So Far, Victories Are Few as Breast Cancer Patients Sue Wyeth Over Hormone Therapy

By Renee Twombly

There is no question that use of combination hormone therapy is associated with an increased risk of developing breast cancer in the population—that was clear in 2002 when the Women’s Health Initiative (WHI) study was halted. But whether the hormone treatment can be proven to have caused cancer in an individual woman who develops the disease is now being played out in courts around the country.

As of November, the pharmaceutical company Wyeth is listed as a defendant on 5,300 cases filed by 7,900 plaintiffs. The company manufactured the best-selling hormone replacement agents Premarin, an estrogen supplement, and Prempro, which contains estrogen and progestin. Other companies such as Pfizer and Upjohn, which produced different brands of hormone replacement therapy (HRT), are also being sued, but as the largest maker of these drugs, Wyeth has become the prime target for personal injury and drug product liability attorneys.

No one knows how far these cases will go or how many will ultimately be filed. The potential liability may be great, given that 6 million women were using the combination hormone replacement when the WHI’s study of Prempro was halted, according to the National Institutes of Health, the study’s sponsor. These cases are also unusual because, unlike the diet drug Fen-Phen, which Wyeth also manufactured, Prempro is still on the market. Wyeth maintains that the risk of developing breast cancer has always been stated in patient information for both hormone replacement therapy (HRT), are also being sued, but as the largest maker of these drugs, Wyeth has become the prime target for personal injury and drug product liability attorneys.

No one knows how far these cases will go or how many will ultimately be filed. The potential liability may be great, given that 6 million women were using the combination hormone replacement when the WHI’s study of Prempro was halted, according to the National Institutes of Health, the study’s sponsor. These cases are also unusual because, unlike the diet drug Fen-Phen, which Wyeth also manufactured, Prempro is still on the market. Wyeth maintains that the risk of developing breast cancer has always been stated in patient information for both hormone replacement drugs. But the cases boil down to whether a lawyer can convince a jury that a drug caused a person’s illness. With Fen-Phen it was clear; not so with Prempro.

Law professors watching the HRT litigation say that so far Wyeth may be winning the judges over, but the wildcard will be the hearts and minds of jurors if a case gets to trial. “Juries are sometimes willing to buy the argument that ‘I have breast cancer. I took Prempro. I am a good person. Therefore, it must be Prempro’s fault,’” said Brooklyn Law School professor Anita Bernstein, J.D.

Since this litigation began in 2006, 21 lawsuits against Wyeth have been decided, although appeals may be forthcoming. Only six have gone to court—12 were dismissed before trial even began, and three judges issued summary judgments in favor of Wyeth before they saw a jury. Juries have been split. Four found in favor of Wyeth, and four others agreed with the plaintiffs: women with breast cancer. But of these four, three with awards between $1 million and $3 million were either overturned by presiding judges or dismissed for other reasons.

The two latest decisions illustrate the split between how judges and juries seem to view these cases. In mid-October, a Nevada jury awarded $35 million in compensatory damages to three women who blamed their breast cancer on Wyeth’s hormones—and then slapped an additional $99 million on top of that for punitive damages because of the company’s “reprehensible” actions. One of the plaintiffs, 67-year-old Arlene Rowatt of Nevada, told the Associated Press, “We got our message out that there are a lot of women out there who are being injured by this kind of behavior.” Wyeth has said that it will appeal.

Later that month, a state district court judge in Minneapolis granted Wyeth’s motion to toss out a different case filed by a breast cancer patient who had used hormone replacement for 20 years. In a ruling that excluded the plaintiff’s expert testimony, District Court Judge George F. McGunnigle said that breast cancer is “unlike toxic exposure, food poisoning, accidents, and many other kinds of causes that cause ailments with a rapid onset and peculiar symptoms.” He added that there is no scientific method that can allow a doctor to determine, in hindsight, the cause of breast cancer in an individual woman and that “even if HT [hormone therapy] can cause some breast cancers, plaintiff cannot demonstrate that HT did cause her particular cancer.”

Warnings on Labels

Attorney Tobias Millrood, J.D., has also had his victories thrown out by judges—twice. He won a $1.5 million judgment for breast cancer patient Jennie Nelson and her husband in a Philadelphia court last October. Seven of the eight jurors concluded that the hormone replacement drugs were a “factual cause” of Nelson’s breast cancer. But the judge overseeing the case declared a mistrial due to a problem with a juror. The case was retried early in 2007 and this time the jurors granted the couple $3 million. The judge overturned the decision but has not yet explained why. When he does, Millrood can decide whether to appeal.

Millrood contends that Wyeth advertised the hormones as a safe and effective treatment for menopausal symptoms even though the company knew that the drugs were unsafe. Use of the estrogen-only supplement Premarin had skyrocketed by 1975, when scientists found that it could cause endometrial cancer in women with a uterus. Millrood said Wyeth suggested that progestin be added to buffer the endometrium.

“When of course, Wyeth was now marketing a known carcinogen (estrogen) to be taken with another promoter of breast tissue growth, progestin, without ever conducting a single study on the effects of breast tissue,” Millrood said. “Wyeth has admitted repeatedly that it never performed any long-term study—on humans or animals—to evaluate the potential liability.
the risk of breast cancer in women taking combination estrogen and progestin.”

Heidi Hubbard, J.D., a lawyer representing Wyeth, strongly disagrees with Millrood’s assertion. The U.S. Food and Drug Administration approved the ads that were first used to promote Prempro in 1995, she said, and the product labeling for Prempro estimated a relative risk for breast cancer of 1.3–2.0, a number that “was approved by the FDA after the FDA analyzed many studies conducted over many years.” That risk was cited even before results of the WHI were announced in mid-2002, leading to a precipitous drop in the use of hormone supplements. “Wyeth conducted or supported at least 20 pre-WHI studies, both observational and randomized controlled, that looked at the potential risk of breast cancer,” Hubbard said.

These lawsuits are different from many other drug liability claims because “these medicines are still on the market, are still FDA approved, and remain an important option for women, according to the FDA and to medical organizations,” she said. “Wyeth acted responsibly in advising doctors and patients on the known risks.”

Taking Research to Court

The WHI clinical trial, a component of the larger, 161,000-participant study, was designed to look at more than breast cancer risk. It also measured cardiovascular and neurological problems and bone health, among other variables, in hopes of finding a risk–benefit profile for use of both single or combination hormone supplementation. The combination Prempro arm was halted 3 years early because of an increased risk of invasive breast cancer in the 16,608 women taking the combination therapy. Researchers found a 26% increase in breast cancer in these patients—a relative risk of 1.26—which translates into eight more cases of invasive cancer per 10,000 women using the agents. They also found increased rates of strokes, heart attacks, and blood clots, as well as reduced rates of colorectal cancer and fractures. Given the conclusions, WHI investigators terminated the trial, believing that, overall, the combined hormone regimen failed to demonstrate a benefit.

But Millrood and other lawyers taking on HRT say that it was the follow-up studies to the 2002 finding that has helped make their case. In particular, they point to analyses that included follow-up for breast cancer incidence in WHI participants: 5.6 years on average. One study, reported in June 2003 in JAMA, found that breast cancers diagnosed in women in the hormone therapy group were more likely to be advanced than in women who were not using the therapy, and they were more likely to have an unfavorable prognosis. The combination therapy also increased mammographic breast density within the first year of use, the WHI investigators wrote, leading them to conclude that “direct effects of estrogen plus progestin on tumor growth cannot be excluded.”

However, the study that most captured the imagination of lawyers representing HRT plaintiffs was one published in September 2006 in the journal Maturitas, which looked at prior hormone use in WHI participants who were randomized to combination therapy. The study found that women who had been exposed to combination therapy before WHI had a higher risk of breast cancer than women who hadn’t taken hormone therapy before, said the study’s lead investigator, Garnet L. Anderson, Ph.D., from the WHI coordinating center at the Fred Hutchinson Cancer Research Center in Seattle. She found that among 4,311 prior users, the relative risk for combination therapy versus placebo was 1.96—about 21 more cases of breast cancer per 10,000 users of combination hormones.

After 3 years, the number of breast cancer cases in prior estrogen–progestin users overtook those in the placebo groups. That crossover happened after about 5 years in women with no prior use, Anderson said. “These findings suggest that use of estrogen and progestin for durations only slightly longer than those in the WHI trial are associated with increased breast cancer risk” and that a safe interval for combined hormone use “cannot be reliably defined,” she said.

Anderson’s relative risk finding of 1.96 is important because some courts require a relative risk of 2.0 before a judge will even hear a case. “Before a lawyer can show evidence an injury was caused by exposure of a drug, a growing number of courts need a relative risk ratio over 2.0 before it will send a case to a jury,” explained Lars Noah, J.D., a visiting professor at Vanderbilt University Law School. “Less than that, the odds are that the illness would have happened anyway. Above that the odds are that it is due to exposure.”

Another study was published in April in the New England Journal of Medicine that found breast cancer incidence dropped by almost 7% in 2003, after WHI results were announced. It is just “proof of the pudding,” Millrood said. “Take away the possible offending agent and look and see if the disease goes away. It does.”

Researcher Forced To Testify

Given her findings, Anderson has been deposed twice by both plaintiffs and defendants and issued multiple subpoenas. “I had continued on page 1835
to give everything to them—all the data, programming, and correspondence related to the hormone trials. And I had to hire staff to pull it all together," she said. “I had no idea they would have the right to get all this information. This is something researchers should be aware of.”

Anderson admits conflicted feelings. “I believe hormones increase breast cancer risk, but it would be very hard to tie that risk to an individual woman. On the other hand—and this is a personal opinion—I don’t think these pharmaceutical companies are blameless,” she said. “The way they advertised these hormones went way beyond what was really known. Doctors relied on that advertising way too much and researchers believed lesser-quality data more than we should have. There is a lot of blame to go around.”

Still, Anderson said, “my understanding is that there were warnings about breast cancer risk on the packaging.”

UCLA breast cancer expert and author of the JAMA study Rowan Chlebowski, M.D., Ph.D., agreed, saying that even if evidence is strong that there is a causal relationship, the drugs have contained warning labels for decades. “If the risk was identified on the label and was part of the risk and benefit discussion that any reasonable physician would have with a patient, the liability issue is like the smoking question now—it is moot,” Chlebowski said, referring to cautionary labels on cigarette packages.

Hubbard, the Wyeth lawyer, said the point is that breast cancer risks were known by the FDA and were in the packaging, so the company’s approach is to defend itself vigorously in these cases. “Our scorecard so far has shown that approach has been successful, and we expect to continue to be successful,” she said.

Predicting what will happen to these lawsuits as more and more are heard in court is hard, said Howard Erichson, J.D., a professor of law at Seton Hall Law School in Newark, N.J. Sometimes a drug company will settle all the cases at once, especially if a drug is still on the market, for the public relations value of keeping the product name out of the news. But others get played out in court by jurors, a good proportion of whom side with companies against plaintiffs who want big rewards, he said. “I generally trust the jury system, so let’s see what happens.”