

FEATURE STORY

Can You Afford Cancer?

BY JO CAVALLO

Escalating cancer drug costs trigger concerns about access for patients.

The good news for cancer patients is that novel therapies are extending lives and even allowing cancer to be treated as a chronic disease. The bad news is they may not be accessible to everyone.

By the time Kara Herynk was diagnosed with large cell neuroendocrine carcinoma of the cervix in February 2005, the cancer had spread to her brain and liver.

Doctors prescribed eight rounds of very high doses of cisplatin and Vepesid® (etoposide) chemotherapy, a craniotomy to remove a large brain tumor and a hysterectomy. She also underwent three rounds of stereotactic radiosurgery to treat six more brain tumors. And more radiosurgery treated cancer in her lymph nodes, adrenal gland and lung.

Earlier this year, samples of Herynk's tumor tissue were analyzed using microarray, a test that identifies tumor protein patterns. The test found that Herynk's tumor is HER2 positive, so doctors prescribed Herceptin® (trastuzumab), a monoclonal antibody the Food and Drug Administration approved to treat HER2-positive metastatic breast cancer. But because the drug isn't approved to treat Herynk's primary cancer type, her health insurance company refused to pay for the treatment, calling its use "experimental."

"It was shocking at first, because the insurance company had never denied anything," says Herynk, 32. "I was excited about Herceptin because my bone marrow was so suppressed from all the chemotherapy, it was the only drug I could take because it wasn't as toxic." In April, convinced that the drug could be beneficial and despite its high monthly price tag of more than \$3,000, the Herynks began paying for the drug themselves, a decision that put her family in a precarious financial situation.

Herynk's husband, Matthew Herynk, PhD, a breast cancer researcher at Baylor College of Medicine in Houston, says coworkers and family members donated money to help pay for the drug and the couple went through their savings when finally, after several appeals, their health insurance carrier agreed to pay for

Herceptin. Still, Matthew says he's willing to go bankrupt to pay for any drug that might make a difference in the outcome of his wife's disease.

"There's no doubt that Herceptin has been a lifesaving drug for me," says Kara. "Since I've been on the drug I haven't had any new tumors. My cancer is so aggressive, I can't imagine where the cancer would have gone if I hadn't had Herceptin." Matthew agrees. "I know enough about cancer biology to believe that this drug is making a difference, so I'm willing to put everything I have into whatever drugs I think will make a difference."

The Herynks aren't alone. Many cancer patients today are facing the same dilemma of how to pay for cancer drugs. According to the 2006 Express Scripts Specialty Drug Trend Report, the cost of oral cancer drugs rose nearly 16 percent in 2005—an average of \$1,600 per prescription. With costs soaring to never-before-seen heights, especially for the new targeted therapies, which directly affect cancer cells and don't have the same toxic effects of conventional chemotherapies, the yearly bill can reach upwards of \$100,000, and carry insurance copayments of \$10,000 or more a year.



Kara Herynk and her husband, Matthew, went through their savings to pay for a drug to treat her rare cancer. Photo by Johnny Hanson.

As a result, cancer patients, doctors and health insurance companies have to consider the cost-versus-health benefit ratio when deciding on treatment, especially if the drug is only expected to have a marginal effect on survival. Compounding the problem is that often the newer targeted drugs have to be combined with conventional chemotherapies to be most effective, driving up both the cost and the severity of side effects.

Leonard Saltz, MD, attending physician at Memorial Sloan-Kettering Cancer Center and professor of medicine at Weill Medical College of Cornell University in New York City, says he's disappointed by what most targeted therapies have been able to accomplish as single agents. "No one set out to combine these drugs with chemotherapy. They were supposed to replace chemotherapy and all of its nasty side effects, but it hasn't worked out that way."

Of the targeted therapies, only Gleevec® (imatinib), which has had remarkable results in the treatment of gastrointestinal stromal tumors and chronic myeloid leukemia, has shown long-term survival rates. For example, a clinical trial of

Gleevec found that 90 percent of CML patients who took the drug were still alive five years after diagnosis. However, the drug has to be taken indefinitely, at a cost of up to \$3,800 a month. “As an individual, the cost is worth it, but from a societal point of view, economists argue that it’s a serious problem,” says Dr. Saltz.

Other medical experts argue drugs that offer any incremental rate in survival constitute a significant advancement in cancer treatment. “It’s important to note that these new drugs are quite good,” says David Johnson, MD, deputy director of the Vanderbilt-Ingram Cancer Center in Nashville and past president of the American Society of Clinical Oncology. “When people make comments like they only affect a two-month improvement in median survival, that demonstrates a lack of understanding of what that means. They’re talking about an average benefit.”

Dr. Johnson, who is himself a lymphoma survivor, says all the benefit doesn’t accrue equally to every patient. It might be that one patient survives four months longer and one patient doesn’t survive any longer.

Plus, says Dr. Johnson, agents like colon and lung cancer drug Avastin® (bevacizumab) are tested in clinical trials of patients with late-stage disease when the chances of survival are small. The same is true of Herceptin, which affected only a modest benefit in terms of overall survival for women with metastatic breast cancer, but when Herceptin was tested in the more favorable setting of treatment after surgery (adjuvant), it resulted in a 50 percent improvement in disease-free survival. “We anticipate that will translate into a substantial benefit in terms of overall survival, so who knows what Avastin is going to do when we start using it in earlier stages of disease as opposed to the worst-case scenarios,” says Dr. Johnson.

Financial Aid

Walter Moore, vice president of government affairs for Genentech, maker of both Avastin and Herceptin, which just received FDA approval for use as adjuvant treatment for breast cancer in November, says the company plans to test Avastin as adjuvant treatment for breast and colon cancer. But the question remains, how will patients—and society—pay for new drugs? The question applies not only to cancer, but also to other illnesses like heart disease, which, according to the Agency for Healthcare Research and Quality, is the most expensive health condition overall in the United States (though the per-person cost puts cancer on top, followed by heart disease).

A voluntary solution puts caps on the price of drugs. It has been reported that a number of pharmaceutical companies are considering caps on high-priced cancer drugs, but so far only Amgen and Genentech have put price caps in place.

Amgen, maker of Vectibix® (panitumumab), a newly approved colon cancer drug priced at \$4,000 per two-week infusion, announced a cap on out-of-pocket copayments after approval of the drug in late September. Patients on Vectibix are now able to get the drug for free once copayment costs exceed 5 percent of their adjusted gross income, regardless of insurance status or income.

Genentech followed suit in October after the additional approval of Avastin for non-small cell lung cancer (FDA approval is still pending on its use for breast cancer). The Avastin program caps the cost of the drug at \$55,000 a year for eligible patients. The price cap, says Moore, was determined by the escalating price of Avastin based on treatment dosage. The current treatment for lung cancer (\$8,880 per month) is at double the dose than for colon cancer (\$4,400 a month), although clinical trials are still ongoing to determine whether lower doses of Avastin would be just as effective. “I’m not sure what will turn out to be the proper clinical dose, but our objective is for oncologists to choose the regimen that produces the best clinical outcome without concern for the additional expense,” says Moore. The Avastin expenditure cap is the first of its kind, putting a cap on spending by all payers, not just out-of-pocket costs from the patient. The program will cover all approved uses for Avastin.

Diane Blum heads CancerCare, a nonprofit organization that provides financial assistance and free services to cancer patients, although it doesn’t directly pay for drugs. As more cancer drugs have been approved over the years, she says momentum has developed concerning the cost issue. “It’s become a critical mass of drugs that are costing a whole lot of money,” she says. “The companies get a lot of negative press about it and understandably—the drugs are very expensive. I think the caps are an attempt to do the right thing so people aren’t shut out of getting the drug but at the same time maintain pricing abilities without interference.” Blum thinks other drug companies will replicate the proactive move of Amgen and Genentech. “There will be pressure for any company that has a newly approved drug to take similar action.”

Apart from price caps, most pharmaceutical companies have patient assistance programs that offer drugs for free to patients who qualify. Nonprofit organizations and government agencies also help low-income patients with little or no insurance get access to needed drugs. Though most middle-income patients who are covered under private insurance or Medicare are ineligible for many patient assistance programs and take the hardest financial hit, some assistance programs offer discounted rates or financial help for patients who are underinsured or who have extreme financial burden because of their treatments.

A study in a recent issue of the journal *Cancer* shows that one in five cancer patients delay or miss needed care because of cost. And, according to 2005 U.S. Census Bureau figures, the number of Americans without health insurance rose by 1.3 million to an all-time high of 46.6 million, putting additional financial strains on an already fragile healthcare system. Blum says she has seen an increase in the number of calls to CancerCare from people looking for financial help. “At the end of our fiscal year in June, we spent about \$4.5 million in direct financial assistance, but it goes primarily to help people pay for things like transportation to and from treatment appointments. If people can’t get to treatment, they simply don’t go,” says Blum.

And, as Kara Herynk found, more and more health insurers are refusing to pay for treatments prescribed off-label. “What we find are extremely concrete and

restrictive interpretations of the FDA approval guidelines as limiting factors for the drug's availability," says Dr. Saltz. "So rather than figuring out a way to deal with [the drug cost], insurers are trying to find ways not to pay for it and, therefore, certain people can't get it." For example, the FDA approved Avastin for colon cancer, which affects the large intestine, so Dr. Saltz says he can't prescribe it for his small intestine cancer patients, because insurance companies won't pay for the treatment.

That practice isn't about to end anytime soon, says Susan Pisano, vice president of communications for America's Health Insurance Plans, a Washington, D.C.-based organization that represents health insurance companies. "We're moving toward a healthcare system that is based on what the medical evidence shows. The insurance companies want the nation to move to a system where we're using the evidence that shows the new treatments are better than the existing treatment."

Physicians admit insurance restrictions and drug costs are impacting the way they treat patients. "Ten years ago I gave very little thought to the drugs that I recommended to the patient, because cost wasn't really an issue," says Dr. Johnson. "Now, sadly, physicians are doing a financial sizing of each patient. Do I want to discuss with a patient a therapy I know the patient won't be able to receive because of cost, or do I want to put on patients the added burden of worrying about mortgaging their home?"

The pharmaceutical companies argue that cancer drugs are expensive because of the amount of time and money it takes to bring them to market. "We discovered Avastin in 1989 and it was approved [for colon cancer] in 2004," says Genentech's Moore. "So you have 15 years and \$800 million to get a drug approved. By any stretch, it's a wildly expensive way to get a new therapy into the hands of doctors and into the bodies of patients." Very few compounds make it from laboratory testing to clinical trials in humans. From there, only one out of every 10 drugs will be approved.

A drug company attempts to recoup its investment before the drug's patent expires 20 years after the application date, because at that point a generic version of the drug is developed and marketed. At a cost of 30 to 80 percent less than brand-name drugs, generics have the same active ingredients and therefore the same effects, causing an immediate drop in price and market share for brand-name drugs.

The cost of drug research and development will continue to rise. In 1991, the cost of developing a drug averaged \$168 million, more than doubled to \$365 million in 1997 and jumped to more than \$800 million in 2003. Since it takes an average of 12 to 15 years to bring a drug to market, by 2015, the cost of developing a drug would cost an estimated \$1.9 billion, according to research published in the *Journal of Health Economics*. In 2005, pharmaceutical and biotechnology companies invested \$51.3 billion in research and development, according to an analysis commissioned by the Pharmaceutical Research and Manufacturers of America, the drug industry's trade group.

The FDA had a hand in founding the Critical Path Institute, or C-Path, which began

operations in mid-2005 to, among other things, simplify the clinical testing process and thus lower the cost of drug development. C-Path reached an agreement in 2006 with eight major pharmaceutical companies, including Bristol-Myers Squibb, Merck, Novartis and Pfizer, to share early-stage drug testing methods.

Drug companies also say a drug's therapeutic value can lead to a higher price. Thalomid® (thalidomide), a drug that's been around for years to treat leprosy, was recently approved to treat multiple myeloma and costs \$3,500 or higher per month. When 65-year-old Dick Wells was diagnosed with multiple myeloma in 2002, his health insurance company covered the cost of the drug and he paid a modest \$25-per-month copayment. After he turned 65 and went on Medicare, Wells purchased supplemental health insurance to ensure he would be covered for the cost of thalidomide. But when he went to the pharmacy to pick up his prescription, he was shocked to learn that his copayment had shot up to nearly \$1,900.

"I told the druggist that I couldn't pay for the prescription and gave him back the pills, but then I started thinking that I have to have these pills. I really didn't have a choice," says Wells. Although he missed several days of medication while he researched other supplemental plans, he finally found one that covered the cost of thalidomide.

Celgene Corporation, thalidomide's manufacturer, justifies the cost because "the therapeutic value of thalidomide is in line with other cancer breakthrough therapies and it's half the cost of existing breakthrough therapies in the multiple myeloma area," says Brian Gill, director of public relations for Celgene. Indeed, the multiple myeloma drug Velcade® (bortezomib) costs about \$6,600 per month, and Celgene's own recently approved Revlimid® (lenalidomide) costs up to \$8,850 a month.

Because cancer is such a frightening disease and patients will do anything to gain access to drugs they believe will help them live, healthcare shouldn't be part of a free-market system in which price is determined by what the market will bear, says Dr. Johnson. "Who's the competition and who's in a position to bargain? There's just something not right about this system."

Is Universal Healthcare the Answer?

John Hornberger, MD, adjunct clinical professor of medicine at Stanford University School of Medicine and a practicing physician who studies drug costs, says drug prices, no matter the illness, are based on a three-legged stool argument.

"You've got to have demand for the drug, and that's clearly the case in oncology. You've got to have innovation to satisfy the demand, and the third leg of the stool is who's going to look at the cost? If there's no one looking at cost, people will charge whatever they want and that's effectively where our healthcare system has been, but it's not sustainable," he says. Dr. Hornberger cites a growing older

population and the increased cost strains it places on Medicare as some of the reasons why. “There are no cost brakes on the Medicare system. Congress won’t let Medicare use cost to decide how care will be provided and people are just using more drugs,” says Dr. Hornberger.

But with healthcare spending projected to soar to \$4 trillion by 2015, outpacing the growth in the gross domestic product by 20 percent—up from 16 percent today—healthcare industry experts and government agencies are starting to look for ways to control drug costs. In October, the National Coalition for Cancer Survivorship brought together representatives from health insurance and pharmaceutical companies, the FDA, the Centers for Medicare and Medicaid Services, physicians and patient advocacy groups to study the problem. The report is pending.

“The drug cost issue has finally come up and hit us square in the face,” says Ellen Stovall, president and CEO of the NCCS and a 35-year cancer survivor. “It used to be manageable because either insurance companies paid for the drugs or the out-of-pocket costs were manageable, but that’s no longer the case.”

Dr. Johnson predicts that rising medical costs will eventually lead to a federal government plan that will provide basic healthcare to everyone. (The United States is the only developed country in the world without universal healthcare, and many developed countries regulate drug prices.) “I think this is going to end up being some sort of crisis, but I suspect that what will ultimately happen is that the country will grow a social conscience and it will decide that we have to do something. It’s unconscionable to me that the wealthiest country in the world has 46 million people without health insurance.”