After 30 years of research, pill for breast cancer approved for use

February 8 2023, by Teddy Rosenbluth

Credit: Unsplash/CC0 Public Domain

After six years of painful injections, Stephanie Walker has had enough.

Every 28 days, she drives an hour to Duke's Cancer center to get 50 mL

slowly injected into her glute muscles. The viscous mixture of castor oil and medicine is painful going in and leaves lumps in its wake.

Then she drives an hour back to her Tarboro home, seat warmers on to soothe the soreness. Walker, who was diagnosed with metastatic breast cancer in 2016, has endured so many of these injections, the tissue around her right hip has turned necrotic, she said.

"My hiney looks like it's been to war," she said. "I just got tired of getting poked."

Walker's regular injections may soon come to an end, thanks to a pill developed across the street from the hospital in Donald McDonnell's cancer biology lab. The Food and Drug Administration approved the medication, elacestrant, in January for use in late-stage breast cancer patients who have not responded to other treatments.

McDonnell expects elacestrant, which will be marketed as Orserdu, to completely replace the injectable treatment regimen. Not only is the pill less taxing for patients, clinical trials also found it to be more effective.

Hot flash's trash is breast cancer's treasure

Elacestrant had several lives before it was finally approved for breast cancer treatment.

First, it was a failed dementia medication. Then, Radius Health tested whether it could help reduce menopause-related hot flashes. It did not.

But Suzanne Wardell, an assistant research professor in McDonnell's lab, was fascinated by the way the pill failed at preventing hot flashes. In low doses, the medication seemed to help with symptoms, but in high doses, the efficacy suddenly dropped off.

She thought that large amounts of the medicine could be breaking down estrogen receptors, a protein that is crucial to many tumors' ability to grow and metastasize.

In healthy cells, these receptors bind to estrogen and cause normal changes in breast tissue. Breast cancer tumors that are estrogen receptor-positive, or ER+, usurp this normal physiological process to use estrogen as a growth signal.

Doctors typically prescribe a medication that stops the body from making estrogen—essentially shutting off the tumor's source of fuel. But in the majority of women with metastatic breast cancer, the estrogen receptor within the tumors eventually mutate, allowing them to progress despite the lack of estrogen.

If a medicine could kill the estrogen receptors in the tumors altogether, McDonnell's lab thought, it could slow the tumor's progression despite mutations in the receptor.

Two weeks after Wardell began looking into the hot-flash drug, she ran an experiment that showed elacestrant could be the drug the lab was searching for.

"That was it—that was the discovery right there," McDonnell said.

Duke University filed "new-use patents" for the drug and in 2017 licensed rights to Radius Health so they could begin to develop it for commercial use.

As part of the deal, Radius Health agreed to pay up to $3.8 million as the drug passed certain regulatory and commercial milestones and a single-digit royalty based on net sales, according to an SEC filing from Radius Health.

McDonnell said some of that revenue would flow back into his department and research program.

"It just takes a bit of pressure off us in fundraising," he said.

As Radius began testing the efficacy of this medication, McDonnell said, they hoped it would be as effective as the injectable drug, so women like Walker could have a less painful alternative treatment.

In fact, the drug was better.

Six months after treatment started, about 34% of patients on elacestrant had survived without their cancer progressing, compared to about 20% of patients on other treatments. Or, as Wardell likes to think of it: "three out of 10 grandmothers that got to go to graduation."

"If it had been equal, I would have considered that a win," he said. "Turns out, it beat it."

A 30-year journey

Elacestrant was not McDonnell's first attempt at bringing a breast cancer drug to market.

In 1996, his lab developed a similar drug, etacstil, which was the first oral medication in this class of drugs. Duke licensed rights to the drug to DuPont pharmaceuticals to run clinical trials shortly after.

But despite promising results, the clinical trials shuttered a few years later when Bristol-Myers Squibb, a pharmaceutical giant, acquired DuPont and killed the project.

"BMS basically decided there was no need for any more endocrine

therapies for breast cancer," he said.

They tried again in 2013, when they discovered that an osteoporosis medication could similarly target and kill estrogen receptors. When they tested the drug on their animal models, they found evidence that it was effective and had few side effects.

But the manufacturer of that drug did not want to associate the medication with cancer, McDonnell said.

"This is a drug which we think is probably as good as elacestrant," he said. "It was another sad story."

The whole process—from when McDonnell's lab first thought to target estrogen receptors to January, when the FDA approved the medication—took nearly three decades.

McDonnell said he's just happy to finally reach a point where his research will help patients.

"People ask, 'Why do you want to work in drug development?'" McDonnell added. "I want to put something in a bottle and last Friday, I saw the picture of the drug in the bottle."