saying, that it’s not just about predicting who’s gonna do well and whether transplant is a possibility or not, the up-front treatments are dramatically different depending on whatever the genomic profile for that patient is.

So, as soon as the patient comes in – and, that’s why my point is that you have to get the concept started right away – you have to send the right – do a bone marrow biopsy, or sometimes off pair for blood, send the mutational testing and this unit genomic profiling, because that dictates the up-front management completely these days, unlike the old times, where everybody got treated with just one treatment. That is no longer the case. So, that is absolutely a necessity to do.
**Andrew Schorr:**
Okay. So, another question for you, Dr. Desai, and that is Jerry was in the hospital for five weeks. Is that what everybody should expect, or are there oral medicines that somebody might eventually be able to take at home? How does it work today?

**Dr. Desai:**
So, it depends to some extent the genomic profile, and also the age. So, the situation currently is that if we have somebody who is younger who is eligible for intensive chemotherapy, then that is usually the way to go, and when we say “younger,” we’re talking about under 60 years old.

So, these people are generally expected to have an induction chemotherapy like Jerry had, so they’re expected to be in the hospital for about two weeks in total, but sometimes, you have a younger patient who is not too well or biologically a different disease, they have lots of comorbidities, or very older patients, where we don’t give them chemotherapy, and many of these treatments for AML, particularly in the older patient populations – they are given outpatient, either IV or a combination of IV plus oral agents. So, these are drugs they can take at home. The patients have to be seen very frequently in the clinic, but you can have an outpatient leukemia induction, basically.

**Andrew Schorr:**
Can that be effective as well, or is that second best?

**Dr. Desai:**
No, it’s actually quite effective. So, the current induction shortage – I’m sure we’re gonna talk about it at some point – these so-called “lower-intensity” oral or a combination of oral and IV treatments are not inferior at all.

They are – in the old days before the current approvals, for example, now there is data on azacitidine and venetoclax, or any hypomethylating agents, and some of the oral drugs, where the effectiveness of remission induction reaches almost the same level as an induction chemotherapy, so for these older patients who did not have a good choice of treatment in the past now have a very good regimen that they can actually handle, and it’s effective as well. It’s definitely not second best. I would consider it first best.

**Andrew Schorr:**
Okay. Dr. Kadia, how quickly have things been changing in AML with the tools that you have and what you see coming?

**Dr. Kadia:**
Quite rapidly. Just in the last few years, we’ve had numerous drug approvals in AML. I talked earlier about the heterogeneity of AML based on the mutations, and people have worked out the biology of a lot of these mutations, and now, we understand that several of these mutations or changes in the DNA actually affect how the leukemia is driven, and so, people have developed inhibitors to these mutations.

So, things are changing rapidly. We went from previously treating everyone with one specific intensive chemotherapy regimen, 7+3, at many places around the country, to now, going to the lower-intensity regimens Dr. Desai talked about, including things like the addition of venetoclax to
hypomethylating agents, the addition of FLT3 inhibitors to chemotherapy. More recently, IDH1 and
-2 inhibitors, which are oral pills, which can be used either as a single agent or in combination with
chemotherapy on clinical trials.

And so, things have really changed rapidly, and they've continued to evolve. Now that we're
becoming more comfortable with using some of these drugs, we're now doing clinical trials looking
at combinations of many of these drugs to understand how we can best match the leukemia that the
patient has to the therapies that we potentially have available. So, the toolbox is quite full where,
previously, we only had a couple of tools, but we're figuring out how to add these things together.

One thing I would say, just as a caveat on a previous question, although many of these new
therapies are oral medications and they're lower intensity, I think it's important to remember that
they're still pretty myelosuppressive drugs, and what I mean by that is your blood counts still drop
pretty significantly. Some of these things can cause a syndrome called tumor lysis syndrome, where
your white count or your leukemia dives rapidly, and then, certain electrolytes and blood tests can
become abnormal frequent.

So, I wanna emphasize the point that Dr. Desai made, that although you may be outpatient, we
really follow the patients closely, almost as if they were inpatient, with either daily or every-other-
day testing. In fact, at MD Anderson in Houston, even some of our older patients receiving lower-
intensity therapy with these new drugs, we often hospitalize them for a period of time because that
first month, that induction month, we really wanna make sure that everything goes smoothly. So,
they may feel well, like they're not getting intensive chemotherapy, but there are still surrounding
matters we need to address.

Andrew Schorr:
Right. Let me mention that to our audience. And, I actually – for another blood-related cancer – take
a very powerful inhibitor, a pill. This stuff, though, is not like M&Ms. The pills for cancer treatment –
some of them breakthrough medicines – are very powerful, and you do need to be monitored
carefully. So, I want everybody to take it really seriously. We've had a lot of progress where maybe
you don't have to be in the hospital or in the hospital for so long, but you have to be in close touch
and monitored by your doctor so things are in equilibrium, if you will.

So, one other question for you, Dr. Kadia – we've mentioned transplant along the way, and I know
that was a staple of AML treatment if somebody was young enough or fit enough to withstand a
stem cell transplant. Where is that now, as you have these additional approaches?

Dr. Kadia:
I think transplant still plays an important role in most places. I think the way we choose patients for
transplant is twofold. First, you wanna look at the risk of the patient. If this is a patient who you
think you can get into good remission with standard induction therapy and have a long-term
remission – or, who falls into something called “favorable karyotype” – those are patients who may
actually not benefit from transplant or even just continue with observation. But, there's a whole
other subset of patients – mostly the adverse karyotype or people who are intermediate who are
persistent minimal residual disease – who we still would recommend transplant. So, I think
transplant still plays a role.

The question is can we modify our transplant approaches? So, can we check minimal residual
disease, which is MRD in more of our people, and kind of decide who goes to transplant rather than
who doesn’t? Can we look at post-transplant maintenance strategies? In patients who have FLT3 ITD mutation, for example, we would recommend chemotherapy with a FLT3 inhibitor, followed by transplant, but now, there are several studies looking at these small-molecule drugs – these FLT3 inhibitors – after transplant to maintain those responses.

Some people who are on the fence about getting a transplant or not getting a transplant – we’re now looking at maintenance therapies for people who are maybe older, unfit, or not so sure about transplant to try to prolong the remission. So, some of these targeted therapies are starting to make their way into pre- and post-transplant to either try to extend the remissions before or after transplant. So, I think it still plays an important role. Whether, in the future, we’re still gonna use some important technologies to replace transplant remains to be seen, but that’s the goal.

Andrew Schorr:
Okay. And, just to be clear, Jerry, you did not have a stem cell transplant, correct?

Jerry Brennan:
Correct.

Andrew Schorr:
So, Dr. Desai, piggybacking off what Dr. Kadia said, a lot of where you are headed now is who needs what, right? And, transplant being one option, or how you maintain your remission from the transplant, or who, like Jerry, maybe wouldn’t benefit, right?

Dr. Desai:
That’s absolutely correct. There’s a few things that we take into consideration from a standpoint of a transplant. One is we are predicting based on the cytogenetics and the genomic profile whether someone would be benefiting or not, so there are some people who clearly benefit and some people who clearly don’t benefit, but there are people in the middle – some who are in the intermediate range – where it is a little controversial on whether it’s an absolute indication or not.

So, for Jerry, we had discussed this – whether we should go for a transplant or not – and we made the decision that we would not go for a transplant because he had a particular molecular abnormality that we could monitor and measure the MRD, or the minimal residual disease, so as long as I was keeping an eye on that, I knew that he was in a solid, deep remission over all the course of these five years.

So, like the same way that we are talking about different treatments, now, transplant decisions – although I agree with Dr. Kadia that transplant is absolutely an important tool in our box for curing patients with leukemia, but how we do transplant, who we choose for transplant, and how we can improve upon transplant both prior to and post-transplant is extremely relevant.

And, for people who don’t want to go for transplant, there’s new strategies coming along to maintain them, but most important, part of this is to monitor people regularly to make sure that they are indeed in deep remissions and are MRD-negative to make sure that that decision stays correct. So, it’s not a one-time decision. You have to constantly monitor to make sure that path is the right path.

Andrew Schorr:
Okay. So, Jerry, how often do you see Dr. Desai now?
Jerry Brennan:
For the last five years after treatment, every three months. My last visit was early September.

Andrew Schorr:
Okay. So, Dr. Desai, Jerry continues to be monitored. We hope that that can, at some point, be considered a cure, but recognizing an AML, most people, there’s a concern about coming out of remission. That’s the case for many people. Now, it seems you have more tools to get people in remission, but how do you sustain that remission, or if they come out of that remission, do you do something different then? Dr. Desai?

Dr. Desai:
So, if patients do come out of remission, then depending on what the situation is, if they were transplanted previously or not, that is taken into consideration. If the patient was not transplanted earlier, then the goal is to put the patient back into remission, and then consider a transplant, but when somebody relapses, it’s a little – it may be different than the original leukemia, so we advocate doing a genomic profiling of the relapsed sample again, even though the original sample, we already know, and most of the time, it’s similar, but we do find that there may be more mutations that have now come up, and that would be important because now, we have all this – so many tools in our bag, so we wanna choose.

It’s almost the same as the up-front management that we choose depending on their genomic profile what they’ve had before in terms of treatment and whether they’ve been transplanted or not. We make a decision on what treatment would be best at this point to maximize the chance of remission again.

Andrew Schorr:
Okay. So, Dr. Kadia, you tell me if I’ve got this right from what Dr. Desai just said. In other words, cancer can change. These karyotypes, or whatever you’re talking about – the genes that went awry and are driving your cancer – there may be different cancer genes driving it the second time around, if you will, and you need to take a look at that to see would a different medicine or a different combination make sense, right?

Dr. Kadia:
Absolutely. So, it goes a little bit also back to the heterogeneity of AML. We talked about heterogeneity among patients, where maybe another patient may have a different version of AML, but even within an individual patient, when you say you have a clone of AML, you may actually have multiple different clones with different mutations within the AML. Now, at the time of diagnosis, one of those clones may be completely dominant.

So, if you had a bunch of Skittles – maybe you have in your bone marrow all green Skittles and a couple of purple Skittles, and you kill off the dominant leukemia – the green leukemia, the green Skittles – but maybe a year or two later, that purple leukemia, which was resistant to the therapy you gave, is now the dominant clone and has relapsed.

And so, what Dr. Desai was pointing out is absolutely correct. At the time of relapse, you wanna make sure that the clone that has relapsed – is it, in fact, the same clone that you treated three months ago, six months ago, a year ago, or has that clone now been treated, but there’s a new clone arising that’s related to the other clone? The reason that’s important is because if that clone now
has a new mutation or abnormality that you can target potentially better with a new agent, then you could potentially try to use that. So, I think that’s an important point to recharacterize the leukemia at the time of relapse.

**Andrew Schorr:**
So, for our audience, we’re in the age of personalized medicine, and now, these two leukemia specialists and their peers around the world have more tools that are personalized, and they’re gonna go to a big convention soon, the American Society of Hematology, where they’re gonna present studies to see are there even new things that they can do?

So, you, as the patient or the family member, wanna draw on that expertise and say to the doctor, "What tests are we having? How do we know what we’re dealing with now, either on initial diagnosis or if remission ends? What’s driving it? What color Skittle" – right, Dr. Kadia – “and do you have a medicine, individual or combination, that lines up with that, personal to me, what we’re dealing with now?” Doctors, did I get it right?

**Dr. Kadia:**
You got it.

**Dr. Desai:**
That’s correct.

**Andrew Schorr:**
All right. So, that’s so important, which is why if this field is changing, you need that consultation with a leukemia specialist, which, Jerry, you would say was lifesaving, right?

**Jerry Brennan:**
Oh, definitely. Without a doubt. It was something that – even in speaking with other patients, how long it took them and their doctors trying to figure out, thinking they had the flu or the symptoms, and to me, it was important that it was found right away, and I think that’s probably a good part of the success as well, that it was caught early, and from my internist to the other specialists he recommended me to, and Dr. Desai, and the whole crew at Weill Cornell, I just was lucky to have all those people from top to bottom there to help me and my family through this.

**Andrew Schorr:**
Right. And, you know should you need it, if something comes up, you’ve got Dr. Desai and a very knowledgeable leukemia team that’s there for you, and I know in my own case with blood cancers, I’m gonna see my doctor tomorrow in San Diego, and I’m very appreciative of that. Let’s get to some questions. First of all, for our viewers, if you have a question, you send it to aml@patientpower.info. We’ve already gotten a number of questions.

So, first of all, I wanna ask the big one. Dr. Kadia, you and I were talking before the program began. Can any of this progress lead to a cure? For instance, if you study up on leukemia, you know that many of the little kids who are diagnosed with acute lymphoblastic leukemia with regimens that were developed can, in fact, be cured. Well, what about with AML? Where are we with that?

**Dr. Kadia:**
Great question. I do this because I’m passionate about it. I think that I am very optimistic that we will define a cure for acute myeloid leukemia. I think the key lies in understanding better the biology
of the disease. I can give you some examples. There’s a type of leukemia – a type of AML, in fact – called APL, where we used to have significant mortality, a very morbid disease. Young people died bleeding all over with this particular disease.

Now, because we learned about the use of ATRA, and arsenic, and the gene rearrangement in APL, we’re able to cure 90 percent plus of these patients with APL. Then, we have carbide fracture leukemia, those with translocation of 8;21 or inversion 16. With the appropriate therapy, which is intensive chemotherapy and one of the new agents called gemtuzumab ozogamicin (Mylotarg), we’re now able to cure 50 to 60 percent of these patients. Five years out, long-term survivors with that particular AML.

So, I think the more and more we learn about the biology of the disease and incorporate specific therapy with known therapy with these diseases, and potentially incorporating in the future immunotherapy to try and clean up whatever residual disease is behind, I think that we are on a track that we will be able to cure this disease.

Andrew Schorr:
I wanna just pick up on something you just said about immunotherapy. Some people have seen, even in the U.S., TV ads for lung cancer, melanoma, or whatever, and they’re advertising these immunotherapies. So, is the idea that when you develop cancer, your immune system did not recognize aberrant cells. Your immune system let you down?

Dr. Kadia:
That’s right.

Andrew Schorr:
And so, if you can, with these chemos or other targeted therapies, kill many of the Skittles you talked about before – bad cells – you could have some of these immunotherapy agents to activate your immune system to do its job that it didn’t do the first time. Is that the idea?

Dr. Kadia:
Absolutely. You got it, Andrew. So, the immune system, like you said, is an important mechanism in our bodies for immune surveillance of cancer. What that means is it prevents the development of cancer when it notices bad cells, and in times of very small-volume disease, it can actually eradicate cancer. In fact, you talked about lung cancer, and you see these PD-1 and PD-L1 antagonists as immune therapy for cancer.

Well, people forget the first immunotherapy for cancer was actually, in my opinion, allogeneic stem cell transplant, where you take donor cells from an unrelated or related donor, and their T cells, when infused into a patient with acute leukemia when they’re in remission, actually maintains that remission and cures those people because there’s something called graft versus leukemia effect, where the immune system of the donor destroys the host leukemia cells.

So, in that manner, there are many new opportunities in AML using some of the drugs that have been used in other cancers to activate the immune system. We have attempted to use checkpoint inhibitors like PD-1 and PD-L1 antagonists in AML. We’ve had some limited success. I think there are new agents along those same pathways which are interesting.
Then, there are monoclonal antibodies, something called bi-specific antibodies or antibodies against certain targets, which also not only target the immune system toward your leukemia, but activate them in order to destroy leukemia. I think the important thing to realize, though, is that you can’t ask the immune system to do too much. If you have a large bulk of disease of proliferating leukemia, I don’t think immunotherapy is gonna work in those environments, but if you can get the disease down to a residual minimal state and then incorporate some of these immunotherapies, I think we can certainly make some difference.

Andrew Schorr:
So, Dr. Desai, I don’t wanna get too technical here, but the idea is can there be treatment that can do the heavy lifting, and particularly what’s in trials now, might there be newer agents that can help you long-term? Is that the idea?

Dr. Desai:
Yes. So, when we do AML treatment, there’s two phases that we call induction and consolidation. The induction part of the treatment is what you were referring to as the heavy lifter. The idea is either chemotherapy, or combinations of targeted therapy with hypomethylating agents, or combinations of targeted therapy, you try to reduce the bulk of the disease and put the patient into a remission, which does not mean that the patient is cured or that we’ve eliminated the last possible cell. The idea is to just reduce the bulk of the disease.

And then, what happens after is what we term as consolidation, and now, maintenance, where we do what I colloquially refer to as the cleanup crew. You come in, and whatever’s left behind has to be wiped out, and the amount of wiping has to be monitored, and now, with these newer agents and an ability with the complicated technologies and testing to actually find these small amounts of clones or leukemia cells, we have at our disposal agents that would help with this cleanup process, and if we can eliminate all of these leukemia stem cells, then that would be the goal to do so that the patient can be cured.

Even for somebody who’s proceeding to transplant, which, like Dr. Kadia mentioned, is the first immunotherapy – transplant is an immunotherapy to some extent; you’re getting donor immune cells to do the job – it only works when you have eliminated the disease to a very small amount so that some of these other agents would help clean whatever’s left behind, and we have more and more drugs to be able to do that.

Andrew Schorr:
Okay. Dr. Kadia, here’s a question we got from Sue. She said, “Our daughter was diagnosed with AML in July” – not too long ago – “and had a stem cell transplant. What is the probability that her AML or leukemia of another type will return?” So, again, is the AML gonna come back, or do we have to worry about yet something else?

Dr. Kadia:
The probability that a person will relapse after transplant is often based on a few things. No. 1, it’s the type of leukemia that went into it. What was the prognostic subset of leukemia? Was it favorable? Was it intermediate risk? Was it high risk? Those patients with high risk seem to have a higher risk of relapse after transplant.

The second thing that determines how people will do after transplant is the state of the disease just prior to transplant. In other words, was the leukemia in complete remission prior to going to
allogeneic stem cell transplant? Most people who are not in morphologic remission tend to have higher relapse rate.
And, to take it a level further, those people who have persistent or detectable minimal residual disease prior to transplant tend to have higher relapse rates than those who do not. So, those three things are factors that would help determine the risk of relapse: The baseline prognostic score, the persistence of disease at the time of transplant, and MRD at the time of transplant. One thing I would say is in many cases, we are now employing methods post-transplant to help mitigate relapses in specific subsets of patients.

**Andrew Schorr:**
Okay, and what about a different cancer developing?

**Dr. Kadia:**
Different cancer developing is an interesting question. If an AML develops shortly after transplant, it is likely clonally derived or related to the original AML, meaning that it may look like the same AML, or it may be a cousin or daughter of that particular same AML. If the leukemia develops years later, it is possible that they may have developed a second leukemia, and if anything else develops, such as sometimes people get TBI or other modalities for their – TBI is total body irradiation – if they get that for their transplant, they can potentially develop secondary cancers in other organs, but those are less likely.

When you have immunosuppression on board after transplant – things like tacrolimus or cyclosporin – to prevent graft-versus-host disease, they can slightly predispose you to developing secondary malignancies, like lymphomas and skin cancers, but again, those are not common, and they’re also not very oppressive in general.

**Andrew Schorr:**
Let’s flip it around. Dr. Desai, people must ask you every time they see you – new patients – “Did I do something to bring this on?”

**Dr. Desai:**
Yes, that is actually a very common question, and many times, I just offer that information before they ask because it’s going in their minds all the time. There is – most of the leukemias we see do not have an identified risk factor in terms of the – it’s not something that they were born with or something that they would pass on to other people.

There is some concern about smoking being associated with a premalignant state that could convert to leukemia, but a direct connection between all of that has not been established. Some patients who’ve had previous cancers and are exposed to chemotherapy for those cancers can develop leukemia as a result of damage that some of these chemotherapies do to the bone marrow, and the leukemia can come as a result of it. We call them therapy-related leukemias.

But, there’s no – that the patient did something wrong that this happens. I always try to emphasize that point. It happens – in older patients, it’s an age-related process where, over time, more and more mistakes happen as our bone marrow cells are dividing, and certain clones get more and more sustained, cause further damage, and lead to leukemia. In younger patients, sometimes leukemia just happens quite suddenly, and there’s no real identified risk factors that would have put them at risk for this.
Very rarely, there are familial leukemias where multiple family members can have leukemia, but those are extremely rare, like a handful of families all over the country and the world, so that is not our first thought about screening their family members or anything. A careful family history is obviously needed, but I wouldn’t emphasize on any particular thing that patients would have done. It’s not like lung cancer, where you have an identified major risk factor that causes the cancer. For the most part, leukemia, we don’t have cause.

Andrew Schorr:
So, Jerry, you shared with me you had an uncle, who was a firefighter, who died of AML in short order, right?

Jerry Brennan:
Correct.

Andrew Schorr:
And, you have two children – two sons – right?

Jerry Brennan:
Yes.

Andrew Schorr:
So, Dr. Desai, Jerry has an uncle who maybe, as a firefighter, might have been exposed to toxic chemicals and stuff like that, which I know could come into play, but he has two sons, so he worries about them. It sounded like from what you said, a hereditary connection is not likely.

Dr. Desai:
Yeah. For Jerry’s case, it’s not. We get some idea – obviously, the kind of family history is important – how many members are affected and whether it’s on one side of the family versus the other – but we also get an idea based on the extensive genomic testing we do where we can sometimes identify a lot of these so-called genes that we know tend to run in familial leukemias, so we generally interrogate all those genes at Cornell when they’re coming in for this testing, and in Jerry’s case, his leukemia was not deemed related or could possibly be something that could be familial, so I did not advocate testing his family members or his kids for that.

Regarding his uncle, we now know that a lot of the 9/11 firefighters that were involved during that time – and, I see several of them – there is murmurs of an increased risk of cancers, and some of them are leukemias. We haven’t completely established what exactly was that, but that program is ongoing, so there’s clearly certain toxic fumes that we normally don’t get exposed to in everyday life that could cause some of these leukemias, or propagate or trigger something, but for the most part, this is not the case.

Andrew Schorr:
Okay. And, of course, you’re in New York City, where 9/11 happened, so you know it well. So, Dr. Kadia, some patients are younger – we’ve talked about older patients, but some patients are younger. So, with these treatments you’re talking about, what about fertility? Can fertility be protected?

Dr. Kadia:
That’s a great question. What I say is usually, even with induction chemotherapy for acute myeloid leukemia, whether it be standard 7+3, which is not used in many places, or higher-dose cytarabine-based regimens, usually, fertility is not — people don’t become sterile after receiving induction chemotherapy of that type, even if they receive several cycles of chemotherapy. You may have a period of time where you may have decreased fertility, where you may not be able to conceive kids right away after induction, but for the most part, most of my patients are able to preserve fertility later on.

In many of our young patients, who we are inducing just to be on the safe side, if they have time, we say maybe we should do some sperm banking. Retrieving eggs, particularly in newly diagnosed patients with AML, which is often an invasive procedure, is difficult because they’re often coming in with severe cytopenia or low blood counts, so it’s difficult to do those procedures, but I tell them that usually, people tend to do okay. We do consult our gynecologists, who use ovarian suppression with hormones to not only suppress menstrual cycles, but to try to protect the ovaries during times of chemotherapy.

So, like I said, with induction and consolidation chemotherapy, fertility may be delayed, but is often not completely eradicated. Now, it’s different when you talk about allogeneic stem cell transplant, where some of the chemotherapies and the conditioning therapy that you get for allogeneic stem cell transplant can actually lead to infertility in a percentage of patients. And so, prior to stem cell transplants for sure, we do – in young people who want to have children – talk about sperm banking in men and egg preservation in females, and so, we refer them to the appropriate specialists we work with.

**Andrew Schorr:**
Dr. Desai, I wanna talk about life after heavy-duty treatment for a while. So, Oliver wrote in, and he asked, "Is a side issue of living with AML weight loss?" Somebody else said they were five years out, and they still feel really crummy. What’s life like after some of these treatments you’ve been giving?

**Dr. Desai:**
This is an important aspect, and we talk a lot about treatments, and our big focus always is get them into remission, try to cure them, get all the treatments. But, patients live through these, and even after the treatments end, they sometimes take some time to recover. So, if somebody has not had a stem cell transplant and has had other forms of consolidation treatment, it can take some time to get back to normal.

Many times, patients feel quite fatigued for up to a few months after finishing all treatment. The weight loss that - this is any kind of treatment, whether it’s lower intensity or chemotherapy - takes a toll on your body. Patients go through infections, appetite loss, sometimes mouth sores, so it takes time nutritionally and psychologically to actually recover from all of these treatments, and it can take some time.

Now, in somebody who’s had transplant, it’s a bit different because when patients finish their transplant and they are discharged, they don’t get more treatment for leukemia per se, but there is a lot of complications that can happen post-transplant that include graft-versus-host disease, some infections that can happen, sometimes the gut is involved with graft-versus-host disease, so people can’t eat or absorb the food that they eat, and because transplant is a much more involved process and more heavy on the body, it can take a while, so most patients start feeling normal after one year
of transplant, and some people who have some of these more chronic graft-versus-host disease can have symptoms from that for many years after transplant, and it takes some time.

So, one of the things we always take into consideration when somebody is being transplanted – the quality of life that they may have as well post-transplant. For the younger patients, I think it’s always justified if the disease biology dictates it. For the older patients, they may choose not to go to transplant because they may have more symptoms and more complications from it. So, it is a fact that even people who have done treatment with or without transplant can many times have persistent symptoms for a while, and we have to support them through it.

There is also a huge process – when people are going through leukemia treatments, they’re not working, they’re out from social life, professional life for months, up to a year sometimes, and going back to their regular life, where they’re expected to go back to work and do their usual thing – parenting – all of that takes a toll, and sometimes it’s a hard transition. You really have to support these patients, not from just a medical, but also psychologically, to get them to understand that this will take time, but it’ll get better.

Andrew Schorr:
Jerry, I just wanna touch base with you on this. First of all, Jerry is a special education teacher in suburban New York. You were able to go back to work. So, Jerry, how are you doing? How has life been like post all those weeks of aggressive treatment in New York City?

Jerry Brennan: It’s going well. Funny that you mention about the stamina – I did lose some weight with the chemo. Fortunately, toward the end of the follow-up treatments, I started getting the mouth sores, but I was fortunate where it didn’t really affect me during the hospital stay and the follow-ups. They did a great job in keeping us busy. I don’t remember the woman’s name, but she would get everybody up in the morning and do a walk. They had signs up over the doors telling you how far you went as you walked around the lobby, and they’d get the group up for a time doing laps.

But, the amazing thing was as active as I was, because I went in with the mindset that I’m not going to be a patient. I never put on a gown, I got up, I had my shorts on, my track sneakers – it was comical. People would come by looking for me and think I was a visitor instead of a patient. But, with that said, I was pretty active in the hospital, walking as much as possible, but when I was out after the five weeks, walking up the five or six stairs to my house, my legs were like rubber, and it was just shocking, and it did take a while before you started to feel completely physically 100 percent.

Andrew Schorr: How are you doing now?

Jerry Brennan: I’m doing okay. I don’t know if it’s the age or what – you feel like you’re slowing down. Sometimes, you’re a little stiffer than usual. You don’t know what it is, if it’s just normal or if it’s something from the chemo, but basically, I’m able to get up and go to work every day and function, and thank God, I feel pretty good.

Andrew Schorr: Great. I wanna underscore a couple points that we’ve been talking along the way. I think we made it really clear – when someone – when AML is suspected, you wanna have this workup where they
look at the genes – the color of the Skittles, going after Dr. Kadia’s analogy there – what’s driving your version of AML.

You wanna consult with somebody like one of our guests, an AML specialist, to say what’s the therapies, whether it’s transplant that’s been around for a while, or new ways you’re doing it, or these other targeted therapies, or what you have in clinical trials. That was the kicker for Jerry – the sweetener that maybe made all the difference – is that something that you can consider now, or if you come out of remission?

And then, Dr. Desai was just talking about the support you need. So, many of these major centers now that are treating AML have support. They’ve got you walking, or at home, there are people who can support you in your community, there are various resources, there are discussions you might have if you work, or if you’re a senior and you’re retired, what support is there for you. And, you need the dialogue with your doctor on how you’re doing. So, it’s not just the test out of your arm, but it may be how you’re doing here, right? Dr. Desai, did I get it right? It’s an ongoing dialogue with your healthcare team.

Dr. Desai:
Yeah. The transition from AML treatment – inpatient, outpatient, and the path towards monitoring – requires a team, and it is not a solo job. There need to be cheerleaders for the patient all along the way – the doctors and nurses, research nurses, the walking club that Jerry was referring to, and outpatient support – social workers, patient support groups – we have a lot of our own patient support groups that talk to each other. It takes a team to make that transition.

Andrew Schorr:
So, Dr. Kadia, you and Dr. Desai have got labs, you’ve got all this stuff going on at your medical centers – some of it is about AML in those labs, in the buildings in New York or Houston, and in other similar medical centers. Are you encouraged – so, here, we’ve got Mrs. Jones or Mr. Rodriguez who’s watching now, or their loved one who’s been diagnosed, and they’re saying, “Okay, I’m on this road; You talked about having more tools, and maybe that’ll help get me in remission. If I’m coming out of remission, do you have stuff in the lab that may do better – fewer side effects, better quality of life, and maybe the road to a cure?”

Dr. Kadia:
Andrew, I would say to the patients out there and everyone who’s listening that I am very encouraged and very optimistic with the things that we have coming up, not only in the lab, which is a little bit early, but also in early-phase clinical trials – Phase 1 and 2 trials – which are looking very promising among patients who are, let’s say, receiving these new tools and new combinations, and if they are starting to relapse or progress, we are trying to assign them or get them onto new studies and new medications which seem to be having some promise.

We’ve had a recent mini renaissance in AML where we’ve had a lot of drugs approved all at once in the last few years, but I think that there is gonna be a trickle, so to speak, of new agents as we learn more and more about the biology, so I am optimistic, and I can tell you that when a new patient comes to see me, often with relapsed AML, we have many options for them to help get their leukemia under control and go to the next level.

Andrew Schorr:
Dr. Desai, how about you? If somebody comes in now, and they’re terrified, and the family is terrified, can you give some encouragement that first of all, you can get a clear picture of what’s going on for them with super sophisticated tests you have now, and that you might well have something that can be pretty effective, and should they come out of remission, you’ll have something else?

Dr. Desai:
I completely agree. This is the time where there’s a lot of hope in AML, there’s lots of newer agents, newer technologies. We can identify how people are different. We’ve been saying AML is heterogeneous. Every patient has a different kind of leukemia to some extent, and our understanding of these specific factors have grown immensely, and the ability to actually target some of these biological pathways is also something that is new, so I’m very hopeful.

Many times, based on the genomic profile, you can have more than one option right out of the gate, and you say you have three options of treatment, and we go through – “Okay, we’re gonna go through pros and cons of each options,” and we pick one. Many times, we already have two options or more lined up if the relapse happens, so there is definitely a lot of hope in AML now.

After all of these drug approvals and new coming around, hopefully, it’s a phase of how to incorporate these drugs best, either in combination, sequentially, for consolidation or eradication purposes – there is a lot of what we call mixing up of strategies that will evolve.

I am considering myself spoiled – the spoiled generation of leukemia doctors – because some of my old mentors who taught me how to take care of leukemia patients did not have any of these agents, and my generation of leukemia doctors have evolved with these newer agents in the pipeline, either as clinical trials earlier, and now they’re approved agents, so this is definitely a new era in AML therapy.

Andrew Schorr:
It is, and it changes fast, and I just wanna underscore – we will be broadcasting live from the American Society of Hematology, where about 30,000-40,000 of these blood experts get together – the hematologists – and AML increasingly is being discussed, and they’re sharing data of studies they’ve been doing around the world. So, for you affected by this condition, that’s part of your active dialogue with your leukemia specialist. Is there something new that you presented or one of your peers at another medical center presented that is important for my care, either now, or next year, or two years, or five years, should we need it?

So, stay tuned to that because being an engaged patient or family member makes a difference once you have the right healthcare team, like specialists such as these, who are either your doctor or advising your local oncologist on a plan that makes sense for you. Jerry, I wanna leave it with you as we wrap up our program. So, here we are, five years out. You’re a very fortunate guy. What do you wanna say to somebody who’s watching or their family member when they’re so scared with an AML diagnosis?

Jerry Brennan:
That’s a great question, and a tough one, but I know it hits you like a brick wall, and there’s no avoiding that. It’s obvious. But, you have to accept it, and then live your life, and come in with a mindset that you’re gonna fight. I don’t know if Dr. Desai remembers the first night, when I went in
there on a Friday evening, and I was like, “Come on. Are we ready to fight this? Get your game face on, and let’s get going.”

I was trying to – when I first met her the couple of times, she’s this beautiful, very short, petite doctor, and I was like – going in there, I was like, “How am I going to be part of this team that’s gonna fight this? They’re gonna give me the medicine, they’re gonna tell me what to do.” The only thing I could do is just like when I played sports – go in there, get your head in the game, and get psyched. I said, “Don’t come in little, mousy, and ask me on it – let’s go and kick this in the ass and get it going, and try to motivate yourself.”

The five weeks was a tough stint, but I always tried to take my mind outside of the hospital. I had a beautiful view of the East River, and the next week, I was supposed to be in Florida on a fishing trip – I don’t know if Dr. Desai remembers – I’m like, “Doc, can we put this off a week? Can I go fishing and come back and start?” She was like, “No, we need to get this done.”

So, in my mind, I was somewhere else. I was going to be sitting on a beach, and not just sitting in a hospital room or on a bed. I’d walk to different parts of the hospital, sit on different benches, try and mix it up a day, say, “I’m gonna sit in the lounge and not come back to this room until lunchtime,” and sit there from maybe 8:00 to 12:00, read a book, watch TV, talk to other people.

It is important to go to the right place to be treated. The doctor who recommended going to the city – I was immediately panicked, thinking that this was over, and gave me one of the best advices he could. He said, “Listen, I can treat you, but why do you want me to? I don’t see this every day. Go to the specialist. That’s all they do.” It makes a difference because during my treatment, when I was past the five weeks, Dr. Desai said, “You don’t have to come into the city all the time. You can do some maintenance in Westchester.”

So, I went for some infusions in Westchester instead of trekking down to the city, and it was really kind of funny because times like that, trying to clear my PICC line, things I saw nurses doing at Weill every two seconds, they didn’t know how to – they were trying their things, but I’m like, “No, they tell me turn my head and cough, and that’ll loosen something up, and that’ll clear it up,” and they thought I was crazy until they tried everything. I said, “Well, humor me,” and things worked. So, it does make a big difference when you’re treating something as serious as this. Go to the people that do this every day.

Andrew Schorr:
Right. Well, Jerry, we wanna wish you a long life and a good quality of life, and we wanna thank you for being with us today and being with your doctor, Dr. Desai from Weill Cornell and New York Presbyterian. Thank you for being with us as well.

Dr. Desai:
A pleasure.

Andrew Schorr:
And, Dr. Tapan Kadia from MD Anderson, thank you for being with us. We wish our doctors here, who are also researchers – go get it, right? See if you can knock this thing out so that we can actually have another conversation sometime before long and say, “You know what? We have the glimmer of a cure.” Thank you so much for being with us.
Thank you to our audience for being with us. We wish you hope, and hopefully, we gave you some confidence. We'll continue to have a dialogue with you on what’s going on in AML. We want you to stay informed, have a discussion with a knowledgeable healthcare team. We wish you all the best. I’m Andrew Schorr, down in Southern California. Remember: Knowledge can be the best medicine of all.

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