

## **PANCREATIC CANCER**

CHRISTOPHER CAMPEN, PharmD, BCOP: Our final presentation of the day in this room is What Advanced Practitioners Need to Know About the Diagnosis and Treatment of Patients With Pancreatic Cancer. Please join me in welcoming Ms. Amy Hacker-Prietz from John Hopkins, and Dr. Joseph Herman from MD Anderson.

DR. HERMAN: I haven't really done this kind of tandem presentation before, so bear with us. We'll probably jump in here and there and talk to each other. This is how our clinic runs, so it's sort of the same thing. You'll get a good taste of exactly what it's like.

Here you can see our learning objectives. It's to summarize available treatments for patients beyond first-line chemotherapy agents for patients with relapsing or refractory pancreatic cancer. Describe the signs and serious toxicities associated with agents used to treat pancreatic cancer as they relate the mechanism of action and approaches to managing the toxicities; identify candidates who are considered high-risk pancreatic cancer and initial screening modalities; and discuss recent advances in the treatment of patients with pancreatic cancer that support an interdisciplinary approach.

I have been a consultant for Oncosil and also have some loyalties from Eleckta, and Amy is just Amy.

DR. HERMAN: The first case is actually somebody that we became very attached to. This gentleman was an 87-year-old, cute little guy, who presented with a 3-week history of obstructive jaundice. His bilirubin was 9.6, and the CT scan, which I'm going to show in a minute, shows a pancreatic head mass compressing the bile duct,

encasing the superior mesenteric artery, that we did get a PET CT, which allowed us to help designate exactly where the tumor is, which can be difficult sometimes in this disease, and it was FDG-avid. And he then underwent an endoscopic ultrasound and ERCP with successful placement of a bowel duct stint, and that's in order to relieve the jaundice, and then a biopsy was positive for adenocarcinoma.

And here you can see his tumor. This is actually a little bit easier to see than a lot of the times when we have a pancreatic mass, but to give you a little bit of overview on anatomy, these are his kidneys, this is the liver here, and then you can see the aorta, this is the celiac axis, and then you can see the mass. And the way you can tell about these tumors, it's hypodense, it's usually a darker mass, and if you play with the window leveling sometimes, it can be very helpful to be able to designate these tumors and separate them from the normal pancreatic anatomy. And here you can see the bile duct stint.

The patient presented to our clinic for a second opinion -- and this is our multidisciplinary clinic, which I'm going to talk about in a minute -- to talk about his treatment option. And I think the point to make here is, you can see that his tumor was completely encasing the celiac axis here. You can see that for a surgeon to remove that tumor, the surgeon would have to basically go in there and carve that out, which means the likelihood of leaving cancer behind is quite high, and that's something we want to try to avoid in this disease. If we leave disease behind, it usually leads to a bad prognosis.

Why is it so tough? You know, people talking about pancreatic cancer is a death sentence, it's a death wish. Why is it so bad? And there's a lot of reasons. One thing is that it's in the middle -- they say, "Location, location," with regards to realtors

and housing. It's basically right in the middle of the body. It's about the worst part to get to. Time is everything. If all of you see a patient that might have pancreatic cancer, the most important thing is to get them to a diagnosis as quickly as possible and manage their health, and that we'll get to in a little bit. The tumor blocks off the bile duct. That decreases the pancreatic enzymes that absorb the proteins and fats that we eat, and that's why these patients, when they present, they've lost a lot of weight, they're very cachectic, and it can take a long time to bounce back from that. And therefore, these patients typically aren't in great shape to be able to get any therapies.

There's a lot of treatment resistance. Unfortunately, there's not many therapies for our patients, there's not much that we can give them, and for that reason, for our job it's been very difficult, because you want to provide home, but you also have to be realistic in what the expectations are going to be. And we don't have a good biomarker, we don't have a PSA, we don't have a great way to diagnose these patients earlier in their diagnosis. And then finally, I think the thing that we both can -- is that we have patients that come to see us and they're given so many recommendations, and because there's not really a great treatment option for these patients, typically these patients come in mismanaged quite often.

What are the numbers? Only about 20% are what we consider to be potentially curable -- that's not many. You can see that the number of cases continue to increase, especially with the Baby Boomer generation, 49,000 new cases now, and it just became the third leading cause of cancer death in the United States; it was number four. The key is a margin negative resection, meaning that you remove the tumor

without leaving any microscopic and macroscopic disease behind is the only way to cure this disease.

And I think the most important thing to take home from today is that staging is paramount. Patients are going to perseverate on, "What stage am I? Where do I fit into this picture? Am I metastatic? Am I localized?" Because that's what they're going to look at online, that's what they're going to look at on the Internet. And as they go through their treatment trajectory, that's what they're going to pay attention to. So I think it's really important to establish that up front.

Why maybe refer a patient to a multidisciplinary clinic, or why create a multidisciplinary clinic within your own cancer center? And I think it's because it really allows patients to get everything in one setting. Some of the benefits are that we work together, we get used to knowing how to work together and what we're going to do for our patients. The patients get -- at the end of the day, they get a plan of what's going to happen to them. That's so key. They come in, they're very scared and anxious, and if we can help diagnose them and get them down the right path, that relieves so much anxiety for these patients, and it really helps their quality of life.

MS. HACKER-PRIETZ: I think it helps us, too, to sit in with other providers in oncology and surgery all at the same time, so we benefit from their education as well, so we can move forward and help patients.

DR. HERMAN: A lot of our advanced practitioners, it doesn't really matter if they come from the surgery end, the medical oncology end or the surgery medical oncology end of things. We all learn together, we work together, and we work in tandem. Amy can talk about how to do a Whipple, as well as the advanced practitioner

with surgery can discuss what radiation is and how it works. And I think that's important, we learn from each other in that environment.

And also, what's very important is cancer clinical trials, and getting patients on trials that will hopefully improve the survival of these patients moving forward is also very important.

This is us. What we do is, a patient would fly in a lot of times at Hopkins, they would get their labs, their imaging, and then they would see Amy or one of the other advanced practitioners or residents, they would get a full history and physical. Do you want to take a minute and comment on that?

MS. HACKER-PRIETZ: Sure. One way I would see the patient, I would review their prior treatments, their imaging, their pathology, discuss their case, get a good well-rounded history from them as far as symptoms and even social aspects. And then I would present their case to the group during the middle of the day, and we'd go through each case. And then in the afternoon, sometimes I would go back and relay that discussion with these patients and their families, and sometimes outside providers, as well as continuing to follow up with these patients for reevaluation. If they weren't, say, getting radiation with us now, we would follow up and see them for reevaluation later.

DR. HERMAN: And I think that's the key. For example, in an academic setting, we do rely on residents to help us a lot, but they rotate. Every 2 months they come and go. And I honestly think that this model would fail without the role of the advanced practitioner. You guys are so paramount and key in the success of this. And it's building that relationship, and as in the keynote discussion today, we really do get attached to our patients. We're their cheerleaders, we're their hope a lot of times to help

get them to where they need to be, whether that's a curative paradigm or a palliative paradigm. And I think the beauty of this is in one day we sit at this table and we discuss each patient, and a lot of times we'll argue about what we think should happen next. What this does, more than anything, is it makes all of us be accountable for what we say and what we do. And when a cancer patient is seen independent of anyone else, at the end of the day, you're going to be somewhat biased by what you do, but when you're at a table like this, you have to be up front and you have to be evidence-based, and it holds everybody accountable, but also it gives you an opportunity to provide the best cutting-edge care for your patient.

I think the other thing that's cool is we're only able to see about six patients a day because it was a lot of time and energy, but we both took an MBA class together to learn how to improve efficiency of healthcare, and with help of another person, another resident, we're actually now able to see about 12 patients in one day. And it's huge, because we can get patients through. And even though it sounds probably too rushed, we share the workload, we sort of share the responsibility, and that way, everybody has a role and we're able to get through it quite effectively and efficiently and still have fun for the most part. It's a tiring day, but we still do a good job.

Timing is everything; timing is everything. And this is why if you're seeing a patient that has jaundice or a patient that has abdominal pain or a new diagnosis of diabetes, it's really important to get them a CT scan, a good quality IV contrast CT scan, so you can see the tumor, and then you can speed up the process here.

Here's a good example of a patient who goes to the traditional clinic, they see the surgeon, finally get diagnosed with maybe borderline resectable, which I'll go

over, then unfortunately, they have a liver metastasis, and then they get to medical oncology, and next thing you know, 6 weeks have gone by. When you can see patients in a one-day clinic, they get everything in one day and you can cut back about 4 weeks of that work-up time and get the patient where they need to be. And that's important, because there's a study that showed if you get a scan 6 weeks later, 25% of the time, that scan is no longer worthy. Those patients have already progressed or something else has changed.

This is that example right here. We found that in our clinic if you look at 500 patients, about 30% of the patients who came to see us in clinic had either a change in their pathology based on looking at a slide, or a change in their cross-sectional imaging that changed their plan or their diagnosis. Time is everything.

How do we work these patients up; what's important? It's a combination of all these things. And I think another good example of where the advanced practitioner comes in is, as a physician at an academic institution, one of my roles is obviously patient care, but it's also writing papers, doing clinical trials, and all those things I could not do without the help of Amy, in helping order these tests and make sure they're done correctly and properly so that everything's done. I do rely on Amy a lot to help order and organize and coordinate all these different tests that we need for our patients and also interpret. From the EUS perspective, endoscopic ultrasound is where most of these -- we no longer go percutaneously unless you have to. Everybody gets endoscopic ultrasound biopsies, fine needle aspirations. As we move towards more genetic sequencing and work-up, more and more patients are starting to get core biopsies, but an FNA is the most common. In some cases, we're going to put markers, like little gold

markers for radiation, which we'll get into. A thin-sliced, multidetector CT scan that allows for 3-D reconstructions is optimal, with also what's called a CT angiogram.

Why do we get all this? It's because -- I'll show you in a minute -- it gives us much better anatomy and helps us stage our patients more appropriately. MRI is not used at all centers, but in a case where there might be a liver metastasis or you can't see it very well or you're trying to differentiate between cancer and a noncancer, like sclerosing mesenteritis or autoimmune pancreatitis, sometimes an MRI can also help, and then an MRCP can give you sometimes some better definition.

How do these patients pan out? Here you can see these are our pancreatic patients. About 20%, as I mentioned, can undergo surgery. Another 35% have what we call localized, either unresectable or what's called now borderline, which I'll get into. Another 40% are diagnosed with metastatic disease. And then 8% -- this is what I call the forgiven orphan population. These are your performance status 2/3 patients that nobody really talks about. There are no trials for these people, there's very little supportive care, and I'm hoping that in years to come, this is a group that we're going to hopefully do a better job with.

We mentioned the anatomy. The anatomy is very complicated. Here you can see the first thing is to differentiate a tumor in the head, the body, or the tail of the pancreas. This is important because this would be a Whipple -- this is where the patient would have removal of the duodenum and the head of the pancreas and leave behind the body and the tail; whereas, if it's in the tail, the patient's going to get a distal pancreatectomy where you cut here, you don't remove any of this, and you remove this and sometimes the spleen. The reason that's important is the Whipple is a much bigger

surgery, as you're probably aware, it takes a lot longer to recover, there's a lot of nursing to get back to normal; whereas, the distal pancreatectomy, these patients tends to recover faster, but unfortunately these patients tend to have a higher likelihood of having metastatic disease at diagnosis.

Here's just another view. This is a cross-sectional view of what we're looking at. And you can see how difficult this is. This is a pancreatic tumor here. You can see how the duodenum wraps around the pancreas, and then you have all these blood vessels that are close by. It's not an easy tumor to deal with for that reason. And then here's an axial view; this is the tumor. See how it's hypodense? It's dense. And then the key part is looking at this vessel interface. Right here you can see there's a fat plain, there's space between the pancreatic tumor, the SMV, and the SMA. That space allows a surgeon to get the knife in there and be able to remove the tumor. But as that space starts closing in, there's less and less room. This is the CT angiography. This allows us -- this is the 3-D CT scan, this is allowing you to visualize the tumor and its relationship to the anatomy. Here's the portal vein SMV coming down, and you can see how it's hugging up against the vessel there. And then this is a CT angiogram, which you can see the stint right here, and it gives you a better sense of what the anatomy is, and this is very important for our surgeons to differentiate a resectable tumor and a nonresectable tumor.

And then here's a couple more images showing you the difference. This is a resectable tumor right here, and it's because there's nothing with the fat plan; whereas, here you can see the two vessels, and they're completely enwrapped with the

tumor. If you think you're not going to be able to get that out in that case, and in most cases this is palliative; whereas, this is potentially curative.

Now there's something called borderline resectable. I don't want to make it too complicated or confusing, but a nice easy way to think about it is, here's your blood vessel, this is your artery, and if the tumor involves less than 180 degrees -- if you can draw a line right through the middle -- then that's borderline. If it's more than 180-degree involvement, that's considered unresectable or locally advanced. This is the tumor, this is the artery, clearly less than 180 degrees, more than 180 degrees, and then this is also where the tumor causes a deformity on the vessel. And as you can imagine, these two are much harder for the surgeon to remove.

Same thing with the vein, same idea. The thing that's important to stress though, is veins can be removed typically. They can go in and they can cut out the vein and remove the tumor; whereas, with the arteries, in some cases it can be done, but as you can imagine, if you cut the artery, you put it back together, and there's a problem, there's a thrombus or it leaks or it fails, that could be fatal for the patient; whereas, the veins, generally, they're going to collateralize and other things can happen to help keep the patient alive.

What's the risk of pancreatic cancer? Who gets it and why? The vast majority of patients, we don't know. There's some interesting clusters of occupational people who live near, let's say, a nuclear waste dump, or everybody in their neighborhood is getting it, but that's very rare. It happens in a 65 to 70 age range, except for these kind of unique situations. And I'm not going to go through all of these, but, I think the one that you might hear a lot of is the BRCA 1 and 2 genes. There's an

association with breast cancer. If patients have a high family history of breast cancer, BRCA mutations, or Fanconi pathway, these are patients who may be more likely to get pancreatic cancer. And then, you can see there's some, like Peutz-Jeghers syndrome, which has a very high likelihood of getting pancreatic cancer. If your patients have any of these, at least it's something to think about. But unfortunately, for most patients, it just happens sporadically.

We see the patients, we diagnose them with pancreatic cancer, we work them up with genetics family history, we get the scan, we get labs, and we differentiate them into these groups of patients. Depending on what they get, it's what we give them. Resectable, generally, they're going to go right to surgery, but in some cases, we give chemotherapy and/or radiation, and that's to help ideally select patients a little bit. Bottom line is, most patients do develop metastatic disease. If we give a couple months of chemotherapy, we see no signs of metastatic disease, then we know that it makes more sense to put them through local therapy of radiation and surgery, and ideally, get them to a curative paradigm.

The borderline, like we mentioned, this is 180 degree or less involvement of the artery, where, if we could just sterilize it a little bit and make it easier for the surgeon to get it out with a negative margin, that could be potentially curable, and then in unique circumstances, we're going to mainly give chemo and either stereotactic, which is a short course of radiation, to these patients. But again, this is the group that typically is thought to be palliative.

What about the timing of therapy? Usually, after surgery, we give adjuvant; before surgery, we give neoadjuvant. If it's locally advanced, we consider it definitive, and, of course, palliative is what we give when there's not much hope.

How do we treat our patients now? Bottom line is that we have converged now, that if they have localized nonmetastatic disease, we're treating them very similarly, where they're going to get maximized chemotherapy, then radiation therapy, and every 2 to 3 months we're reevaluating these patients. They're coming into see us. A lot of times they'll fly in to see us, or they'll see their local doctor, they'll send us scans, we'll look at the scans, we'll call them, and we'll talk about what the next steps would be.

And then the next question is, do we keep them on maintenance therapy? Unfortunately, we don't know what the right treatment is right now. And I guess, again, this is why I take into account what the patients want and others; we try to do that.

To familiarize with what are the most common chemotherapy regimens being used today. And there's these two that are the most common, and the standard of care used to be gemcitabine alone, and it worked okay, but it wasn't super effective. And then there were two different trials that looked into gemcitabine versus FOLFIRINOX, which is 5-FU, irinotecan, and oxaliplatin, or another trial looked at gemcitabine versus gemcitabine plus nab-paclitaxel. Both of these trials showed a survival benefit compared to gemcitabine alone. The take-home is that these are the two most common regimens we use now in pancreatic cancer, this is what I would fight for for your patient, as long as they have an okay performance status. FOLFIRINOX, a

little bit tougher. And these are really your ECOG 1. There are some indications for ECOG 2 for that regimen.

The other thing, as a quick reminder, is that if they do have a BRCA mutation or other DNA repair, a cisplatin or an oxaliplatin or a PARP inhibitor are also things that we want to try to consider in this setting.

As mentioned earlier, it's a very tough place for surgeons to get to, and the area where it most likely comes back, is this area right here, which is called the retroperitoneal margin. We want to generally give radiation to kind of cover that area and sterilize that area. Radiation has come a long way. This is 10 years ago when I got to Johns Hopkins, we were treating these really big areas with radiation, and then we got what's called intensity-modulated radiation therapy, or IMRT, which allowed us to give very focused radiation with multiple beams, like multiple flashlights coming around, and honing in on the tumor. And then, this is what it looked like next, which is with IMRT. You can see the tumor here, and the color here represents dose. This area is getting full doses of radiation, whereas this area is getting a lot lower dose. When you breathe, the pancreas moves. So we realized that in order to get a smaller margin on our tumor, if we can have patients hold their breath for about 30 seconds, we can actually freeze the tumor in space and radiate it, and that's called active breathing control. Then, if we put markers in the pancreas, we could actually, like target practice, we can track it. That allows us to shrink our margins way down, and that allows us to do what's called stereotactic body radiation therapy, or SBRT, and now, we're able to give a very, very tight margin. That allows us to radiate these tumors 5 days now, instead of 28 to 30 days.

Why is that important? It's very important, because our patients can come in, get 5 days of radiation, and go home. Their quality of life right then and there is so much better. And I didn't have time to talk about it, but, we've done a couple trials which does appear that the 5 days of radiation is as effective as the 5 weeks. And what you can see here is, it allows to really -- this is a very large tumor, but you can see it allows us to give a very a high dose. The orange is going up to 40 grey, and grey is a milligram of medication; it's the way we describe our radiation, but it allows us to escalate the dose to the tumor. And ideally, in the future, we'll be able to sterilize these tumors and maybe not have to take them to surgery. That's the goal we're trying to get to. And in lung cancer, that's already a reality.

A couple take-home points for everybody to think about with these patients is that we try to give everybody pancreatic enzymes, pain control. Amy's going to go into this in a little bit more detail. I try not to do stereotactic radiation. If the tumor is invading into the duodenum, it can actually cause an ulcer and these patients can bleed. So I'm very careful; in those cases I would usually give the 5 weeks of radiation and keep the tumor small. And then we put the fiducials in. These are what the little gold seeds look like, the little fiducials that we put in the tumor to track it. They look like a little piece of rice. They're a little bit more expensive though. We had one patient that we put them in, and the patient had surgery and then they kept them afterwards; they wanted them back.

This is what it looks like. We put a patient through a CT scan and we have them in a little cradle so they don't move around. And it's all about target, keeping people in the same position every day. And then you can see, this is the dose of

radiation right here on the bottom, and then along here you have the volume. And you can see that the tumor gets a very high dose of radiation, but all the normal tissues, the liver, lung and everything else, gets a very low dose of radiation.

And then this is an example picture showing the stint, and you can see the little gold fiducials. We're basically treating these tumors with millimeter accuracy. So we're able to get a very high dose. And these patients literally go out to the ballgame. Like they'll come and they'll go to Camden Yards and they'll have burgers and a beer, maybe against our advice, but they feel pretty good. There's very little toxicity associated with this.

With our patient, this is what it looked like. This is his tumor up front, and after radiation, about 30 months later, you could see -- he was not in any shape to go to surgery, but he had a really nice response. He lived almost 5 years without surgery.

Where is the future going? The future is about genetics and about selection. And what we're doing now is, we're taking core biopsies of the tumor up front and we're looking at the tumor, we're looking at the immunos, the chemistry, or the protein expression, and we're also sequencing these tumors, and we are finding that there might be certain genes that will allow us to better select the therapies for our patients moving forward.

And along those lines, one thing that we're very excited about is the unresectable patients, where there were not many treatment options for these patients. And with aggressive chemotherapy and a short course of radiation, we've gone from -- this is our population at Hopkins. Historically, only about 10% of these patients go to surgery. Now, we're up around 40% of our patients going to surgery, and these patients

are having R-0, or margin-negative resections 90% of the time. These are those patients that have more than 180-degree involvement of the vessel, but we're sterilizing it, the surgeons are going in and removing it, and it turns out the tumor's basically dead; there's not much left behind.

However, there's still patients that, unfortunately, are getting metastasis where we can't remove it, or their performance status isn't good enough for us to get them to that point where they can get surgery.

And some of the predictive variables that we found is that if you can get your patient more than one chemotherapy, that tends to lead to a better outcome, and if they can get a higher dose of radiation and at least 4 months to chemo prior to going to surgery, these are things that tend to be more likely to get the surgery.

And here's our Kaplan-Meier's survival curves. You can see that of those patients who go to surgery, the survival is better than those who do not make it to surgery. If we can "select" the right patient to go to surgery, then we can improve survival for at least a big group of the patients that we see. And this is also just showing that margin-negative resection is better, which makes sense.

The other thing is, what does it look like? I know this is the pancreas tumor, and it's white because it's been radiated. And you can see how sharp the edges of radiation are. This is normal tissue, and this white area is the fibrosis that's been caused by the radiation.

The other question is, what does it look like under the microscope, and can we maybe cure these patients without even taking them to surgery? In addition to that, do we need radiation at all? Can we just give chemo? Do we have to give the

radiation? And here's another example of the tumor here, and here is the response here. And the question is, do we need the radiation at all? Because some of our medical oncologists were like, "Hey, the chemo's working great. We don't really need this radiation stuff. It's expensive and we don't really need it." So we wanted to look at this and see if it's really needed. We looked at the patients who got chemo alone and compared them to patients who had chemo plus radiation therapy. And when you look at the likelihood of having a margin-negative resection at the time of surgery or a node-negative resection at the time of surgery, whether it's borderline or locally advanced, there was a much higher likelihood of having a margin-negative resection and a node-negative resection with the addition of 5 days of radiation. It's not a randomized trial, but it at least suggests that radiation is helpful.

And then the other question is, can we sterilize a tumor, and does radiation help with sterilizing or causing a pathologic complete response? And here you can see that if you look at just the SBRT arm, having a complete pathologic complete response. Unfortunately, it's only 8%, it's not a big number. Clearly, we need to do better. But if you look at near pathologic CR, which means there's only some cells that are alive, we killed most of it, but there's a couple cells that are residual, you can see that radiation almost doubled the likelihood of that happening. It suggests that the combination of chemo and radiation is more likely to be beneficial.

There is a trial that's opening very shortly, and if it's not in your institution, please consider it. It's the Alliance trial, and it's comparing FOLFIRINOX alone followed by surgery in borderline resectable patients following by chemo or the same thing with

the radiation arm in there. The idea is to show that there is truly a benefit with radiation in this patient population. This is just the short course, 5-day course of radiation.

In conclusion, pancreas cancer has a very poor survival, but with better chemotherapy, better radiation, better care, better multidisciplinary approach of care, we can take better care of these patients and improve the survival. CT staging is important to determine -- we've got to put patients in the right bucket in the very beginning so that they know where they are and we know where they are. That's very important moving forward. Multi-agent chemotherapy improves survival, and SBRT does appear to improve survival in these patients, but we need a randomized trial to prove it.

Now we're going to switch gears. I'm going to hand it over to my partner here.

MS. HACKER-PRIETZ: The 2015 consensus for advanced practitioners, there's about 333,000 practicing in the U.S., and only about 2.3% are in oncology. Breaking that down even further, there's only 217 physician assistants in radiation-oncology. So I am one of 217.

There's a strong need for advanced practitioners, especially in oncology with advancing technologies in radiation and systemic treatments. Patients are doing better, they're living longer; they're living longer with disease and having to manage more side effects, and they're on treatments longer. Advanced practitioners are great for daily day-to-day symptom management for direct patient care, performing procedures that are reimbursable, can act pretty much independently, and have prescriptive authorities. There is also an educational push by ASTRO in 1997 on the

Joint Committee for educational implementation of advanced practitioners' inter-oncology practices.

This is actually my job description directly from there. It's a little overwhelming, and there's a lot of random things that I do. But for the most part, in the GI radiation oncology, I will see new patients in consultation, I will see follow-ups and reevaluation patients, and also participate in the pancreatic multidisciplinary clinic, as well as the rectal multidisciplinary clinic. Big role in symptom management for all of these patients, whether they're on daily treatments or they're just coming through for follow-up or coming in as a new patient. I'll consent patients for radiation therapy, as well as a big part of clinical trials, supporting those trials, as well as clinical trial documentation, eligibility criteria, toxicity assessments.

DR. HERMAN: If I can cut in here real quick. I have to really stress the importance of this. I think some institutions, if there's a separation between the clinical care and the research care -- Amy is a coinvestigator on every single one of our trials. And I think that's really key to work as a partnership. That way, there's an understanding. She understands exactly what medications they're on, what trials they're on, what they're going through. It is important to meld those worlds together and not make it a separation.

MS. HACKER-PRIETZ: And it's important later when you're going back through all of that data, you can say, "Oh, I remember that patient. That wasn't related to their treatment. They had something else going on at that time."

I'll order the majority of the diagnostic imaging. Just the way practice is set up these days, when you get results back, if a resident's ordering them and they're off

the service, it's kind of hard to follow some of those things. I'm involved with a lot of resident training, as well as tumor board discussions of patients.

The biggest -- the toughest part for me is symptom management, especially for these pancreatic patients. It is a big team effort. In the GI service -- in radiation oncology, we do have a big team, the attending physician Joe, myself, we have a nurse, we have a resident, a clinical coordinator, administrative assistant, as well as our research staff. And I think it helps provide continuity of care with me on the service. Like I said, residents change, and in our department it's every 7 weeks. Those residents don't see this continuity of care so much. And there's a big need for direct patient care while these patients are undergoing therapies, and a lot of times the physicians, especially in an academic setting, are tied up with other things and don't have the time to actually sit down face-to-face.

As you can see here, the majority of patients coming in with pancreatic cancer diagnosis, about half of them have metastatic disease, but the survival rate is pretty poor overall; survival at 5 years is about 7% to 8%. Most of these patients are undergoing active therapies. There's a big need to address their symptom management, whether it be disease-related or treatment-related, and a lot of times it's just unclear.

When you're talking with pancreatic cancer patients, there are things you want to learn from them, so you can help others moving forward. You want to know their goals. What are they expecting to get out of treatment? How do they want to live their lives? What do they do for fun? How will these treatments impact maybe some of those hobbies that they have? Talk to them about their support systems and where they live.

Are you going to be bringing them back and forth to a facility that's far? Can you combine things for them? If they're young couples, do they need family planning? Do they need fertility advice? Do they need daycare advice for their children? These are important things to consider when talking about these patients.

DR. HERMAN: I think one thing to add that's really important is, I know a lot of places will say, "I have a tumor board. We don't really need a clinic; we're good." But, if you see that patient, having that discussion about that patient can be very different. And I think, you know, having someone who has the experience, see the patient up front, and say, "I know you guys are talking about FOLFIRINOX, but Mr. Jones doesn't want FOLFIRINOX. He wants to go fishing. And oh, yeah, but the way, he barely got up on the table, so let's be realistic here." And we need that sounding board. You need somebody to speak up.

I think the other part about this is, we really encourage people to be vocal, and we have to empower every part of the team. And personally, I value it, because the worse thing is to do something that's going to hurt somebody. So please be vocal, be part of that, and don't be scared to say, "Hey, it's great you guys are having this educational academic discussion, but we have to be real here about what's important for this patient."

MS. HACKER-PRIETZ: And talk with their families. A lot of times their families know better. The patients are pretty stoic at times and don't always express some of the things that they're going through or what their expectations are. So it's important to sit down with the patients and educate them, as well as educate yourself about your facility's services. What things can you offer them as a team, social work, nutrition, pain

and palliative care, housing, financial things, support groups in the area? Talk to them in detail about the treatment flow, what is expected in that treatment process, how long is their treatment going to last, what are they going to be doing when they come in all the time, and make sure they have all the education about the department they're going to be with you in.

The biggest thing for me is symptom management. I think a lot of times it's hard to differentiate is it disease-related, treatment-related, or is it just a combination of other things? And these pancreatic patients, unfortunately, they have a lot of symptoms going on, whether it be obstructive symptoms or GI symptoms, such as diarrhea, constipation, nausea, vomiting, their diabetes, they have a lot of pancytopenias from their treatments, failure to thrive, they have clots, weight loss, fatigue, weakness. Mental health is a big concern. Two of the bigger ones are pain and exocrine pancreatic insufficiency. A lot of these will put patients on these slippery slopes where it's hard to recover from if they're not managed appropriately.

Pain affects about 70% of cancer patients, and for pancreatic cancer patients, about 75% to 80% of them present with that symptom as their first symptom, and even survivors do have a good portion of pain. A lot of patients have multiple sites of pain and require opioid therapies, and it's a big impact on their function and quality of life. Pancreatic cancer patients with this big presentation of pain is a really scary thing for them. Even if they're not having pain, they're anticipating it, they're afraid to have pain, and sometimes it's hard for them to express that.

In defining pain, you really need to take a good history and physical, find out when their pain is coming on, what's going on at the time. Have them create logs. A

lot of times they come in in front of you and they almost forget that it was that big of a deal before, but then their spouse or partner or family are saying, “Yeah, they were in a lot of pain.” Review their data, look at the scan, see if there’s something that you can pinpoint to maybe better address the pain. It’s hard to differentiate sometimes where the pain is originating from. And there’s a lot of different special populations to consider if they have comorbidities and things like that. I know we’ve all seen these pain scales, and they’re really tough. Everyone is different with these. Sometimes the scales like this might be a little bit easier, where they can directly point to the pain, or show you in a color scheme of what their pain is like.

Pancreas cancer patients have a lot of variable pain, and it’s hard to say if it’s tumor-related, or is it treatment-related. Do they have a lot of generalized abdominal pain, epigastric pain, post-perineal pain, back pain, right upper quadrant pain, do they have a bowel obstruction or a (indiscernible) cystitis, peripheral pain from neuropathies? When you’re discussing pain treatments, you want to discuss what kind of treatments you want to move forward with and what’s more comfortable for the patient, whether you’re going to use opioid versus nonopioid actual medications, or are there some interventional procedures that can be considered? Can you consider radiation therapy for palliative pain, or do they have a compression fracture and need vertebroplasty or pain blocks for pain, or do they have sites that’s causing pain and maybe benefit from a drain? There’s also a lot of nonpharmacological therapies -- I think a lot of us forget these things -- that really do help with pain, such as exercise, physical therapy, occupational therapy, acupuncture massage, meditation. Sometimes they’re not

available at your facility, but educate yourself of where you can find these for these patients, and of course, psycho-social assistance.

DR. HERMAN: I think the other thing is diet. Increasing protein can help third spacing and help bring those fluids back into the vasculature, and is also very important. And then I think the other thing is we have patients a lot of times, they have pain and their local oncologist will just give them a narcotic, and then all of a sudden, it's getting worse and worse, and it turns out that really, it was due to pancreatic enzyme deficiency. What you're doing is, you're just causing them to be constipated on top of the fact they're enzyme deficient. So it's really important to try to differentiate, is it the pain that goes through the back, like piercing pain, or is it a lower bloating pain that could be more associated with the deficiency?

MS. HACKER-PRIETZ: This is the MCC guidelines for screening for pain, and the biggest thing is to screen for pain. Screen for pain at every visit. Even though the first time they come through they don't have pain, make sure you ask it each and every time. And if you make adjustments to their treatment regimens for pain, continue to ask them, "How is it working," follow up with them, spend the time to find out what's going on with their pain, is it getting any better, any worse.

The other thing I wanted to talk about was exocrine pancreatic insufficiency, which is a big problem for a lot of pancreatic patients. It can be caused by a multitude of factors, and sometimes it's just the loss of the pancreatic parenchyma due to pancreatitis or just inflammation from treatments. They can have obstruction of the pancreatic duct from even just the tumor location or just fibrosis over time, or surgical injury or removal of the gland with a pancreatectomy or just a bypass surgery

can cause these patients to be deficient in their enzymes. Their enzymes are going to be amylase, protease, and lipase -- all involved in digesting your starch, proteins and fats, and if these patients are not producing those enzymes or they're not getting into the small bowel to help digestion, they're going to have a lot of these symptoms. They're going to have loose stools, they're going to have steatorrhea, distension, weight loss. That's the biggest thing. These patients are eating well, but they're continuing to lose weight and now absorption.

DR. HERMAN: I think this is very key. We have so many patients that come to the clinic, they've lost weight, and it took maybe a couple months to get to us, and no one even thought about giving them pancreatic enzyme supplementation. If there's one thing that you remember from the entire hour, it's the pancreatic enzyme insufficiency and making sure that you're aware of that and to consider starting them on.

MS. HACKER-PRIETZ: It's important. It's easy to start to have them try it. If it doesn't work, unfortunately, it doesn't work, that wasn't the problem. If it works, then it works, great. It actually can help a lot of these patients with their symptom management. Use appropriate dosing, trade up. Keep in mind the cost though. Sometimes it can be very, very expensive, so you may have to navigate some programs for these patients -- dosing by weight, take with every meal. Even if they're taking some of these supplement drinks, they do have nutrition in them that they need to digest, and sometimes patients forget that.

Going a little bit to the multidisciplinary clinic. I'm not going to touch on this too much. We have a whole team of colleagues involved with this clinic. It's a 1- to 2-day process. Patients come in from all over the world, get their imaging, have a full

discussion with all of these providers. We started with about four to six patients, now we're up to about 14 patients every single week, and that varies from week to week, but we accept up to about 14 new patients.

These disciplines that we speak [about] with these patients, we usually have the ones that are applicable to their care at that time frame. And surgery is not always talking about a curative surgery. Sometimes they're talking about palliative bypasses for these patients. Medical oncology is going to go through standard therapies as well as clinical trials. They will talk about radiation therapy in different settings, as well as our GI endoscopy team, we'll talk about different biopsy attempts, if they need stints placed in their bile ducts or if they need pain blocks.

DR. HERMAN: Or even duodenal stents. In some cases, the duodenum is completely closed off, and endoscopic duodenal stents can help palliate and allow the patient to eat.

MS. HACKER-PRIETZ: We have pathology, genetics there, radiology, pain and palliative care; not only talk about medications, but also interventional procedures, as well as hospice discussions and things like that. And research not only talks about therapeutic regimens that they have available, it's also quality of life studies that they have.

Some other disciplines that aren't directly involved with the clinic, but are something to consider, is interventional radiology can discuss if they need a catheter, drains placed, or biopsies done. Integrative medicine, find out what's available for these patients. Ultrasound can do drains and lines in site, and nutrition is a big part of this that

should be integrated sooner than later. Even survivorship programs and social work aspects.

What else can advanced practitioners do with these pancreatic patients? I think educating themselves of what's available for these patients, as well as taking the patient as a whole and with their families involved, and understanding their social aspects are big. I'm involved with a pancreatic cancer couple's retreat that is a 3-day process for patients, as well as their spouses, to come together and meet up to 11 other couples for the weekend, and it's a lot of practical things as well as fun social events. And I'll show you a little bit about that in just a little bit.

Creating and supporting clinical trials, research, and publications and meetings, just like this, and adjudicating and mentorship of others in the field.

DR. HERMAN: And she's given her own talks at national meetings, which I'm very proud of. And I think that's the other thing, understanding that the role of education is key.

[VIDEO ABOUT THE PANCREATIC CANCER RETREAT PLAYS ONSCREEN]

MS. HACKER-PRIETZ: [They] kind of open up to each other, bond, talk about things, share different stories, different experiences, learn from each other, and have a good time.

We have a welcome session where basically, we talk about what the retreat environment should be like, trust, care, respect. We have a nutritionist that comes on Friday night to talk about nutrition. We do a physical and medical rehab session first thing Saturday morning, bright and early to wake everyone up before we have breakfast. And then we bring in experts to talk about quality of life, talk about treatment

options, what's new on the horizon, what treatments are coming down the pipeline that we may not know about yet.

We also do kind of an arts and crafts session in the afternoon. Sometimes writing it down helps. We also have a session about advanced directives in healthcare decision making as well as other legal and financial issues that we discuss. And of course, we have discussion with the caregiver.

One of our goals is to bring laughter and smiles and fun into the weekend. And that is one of our primary goals, breaking down a little bit of some of the barriers, between even the patient and their caregiver. They haven't had an opportunity to forget about cancer and hit the pause button and say, "Okay, we're going to laugh and just be goofy for the night."

Then on Sunday, it's more of the spiritual mindful meditation reflection period, where our minds are with all of this process. And then we have a closing. It's a wrap-up and a goodbye session, and a further time to take pictures and to say goodbye and how we're moving forward from the retreat.

DR. HERMAN: I want to stress that the vast majority of this was actually done by Amy, and I think it says a lot about the commitment.

MS. HACKER-PRIETZ: It's a great program and it's not just open to Hopkins's patients, it's open to anyone across the world. If anyone's interested, please send their patients. We do it once a year. And there's a full video if you want to look at it on YouTube. It's about a half hour long. It goes into a little more detail about this session, and if anyone's looking to implement something like this at their facility, let me know.

Going back to wrapping up. Pancreatic cancer patients have a lot of symptoms that [are] multifactorial at times and can require a lot of time and attention, and it's nice that the advanced practitioner role sometimes does allow you to have that time. And I think that's important with patients, to offer your time. There's a push with advanced practitioners now with the increasing awareness and how to use them appropriately, especially in oncology clinics, and can help with patient flow and provider flow and overall patient care, and it's cost effective and time efficient for symptom management and can help fill that deficit of increasing demand of our oncology patients. And they're useful in the academic setting as far as teaching, publication, and clinical trials.

So, just a little thanks to everyone.

(End.)