Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/frontlines-metastatic-breast-cancer/the-past-present-and-future-of-metastatic-breast-cancer-care/39718/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

The Past, Present, and Future of Metastatic Breast Cancer Care

Announcer:
You're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. And now, here's your host, Ryan Quigley.

Ryan Quigley:
Welcome to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Ryan Quigley, and joining me to discuss the history and evolution of metastatic breast cancer care is Dr. Gregory Vidal. He's a medical oncologist at West Cancer Center in Memphis, Tennessee, and an Associate Professor at the University of Tennessee Health Sciences Center.

Dr. Vidal, thank you so much for being here today. Really appreciate you doing this.

Dr. Vidal:
Oh, you are welcome. Thank you for inviting me.

Ryan Quigley:
So, Dr. Vidal, to start us off, I'd love it if you could set the stage for us a little bit. When clinicians first began to define metastatic breast cancer as a distinct clinical entity, how was it understood, and what did it mean for patients at the time?

Dr. Vidal:
If we go back in history, a lot of patients were dying of this disease and, once it became a separate diagnosis, metastatic breast cancer probably was established very early. I think where we started differentiating is, how do we cure when we see patients early? And how do we define that and separate those?

I think metastatic breast cancer is probably what most physicians were dealing with, because most patients who presented early would eventually end up with metastatic disease. It's how we then figure out, how do we treat metastatic disease and how do we prevent patients from becoming metastatic?

And that, over time, has evolved to where we are today.

Ryan Quigley:
So looking back to the mid to late 20th century, what were some of the major treatment milestones that first began to change outcomes for patients with metastatic disease?

Dr. Vidal:
I don't think you can talk about metastatic disease without talking about the early disease. So, for breast cancer particularly, we thought very early on that it started in the breast—you just do surgery. And you had really radical mastectomies, taking away muscle and lymph nodes and just leaving ribs, and then those patients would still end up having metastatic disease.

So then, there was the recognition that maybe those cells are escaping the breast prior to all of these radical surgical maneuvers. And we then also now need to focus on killing those cells that are circulating around that already left the breast to prevent them. And so that's where systemic therapy started developing.

In the early, I think, 1890s was the first realization that estrogen plays a role, when physicians would, in premenopausal women, remove the ovaries and see responses in the breast. And so there was a recognition that the hormones—estrogen—may play a role.

It wasn't until, say, the 1950s when estrogen was cloned. In the 1980s and 1990s, we started seeing differentiation between estrogen

alpha and estrogen beta. And in the 1970s, we got a drug like tamoxifen, that could then target estrogen-positive tumors.

Again, in the 1970s, 1980s, we could figure out which tumors are estrogen-dependent versus not, and then develop a drug. So, in the 1970s, we started developing treatments that are focused on controlling diseases from a systemic perspective. You take it in your mouth, and it goes everywhere. And so that's some of the development.

In the later 90s, we have HER2. We also figured out that there are not only estrogen-positive tumors or hormone-dependent tumors, but there may be a subset of tumors called HER2-positive tumors. Those were really bad actors. Those patients died at a median survival of 18 months. But then, the recognition that this was driven by HER2 caused the development of therapies in the late 1990s that targeted HER2 and showed significant improvement in disease control and overall survival for those patients by using a HER2 target.

And then, later on in the 2000s, we had adjuvant settings, where we are curing more patients. And now that—which was the most deadly—probably has some of the best outcomes now. And we're still trying to figure out what we need to do for other subsets of breast cancers.

Ryan Quigley:
For those just joining us, this is *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Ryan Quigley, and I'm speaking with Dr. Gregory Vidal about key milestones in the evolution of metastatic breast cancer care.

Dr. Vidal, as research has progressed here, how did the growing understanding of breast cancer biology, particularly hormone receptors and, later on, HER2, begin to reshape metastatic disease and how it was approached?

Dr. Vidal:
Yeah, that's how science is so beautiful. Before, we used to do medicine with just bloodletting and using different ways to try to cure disease, and it wasn't until we used science that we figured out empiric reasons for why this thing is happening and how we target it.

So we talked about the estrogen development, and the fact that anti-estrogen, and recognizing hormonal therapies or anti-hormonal therapies, may be a treatment approach. We talked about HER2, but we started moving even further after we were able to sequence the human genome. We started recognizing that there are particular mutations that cause tumor genesis. Or the tumor started forming because of particular mutations—what we call driver mutations. And maybe, if we target those mutations, then we could shut down these pathways and have increased cell killing. And once it becomes cheaper and cheaper to do those sequencings of DNA, we can then, in a particular cell, have more of a precision-type approach and figure out, in that cell, what is the mutation driving that cell.

Pharma and academia come together and can further science to say, "Okay, I've seen these patients. You can get a mutation in your estrogen receptor—ESR1 mutation. Maybe if we got a drug that binds to each much better, we could have better cell killing. Things like PI3 kinase mutation happens in about 30 to 40 percent of estrogen-driven tumors. That confers more resistance or a higher-risk tumor. Can we target that pathway and shut it down?

That led to approval. Now we're doing ctDNA, where we can actually monitor the amount of DNA, and that can give us response recurrence information that we never had. And so science is driving all of this, and it's only done once we understand what's happening on a cellular level and be able to more specifically target those.

I have so much hope for the future in this realm, and science will continue to drive us. Hopefully we can get a cure for this disease.

Ryan Quigley:
So Dr. Vidal, before we wrap up, let's think big picture here. When you look at today's treatment landscape through a historical lens, what lessons from the past continue to shape how we think about the future of care?

Dr. Vidal:
That's such a very good question. I cannot talk about cancer care and lessons from the past without thinking about equitable distribution of treatment.

We have better tools, better drugs, and more effective drugs. But if everybody doesn't get it, everybody doesn't get the same outcome. We have to learn from how we behaved in the past to change how we behave in the future. And the cost of drugs is getting so much such that we are creating even greater disparity in who can and who cannot afford it. And so that's one of the learnings that we need to apply from the past to make the future better.

But from a pure scientific perspective, it's knowing that the cells itself and the tumors often have the answer to what the treatment could be. And we also have to go beyond just the cells, because the microenvironment in or around the cells is also very important in trying to figure out the best approach. Because that cell doesn't leave the tumor and go to the rest of the body without navigating through the tumor microenvironment. And the tumor microenvironment has to be open for that cell to be able to do that. And so managing all of the

area is going to be very important in trying to get to curing. And some of those cancers we may never cure, but at least if we make it a chronic enough illness such that patients die of something else and not the cancer, that's also something I'm looking forward to.

Ryan Quigley:
And that's as good a point as any to round out our discussion here on how the understanding and treatment of metastatic breast cancer has changed over time. A special thanks to our guest, Dr. Gregory Vidal, for sharing his insights with us today.

Dr. Vidal, thanks so much for doing this and joining us on the program.

Dr. Vidal:
Thank you very much for inviting me.

Announcer:
You've been listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. To access this and other episodes in our series, visit *On the Frontlines of Metastatic Breast Cancer* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!