LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Patient-Doctor Perspectives: Groundbreaking Research in CML'

Description:

Join us in this next installment of our series, *Patient-Doctor Perspectives*, where we explore a diagnosis from the view of a patient and doctor. To celebrate the 100th episode of *The Bloodline with LLS*, we will be speaking with Mel Mann, a chronic myeloid leukemia (CML) survivor and Dr. Brian Druker, a physician researcher at Oregon Health Sciences University (OHSU).

Mel shares how Dr. Druker's research saved his life with the drug, Gleevec®, and we get to hear his inspirational message of how one person can make a difference. Dr. Druker discusses this revolutionary therapy, how it transformed the lives of CML patients like Mel, and how targeted treatments are continuing to transform how we treat cancer.

Transcript:

Elissa: Welcome to *The Bloodline with LLS*. I'm Elissa.

Edith: I'm Edith.

Lizette: And I'm Lizette. Thank you so much for joining us on this episode.

Elissa: To celebrate the 100th episode of *The Bloodline with LLS*, we will be speaking with Mel Mann and Dr. Brian Druker. Mel was diagnosed with chronic myeloid leukemia, or CML, in 1995 and is the longest living Gleevec® survivor.

As an Army Major given only three years to live, Mel was unable to find a bone marrow donor and entered a Phase I clinical trial for Gleevec as his last hope. The trial was successful, and Mel has now been in remission for 23 years. He has since become an advocate for blood cancer patients, writing for numerous publications, serving on panels, and as an ambassador for multiple organizations, and recently serving as a

National Community Outreach Coordinator for LLS's Myeloma Link program. He is passionate about sharing his cancer story to help patients with blood cancer.

Dr. Brian Druker is the Director of the OHSU Knight Cancer Institute in Portland, Oregon, Associate Dean for Oncology at the OHSU School of Medicine, and the Jeld-Wen Chair for Leukemia Research. Dr. Druker performed preclinical studies that led to the development of imatinib, or Gleevec, for CML and then spearheaded the highly successful clinical trials which led to FDA approval of the drug in record time.

This work changed the life expectancy of patients with CML from an average of three to five years to a 95% five-year survival rate and has resulted in a paradigm shift in cancer treatment from nonspecific chemotherapy to highly targeted therapeutic agents.

In this episode of our patient-doctor perspective series, we will be discussing the development of Gleevec, how that transformed the lives of CML patients like Mel, the latest advances in CML research, and how targeted treatments are continuing to transform how we treat cancer.

Welcome Mel and Dr. Druker.

Brian Druker, MD: Thank you.

Melvin Mann: Thank you.

Elissa: So, let's start with Dr. Druker. What got you started in the field of medicine and studying leukemia?

Dr. Druker: Well, thank you, Elissa, for having us here.

My interest in leukemia started when I was a first-year medical student, and we traced the history of the cure of childhood leukemia. It was a fascinating history because every article from the 1950s started with "Childhood leukemia [acute lymphoblastic leukemia (ALL)] is the most common cancer in children, and average life expectancy is

six weeks, and all efforts should be directed at relieving the horrific bone pain that the children experience. Over the 1950s and '60s, treatments like methotrexate and others were introduced; and by the 1970s, this was a highly curable cancer. And now we expect a 90 to 95% cure rate for children diagnosed with this leukemia.

But I looked at that and thought, we're giving these children two years of toxic chemicals to get to this endpoint; there has to be a better way. And in my final report, I wrote the best way forward would be to understand what's different between cancer cells and normal cells and to target that. And that's what set me on my path.

Elissa: Oh, that's great because back then it was 100% fatal, correct? Back in the '50s?

Dr. Druker: Yes, not when I was in medical school. I'm not quite that old. But, yes, in the 1950s, it was 100% fatal.

Elissa: It's amazing how things have improved since then.

Dr. Druker: Yes. It was an inspiring story to learn about that cure; but again, I just felt there had to be a better way of treating cancer instead of using these toxic chemicals for years at a time.

Lizette: Dr. Druker, our main focus today is on chronic myeloid leukemia, or CML. Could you explain to our listeners what that is?

Dr. Druker: Yes, chronic myeloid leukemia is one of the four common types of leukemias. It predominantly is a leukemia that is diagnosed in people in their 50s and 60s or maybe even a little bit older. Generally, it's viewed as too many white blood cells. So, if you think about a normal white count which should be 5,000 or 10,000, the average white blood count at diagnosis for a patient with CML would be anywhere between 50,000 to 500,000. So easily 5 to 10 and maybe 50 times the upper limit of normal. And what's happened is, is that there's been a trigger in a blood cell in the marrow that drives the uncontrolled growth of these white blood cells. Now we can

control the white blood count, but the problem with this disease is that over three to five years, it transformed from a chronic leukemia into an acute leukemia; and that acute leukemia is extremely difficult to treat and is almost uniformly fatal.

Elissa: So, a lot of leukemias have genetic mutations, which end up kind of causing leukemia. Is that the case with chronic myeloid leukemia?

Dr. Druker: Yes, there's a fascinating and storied history of the scientific discovery in chronic myeloid leukemia. It dates back to 1960 when Peter Nowell and David Hungerford, working in Philadelphia, identified an abnormal chromosome in the blood and bone marrow of patients with chronic myeloid leukemia; and they called it after the city they work in, the Philadelphia chromosome.

Now in the 1960s, people thought that was an associated abnormality that had absolutely nothing to do with the cause of the leukemia. But by 1973, Janet Rowley, working at the University of Chicago, showed that the short chromosome 22, the Philadelphia chromosome, came about because of the swap of segments on two different chromosomes, chromosomes 9 and 22.

In the 1980s when oncogenes, these are the driving, genetic abnormalities we see in cancer, were mapped to different chromosomes, it became clear that a specific gene abnormality drove the growth of these leukemia cells; and that's something called BCR-ABL or BCR-ABL for short. We now know what Nowell and Hungerford discovered in 1960 is abnormal chromosome leads to BCR-ABL, and that drives the growth of this leukemia.

When I got into this field in the late 1980s, early 1990s, it was pretty clear that this could be the target for treatment if we had the right drug; and so that's what I set out to do in about 1988 to 1990.

Edith: That's really interesting Dr. Druker. So, Mel, you were diagnosed with CML in 1995. What signs and symptoms led to your diagnosis?

Mel: Well, initially I had fatigue and severe back pain. I had tried traction and medication and therapy, and nothing was helping it.

And so, the doctor ordered an MRI; and the MRI revealed that it was something much more seriously. But the back pain was the main issue because it had gotten so bad that it was hard to do my job without being in severe pain.

Elissa: So, what was the plan for treatment once you did get diagnosed?

Mel: Well, it was kind of like a slow process because initially they had to confirm that I did have CML. I had went up and I got a second opinion. I was living in Michigan at the time, but the military flew me up to Walter Reed to get a second opinion. Between the time I was diagnosed and Walter Reed, they put me on Hydrea to get my white count down. And then once they confirmed it, they put me on interferon; and I did daily injections of that. But the plan was to find a bone marrow donor because at that time the only possible cure or hope for a better outcome was to find a bone marrow donor and have a bone marrow transplant.

Elissa: After hearing that you needed a bone marrow transplant to save your life, you set off on a search for a bone marrow donor.

Mel: Yes.

Elissa: And African Americans and other people of color tend to have a more difficult time finding donor matches. Could you tell us about your search?

Mel: Yes. Well, I had one sister, and she did not match. And then the next plan was to look on the National Registry, and there was nobody on the National Registry at that time; and this is 1995, so this list is not very big to start off with. There's like less than a million people overall in the world on that list. Now it's like 23 million.

But my search, my plan was to do bone marrow drives; and I contacted the Red Cross, and the lady at the Red Cross had told me, , "It's probably better for you not to do this

because it takes a lot of energy to do the drives and have some other folks perhaps do it, as far as doing all the work and appearances and stuff like that, to have them do it.

But I figured it would be better, I could create more empathy for my situation if I was the one actually out there doing the promotions and the drives.

Elissa: Were you very successful with getting people to sign up for the registry?

Mel: Yes. We did a bunch of drives. We did drives in churches, at the malls. The military was a big one because I did drives on the military side and on the civilian side. And I had such support. I had a good team. The folks at work, they became like my planners. They would man the tables and do all the leg work. And then I had other friends from church that would go around to help out with the different churches, to do those drives. And then would do drives at fraternities and other places. So, yeah, it was big.

Dr. Druker: Mel, do you remember how many drives you did?

Mel: I did a lot. I would say at least 40 in those first few years. It was really me and the people like the Red Cross lady who was in charge. She was very good, so we would like just work hand in hand and trying to get as many drives as we could.

One year she did 60 drives in one year, not all for me, but overall. So, it was like a whole bunch of drives. And we did this, and some drives you only get like a few people; and some drives you get a whole bunch. I said I wanted to do this drive at this church. And she said, "Are you sure you want to do this drive because we've already done a drive at this church for two little girls with leukemia, and they only had two people show up." And I said, "Yeah, I'm just like planting seeds. Just keep trying."

So we did a drive at that church. She called me and said, "Hey, you know that church with the two little girls?" She said, "We just set a world record. We had 5,000 people show up for that drive."

Lizette: Wow.

Mel: So, yeah. It was great. And for every 430 people that joined the registry, one match is made. So that's great.

Elissa: What's great is even if you couldn't find yourself a bone marrow donor, you probably saved so many lives by getting people signed up for that registry.

Mel: Yes, we were very successful in that, and I was counting on somebody else doing the same for me. So, we're all like on the same team, and then sometimes people from around the country will meet up and discuss different techniques on how to get more donors.

Elissa: But then you weren't able to find a donor for yourself?

Mel: No. Not at all.

Dr. Druker: And Mel, for me what's amazing, not only were you doing all these drives, but you're doing this while you're on interferon. And I can't imagine you're feeling that great when you're on interferon.

Mel: Right, right. I started losing weight; and from time to time yeah, I would inject myself; but I would have like an infection like on my leg or something. So, it would be somewhat difficult.

Elissa: Now Dr. Druker, as Mel was desperately searching for a bone marrow donor, you were on your way to developing Gleevec. Could you tell us about the development of that drug and also how LLS played a role in that funding?

Dr. Druker: Yes. So, the recent history of Gleevec started in about 1993 when I moved to Oregon Health & Science University. And prior to that I had helped a drug company which was, in those days, Ciba-Geigy and is now Novartis, establish a drug discovery program looking for inhibitors of this family of enzymes that we knew drove the growth of some cancers.

When I moved to Oregon in '93, I contacted Nick Lydon and asked, "Hey, Nick, do you have any drugs that might target this BCR-ABL enzyme that drives the growth of CML? And he said, "Well, as a matter of fact, we have a few. Why don't I send them to you when you get to Oregon?" So, within six weeks of arriving in Oregon, I had a handful of compounds, and I started testing them in a bunch of assays that I'd never done before. But there was one drug that stood out among all of them at killing CML cells without harming normal cells. And that actually turned out to be Gleevec. But Nick had sent these compounds to me blinded, so I had no idea what I was getting. And when I contacted him and said, "Hey, there's one that looks really good," he said, "You got it right, Brian."

So, after that, I was struggling to convince the drug company to move this drug into clinical trials. There's obviously a lot of work that has to be done – toxicity studies, formulation. But the biggest hurdle was going to be a return on investment for a relatively small, rare disease, 5,000 people in the United States, and also a drug that in at least their initial studies had some toxicity in animals. So, there was a lot of concern about whether this drug would be toxic, whether it would be financially viable, whether it would work. Nobody ever tried this approach, and I was just struggling to keep my lab afloat.

And then in 1996, while I was working on this project, The Leukemia & Lymphoma Society launched their Translational Research projects. And the goal behind those projects was to identify researchers who had drugs in their labs that could be moved into the clinic. That's exactly where I was when I looked at that and thought they must know exactly what I'm doing.

I applied. I was in the first group of recipients, and that helped me continue to do the laboratory work that I needed to do, ultimately get Gleevec into the clinic in mid-1998.

Elissa: How long does that usually take? So, from the time you really started testing these out, and seeing that, hey, I think this could actually work to the time when you can start the trials?

Dr. Druker: The timeline there, Elissa, can be highly variable. In large part it depends on lots of properties of the drug. Is it something that is going to be able to be taken by people or not? And that's this formulation process. And some drugs are easy to formulate and can be done in years. Some drugs will never make it. Then there's all the toxicity studies. If the studies in animals show that these are highly toxic drugs, you might not want to move them into a clinical trial. So, there's a lot of variables that can take anywhere from a couple of years to 15 years and sometimes never. So, it's really hard to put a specific timeline on this, but this was one that was moving actually quite quickly from the generation to compound to the formulation and to all the things that needed to be done to get it into clinical trials.

Elissa: People wonder about the toxicity of chemotherapy and other medications. It has to be just enough to kill the cancer cells but not kill the host.

Dr. Druker: That's exactly the point is that there is a fine line; but as an oncologist who gives lots of chemotherapy drugs, this one I was working on, Gleevec, looked pretty benign compared to some of the chemotherapy drugs I'm used to giving. So, I felt it was worth a try in people, and I always felt that if we got to effective doses that people could tolerate, it should work. But the wildcard was how well tolerated is it going to be in people?

Lizette: Yeah, definitely. And Mel, Gleevec started clinical trials in 1998, near the end of your initial three years that the doctor actually gave you to live. So how did you end up at MD Anderson and get enrolled in clinical trials for Gleevec?

Mel: I moved down to Atlanta at the end of 1995. And I kept doing the marrow drives. And my wife's aunt was doing a drive for me in Columbus, Georgia, later like mid-1996. And so, my wife and my daughter, we went down to Columbus, and this

guy came to the drive; he had hairy cell leukemia. He had been out to MD Anderson and said that he had been near death; and that he turned it, his leukemia was in complete remission. And he recommended that I give these experimental drugs a chance. So that's how I got involved with initially doing clinical trials.

And I talked to that gentleman about three or four weeks ago, and I keep him updated.

And, yeah, yeah, he's still doing good after all these years.

Lizette: That's great.

Mel: In fact, he had been diagnosed six months before I was, so it's great.

Lizette: Wow.

Mel: And so I went out to MD Anderson. The doctor looked at my records; and, you know, I'm already like 18 months into my diagnosis, and he says, "We still have time, and I'm going to put you on clinical trial after clinical trial." At first, he increased my dose of interferon. I don't think it was strong enough. But then he started adding these other drugs, and something called ARC and homaheritan and these different things.

And then I started doing these other clinical trials like PEG-interferon, and, then it would improve for a little bit; but then it would just like go back to where it was.

So, at the three-year mark, it was starting to go back the other way; but that's what I had been told, you know, three years.

So, I asked the doctor if there was anything else; and he mentioned this drug that was in the lab. There's still some toxicity problems within animals and that he would give me a call if they got approval to use it in humans. He called me about six months later and said, "Hey, it got approval." And he said I would be the first person at MD

Anderson to use it, but then the secretary said, "Well you just told somebody else that. So, you'll be the second person to use it." So, well not his secretary, but his nurse.

Elissa: Right.

Mel: Yeah, I'll be the second person. So, I was happy to get on that trial because, there was like 20 from like the three different sites; and I was one of those 20 at MD Anderson. So that's how it started.

Lizette: Yeah, but how did you feel knowing that you'd be the second person?

Mel: Well, I knew there was a lot of people that had CML. And I really just wanted to be one of the 20 because I was already at three years. I couldn't wait too much longer. So, it just felt good being part of the trial. And I didn't know if it was going to work or not because there's no promise that it's going to work. But when you start the trial, you have that hope.

Lizette: Yes.

Mel: And that gave me a lot of hope that this could be the drug.

Lizette: Definitely. I think clinical trials bring a lot of people hope, that hope that we need. And I know I should save this till the end, but you're really showing us how one person makes a difference, right? So that one person that had hairy cell leukemia telling you that you could go somewhere and there was this possible therapy that maybe they could help you like they helped him. And then you doing all these drives, one person doing all these drives to help other folks that would need a transplant.

And Dr. Druker thinking, okay, we have to do something; and one person with that spark to come up with a treatment. People say, what can one person do? And this is what one person can do. This is amazing. This story about how imatinib, which is Gleevec, was found and how, Mel, you're still here with us and how Dr. Druker is going onto even more research and helping more and more patients. I just want to thank

you for sharing your stories with us. This is really impactful and just knowing that these trials are so hopeful is really big for our blood cancer patients.

Mel: Well, I'm glad that Dr. Druker spent all that time in the lab because, you know, if he hadn't been burning that midnight oil and like really studying this issue, I wouldn't be here. It's just plain and simple. I was able to see my daughter grow up and become a physician herself. I mean it's like a miracle. And I'm just glad that he was there, that he decided to study science, and become a doctor. I didn't have to wait for the next person to make the discovery or whatever. But it was him and right in the nick of time.

Dr. Druker: What is remarkable, there's a story about my future wife who actually is a writer; and she came to interview me around 2000. And she was asking me some questions about other people she could interview and people that knew me well; and I looked at her and said, "Well, my life is, I work, I work out, I eat, and I sleep." And she looked at me and said, "You're pathetic."

The story has a happy ending. After her story was published in *People* magazine, we started dating. I have three wonderful children now.

But most importantly, I get to hear the stories from people like Mel who 22 years later surviving, thriving. It made every bit of work I put into it absolutely worth it and so incredibly rewarding. So, thank you, Mel, for sharing this story because you're why we do the work.

Mel: Thank you.

Elissa: Now Dr. Druker, many people aren't familiar with clinical trials. Could you tell us what the significance of a Phase I trial is for a patient?

Dr. Druker: Yes. So, Phase I trials are really designed to determine the safety of a new medication because it's the first time it's being given to people. And it's also being used to determine whether there's what's called a maximally tolerable dose.

And so typically what you do in a Phase I trial is you start people at a very, very low dose. You enroll three people. If they tolerate that, a month later you enroll three more people at a slightly higher dose. And you keep repeating that until you run into essentially a toxicity wall where people can't tolerate the dose. Then you drop the dose back one or two notches, and then you run a larger expansion to see whether the drug has any activity. But a typical Phase I is not to determine whether the drug is active. It is to determine whether it's safe and what the right dose is.

But we did something interesting in this clinical trial, and I lobbied Novartis that the only people that should be enrolled on this trial were people with CML. In a typical Phase I trial, you enroll anybody with an advanced cancer because you really aren't looking for whether the drug's going to be effective. You just want to see if it's safe. But I argued that this was a targeted drug. It was only going to work in people with CML, and it was unethical to enroll somebody with breast cancer or lung cancer that had absolutely no hope of benefitting.

In addition, by limiting it to patients with CML, we might see some early hints of activity which could actually speed the development of the drug. So, this was a highly first-of-its-kind Phase I trial where we limited enrollment to the disease where we thought it would work. And that turned out to be exactly the right way to do it because we saw activity in the second and third dose cohorts, including somebody like Mel.

Elissa: Now Gleevec ended up finally being approved by the FDA in May of 2001, so we've just hit the 20-year anniversary. Dr. Druker, what has been the impact on patients during that time?

Dr. Druker: Well first of all, I should just note that in that Phase I trial, by the time we hit effective doses, we had a 100% response rate-

Elissa: That's amazing.

Dr Druker: -and that had never, ever been seen in a Phase I trial. And that helped speed it through the FDA in record time. That's why we just hit the 20-year milestone.

But this has opened people's eyes to this whole field of precision medicine, targeting cancer by understanding what drives its growth and then using that information to develop drugs to target those molecular abnormalities. On the heels of the development of Gleevec, there are hundreds of these targeted drugs that have been FDA approved and thousands more in clinical trials and development. So, it's completely revolutionized the way that we think about cancer and the way that we treat cancer.

And that's been just an absolutely spectacular benefit of the work that we did and the path we showed.

Edith: That's really amazing, Dr. Druker. So Mel, how did Gleevec impact your own life?

Mel: Well, it saved my life because, I was diagnosed in '95; and the drug was not approved until May 2001. So that was 6-1/2 years after I was diagnosed. I was able to get on the clinical trial at least three years before it was approved.

And it saved it so I could go back and lead a pretty much normal life. I was able to run a marathon in 1999, even before Gleevec was approved. I cycled 111 miles, and so I've been able to physically get back into life and mentally.

It saved my life, so that's what it did in essence. And this is my 36th wedding anniversary. I just celebrated that in November. So yes, it's great.

Lizette: Congratulations and also congratulations to your daughter for becoming a physician. That's wonderful.

Dr. Druker: But also, Mel's experience running a marathon while on treatment for leukemia with Gleevec is absolutely a remarkable testament to how well tolerated this

drug is. Now it doesn't mean that there aren't people who have side effects. There certainly are and there's certainly some people who have some pretty significant side effects. But most people, like Mel, they're doing extremely well and have really minimal toxicity from this drug; and that to me was the biggest surprise. I had no idea what that side effect profile was going to look like. And it was just amazing to see how well people have done and how many people are able to maintain normal, active, healthy lives and really are thriving despite this diagnosis. And that to me was the best gift of all from this treatment.

Lizette: Yes, definitely.

Mel: Yes, it's just a pill.

Lizette: That's what I was going to say Mel. It's a pill, so it's a different way of actually getting medication. So, everybody or most people when they think of cancer, when they think of leukemia, think of chemotherapy. And this is a whole new shift of getting a pill instead of getting an infusion, getting different treatments. And I think that's something that also lends to why this is so revolutionary, right, because it actually does affect your quality of life-

Mel: Yes.

Lizette: -if you can take a pill and not have to go to a hospital, not have to do the traveling to get your medication.

Mel: For me, when I was initially told that I needed the bone marrow transplant, I imagined all these big machines and being in this isolation bubble; and just needing all this support as far as caregivers. And then it was kind of hard to go from that to just this little pill that you take once a day. It doesn't need to be refrigerated or anything. You can put it in your pocket and go about your business.

So yeah, that was a big paradigm shift in treatment. And it took me a while to process that.

Dr. Druker: Now there's a great backstory to the development of this as a pill and enormous credit goes to Nick Lydon who was at Novartis and the head of the Drug Discovery program that developed Gleevec.

And Nick and I had conversations because the initial trial was actually going to be an intravenous formulation where you hook people up to a continuous infusion. And Nick and I debated this, and Nick said, "You know, if we're going to give people this medication every day, there has to be a pill form." And I said, "Nick, I'll take an effective drug no matter how it's given."

And to Nick's credit, he pushed forward with the oral formulation of this medication, ultimately this intravenous formation that we're going to go to clinical trials in about 1996 couldn't be given because when animal studies were done, it caused blood clots at the end of the catheter tips that we used for the infusion. So, the intravenous formulation got killed. Because of Nick's foresight to have a backup as a pill, the compound continued to advance forward, and we went to clinical trials. It was a pill.

Lizette: Wow, I did not know that. Did you know that, Mel?

Mel: No, and it's good to know.

Lizette: Yeah, that's really interesting and I know that, with it being a pill, there does come some issues now with some of our folks with insurance coverage. It led to the oral parity laws. Dr. Druker, how did Gleevec play a role in oral parity laws being passed across the country, starting, in the home state of Oregon?

Dr. Druker: Yeah, so the story there is that many oral chemotherapy cancer drugs weren't covered by insurance. Unless you went to an infusion unit at a clinic or a hospital, you didn't get coverage. So, I forget what year it was, but this oral parity law ultimately made it through federal legislation.

But one of the things that it left was this so-called doughnut hole for Medicare patients. And so, what that means is that you have to pay up to a certain amount, and

then your coverage will kick in. So, some of these medications are still pretty expensive, despite the fact that at least we have coverage for them so they're not the $100,000 a year; but they still, for some people, are unaffordable.

Elissa: Yeah, LLS has our advocacy arm; and that's one of the things that we're really trying to change is make it so these loopholes, these doughnut holes can go away so that patients won't have this extraordinary cost. And of course, we have our copay assistance as well to help with that in the meantime. But it is an enormous expense. While it is nice that insurance is paying some of it, there is still a huge cost associated with this drug.

So, Mel, since your life was saved as a result of Gleevec, you have been very open about your disease and have a passion for helping other patients. I mentioned in the introduction how you have written for numerous publications and also served as an ambassador and on panels for various organizations. Tell us about that and what it has meant to you.

Mel: Well, I've pretty much was an advocate from the beginning because I had to get out and do the bone marrow drives. But, once the success of Gleevec was known and I saw it, I immediately started telling other people and I started advocating for clinical trials.

They would look at me and they'd say well it works because he had terminal leukemia and look at him now. He's running marathons.

So I used that platform for many years to just get out and speak with people and encourage clinical trials, encourage people to sign up for the marrow registry. And, also, being connected with The Leukemia & Lymphoma Society from really the very start; I was able to be a part of the Myeloma Link program, and that focuses on the African American community as far as spreading awareness about myeloma because it affects blacks twice as much as whites.

I've been able to go out to the churches, and pretty much the same places that I went to do the bone marrow drives and just spread the news as far as early awareness. You know, stop it as early as you can. Get that information as early as you can so you can get out there and you know about these different things.

And it's been very successful. It spread out. I think it's in 17 cities. It's good because you get that information out, and you help people navigate that cancer terrain. I'm very pleased with that. My wife has been a good part of that too.

It's just what I do. Because I know that you have to be aware of the issues. The information is very important. So, I just do it all the time.

Elissa: That's so great that you've been able to just use your experience as a leukemia patient to also help other blood cancer patients and really get the word out-

Mel: Yes.

Elissa: -about myeloma. That's a very important program that we have, and we'll have a link in the show notes for our listeners who want to learn more about it. But it's just so great that you've been able to do so much with your experience. And from the very beginning, helping increase the donor registry and then continuing this journey over 23 years to help people. I mean it's just amazing.

Mel: It's all one big team, yes.

Dr. Druker: Yes, Mel, I would just echo you're such an inspiration to all of us. And despite the fact that you were given three years, you were out there doing what you could to help others, and you've continued on that journey for 23 years, and countless people have been helped because of what you've done, and so you've taken that gift of life, and you've given it to so many others, and so thank you from all of us for, for continuing to do that.

Mel: Well, thank you. I'd like to add this one little story that when I was first diagnosed, and I was at my desk at my office in Michigan in the military. And this lady comes by, and she has this little clipboard, and she says, "Hey, would you like to support me for, well, it was the Leukemia Society back then, the Leukemia Society's Team In Training marathon. And I'd just been diagnosed, and at the top it had something called Cure 2000. That was the slogan for LLS back in 1995. And I asked. I said, "What's that?" And she says, "Well, we're going to cure leukemia by the year 2000." And it was 1995. I had three years to live, and I counted the years. It was like, "Well I need my cure by 1998." So, I felt like left out, you know.

But amazingly enough, in 1998, the clinical trial for Gleevec started. By 2000, I was good to go. I had already run a marathon and so hey, that's just the way everybody makes a difference in this.

Elissa: That's awesome. I love it.

Dr. Druker, so what has been the latest developments in CML research; and how has all of this work changed the landscape of cancer treatments, and where can we go with these targeted treatments, even for other cancers besides CML?

Dr. Druker: Yeah, so first of all, as Gleevec was developed, The Leukemia & Lymphoma Society started their specialized Centers of Research program. And our team, including myself and Charles Sawyers, who was one of the participants in the Phase I trials as an investigator, and I, put together a grant to look at what mediates resistance to some of these drugs? And out of that grant has come four or five new drugs to treat patients with CML in the chance that they become resistant to one of these medications.

So, with Gleevec, about 15% of people become resistant at five years. That still means the majority are doing great like Mel. But for the 15% or so that become resistant, we need something else. We figured out why some people become resistant, and it turns out that the drug doesn't bind to its target. And so, companies

have developed new drugs that can still shut down this enzyme that's driving the growth, and now people have four or five different options to treat this leukemia.

Elissa: Oh wow!

Dr. Druker: We've also learned that some people with CML will end up with undetectable amounts of leukemia, so no detectable leukemia. It runs about 20% to 40% of people overall. And half of those have been able to stop therapy now with five to ten years of follow-up. So, there's a small percentage of patients who are actually what we call, we'd like to say cure, but we're very careful with that word because we know they're going to need to continue to be followed.

But one of the most active research projects in my lab is to try to figure out how do we make that number bigger. So instead of 20% to 40% of people are undetectable, why can't we get that to 80%? Instead of 50% of people are undetectable being able to stop therapy, why can't we get that to 60-80%. So that's one of the things my lab is working on.

But in addition, we've taken this targeted therapy approach to other, much more difficult-to-treat leukemias like acute myeloid leukemia, or AML. We know a lot about the abnormalities that drive the growth of AML, and with The Leukemia & Lymphoma Society support, we've started a huge clinical trial called Beat AML with the goal of matching patients to the best therapies based on what we know about their leukemia.

In very early stage of that trial, we've already shown improved outcomes for people that go on one of these targeted therapies. So, we think we're on the right path. We just have to keep working as hard and as fast as we can to get these new treatments to patients.

Elissa: That's great. And Gleevec was really one of the first targeted treatments, right, that really went after a particular protein or something along those lines.

Dr. Druker: Yes, that's absolutely right. And like many leukemia drugs, we learned that it might have activity against solid tumors. So, for example, gastrointestinal stromal tumor or GIST for short is a relatively rare, but deadly sarcoma that occurs in people's abdomens. No effective treatments were available. My laboratory showed that Gleevec also shut down the target that drives the growth of that cancer, and now people are alive and thriving on Gleevec and other related medications with that deadly cancer.

Elissa: I'm curious how that ends up working. How do you end up testing the drugs that you have manufactured already for blood cancers to use on tumors and try them out?

Dr. Druker: In this case, it was just much like Gleevec for CML. We knew what drove the growth of CML, and we had a drug that targeted that. For GIST, we knew what drove the growth of that cancer, and Gleevec targeted that, so it was pretty simple to go from CML to GIST. We knew the dose. We knew it should have activity, and it worked in the very first patient that got it.

For other cancers where you're not as clear about what drives the growth, it can be a little bit harder to figure out what drugs to use; but we're getting so much better at matching patients based on the driving molecular abnormalities. And plus, we also have other treatment options in our armamentarium, like these amazing immune therapy drugs, many of which were supported, again, by The Leukemia & Lymphoma Society researchers.

Elissa: Now one thing that you're doing over at OHSU is having kind of more collaborative environment with all different types of cancers. Do you see that as the future in research, having that collaborative environment to be able to utilize one drug to treat multiple cancers?

Dr. Druker: Yes, so our motto is one person isn't going to cure cancer. And even though much of the work I did was on my own, I recognize that I had a huge team

behind me. I had collaborators, and we always did better when we worked with others. We got diversity of ideas, diversity of people, and we recognize that that's the way forward – to collaborate, to get expertise from outside of your own areas, and really move things forward as quickly as possible.

Mel: You know, it's really amazing to me that, that Dr. Druker and his team has saved so many lives because you look at how many people are living with CML today – it's hundreds of thousands. And then you add in GIST and then you add in the other TKIs and kinase inhibitors that came from that, and then you're up in the millions. It's just phenomenal. There's no words to describe it.

Dr. Druker: Well but Mel, it'll all come back to people like you; and that's what it's all about.

Mel: Well, thank you.

Edith: Mel, on our patient podcast homepage, we have a quote that says, "After a diagnosis comes hope." Based on your cancer journey and advocacy, what word would you choose to complete that sentence? "After a diagnosis comes-?"

Mel: Well, I would always say hope because I was told early on to never lose hope because once you lose hope, a lot of the battle is lost. So, keep hope as long as you can. So hope is the word.

Elissa: Now regarding hope, a question to you, Dr. Druker. After the development of Gleevec and continued research on targeted treatments, what would you say to patients and their families to give them hope after a diagnosis of CML?

Dr. Druker: Well, I'll go back to the interview with my future wife, who asked me, "What lesson have I learned from my patients?" And as an oncologist, you probably are supposed to say, "Well, I deal with people who have death sentences, and I realize that I need to live each day to its fullest." But as I said, I was working my butt off in

those days; and I couldn't really exactly say, "I'm living each day to its fullest. I'm trying to move this project forward."

But I harken back to a day in clinic, and it was about April of '99. And in those days, I was so worried about whether the benefits from Gleevec would last, and I had three patients in a row, much like Mel, who had been told, "Your three to five years is up; get your affairs in order." And they had found their way to me, and this was their last hope. And now all of a sudden, their blood counts, which hadn't been normal in years, were back to normal. They were feeling well, and they began to plan for the future and have hope for the future.

And I realized in that moment that the greatest gift was hope, and to be able to give that to patients and tell them there is hope, there is something we can do, that is so powerful. But what I've gotten in return is 20 years of stories of what people have done with that gift. And to me that's the greatest gift that I have received in return. So, I've learned so much from my patients, and I continue to learn from them on this journey. And I want to continue on this journey of providing hope to patients with blood cancers and leukemia.

Lizette: We didn't know what you were going to say, Mel, as to your word. And it was hope. And I think this brings it full circle. Right, so we started with hope and for our 100th episode, you both were able to really kind of make the hope real. So, I want to thank you both for that.

Mel: Thank you. Dr. Druker said that we didn't know if it would last. So, I was part of that patient population where it's working. And then, I get to the 5-year mark and 8-year mark, and then I said, "Well, I think this thing is going to keep on. And hey, now it's 26 years, so.

Lizette: Wow.

Mel: They know that somebody has been here 26 years. They don't have the same worries that I had when I was diagnosed.

Dr. Druker: Yeah, I went through a phase in clinic where when I trained, it was CML, three to five years. And there was a phase I went through in clinic where, maybe five, ten years ago I'd see somebody had been diagnosed with CML 20 years ago. And I'd look at that, and I'd have this reaction. Like how is that possible? Oh, yeah, that drug Gleevec.

Elissa: You know, that one.

Dr. Druker: Yeah, so then again, because I had just been so engrained, three to five years, it was just wow, 25 years from diagnosis. But now, I've gotten past that; and I'm so used to seeing these big numbers from diagnosis that it doesn't phase me anymore.

Elissa: It's amazing, even over the past few years how successful treatments are getting and how many new treatments are coming out. I mean I was diagnosed with AML in 2016, and the amount of drugs that have come out for AML since 2016 is just incredible. And out of all episodes for our 100th episode, Gleevec has had such an incredible impact on patients that we figured it would be a perfect 100th episode.

Elissa: Well, thank you so much, Mel and Dr. Druker for joining us today. It was so amazing to just hear about the development of Gleevec and what it has done over the past 20+ years for patients like Mel and also changing that landscape of cancer treatment so that we can hopefully find a cure for all of these different blood cancers and other cancers as well. It's just so exciting to see where the research is going, and we really appreciate you both joining us today and hearing about all of the great things with CML treatment.

Dr. Druker: Thank you. It was our pleasure.

Mel: Thank you.

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Elissa: And thank you to everyone listening today. *The Bloodline with LLS* is one part of the mission of The Leukemia & Lymphoma Society to improve the quality of lives of patients and their families.

To help us continue to provide the engaging content for all people affected by cancer, we would like to ask you to complete a brief survey that can be found in the show notes. This is your opportunity to provide feedback and suggested topics that will help so many people.

We would also like to know about you and how we can serve you better. The survey is completely anonymous, and no identifying information will be taken. We hope this podcast helped you today. Stay tuned for more information on the resources that LLS has for you or your loved ones who have been affected by cancer.

Have you or a loved one been affected by a blood cancer? LLS has many resources available to you: financial support, peer-to-peer connection, nutritional support, and more. We encourage patients and caregivers to contact our Information Specialists at 1-800-955-4572 or go to LLS.org/PatientSupport. You can find information specific to chronic myeloid leukemia at LLS.org/CML. All of these links will be found in the show notes or at TheBloodline.org.

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