Improving Response and Expanding AML Treatment Options

Uma Borate, MD, MS
Assistant Professor of Medicine, School of Medicine
Oregon Health & Science University

Hetty Carraway, MD
Associate Professor
Cleveland Clinic

Harry Kuligofski
AML Patient and Advocate

Eunice Wang, MD
Chief of Leukemia Service
Roswell Park Comprehensive Cancer Center

Amer Zeidan, MBBS, MHS
Associate Professor of Internal Medicine (Hematology)
Yale Cancer Center

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Andrew Schorr:
Hello, and welcome to Patient Power. I’m Andrew Schorr. We’re on location in Orlando, Florida. Why are we here? Because across the street at the big convention center, we’ve had more than 25,000 people who study blood-related conditions and treat it, and of course, fortunately now in recent years, we’ve had a lot more to talk about in acute myeloid leukemia. It offers great hope to people who are affected by this acute condition.

Joining me now are four leading experts, and we’re here to discuss this, and also in a little bit we’ll be joined by a patient who’s been treated successfully for AML, and that’s the good news. All right? So, let me introduce our guests. I’m going to let them introduce themselves as well, but first, let’s go way down to the end. Dr. Uma Borate, from Oregon Health and Science University in Portland, Oregon. What’s your title there? What’s your area of study?

Dr. Borate:
So, I work at the Oregon Health and Science University. I’m an assistant professor, in our Section for Hematologic Malignancies, and I mostly study the blood cancers known as myelodysplastic syndrome and acute myeloid leukemia, or AML.
Andrew Schorr:
Okay, and you’ve been on Patient Power before. Welcome back.

Dr. Borate:
Thank you.

Andrew Schorr:
Okay, let’s go to Buffalo, Dr. Eunice Wang.

Dr. Wang:
Hi, I’m Dr. Eunice Wang. I’m the Chief of the Leukemia Service at Roswell Park Comprehensive Cancer Center. We run a very active clinical service and clinical file portfolio focusing on early phase clinical trials, those drugs that are very, very early in development. I also run a transitional research lab, where we are doing experiments in cells in mice to come up with the next best thing to treat AML patients.

Andrew Schorr:
Okay, great. All right, we’re working down the East Coast, we’ve made it to New Haven, Connecticut, Yale University, Dr. Amer Zeidan.

Dr. Zeidan:
Correct.

Andrew Schorr:
Right, and what’s your area there?

Dr. Zeidan:
Yes, I’m an associate professor of medicine at Yale University. I also focus on myeloid malignancies, especially patients with myelodysplastic syndromes, as well as older patients with acute myeloid leukemia. So, I also do clinical trials focusing on targeted agents as well as immune therapies for those patients. I also do a lot of large database and outcomes research, which I think is very important compliment to understand—not only how these therapies work in the real-life setting, which is most important on the patient level, but also how we can learn from that and try to improve the outcomes, what they are.

Andrew Schorr:
What’s the impact?

Dr. Zeidan:
Correct.

Andrew Schorr:
Yeah, yeah, okay, and now let’s go to Cleveland. Dr. Hetty Carraway from the Cleveland Clinic, and Hetty, what’s your area there?

Dr. Carraway:
I currently am an associate professor in the hematologic malignancy program at the Cleveland Clinic. I also serve as the vice chair of strategy and enterprise development at the cancer institute as well. I spend most of my time taking care of myeloid malignancy patients, MDS, AML and other leukemias as well.

Andrew Schorr:
Okay, let’s start with you right here. So, what’s the buzz about AML? You have so much that you’ve been able to talk about in the last couple of years, and I’m going to ask all of you, and you can sort of be added in, but what’s impressed you?

Dr. Carraway:
Well, the landscape of AML is really changed in the last two years. We now have drugs that are approved, that we never really had the ability to use combinations, that we now can test and use for patients. I would say in the last two years we’ve had about seven or eight novel drugs that have been FDA-approved for patients with AML, and in the last 30 to 40 years
that hadn’t happened, so it’s a very exciting time to be in this arena, not only because of the drugs, but because of the testing that we’re doing, looking at specific mutations, that are on the leukemia, that help us focus the chosen therapies that may best fit a patient.

Andrew Schorr:
So, AML is not a one size fits all?

Dr. Carraway:
Currently, no. We’re learning that there may be populations of patients that may benefit more from one targeted therapy, for example, than another. So, it’s a very heterogeneous disease, and I think our discussion today will probably highlight a lot of that.

Andrew Schorr:
Let’s get to that, Dr. Zeidan. So, if people are different, then you have to do testing now, and testing has improved as well, so a patient comes to you, you can get a clearer picture of what version of AML you’re dealing with. That testing is critical, isn’t it?

Dr. Zeidan:
Correct, yes, so the testing is very important on two levels. The first one is to actually confirm what the patient has, whether they actually have acute myeloid leukemia. In certain situation, the diagnosis itself can be challenging, and some patients are diagnosed with what we call higher risk MDS, and some patients are diagnosed with acute myeloid leukemia. Sometimes, the definition of where the cutoff between the number of the blasts, the number of the cancer cells in the bone marrow determines that. The second level is to try to pick up the best treatment, and also understand the prognostic outcome, like how well, or poorly is the patient likely to do, based on the genetic studies that we have for them? So, testing for those mutations is becoming extremely important, and becoming, really, a part of the standard of care that I think every patient with acute myeloid leukemia should really have.

Andrew Schorr:
Right. I just want to interject. We’ve been interviewing a lot of AML experts, and so, it’s an acute condition for you or your loved one. You need to make sure, wherever you are, that your situation is clearly understood, specifically with testing. Is the diagnosis correct, of course, which illness? You talked about which version of AML. Have the right tests been done? If you’re not near one of these major centers, maybe you and your doctor make a call, or you get to one of these centers, so that, with this changing landscape we’re going to talk about, is brought to bear in your case. Okay, so, Dr. Wang, things that have impressed you here, news, you have poster sessions, presentations and all that. What is standing out now?

Dr. Wang:
There are a lot of exciting new therapies and lot of exciting new approaches that are in development. Some of the most exciting news that I’ve seen is the development of an oral drug, that can actually be used for what we call maintenance therapy. So, patients that are getting up-front intensive chemotherapy, often times when they finish their therapy, we just stop, and unfortunately, up to half of those patients could relapse, and now there is an oral version of a drug called azacitidine (Vidaza), which has been shown, if you take it for a couple weeks out of every month, that it can dramatically prolong survival and prevent the disease from coming back, so it’s...

Andrew Schorr:
That’s not a new drug.

Dr. Wang:
...no, it’s a new formulation. It’s an oral formation of a drug that we typically use for combination of up-front therapy for myelodysplastic syndrome, and AML, and this new pill version, convenience-wise, adherence-wise, compliance-wise is offering a way to, on a day-to-day basis, provincially delay, or prevent the disease from recurring. So, I think that is a major development, and I think we’re going to see more of that drug. I think we’re moving further and further into oral chemotherapy for our disease, away from that high, intensive chemotherapy that requires people to be in the hospital for weeks and weeks and weeks.
Andrew Schorr:
One of the drugs I’ve heard about, also another oral. I have chronic lymphocytic leukemia, so they came out with this drug, venetoclax (Venclexta), that’s used in AML as well, sometimes in combination with others.

Dr. Wang:
Yes, so, venetoclax has astonishingly now also become a standard of care therapy for acute leukemias, based on some of the data and the safety profile from individuals like yourself, who have taken it for chronic leukemia. It has improved the results of azacitidine for acute myeloid leukemia patients. We’re now seeing about two-thirds of patients with newly diagnosed acute myeloid leukemia, particularly older individuals, 70s, 80s, patients that don’t want to get intensive chemotherapy, be able to take a pill and a shot chemotherapy together and have a response rate of 60 percent to 70 percent. That’s a game changer for us, and that type of chemotherapy can be continued in the outpatient setting. So, that sort of changed the way we think about it. Now, we used to think high-dose chemotherapy, put you in the hospital, nausea, vomiting, low blood counts, and now we’re moving towards being able to treat older individuals safely in their own homes.

Andrew Schorr:
Dr. Borate, you’ve been nodding your head. So, typically people with AML are older, typically. So, here, having these oral therapies then, as Dr. Wang was saying, it’s a game-changer as people can live a more normal life.

Dr. Borate:
That’s correct, and just to elaborate a little bit of what’s already been mentioned, as Dr. Zeidan said, the first step is really testing and figuring out if you have AML, but also, what are the different genetic changes, also known as mutations, that are present in your AML? Based on the type of mutations that are present in your AML, we have different therapies that can target those mutations. Majority of them are now oral therapies, so a common mutation is an IDH1, so a lot of letters and numbers, or IDH2, and now we have two approved oral agents that you can actually give patients that they can take in their own homes. And just as you mentioned combining this drug called azacitidine with another oral agent called venetoclax. We could combine, and there’s data presented at this meeting of combining these different oral agents that are targeted for IDH1 and IDH2 mutations, that is azacitidine. that can then even improve on the response that we’re seeing in AML patients that have these particular mutations.

Andrew Schorr:
Okay, so, Dr. Carraway, so let’s say you try one of these combinations or a certain drug. If you’re measuring and you’re seeing, you’re not getting the response you want, do you have another horse to ride? Do you have another choice?

Dr. Carraway:
That’s a great question. I think I always go back to, “Are we really convinced that we’ve failed the first therapy?” These therapies, we want them to work quickly, and I think one of the first principles is that they don’t often work quickly alone. So, we talked a little bit in the up-front setting that you can use some of these agents even in the relapsed setting, we’re able to use some of these targeted agents as well. So, venetoclax has really changed things for many of our patients, even in the up-front and in the relapsed setting for patients. What we’re struggling with now, is, what’s the next best therapy after people have failed these agents? But we really need to clarify those populations, and again, what ends up being very important is, when the drugs have failed the patients, that molecular profile, that mutation profile, again becomes important, because it can be different...

Andrew Schorr:
Test again.

Dr. Carraway:
...at the time of relapse, compared to the time of presentation.

Andrew Schorr:
So, this is genomic testing, is that what we’re talking about?

Dr. Carraway:
Mm-hmm.
Andrew Schorr:
In other words, not genes that affect the color of your eyes or whether you have hair or not, and go bald like your father or mother, but it’s cancer genes.

Dr. Carraway:
Mostly, yeah genes that are allowing tumors to progress and cause leukemia.

Andrew Schorr:
Okay, so, you mentioned, Dr. Zeidan, about the immune system. You’re studying that, too, and there’s discussion across the way, and I’m sure you’re involved in it. Are we looking into ways to harness the immune system that let us down when we develop cancer cells in the first place? The aberrant cells proliferated, where you can turn that on and knock the cancer back.

Dr. Zeidan:
Yeah, I think that’s definitely a great question, and in an area in which a lot of research is going on. The development of those immune checkpoint blockers, and so the tumors have been a major breakthrough.

Andrew Schorr:
Yeah, lung cancer, melanoma.

Dr. Zeidan:
Yeah, yeah, we’re seeing amazing responses in patients who have very advanced melanoma and lung cancer and other multiple forms of cancer, so the tumors basically, are living much longer and are doing much better. We look at this in the leukemia field, and we say, “Well, we’ve been doing some forms of immunotherapy for many years, bone marrow transplant.”

Andrew Schorr:
Which is immunotherapy.

Dr. Zeidan:
“...which is, basically, a form of immunotherapy, so, it makes sense that some activation of the immune system would lead to control of the leukemia.” We still don’t fully understand, for example, why some patients who get chemotherapy, intensive chemotherapy, are cured and why some others are not, and probably also have to do with their immune system being reactivated in some fashion. So, I do think there is a lot of interest in this area.

I think that some challenges that are unique to this area of study is that acute myeloid leukemia, although we live it every day, is relatively rare, you’re talking about 20,000 patients a year, compared to much more common tumors. So, trying to get the number of clinical studies that you want, especially in this setting, where you have many other agents, has been somewhat difficult to conduct the type of big studies that can give you these results.

The second part, I think, that’s important is that many of these studies that are looking at these, have used different types of immune activators in smaller settings. Sometimes in combination with other agents, sometimes single agents, sometimes at the beginning, sometimes later, and without all of the understanding of the science at the level of the bone marrow and the blood, a lot is actually changing. So, I think some of that is changing. We are getting a better understanding of how all of these processes work, and I’m optimistic that we are going to find a good way to use these agents in some fashion to help our patients who have acute leukemia.

Andrew Schorr:
So, Dr. Wang, I have a basic question you must get asked in clinic all the time.

Dr. Wang:
Sure.
Andrew Schorr:
Family comes in and they said, “Did we do something to bring this on?”, A) and B) “If mom or dad has developed this, do the other members of the family, the younger members, have to worry about that too?”

Dr. Wang:
So, that’s a great question, Andrew, and that’s something that was, a primary question, that when people get diagnosed with cancer, is, we always get. I think in the majority of cases, we tell patients that their major risk factor to develop cancer is really their age. As you know most of the cancer screenings that we do, colonoscopies, mammograms, prostate cancer screening, all occur at certain ages. And we know that in the bone marrow of individuals, as you age, these cells age, and they acquire, what we call, age-related mutations, and over time those mutations can contribute to development of acute myeloid leukemia and other bone marrow problems. However, those are due to you being exposed to various things and mutations that occur. That being said, a small percentage of individuals who develop myelodysplastic syndrome, or acute myeloid leukemia, particularly in younger ages, or ones that have specific mutations may have inherited genetic predispositions.

So, typically what we would do, is we would say, most likely, the typical age of presentation of acute myeloid leukemia is 67 to 70. Most cases are going to be age-related, but it is becoming standard now, that we do a very careful family history, and we look for individuals in the family that might have developed blood cancers, who might have, for example, low platelets or other blood cell abnormalities, and if we see a pattern, we have a protocol at our center. We have genetic counselors, and typically we turn to those experts or to specialized clinics and ask them to do the same thing: to do a detailed family history, and to assure these individuals that is there something that they need to be concerned about?

Andrew Schorr:
Okay, so, Dr. Borate, so, if somebody is treated with one of these drugs, can you give them some confidence that they can get back to their life for a while, or because it’s acute, it often came on, “phew”, maybe you put them in the hospital right away. Pretty scary. Can things calm down for them?

Dr. Borate:
So, I think that’s something that’s very gratifying, that we as physicians have been able to do in the last few years with some of the therapies that have already been discussed. Instead of putting the patient in the hospital for an extended period of time and telling them that the next six months to a year or two of their lives is going to be, really, time spent in the hospital. Now we can provide options for various therapies that can be at what has been described before as less intensive. That can allow them to have a good quality of life, where they’re spending more time with their loved ones at home, maybe even working, if that’s what they want to. Now, this may not happen immediately, because as you mentioned, acute myeloid leukemia is fairly aggressive, and when we start treating the patient, they are going to experience some side effects as the cells die and the cancer dies. So, we do want patients to be careful in the beginning until we know that we have gotten rid of most of their disease, but once they reach that stable point, we can continue these treatments mostly as outpatients, and allow patients to live a relatively normal life.

Andrew Schorr:
Dr. Borate, thank you for that. Alright, let’s meet a patient, like you’re describing. Harry, come on in, come take a seat. Want to make sure I get your last name right. Kuligofski.

Harry Kuligofski:
Right.

Andrew Schorr:
All right.

Harry Kuligofski:
That’s right.

Andrew Schorr:
Harry is from nearby, not too far, in Florida, in central Florida. And you have been treated for AML.
Harry Kuligofski: Right.

Andrew Schorr: How are you doing?

Harry Kuligofski: Very good, they tell me.

Andrew Schorr: So, how long ago did this acute leukemia start?

Harry Kuligofski: I started in May.

Andrew Schorr: So, not that long ago?

Harry Kuligofski: No.

Andrew Schorr: And I heard you had two medicines. Vidaza, I think, and Venclexta, or venetoclax.

Harry Kuligofski: Right.

Andrew Schorr: How do the doctors say you’re doing?

Harry Kuligofski: Well, they had to cut the dosage down, because it was killing everything too fast.

Andrew Schorr: Mm.

Harry Kuligofski: But they’re very pleased with what’s happening.

Andrew Schorr: And you’re pleased?

Harry Kuligofski: Very pleased.

Andrew Schorr: Okay, do you have children or grandchildren?

Harry Kuligofski: I have a daughter.

Andrew Schorr: Okay, and a wife?
Harry Kuligofski:
And a wife.

Andrew Schorr:
How long you been married?

Harry Kuligofski:
Fifty-six years.

Andrew Schorr:
Okay. Alright. So, doctors, so, Harry, at his age, and hopefully long marriage. That’s often typical, right, of somebody with AML? These are your patients, right, Hetty?

Dr. Carraway:
That’s correct.

Andrew Schorr:
Okay, so, let me ask you, how did the symptoms come on?

Harry Kuligofski:
Well, it was really strange, because I got the flu, and it wasn’t going away, so we called the doctor, our family doctor, primary, and he brought me in and said, “Let’s do some blood tests to see why you’re not responding.” And they caught it there.

Andrew Schorr:
Okay.

Harry Kuligofski:
And they sent me to a hematologist, and he immediately called Moffitt.

Andrew Schorr:
All right, so when they use that word Leukemia, a cancer, that’s pretty terrifying.

Harry Kuligofski:
Yeah, that was a kick in the stomach.

Andrew Schorr:
Yeah, I’m sure it was, and then how rapid, were you hospitalized, or what happened?

Harry Kuligofski:
Briefly, I was for two weeks, or for two days and then I, they let me go and I came back in for a week, and that was really, my wife can tell us more. She’s a lot, some of the dates. She kept better records.

Andrew Schorr:
Might have been kind of a blur for you.

Harry Kuligofski:
I just took care of the CML.

Andrew Schorr:
Yeah, AML.

Harry Kuligofski:
Or AML.
Andrew Schorr:
Yeah, right. Okay, let me ask you, Dr. Wang. So, some people go to the emergency room. Is that flu-like symptoms?

Dr. Wang:
Right.

Andrew Schorr:
How is it present, and then boom, your upstairs in the hospital, and other people are not. So, how does it present? It varies, it seems, among people.

Dr. Wang:
Yes, so, I mean this is a really rapidly moving disease. So, like Harry, you probably felt, when you think about it, you might have been feeling a little tired, a little weak, for probably a few days to weeks before this came about. So, because of the rapid rate at which the disease grows, it can be a little bit subtle, but most people present with compromise of their normal blood count. They have infection because their white count is low, or they’re really tired because their red cell count is low, or they’re bleeding because their platelets are low. Many of these individuals, you’re older than maybe in age, as 67 to 70, many people, half of people, present over the age of 70. So, you just think, I’m just getting old, and it’s really hard to pick that up until you do some blood tests and a complete blood cell count.

Now, in the past, somebody like Harry yourself, you might have gone to the doctor and they would have said, “You have acute myeloid leukemia, and we’re not going to be able to do anything for you, because you’re too old for treatment. One of the great things and one of the major advances, I think, in the field of AML therapy is that we now have drugs and drug regiments specifically for people over the age of 75. You have to be 75 and above to really be eligible. You have to have some other problems for treatment with venetoclax and azacitidine.

Andrew Schorr:
He’s 78.

Dr. Wang:
Seventy-eight, so you had your disease at just the right time. I mean really, I mean, and I think that our recognition that patients like you need treatment and can get treatment and can tolerate treatment, is, I think, really opened the field. I think if you had presented five years ago, ten years ago, there’s a possibility that they might have said you’re too old for treatment.

Harry Kuligofski:
Yeah, basically, go home or put your affairs in order.

Dr. Wang:
Right.

Harry Kuligofski:
Is what had been said.

Dr. Wang:
I think, also, the quick recognition, making the diagnosis, getting you to a major academic center, getting you to the specialist like Dr. Zeidan mentioned, that they were able to make that diagnosis quickly and start you on therapy, I think is outstanding by your primary care physician.

Andrew Schorr:
So, Dr. Zeidan, it used to be, that if someone was older with cancer, and Dr. Wang was just referring to this. That’s aging, that’s the way it goes, and the treatments we have are too hard. But now, Harry’s been treated, you seem to be doing pretty well today, that it’s tolerable even if you’re older or have other conditions. You might have diabetes, might have a heart condition, right? It’s tolerable.
Dr. Zeidan:
Correct, and I think that’s very important, because for a long time as we just heard basically the only option was really that strong chemo that, and patients who are older and have multiple medical problems, it can be too toxic, and we can end up doing more harm by giving those strong treatments. I think things have changed significantly, really from the mid-2000s, basically since 2004 when the first drug, the Vidaza, azacitidine was introduced. Since then I think there has been more use of this drug. However, until today, and I’ll show you some of the data we just presented in this meeting, like up to the year 2013, 40 percent of AML patients who are older in the U.S. are still not being treated with any kind of treatment, and I think some of that is related to the fact that probably some of it is lack of education, some of it is on the part of the physicians like basically, or some of it that those drugs don’t work particularly well, so I think getting the patients to the right specialist who can keep up with all the pace of all of those new therapies that are coming is extremely important, because things are really changing at a very rapid pace, and I think, one, we cannot cure leukemia in someone in your age, for example.

Our goal is to try to control it for as long as possible. Ultimately, I think, in an ideal world situation, to make it into a situation where it’s like diabetes, or hypertension, or someone can have it for many years, and even treat it with oral drugs. I think this is the way in which we are heading.

Andrew Schorr:
Okay, so older people, I’m going to catch up with you there, Harry. I’m 69, but as we get older, we heard about cancer being often a disease as we age, you deserve state-of-the-art care. Seek that out. Ask about it, and as Dr. Zeidan was just saying, unfortunately, with so much changing, the local doctor you see may not know, because they have to treat, perhaps, every cancer and unfortunately, the number of cancers, things are changing, it’s a lot to keep up with. Okay, Dr. Borate, so let me ask you about this. Why is it important to start treatment with the strong combo perhaps, right away, to achieve the greatest response and go after those blasts, and have the most favorable outcome?

Dr. Borate:
So, there’s a couple of reasons, as Dr. Wang mentioned. It is a rapidly moving disease, and as Harry felt, he had an infection that wouldn’t get better. We know that once it’s diagnosed, we want to hit it hard, and by hitting it hard, we want to hit the cancer hard, not the patient hard. To hit the cancer hard, we really often need two drugs to actually hit the cancer in two different ways. So, sort of give it a double whammy, attack it from two different directions, and that’s the way that we can kill most of these leukemia cells or blast cells, as we call them.

This achieves two things. It achieves killing a large amount of the cancer, thus making the patient and his or her blood counts better, and make the patient feel better. But it also minimizes what we call the margins of resistance, meaning cancer cells, unfortunately, are smart and tend to figure out after a while that therapies that we’re giving them, and try to find a way to live despite the chemotherapy or the targeted therapies that we’re giving, and so when we give two or more drugs together, the risk of this resistance emerging in these cancer cells is also minimized.

Andrew Schorr:
Okay, makes sense. Now, you want to do that because I know when it rears its head again, if you didn’t treat it as effectively as you want, it’s tougher to treat. I’ve heard that right, and it’s more difficult and you all are still grappling with what to do in those situations, right?

Dr. Carraway:
That’s correct. I think we struggle with what to do in those settings, and I think that’s one of the reasons why we all convene in a meeting like this to say, “What is working well? What are the promising agents, and what do we really want to pursue that are the best candidates for next therapy?” And one of the reasons why it’s important to have an understanding of how these cancer cells evade, that teaches us about the biological pathway that we then want to target, and uses combination therapy, again, in the up-front setting, not necessarily in the relapse setting. So, again, kind of doubling down on time.

Andrew Schorr:
Get it right the first time.
Dr. Carraway:
Get it right the first time, even if we need to deploy a strategy to hit multiple arenas to anticipate, this is going to be the resistant pathway, let’s get that before that happens.

Andrew Schorr:
Okay. Now, over time, though, you may be testing a patient, like Harry, more than once, right, to see not only how’s he doing, but also are those cancer genes changing, right? So, that’s maybe subsequent again genomic testing?

Dr. Carraway:
That’s right.

Andrew Schorr:
Okay, so this whole idea of testing, that’s something the patient needs to advocate for, too. So, Dr. Zeidan, you were talking about hoping that your doctor knows about the latest treatment, but also about the state-of-the-art testing.

Dr. Zeidan:
Correct, and I think some of that also might not necessarily be only about the physician not knowing, right. There are many good physicians, but some of it could be related to the local resources. Sometimes, in bigger institutions you might have results come back relatively quickly, where you decide on using a certain treatment if you have certain mutations. While, if you are sending it basically to a send-out lab from a smaller center, that might take several weeks. So, some of it is related to the resources that are available. Some of it is related to the knowledge, and I think, with so much going on, you are definitely right, that I think, having that advice from someone who is very involved in this area is very important, because we definitely see situations where someone has already decided to go on a treatment that might, in our view, might not be the best way. For example, if you are maybe five, six years younger, someone might have given you the strong intensive treatment rather than think about this is azacitidine-venetoclax approach, which we are realizing more and more, that those type of treatments might be actually good, even in patients who are not necessarily too old for treatment. This is a somewhat evolving field.

Andrew Schorr:
Make your move earlier.

Dr. Zeidan:
Correct, but I think some of the mutations testing, what type of mutations that you have can affect that decision, so it’s not only how fit and strong you are, but also those mutations play a part in what type of intensity and approach we use.

Andrew Schorr:
Harry, tell me a little bit about yourself. You said you have a child, right?

Harry Kuligofski:
Yes.

Andrew Schorr:
Okay. Any grandchildren, not yet?

Harry Kuligofski:
No.

Andrew Schorr:
Okay, and what do you like to do?

Harry Kuligofski:
Well, before I got this, I was playing golf and fishing.
Andrew Schorr:
Okay.

Harry Kuligofski:
And had a little shop in the back that I worked in.

Andrew Schorr:
So, what’s your plans now? So, you’re doing okay? Obviously, you got to recover. What’s your hope for the future?

Harry Kuligofski:
To get back to where I was.

Andrew Schorr:
Get back to normal.

Harry Kuligofski:
To be able to play golf again and take the boat out fishing.

Andrew Schorr:
So, Dr. Wang, what do you tell your patients if they say, “Well, how do I get back to normal? How do I view the future with this diagnosis?” What do you say? I mean, I know it’s going to vary.

Dr. Wang:
Well, I say the first thing that we want to do, we want to make sure we have the diagnosis right, and we want to make sure that we have the treatment right. For me, that’s taking into consideration who Harry is, what he wants to do, what he is looking for, what kind of lifestyle that he wants to get back to. I certainly have, I had a patient who wanted to climb up, his job was to climb up those utility poles, and fix the electric wires in the middle of winter storms.

Andrew Schorr:
Maybe not.

Dr. Wang:
That might not be a reasonable goal. I’ve had people that are bookkeepers, or who want to spend time with their grandchildren. That is much more reasonable. So, I say to them, depending on what your goal is, and we’re going to tailor the treatment to either inpatient/outpatient, intensive/non-intensive. Some people with AML want to go for the cure, and sometimes that involves a bone marrow transplant in younger individuals. So, I think that there are, with the newer developments, and with our ability to treat older people, younger people, people in their older age, twilight years, as well as children, we have much more options to offer to Harry, and to try to get him back to where he was. Everybody wants to go back to their lives, and I think it’s our goal to understand, with the variety of treatment options that we have, and the disease that you have, how we can get you there.

Andrew Schorr:
I hope we can get you back on the golf course, too.

Harry Kuligofski:
I hope so, too.

Andrew Schorr:
Do you drive, use a golf cart?

Harry Kuligofski:
Oh, yeah.
Andrew Schorr:
Okay, all right, so you can ride.

Dr. Wang:
Were you good at golf before, or you're?

Harry Kuligofski:
Pardon me?

Dr. Wang:
You want to get back, and you want to be better at golf than you were?

Harry Kuligofski:
I don't think that's going to happen.

Andrew Schorr:
Okay. Dr. Borate, Dr. Wang brought up something, though: transplant, for younger patients. That's been around for a while. Is that gone with all these other medicines, where does that fit in?

Dr. Borate:
So, transplant is not gone. I don't think it'll ever go, because it is one of the most long-lasting therapies that we have for what we call long-term remission, and hopefully that translates into a cure, meaning the disease never comes back. What has changed, though, is the type of transplants we're doing for older patients. So, instead of doing what we call myeloablative transplants, where we would give a very, very high dose of different types of chemotherapy, to wipe out a patient's bone marrow. We now do what we call reduced intensity conditioning, where we're doing the same agents, but we're doing them at lower doses. So that, if a patient is older, and does proceed with a stem cell or bone marrow transplant, that they can, not just get the transplant successfully, but survive it and not suffer from some of the long-term side effects that people get when they go through a more intense transplant.

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Andrew Schorr:
Okay. Dr. Carraway. So, at this medical convention, in a number of different conditions: lymphomas, myeloma, chronic lymphocytic leukemia, either approved or investigation, they talked about another approach: CAR T-cell therapy, chimeric antigen receptor T-cell therapy, an immunotherapy, taking cells from you, going to lab, making a drug out of it, injecting it back a couple weeks later. Does that have any place in AML? What do you think?

Dr. Carraway:
Yeah, we had a fantastic lecture today, really talking about this exact therapy, and again, some of the things that we've talked about with resistance and resistance mechanisms come into play. I definitely think this is a type of therapy that will be very important in leukemia. I think currently it's not as durable as we want it to be, but we will get there, I believe, in some period of time. We're learning about how these cells don't consistently stay present to keep the leukemia away, and we're learning the techniques and how those leukemia cells avoid that, so that we can also then nip that in the bud, and figure out how to make these cells work specifically to the leukemia, and have them be durable. So, that's the really the key, some of the key research that's happening now. It may change the future of transplant for patients as well, so there's lots of questions that still remain in this space.

Andrew Schorr:
Okay. So, do you think down the road, that what we'll learn how to do, it's like what they would do on "Star Trek" or something, is really have some approach, non-toxic, that turns your immune system on when you've developed the earliest tested signs of cancer, and it just bops it on the head, and it has this radar that keeps looking for those cancerous cells, so they never become a tumor, or an acute condition. Is that, do you think we're going to get there?

Dr. Carraway:
Yeah, that's a big question. I think for Leukemia, my hope is that the answer to that is yes, but it's such a smart cancer and there's lots of heterogeneity to it, so that each patient's leukemia can also be very different. So, it's very challenging. We
just have to stay persistent and keep with it. But my hope is someday, yes.

Andrew Schorr: All right, the someday, though, requires our help as patients. Dr. Zeidan, how can we help you, whether it’s in Cleveland Clinic, or Yale, or Roswell Park, or Oregon Health and Science? How can we help you? So, should clinical trials be part of the discussion? You have all of these medicines, but you’re trying new combinations? Should we as a family, affected by AML say, “Tell me what’s approved, but tell me what may be experimental,” but we should talk about?

Dr. Zeidan: Yeah, that’s a fantastic question, because each time we talk about this disease, we have some improvements, but I think we are definitely not where we want to be, I think there’s still a lot that needs to be done. In my view, I think every patient with acute myeloid leukemia, or any kind of cancer, in reality, should be treated within the context of a clinical trial. Now, there are some misunderstandings about clinical trials that I think are important to know. Each clinical trial, when they are designed, they are done in a way that ethically is very stringent. It goes through multiple layers of review, so you would never get any treatment in a clinical trial that is inferior to what you’ve gotten otherwise. I think that’s important, because one of the gut reactions that sometimes we get when we talk to patients about clinical trials, is some of them think of it as, “Am I going to be a guinea pig?” And I think that’s very important.

Andrew Schorr: And there are no placebos here.

Dr. Zeidan: Correct, so, if there’s a placebo, it usually would be in the context of adding it to something else. So, it would be, for example, Vidaza plus something, versus Vidaza plus venetoclax. So, it would never be, we’d never give something placebo, when we have something we know works better.

Andrew Schorr: In that care?

Dr. Zeidan: Yeah, that would never happen. The second thing is the logistical aspects, and I think that tends to be problematic sometimes. Maybe if I may, I can ask Harry, I mean, was that something that was discussed with you?

Dr. Zeidan: I think that’s good, because again, I think the thinking is always there in a great center like where you were treated, I’m sure that’s there all the time, and of course, this is part of why I’m saying things are done in a very, I think, patient centered way, because we know this treatment azacitidine with the venetoclax is so strong we would be very hesitant to put you on anything that we think is inferior to that. So, that’s probably part of the thinking. The other part is that sometimes patients might live far, right, clinical trials require you to come to the big center, you might not be able to do it where you live. So, I think it comes on us, and the community of the researchers working with that. You know with the pharmaceutical companies’ design trials that can also come to the patients, can be done in the smaller places. So, even if you live far from a big center, you can still go on a clinical trial that might give you something beyond what you get as a standard treatment.

Andrew Schorr: So, Harry, just a couple of questions for you, and that was, when you weren’t feeling well, you thought you had the flu, with your wife of many years, who encouraged you to call the doctor to get? Did you do it? Did your wife do it? What made you?
Harry Kuligofski:
Well, I did say I just felt like something was wrong and it wasn't getting fixed. She took care of it from there.

Andrew Schorr:
That’s often the spouse. Right, okay, and then your general practitioner was pretty smart about getting you to a hematologist. I bet you’re really grateful for that.

Harry Kuligofski:
Yeah, I’d say we credit him for the fact that I’m still here.

Andrew Schorr:
Yeah, yeah, that’s the thing, is having good team. So, first of all, hopefully you have somebody in your life, who, when you’re not feeling well, you don’t let it go. That’s the first thing. And then you can get to care that’s knowledgeable and knowing in people who are older, Acute Leukemia can happen, and then you can connect with the right specialist. So, ok, I just want to wind up by saying, it seems like there’s a great deal of hope, so Dr. Wang, what about you? I mean, we have a message for people that’s not perfect, right? We haven’t heard the “cure” word, but here’s Harry, who was treated successfully, now, and hopefully to get back on the golf course. It’s a much more positive story, right?

Dr. Wang:
Yes, I think that we are very optimistic with the participation of people like Harry, and our clinical trials being referred to our centers, getting the diagnosis, getting the good care, having a partnership with you, your family, your wife, your Oncologist, maybe a clinical trial center, that we can really work towards beating this, and giving you more time fishing, more time with your grandchild. One of the things that you talked about as you’re on this therapy, one of the things that we’re doing across the street is having discussion among discussion. Which patients do well with this therapy? What to when somebody like you, when it stops working? And we’re actively debating that as we sit on this side and talk about how glad we are that you got this therapy.

Andrew Schorr:
Okay, Dr. Borate, final comment from you. Feeling more positive in your field now?

Dr. Borate:
I’m feeling extremely positive in our field, and I wanted to say that, Andrew, you mentioned that we’re not hearing the word “cure” yet, and while we may not be hearing the word “cure”, the word we’re hearing a lot is quality for a long time. For somebody like Harry, that means, doing what he was doing before he got sick, and if he can keep doing that for as long as possible, then I think we are definitely helping people achieve their goals of care, and hopefully that will translate to a cure, but I think we have to do it with quality as well.

Andrew Schorr:
So, Harry, we have families out there on that camera, who are living with AML, or affected by AML. Any words of comfort you want to give them? You’re an example of what can happen with the latest medicine.

Harry Kuligofski:
There is hope, and I appreciate the effort that Moffitt Cancer Center is taking to get me back.

Andrew Schorr:
Right, well, these are their brother and sister centers here, and others around the world working, so I want to wish you the best...

Harry Kuligofski:
Thank you.

Andrew Schorr:
...the best of good health. Back on the golf course. Back fishing. And I want to thank our doctors for being with us, Uma Borate, from Oregon, Eunice Wang from Buffalo, hopefully you have a good winter, okay? Amer Zeidan from New Haven.
And Hetty Carraway from Cleveland. Thank you so much for being with us on Patient Power. I’m Andrew Schorr, bringing you the latest news. Stay tuned as we have a continuing discussion about AML. We welcome your questions. You can always send them to AML@PatientPower.info. Remember, knowledge, and some responsibility and action by you, can be the best medicine of all.

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