Kendal Williams, MD (Host): Welcome everyone to the Penn Primary Care podcast. I'm your host, Dr. Kendal Williams.

So in this podcast, we thought we'd continue our discussion of breast cancer.

In the first section of this series, we discussed breast cancer screening and mammography and so forth. And we decided today that we would focus on the management of breast cancer, once it's diagnosed.

With us to discuss this are two experts, Dr. Leisha Elmore is an Assistant Professor of Surgery at Penn. She completed her medical school and residency as well as a master's of population health sciences at Wash U in St. Louis. She did her fellowship training at MD Anderson. She is the Chief of Breast Cancer Surgery at the Philadelphia VA and sees patients both at Penn Presbyterian Medical Center and Top.

Leisha, thanks for coming.

Leisha Elmore, MD (Guest): Thanks for having me.

Host: Dr. Mary Mahler is a Medical Oncologist at Penn based out of Penn Presbyterian Medical Center. She's actually Canadian but attended medical school in Ireland at the University College of Dublin. And then went back to Canada for residency and fellowship training in Toronto. Her focus is on breast cancer oncology.

Mary, thank you.

Mary Mahler, MD (Guest): Thanks for having me.

Host: And I'm honored to welcome back Dr. Amber Bird who co-hosted the previous episode on breast cancer, and you all know Amber by now I think. She's an Assistant Professor of Medicine at Penn and Associate Program Director in the Penn Internal Medicine Residency Program.

Thanks for coming to Amber.

Amber-Nicole Bird, MD (Guest): Thanks for having me back, Kendal.

Host: Today, I thought we would have a relatively straightforward discussion of the management of breast cancer, sorting through the various types of breast cancer and how they're managed. And that we'd really keep sort of to the fundamentals.

I wanted to start by just going over some of the basics of breast cancer and Mary and Leisha can correct me, but you know, breast cancer is a cancer primarily of the epithelial lining of the ducts and lobules of the breast. You can think of the ducts and lobule structure is being like an eyedropper or a pastuer pipette or uh, straw with a balloon on it, with the lobule being the balloon part and the duct being the straw.

So you have cancers to develop in the inner skin, if you will, the epithelial lining and if they remain within the duct or within the lobule they're considered in situ, but then of course they can evade through the basement membrane and become invasive cancer.

And so, you know, the first stage zero is ductal carcinoma in situ. So you have epithelial carcinoma that begins within the duct has not invaded. And DCIS as it's known has been, I suppose, one of the most interesting areas of breast cancer, because we've in a sense changed how we treat that.

I'm going to punt it out to Leisha and Mary—first off is my description accurate of the nature of breast cancer? Let's just start with that question. Is that how you think about it?

Dr. Mahler: I think that was a really good summary. Leisha, what do you rthink?

Dr. Elmore: Yeah, I completely agree. I think that was a perfect synopsis of the way we think about breast cancer developing.

Host: So let's talk about DCIS. You know, when I was in training, DCIS was not considered breast cancer yet, but now we're treating it more as breast cancer. We do treat it as breast cancer now, which has increased the rates of breast cancer around the world, or certainly in the country.

Let's talk about DCIS. Leisha, how do you think about DCIS?

Dr. Elmore: Yeah, absolutely. I think to understand how we have changed our paradigm of thinking about in situ disease in general, it's important to think both about DCIS and its cousin LCIS that started in the lobule.

Historically, we actually used to consider both of those one in the same. And now we know that the behavior is quite different. And in fact, lobular carcinoma in situ, we now think more of a precancerous lesion and the most updated staging guidelines have actually removed it altogether from cancer.

And so, over years of studying the epidemiologic behavior, the biological behavior of DCIS, we now understand that the way it behaves is similar in terms of growth and survival to our invasive cancers. But obviously, it's more favorable, but that distinction between DCIS and LCIS really is what moved DCIS into the consideration of stage zero cancer.

Now, Mary, do you have any thoughts?

Dr. Mahler: No. Yeah. I mean, I agree with everything that you said and agree with that, that we sort of think of LCIS, I guess, of being the more favorable subtype of the two and that DCIS like what Kendal was saying, we sort of treat like we do other breast cancers in the sense of it being treated with surgery upfront and then consideration of adjuvant therapies thereafter.

Host: And those are the two main breakdowns it's either ductal or lobular right?

Dr. Elmore: Correct. Yes.

Dr. Mahler: I guess maybe what I will say is there are rarer pathologies of breast cancer. I don't think it's necessary for all primary care providers to know about those. But those are definitely the vast majority.

Dr. Bird: And then Kendal, before we go beyond LCIS and DCIS, I think on a practical level, one thing that's always good to hear is how you might describe these to patients. Because I think one of the challenges that we sometimes see in primary care is we're trying to explain LCIS to patients and the nuance of something that is not technically considered true cancer, but still increases risk for future breast cancer for patients.

I'm just curious if either of you have, you know, ways that you describe this that have resonated well with patients.

Dr. Elmore: Yeah. I think that's a very important point. What I like to describe to patients is that LCIS is really, a pre-malignant lesion that places them at higher risk for breast cancer, but in and of itself, you know, does not represent, anything in the spectrum of breast cancer. And so I think what's really important for patients is understanding that, you know, as we've come to better understand LCIS, it does not represent a cancer, but really a marker of high risk for development in the future.

And that's important because it helps us understand how we can best screen them to detect potential cancer that would develop in the future. Because LCIS, is associated with a risk of about eight to 10 times risk of breast cancer compared to

a patient, you know, at average risk disease.

Dr. Bird: Great. That's really helpful.

Host: So, what is the screening paradigm for LCIS, Leisha? Is it the same? Do we do anything differently once somebody has been diagnosed?

Dr. Elmore: Yeah. So if someone has LCIS, I typically calculate their lifetime risk of breast cancer using one of the many models that exist, which include the Gail score or the Tyrer-Cuzick score. And what that does is give us you know, a lifetime risk of breast cancer in comparison to sort of an average risk individual.

And so if that risk is greater than 20% and someone with a history of LCIS, it typically is, then we would add MRI in addition to mammogram, to their screening regimen.

So every six months, they'd get diagnostic imaging of the breast. And so they'd get, screening mammogram alternating with an MRI.

The other thing that's important to note is we also consider chemo prevention in these patients. So you know, we know that consideration of chemo prevention with something like Tamoxifen can actually decrease their risk of breast cancer development in the future.

Host: So DCIS is a different entity, right? It's treated as cancer now.

So Leisha, you're probably going to see a patient first with DCIS. And how do you approach that patient? What are the steps you take?

Dr. Elmore: So typically by the time an individual comes to me, they have had, you know, their diagnostic imaging as well as, biopsy. And so with that diagnosis really it's the counseling of upfront surgery.

And typically, DCIS is caught, you know, with our advances in screening, it's usually caught before it is a very large size. And so most of those individuals are candidates for breast conservation. And so I really counsel them on their surgical options, which for every patient there's sort of two main categories, for surgery. And so that's breast conservation or mastectomy.

And so what's important in counseling, DCIS patients is because it is confined to the duct, the risk of spread to the axilla is effectively obsolete. And so I think that's important to realize because many patients have done their research when they come to me and so they're asking well we need to look at my lymph nodes and I

always counsel them that in order to spread to the axilla, it must first spread outside of the duct. And so the first step for the vast majority of these patients is breast conservation.

Host: That's recommended for all patients?

Dr. Elmore: Yes. So there are rare patients where the size of their DCIS or the extent of disease involves a large portion of their breast. And so for a select number of patients, mastectomy, can be considered in that case. But what's important to note is that there's really great data that shows that breast conservation coupled with radiation has equivalent survival outcomes to mastectomy.

Host: And, you know, the controversy, I guess, with DCIS and Chris Racine had noted this in our previous podcast on this issue is that, some DCIS is indolent, some is aggressive and we can't really tell the difference. Right? So we treat everybody as if they're aggressive, is that accurate?

Dr. Elmore: Yeah, I think that's an accurate way to look at it. And I think that the way that we treat patients today and the way that we're going to treat them, you know, five, 10 years from now, is going to be different. We've actually, as you mentioned earlier, we deescalated therapy, for DCIS. And so, you know, if we have a patient over the age of 70, for example, there's, good data that shows, you know, if they've got a DCIS, we don't even consider radiation where it was standard of care to radiate everyone in the past.

So I think, the marker of DCIS and how we think about its treatment is, you know, it's much more indolent than we used to think in the past. And we've really deescalated therapy over time.

Host: So when you get to the actual cancers that are invasive, you start to stage them. DCIS is stage zero, let me just go over this briefly. I know Mary and Leisha, you know, this intimately, but breast cancer is stage one through four. With stages two and three being broken down further into A, B and then in the case of stage three, a C stage as well. And really the as a stage four is metastatic disease.

And the difference between stage one, stage two and stage three really depends on the size of the tumor and the degree of lymph node involvement with sort of two centimeters and five centimeters being a typical breakpoint. The prognosis, the five-year survival decreases as stages evolve as you get to the latter stages.

The five-year survival for women with stage three B disease is 48% and is as high as 99% for patients with early stage disease. So, you know, still half of patients, even with three B disease are having five-year survivals that are half of them are

making it to five years. That's sort of my general summary of stages from what I've read.

Leisha and Mary, is some other way to think about that?

Dr. Mahler: The truth is that staging for breast cancer has become fairly nuanced because the most recent eighth edition of the AJCC Staging has incorporated biomarkers, which I think we're going to talk about a little later on in the podcast. The reason that this is the case is because your biomarker status also weighs quite heavily into risk of relapse or prognosis.

So, I find staging to be very difficult to sort of rhyme off the top of my head just based on size and lymph node involvement, because there are so many factors to take into consideration.

Roughly Kendal, absolutely. I think what you said is right in the sense that, you know, it's the size of the mass and the nodes that really dictate things in addition to receptor status.

Dr. Elmore: Yeah. And to piggyback a little bit off of what Mary said, because staging is so nuanced, I think to break it into the most simplest sense, I like to think of breast cancer as early, locally advanced or metastatic.

So early stage patients are really those, that have, T1 or T2 two tumors, which are those less than five centimeters and no axillary involvement. Most of those patients are cured with surgical therapy and radiation alone. So local control with consideration of hormonal therapy or some element of systemic control.

But really, local regional control is the name of the game for early stage cancers. When you look at advanced stage or locally advanced, that's sort of the other category, I think of and so those are really larger tumors. Those that are bigger than five centimeters, those that have lymph node involvement. And, for those, you know, systemic control plays a big role.

And then the third category is metastatic disease. So really, even though there's a lot of nuance, you can really think about it in those three categories.

Host: So I think that's helpful because that's the way we naturally think about it. Because as you had alluded to that, that breaks down into treatment strategies. I want to go back to this biology and I'll skip ahead a little bit in our outline and talk about estrogen and progesterone receptors as well as HER2 positivity.

So, you know, breast cancers are defined by pathology and stage, further by

whether they express these receptors, estrogen, progesterone, and HER2. So Mary, maybe I'll, take this back to you because you brought it up.

Can you help us understand each of those aspects, each of those receptors and why they're important?

Dr. Mahler: Sure. So, yeah, like we said receptor status is hugely important, both in terms of prognosticating breast cancers, as well as predicting which therapies they will respond to best. Three big receptors that we look out on the pathology is the estrogen receptor, the progesterone receptor and the HER2 receptor.

And the big buckets that I sort of put breast cancers into is hormone receptor positive, HER2 positive or triple negative.

Of course, patients can be triple positive. Meaning if they're hormone receptor positive and HER2 positive where they can be a little bit more nuanced in that they're just estrogen receptor, but not progesterone receptor positive.

Those three buckets sort of cover most of your bases as far as treatment. When we look at the frequency of breast cancers, hormone receptor positive is by far the more common of the breast cancers, this accounts for about two thirds of breast cancers, whereas HER 2 positive and triple neg, both the account for about 10 to 15% individually.

Mentioning that both the receptor statuses are prognostic and predictive. So as far as prognosis being hormone receptor positive is certainly the best prognosis. Whereas HER2 positive disease or triple negative behaves more aggressively.

However, I say that HER2 is sort of, our hero story in cancer in that it has a poor prognosis when it is not treated. However, given that we now have so many targeted therapies directed against HER2, it actually now with treatment has a very good prognosis.

So it went from having the worst prognosis in the metastatic setting to now having the best prognosis of all of the receptor statuses, which I think just goes to show how great our advances have been in targeting these receptors as far as systemic treatments go.

Host: It's sort of akin to lymphoma in a sense, you know, a high grade lymphoma is a bad thing. Obviously you have an aggressive cancer, but it's actually the most curable. Because of the intense cell proliferation that's going on, but I sort of, maybe I'm making a connection that doesn't exist.

Dr. Mahler: Yeah. You're obviously right in the sense that, you know, yeah, like many years ago, a high-grade lymphoma would have been terrible news. Whereas now you're sort of like, well, this is something we could actually strive for cure. So that's a great connection. Absolutely.

Host: So, HER2 are more aggressive, but more treatable. So it's a good thing to have HER2 positivity, as well as estrogen and progesterone positivity, which is why we say triple negative are the worst because you don't have those hormonal or Herceptin options, right?

Dr. Mahler: Right. And in triple negative, you're mostly relicated to chemotherapy. As well as more recently, the addition of immunotherapy in certain circumstances.

Host: Okay. Now that we understand the biology a little bit, let's go back to sort of the practical issues. We sent a patient for a mammogram. They have on their mammogram, maybe clustered calcifications or some density that is a spiculated or there's architectural distortions, things that suggest cancer. All of those will lead to a diagnostic process from that point forward.

Leisha, can you take us through that process, when a patient has a positive mammogram and what happens?

Dr. Elmore: Absolutely. So if someone has a positive screening mammogram, it will next prompt diagnostic imaging which includes a mammogram and typically an ultrasound.

I like to think of breast cancer management and workup as a team sport. And, so at each kind of stage of a workup, a different person shepherds an individual through their care.

And so breast radiologists are really excellent navigators through this portion of care and can work intimately with referring providers to help them figure out what the next imaging stage is. But after a screening mammogram, comes a diagnostic mammogram, and ultrasound.

What the difference with this is that there are additional views and magnifications of the area of concern in order to get a better idea of what it looks like because in many of cases, actually, with additional diagnostic imaging those findings go away. It turns out to be nothing. But if those findings remain on diagnostic images, biopsy would come next.

A biopsy can have multiple different flavors. It can be done using a mammogram which we call a stereotactic biopsy. It can be done under ultrasound or if a patient has had an MRI it can be done, and if it's not visible on mammogram or ultrasound, that biopsy may come through MRI.

Historically, we may have heard about excisional biopsies or surgical biopsies. Given our radiologic advances, it's rare to need a surgical biopsy for diagnosis. And our radiologists are really capable of obtaining that diagnosis. And so after the imaging and the biopsy is performed and our pathology provides a diagnosis, at that point it would be an appropriate time to refer to a breast specialist.

Dr. Bird: And Leisha, just to ask a question, a follow up question in regards to that.

You know, I think that oftentimes in primary care we may have people who are anxious as soon as they get that abnormal mammogram, or a diagnostic mammogram with a recommendation for biopsy. Oftentimes, when we're trying to counsel patients on the reason to take it one step at a time and do that imaging based biopsy next before heading right to the breast surgeon is my understanding is really just because we want to have a good understanding of the type of breast cancer as that may affect eventual treatment options, specifically the type of surgery that might be recommended by the time they make it to your office.

Is that correct? Is that the way we should be thinking about this?

Dr. Elmore: Exactly. I think that's a perfect way to think about it.

And from my experience, seeing patients in clinic before they have that diagnostic information really leads to a visit that's not particularly productive, and can actually heighten anxiety in patients.

So, I think it's really helpful to have all of that information coming in, so that we can make a true treatment plan and the patient can truly understand what's coming next.

Host: And Leisha it's to you as a surgeon that a patient would first go, right? There's not a referral to an oncologist at that point you are sort of the next step in that process. Right?

Dr. Elmore: Absolutely. In the absence of metastatic disease, the first step would be a referral to a surgeon. What we're seeing now is multidisciplinary care and multidisciplinary clinics, that's kind of the direction oncology care is heading.

And so in our particular practice, Mary and I actually see patients at the same time. So if a patient is appropriately referred, to me, I review their chart. And then I also get them scheduled with Mary or with, you know, a medical oncologist so that they can see us both because you know, critically important and we both serve important roles.

And I think it's important for a patient to understand what their plan is, both from beginning of treatment to cure.

Host: And so that's one way to get into the process. The other way is to present with a breast lump, right?

So they either present, we detect a breast lump either your gynecologist and you appreciate it, or we note it on one of our exams as primary care physicians or patients come in complaining that they've noticed it.

So, you know, obviously lesions that are firm, tethered, irregular, or have any overlying skin changes, particularly the Peau d'orange sort of orange peel like appearance are concerning.

But Leisha, maybe if you could take us through what happens when a patient comes in with a breast lump?

Dr. Elmore: If a patient comes in with a palpable lump, it's important to go straight to diagnostic imaging. So you basically skip the step of screening imaging.

The next step would be to order a diagnostic mammogram with tomosynthesis, as well, as an ultrasound. And based on the results of that, the radiologists will provide a recommendation for biopsy.

And the next step would be to biopsy that finding typically under ultrasound.

Host: And that's still done by the radiologist and the same process you described.

Dr. Elmore: Correct.

Host: So let's go through the treatment options once a patient's been diagnosed and they present to the multidisciplinary breast clinic. You know, we know about lumpectomy and mastectomy and radiation therapy, and then there's hormone based approaches as well as chemotherapy itself.

Leisha, you had started a discussion of this in terms of the DCIS, but let's go back to that framing that you had made before of localized disease. Maybe you could

help me with this, what you had said before and so you said localized disease, regionally advanced disease, and then metastatic disease. Right.

Dr. Elmore: Correct yes. And so, I'll tackle early stage and then maybe I'll have Mary tackle locally advanced disease.

So, if a patient comes in with early stage disease, the first step in their therapy almost every time is upfront surgery. And so that would either be breast conservation known by many names, as partial mastectomy, lumpectomy and followed by radiation to minimize risk of recurrence.

Host: You had highlighted times when you would just do the lumpectomy and not XRT, but anybody with stage other than zero after the description is going to be getting XRT. Correct.

Dr. Elmore: Typically yes. So it's become more nuanced. So as I mentioned, previously, deescalation of therapy is something that we're finding to be a common theme in breast cancer care because we've noticed there we've identified based on a lot of data that many patients have significantly improved survival without kind of the aggressive therapy, we used to do in the past.

And so one subset of those patients is patients over 70, and so we know there was a big trial that was done that basically showed for patients over 70 with hormone receptor positive, early stage disease and no nodal involvement, based on clinical examination, we can typically oh safely omit radiation therapy in those patients and omit sentinel lymph node biopsy in those patients.

Dr. Bird: And I guess just a follow up for our understanding, oftentimes patients may come and see both you Leisha and Mary and discuss their options and then come back to us with questions.

And traditionally, I think when we think about this, you know, the question is always, should I get a lumpectomy or should I get a mastectomy based on a diagnosis of local disease. And typically we'll kind of think of the lumpectomy if combined with radiation therapy, being about equivalent to mastectomy.

Is there a time when you're choosing mastectomy first? Is it just based on patient preference or risk for side effects related to radiation therapy? Is there something else we should be considering there?

Dr. Elmore: So when I think about which patients would benefit from mastectomy, it's typically those patients that have larger tumors or a relative tumor size to breast volume that would leave them effectively with an unacceptable

cosmetic defect in the setting of a lumpectomy. So that's kind of one indication for doing a mastectomy.

We understand that now that most patients are going to have a long life beyond cancer. And so it's important for us to not leave them cosmetically deformed based on our surgery.

Another indication for considering mastectomy would be someone with multicentric cancer. So, what that means is breast cancer in multiple quadrants of the breast.

And then another reason we would consider a mastectomy, as you mentioned, is for an individual that has a contraindication to radiation. And then a final consideration would be someone who has a known genetic mutation, such as BRCA is the one that we've most commonly heard of. And so we know in those patients' consideration of mastectomy and even contralateral prophylactic mastectomy can be associated with improved survival.

So those are typically the reasons I'd consider mastectomy.

Dr. Bird: Great. Yeah, that's really helpful. And I guess this is my last follow-up question. And then I'll toss it back to Kendal to talk about other treatment questions we have, I guess when you're talking about multi-focal disease, does that also include women who maybe have multiple primary breast cancers?

So, you know, 2022, they have one local breast cancer that can be treated with lumpectomy, but in the next year they have another quadrant of the breast with a new primary breast lesion.

Is that another time when you might be thinking about mastectomy?

Dr. Elmore: Yes, that's another great point because there's a maximum dose of radiation that a patient can receive without having toxic side effects.

Typically, if a patient has been treated in the past for breast cancer, they would have, you know, with breast conservation, they would have received radiation. And so we can't really provide additional radiation again in that breast. And so in that instance, we would consider a mastectomy as the standard of care.

Host: Leisha, I had a friend who had multiple primaries and it surprised me a little bit. How often does that happen?

Dr. Elmore: Yeah. So and when you say multiple primaries or you mean recurrent

disease, cause what the situation we just talked about with the patient, with their recurrence, do you mean different subtypes of breast cancer can currently or recurrent disease?

Host: My understanding was she was diagnosed with one cancer and when they did the MRI found a second primary within the same breast.

Dr. Elmore: Yeah, And so that raises a question of, is this truly a second primary or is this just a larger extent of disease than we initially thought? So, main kind of big picture question is, is this multicentric disease or is this two separate primaries?

And so that would require a biopsy of each lesion to determine whether this is really two different breast cancers, or if it's one breast cancer, that's more extensive than we thought, but it's not uncommon for us to see a patient that has either multi-focal, so multiple tumors in the same quadrant of the breast or multicentric disease. So tumors in different quadrants of the breast.

Host: So let's talk about the surgical approach. And when you do a lymph node dissection and a sentinel node biopsy and so forth, can you just take us through that?

Dr. Elmore: Absolutely. So for a patient that has what we consider a clinically node negative axilla, so no evidence of lymph node involvement on physical examination and they have an invasive breast cancer, standard of care is sentinel lymph node biopsy.

And so sentinel lymph node biopsy involves injection of a blue dye. Which is either methylene blue or isosulfan blue and a radio tracer, or technetium, which allows us to detect the sentinel lymph nodes. In most cases, we remove one to five lymph nodes and send them for pathologic evaluation.

And so the vast majority of, patients, you know, that with early stage disease, are able, to be treated with sentinel lymph node biopsy. Now is the question that gets a little more complex so when do you perform an axillary lymph node dissection, and that's much more nuanced now than it used to be in the past.

And so axillary lymph node dissection is typically reserved for patients that have a high volume of nodal disease in their axilla or they have a on sentinel lymph node biopsy, a significant number of positive lymph nodes.

Host: So as we see patients who have had breast cancer surgery and come back in and have lymphedema and so forth, I imagine that depends on the number of lymph nodes they have removed, right?

Dr. Elmore: Yes, that's actually a very great point.

So with a sentinel lymph node biopsy, the risk of lymphedema is really in the order of two to 5%, so quite low, but with axillary lymph node dissection, it's much, much higher and can be anywhere 20 upwards of 40% risk of lymphedema in those patients based on the literature that exists. So that's a big impetus for us, really trying to deescalate therapy in the axilla as well.

Another important note that I think is really important is we've historically heard that if someone has axillary surgery, they should not have venipuncture or blood pressures taken in the arm on the side of axillary surgery. And there's actually been a reasonable amount of data that shows that this doesn't truly impact their risk of lymphedema.

I actually counsel patients after a sentinel lymph node biopsy, that it's okay to have blood pressures checked and blood drawn, on the side of their surgery. I am still hesitant. I consider it a relative contraindication in someone with an axillary lymph node dissection.

So if possible, avoiding blood draws and blood pressures on that side, but again, not an absolute contraindication, like we used to think about in the past.

Host: And avoiding PICC lines and midlines on that side too, or I'm sure fall in the same category.

Dr. Elmore: Yes. For those axillary lymph node dissection patients.

Host: That's actually very helpful. It comes up a lot.

So let's talk about the after surgery and this is going to take us into hormonal therapy and Mary we'll pull you back in here.

Well, let's talk about hormone therapy. Let's say somebody is, well, let me ask a question first. If a patient is hormone receptor negative, are they a candidate for hormone therapy? Number one, and then two, how do you treat somebody if they do have estrogen and progesterone receptor positivity?

Dr. Mahler: Sure. So generally, no, if somebody 0% estrogen receptor or progesterone receptor expression, we don't routinely offer adjuvant hormonal therapy.

Mostly because we don't think that it will, you know, we don't think that's what their breast cancer is trying to use to grow. So we don't think that it will have much in the way of effect. So when their receptors are negative, then no, we don't necessarily consider it.

But most women with invasive breast cancer, who express estrogen receptor or progesterone receptor, we do talk to them about adjuvant hormonal therapy. We of course have more nuanced discussions when women are elderly and have less life expectancy.

So what are we really trying to prevent? And that's a more nuanced discussion, but it certainly is something that we consider in the majority of the women that we see. When it comes to the selection of which hormonal therapy you use, their menopausal status largely comes into play.

So for premenopausal women, our most common medication that we use is tamoxifen. We certainly can use other medications, such as aromatase inhibitors in high risk premenopausal women. However, if women have intact ovarian function and you use an aromatase inhibitor, it can actually have an opposite effect and cause their estrogen levels to spike.

So if you're going to do that, you have to couple it with ovarian suppression. And so understandably if we're putting someone into medically induced menopause, we really only do this in very high risk premenopausal women.

When women are post-menopausal, our preferred agent generally is an aromatase inhibitor. Both Tamoxifen and aromatase inhibitors have a lot of similarities in that they can cause menopausal type symptoms like hot flashes, but some of their differences that we often look to help us with decision-making is that Tamoxifen can increase risk of blood clots as well as uterine cancer in post-menopausal women.

So those are things we take into consideration. And then not similarly aromatase inhibitors can increase the risk of osteoporosis, which Tamoxifen does not do so in women with very high risk of osteoporosis, that's something that we also take into consideration.

Host: And length of time you use Tamoxifen or aromatase inhibitors is limited, right? It's five years in some cases, 10 years. Right?

Dr. Mahler: Yeah, so you're absolutely right, Kendal. I'd say that five years is the most common, but again, in higher risk disease or in particularly young patients, sometimes we consider it out to 10 years.

I usually, when I'm speaking with women, say to them, you know, what I try and aim for is five years. And then depending on how you're tolerating things, we can have the discussion at that point about whether or not we extend therapy.

Host: So, when do you consider non-hormonal chemotherapy? This is obviously for patients with more advanced disease, metastatic disease, certainly, but even in the early stages, you consider it as well?

Dr. Mahler: Yeah, so that's a tricky question to answer like straight up, but basically their receptor status comes into play with how we decide who gets chemotherapy in either neoadjuvant or adjuvant setting. So maybe sticking along the lines of hormone receptor positive women.

In this situation, we really try our best to deescalate therapy, meaning that we don't like to give chemotherapy unless women really need chemotherapy. And oftentimes in hormone receptor positive disease, we will have them go to surgery first. And then on their final pathology, we will do extra molecular testing to give us a better idea of how their cancer will respond to chemotherapy to try and guide our decisions.

Of course, exceptions to this rule in terms of women who have very locally advanced disease, that's not operable upfront. Then we may consider chemotherapy upfront.

But for the majority of women with hormone receptor positive disease, we consider chemotherapy in the adjuvant setting. And we really use these sort of molecular tests to help guide our decision.

Now, when we think of triple negative disease or HER2 positive disease, I think that medical oncologists will give chemotherapy much more easily to these patients. For HER2 positive disease, we have to give chemotherapy in order to be able to give herceptin or HER2 targeted drugs. So that's why these women will often get chemotherapy. And then similarly for triple negative due to its high risk of recurrance, a lot of these women will also get chemotherapy.

One of the changes in our treatment paradigms in more recent years is that for HER2 positive and triple negative disease, we are giving a lot more neoadjuvant chemotherapy than we used to in the past. Part of this is because there's been a lot of recent evidence that's come out about looking under the microscope at the time of surgery to see how the disease has responded to the neoadjuvant treatment.

We often throw around the term of pathologic complete response, being that patients who will then go to surgery and have residual disease that's visible under

the microscope have a much better prognosis than women who still have residual disease at the time of surgery. And we sort of use this result to help better guide our adjuvant therapies, whether we escalate adjuvant therapy or deescalate adjuvant therapy.

Host: If you give chemotherapy with the modern agents, what can women expect in terms of side effects?

Dr. Mahler: Yeah, so it, it definitely depends on which chemotherapy you're using.

Some of the most common regimens, I say common side effects are things like fatigue, not having the same energy levels. They certainly can be nauseating. However, I counsel all of my women that if you feel slightly queasy, that's normal. I do not want you to be throwing up. If it's to that point, I want you to call me because we have a lot of great supportive antiemetics these days that that should not be the case for women. It certainly can suppress your immune system.

So I counsel women on if you're feeling unwell, I want you to check your temperature. And if you have a temperature to come to the emergency department. Not all chemotherapy regimens, but some regimens require sort of GCSF boosting to try and prevent febrile neutropenia. And then depending on which medications they get, certain medications can cause hair loss, which is one of the common things that you see in breast cancer patients. They can cause neuropathy as well. And those are some of the neuropathy is one of the long-term side effects that I really try my best to prevent in patients because likely as you said, a lot of our women go on to live very full lives afterwards.

And the neuropathy is one of the things that can sort of be a reminder of treatments of the past. And then more uncommon side effects, but serious ones that we always think about is the effect that it may have on women's heart. Certain chemotherapies, particularly adriamycin can have that effect. And then also the, HER2 directed therapies like Herceptin can have those effects.

Host: What do we need to know about Herceptin, long-term that comes up?

Dr. Mahler: Fairly often. Yes. So I mean, what I counsel women on about Herceptin long-term because a lot of women who are getting this in the curative setting will be on it for a year after their surgery. And then in the metastatic setting can be on it for many years; is that a lot of times for these women, we will get a port, which we don't get for all of our cancer patients. And part of that is just kind of typically given intravenously every three weeks. And so that way they don't have to get peripheral IV pokes every time they come in.

Generally, it's really well tolerated. It's Herceptin's not like once a year not getting it with chemotherapy and you're just getting single agent. It's not immunosuppressive. It doesn't cause nausea. Women's hair will grow back. They will really start to feel more like themselves again.

One of the possible toxicities that we always keep an eye out for is the risk of it reducing women's ejection fraction. So especially when I'm giving this in the curative setting, I will make sure that I'm getting echocardiograms done every three months. As if you catch drop in ejection fraction early, this can be reversible and I'll have a very low threshold to hold the medication and involve cardio-oncology.

That being said, I do also stress to women this is not a common side effect, but one that all of us oncologists will see in our practice at some point. And so a serious one that we want to try and pick up early.

Host: So. In nearly half of women, even with advanced stage three disease, stage four is not curable, but stage three is curable. Nearly half of women are going to live more than five years, according to the statistics. But when do you consider someone cured?

Dr. Mahler: So, I mean, this is a tricky question, right? Throwing around the word cure. I always am a little bit hesitant to.

What I often say to women is that breast cancer is not like some of the other cancers that we treat where we do surveillance scans up to five years. So then at five years, people are like, okay, great. I'm done. We don't do routine surveillance scans after breast cancer treatment. And so what I often explain to women is once you've had your surgery to the best of our knowledge, all of your cancer has been removed. And any treatments that we consider after that are really with the goal of killing any possible microscopic cancer cells that are left behind that we can't see to the naked eye or to any forms of scans.

And that's sort of how I explain it to patients is, you know, once you've had your surgery, I sort of think of that as this, the cancer being gone. Breast cancer is one of these cancers, particularly hormone receptor positive that the risk of recurrence continues many, many years out.

So that's why I'm very hesitant to ever say, this is the timeline where you're completely in the clear, if that makes sense.

Host: I had always thought of 10 years as a good marker that if someone got beyond 10 years, their chances of recurrence is diminished, that may be old information.

Dr. Elmore: Yeah. We know that the likelihood of cancer recurring is highest within the first five years. And so that's typically what I counsel my patients on. And even though beyond five years, that risk does continue to increase; we know that the vast majority of women that are going to have a recurrence will be within that five-year timeline.

Dr. Bird: And I think that's probably helpful on our end, too, just in thinking about how we consider ongoing screening for breast cancer. Because certainly in that initial five years I think, obviously continuing with annual screening, there certainly are women who at some point in time are interested in decreasing the frequency of screening mammography, and it's always hard to decide, like what, at what point does that happen? And particularly women who might be older at the time of their diagnosis, and you're kind of pushing beyond the five-year mark.

When can you start to feel comfortable, maybe decreasing from annual mammography? I think in primary care, we oftentimes feel comfortable when there's other chronic diseases that might change how a woman thinks about a subsequent breast cancer diagnosis.

But I'm just curious in, your opinion, Mary, are you kind of annual mammography at least in 10 years out for most women, unless there's some other chronic health condition?

Dr. Mahler: Yeah, I guess that's a, I don't know that I have a set number of years that I say, okay, after this point I stop. I agree with you, Dr. Bird, that it's kind of it depends on their other co-morbidities, depends on their age. Depends on the patient. Right.

I think that we all know that we have some patients who, if you say to them, I think we are at an age that we can stop doing your annual mammogram, they're not going to be happy about that. And then there's other patients that we all have that every year. You're like, you know, you have to go for this again. And they're like, oh, they don't want to go.

So I think part of it too, is about patients and what their wishes are about how frequently they want to go. Leisha, I don't know if you have a set timeline that you think of.

Dr. Elmore: I tend to follow the American Society of Breast surgeons Consensus Guidelines on this topic. And so after curative intent treatment, I typically will image people every six months for two years, and then annually thereafter until

their life expectancy is less than 10 years at which time, you know, obviously that's a hard thing to assess.

And so that's sort of, you know, my thought process in terms of imaging, but after someone's been treated for breast cancer beyond that two year mark, where I get more frequent imaging, I still continue with annual mammogram.

Dr. Bird: Yeah. And I suppose I should have been a little more specific because I think the question that typically comes up or that we're faced with in primary care for average risk women. So women who haven't actually had a breast cancer diagnosis is the annual versus biennial. So every two years, and I think in general, we shy away from that in anyone who's had a prior breast cancer diagnosis and it sounds like there's no real good guidelines on that. Other than the more intensive screening initially after treatment.

Dr. Elmore: Yes, exactly. And even in average risk patients, I think, you know, what's become particularly confusing is there are at least you know, I think six different societies, that have six different guidelines for screening. But I, still tend to, even for average risk patients do annual mammography in which again, follows that American Society of Breast Surgeons Consensus Guidelines.

Host: And when do you guys have your patients go back to primary care and stop seeing you? At what point do you say you no longer need to see me?

Dr. Elmore: On the surgical side of things, once someone has hit five years, I sort of transition them. But the terminology I use is from active surveillance to survivorship.

And so at that five-year point, I turn them back to their primary care provider for additional imaging.

Dr. Mahler: I usually follow women as long as they're on systemic therapy. So for a lot of these hormonal therapy women, that could be five or 10 years. For the women who have let's say triple negative or HER2 positive that aren't on these long-term treatments. I often similarly to Leisha, will try and follow them up to five years out and I'll try and stagger my visits with the surgeons so that every six months they're seeing one of us.

Host: Well, that's great. Thank you to both of you for coming on.

And Amber and I are constantly managing breast cancer on some level, either screening for it. It's probably, you know, in my average day, it happens a dozen times that I make a decision or an intervention related to breast cancer, either

having to do with somebody who's a survivor, who's coming back to me or I'm in the screening process. So this is something we see quite often.

Is there anything that comes up that you would say in your practices that you want to communicate back to the primary care community, some sort of pearl or things that bother you that you want to tell us about?

Dr. Bird: Now's your chance. Tell us now.

Dr. Elmore: I think we already touched on the main thing, which I will say people that come through the Penn system are very well worked up, but I would say getting that diagnosis and completing the workup prior to referral is incredibly helpful for both you know, from our standpoint for counseling the patient and to kind of quell that the anxiety associated with that visit.

Dr. Mahler: Yeah. And I think that my big thing is just, I find early on in treatment, a lot of women want someone that they know and trust to be able to offer them support and sometimes walk them through things a second time in the sense that.

When they see us, they're oftentimes in shock and don't absorb everything. And I, find it always super helpful at the third or fourth visit when they say, yeah, I followed up with my primary care doctor and they walked me through things as well, which made me feel much more comfortable. So I'm always very grateful to primary care doctors for sort of touching base with women when they're first meeting us. Because I think that it offers them a huge amount of emotional support.

And if you ever have questions about our treatments or what we're doing, I always encourage people to reach out I'm somebody that sends it sends a lot of messages to primary care doctors.

Host: And this is the purpose of this podcast because we do engage in these discussions often and patients do come back to us a lot, trying to just have somebody they trust, talk it through with them. So this is very helpful. The discussion, this has been great.

Dr. Bird: Thank you. This has been wonderful. And certainly some great counseling pearls that I will take back to my own practice.

Host: So, thank you all for joining us again for the Penn Primary Care podcast. We hope the information tonight is going to be useful to you in your practices. And please join us again next time.

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