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00:00:00.076 --> 00:00:21.807 Announcer Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers with the director of the Yale Cancer Center, Doctor Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Doctor Winer.

00:00:21.884 --> 00:00:52.615 Eric Winer Tonight, we're going to talk about advances in the treatment of leukemia. A number of weeks ago, we had doctor Max Stahl on this show, and we had a great conversation and decided to invite him back to to talk a little further. Max is the director of the Leukemia and Myeloid Malignancy program here at the Yale Cancer Center and chief of the Duffy hematology firm at Yale New Haven Hospital.

00:00:52.692 --> 00:01:24.384 Eric Winer He's also an assistant professor in medical oncology at the School of Medicine. And the bottom line is, Max is a leukemia expert, a great clinician and a researcher. So Max, welcome. It's really a pleasure to have you here. Thank you for having me back, Eric. So I don't want to cover a lot of the territory that we covered the last time, but maybe a bit of a refresher if you can just remind us as we start talking about leukemia.

00:01:24.461 --> 00:01:33.730 Eric Winer Tell us how many, how many cases of leukemia there are in the United States. Each year. And I think we're really talking about acute leukemia here.

00:01:33.807 --> 00:02:00.846 Max Stahl Yeah. So leukemia is still what we would consider one of the rare forms of cancer in, in comparison to other types of cancer. It's probably about 50 to 80,000 new cases of myeloid leukemia. They're less cases of what we call acute lymphoid leukemia. That's a disease that is a little bit more common in in children and young adults, although we do see plenty of cases here as well.

00:02:00.846 --> 00:02:15.884 Max Stahl And then there are a bunch of other cases we see that are in the umbrella term of myeloid malignancies. And I think we discussed that at in our last session, which, you know, really cover pretty broad spectrum of other blood cancers.

00:02:16.192 --> 00:02:29.269 Eric Winer Sure. Well, I mean, you know, 50 to 80,000 is a fair number. And of those the ones that are acute lymphoid leukemia, less than 10%.

00:02:29.423 --> 00:02:55.769 Max Stahl Yes. Correct. Yeah. Yeah, it's definitely the rarest form of I think the diseases that we treat is acute lymphoblastic leukemia. It is definitely more common in young adults, which I know has been a focus of some of your prior discussions. Cancer and young adults. And in those patients actually al is a more common leukemia compared to AML. AML is often a disease of older patients.

00:02:55.884 --> 00:03:06.884 Eric Winer But AML is also a disease of people who are in their 20s and 30s and really all ages. I mean, it becomes more carbon as you get older. Correct.

00:03:06.884 --> 00:03:25.576 Max Stahl That's right, that's right. We have a bunch of younger patients with acute myeloid leukemia. And when they first read about the disease, you know, their first reflexes, I should not have this disease. This is really a disease of older patients. But exactly like you point out, it definitely happens throughout the age span.

00:03:25.653 --> 00:03:29.807 Eric Winer And I'm guessing the median age is probably in the 60s.

00:03:30.000 --> 00:03:48.269 Max Stahl Yes, the median age of 60, 65 to 67 years old. But that is a median. And and with every meeting, yeah, you're going to have cases who are younger. And we also have quite old patients that we treat now for leukemia. And they're diagnosed in their 80s and 90s even.

00:03:48.346 --> 00:04:17.000 Eric Winer You know, I think that the incidence by age curve might be very similar to what we see in what I do, breast cancer, where the median is in the early 60s. But there is still quite a number of cases of people in not so much in their 20s, few, but in their 30s and 40s and 50s. And so it really is something that does not necessarily spare young people.

00:04:17.076 --> 00:04:43.346 Eric Winer And here I'm talking about both breast cancer and and leukemia, and for that matter, almost every cancer we deal with there, there are very few that don't occasionally affect any people. Okay. And then of those people who are diagnosed with acute myeloid leukemia, do half of them lose their lives to this disease or is it more still?

00:04:43.423 --> 00:05:08.538 Max Stahl Yeah. That's a that's a good question. You know, when you look at overall the entire I think population databases which are often formed on older patients still that more than half of their patients lose their life, I would say, and this is a scary number, I think when patients read about this information, you know, it is certainly a serious disease and it gets presented that way.

00:05:08.615 --> 00:05:27.615 Max Stahl But I would say the flavor or the different type of the disease really matters. When I meet with patients, I try to explain to them that AML is probably 16 to 18 different diseases. And I think that's not so much indifferent from breast cancer, where there are many different forms of breast cancer. And it all makes a difference.

00:05:27.653 --> 00:05:57.192 Eric Winer Yeah. No. It used to be when I was in training, that there were six types of leukemia, and that was all based on classification that pathologists did by looking at the microscope. But now you do so much more in the way of molecular testing that you're able to identify these subpopulations that are that are really quite distinct. And do you think at some point that you know, that 16 different types of cases was going to become 60?

00:05:57.269 --> 00:06:22.884 Max Stahl No doubt. I'm pretty sure that's exactly what's going to happen. You know, with us learning the biology better, we're discovering rarer and rarer subtypes of leukemia. And that I think the number of different types that we can distinguish and most importantly, that we can target with different types of specific therapy is only growing. And I think this is this is when we meet with patients.

00:06:22.884 --> 00:06:41.269 Max Stahl We really always say to them, one of the most important steps before we even try to tackle the problem is to know exactly what the problem actually is, and that is exactly identifying the subtype of leukemia. So we treat it correctly, and I'm sure that will only increase in time.

00:06:41.346 --> 00:07:04.192 Eric Winer But you know, one of your challenges, you don't have weeks and weeks to figure that out, because oftentimes you're seeing people in a very acute situation who are quite ill, who don't have white cells, who don't have platelets or anemic and need to get therapy that will clear out there the bad cells from their bone marrow so that they can start producing normal cells.

00:07:04.269 --> 00:07:28.576 Max Stahl Yeah, yeah. You absolutely right. I think time is of the essence in leukemia treatment. And that's why we have here really optimized our diagnostic approach. When patients come to our emergency room, they always say, you know, yesterday night a nice young fellow came and then they drew 30 different tubes of blood from me. And that's exactly. So we start to work up literally the moment they arrive.

00:07:28.615 --> 00:07:52.269 Max Stahl And usually even in the first couple of days, we already have certain tests back that guide our treatment choice. But we're very conscientious about exactly what you say, that we don't have weeks to make decisions, we have to make decisions quickly, but we have to make the right decisions. And we want to pick the best treatment, not always the fastest treatment, but we want to pick the best treatment, the fastest we can.

00:07:52.307 --> 00:08:21.538 Eric Winer Yeah. So I know things have evolved. Years ago, everyone received what was called seven and three, and it was one drug for seven days and another given three times. And that has really come a long way. And maybe we could talk about some of the non chemotherapy options that have arisen. And when you actually start therapy with something other than chemotherapy.

00:08:21.576 --> 00:08:42.038 Max Stahl Yes, absolutely. So seven and three what you mentioned seven days of one drug and three days of a different chemotherapeutic has been kind of the standard of care since 1973. And there were not many changes for almost 50 years. So you didn't have to, you know, be so much up to date because the treatment didn't change in a long time.

00:08:42.076 --> 00:09:14.730 Max Stahl And that has now rapidly changed, as you mentioned, you know, since 2017, there were multiple new drugs approved, and they all go after the specific biology of the, of the leukemia. And and this

has improved so much because we understand the biology of the leukemia. We understand the genetic alteration that causes the leukemia. And that is exactly what we try to target with therapies that are much more specific for that specific alteration.

00:09:14.730 --> 00:09:37.884 Max Stahl And hopefully, as a consequence of that, have less the kind of general side effects that chemotherapy has. And we have now multiple different mutations in leukemia that we can target with so-called small molecule inhibitors that try to go specifically after this abnormality. How do I explain it to patients sometimes is it's almost like a key and a lock.

00:09:38.000 --> 00:09:50.538 Max Stahl And the and the key will only fit in that specific lock. And that's why it's so important for us to identify exactly what the driver of the leukemia is. So we pick the right drug against that specific leukemia.

00:09:50.615 --> 00:09:59.269 Eric Winer And it's a key of the lark versus the seven and three approach, which was more like bombing the whole city.

00:09:59.346 --> 00:10:14.692 Max Stahl Yes, exactly. It's like a it's like a cruise missile compared to a carpet bombing kind of approach. And we do sometimes combine those specific drugs still with chemotherapy and sometimes we use them instead of chemotherapy.

00:10:14.730 --> 00:10:18.230 Eric Winer It depends on the same seven and three.

00:10:18.307 --> 00:10:21.461 Max Stahl There's there's still patients who get treated with 73.

00:10:21.538 --> 00:10:23.576 Eric Winer Is John and.

00:10:23.769 --> 00:10:37.730 Max Stahl And Sitara been. Yes. Yeah. So still some patients get treated with that. But increasingly we add those specific treatments to 7 or 3 or we use it entirely instead of seven and three chemotherapy.

00:10:37.730 --> 00:11:10.192 Eric Winer So tell us about some of those newer treatments. And I think it's just worth making the point that these treatments come as a result of research that is done in laboratories across academic centers around the world, and that research and laboratories then gets at times done or replicated by pharmaceutical researchers. And then it's largely the pharmaceutical industry that does, in fact manufacture the drugs.

00:11:10.192 --> 00:11:24.500 Eric Winer And it takes fundamental research and cancer centers everywhere and other academic institutions to get this moving. And then it's collaborations that actually translate this for patients.

00:11:24.538 --> 00:11:48.115 Max Stahl Yeah, I couldn't agree more. I think it's often the story behind many of those treatments. And I can give you some examples in a second, is really decades in the making and very hard work from

basic science researchers in cancer centers like this one that then get translated step by step and and derive benefit for patients. One specific treatment to mention maybe a so-called Menin inhibitors.

00:11:48.115 --> 00:12:13.423 Max Stahl I think there's a lot of excitement about those new drugs. What they target is a protein called menin. And men in is part of a multi protein complex that is altered in different subtypes of leukemia. And it's one essential part of that protein complex. So it's almost like a very delicate house of cards that have been built. And when you remove this one card, the entire house of card collapses.

00:12:13.423 --> 00:12:38.615 Max Stahl And those specific drugs, the men in inhibitors target that specific protein called menin. And that has really made a huge difference in the in the treatment of, of patients with acute myeloid leukemia that allows us to target 30 to 40% of acute myeloid leukemia. Patients have an alteration where this protein menin plays a key role.

00:12:38.653 --> 00:12:44.346 Eric Winer Wow. And can you use this instead of chemotherapy? Or is this one that's given with chemotherapy.

00:12:44.538 --> 00:13:17.500 Max Stahl Yeah, it was actually the approval by the Food and Drug Administration. The FDA is for patients with a disease that has come back after prior chemotherapy. So what we call relapsed leukemia. And in this case it's actually instead of chemotherapy it's just given by itself without any chemotherapy with it. Because it worked so well in this setting. We now have multiple clinical trials that try to use this drug right from the beginning.

00:13:17.500 --> 00:13:27.230 Max Stahl So not waiting for a relapse to happen, but prevent that relapse in the first place. And in that specific case, it is often combined with different types of chemotherapy.

00:13:27.269 --> 00:13:44.884 Eric Winer When it's given in this relapse setting. Are there some patients who then have the kids are controlled for a long period of time, or even or any of them cancer free for, you know, years and years? I'm hesitating used the word cured, but I guess we could say cured.

00:13:45.038 --> 00:14:08.730 Max Stahl Yeah, I think that's a that's a great question. So in most cases where you get really long disease control or, or cure, you know, for lack of a better word here. Those are patients who got this drug. They get into what we call a remission, meaning that the leukemia goes away on the microscope. And then often they receive a transplant afterwards to deepen that remission.

00:14:08.807 --> 00:14:27.192 Max Stahl The drug by itself, if you don't follow it up with a transplant, does not cure patients yet. And this is one of, I think, one of the major motivators for us in our group to use this drug earlier with the goal to actually cure patients of the disease, sometimes even without a bone marrow transplant.

00:14:27.230 --> 00:14:35.692 Eric Winer Yeah, but the challenge when is relapse is you need something that will put them back into remission in order to allow them to have a transplant.

00:14:35.846 --> 00:14:49.807 Max Stahl Yes, that is absolutely true. And that is in fact the goal, I think for every patient with red ops or refractory disease is to get to a remission and allowing them to to proceed to this life saving treatment, which is a transplant.

00:14:50.115 --> 00:14:54.115 Eric Winer All right. Well, listen, we're going to have to take a brief break. We'll be back in a minute.

00:14:54.307 --> 00:15:12.884 Announcer Funding for Yale Cancer Answers comes from Smilow Cancer Hospital, where artificial intelligence works together with the latest imaging technology to help diagnose cancers at earlier stages and treat them more effectively. Learn more at SmilowCancerHospital.org.

00:15:13.038 --> 00:15:40.230 Announcer Over 230,000 Americans will be diagnosed with lung cancer this year, and in Connecticut alone, there will be over 2700 new cases. More than 85% of lung cancer diagnoses are related to smoking, and quitting, even after decades of use, can significantly reduce your risk of developing lung cancer each day. Patients with lung cancer are surviving thanks to increased access to advanced therapies and specialized care.

00:15:40.423 --> 00:16:08.576 Announcer New treatment options and surgical techniques are giving lung cancer survivors more hope than they have ever had before. Clinical trials are currently underway at federally designated Comprehensive Cancer Center, such as the battle two trial at Yale Cancer Center and Smilow Cancer Hospital. To learn if a drug or combination of drugs based on personal biomarkers can help to control non-small cell lung cancer, more information is available at YaleCancerCenter.org

00:16:08.653 --> 00:16:12.269 Announcer You're listening to Connecticut Public Radio.

00:16:12.346 --> 00:16:45.384 Eric Winer Hello again. This is Eric Winer back from the second half of Yale Cancer Answers. I'm here with my guest, doctor Max Stahl, who directs our leukemia program and himself is a leukemia clinician and researcher. Max, maybe we could talk about a couple of other new approaches to leukemia. There's been talk about these Flt or Flit three inhibitors. This is something that's been worked on for now over a decade.

00:16:45.423 --> 00:16:51.384 Eric Winer And there have been large clinical trials looking at these drugs. Would you what are they? Would you use them?

00:16:51.423 --> 00:17:16.615 Max Stahl So Flt three or Flit three is a mutation that is present in about a third of acute myeloid leukemia patients. And it's the best way maybe to explain it is almost like it's a gas pedal that's always on drive. And, you know, it really drives the car forward and it doesn't go off.

And with those new drugs, we try to kind of release that gas pedal and make the car stop.

00:17:16.653 --> 00:17:43.192 Max Stahl The multiple different flip three inhibitors now, and they have been added to chemotherapy or use by itself. And they have improved survival of patients with those mutations. We also use them now after transplant for patients who go to a bone marrow transplant. And we look for this mutation with a very sensitive next generation sequencing to look whether it's still present and if it's still present after transplant.

00:17:43.192 --> 00:17:52.000 Max Stahl We give this drug a so-called maintenance therapy, which has reduced the relapse rate post-transplant dramatically. So we use it in many different settings.

00:17:52.038 --> 00:17:54.884 Eric Winer Side effects with the drug. Is it a oral drug? Correct.

00:17:55.000 --> 00:18:17.115 Max Stahl It is an oral drug. Yes. I think the biggest side effects are some GI side effects. Some people have nausea or diarrhea, and it can still suppress blood counts less so than chemotherapy. But it can suppress normal blood counts. And that means we have to watch out for infections and bleeding and other complications of low blood counts.

00:18:17.230 --> 00:18:20.692 Eric Winer But people are able to tolerate it for long periods of time.

00:18:20.769 --> 00:18:44.461 Max Stahl Yes, yes. And in fact, like for this maintenance therapy that I mentioned, patients are on treatment for two years post-transplant. And they take this pill every day and most patients do very well with it. And this has, you know, transformed this disease actually, in order classifications of acute myeloid leukemia, flat three mutations were always a very adverse risk marker of of the disease.

00:18:44.461 --> 00:18:53.076 Max Stahl And this is not the case anymore to the same extent with better treatments our prognostication changes, which is, I think, a good thing.

00:18:53.115 --> 00:19:24.269 Eric Winer Yeah. No, it's it's an amazing thing. Again, referring to the world of breast cancer, her to positive breast cancer used to be one of the worst types of breast cancer. And it's now one of the most favorable because of our ability to inhibit the Her2 protein. And speaks again to the fact that when we understand the biology of what we're doing and where, when scientists can then take that biology and develop drugs, it really makes the difference.

00:19:24.269 --> 00:19:51.884 Eric Winer It's why drug development has improved so much in cancer over the last 5 to 10 years, because we understand the biology. So so that's for three inhibitors. And then there's this drug that's been around for a long time. I feel like at one point it was tested in other malignancies as well. Maybe myeloma. And it's a drug called Vanita Clark's.

00:19:52.038 --> 00:20:17.423 Max Stahl Yeah that is a fascinating drug. So it it targets a protein called BCL two. And BCL two is how I try to explain it to my patients in clinic is it's almost like when we shoot at cancer with our chemotherapy or targeted therapies. Those are arrows we direct at the cancer. And cancer has found a way to raise up a shield to protect itself from those arrows.

00:20:17.423 --> 00:20:47.615 Max Stahl We're shooting at the cancer. And this shield is this protein called BCL two. So it prevents something called what we call apoptosis or programed cell death, which all our targeted therapies and chemotherapies we try to promote. And if the shield is up, it can, you know, mediate resistance against all those other treatment options. So by lowering the shield or taking the shield out of the hand of cancer, we're able to target cancer much more efficiently.

00:20:47.615 --> 00:21:12.269 Max Stahl And in fact, we can use arrows that are less toxic because the shield is down and those arrows can reach the cancer so much easier than when the cancer is protected with a shield. So the Netflix has really transformed the entire treatment of leukemia. It was first studied in mainly older patients who could not tolerate the intensive chemotherapy we were giving them.

00:21:12.269 --> 00:21:46.038 Max Stahl And because of the significant success and the excellent response rates and tolerability as well, with this treatment, we have now moved it to patients who are younger and who can tolerate chemotherapy. And we have found in a large randomized trial, actually that that this therapy is as effective and in some cases more effective than the toxic chemotherapy. So more is more toxic does not always mean more effective, I think and I think this is a wonderful change in the in the treatment of AML.

00:21:46.076 --> 00:22:28.500 Eric Winer It's sort of incredible that we're having this conversation about leukemia because, you know, in other malignancies, of course, where we're doing very well, we are having the same conversation, but there's been so much of a need for progress in leukemia that backing off on treatment is not something that certainly anyone thought about ten years ago. And can you use vendetta lax by itself, or do you need to lower the shield and then use something to stimulate the cancer cell to, to go on and at a lot and die on its own?

00:22:28.576 --> 00:22:51.692 Max Stahl Yeah, that's actually a very important point when when it was first studied by itself, people were actually disappointed with the drug in acute myeloid leukemia. And, you know, because in other cancers, such as chronic lymphocytic leukemia, you can actually give the drug by itself. And it works in acute myeloid leukemia. The response rate by itself was quite low and people almost gave up on the drug.

00:22:51.692 --> 00:23:06.307 Max Stahl And but then people understanding the biology, exactly like you were saying, they were saying, well, if you lower the shield, you might still need an arrow to go after the cancer. And, and and

that has really made the huge difference combining the needle packs with other therapies.

00:23:06.346 --> 00:23:26.346 Eric Winer So vanilla lax protects the cancer cell from apoptosis which you want to achieve so programed cell death. And then you lower the shield and you then need to help induce the program cell death a little bit more than by just lowering the shield.

00:23:26.423 --> 00:23:42.346 Max Stahl That's right. And we use in order to induce this apoptosis we use very low dose chemotherapy that is quite well tolerated and that we can give to even, you know, patients who are quite old or who are quite frail.

00:23:42.384 --> 00:23:44.384 Eric Winer What do you use in this situation?

00:23:44.423 --> 00:24:09.384 Max Stahl Yeah. The most common drug that we use is something called the hypermethylation agent, something called as cytidine or decided been. And those are drugs that we can give to patients in their 70s, 80s, even 90s. But by themselves, they're also not very effective because cancer uses this shield to shield itself very effectively. But without the shield, it's vulnerable even towards lower dose chemotherapy.

00:24:09.500 --> 00:24:41.846 Eric Winer Yeah, that's very remarkable. Well, let's let's end by talking about something a little different. And that is survivorship needs after one has had treatment for acute leukemia. Because there are an increasing number of individuals who have had leukemia who are in remission. Hopefully most of them are cured. Some of them have had a transplant, some of them habitat a transplant.

00:24:42.076 --> 00:24:52.615 Eric Winer And maybe we can touch on that needs these people have because they've been through many of them through quite an experience.

00:24:52.653 --> 00:25:15.038 Max Stahl Yes, absolutely. And I think in experience that can be traumatizing to, you know, to patients in a way that we have survivorship and we have those issues to tackle with it is is good news. You know, it means patients are doing well. And and they got through their disease and they got out on the other end and can hopefully live a meaningful and and in long life.

00:25:15.038 --> 00:25:38.500 Max Stahl But there are issues to tackle. And I think to your point, it is a dramatizing experience. You know, leukemia treatment is very tough. The disease is tough. Treatment is tough as well. And it has impacts psychologically and and on the body itself. I think I would maybe group it in a couple of things that we try to look after patients after we complete treatment.

00:25:38.500 --> 00:26:08.153 Max Stahl One is to look very carefully and monitor them very closely for any signs of relapse, because we know relapse can happen even several years after they finish treatment. And our goal is always to

detect relapse as early as possible, even before a frank relapse happens. When there's any evidence of that, the disease comes up. We want to go right after because treatment is usually easier when we do it than later.

00:26:08.230 --> 00:26:45.000 Max Stahl So that's I think is one big part of it. Another big part of it is, and we think actually of this kind of right from the beginning is fatality for younger patients. You know, many of our chemotherapeutic can affect fertility. So we try to do sperm banking or site retrieval right before we start chemotherapy. And and we have them, you know, follow very closely with our, you know, gynecologists or fertility specialists when it comes to a time that they I would like to to start a family.

00:26:45.038 --> 00:27:01.153 Eric Winer Do you have time to do you say retrieval or egg harvesting, as some might call it, because oftentimes one needs to stimulate the production of the of the site with various kinds of hormonal therapies.

00:27:01.346 --> 00:27:26.269 Max Stahl Yes. In in women, exactly like you say it, it is a challenge, you know, and it's a challenge that we face. And sometimes it is not possible because the disease is so rapidly moving and it's really a threat to the patient. I mean, we have to we have to go ahead. But I have several examples of of patients of mine where they presented with acute leukemia and they were sick and we still got them through this.

00:27:26.307 --> 00:27:49.269 Max Stahl You know, it is definitely, I think, one of those moments where as a physician, you sometimes have a little bit of sleepless nights, you know, getting a patient through this and waiting and you feel like, do I do the wrong thing, you know, should I, should I start treating? But it is for some patients, it's such an essential part of what they want in their life, particular some of our young women with leukemia that we treat, that we make it every effort.

00:27:49.307 --> 00:27:51.538 Max Stahl You know, sometimes it is just not possible.

00:27:51.576 --> 00:27:54.653 Eric Winer And, you know, because it's a minimum of a couple of weeks.

00:27:54.692 --> 00:28:16.538 Max Stahl Exactly, exactly. And I had a patient very recently of mine, you know, who went through this. And I think we all held our breasts. And we had this patient come to clinic like 3 or 4 times a week to make sure we at the first sign of that, the disease is really moving to quickly. We can change pace, but we managed to to do it, you know.

00:28:16.538 --> 00:28:24.115 Max Stahl And she is through treatment now. She's in remission you know. And and she's very happy that she, she did it.

00:28:24.153 --> 00:28:38.423 Eric Winer Well listen, Max, it's been a pleasure having you on. And to our listeners signing off now, this is Eric Weiner, and I've been with our guest, Max Stahl, a leukemia expert here at Yale.

00:28:38.615 --> 00:28:57.653 Announcer If you have questions, the address is CancerAnswers@Yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you'll join us next time to learn more about the fight against cancer. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.