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### Investigating the Impact of Cannabidiol on Breast Cancer Cell Viability

Announcer:

You're listening to Breaking Boundaries in Breast Cancer, sponsored by Lilly.

Dr. Birnholz:

This is ReachMD. I'm Dr. Matt Birnholz.

I'm joined by Dr. Luka Dobovisek. He is a medical oncologist and, aspiring Ph.D. candidate at the Institute of Oncology at Slovenia. He's presenting a preliminary study on cannabidiol increases, , in the potency of tamoxifen in inhibiting breast cell cancer viability.

Dr. Birnholz:

Dr. Dobovisek. Welcome to you.

Dr. Dobovisek:

Hello.

Dr. Birnholz:

Well, it's great to have you on the program. What I'm fascinated by in your – in your preliminary study here is that when we think of CBD or cannabidiol, we typically think of the palliative affects um – and its applications in that arena, but there've been some recent studies that you've eluded to that have started looking at cannabinoids, um, beyond palliative treatment and perhaps, as something that's more antiproliferative, anti-anti- metastatic for cancer. Um, can you talk about that as a background to your study?

Dr. Dobovisek:

Yeah, sure. So, I'm coming from a clinical point of view here because we recognized a very dire need basically in our patients to like resolve the question if CBD or cannabinoids are safe in breast cancer patients because so many of our breast cancer patients, , take cannabinoids in one form or another during their treatment and they're asking us this question, , almost every day in our clinical practice, Should I take cannabinoids? Will they help me, What sort of cannabinoids should I take? Should I take THC, CBD, or a combination of both? Or, so, this is a very important topic I think and it's not being discussed as it's – as much as it should be, basically.

Dr. Birnholz:

And that – that's certainly has been known to be the case, although it's sort of eye opening I think for many people when they hear, is it possible that CBD could have some effect on cell viability for cancers and an anti-tumor affect? Uh, where do the grounding for that theory come from?

Dr. Dobovisek:

Sure, So our first concern was that is it safe, right? Of course, we did not answer this with study just from breast cancer cell lines, but we wanted to see like if CBD has effect on breast cancer cell lines and what that affect is. So, we took like hormone receptor positive and hormone receptor negative or triple-negative breast cancer cell lines and exposed them to different concentrations of CBD. And what we saw, basically, that increased doses of CBD decreased the proliferation of – of different breast cancer cell lines, and it – maybe it depends on the type of cell line, we are exposing CBD, um, we're exposing it to the CBD. So, the next step we – we – we thought – we thought about how if the CBD effects different treatments, standard treatments of, um, breast cancer, our background logic behind this was, we know now that, CBD or okay – better – tamoxifen acts as an inverse agonist on CB1 and CB2 receptors. So now we know that this molecule, which is like a standard treatment and – used for very long time in breast cancer treatment, also works on the – endocannabinoid system. Also, there are some data that, endocannabinoid system and the estrogen system where the sex hormones in

the human body are connected. Like there are two studies who showed that increased levels of estrogens during ovulation also caused the increased levels of endogenous cannabinoids, so, this is also a, um, this correlation between sex hormones and the other in the one side and the endocannabinoid system on the other side just begs the question, but will different cannabinoids effect the treatments in hormone receptor positive breast cancer, right? So, this was our main focus, and we tried to do some preliminary studies on that.

Dr. Birnholz:

So, let's talk about that for a minute. What were these preliminary studies? What did you investigate in? What were some of the initial results?

Dr. Dobovisek:

Yeah, so, we took, like I said, we took different breast cancer cell lines, hormone receptor positive, and hormone receptor negative breast cancer cell lines and first we applied different doses of CBD and we got, like, a nice, um, dose responsive, um, curve there. So higher doses of CBD decreased the viability of the different breast cancer cell lines and this was our first – this was the first part of the study. Also, we – of course – confirmed the expressions of CB1 and CB2 receptors in breast cancer cell lines, and we confirmed that both the breast cancer – different breast cancer cell lines confirm, um, expressed both CB1 and CB2 receptors, but this was also done to some degree – this was also done before, right? What – what was not done before is basically, um, see if the CBD effects different, treatments – standard treatments for breast cancer, right? So, and our results are like I would say the main message from our results is there was not adding CBD to standard treatments – what - did not result in increased viability, basically. It – it was not worse, right? Many times it showed decreased viability and there is also some evidence that CBD increases potency of tamoxifen and inhibit – inhibiting like hormone receptor positive breast cancer cell lines but basically all the studies, um, all the experiments we did, um, did not show a – an increased proliferation with CBD, which may- may – which may speak to that – that CBD is actually not, something we should be so afraid in the breast cancer setting, but indifferent – like in hormone receptor positive and hormone receptor negative or triple-negative breast cancer setting.

Dr. Birnholz:

at this point, it is hard to know whether that affect appear actually might be something in the – in the mechanism that is inhibiting, uh, growth, but there could be something there to investigate.

Dr. Dobovisek:

Sure, so, um, of course, I totally agree. This is very – a very preliminary study and I would say that, um, it is important to understand here that endocannabinoid system is very complex, right? And so, CBD is basically, it works on both CB1 and CB2 receptors. Also, we don't – we do not know how this translates into like a, um, person, somebody who smokes marijuana, who gets THC, CBD, and many other cannabinoids, right? So this is very unclear, um, but, um, there are also a lot of studies that show that cannabinoids effect, um, the secondary messages or the molecular mission of the cell in the – in the antiproliferative way, but I would say the big unknown here is the, uh, immune system because like you can study, um, all you want, the mechanism or the – the decreased viability of breast cancer cells in breast cancer cell lines, but we also know that cannabinoids effect the immune system in probably most – more immunodepressant way. So this is not very good for cancer, right? We would not want any immunosuppression in cancer patients, as we know the immunotherapy and so on, it's very big these days. So, maybe these results would not be so evident in where also, um, the immune system would be suppressed, but I would like to ex – say once again that like a lot of this studies have already been done. They are very fragmented. They – they are not systematic. There are some results are contradictory. So, our main focus was to see if there is a – if the tamoxifen – uh, if standard best ca – cancer treatments are effected by CBD and basically, maybe they are, but in a good way, not in a bad way. We can say, of course, it's preliminary research, but this does not and, um, translate into a clinical practice at all at this point, like, there are so many steps between that, um, at this moment.

Dr. Birnholz:

So what would you say is the next step for you and your team in Slovenia?

Dr. Dobovisek:

So, what we are planning to do next is, um, go to a animal – to go to animal models and see, um, what other defects are there. So, of course, animals have the immune system, , and the breast cancer cell lines don't, so, this is one way we can say if this is also effective, um. So we have the component of the immune system there. and then, we will also do like a clinical research in, um, patient samples, who were patients who were treated with tamoxifen as an adjuvant treatment and so we will do the – we will see the expression levels of CB1 or CB2 receptors in that patient population. So, we will see if the expression levels of CB receptors actually, um, translates into a – as a predictive base – prognostic marker for overall survivors or so on. So the clinical implications of that. So, um, this one thing, but maybe in the future, there will be a window trial with some – with maybe with CBD, I don't know, um. We will see that like how the CBD if, um, took in adjuvant setting, if it's actually makes, uh, what are the effects on the tumor itself in the patients, um. So this – this will – I would love to have this as a next or the late step in the research, but I don't think we are there yet.

Dr. Birnholz:

A little bit more time, uh, before we get to that place. Well, I really want to, uh, thank you for your time. It's been great talking with you about this, uh, novel study, and I hope that the next steps prove successful and, um, that there be many of them coming in the future.

Dr. Dobovisek:

Thank you very much.

Dr. Birnholz:

I've been speaking with Dr. Luka Dobovisek from the Institute of Oncology in Slovenia. and we've been speaking about the possible role down the road for cannabidiol in antitumor activities for breast cancer. thanks again.

Dr. Dobovisek:

Thank you very much.

Dr. Birnholz:

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

Announcer:

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