HEALTH

Chemotherapy, a Trusty Weapon Against Cancer, Falls Out of Favor

Breast-cancer doctors are at odds over whether some patients should get less chemo—or none at all

By Lucette Lagnado
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Chemo or no chemo? That is the question.

Doctors are at odds over whether some women with breast cancer should have chemotherapy—one treatment among the arsenal long seen as crucial to fighting the disease, along with surgery and radiation.

Many oncologists are shunning chemo as risky and ineffective at combating some early-stage breast tumors. Traditionally, the majority of women with invasive breast cancer were treated with some combination of surgery, radiation and chemotherapy.

A shift to less chemotherapy or none at all, called "de-escalation," is being hailed by some as revolutionary, following what some doctors see as years of overtreatment with drugs that may have harmed more than helped. Proponents of de-escalation say chemotherapy—the use of chemical agents to treat the disease—should be used only when it appears likely to reduce the chances of the cancer spreading.

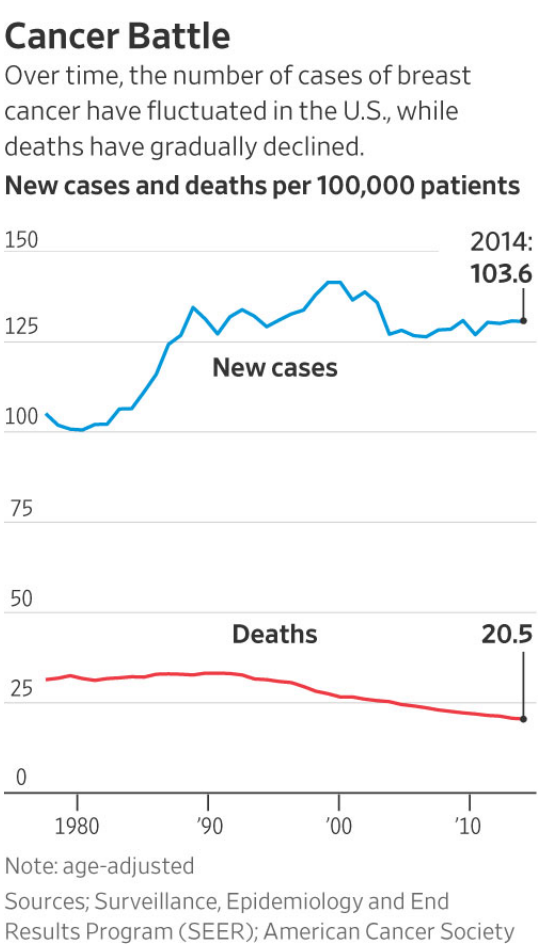
De-escalation has exposed a rift among oncologists, with some worrying that women may not get the treatment they need to survive. Cancer mortality rates have improved since the late 1980s and some researchers credit chemotherapy for playing a role. In use since the 1940s, chemotherapy has become generally less toxic and more effective since the early days of nitrogen mustard. While it has side-effects such as nausea, doctors are more skilled at controlling them.

The fault lines over chemotherapy are emerging amid a larger debate about over-treatment. Concerns include whether too many antibiotics are being prescribed for ailments that don't warrant them and whether surgery has been foisted on prostate-cancer patients despite tumors that posed little risk.

Some doctors say the time has come to reassess treatment for breast-cancer patients, too.

"Tens of thousands of women were over-treated, they got surgery they didn't need, they got radiation they didn't need, and they got chemotherapy they didn't need," says Steven Katz, a professor of medicine at the University of Michigan, and a supporter of de-escalation, an approach that extends beyond chemotherapy to other treatments and other maladies. Chemotherapy, he adds, "knocks the hell out of people and oncologists have gotten more sensitive to the harm" it can cause.

In the past, chemotherapy was widely considered crucial to care. But advances in understanding tumor biology have changed the way many doctors approach chemotherapy. With genomic testing—which looks at genes that affect cancer—a tumor is given a score. A low score means a woman has a good prognosis and won't benefit from chemotherapy. A higher score suggests a greater risk of recurrence and a need for conservative chemotherapy treatment. The middle scores—which are fueling physicians' angst—are in a gray zone in terms



Faye Ruopp, left, at her son's wedding in 2015 with her sister, Elaine Nisonoff. A year earlier, Ms. Ruopp was diagnosed with breast cancer and opted for surgery, radiation and hormonal therapy, not chemotherapy. PHOTO: LOLA FARRA

of data on whether to prescribe chemotherapy.

In 2014, Faye Ruopp, of Chestnut Hill, Mass., learned she had invasive breast cancer. Her tumor was 1.3 centimeters and "growing fast" says Ms. Ruopp, a former math teacher. On the genomics test, her tumor got an ambiguous score—"at the top of the low end."

Ms. Ruopp's physician, Eric Winer, director of the Breast Cancer Program at Dana-Farber Cancer Institute in Boston, says her case wasn't a "slam dunk." Indeed, Dr. Winer says, "there was the very real possibility we would give her chemotherapy." Patient and doctor discussed the pros and cons and decided: no chemotherapy. Her treatment consisted of the original lumpectomy surgery, radiation and hormonal therapy. Ms. Ruopp, now 67 years old and a math coach, had hoped to avoid chemo and says she has no misgivings: "You need to trust your oncologist."

Treatments for those who decide against chemotherapy still include surgery and radiation. Women whose tumors are deemed receptive to the hormone estrogen, will get hormone therapy. They can take pills, such as Tamoxifen, which reduces the risk of recurrence.

Use of chemotherapy to treat early breast cancer has been declining, according to a study led by Dr. Katz and Stanford oncologist Allison Kurian published in December in the Journal of the National Cancer Institute. The study of about 3,000 women with early-stage breast cancer—and some 500 doctors who treated them from 2013 to 2015—found that use of chemotherapy declined overall during that time, to 21.3% of cases from 34.5%.

In an accompanying editorial, the senior author, Dana-Farber's Dr. Winer, highlighted chemotherapy's drawbacks. While chemo can have "limited" benefits, he wrote, "toxicity can be formidable" and long-term effects can include leukemia, heart failure, neuropathy, premature menopause, and infertility.

A suite where patients can receive chemotherapy at Dana-Farber Cancer Institute's Yawkey Center for Cancer Care in Boston. PHOTO: SAM OGDEN

Dr. Eric Winer, who heads the Breast Cancer Program at Dana-Farber Cancer Institute, says the challenge of chemotherapy is balancing its risks and benefits. PHOTO: KIERAN KESNER FOR THE WALL STREET JOURNAL

Dr. Winer says he is "not afraid of chemotherapy," which he prescribes when necessary. The challenge is balancing risks and benefits, he says; for some patients, the risks are substantial but there is little or no benefit. "The medical community has underestimated the side-effects and impact on a woman's life," Dr. Winer says, adding that thanks to strides in understanding breast cancer, "we may be able to do less without compromising outcomes."

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Among the chemotherapy drugs commonly used against breast cancer are Cytoxan, Adriamycin, Taxol and Taxotere, which are administered intravenously. In addition to nausea, side-effects can include hair loss and fatigue. The de-escalation debate, Dr. Winer says, isn't about these drugs, which oncologists generally agree can be effective in certain cases. Rather, the debate is about which patients and their cancers would benefit from such regimens.

Other doctors at major cancer centers worry that a less-aggressive approach poses dangers. The attacks on chemotherapy are scaring patients, they say, and could prevent them from

making life-saving decisions. Meanwhile, data on the effect of withholding chemo from more complex breast cancers is still lacking, they argue.

At Memorial Sloan Kettering, Physician-in-Chief José Baselga says that while there is data to support forgoing chemotherapy on certain women with early-stage disease—and he himself has been prescribing less—these are only "a fraction" of cases. In some cases withholding chemotherapy carries big risks, he warns: "People will die because they will not get the therapy they need."

One of Dr. Baselga's patients, Evette Fairweather, was diagnosed with early stage invasive breast cancer in 2013. Her 1.5-centimeter tumor had a genomics test score of 19, placing Ms. Fairweather in the ambiguous zone of whether to have chemotherapy. After Dr. Baselga said it would reduce her risk of recurrence, Ms. Fairweather, who is now 51, decided to overcome her fears of the treatment and proceed with it.

While receiving chemo drugs over several months, Ms. Fairweather, a payroll processor, kept working. "I won't say I felt great, but I was able to bounce back," she says. "I didn't throw up, I ate a lot." Now relocated to Atlanta, she comes to New York twice a year to see Dr. Baselga and feels fine. She has no regrets about her decision.

Dr. Baselga worries there is a "pack behavior" in the breast-cancer community that could lead doctors to embrace doing less before such an approach has proved itself through rigorous studies. For more complex cases, "We need to make clinical decisions based on data not on beliefs or wishes," he says.

De-escalation supporters "have these buzzwords they use quite lightly such as chemotherapy being a poison: Are you kidding me?" he says. "Chemotherapy has saved many, many lives. There is zero question about that."

The breast cancer field, he says, is littered with once-vaunted treatments that subsequent research proved to be failures. In 1990s breast-cancer patients were given bone marrow transplants and high intensity chemotherapy—a costly, agonizing treatment that didn't work. Now the pack is headed in another direction, he says. "One day we are going to transplant everyone and the next we are not going to do chemo," he says.

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A paper published in the New England Journal of Medicine in 2015 gave de-escalation supporters powerful ammunition. In a study of more than 10,000 women, 1,626 who had early-stage breast cancer with no lymph node involvement were given hormonal treatment alone, without chemotherapy.

The study, led by Joseph Sparano, an oncologist and professor of medicine at Albert Einstein College of Medicine, found that those with a low score also had "very low rates of recurrence at five years with endocrine therapy alone." In other words, they did fine without chemotherapy.

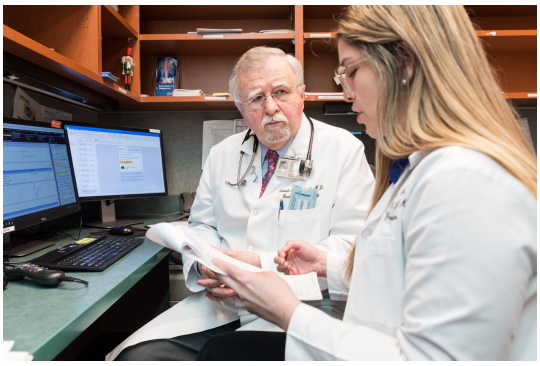
Oncologists are awaiting the results from the next phase of his research. Dr. Sparano, an oncologist at Montefiore Health System, will be focusing on more ambiguous and complex breast cancer cases with mid-range scores.

The conundrum lies with these "close calls," says Stanford's Dr. Kurian. Will de-escalation lead to errors? "I would hate for doctors and patients to say chemotherapy was oversold," she says. "Some patients don't need it, but a subset does need it to reduce their chance of death."

According to Otis Brawley, chief medical and scientific officer of the American Cancer Society, in the late 1980s the mortality rate for breast cancer was 32.2 deaths per 100,000 women; by 2015 the death rate was 20.5 deaths, or a 39% decrease. Dr. Brawley backs de-escalation, saying that with genomics testing, "we are hopefully identifying the women that need the chemotherapy and more importantly the women who don't need the chemotherapy."

At the MD Anderson Cancer Center in Houston, oncologist Gabriel Hortobagyi, in practice for more than four decades, can still recall the years when high percentages of women died from

breast cancer. He credits chemotherapy for helping achieve a turnaround, saying "tens of thousands, maybe hundreds of thousands" owe their lives to it.



Dr. Gabriel Hortobagyi, seen with nurse practitioner Ashley Martinez in the breast cancer clinic at MD Anderson Cancer Center, says a 'civilized discussion' about chemotherapy is needed. PHOTO: MD ANDERSON CANCER CENTER

Genomic tests can help determine who can benefit from chemotherapy, says Dr. Hortobagyi, but he worries about "pejorative" attacks on chemo.

"There is clearly a need for addressing the toxicities of the treatments," Dr. Hortobagyi says, "but we have to do it responsibly and on the basis of the highest level of evidence. We can't simply go out and say, 'As of tomorrow, I will go and give half the chemo,' in the absence of evidence that [it] would work."

Besides, he adds, "the worst toxicity is death."

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