Breaking Barriers in Lung Cancer: New Treatments, New Hope with Dr. Peter

**Speaker 1** 00:02

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**Dr. Bill Evans** 00:20

Well, welcome to the cancer assist podcast with your host, Dr Bill Evans, and today we're going to be talking with an expert in lung cancer. And lung cancer is a really important issue for us to discuss. But before we get into it, I wanted to say a few words about the cancer Assistance Program, which provides a variety of free services to patients in the Hamilton area. Amongst other things, free rides, free access to some nutritional supports and incontinence supplies. And what I find really, really exciting is they can provide you a lot of different pieces of equipment that could keep you safe and moving around your house more easily or getting out. So you have wheelchairs and ambulators and canes and commode chairs, a variety of pieces of equipment that are really helpful to individuals who are facing cancer and have some limitations. And you can borrow them for as long as you you need them, and it's all free. So those are services of the cancer Assistance Program. And of course, the podcasts are part of the services and providing educational resources to individuals who are facing cancer. So today we're going to tackle a big problem. It's called lung cancer, and it is a big problem. It's still the biggest cause of cancer death in Canada. I was looking at some stats this morning, something in excess of 31,000 individuals who will experience or be diagnosed with lung cancer this year, and unfortunately, a pretty high proportion of them will pass away. And I've seen in my own career quite a change, and we're going to hear about that from my special guest, Dr Peter Ellis. He's a medical oncologist at the Juravinski Cancer Center, and he's made that the focus of his research. And Peter, welcome to the program.

**Speaker 2** 02:08

Well, thanks Bill, and thanks for the invitation to come on and talk and to really provide an update on lung cancer, because it's just a very exciting time for someone that's treating lung cancer. It

**Dr. Bill Evans** 02:19

really is. I'm just in awe of how much it's changed, actually a little bit overwhelmed because there's so many drugs now, compared to when I was treating lung cancer early on in my career. But before we get into the lung cancer per se, tell us a little bit about your personal story. I know you came from Down Under and came to Canada sometime in the 2000s I can't remember the exact date, but how did you get to be a physician in the first place? And then maybe how you got to be interested in lung cancer? So

**Speaker 2** 02:50

some time ago, one of my colleagues gave a talk at the Cancer Center Research Day that was entitled The lung unwinding road. And I, you know, it really paralleled my story. So I'm honest with you, when I was 16, I wanted to fly jet planes, and I'd always been the top of my class, and I thought to myself, I might as well, you know, apply for a scholarship, because why not get paid to finish high school? And so I went for this testing, and they told me that I didn't have the aptitude, and I was devastated. And so then I went away, and I thought, Okay, well, let's be serious about what I want to do. And so I decided that I was going to go into medicine. And it was a very, you know, to me, going into medicine was very altruistic thing. It was about helping people. And I got to the end of my medical school. So medical school in Australia at the time was straight out of high school. And I thought to myself, I don't want to do another exam ever. And so I got to my intern year, which was the sort of post graduation, pre licensing year in Australia, and I very quickly realized that I didn't want to do family medicine, and that was the only course that I could have taken at the time that didn't involve exams. And so I realized I was going to have to do a few exams. And to cut a long story short, 10 years later, training in internal medicine, medical oncology, a master's and a PhD. I finally finished my training.

**Dr. Bill Evans** 04:15

I gather you have a PhD in epidemiology. I think is that not correct?

**Speaker 2** 04:20

So I have a master's in clinical epidemiology and a PhD in Health Service Research, okay? And so I was, wasn't looking for job overseas, and I was, I've gone for a few jobs, and because I had taken a different track to a lot of my colleagues back in Australia, I stood out. And unfortunately, I stood out for the wrong reasons. And so I was having a little bit of difficulty in finding a job. And I saw this job at McMaster University, which offered everything I had was interested in, and sent my information, thinking, Yeah, well, that's the last I'll hear about that. And I got these replies back. And the CEO the Cancer Center at the time was George Broman, who was one of the leaders and pioneers in the in the concepts, of course. Clinical Epidemiology and evidence based medicine. And George is emailing me, and I'm thinking, Oh, wow. So I came March Break in 2000 and spent some time, spent a week here, went through some an interview process, and then came back about four or five months later with a job, really. Most of that was just sorting out immigration issues?

**Dr. Bill Evans** 05:20

Well, I remember some of those immigration issues because I was at the Provincial Office of Cancer Care Ontario, and I was one of the people who had to process your application through the College of Physicians and Surgeons, and it wasn't easy in those days, but with your excellent training and the Masters and PhD, it seemed ridiculous not to welcome you to Canada and take advantage of all your knowledge and skills in our environment. So we made it happen. We're glad you ended up in Canada.

**Speaker 2** 05:47

And you know, I came thinking that breast cancer was going to be one of my, my sort of key interests, and I still treat breast cancer. But I looked, I got it to the cancer center, and I looked around, and I looked at the people that were there who really were experts in breast cancer. And I was trying to find where would my niche be, and we would buy opportunity to contribute from a research perspective, and lung cancer was a secondary interest at the time, and yet, you know, that's where the opportunities were. And so I just went from strength to strength in in like treating lung cancer Well, got involved with a guideline group, which you were chairing at the time and for which I took over when you stepped down.

**Dr. Bill Evans** 06:25

Well, things have changed hugely since that time. I as I said at the beginning, I'm almost awestruck by the amount of change, and it's brought a lot of hope for lung cancer patients. And that's what we want to want to talk about today, by the way, that's a very interesting path you took. It is a winding road, but you're not yet the most interesting guest I had one who said he started as wanting to be a hot tub salesman. So my jet aircraft is right up there with hot tub salesmen. I think that as a way of thinking, you're going to have a career and end up in medicine and doing oncology. So we're the better for your choice. So when I reflect back on treating lung cancer, and this is starting sort of mid to late 70s, gosh, it was pretty simple and not very effective, we're basically two types of lung cancer, basically determined by how cells look like down the microscope. They were small cells, so therefore they were called small cell lung cancer, and then different kinds of cells that we call non small cell lung cancer. Really creative classification system, and those could be subdivided into some other subtypes of squamous and non squamous and large cell adenocarcinoma and so on, but the drugs we had were particularly ineffective, and they were quite nauseating and caused other side effects. So that really was a question, are we helping or harming individuals back in those days? But we tried, and we kept trying newer combinations, and eventually some even showed some survival benefit, and I was able, with colleagues in Ottawa, to show they're even cost effective, which surprised everybody. But those were the old days, and things have evolved so hugely from there, and part of it's understanding the biology of lung cancer and the variance of the oncogenic drivers in in the cancer cells, and maybe you could pick the story up there and how it's, how it's been transformative. It's,

**Speaker 2** 08:29

it's a really good point, I think that, and I'm not one to write off chemotherapy completely, because I think chemotherapy has a role. And we know that people with lung cancer are often feel very unwell. They often have a lot of symptoms, and the best way to improve the way they feel is to control their cancer. And I think that any treatment that has some ability to control their cancer is going to be helpful in terms of improving quality of life. And if that can help people to live longer, then I think that that's a win situation. You obviously have to balance that against the potential side effects of treatment. But I think we probably have got a lot better at managing side effects. But the really exciting sort of things have happened in the last probably 15 years, and people have grown or the understanding of lung cancer has grown enormously, and there's been a lot of research at a basic science level, and we've come to understand that that there are subgroups of lung cancer that are driven by what we'll call molecular abnormalities. So these are abnormal genes that things that have gone wrong in the in the cell, that then are driving the growth of the cancer, and the technology for developing new drugs has also changed enormously, and so the ability to find drugs that will turn off that particular gene that's driving the growth of cancer is is just amazing. And you would probably remember as well, Bill, I would say to people you know. Even with treatment that half these people that I was seeing 20 years ago would probably be dead at a year, and maybe 10 or 20% of them might live beyond two years, and now we're talking about 20% of people living five years. That's all comers with stage four lung cancer, if we look at patients that have a molecular abnormality of a gene called ALK, these people have some fantastic options for treatment. Last year, at the American Society for Clinical Oncology meeting, they provided an update on a trial of a drug called lolatinib. So this is a drug that that targets or turns off the ALK gene. And in this particular disease, 60% of people are still on their first or their initial therapy at five years, meaning that that you're probably talking about half of these people living eight or more years. And it is phenomenal for a disease that we used to think, you know you'd be doing well if you lived more than a year. And there was so much nihilism about treating lung cancer that people didn't even necessarily get sent to see somebody like me, because it was like, Oh, you got lung cancer. It's no use. That's

**Dr. Bill Evans** 11:13

absolutely the case. And I remember when I started the trial general and we saw a lot of lung cancer there, because it had a very large thoracic surgical group, so it attracted a lot of referrals. And I was told by colleagues, repetitively, Bill, don't you think the best thing is just to send them on a holiday or tell them to take a vacation in Florida? And that was a level of enthusiasm for managing lung cancer. And one of my colleagues I shared an office with, said, Bill, you're a nice guy, but I just don't understand why you do what you do. And it's persistence and trying to treat a very difficult disease, and the increased understanding of the biology that's really led us to the part where you can talk about an average survival time of eight years with a subtype of lung cancer, like that's that's incredible, and we keep inching forward, it seems to me. And there's so many of these oncogenic or cancer driving genes that are turned on, and of course, to to the average lay person is going to sound like alphabet soup or something, you know, the EGFR, the ALK, the RET, entrack, met, etc. So what I'm trying to get across is that there are a lot of different subtypes of lung cancer now compared to when we started, which was what I was trying to explain on basically two broad types and and in fact, now we can slice and dice them into these molecular forms and test for them, and then there's a specific, targeted therapy that you can prescribe that is far more specific in its action and generally less toxic. I think too,

**Speaker 2** 12:56

that's definitely true. So there are probably at least eight or nine molecularly defined subtypes of lung cancer. There are varying series that report different percentages, but over half of people that have an adenocarcinoma, which is probably about 70% of lung cancers, so nearly half of those people will have some underlying abnormal gene driving the growth of their cancer. Now, KRAS is the most common, and unfortunately, we've been a bit less successful in getting therapies that target KRAS, although some are in development, and there's so many drugs that are coming through that I think that has to improve. But there's probably 30 or 35% of people that have an underlying molecular abnormality where the best initial therapy is going to be an oral therapy.

**Dr. Bill Evans** 13:48

Now, you mentioned there's still a place for for chemotherapy, and we also have to talk about immunotherapy. So this is where it gets really complicated. It seems to me, the decision making process about when you choose what and maybe in our conversation, the place to go next might be to talk about immunotherapy, and then try and link all those three different types of therapies together,

**Speaker 2** 14:14

because you can slice and dice lung cancer in multiple ways. You can look at the type of lung cancer. So under the microscope, is it a squamous cancer? Is it a everything else we call non squamous but most of those are adenocarcinomas. You can look at whether there's an underlying molecular abnormality that we've talked about, and then you can look at whether cancers express a signal called program death one or PD one that helps the cancer hide from the immune system. And these immunotherapies, in some ways, are a very simple concept, and we've known for many, many years that cancers are able to hide or escape from the immune system. Now our body's immune system is meant to. To see things that are meant to be in your body and ignore them and attack things that aren't meant to be in your body. So bacteria, or, you know, in cancer as well. But the cancers are able to send out signals to the immune system that, instead of being considered an enemy, it says, Hey, I'm a friend. Leave me alone. And at the simplest level, these immunotherapies block that signal. So instead of the cancer cell being able to hide from the immune system, all of a sudden, your body's immune system can now see this cancer cell as being something that shouldn't be there, and they attack it. And in some forms of lung cancer, so ones that have a high level of this signal called PD one, the immunotherapy represents the best treatment on its own. In others where there's a little less expression of this signal, PD one, then or Pdl, one, the cancer isn't as effectively treated by immunotherapy on its own. And so what we know then is combining the immunotherapy with chemotherapy becomes a better treatment than chemotherapy on its own. And so when you were treating lung cancer, and even when I started treating lung cancer, we might have said to people, you know, 20 or 30% of these people are going to have a meaningful shrinkage of their cancer with with therapy. Now there'd be a group that would have their cancer sort of stabilize, and there'd be people where their cancer would grow despite treatment. Now it's about 50% of people will have a meaningful shrinkage of their cancer. The amount of time the cancer is kept under control is now longer, and survival has not quite doubled, but the average survival, you know, is now up around two years, even in people that don't have these molecular targeted lung cancer. So I think there's now a lot of reason, you know, to to think that we can have a meaningful impact on people's lives even when they have stage four lung cancer. And I think it's very important that people get to see, you know, someone that's experienced in treating lung cancer, rather than to be told, Well, you've got stage four lung cancer and you're going to die and go away and just get your affairs in order. That's

**Dr. Bill Evans** 17:14

a really important message for people to hear, because I do wonder how many people, perhaps, in you know, more remote areas, perhaps family physicians, perhaps aren't aware that there's been progress in lung cancer. They need to hear that there's been this kind of progress. It's a fascinating story, because I think we suspected that the immune system should be doing something, and occasionally it's given us clues, like we do, see rarely regression of some cancers, like more like melanoma or kidney cancer. They people have seen these things happen and then, well, that's could only be by an immune mechanism. And of course, there is the work of was a surgeon, Cooley, who created a mixture of various bacterial things to stimulate the immune system and reported some regressions of cancers way back in time, but it did stimulate thoracic surgeons to try and use some immunotherapy in the form of BCG and coriobacterium Parvum and Pseudomonas vaccine, various things that we tried back then, but we didn't understand the biology. It's really been the understanding of the biology and how, how this PDL one, and it's ligand, or PD one, and it's ligand work and and how it basically shuts down our immune system, or how the cancers are able to shut down our immune system. And now we can turn the switch the other way and get the immune system, the T cells, working to kill the cancer cells it it's a phenomenal piece of research earned Allison a Nobel Prize. So pretty, pretty, fine piece of work. But are we? Are there newer strategies in the immune area? Because there are multiple of the multiple types of immune checkpoint inhibitors, as I understand it, and we're working with just a couple of them at

**Speaker 2** 19:05

the moment. So there are, there's a series of of switches that will regulate the immune system, either by turning the immune system on or turning the immune system off. And there's a lot of work that is going on trying to add on to the varying immune therapies that are that are currently sort of licensed, then in practice, unfortunately, to date, they haven't been that successful. So as an example, there was a target called tidit, which is another inhibitory, or, you know, signal in the immune system, and there's now several sort of drugs that work by blocking that signaling that have not been able to improve on the results of just an immune sort of inhibitor, like pembrolizumab. But there's new technology, and we're looking now at. Are what are called bispecific antibodies. So a drug like pembrolizumab is what's called a monoclonal antibody. So it's an antibody. So that's a that a way that the body signals varying cells in the body, like T cells, and so the the newer technology has now developed these drugs that actually work by turning on or turning off two different signals at once. And the idea then you can, you know, with that one drug, you're bringing together or blocking these two separate signals simultaneously. And so there's now interest in whether or not that can be more effective. So I was just at a meeting over the weekend where there is one of the companies that have several of these compounds that one of them blocks, PDL one or PD one and and tid another one blocks, both PD one and then another sort of signal in the immune system called CTLA four. Now you potentially add to side effects by combining these, these drugs together. So I think we're going to need to learn about what's the appropriate dose. We're going to need to learn about how to manage some, you know, some of the side effects, you know, in small cell lung cancer that we're not talking we haven't talked about, there are. There's a very exciting drug that is what's called a bite. So it's called a bispecific T cell engager, and that works by bringing together T cell with a cancer cell, and the compound works by as the sort of the intermediary. And again, it's another way of trying to more effectively activate the immune system to specifically attack those cancer cells, and this is a drug which is available through compassionate programs across the province, will be hopefully publicly funded in the near future, but there's always delays In that process with the drug funding,

**Dr. Bill Evans** 22:01

not in Canada. Surely we could talk about that, couldn't we? And actually we have on this podcast, there are challenges, but I think for our listeners, they might be getting a bit overwhelmed by the complexity of all this. And it is complex, and hence there's a lot of testing that needs to be done to decide whether an individual with a particular lung cancer has some of these genetic markers, is expressing certain immunological features on their cancer. And then physicians need to contemplate the extent of disease, having done all the staging procedures, and come up with a plan, and maybe you could talk a little bit about how that happens.

**Speaker 2** 22:45

So again, if we think back two decades, all we asked our pathologists was to say, is this small cell lung cancer, and if it wasn't small cell lung cancer, then everything else was non small cell lung cancer. You needed just a few cells, so you needed very little tissue. And if you jump forward to today, we're doing complex testing on these patients. So the first thing we need to understand is what type of non small cell lung cancer it is. And so that takes a few, sort of a few samples of tissue that the pathologist will need to look at to separate out squamous cancers and adenocarcinomas, then we want to know, do these cancers have you know, do they express this marker called PDL one or program death one ligand, because that helps in sorting out about immunotherapy on its own, or immunotherapy with chemotherapy. And then we need to understand about whether or not patients have these underlying abnormal genes or molecular markers, and that requires really complex testing, something that's called next generation sequencing. So the technology is such that you can take a sample and you can in the molecular biologists will will hate me for saying this. You can put it in a machine and it'll spit out an answer several days later. But what goes on inside the machine is complicated, testing where they're looking at analyzing the DNA of those cancer samples to determine whether common genes are abnormal or mutated, and our testing routinely looks at eight genes. There are some places that would test a few additional genes that might help understand about whether or not someone's cancer may have some level of resistance to the treatments that we talk about, and then you can look at the technology that's been developed, where they can analyze up to 300 or 350 different genes or molecular abnormalities. Now, do you need that? That's debatable, but the technology is there to do that. And so you can. Imagine that we've gone from needing just a few sort of cancer cells under a microscope to a situation where we need a lot more tissue. And then you have to think about what happens so in Hamilton, for instance, fortunately, most of our patients come through the lung diagnostic assessment program at St Joseph's Hospital, which has really been a great sort of step forward in coordinating care. And so the pathologists that report, you know, the for lung cancer, are largely based there at St Joseph's Hospital. And certainly when you're talking about getting samples for this molecular testing, it has to go through one of those pathologists. So the first sort of steps in all of that testing are in one place. But then the molecular testing is now done at the Juravinski hospital. So then it has to go to a pathologist at St Joseph's, who has to look at it, mark out the areas that need to be tested, and then send all of it to up to the Juravinski where the testing is done. And this, and it gets even more complicated. So if you were diagnosed with lung cancer and had your procedures done at the Juravinski. It's probably going to be sent down to St Joseph's hospital to be looked at, then it's going to get sent back to the Juravinski to have the molecular testing. And you can imagine then that these processes take time. And so the probably one of the biggest challenges we face is the time that it takes to get some of this testing done. And it, you know, the lab says their turnaround would be two weeks, but if you add that's two weeks from when they get the sample. And so, you know, if your cancer has traveled around Hamilton to multiple different places, first it might be three or four weeks. And in some places, you know, if you're at Cambridge or Kitchener or Guelph, then they're going to have the pathologist do some initial testing there, and then it's going to get sent to Hamilton or to Brampton or to Toronto. So it takes time, and one of the biggest, I think, concerns is, is that time that and then the potential delays in getting treatment started, because you need all of this information to be able to make the best treatments for each individual patient,

**Dr. Bill Evans** 27:03

and that's got to be hugely stressful time for patients, as they're waiting to hear and thinking that they got something that's growing in their in their body so well, I guess that's a challenge to figure out how to make it all work more efficiently. I feel like we've been drinking from a fire hose with all these terminologies and new forms of therapy. So we'll take a little break now to hear from the cancer Assistance Program, and we'll be right back to talk a little more about the management of lung cancer, particularly in the earlier stages disease, where we apply some of the learnings from advanced disease and bring them forward to individuals who have a better prognosis, but still are at risk of their disease recurring. So we'll be back in a moment.

**Speaker 1** 27:45

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**Dr. Bill Evans** 28:27

So we're back with Dr Peter Ellis, talking about lung cancer and some of the amazing changes that have happened in terms of treatment of advanced disease. When we started to talk Peter, we didn't talk too much about sort of causes of lung cancer, I think most people are aware that smoking is the commonest cause, and we generally say somewhere upwards of 80, 85% of lung cancers caused by smoking, although I've heard lower percentage and the prevalence of smoking and the incidence of lung cancer are are both declining, which are positive things, but still, there's a lot of individuals who continue to smoke. And even amongst those who stop smoking, they can remain at risk for a very, very long period of time, the age group, the sex distribution, talk about some of those things for our audience.

**Speaker 2** 29:18

So lung cancer increases with age. So when you look at the the absolute numbers of lung cancer, it's uncommon in young people, and progressively increases, you know, up until probably the mid 70s, and then the rates sort of start to drop off, because at that point, people are dying from other things like heart attacks and strokes. But what we've seen is that there's a an increase, sort of, maybe not A, not an increase in number, but there's certainly a greater awareness that people who get lung cancer at a young age are often not smokers, and so these are people that more commonly have these underlying molecular abnormalities. They can be very young. So. You know, I have somebody in my practice, at the moment, in their 30s with stage four lung cancer who does have one of these molecular abnormalities. And so I think it's important to recognize that, firstly, not everybody who gets lung cancer has smoked, and those people may have different forms of lung cancer. And I think that smoking, as you said, is the largest cause of lung cancer, and we need to be very careful, and we need to be as very important point is to not put blame on people. Unfortunately, you know, in the past, the I the thought was there that people brought this on themselves, that people smoked, they got lung cancer, and it's their own fault, and we need we've got to be past that. You know, smoking is a highly addictive sort of behavior. Smoking was far more acceptable in the population than it may be today, and even if people are current smokers, these are people who need care. These are people who need treatment and will benefit from treatment as well. You know, I think really wants to try to ensure that every effort is made to look at smoking cessation, and I think that's trying to encourage the population to stop smoking, but to encourage our patients to stop smoking as well. And we know, and big bugbear of yours, Bill, we know that even if you've developed cancer, and not just lung cancer, that stopping smoking will reduce the complications of treatment, reduce things like infection. Smoking induces a whole lot of enzymes that can break down our treatments faster. And so people who smoke may effectively get less therapy, because, you know, the compounds from their smoking are breaking their drugs down faster. And so there's lots of reasons why we think that stopping smoking is a good thing, and there's some data that just say that people who stop smoking live longer as well. So I think that's got to be a focus, not only of smoking cessation in the population, but taking whatever opportunity we have to encourage people to stop

**Dr. Bill Evans** 32:12

smoking. Well, thank you for saying that, because it is a very important message. And I think even amongst healthcare providers, there's often the view that so you have advanced lung cancer or some other type of cancer, and it's, it's too late. It's and we like to, I like to deliver the message, it's almost never too late. And it makes a difference to how effective our drugs work, how effective the radiation works. It makes a difference to the amount of toxicity from treatment. So really is important to try to help our patients to stop smoking, acknowledging that it is a really difficult thing to do because nicotine is highly, highly addictive, and so we have to be empathetic and supportive to the patients who are currently smoking and struggling to stop when we encourage them to do so for the better outcomes from their cancer treatment. Now, before the break, we talked about all the advances in lung cancer and advanced disease and the tendency in oncology generally, as we work in the advanced disease situation first and test out new strategies, new drugs, and if they work, then we tend to move them to earlier and earlier stages of of a disease. And that certainly happened in in lung cancer as well. And we could sort of back it up to stage three disease, or all the way to stage one with bad prognostic features. I'll throw that to you and know that you tackle it any way you want, because the evolution has been a little hasn't been exactly sequential, and in many respects, it probably was more adjuvant after people had resections than it was for Stage Three disease, but both are important stories to tell

**Speaker 2** 34:03

so so thanks for that bill. I mean, what we've seen is that the treatments that have been shown to result in longer survival, better quality of life in patients with stage four disease are now being have been tested and now being implemented in early stages of disease. So if we think about someone who has lung cancer, that might be a candidate for surgery, so that could be anyone from stage one to stage three, even then, we used to give these people chemotherapy after surgery, so they would go, they would have the surgery, you know, if not the really very tiny cancers, but people that had cancers more than four centimeters, or whether cancer had spread to lymph glands nearby, they would all be considered for chemotherapy. And again, there's an often quoted figure saying that that results in a 5% improvement in survival, but that's like putting everybody together. But if you think at the higher the stage, the more band of. So someone with stage three disease might have had as much as a 15% improvement in their survival from that. But again, you're right that these people still had high rates of recurrence. And so what we've seen more recently is a shift to using chemotherapy together with immunotherapy in these patients, and not giving it in the period after surgery, but giving it before surgery. And it's an interesting idea, because people are probably in a better shape at that point. And what these trials have shown is that by combining chemotherapy and immunotherapy together, firstly, one in four or one in five people by that when they go to surgery, their cancer will all be dead. That's called a a pathologic complete response. And that's the best thing, because that you can hope for, and that really identifies a group of people that have a really very good outcome, where you know their risk of recurrence is probably no more than about 10% but even in people who don't, who have a complete response. So who still have some cancer remaining? Those people still show a reduction in the risk of their cancer occurring. And as we follow these trials a little longer, it's showing people have improved survival. And so these treatments really have resulted in improvements for patients, and these treatments are being implemented. And so you know that then you have a challenge where with stage three disease, which is a very complex sort of disease, where some people aren't candidates to have surgery, their cancer is too extensive. It's wrapped around important structures, and those people would typically be given chemotherapy together with radiation. And again, probably the last five years, we're offering those people immunotherapy after their chemotherapy and radiation, because that, again, has been shown to improve survival. And then these molecularly defined lung cancers, like people that have mutations or abnormalities of the epidermal growth factor receptor gene, and even now, well, the data is coming anyway, for the ALK that giving these targeted therapies after chemotherapy and radiation can also significantly lower the risk of the cancer coming back at the American oncology meeting last year, they presented a trial where Patients were who went through chemotherapy and radiation, were given a drug called osimertinib, which is a drug that blocks this epidermal growth factor receptor. And at the end of the presentation, you know, there was a standing ovation from the room, like we're talking 6000 people in a room. Now, maybe the pharmaceutical company who sponsored the trial started that, but it nevertheless, it shows how important and how meaningful some of these new drugs can be in terms of improving outcomes for patients.

**Dr. Bill Evans** 37:49

Yeah, that that is, you know, phenomenal. And I, again, I'm sort of awestruck, because it's so such a dramatic change from the past and so much more hopeful, and it's taking all the learnings from more advanced disease and bringing them forward. But it does make decision making far more complicated. So you're involving surgeons and radiation oncologists and medical oncologists, and the surgeons are at St Joe's here in Hamilton, and the med oncs and the radons are up at the jurovinsky So how does all that decision making get made and the care coordinated?

**Speaker 2** 38:28

So most cancers will have meetings called multidisciplinary case conferencing. So this is a meeting. So for our lung group, we meet and it's done virtually, so we're meeting on still on Zoom, so our surgeons will join from St Joseph's. In fact, they can join from home, if they're working at home that day. You know the medical oncologist, the radiation oncologists, are there. We have a radiologist who provides a very important role in providing a detailed review of the of someone's CAT scan or PET scan, so that we can all look at these pictures and provide input into how to best manage it. Now there are times where pathology is a little bit unclear, and so we have a pathologist who regularly joins those meetings as well. So all of the people who are important in managing people with lung cancer take part in that meeting. And let's not forget our nurses. And nurses take pride in those meetings as well, because they're the ones that are going to be doing the the you know, the care, the coal face, so to speak. And so they have a crucial role too. And so people bring forward in some cases are fairly straightforward, but the cases where there's more than one discipline involved, or where there might be more than one option for treatment, those cases are brought forward. They're discussed, we review their scans, and then have a discussion about what's the best option. You know, do we agree 100% of the time? No, you don't get that. You never get hurt. Of us in agreement, but by and large, we'll get a consensus about what is the best way to try and move forward.

**Dr. Bill Evans** 40:07

And that's such a change from how practice existed in the past, and it tended to be if, you know, if a medical oncologist saw the patient first, they probably would get drugs, and they saw a radiation oncologist, and it was locally advanced disease, they'd get radiation and medoff would not be involved. So it's such a change, and I think it's such an important message for people to hear that the decision making is not all by one person, because none of us have all the knowledge and all the things that are happening, the results of all the trials, but it's by a group of people who are expert in lung cancer who put their minds together to try and come up with the best possible tailored therapy for the situation of the individual in front of them. I think that's a really important message for people to hear. I guess, another important message you used the word trial a while back, and important to touch on clinical trials, because people see them different ways. Some people see them as an opportunity and an opportunity to get some new treatment, something innovative that may be better than what the current standard. Other people see them as experimentation on them, and they don't really want to be part of an experiment because there's a lot of uncertainty associated with it. But if that's how we make advances, is through clinical trials, and maybe talk a bit about the trials that been going on in the joravinski and maybe something specific in the lung cancer area.

**Speaker 2** 41:36

So I think you're right that clinical trials are a very important part in practice. So just this weekend gone by, I was at the Canadian cancer trials group meeting. So this is a national organization that coordinates academic clinical trials in Canada, and then we were just musing about the fact of where we were 20 years ago and how the advances that have happened have happened because of well designed clinical trials, and I won't say all of those trials, but there have been very important practice changing trials that have been coordinated in Canada over the last two decades, some of which were run by you, Bill. And so trials really represent an important way in which we move forward. And there's a lot of misconceptions about clinical trials. You know, the focus of my PhD was really looking at understanding and and sort of attitudes towards clinical trials in in patients. And so the idea that maybe you'll be a guinea pig, maybe that's a little maybe that's not quite as prominent, but that's still there, that this is an experiment. And there are certainly some people who don't like the idea of of a clinical trial, because maybe there's more side effects. But the reality is, is that this is how we move forward our knowledge. And I always look at each patient to sort of say, Do I have a clinical trial that I could offer you and make sure people understand what their standard options are. And again, sometimes people think that a clinical trial is a placebo. So you some people will get something, and other people would get nothing. But it's always about looking at what would be the standard treatment, and mostly trying to build on from that. And so, you know, there is, there's rarely a situation where you would have a clinical trial looking at some treatment versus no treatment. And so we've been involved in a number of clinical trials. We've had a few sort of limitations with our clinical trials department, just in the very recent past, around resources, which I think is a common thing within the healthcare system. But we've, we've, we've had some important trials where we're going to be opening up very soon, and a very interesting clinical trial which is looking at trying to understand the importance of measuring DNA in the blood. So this is a trial where patients start standard, whatever their standard treatment is, and in this case, it's immunotherapy. And after a couple of cycles of treatment, they have a blood test. And we didn't when we talked before about molecular testing on next generation sequencing, we were talking more about tumors, but it's possible to take a blood sample and try and find DNA from the cancer in the blood and then do testing on that. So this is a sensitive test where if there is still tumor DNA in the blood at the end of six weeks, the idea is that maybe that person has some resistance to the treatment that you're getting. And so the trial is then looking at whether we should add chemotherapy onto that, or just continue the same immunotherapy, and then following people over time to see whether the group that had chemotherapy do better. And so that's a that's a really novel and interesting sort of way of using technology to see whether we can improve our understanding about how tumors behave, and whether we can modify treatment based on some of these tests.

**Dr. Bill Evans** 44:59

So that is real. Really an exciting concept. And I think one of the things that people should know about clinical trials as well is that you're really very carefully monitored during clinical trials, so you actually get a lot more supervision and attention to side effects and so on. And invariably, patients in clinical trials tend to do better. So it's another reason why people, when confronted with a suggestion from their physician that there's a trial that might be suitable in their situation, should really give it serious consideration. And it is, I think Canada is actually hit above its weight in contributing to advances in cancer medicine through the clinical trials that have been conducted in Canada. So love to see that continue. Well, we're sort of getting to the wrap up phase here. We've heard a lot of very positive things, and I'm going to give you a crystal ball now to gaze into and to maybe give some ideas the audience where you think things are going what? Wait? What might we expect? You've already alluded to a few, even talking most recently about liquid biopsies or sampling the blood to look for tumor DNA in cells, and talking about bites and but what do you think in the next if I bring you back in 10 years and I'm still doing podcasts, what will we talk about then? What would be the big advances I'll

**Speaker 2** 46:25

have retired in 10 years time? I think what? There was a really interesting proposal on the week, at the weekend, at the Canadian cancer trials group meeting, which was looking at fecal transplants. And there's probably a lot of people out there that are gonna go he didn't say fecal. Yes, I do. And so the the concept is that the the bacteria in the bowel have some effect in terms of regulating the immune response, and there are varying things that can affect the spectrum of bacteria that are there, including antibiotics, some chemotherapy, can do that as well. And so there's a lot of interest in studying the effect that that has. And now people are moving forward to say, Well, okay, maybe, maybe what we need to think about our pico transplant. So the concept is that you have stool that's donated from healthy donors, and it's it's packaged up into little capsules, and then the transplant part of it is you take a whole series of these capsules to then try to repopulate the normal bacteria in the bowel. And so this is being done, or the proposal is that this would be done in combination with chemotherapy and immunotherapy for people getting that treatment for lung cancer, and then half the people would get the the fecal transplant, and then half the people wouldn't, and then the idea is to see whether that actually improves the response to therapy. And I think that's a really novel and interesting sort of concept. I think what we're going to see is that there will be new and better drugs. The technology for developing drugs is has just changed. It used to be that people would stumble across a drug, you know, a compound, and then discover that it had affects the anti cancer effect.

**Dr. Bill Evans** 48:24

So a long way from the bark of trees of Taxol or Taxotere and those sorts of things.

**Speaker 2** 48:31

But now they do it in the reverse direction. Now they sort of say, well, okay, here's what we want to achieve. And then, you know, these very clever sort of chemists work backwards from the target to develop a compound which will be active against that target. And so there's so much work in trying to develop better and improve drugs that will overcome some of the resistance, you know, in patients that have the an abnormal gene called the epidermal growth factor receptor, we would be treating them, you know, with an oral drug. So now there are studies that look at combining chemotherapy together with that, or combining a second compound that is active against this epidermal growth factor receptor that may help prevent the development of resistance. And so I think we're going to see some of these, these drugs that are used as single agents, they're going to end up being used in combination with either new drugs or some of our existing therapies.

**Dr. Bill Evans** 49:34

So there's a lot that's been happening, and there's even more on the horizon that looks really exciting. One of our mutual colleagues from Vancouver actually said to me a couple of years ago, it's a great time to be a lung oncologist. I never thought I'd hear that, certainly back when I started and options were so limited for our patients, you couldn't have said it then, but it truly is a very hopeful time, and there's been so much that's changed, and I really want to thank you. Peter. For taking the time to elucidate these changes for our listeners and to give us some insight of where we may be going in the future. So thank you very much. Well,

**Speaker 2** 50:10

it was my pleasure. Thank you for the invitation, and thank you for the opportunity to just share some of this excitement. Oh,

**Dr. Bill Evans** 50:17

until the next time. Goodbye for now.

**Speaker 1** 50:22

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