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Are PARP Inhibitors the Future of Treating Triple-Negative Breast Cancer?

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 European Society for Medical Oncology's annual congress in Barcelona, Spain, this is Reach MD. I'm Dr. Matt Birnholz. I'm joined by Dr. Hans Petter Eikesdal from the University of Bergen in Norway. Dr. Eikesdal I'd like to talk to you a little bit about the study that you and your colleagues have been presenting. It's sort of turning heads because it's, as you put it, you said it's in a way the idiot study because it's very counterintuitive, but you're finding some interesting new results regarding looking a PARP inhibition in primary triple-negative breast cancer. Can you talk a little bit about this study, and what you were hoping to find?

Dr. Eikesdal:
Well, I mean it's trial of trying to find targeted agents that we can use instead of chemotherapy in this patient population. And these patients so far, basically only had chemotherapy, chemotherapy, and even more chemotherapy. So it's of course a lot of side effects and a tough treatment for the patients to get. And at the same time, there is a soft population within triple-negatives that are BRCA mutated – germline BRCA mutated, and it has been known for a long time that they respond really well to PARP inhibitors. But we tested it. This is in patients with triple-negative breast cancer because we also know that there's a lot of DNA damage defects within triple-negatives. And we wanted to see if we could have an effectiveness compound in first line. The reason why I said it's kind of an idiot trial is because this has been tested before in the advanced setting in patients with late stage triple-negative breast cancer, metastatic, where there was no efficacy of PARP inhibitors. But of course looking at first-line setting and treatment-naïve patients, it's a very different situation. The genomic picture and the tumors are probably very different. So we found a very high response rate to this treatment given in the neoadjuvant setting

Dr. Birnholz:
It is very much a head-turner. We've seen more sobering accounts, even here at ESMO, relating to keynote 119 clinical trial saying that even some of the heavy-hitter immunotherapies and other targeted therapies didn't seem to be very effective for triple-negative breast cancer. But your findings are indicating that maybe there is hope on the horizon. Is that correct?

Dr. Eikesdal:
There is definitely much more to gain by using PARP inhibitors than with immunotherapy in this patient population, to my opinion. I haven't seen those kind of high frequencies of response in using immunotherapy in this patient population. I think you need better biomarkers if you're going to give immunotherapy for triple-negatives. Whereas, with this kind of treatment, it's very low toxic. The patients are – most of the patients were still working, they had minor side effects such as a little bit of fatigue, a little bit of nausea, but it was nothing compared to chemotherapy.

Dr. Birnholz:
It's remarkable. So do you think it's going to be still years from primetime as far as being able to incorporate this into practice? Or will this type of practice change if using this in more than the neoadjuvant setting gain traction quickly, as to your point, you look at fewer side effects, potential efficacy, that's beyond what people would have expected?

Dr. Eikesdal:
Well, I mean, it's – this is a small trial. It's only in 31 patients, so it's not kind of ready for going into routine use. It needs to be confirmed in a larger trial, which would have to kind of go internationally because we don't have enough patients in Norway to do this in a larger setting. At the same time, it's really affected this treatment. It regresses the tumors pretty dramatically in 65% of the patients, but it's not going to take the tumors down to zero, at least not if they're locally-advanced breast cancer. So you need something else after the PARP inhibition or combined with it. And what that would be, we've been testing different types of chemotherapy after the PARP inhibition which might – which gives something. And there are also of course preclinical data that you can combine this with. For instance, immunotherapy, that PARP inhibitors are kind of triggering an immune response. But we don't really know.

Dr. Birnholz:
So it sounds like there are a few next steps; almost too many to count. But any immediate next steps on the horizon for you and your team?

Dr. Eikesdal:
Well, what we're doing now is focusing on the comprehensive genomic analysis of these tumors to really pinpoint what kind of genomic aberrations we are predicting for response to PARP inhibitors or to the chemotherapy that we're kind of giving in sequence. So that's our main focus currently. And then we'll take those results into kind of starting a next trial of personalized breast cancer therapy where we test different subtypes of breast cancer.

Dr. Birnholz:
I really want to thank you for your time. Before we go, one last question for you, just for our healthcare professional audience. Clearly, this trial helps turn people's heads around based on what they – questioning their assumptions, which I think is a very powerful motif in this entire conference. Are there any other messages that you would want to provide to healthcare professionals, breast cancer specialists in particular, after what you've uncovered from this study?

Dr. Eikesdal:
I think kind of the main message is don't give the same kind of treatment to all patients in the neoadjuvant setting. It's not a one-size-fits-all, and it's definitely not correct for neoadjuvant treatment of breast cancer. You need to individualize.

Dr. Birnholz:
I've been speaking with Dr. Eikesdal from the University of Bergen, in Bergen, Norway. Dr. Eikesdal, thank you for your time.

Dr. Eikesdal:
Thank you.

Dr. Birnholz:
For access to this, and other episodes, visit ReachMD.com. I'm Dr. Matt Birnholz. Thanks for joining us.

Announcer:
You've been listening to this special focus on breast cancer from *Advances in Women's Health.* To revisit any part of this discussion and to access other episodes in this series, visit ReachMD.com/Advances-in-Women's-Health, where you can join the conversation and Be Part of the Knowledge. Thank you for listening.