Cancer Assist Podcast: Multiple Myeloma: What is it, And Can It Ever Be Cured?

**Narrator** 00:02

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**Dr. Bill Evans** 00:20

Welcome to the cancer assistance Show. I'm your host, Dr. Bill Evans. On this morning, I'm talking with Dr. Ronan Foley, who's our hematologist and oncologist at the Juravinski Cancer Center and a specialist in the management of multiple myeloma and the treatment of malignant diseases with car T cells, which are going to be talking about later today. But before we dive into conversation with Dr. Foley, I thought I just mentioned some of the services of the cancer Assistance Program offers. And the mission of cap, as we sometimes call it, is to support educate and empower individuals and families touched by cancer, through our programs in the services, which are all provided free of charge, and they include free rides to and from the cancer center or their medical appointments, the loaning of free equipment to help people stay safe in their homes and emulators, wheelchairs, other aids, nutritional supports and continence supplies and a host of other things. So the cancer Assistance Program really provides practical aids to people who have cancer. And so if you're listening to this, and you're in the Hamilton area, check out the cancer Systems website, cancer assist.ca. There may be services that we can offer through the program that will be helpful in your cancer journey. So welcome, Dr. Foley. I'm really pleased to have you here today and to delve into a disease that isn't that common, but is terribly important. Multiple Myeloma disease was kind of a strange name in a way. But maybe you could tell us a little bit about what Multiple myeloma is. We know it's a disease of the bone marrow, but much more than that, probably our listeners don't know. Yeah,

**Dr. Ronan Foley** 02:03

no, it's it's a great question and a name multiple. So So Thanks for being here today and having me also agree 100%, that the cancer Assistance Program does amazing things. And I hear from the patients every day, so So God bless her that Multiple myeloma is essentially a cancer of white blood cells. So the white blood cells we have that protect us and prevent foreign invaders and germs and things like that. They're the cells that ultimately become multiple myeloma cells, these white blood cells, typically, they're called B lymphocytes. And their kind of goal in life is to produce antibodies. And so, which is an extremely important part of your immune system keeps us healthy. And of course, when you go and have a vaccine, be it flu vaccine, or COVID. It's these plasma cells, these white blood cells that produce the antibodies are the ones that are kind of doing all the work. So again, very important, but for reasons we're beginning to understand, these white blood cells, or plasma cells, like a plasma TV, plasma cells begin to grow on their own in an uncontrolled manner. their zip code really is in the bone marrow is where these cells end up being their home, that is their home. But occasionally, they as they become more and more malignant, they'll they'll leave the bone marrow and start to grow in other places. The condition occurs when you have more than 10% of your bone marrow with these myeloma cells. And you have other myeloma defining things like kidney failure, anemia, and then holes in the bones like that can be quite painful. Another condition where the calcium level goes high, and So taken together, we call that crab.

**Dr. Bill Evans** 04:07

Yes, I've seen that acronym. And it's one way of remembering all the signs and symptoms of the disease, right.

**Dr. Ronan Foley** 04:12

And it's also important to know that the condition exists in earlier phases, there's something called an M Gus, which is just having an abnormal protein in your blood. And then there's a more distal condition called smoldering myeloma. Neither of those need treating, but most people will progress and then eventually develop myeloma. And of course, it's our job to properly diagnose it.

**Dr. Bill Evans** 04:35

And that's a bit of a interesting part of the disease, too. How, how do people typically present with myeloma? And because I'm thinking particularly for the family physicians point of view is not a common diseases, right, about 1% of all hematologic malignancies are taken right? And it's only a few people per 100,000 that will get it in their lifetime. So it's It's really relatively rare. So I feel for the family doctor who might have someone come into the office with complaints of fatigue, because of the anemia, maybe thirst, peeing a lot because of the elevated calcium, things like that, or bone pain.

**Dr. Ronan Foley** 05:18

All of the above. I mean, I mean, you're 100%, right, so the group constellation of symptoms, the crab, hypercalcemia, renal failure, anemia, and bone lesions, it could be any one of those. But more commonly, because you have a population of plasma cells producing these antibodies, the levels of protein in these antibodies get very high. And sometimes screen color protein electric Rhesus, which is a simple test that happens in a family doctor's office. That's where you see it. And so you'll see a large spike of a monoclonal protein. And that tipsy off, there's something wrong. So any one of those things is how people present.

**Dr. Bill Evans** 06:01

And then the further diagnosis, the bone marrow, and bone marrow is required and X rays are interesting, helpful. Some very characteristic things can appear on an x ray of the skull, I gather.

**Dr. Ronan Foley** 06:16

Yeah, so it's, it's interesting, the myeloma cells send messages to the bones that want to destroy the bones. And so if you have a cluster of cells in a certain marrow forming area of a bone, those local secretion of those called osteoclasts, activators, will cause actually holding the bone. And so even on a plain X ray, you will see a lytic lesion. But of course, nowadays, we have escalated imaging more, so two, MRI, and something called the whole body CAT scan. So we can get much more sensitive about seeing the smaller the lesions, and at an earlier stage of diseased.

**Dr. Bill Evans** 06:59

And just for clarification to listeners, oolitic lesions kind of punched out area where the broken bone has been eroded. So he kind of looks like a whole lot of dark spots where you should see white on an x ray from the calcium in the bone. So it's, it has a very interesting presentation. And you mentioned, I wasn't aware you're doing whole body CAT scans to identify the important thing about doing that, I guess it was to see where the bone might be weakened, and therefore at risk of breaking, right.

**Dr. Ronan Foley** 07:30

100% true. And that that certainly is one of our biggest worries, in dealing with myeloma patients is, you know, are there any lesions that are unstable, and sometimes you have to draw in orthopedic colleagues to give advice about pinning them or even my dealing with with the fractures, but that, you know, in itself, not just because of the pain of a fracture, but you'd become functionally limited afterwards. You know, if you've broken a hip or an arm or a leg, your journey through your treatment is going to be that much harder, difficult with with those limitations, so certainly, breaking bones is something we go, you know, we make sure that doesn't happen. The second thing that can happen with this condition is the tumors can grow out of the spine. And that can put pressure on the spinal cord and even impair its function like a paralysis. So breaking bones and spinal cord compression are kind of the big risks or things we want to make sure are going on.

**Dr. Bill Evans** 08:33

With the plasma cells taking up more and more space in the bone marrow, these will crowd out other cells and functions as a result, does it have an effect on your ability to fight infections, you're producing this antibody, but it's a monoclonal meaning just one one type, you need a whole bunch of them them fight all the microbes in the environment, does it make you more rested?

**Dr. Ronan Foley** 08:56

100%, right, it has an effect on the remaining healthy immune cells. But as we'll get to, the concern about infections is actually made worse by the treatments. The treatments are remarkably effective, but they ultimately have a risk of infection. So so that becomes more and more important as patients get treatment.

**Dr. Bill Evans** 09:19

It was like a refresher course in myeloma for me, way, way back when I trained. I actually trained under someone who was considered a world expert at the time. Dr. Daniel Birdseye Gollum wrote the chapters in the major textbooks about multiple myeloma, but it seemed a lot simpler than especially around the treatment aspects. As once we went through those diagnostic tests that you were mentioning, and they were a little more limited than I think. We had only really one therapy to offer which was an oral agent called melphalan. And we combine either with prednisone witschi, it's catabolism is the protein more quickly, and people did benefit from the treatment and we watched the spike in the so called M protein come down. And those patients would do well for a time. But after that got a little more desperate. And we try some things like cyclophosphamide and prednisone or, CCU and, and prednisone. But they didn't, we didn't have the panoply of therapies that we have today. And it seems to me about maybe 20 years ago, all of a sudden things changed. And tell us about that change lives is really quite exciting.

**Dr. Ronan Foley** 10:41

Yeah, it's, it's, it's, it's been a remarkable journey. And, you know, Bill, me like you, I remember it was melphalan, and prednisone. And sometimes dexamethasone, but that's all we had. And, you know, typically, patients would do well for a period of time. But then when the disease became refractory, or came back, there really wasn't much to treat people and sometimes we would get some radiation. So the the journey of all these drugs, and it has been a remarkable journey. The first sort of major bit of success was was with the drug you, you talked about melphalan, which is the first drug, but we realized we could give it in very high doses in the context of a stem cell transplant. And that was really the first time we moved the needle with this disease that people would go into remission, and the remissions would be quite durable. The next phase was novel therapies. And, and they have really dominated the last 10 years with with drugs that work differently than chemotherapy. They have different mechanisms of action. And there are three big ones, something called a proteasome inhibitor, the PIs, there's a few of those, something called an Emmitt, which is an immunomodulatory. And that's a drug called lenalidomide. And then the third one is a monoclonal antibody, so an immune type of therapy that targets CD 38. That's called Dara tumor map. And so those agents coming into the game and used in different combinations, really, the whole thing took off from there. And whereas the median sort of time with disease would be three years, it's now all well over 10 years for for a majority of patients. That's remarkable.

**Dr. Bill Evans** 12:31

Yeah, but still not a cure. That's the holy grail world. We're still seeking after here. It's getting closer.

**Dr. Ronan Foley** 12:39

Yep, that is correct. So you know, it's not just about going into remission. Now, it's going into deep remissions where you can't you can't find any evidence of disease. And we do that through testing called Mrd. And this is a very sophisticated high level test that can get down to hundreds of 1000s of cells. And if we can't find any myeloma cells, then you're considered Mrd. Negative, that will be the path to cure. Deep remissions. MRD, negative. And then eventually,

**Dr. Bill Evans** 13:12

the curious is what I believe in your lifetime.

**Dr. Ronan Foley** 13:16

Close. Yes,

**Dr. Bill Evans** 13:18

we hope Yes. Oh, when people are on the stream is let's take the first two the the proteasome inhibitors and the the imminence, how would people feel? Are they? Do they have a pretty normal life and able to do things? Or is it something everybody knows? Chemotherapy makes you sexy? Right? Is it the same with these drugs? Or is a much better?

**Dr. Ronan Foley** 13:41

Yeah, it's a great question. I mean, the you know, every drug, nothing comes free. So I mean, every drug has something. But but you know, without question, not even a maybe these drugs are very well tolerated. So they're not hair losing vomiting, chemotherapy drugs, the way they work is entirely different and a lot more sophisticated. And what we've what we're able to do, and what has always been the limitation with this disease, what we're able to do is attack it from different directions. And that turns out to be extremely important. Myeloma and you're 100%, right, it isn't curable. And the reason it is incurable, as you treat it, it becomes resistant, you treat it, it becomes resistant, you treat it becomes resistant, and each time that remissions get shorter and shorter, until eventually it's entirely refractory. By combining drugs, the chance of it becoming escaping and becoming refractory is a lot less. So these combinations. Initially were two combinations, but now three combinations of drugs have been unbelievably effective. The thing is, you got to stay on them. And so that's that's the challenge right now is people are on the drugs, they're doing well to have a good quality of life. They Have manageable side effects, but they can't necessarily stop. And so that's that's one of the challenges.

**Dr. Bill Evans** 15:07

One of the more recent additions to the therapeutic armamentarium, if you will, was the monoclonal antibody. You mentioned the Dara tumor. Ma'am. Can you talk a little bit about what it's targeting? And then how it's kind of moved from a third line therapy? Yeah, up towards the front end of treatment. Yeah.

**Dr. Ronan Foley** 15:27

Dara, Dara tumor map has been a complete success. It kind of took from the took the game buck from from treating lymphomas with a different target. But these are manufactured antibodies, that a very specific target on them. And if the if the tumor cell has that target, these guys can come in bind and essentially kill the cell. So it's very, it is very targeted. And that means the side effects are a lot less because you have, you don't have as much off target effects. It's all going after the myeloma certainly in the case of lymphoma, monoclonal antibodies knocked it out of the park, they were, you know, making people live longer. And they were a game changer. And it took a little bit of a while but but, you know, the same strategy came into myeloma with Dara tumor map. In the beginning, we're just giving it by itself, we realized it was very effective, you could combine it with other drugs. And then the results are even more amazing. And now it's it's used up front. So if you're not having a stem cell transplant, you'll be getting Dara tumor map in the front line. And of course, all drugs work better in the earlier lines. So it's found its place, it's found its home. It's now given subcutaneously over five minutes. So it's quite convenient. And it's been a game changer. Without question. I guess

**Dr. Bill Evans** 16:56

the only negative associated with it is something called cost. Yes, there's all these drugs tend to be expensive until they become generic, and then prices start to fall. But as they enter the market, they're like $10,000, a month or more. And remember, all the monoclonal antibodies are in that kind of class, aren't they? Yeah,

**Dr. Ronan Foley** 17:17

no. And I suspect if you if you looked at the global budget bill, you'd probably know better than than I suspect. It's up there in terms of, you know, drugs that are costing money. You know, that that said, and you know, this is kind of going back into the memory banks a bit but you know, I used to remember myeloma patients coming in, they'd have terrible pains hobbling in, and, you know, you try to figure out ways to control their pain. People come in now, and they're telling me about their golf score. And you know, what, they're up to the cottage on the weekend, and this and that, so. So if you get the disease in remission, and the medications aren't too bad, people have good life. And that's kind of where we're at now. Obviously, from my end, it's worth the money. From what I see, but I'm

**Dr. Bill Evans** 18:06

sure from the patient's perspective, and thank heavens, we live in a publicly funded healthcare system. Yeah, yeah, absolutely. I couldn't agree more. Because the financial toxicity if you were to have to pay for this, it

**Dr. Ronan Foley** 18:17

would be impossible.

**Dr. Bill Evans** 18:20

Now there is a role for bone marrow transplant in some patients is or not, yes, yes. And you talk a bit about that and how you select the patients who are a bone marrow transplants or how their initial treatment would be different from say, a 75 year old who's got some comorbidities.

**Dr. Ronan Foley** 18:36

So your your best results with a patient I tell patients this all the time, your best results come from what we call one L therapy or first line therapy and a patient remember, they may go through one L two L three l four L. But your first line of therapy one L is when you get your most bang for the buck. And for patients that are young enough fit enough that we feel can safely tolerate. We don't want to put people in harm's way. a stem cell transplant is the way to go. And we find that patients having the stem cell transplant very often go into into a deep remission. And then they can receive a medication afterwards called maintenance to keep them in remission. And they after a transplant can be 5678 years before the disease comes back.

**Dr. Bill Evans** 19:34

So they can get a very long remission and essentially minimal maintenance therapy. Right, right. Just

**Dr. Ronan Foley** 19:41

just very well tolerated maintenance therapy. We, you know, is interesting so so the the stem cell transplant data always look better than people that will, as you said we're no ineligible for transplant. It is interesting to note with the derrick Huma Mab coming up front now and combined with Reverend lead Revlimid and dexamethasone, they do virtually as well as the stem cell patients now, so So the, the drugs have caught up with doing the transplant. But to your point, the transplant remain standard of care for certain patients, you know, maybe up to the age of 70 You have to have a good heart, good lungs, good kidneys, you have to be you have to sort of be what we call ECOG mobile and, you know, functioning and all that stuff in bed all the time and things like that. So for a while there, we were getting up to 300 stem cell transplants at Juravinski. The majority of them were myeloma. It's kind of backed off now with the new drugs and as an option there isn't quite as many stem cells but probably about 120 to 150 patients come into Juravinski from from around our Linn Credit Valley, Trillium Health Partners, Grande River, to have transplant. So that's still happening quite frequently.

**Dr. Bill Evans** 21:06

So I think we'll take a break here and come back in a moment to continue the conversation and, and focus on a really exciting area called car T. Cell Therapy, which is another relatively recent addition to the therapeutic approach to multiple myeloma and really a very dynamic lead. We'll be right back.

**Narrator** 21:27

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**Dr. Bill Evans** 22:12

All right, we're back with Dr. Rona Foley talking about multiple myeloma. And we've already heard the tremendous progress that's been made in treating this disease. But more recently, it really has taken Cena BREP abrupt turn to towards a dramatic introduction of a therapy called chimeric antigen receptor T cell therapy and it's quite a mouthful. That's why we call it car T. And I gotta leave it to you run into explain what car T cells are number one in where they should in the therapy for multiple myeloma.

**Dr. Ronan Foley** 22:47

Yes, a bit of a car tea party. So no, it's it's a great question. Maybe I'll just step back a little bit. And you know, Bill, as you know, the war on cancer always kind of involved the historically involved radiation surgery and chemotherapy. You know, the fourth dimension is immunotherapy. And that's harnessing the immune system to to attack the cancer cells, which which probably is what it's meant to do in normal situation. For whatever reason, the immune system doesn't recognize the cancer and the cancer grows. So like other diseases, immunotherapy looms large now in in myeloma, and it turns out, some of our best results happen when we're, we're engaging or targeting the immune system to treat the cancer. So car t is just a beautiful example of that. We we had in the beginning, we said that the primary myeloma cell is a B cell derived from a B lymphocyte, called the plasma cell. But in car T, we're talking about the other side of the house, which is T cells or T lymphocytes. T lymphocytes are a remarkable part of our body and part of our immune system. They have the ability to kind of in a hand to hand combat, identify a cell and kill it through various mechanisms of granzyme and peripheral and these T lymphocytes also have a remarkable ability. If you get sick, if you get a viral infection, they can go from 10 cells to 10 billion cells in about 24 hours. So they have a remarkable ability to expand. And of course, they become the soldiers to fight the infection. And they can persist. So every time there's a reaction, some of them kind of pull back and remain as memory cells. So watching or seeing a patient going through an infection, this rapid increase in these lymphocytes, which are powerful killer cells, you think She's Why can't you harness that to kill the myeloma. And for whatever reasons, the cells are there kind of swimming by but they don't recognize the myeloma. So the myeloma kind of gets off free. Without without the attack. If you collect those lymphocytes from a patient, and we're talking about billions of these lymphocytes, we do that through a procedure called Luca for Rhesus. And which is similar to dialysis, it'd be go on a machine for a few hours and collect all your white blood cells and T lymphocytes. Those cells, the T lymphocytes can be genetically modified to have a very specific receptor on the they produce it. So into their DNA goes a new gene, this is Gene therapy. And from that day on, that cell will produce this receptor to recognize the myeloma cell. But not only that, that cell gives rise to daughter cell to daughter cell to daughter cell 1000s and 1000s of times, so one cell can quickly become 1000 cells. And so, Carty therapy, ultimately is a living drug. Because you put these cells into a patient small number, they expand and expand, they wipe out the myeloma through this mewn mechanism. And then they stay in the body. For we've seen them now three, four years, they're still there. If the cancer tries to come back, they just get snuffed out and and that's that's the procedure. It's

**Dr. Bill Evans** 26:35

fantastic. And you made it sound simple. But I know it's not. Because there's a whole process after the look of Reese's of manufacturing, which is kind of a almost a weird concept to think about that you're taking somebody's cells and then sending them off to a manufacturing center to actually be tailored for their job as a new foot soldiers in your analogy to fight the myeloma. Maybe just talk a little bit about the logistics their boats. Now, after you've taken the cells, where are they going to? And how do they get there? And what happens when they get there? That sort of thing?

**Dr. Ronan Foley** 27:13

Yeah, no? Great question. So yes, the cells are collected at Juravinski. But then often that night, they are shipped off to California or New Jersey, there's a few of these manufacturing labs, depending on what product and of course, this is taking off big time. With multiple new diseases getting Carty therapy, so there's a lot happening in this area. Basically, the cells arrive, and they go into a laboratory where people are wearing hazmat suits. And it's it's the real deal. The cells are initially selected, purified for the right lymphocytes that we want, they then undergo this gene therapy through a viral insertion of the of the gene product, they're then expanded. But it's mainly laboratory things and cells growing and incubators and things like that, it takes about 10 days to get the product fully, fully ready to come back. So the cells fly out, you know, they go through customs and all that there's a ton of logistics to it, as you might imagine. And of course, the place down in California has to be ready for them. And so a ton of paperwork and labeling and preparation. And so we have absolutely excellent coordinators at the Juravinski to kind of take care of all all of those things. Cells come back, they arrive, and then we get started and use them right away.

**Dr. Bill Evans** 28:48

So there's a bit of a delay Yes, I'm the cells are taken to the time that's correct. Manufacture cells can come back, do you have to do anything in the interval of the patients, you know, diseases progressing and then have to bridge them over with drugs?

**Dr. Ronan Foley** 29:03

So you know, the thing about the car T cells is they don't necessarily care what what has been used before. If you have the target on that cell, it will kill it doesn't matter if it's had radiation or what chemo is it said in the past. So it's very powerful thing. However, you do kind of conceptually want as little tumor in the person's body when when when you start the reaction, and that kind of favors more than car t, if you have you know, you'd rather be treating ants than elephants. But on the other hand, that that period of time you're 100%, right? Well, it's what we call bridging therapy, kind of, you know, putting a lid on the boiling water as it were just to kind of keep things over and some people need that. We don't know if bridging is good or bad at this stage, does it somehow an open question is still an open question but sometimes you have no choice. Patients is progressing very quickly. And then the other, you know, the other part of it and, you know, hats off to the team at the Juravinski. And, you know, this is a multidisciplinary approach, you know, setting the table for curtsy and Juravinski, we were the second center in Canada to do this. But but a really a lot of people came under the tent to do this all with expertise, because it's a remarkable journey for a patient from from start to finish. And it needs a lot of expertise.

**Dr. Bill Evans** 30:29

I imagine there's a lot of training that goes into getting everybody ready to do this. And, and, frankly, some of the background to being prepared to do it comes out of preparation for stem cell transplants as being accredited as a senator that can do that kind of work, if he could do that kind of work. You can kind of graduate to this kind of work. But if you've never done stem cells, it's must be a huge leap. Or maybe it's not a leap, you can even attempt as a result of not that many places in Canada do this kind of work coming up with what's his current situation? Well,

**Dr. Ronan Foley** 31:04

so you've hit the nail on the head, it's it's so because of stem cells centers will be fact accredited, just just like you said, and, and they're in a better position to take this on with with the expertise they've developed, but there's only about 13 centers across the country that would be in that situation that would be fact ready and able to do this treatment. And clearly, given the size and geography of Canada, we need a lot more centers. But it's hard. I mean, you know, Bill from from, you know, when you ran the cancer center, just start up something like this, nobody's giving you any money to you know, the startups you're seeking in kind and it's it's a real challenge. Will there be a day when when when smaller centers, community centers, maybe even rural centers are able to do this? I don't know. It's what you said, there's so many pieces to this and regulations and, and things, you know, it would be a lot, a lot to take on. We have started looking at, we treat the patients, we give them their cells, and then shortly after they can go back home. And that works for the stem cell transplants, like you mentioned, and we're trying to move in that direction. As it stands right now, if you're having Carty therapy in Hamilton, you have to come and stay for 30 days, we put people up at the Staybridge and families and caregivers stay there.

**Dr. Bill Evans** 32:34

Well, it's not simple to get it up and running. I mentioned 13 centers in Canada, do stem cell and Carty and car t now Well, that's a change in the last yes decade from the things you were mentioned, you were the second in the country seem to remember when there were only about three or four centers that were capable, which created a lot of challenges about selecting which patients have access and and is that still an issue now that there's more patients than slots to put them into for treatment?

**Dr. Ronan Foley** 33:09

I mean, I think that's correct. Now, you know, some of the barriers to Carty. So, you know, Hamilton's got this amazing new therapy, but if you live eight hours away, and you might be eligible, the thoughts of it might be I don't want to leave my home for for for 30 days and go live in Hamilton. So, you know, Bill, I don't know what's out there, what we're still learning about access, but there's clearly access issues. But we kind of need a plan B for the people that don't, aren't able to get down here and commit to the whole the whole journey or don't want to quite frankly. So there's a lot of fear and anxiety about about doing it.

**Dr. Bill Evans** 33:56

And I imagine there's some parts of our country that just don't have the resources to put in place like some of our smaller provinces and can't, you can all have car T centers, so they're going to have to send their patients somewhere. And it raises some very interesting and challenging ethical issues to think about how you make decisions for patients who have the more remotely and then may have financial barriers to coming to live in another city for a period of time with their family while they go through a therapy like this. Wanted to step back a couple of steps. So I I don't think the manufacturing process is 100% perfect right now. And then when it started, perhaps a more modest percentage were actually successful or they're getting up in the 90% sort of range or

**Dr. Ronan Foley** 34:46

I know that they are it is somewhat product specific. So some some products struggle a bit more and what you're talking about is 100% Right. Products that haven't met At the specifications so. So to get the product approved by Health Canada, it has to meet the certain specifications, something we call a CLT C COA or certificate of analysis. And it, it's multiple points with very specific cut off points. And if you miss just one single cut off, the product is out of spec. And so it's what's called a manufacturing failure. And then either you have to go back and get more cells try again, or in some instances, you can actually give the product sort of in a research type of way where they still make the product available. And you can try, but but it is out of spec.

**Dr. Bill Evans** 35:41

It's probably around 90 to 95%. Now, if the products are successful, it must be very upsetting to say, yes, yes, you prep them for all this harvest or sells, you send them off, they're waiting expectantly to get their treatment, which, if not curative, at least has the promise of a very long remission a little bit. And then you have to tell them that they couldn't grow yourselves

**Dr. Ronan Foley** 36:04

or so well. And of course, as you know, you we prepare people for this ahead of time, right that this could happen. And here's the numbers. But, but you're right, the stakes are high, and the emotions are high. You know, the thing about car T is it's a remarkably effective therapy, but it's not 100%. So, you know, certainly people that go into deep remission for a long time, that that's what they were thinking, but there are still people where it doesn't work. And that can feel devastating, because you are all set up for this remarkable thing. And then push. Yeah, yeah. So your, your whole. So again, that's right, you try to you try to set the expectations with the understanding, this isn't 100%, this could fail, we could be looking each other in the eye and two months, and I'm telling you that it didn't work. So that least people are prepared for that.

**Dr. Bill Evans** 36:59

And in car T cells have some interesting potential side effects to their on unusual for therapies that we offer for other therapies for myeloma or other therapies for other cancers. One of them because it works so well can causes cytokine release syndrome, and maybe just explain what that is. And I think early on, it was kind of a frightening thing for clinicians, and not to mention patients, but that you'd learn to manage that, perhaps a little more expectedly and jumping on it earlier. So it's not such a big deal anymore. But then there's also neurological potential side effects. And this can cause I think people will be interested to hear but both of those. Yeah,

**Dr. Ronan Foley** 37:45

no, those are. Those are big challenges for patients going through car T. I mean, essentially, to to explain it, you have a car T cell that's kind of loaded up with this special receptor that can identify the myeloma cell, they come together in the car, T cell kills it. But every time it kills, there's a little bit of what you said, a cytokine is released. And so so the cytokines get released on the killing that cell then divides and divides and divides, it becomes 1000 cells or 10,000. Cells, killing tumors very quickly within hours. And so it's it's like a chain reaction in the nuclear thing that the over 12 hours, you can have this massive expansion and massive killing almost too quickly. And of course, you don't We don't have the control on that at this point. I mean, the cells go in and they start cooking. And if they want to go in that direction, they will. And so all those cytokines, build up, build up, just like you said, a cytokine release syndrome, and that can make people very sick. So their blood pressure can become low, they develop temperatures up in the 40s. They can have liver failure. And very oftentimes they have to go to the intensive care unit for pressors. And sometimes intubated. So you know, within two or three days you can have somebody who's you know, sitting in bed stable in and being in the ICU, in its worst scenario, that only happens about somewhere five to 10%. But but it's still, you know, you need a hospital has an ICU. And then sometimes in those bad cases, just like you said, it affects your brain. And patients stop talking. It's almost like they've had a stroke. And they can go become obtunded. And they can develop a demon in the brain, some very serious things. And, you know, so we're aware Have it you know, we're the whole teams at the ready when a car T patient comes in, we have an antidote called Tocilizumab. Another somewhat expensive drug. But recognizing when this starts and getting on it right away is is critical. So so all eyes are on the patient. And early intervention gets away from those tragic cases in the ICU where, you know, and people have passed away from that. So it's, it's a devastating thing, what it happens.

**Dr. Bill Evans** 40:31

But getting on it early with that particular drug, yes, seems to be the answer. Yes, most cases and,

**Dr. Ronan Foley** 40:37

and good old corticosteroids, steroids, dexamethasone, and it's recognizing it's starting. So it's really having that education baked into the system with you know, and you know, Bill, it could be a nurse, it could be a house staff, it could be an r1 resident, I mean, whoever's sort of involved in the case. So we have very explicit algorithms for car T patients. In fact, car T patients have a special band on their on their arms to tell tell of somebody that they are car T. And that then will ignite an algorithm that rapidly gets on top of it. So that's what the education was, was huge in setting the table.

**Dr. Bill Evans** 41:20

And one of the things I find interesting and a bit challenging and trying to keep up with the literature, there are a lot of new car T cell products. So I guess we had Korea initially and yes, Carta. And now we have Ida cell and need to sell some other cells. So and so. And so. So the cell, yes. And then how do you decide who gets what? And are we administering all these different types of car T cells in a single center? Does a center select one or two and work with those manufacturers? How's this playing right now?

**Dr. Ronan Foley** 42:00

Well, it Juravinski we're, we're using them all for? And but you're right, it kind of creates some challenges, because there are product specific side effects. Perhaps the product is handled differently based on on, you know, what the company recommends for it? So there's several sets of books with, you know, one for each product. And, you know, I do wonder to your point, I mean, how far can can that go? You know, is there a red line of, okay, well, we can't have 40 different products, you know, there has to be some consistency or some odd you know, some it has to be homogeneous to some degree. But they all they all do have their their different quirks and you have to have that experience, which which product it is me may change how you treat it. And, you know, of course, this car T is the dawn of a new era, and it's coming in many diseases now, lymphoma, myeloma, but other ones, that may it may come into solid cancer tumors as well, ocular melanomas and things like that.

**Dr. Bill Evans** 43:08

So it really is changing the face of, of cancer therapy hugely. And it also changes what you need a hacer setter to provide care. It seems to me it's like a shifting pendulum. I've seen over my career where initially, so much was done in hospital because we needed to support the patients because we had chemotherapy, nothing else and it was all quite sickening, fair, and then we got good antiemetics and we could move a lot of the chemotherapy to help patients and then along came oral drugs and the oral drugs were easy to deliver in the outpatient so he kind of to canted things out of even the cancer side or in large measure, it could just do it in the clinic and prescribe it me took it at home and how he got the pendulum swinging back towards the need for 30 days in hospital for car T cell therapy. So it can never quite predict the future.

**Dr. Ronan Foley** 44:06

No, no, no but but you know, to your point there are efforts to try and transition this to outpatient you know, various instances of the journey there are times where a patient could be safely at home but it's all about safety and

**Dr. Bill Evans** 44:21

I even hear about off the shelf car T which is something else that may come along if people can develop the products we might see this whole I guess manufacturing process and that time delay right. So I guess we'll just have to wait and and see what happens and

**Dr. Ronan Foley** 44:38

for sure that is one of the biggest limitation of car T is it takes time. Start to finish is going flat out is about 60 days, which for somebody with a malignancy that can be along 60 days especially if their diseases unstable. So so the products you talk about that are pre made kind of off the shelf often can be given within 48 hours, you know, we'll we'll solve that issue. The only issue there is if the cells aren't the patient's own cells, then there's always a risk of, of a graft versus host, the sort of process which which is, can be terrible.

**Dr. Bill Evans** 45:17

So we have the complexities of car T cells in the multiple products. Now, we didn't talk about it, basically, because I can't pronounce the names of most of the drugs. But for all those proteasome inhibitors and imines, there are second and third generation, probably fourth generation drugs that can be used and, and it gets tremendously confusing. And they're often used in combination. So he had so many acronyms, death, swinging around up there, that it's a bit overwhelming. And I'm sure it's overwhelming to funders. And I guess one of the things that's recently appeared in the Canadian scene as the an initiative by what was called Kadath, Canadian agency for drugs and therapeutics and health. Now, that Canadian drug agency easier to say, right, our provisional funding algorithms where they bring together practitioners, I gather five or six oncologists who review the evidence and also bring their experience to bear on what should be the sequence. And what do you think of the process that he had been involved in it for myeloma is certainly would be helpful to have a roadmap that had all the signposts clearly marked as to what's the next step? Well,

**Dr. Ronan Foley** 46:38

I think it's clearly an important thing, and what you know, what, what Kadath has done in terms of laying out the sequence in the sequence of treatment options? And again, it comes back to, you know, are you first line? Are you second line, third line, fourth line, sometimes fifth line? You know, what should you be doing? Because it's, it's unbelievably complicated. It's a success story. But there's so many drugs, so many combinations, there's, uh, you know, hundreds to 1000s of clinical trials that you're, you know, as always, that's what we're basing our decisions on. And so that, as you said, there was, you know, expert review. And keeping in mind, the Canadian scene, you know, what, what things are available to Canadian practitioners? And I think it's very good. I think it's very comprehensive, very accurate. I mean, it may change in six months, it may change in another six months. But no, I think I think that's been important. I think the challenge is educating physicians across the country who may be in very different situations. I mean, those of us that work in academic centers are heavily exposed to the trials and rounds and things like that. But if you're, you know, if you're working in a remote place, and you're seeing breast cancer and renal cancer in myeloma, it'd be very hard to, to, to, to fit, you know, keep up to that level of care, but that, but that's important. So education becomes huge groups like myeloma, Canada, that, you know, our full court press on educating the whole country in these types of things. So, and even sometimes pharma themselves go out and give educational talks, which are very useful, you know, provided their fair and transparent about it. But education is a big is a big, big piece.

**Dr. Bill Evans** 48:33

So you touched on the topic of clinical trials, which is where he's gonna go to, probably next and last. Because I know the Juravinski is very active in clinical trials, and you've been a leader in clinical trials of car T cells. What's happening there now, and maybe a little bit of prognostication. Where do you think this is gonna go? And what's it look like in 510 years? Yeah.

**Dr. Ronan Foley** 48:59

Well, the clinical trials are exploding mica, you know, she had so many drugs, and, you know, infinite numbers of combinations that, you know, all driven by science, I mean, they all have sort of a mechanistic rationale to them. But there's a lot of trials. And, you know, as you know, some of them are phase three studies. So you're really confirming that a drug that looks very promising. Some of them are just trying out some new drugs, and some of them are first in human, they're trying drugs that have never been tried before. So, so it's a challenge for us, you know, which trials should we be doing? Or where should we be focused? Kind of, we kind of have a blend of, of different types. But that's one of the challenges for the research team up of Juravinski is, you know, should we should we kind of be focused on one type of trial, the end of the day, we we weren't the trials so that we learned but we really want the trials as opportunity He's for patients who go to get access to drugs they otherwise wouldn't in Canada. So we we always keep our eye on that.

**Dr. Bill Evans** 50:06

And your prognostication for five and 10 years from now? Well,

**Dr. Ronan Foley** 50:11

you know, I think I think you're alluding to cure. So, you know, cure is a tough a tough thing to talk about in that, you know, how long do you have to wait before you've you've done it, you know? So what I think is happening is a test we talked about before, it's called MRD, or minimal residual disease, people who are MRD, negative, we think those are the ones that may in time be cured. The myeloma does not come back. And it has always come back. So when it stopped when it when it happens, that it's not coming back. You'll that will kind of be the moment where you realize, Wow, we may have cured people. Are we there yet? I don't think so. Between the Dara tumor map that we talked about in the car T, I believe there will be some cures. And so just will take time to see that. That's kind of going out there a little bit. But But no, in terms of your question. It's a new era. And it's really exciting stuff. But a lot of moving pieces

**Dr. Bill Evans** 51:16

are certainly a very hopeful era, very hopeful. And I think for anyone listening who either has multiple myeloma or a family member has multiple myeloma, you're hearing how much the treatment scene has changed, particularly in recent times, how it's very positive and therapies are really yielding a lot of success and maybe cures just a little distance away at the moment, but perhaps not too far distance. So it's been a really interesting conversation. Dr. Foley, really appreciate your time, your expertise and sharing that with us. And is one of the purposes of cancer assistance programs to bring practical aids to patients, whether it's travel to and from the cancer center, free equipment loans, but this podcast is practical aid to help people who are out there who are confronting a type of malignancy and want to know what it's about and how it's being treated. And we hope that this podcast has shed light on the topic of multiple myeloma, do what affect the Hutton family and Family Fund funds this podcast and we couldn't do it without them. So, again, thank you very much for your time today and to our listeners. Thank you for listening. And just a reminder, we've done over 50 podcasts so they're still available and cancer assess.ca. You can go back and into the vault, so to speak and find any number of podcasts on various tumor types, supportive care services in our region, amongst other topics. So thank you for listening and we'll look forward to talking to you next month.

**Narrator** 53:00

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