Understanding Advanced Stage and Metastatic Cancer

Scott Redding: Welcome to the 3Ps of Cancer Podcast, where we'll discuss prevention, preparedness, and progress in cancer treatments and research, brought to you by the University of Michigan Rogel Cancer Center. I'm Scott Redding. We're here with Michigan Medicine, assistant professor of radiation oncology, Daniel Wall, to talk about advanced stage and metastatic cancer. Dr. Wall is a physician scientist specializing in cancers of the central nervous system. His research focuses on the development of new treatment strategies for brain tumors, and his laboratory group is especially interested in interactions between radiation and abnormal metabolism and glioblastoma. Welcome Dan.

Daniel Wall: Thank you, Scott. It's a pleasure to be here.

Scott Redding: I'd like to start off... Is there a difference between advanced stage and metastatic cancer?

Daniel Wall: Yeah, it's a good question because there are a lot of terms and terminology around cancer and a patient's cancer diagnosis, and it's important to understand what is what. Because doctors might use one or the other, and a patient might say like, "Why is he calling it this? Why is she using this word instead of that word?" And so, yeah, just for a little bit of clarity on that. For starters, metastatic cancer really means a cancer that has spread elsewhere in the body, from its original site. And so, examples of that would be a breast cancer that started in the breast, but a spot has spread to the lungs or the bones, we would call that a metastatic breast cancer. Or same thing, like a lung cancer that started in the lungs, and then had spread elsewhere, like to the brain, would be a metastatic lung cancer. And so that's really what that word means. Metastatic is spread elsewhere in the body. And that's important because for many, but not all cancers, metastatic implies that the stage IV diagnosis that patients might also be familiar with, but they're not always synonymous.

So really, what does metastatic mean? It means spread elsewhere, more distantly in the body. Now, advanced stage cancers is kind of an overlapping in different term. Advanced stage doesn't really have a precise medical definition. I think the best way to think about the words advanced staged are cancers that we as doctors think we are unlikely to cure. Okay?

And so, would a lung cancer that has spread to the brain and elsewhere, would we call that an advanced stage cancer? Yes, we'd call that an advanced stage cancer. But would a large lung cancer that has only gone to the nearby lymph nodes, but that we also think we're unlikely to cure, even though it hasn't spread far elsewhere in the body? Yeah, we'd probably call that an advanced stage cancer too. So it's maybe more of a less... It's less of a precise term, advanced stage cancer, and more of a physician or team of physicians opinions about the likelihood of being able to cure this cancer. That make sense?

Scott Redding: Yeah. But if I think back to the staging, there's stage... You hear people say they have a stage I breast cancer. Maybe they haven't had any other breast cancer, but they get diagnosed with a stage IV. Is that considered metastatic, or is that considered advanced, or does it depend on the tumor type?

Daniel Wall: Yeah, it's complicated because all of these definitions are like Venn diagrams with some amount of overlap. So if someone said I was diagnosed with a stage I breast cancer, I would know that this is a breast cancer that is localized in the breast and hasn't spread elsewhere in the body. That's how... We use our staging system, this stage I, II, III, IV as tools to tell us how a patient is likely to do, in terms of outcome with their cancer, how long are they likely to live after they're being diagnosed. And traditionally, the things that have gone into a stage, can be how big is the tumor in the breast? Has it spread to any nearby lymph nodes? More and more, we're starting to determine the... Look at the biology of the tumor, as it relates to stage. And so is it predicted to respond to standard therapies? Doesn't have these receptors that make it more responsive to therapy? That can affect the stage.

But I think the way that we think about stage really is at the initial diagnosis of a cancer. And so, the way I was always taught this is that your cancer is given it's formal stage one single time, at the time you are diagnosed. And so, you can imagine the unfortunate situation of a patient who is diagnosed with a stage I cancer, and is treated for that, has an appropriate surgery and maybe some radiation treatment and some systemic therapy, meaning chemotherapy or endocrine therapy, afterwards for their breast cancer. And five years later, unfortunately we find spread to the bones. Right? And so now, what was a stage I cancer five years ago, has now become metastatic.

There's some disagreement, but a lot of people would say you don't call that a stage IV cancer because, well, it was stage I at diagnosis and then it spread. Whereas the staging system is really to be used just at that original diagnosis of a cancer because that's where all of those data were generated. And so, that's a complicated... It's really more of a semantic issue because a patient who's diagnosed with metastatic cancer upfront is said to have a stage IV cancer. But someone who is diagnosed with a local cancer, and then it spreads years later, still has metastatic disease and their treatment might be very similar, but we wouldn't necessarily call that a stage IV cancer.

Scott Redding: On the metastatic aspect that you mentioned, if someone gets diagnosed with metastatic upfront, and earlier you'd mentioned that metastatic usually means it spread from somewhere, how is that person determined what their cancer? So, for instance, someone has a metastatic cancer with a brain tumor. Is a brain tumor their primary cancer or could it be another cancer, and how is that determined?

Daniel Wall: Yeah, it's a good question. We see this a lot. Sometimes I see patients who have maybe had a lung cancer a few years ago, had a kidney cancer a year ago, and more recently, was diagnosed with a melanoma, right? And so, all of these things, there was a spot on their kidney, they had it taken out, it was a kidney cancer. There was a spot in their lung, four years ago, they had a surgery, it was a lung cancer. And then a year ago, they had a melanoma on their skin and it was taken out. And then maybe a year after this, they have a tumor found in their brain. Let's say a patient has headaches or stroke-like symptoms and a scan shows a spot in the brain, and we think to ourselves, "Is this a tumor that started in the brain, or is it something that started from one of these three other cancers and then went to the brain?"

And that matters a whole lot because it tells us which one of these cancers is behaving badly. Which one hasn't been cured and which one... How should we... The treatments for all of these three cancers are very different and how do we decide which treatment to give? And usually what we do in those types of situations is we work with our neurosurgeons to do a surgery and remove the tumor in the brain, if it's at all safely possible. And then from that tissue that's removed in the brain, our pathologists, by doing molecular tests and looking at under the microscope, are usually able to tell, "Aha, this spot in the brain came from the melanoma." Or it came from the lung cancer, or it came from the kidney cancer. They can help figure that out by doing either molecular testing or looking under the microscope. And then we know, let's say it's from a kidney cancer, then we know that, "Hey, this melanoma and the lung cancer are doing just fine, but the kidney cancer has spread to the brain."

And so now this patient has metastatic kidney cancer and then their future treatments would be designed around kidney cancer treatments, not lung cancer treatments or melanoma treatment. So the big picture is, if a patient has a main cancer that started in one of... Some organ, a kidney cancer, and it spreads to the bones, and we do a biopsy of the bone and it shows kidney cancer, the way we think about that and what we call that is kidney cancer that has metastasized to the bones or renal cell cancer. We don't typically call that a bone cancer. And our treatments are designed around where the cancer started, the kidney cancer treatment. It's not designed around where the cancer ends up, the bone cancer, for example. Bone cancers, like multiple myeloma that start in the bones, have very, very different treatments than kidney cancers. And all of our treatments are kind of designed around where the cancer started and the molecular features of the cancer and where it started.

Scott Redding: So in that example of kidney cancer spreading to the bones, would part of that treatment also include any kind of orthopedic oncologist involved in that care as well?

Daniel Wall: Yeah, it can. And it depends on kind of which bones are involved. And so, when I, as a radiation oncologist, I often see patients who have cancer spread to

bones, but when it's causing pain, because our radiation treatment can often relieve that pain. And one of the questions I asked myself anytime I see a patient with cancer in the bone causing pain is, "Does this patient need to see an orthopedic oncologist before I offer them radiation treatment? Am I the right doctor to be seeing this patient right now?" And one of the ways I make that decision is, "Which bone is involved and how serious is this bone involvement?" And so the ones that we really worry about, kind of stability or fracture, or let's make sure that this bone is strong enough before we do anything else, are the weight-bearing bones of the body.

So those are usually the legs, the femurs. And if a patient came in and they told me that, "Every time I step on this left leg where I have cancer involvement, I have pain and it's been getting worse over the last week." That's a patient who would get some scans on an X-Ray, and ask our orthopedic oncology colleagues to see them, to talk about, "Does this need to be stabilized by putting a little supporting pin in the bone, for example, before moving along with any other treatment?" Because we really want to avoid having a fracture if we can avoid it. Something in a rib, that's not bearing a lot of weight, much less likely to have involvement from an orthopedic surgeon.

Scott Redding: You kind of talked a little bit about it earlier, but what kind of treatment options are there for those with advanced stage or a metastatic cancer?

Daniel Wall: There are a lot. So, we think... And I guess we can bin our therapies into the two or three main local therapies, meaning treatments that we aim at a particular part of the body, or we're focused on a particular area. And those are surgery, doing a resection of a cancer. And there's radiation, which is what I do, where we use high energy X-Rays aim to kind of exactly where we want them to go in the body, not throughout the whole body. And then there's some other local therapies that are emerging, as well. Being able to ablate a tumor with high temperatures, or radio frequencies, or microwave ablation to use kind of localized energy to kill cancers in the liver or the lung or... Gosh, sometimes even in the brain. So those are localized therapies. We see cancer someplace and we take it out of that place.

Then the other big categories... And those are really typically used for more localized cancers, things that aren't spread all the way throughout the body. Then there are systemic treatments. And systemic is a big category and all it means is that the treatment is going throughout the body. So things that's going to go through the bloodstream to get where it needs to go. And I think about three main categories of systemic therapy. Traditionally, chemotherapies was the first pillar of a systemic therapy. So these are things like Platin, that you may have heard of, or doxorubicin, or mitomycin-C, things that interfere with a cancer cell's ability to divide. And there's the several ways that these work, but they're... People think about them as interfering with the ability of cancers to divide and kill them by damaging their DNA, for example. Okay.?

Then the second main category of systemic therapy are so-called targeted therapies. And these are small molecules that have been designed to interfere with precise signaling pathways within cancer. So not like a chemotherapy that's going to go in and damage a whole bunch of the DNA in the cancer so that it dies and also kill some nearby normal cells as well, because everything has DNA and... But these targeted therapies, people have used information to figure out, "Hey, there's a mutation in this signaling molecule in this cancer. And so this one molecule looks different in the cancer cells than it does in all of the other cells in the body. Let's design a drug that specifically targets this different molecule in the cancer cell."

And the gold standard example of this is Gleevec or imatinib, that's used for a type of leukemia that has a rearrangement, that's only makes this one signaling molecule only present in the cancer, so you can take drug for it and it can stop the leukemia from growing, but doesn't really affect the rest of the cells in the body. And this type of therapy has had success now outside of leukemia, to many other cancers. Kidney cancer, lung cancer, many of them can be treated by these targeted therapies. So [crosstalk 00:15:21]-

Scott Redding: Targeted therapy, is that like immunotherapy?

Daniel Wall: So immunotherapy, I'm putting in a different cast, its own category. So chemotherapy, targeted therapy, and immunotherapy, and that's kind of like the three... Well, I mean, I'm not a medical oncologist, but if that's how I think about the armamentarium of systemic therapies.

Scott Redding: Can you explain a little bit more, obviously with your background being a lot on the nervous system and in particular glioblastomas, how many cancers metastasize to the brain, or is that just kind of only certain ones, or is brain kind of one of the higher ones? Where does cancers usually metastasize and then how is it treated from the brain standpoint?

Daniel Wall: Many cancers can metastasize to the brain. And the most common ones we see spread to the brain are lung cancer, melanoma, and breast cancer. Some cancers rarely spread to the brain. For example, prostate cancer. And it can happen, but it is less like. The way we treat a cancer that has spread to the brain depends a lot on how symptomatic that spot is in the brain and how many of those spots are there. And so, those are two main questions. Another question is, do we know what that thing in the brain is? So one of the examples I gave you earlier was a patient who had three prior cancers and now has something new in the brain, but we don't know what that new thing is. We don't know whether it's a lung cancer or a melanoma, or a kidney cancer, and all of that factors into our decisions.

What we say is, traditionally, the two main treatments for cancers that have spread to the brain are surgery and radiation, these local therapies. And the

reason we've said that for a long time is because chemotherapies, targeted therapies, a lot of them don't get into the brain well because of this physiologic feature of the brain called the blood brain barrier that prevents a lot of these drugs from achieving effective concentrations in the brain, and for some, even pumping the drugs out, because our body has developed this protective feature to prevent against poisons or toxins entering the brain. That's starting to change maybe a little bit. There are drugs that can get into the brain, but I think it's still reasonable to think about, for most cases, surgery and radiation being the two main treatments for cancers that have spread to the brain.

So first things first, if I see a patient who is having bad symptoms from a spot in the brain, it's causing swelling, it's causing bad headaches, or nausea, or vomiting, this is a patient who, almost always, I will ask one of my colleagues in neurosurgery to evaluate. To see if they think that there is an option to resect this tumor. And that's because this type of patient who is having a spot in the brain that's pushing on all of this, has a lot of mass effect that needs more urgent relief than we can offer with radiation or with a systemic therapy. So surgery is one of the mainstays of treatment of cancers in the brain. And even if there are larger box of cancer that aren't causing bad symptoms like that, surgery is often the first step.

And of course, the other thing that surgery can get us that other treatments can't, is pieces of tissue to look at under the microscope, do molecular testing on, and help aid us in the diagnosis, if we don't have that diagnosis yet. And so those are the two main reasons when I asked my neurosurgeons to see a patient. Now, for a patient with very small spots in the brain, where we know that they have cancer elsewhere in the body, these are patients for whom radiation by itself might be an excellent treatment option. And so a patient with a melanoma that has spread to several places throughout their body, but is three new spots, small new spots are found in the brain, this is someone that I'd feel very comfortable treating with focal high dose radiation to those three spots, really to prevent them from growing and causing stroke like symptoms, headaches, these mass effect symptoms that I was mentioning earlier. And so those are just two possible ways that we treat patients with whose cancer has spread to the brain

Scott Redding: With these options, of the existing options, are there clinical trials or is there research being done on other ways to be able to either better manage or to treat these kind of cancers?

Daniel Wall: Yeah. I mean, I think that we here at Michigan have a number of clinical trials open for patients with cancers in the brain. So for metastatic cancers that have gone there from elsewhere, there's an open question about whether... I kind of gave you the example of a patient with three spots of cancer, and I said I'd treat each one of those individually. But what if I saw a patient with 11 spots of cancer? Should I treat pinpoint radiation to each of those 11 spots? Or should I

treat with radiation to the entirety of the brain because I'm worried that if I treat these 11 spots right now, and I get a repeat MRI in three months that there might be 11 more spots, and some of them might be even bigger and causing the patient to get really sick?

And so that's a question we don't know. So we have a clinical trial opening very, very soon to ask that question. Patients with a larger number of metastases in the brain, should we be giving them focused radiation, or should we be giving them radiation to the entirety of the brain? And there are risks and benefits of each approach and I think most doctors don't think they know the right answer here, and so that's where we're really trying to answer questions like this.

We have other clinical trials that are working on the thing I mentioned about, how do we make our systemic therapies, that go through the blood, work better for patients with brain metastases? There's an active research program focusing on patients with a certain subset of breast cancer, trying to figure out, are some of these newer targeted drugs actually effective for patients who have breast cancers that have spread to the brain? So we have active trials open there, as well. So there's a lot going on, both to try to figure out the best way to do radiation or surgery for these, but also to come up with some newer therapies to try to help these patients.

Scott Redding: I want to back up a little bit on a mention of... You mentioned that lung cancer can metastasize to the brain. So my first part of this question is, it's interesting because don't some cancers also metastasize to the lungs? And so, if that's the case, how do you know which came first and last does? Brain tumors or brain cancer, do they spread elsewhere, or is it because if it's in the brain, that's as far as it goes?

Daniel Wall: Yeah. So yes, it's a good question and it can get complicated. A lung cancer that starts in the lung, and it really... I mean, let me back up. A lot of this has to do with the circulation of blood throughout the body. If we think about the way the heart is pumping blood, the left ventricle pumps blood out to all of the body, except for the lungs, right? It is pumping blood that has high levels of oxygen out to the kidneys, out to the brain, out to all the muscles in the body. The body uses up this oxygen, and then through the veins, it goes back to the heart, and now the right ventricle pumps that blood that's low in oxygen out to the lungs, right? And the blood goes to the lungs, then it goes back to the heart, and now it's got high oxygen, it ends back up in that left ventricle, and then gets pumped out to the rest of the body.

And well, this is... We're talking about cancer and why am I talking about the physiology of how blood is circulating through the body? But that starts to explain why lung cancers go to the brain so frequently. Because cancer is in the lung, some of those cells break off, they're in the blood, and then they go right into that left ventricle, and then pumped out to the rest of the body including

the brain. It also explains why other cancers like, for example, kidney cancer, might stop in the lungs. Spots might develop in the lungs first, and then go to the brain.

So you can imagine a cancer in the kidney. Some of it... Some cancer cell has acquired some molecular features that allow it to break off and spread through the blood. The blood is flowing from the kidney back to the lungs, so that's the first place they end up, and spots of cancer might grow in the lungs. And that's again, kidney cancer now grow in the lungs, and then it grows there for a little bit, and then pieces break off again, and they go into now from the lungs into the left ventricle, and then get pumped out to the rest of the body, including the brain. And so now we have a kidney cancer that has spread both to the lungs and to the brain. And so, cancer is often... We see spots of them in the lungs before going to the brain, but not always. Sometimes, for whatever reason, that cell that breaks off of the initial cancer, it might have some mutation or molecular feature that makes it want to go in the brain or grow especially well there.

And so, yes. And how do we tell the difference between all of these? It's really based on the clinical setting, and based on the molecular features of the cancer. So, let's say I had a patient who had a kidney cancer that had spread to a lot of nearby lymph nodes and had spread to the lungs. And we knew that because we had done a biopsy of a spot in the lung, and when we looked at it under the microscope, it didn't look like a lung cancer, it looked like a kidney cancer because of its molecular features and the stains that our pathologists did.

And let's say, six months later, that same patient developed a new spot in his brain. I would then say that, based on this clinical picture, this is now a patient who has a kidney cancer that has spread to the lungs, but also the brain. Which that we wouldn't say like, "Hey, is this a new lung cancer that has spread? Is this a new brain cancer?" We would say, "Just based on all these features, we know how kidney cancer behaves, this is almost certainly just one more spot that your kidney cancer has gotten."

If we had a different situation, a patient who had a lung cancer five years ago, that has a new... And we treated them, we thought they were cured. And then five years later, there's a new spot in the brain, we would scratch our heads a little bit and say, "This is probably from the lung cancer, but we don't know for sure. And is our uncertainty enough that we need to do a surgery? Is there cancer anywhere else in the body?" If we found a spot in the bone and we biopsy that and that showed lung cancer, we would make the inference that this new spot in the brain is probably from the lung cancer as well. It makes more sense that a patient has one cancer that has spread many places than two cancers independently developed, both of which had spread. That can happen, but it's much less common.

And if we couldn't find spots elsewhere in the body, we might, again, ask our neurosurgeons to help us do a resection of that spot in the brain, to tell us, "Oh, this is from that lung cancer from a few years ago that we thought we had cured." I would say all of this contrasts with the kind of cancer that I specialize in, which are the brain tumors that start in the brain, like glioblastomas, or oligodendroglioma, or IDH-mutant astrocytomas. So these tumors, they start in the brain and they stay in the brain. They don't spread elsewhere in the body. And so, the concept of metastasizing doesn't really exist for these brain cancers. And so, they're kind of like a different beast than most of the other lung, kidney, melanoma cancers that we've been talking about already.

And what this means is a lot of the terminology that is commonly used for cancers, I don't use it in my day to day conversations with my patients. I don't talk about a glioblastoma metastasizing. I don't talk about this glioblastoma is stage II, or this glioblastoma is stage IV. These things are graded, they are given a assignment of how aggressive they think... Pathologists think they are, but they don't get staged in the way a conventional cancer does. And we think the biology is that these things just need the environment of the brain to exist and to thrive, and that's why they don't spread elsewhere.

But it also means that, from my conversations with patients, and I think a lot of our oncologists do this for other cancers, as well, we're really trying to get across a meaning or understanding of what the diagnosis needs. When I see a patient with a glioblastoma, the most aggressive brain cancer that adults can get, is it's what's my lab specializes in. And what I usually tell them is, "This is a very aggressive cancer. It's a cancer that we have effective treatments for." Surgery, radiation, chemotherapy, a couple of other things emerging, but the goal of our treatments, for the most part, is to push off the time until this tumor comes back. Only exceptionally rare circumstances would we think about talking about getting rid completely of one of these tumors.

And so what I tell my patients is that I've had patients with glioblastomas that I have treated, and sometimes we can push the recurrences off two, three years, but for some patients, those recurrence happen earlier. We do our treatments over three or six weeks, and sometimes by the end of treatment or a month or two afterwards, the tumors are always already coming back and causing problems. And what I tell patients is, I explained to them that I do not know where they're going to fall kind of in these ranges. That yes, this is a serious cancer, but for some patients, it's very, very bad within a matter of weeks to months, and for some patients, they do well for a couple of years before the cancer really takes off.

And for most patients, when I'm meeting them at the first visit, that is the information that I have. I don't know how they're going to do. I don't pretend like I know exactly how long a patient is going to live. And as long as I can get

across some of that uncertainty, this is serious, but uncertain, now that's really what I want a patient to take away and understand, regarding their cancer.

None of us know exactly how an individual cancer is going to go. Some go very badly, some go very well, and there's always, always, always a range. And that's important for a patient to know, even if you're told you have a metastatic cancer. Is it possible to live for years and years with this? Yes. If you are told you have a very early curable cancer, is there a slight chance that things go badly and it spreads elsewhere very soon? It's possible. So I think really speaking with detailed conversations with your oncologist and having a healthy understanding of the uncertainty in all of this, is really, really important, both for patients and for oncologist.

Scott Redding: Great. That's a lot of information and really appreciated. I think that these are questions I know a lot of people have been asking, as we hear about celebrities and people we might know that have been diagnosed with whether it's a brain tumor, pancreatic cancer, ovarian cancer, late lung cancer, even some liver cancers where it always seems to be diagnosed very late and people worry about that. So I think that knowing that there's a lot of variables and that people can live a while with these kinds of cancers with the right treatment, with the right knowledge, and the right team, and the right hope that they have themselves. So that's really good to know.

Daniel Wall: Yeah, exactly.

Scott Redding: As we wrap up, and I really appreciate the time today, Dan, but as we wrap up, what would be kind of the takeaway message that you would like people to have after listening?

Daniel Wall: The biggest takeaway that I would want patients hearing this to think about is that every situation is unique and there's information that makes one case different from another, and that the words we use are not always precise. So some patients with metastatic stage IV cancers are cured, and cured relatively regularly. A metastatic testicular cancer, a lymphoma that has spread elsewhere in the body, still a very high chance of being able to cure these diseases. Some cancers, even if they haven't spread elsewhere in the body, can be very serious. So, even if a lung cancer isn't metastatic, that spread to the nearby lymph nodes, or a pancreatic cancer that hasn't spread, but can't do surgery on because it's in nearby blood vessels, that can be extremely, extremely serious. A glioblastoma that hasn't spread elsewhere and isn't going to, can still be very, very serious.

And so instead of focusing on these words... And one patient with a stage IV cancer, it might mean, "Gosh, I'm sorry, but most patients with this end up dying within six months or so." And some patients with a stage IV cancer, many might live five, six, seven years. And so I would like patients to have an

oncologist to have detailed conversations with one another about, what does this mean for me with my exact cancer, with the biology of my cancer, with the mutations that I have and the treatments available to me? I know there's uncertainty, but how do patients with this typically do? What are the ranges are we looking at? And not to focus so much on metastatic cancer equals I'm going to die, or locally advanced cancer equals there are no effective treatments for this.

And just having a understanding of that uncertainty and one of the ways to fight it is by having detailed conversations with your oncologist. The other big piece of this is that the state of the field right now does not equal the state of the field in one, two, three, four years from now. And so all of us oncologists are working as hard as we can to make these treatment options better, right?

And there's a lot of ways to make things better. We can make treatments less toxic. We can make them less costly. We can figure out when the cancer's arrive earlier, or try new ways to diagnose them earlier, so we can give more effective treatments earlier on. My laboratory is working on how to make radiation treatment more effective for these aggressive brain tumors like glioblastoma. There's clinical trials ongoing at Michigan and elsewhere for all of these concepts. And so I think there is hope. Hope is important and I think there is a plan to make that hope actionable. That in, through these clinical trials, in two to three years even, we could have a new treatments available for these patients. So just the state of the ground right now is not the state in the future. And so treatments are constantly improving. So that's what I would just hope patients take away with.

Scott Redding: I appreciate the time today, Dan, and thank you.

Daniel Wall: It was my pleasure, Scott. Thank you for having me.

Scott Redding: Thank you for listening. And tell us what you think of this podcast by rating and reviewing us. If you have suggestions for additional topics, you can send them to cancercenter@med.umich.edu, or message us on Twitter @UMRogelCancer. You can continue to explore the 3Ps of Cancer by visiting rogelcancercenter.org.