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### The Steep Toll of Endocrine Therapy on Breast Cancer Patients

Announcer:

You're listening to a special Focus on Breast Cancer from Advances in Women's Health, sponsored by Lilly.

Dr. Birnholz:

Coming to you from the 42nd Annual San Antonio Breast Cancer Symposium, this is ReachMD. I'm Dr. Matt Birnholz. Joining me today is Dr. Dawn Hershman, Professor of Medicine and Epidemiology, and Leader of the Breast Cancer Program of the Herbert Irving Comprehensive Cancer Center at Columbia University. Dr. Hershman is presenting on the subjects of Toxicity, Cost, and Adherence to Endocrine Therapy with the overriding theme that everything comes at a price. Dr. Hershman, welcome to you.

Dr. Hershman:

Thank you. Happy to be here.

Dr. Birnholz:

It's so great to have you on this program. I want to set the stage for this challenging topic that is, hopefully, near and dear to everyone in the oncology space and, to start, how did you come to focus on the tolls of endocrine therapy for this year's symposium?

Dr. Hershman:

Well, this has been a longstanding interest of mine. I think very early in my career it became apparent to me that we had a lot of really fantastic treatments that people didn't initiate, they didn't complete, and they weren't really getting the benefits of the standard treatments, but we were putting so much focus on incremental, small gains without really focusing on the big gains we could get with something as opposed to nothing. And so, I really focused my research initially on understanding what the rates of adherence were to people completing their chemotherapy, and, and that got me into endocrine therapy and one of my first large studies looked at 8,000 women in Kaiser Permanente and we were shocked to see that about 25% of patients didn't complete their five years of endocrine therapy, and then an additional 25% were taking it intermittently. So, big gaps of time while they weren't taking it over that five-year period and, low and behold, women that took it lesser, stopped altogether, had worse outcomes than those completed their therapy as prescribed.

Dr. Birnholz:

That's a-a massive disparity – uh 25 and perhaps even greater percentage of drop off of these patients. Your talk today centers on these three factors – toxicity, cost, adherence – interconnected in many respects. Does one form of barrier predominate in your mind? Or do they all rest on the same playing field and the same level?

Dr. Hershman:

Well, you know, they all are modifiable to a certain extent, but we know for sure that the most common reason people stop their medications is due to toxicity. That is, without a question, the most common reason. But, factors are at interplay with each other because patients that have uh high copayment and they have side effects may be even more likely to stop taking their medications. Or if you have not a good belief that the medication works and then you have some other factor on top of it, it may be just enough to push you over the, over the edge. So, there's probably multiple things going on, but when you look at the data and you look at – talk to patients, the most common reason people stop is due to side effects.

Dr. Birnholz:

Now let's dig into that for a second because on one level it's very intuitive to say side effects are a major reason why patients would

discontinue endocrine therapy, but from an oncologist's or an oncology clinician's standpoint, what are some factors that either get overlooked or maybe not get placed top of mind when it comes to side effects and truly prioritizing them in, in the, the minds of the patient's eye.

Dr. Hershman:

Right. Well, that's actually a great question because sometimes as oncologists we're used to side effects that are life threatening and are obvious – a drop in your ejection fraction so you can't breathe or high fevers that put you in the hospital, but it's the chronic side effects that interfere with the activities of daily living and women's quality of life that really have a big impact on, on long-term adherence to treatment because people have to take this for a long period of time. So, sometimes questions we don't always ask patients are the things that make them the most miserable – their mood, depression, that they don't feel like they're the same person that they used to be. The most common side effect from aromatase inhibitors is joint pain, so people complain, I can't get up from a chair. This medicine's making me feel like an old woman; I can't open a jar. And while those aren't life-threatening side effects, they alter your experience day in and day out, and if you don't have any evidence of disease, it becomes hard to take a medicine that's causing side effects when you don't know if your cancer's really ever gonna come back.

Dr. Birnholz:

And I imagine the increased awareness of that – these quality of life side effects – we often bandy that term around, quality of life, but then we don't do much more than just put it into a review of systems and you say, any joint pain or anything like that – and check it off or don't check it off, how has your care for breast cancer patients changed in the wake of discovering these effects that don't always make the top of line item but are very, very important.

Dr. Hershman:

Yeah, I mean I think it's important to talk to patients and engage them and understand and let them know that these side effects are, are normal, but then also to try to work with patients to overcome them or come with suggestions of things that might work to alleviate their side effects. A few years ago, we presented here at San Antonio a very large study that we did that looked at the role of acupuncture for alleviating this side effect. It was a large, randomized, multicenter trial and it actually got a fair amount of press at the time because it did show a substantial benefit of acupuncture compared to either sham acupuncture or waitlist control in reducing this symptom and that we were able to show that the pain reduction was not just during their treatment, but it was also after they completed it. So, you want to be able to partner with patients and try to come up with solutions. You also want to be able to really be able to explain the benefits to say, well maybe also maybe this brand isn't working. Let's try a different brand. Or, maybe the aromatase inhibitor isn't the right medicine for you, let's try tamoxifen. But it has to be a process that you spend a lot of time and effort because that's really where you get the benefits of these tremendous medications.

Dr. Birnholz:

Well, let's contrast that process, which is sort of a, a working discovery with patients based on their experience, and contrast that to cost of medications, which is another major barrier that you're going to be speaking about today. What can clinicians not afford to overlook in this case? No pun intended.

Dr. Hershman:

Yeah, well, you know, it's actually was fascinating. We, we also were one of the first groups to look at just the issue of copayment about five or six years ago, and aromatase inhibitors, at the time, were not – there were no generic versions yet. And, you know, the out of pocket cost if you had no insurance was over \$200 a month. But we were finding a big range in terms of copayments being anywhere from \$0 to \$50 to \$100, depending on the kind of insurance you have and, low and behold, the amount of copayment you have was highly correlated with adherence rates. We looked at type of insurance and found similar things, and we looked at when all of these medications switched from being branded to having generic versions, and we found that women that started with lower cost medications were more likely to be adherent than those that started with higher cost medications. This was really important because it suggests that policy interventions that make drugs more affordable can have an impact on adherence. And, you know, this is really the tip of the iceberg because since that time, about hundreds of oral medications for cancer therapy have become available, many of which cost \$11,000+ per month, which is hugely different than the \$200 or \$300 copayment for the aromatase inhibitors, and so the out-of-pocket cost can be astronomical. And so, you know, subsequent research has shown that a patient's likely to initiate treatment or be on it for any extended period of time is directly related to those copayment amounts as well. So, you know, overcoming one barrier is making drugs accessible.

Dr. Birnholz:

Right. Do we have a sense of outcomes differences for those based on the disparity of adherence rates?

Dr. Hershman:

Well, we really just know what nonadherence does, not what each individual factor that contributes to nonadherence, how that contributes to outcome.

Dr. Birnholz:

Coming back to adherence rates, you have done an enormous amount of research. In fact, I wanted to ask you if there was any facet of these barriers that you have not actively investigated – among your 250 publications.

Dr. Hershman:

Well, I mean I think that, you know, we're always looking at better ways to improve adherence and it's the behavioral interventions that are the most challenging. There are challenges in terms of how you design these studies and measure adherence, but there're bigger challenges trying to come up with a fix. It's not so easy to come up with an intervention that you can give long term that works. We showed that in a presentation we gave at ASCO this past summer because we presented results from a large randomized trial of text messaging to see if reminding people to take their medications but also in that text message reminder, educating them about the importance of the medication and how well it works and what to do if they have a problem, if that would improve adherence rates, and we really found that that intervention was not effective and that most of the research in that area of behavioral interventions look at, you know, can you improve something over six-week or 12-week period. We looked at three years, and if you look over time, those kinds of interventions fade. So, really trying to think of ways of changing people's behavior is complicated and a big challenge.

Dr. Birnholz:

And I imagine it's very hard to tweet out all the factors that go into nonadherence over that kind of time span, but if cost were not an issue – say in some areas where policy is such, whether it's in this country or other countries, that people can access the medication frequently, routinely – would adherence be expected to be on a more even trajectory? Or is that still...

Dr. Hershman:

Because that's just one of many factors, um, you still see issues. And, as I said before, the most pressing issues are probably related to the toxicity, and finding interventions to treat that toxicity that people tolerate is complicated because patients don't want to take a medication that could have its own host of side effects to cover the side effect of another medication, and so that's where we have to really be creative and openminded because while some pharmacologic interventions, such as duloxetine, otherwise known as Cymbalta, can reduce pain, most patients don't want to take it, uh, because it, it also causes its own secondary effects. So, trying to think of ways that, that are accessible to patients to, to control these side effects, I think has been a big challenge.

Dr. Birnholz:

So, moving forward, so much of the focus on endocrine therapy is what's in the future? What's the next trend? What's hot in this area? What I love about your, your talk is that it forces us to truly take stock of where we are, what the barriers are, what the challenges are – and how to think creatively. What is next on the horizon for you and your colleagues to try to creatively get around some of these really thorny issues?

Dr. Hershman:

Yeah, I mean I think, you know, we're always trying to investigate new ways to control side effects that are nonpharmacologic and nonopioid based. You know, a variety of things can be effective, such as exercise and acupuncture and meditation. At the end of the day, if it keeps somebody on their medication, that's the most important thing. So, really trying to come up with ways of predicting who's going to be less likely to adhere and based on what factors that they may have at baseline that may lead us into whether or not somebody's going to need intervention for symptoms or whether or not they're going to need an intervention that helps make them remember to take their medicine, or whether or not they're going to need other types of educational or support to help them get through it. And so just like we need to personalize our treatment based on characteristics of patients, we probably need to personalize our interventions also based on baseline characteristics of patients.

Dr. Birnholz:

That's a really great comment to close our interview, looking at those interventions, but before we do, anything at the San Antonio Breast Cancer Symposium that you're particularly excited about, whether it's new data that's coming, new investigations, workshops that are happening?

Dr. Hershman:

Yeah, I mean there's – this is the meeting if you're involved in breast cancer from, on, on every level it covers the entire continuum from prevention to advocacy to treatment, surgical treatment, radiation treatment, treatment for advanced disease – there's lots of interesting data being presented about new drugs to treat HER2-positive breast cancer. There's a lot of buzz around that. Also, there's a lot of excitement about CDK4/6 inhibitors and whether or not there'll be evidence to try to move them earlier along with endocrine therapy for patients with nonmetastatic disease. A lot of interesting abstracts looking at IO, or immuno-oncology agents, in patients with triple-

negative breast cancers which have been so difficult to treat, so there's going to be a lot of exciting presentations at this meeting that will undoubtedly change practice.

Dr. Birnholz:

Well, with those promising avenues on the horizon, I very much want to thank my guest, Dr. Dawn Hershman, for joining me to think through these most prominent barriers to endocrine therapy and ways that we can creatively move past them in the future. Dr. Hershman, it was fantastic having you on the program.

Dr. Hershman:

Thank you very much for having me.

Dr. Birnholz:

To access this and other episodes covering innovations in breast cancer treatment, visit [ReachMD.com](https://ReachMD.com) where you can be part of the knowledge. For ReachMD, I'm Dr. Matt Birnholz, and thank you for listening.

Announcer:

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