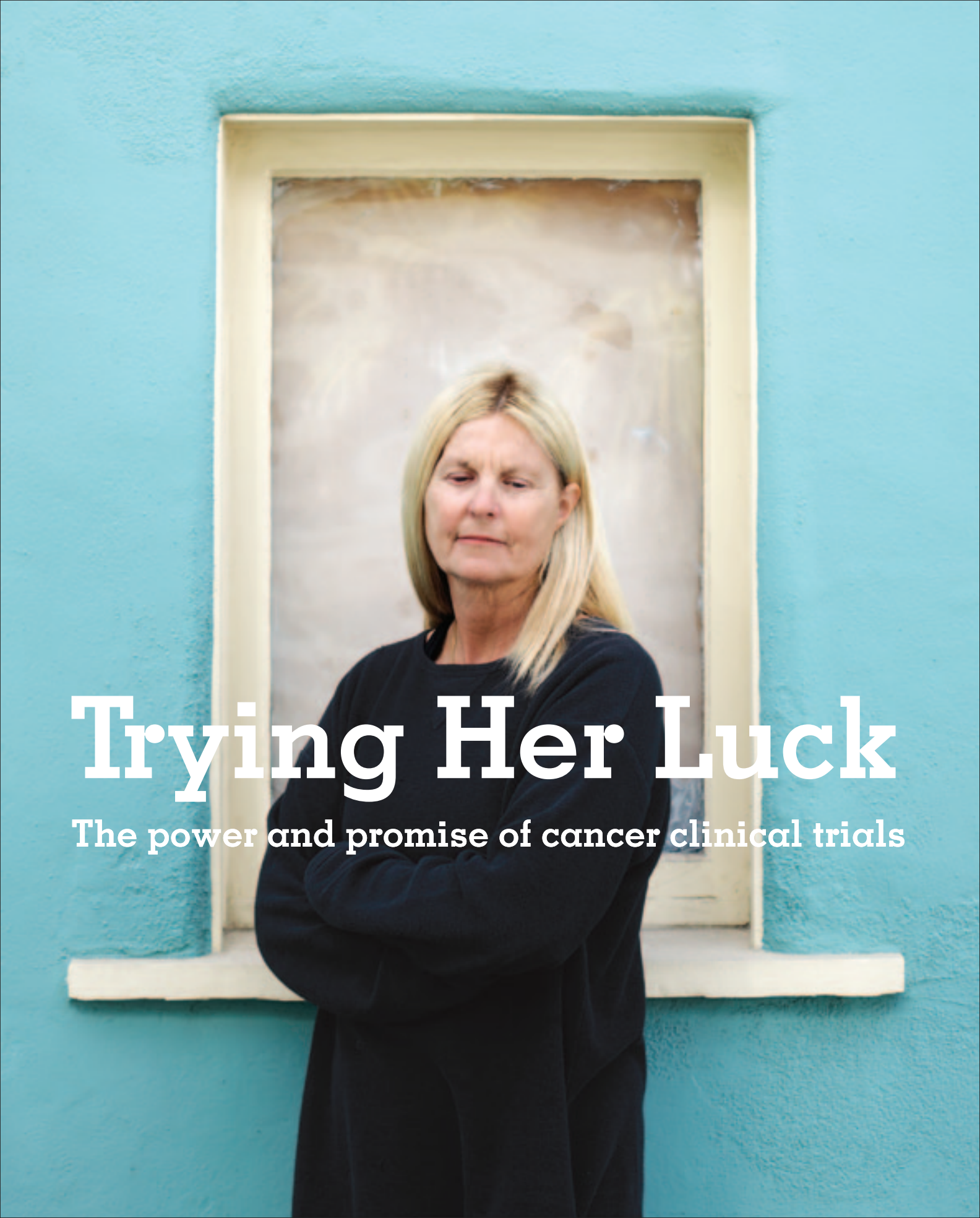


Trying Her Luck

The power and promise of cancer clinical trials

Jan Lesser has traveled to the Gallapagos Islands, Micronesia, and the tiny Caribbean island of Bonaire. But her most profound voyage has been from health to near death and back to health again. The lifeline which brought her from terminal cancer to eight-year remission—a clinical trial. **By Nancy Sokoler Steiner**

A petite blond with skin sun-kissed from living for three decades in Manhattan Beach, Jan Lesser sits with her husband Rick in the weathered beachfront home they share with a dog, three cats, and a small platoon of parakeets and turtles. Her carefree demeanor shows no trace of the ordeal she experienced nine years ago.

The year was 2000. Jan was 47, busy raising her children, then 10 and 16. She barely noticed that she'd started having frequent headaches. She began to worry when she was unable to read to her children each night at bedtime. "I couldn't make out the words on the page," Jan remembers.

Jan was diagnosed with Stage IV lung cancer, the most advanced form of the disease. And it had spread, forming two tumors in her brain and two more in her liver. Rick asked what the odds of his wife's survival were, and he was given a simple answer—zero.

Jan had surgery to remove her brain tumor and then underwent radiation. That successfully treated the brain cancer, but the lung and liver tumors remained. She started on a chemotherapy regimen, then another, but the cancer kept growing. A third chemotherapy treatment failed to shrink the tumors.

KEY POINTS

Clinical trials are research studies that test how well new medical approaches work in people. Each study is designed to find better ways to prevent, screen for, diagnose, or treat a disease.

Clinical trials follow a strict sequence of steps or phases and can last between 4 and 8 years.

Participants in clinical trials can gain access to new research treatments before they are widely available, and help others by contributing to medical research.

Fewer than one out of 20 adults with cancer—less than 5 percent—will take part in a clinical trial.

A Breath of Hope

With hope all but vanished, Jan's doctor told her about a clinical trial at Cedars-Sinai Medical Center involving a novel treatment for lung cancer. Unlike conventional chemotherapy which kills the cells themselves, this drug targeted a specific biological process that drives the growth of cancer. After undergoing tests to see if she fit the criteria, Jan was accepted into the trial and met Ron Natale, MD, a medical oncologist in Cedars-Sinai's Samuel Oschin Comprehensive Cancer Institute.

"All treatment advances for cancer result from clinical trials," explains Dr. Natale, who described the experimental medication Jan would be taking as "a revolution in oncology."

Dr. Natale likened the targeted therapy to "putting gum in the lock of the mechanism which allows the cancer to grow." The medicine, called Iressa, had been tested in the laboratory and had stopped the growth of lung cancer cells in mice. In Phase I trials, it was given to patients with terminal lung cancer whose tumors remained despite trying all available treatments. Because the side effects of the new drug were unknown, it was given to a small group of patients at a moderate

Photograph: Max Gerber

dose. When they tolerated the drug, it was given in slightly larger doses to a second group. The process continued until 243 patients—100 with advanced lung cancer—were treated. At that point, researchers had a better idea what doses might work and what side effects to expect.

Jan Lesser was one of 27 participants treated at Cedars-Sinai Medical Center for the Phase II trials.

Jan doesn't remember many details from the time she was undergoing chemotherapy. "I lost time," she says. "It took two or three years for me to come back to my head." But compared to chemo, participating in the trial was manageable. There were no technicians dressed in plastic coats and goggles administering a toxic substance into her bloodstream. Instead, she swallowed a little, round, reddish-brown pill once a day and came to Cedars-Sinai for monthly scans and blood tests.

A Trying Process

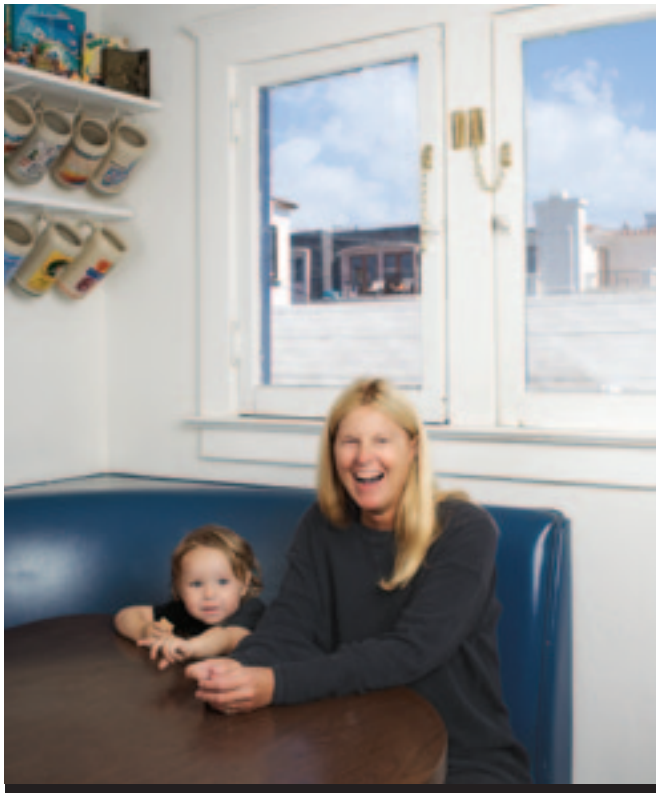
Steven Piantadosi, MD, PhD, is one of the world's leading designers of cancer clinical trials. He joined Cedars Sinai in 2007 as the Samuel Oschin Comprehensive Cancer Institute's first director and is on a mission to expand the Institute's volume and scope of research.

"The benefits of participating in a clinical trial are tangible and substantial," states Dr. Piantadosi. "You may get access to a new therapy in the earliest possible stages of its development. Especially for those with serious illnesses, access at that early time can literally be life saving."

Clinical trials follow a strict sequence of steps, so any treatment that passes through the required phases must surmount many hurdles. According to Dr. Piantadosi, "The system has evolved for good reason. The pipeline is designed to make sure whatever gets through is a true advance in medicine."

Dr. Piantadosi estimates that clinical trials cost between $5,000 and $8,000 per patient, although that figure can reach as high as $40,000 for one patient. Trials also take time. An average of eight years elapses between the time that a cancer drug enters clinical trials and it is approved.

Dr. Piantadosi adds that, while not all treatments studied in clinical trials will offer an improvement over the conventional therapy, they may offer benefits—such as lower toxicity or easier ingestion—which can improve the quality of a patient's life.



"It is a gamble to try a treatment that is essentially untested, but when the results of the traditional treatments are disappointing, it is a gamble worth taking."

Nevertheless, perhaps the biggest hurdle in cancer research (according to Dr. Piantadosi) is the shortage of clinical trial participants. Fewer than one out of 20 adults with cancer—less than 5 percent—will take part in a clinical trial. That, says Dr. Piantadosi, is "a national shame."

Shrinking Tumors

Jan Lesser started taking Iressa on November 29th of 2000. She began feeling better almost immediately. There was no more nausea, no more fatigue. Jan spent Thanksgiving lying on the couch at her mother's house, and by Christmas, she was hosting the family's

celebration. But was she energetic only because she wasn't suffering from the side effects of chemo?

Jan recalls that an unusual decoration was hanging from the ceiling in Dr. Natale's office when she first met him there—a plastic pig with wings. It seemed that pigs, indeed, could fly: Jan's lung and liver tumors had shrunk dramatically. Eventually, they completely disappeared.

Not everyone responded to Iressa as dramatically as Jan had. Fourteen percent of the patients in the Phase II trial saw their cancers shrink. For another 35 percent, the cancer didn't decrease but it stopped growing.

The drug did not perform as well in subsequent trials outside the country and the FDA eventually pulled Iressa from the U.S. market. It is still used in Europe and Asia, but is restricted in the U.S. to patients for whom it had already showed success—including Jan Lesser.

"In retrospect, the trial probably included too many patients with lung cancers that were resistant to all known treatments, making Iressa's task of improving survival nearly impossible to achieve," reflects Dr. Natale.

For Dr. Natale, the Iressa trial has provided invaluable information on a different treatment approach to lung cancer. "This was the first study of its kind that showed we could identify a target commonly expressed in lung cancer; that we could develop a medicine against that target; and that—at least in some patients—it could produce tumor regression, improve survival, and improve quality of life," says Dr. Natale. "This marked a sea change in our thinking." Today, dozens of biologically targeted cancer drugs are undergoing clinical trials in institutions across the country.

Making Research a Priority

The Samuel Oschin Comprehensive Cancer Institute is the hub for cancer research at Cedars-Sinai, implementing numerous clinical trials to test the best discoveries and translate them into new care options that are measured and delivered on-site.

Academic medical centers like Cedars-Sinai are poised to identify the basic scientific discoveries with the most potential for yielding transformative treatments. Having an infrastructure that enables researchers to speed the translation of laboratory discoveries into new cancer care approaches is essential. It means that promising therapies are available in the shortest amount of time even before they receive approval by the U.S. Food and Drug Administration. For a patient facing a grim cancer diagnosis, every minute counts.

"Research and clinical care synergize with each other," explains Dr. Piantadosi. "Patients who enroll in clinical trials receive better care, better nursing, and better support and tests because of the additional attention on the research study," he says. "And the kinds of practitioners who perform trials generally are more up-to-date, more informed and more expert than those who do not. You have a much more sophisticated view of the therapy and the disease if you are engaged in research."

The Institute is developing a Phase I testing program and a treatment unit equipped to conduct cancer-specific clinical trials. Add to that a broad local base of patients from across the Los Angeles area, and Cedars-Sinai is positioned to undertake clinical trials on a scale that most other institutions are not.

Dr. Piantadosi plans to establish a shared resource model across all cancer specialties that would handle administrative and managerial tasks, freeing investigators to focus on their research. "Principal investigators need data coordination, computer and administrative support, and time for scientific meetings and travel," says Dr. Piantadosi, who wants to expand the Cancer Institute's portfolio of active trials—currently 288. His goal is to see the Samuel Oschin Comprehensive Cancer Institute become a federally designated National Cancer Institute Cancer Center within the next decade.

Jan and Rick Lesser know that not every clinical trial will have dramatic results, and they are grateful that Jan's did.

"We have come to appreciate that every new drug that might have promise has to start with a clinical trial," says Rick. "It is a gamble certainly to try a treatment that is essentially untested, but when the results of the traditional treatments are disappointing, it is a gamble worth taking."

"My wife would have died in the spring of 2001," he adds. "We've received a gift of eight years ... and counting."

MORE ONLINE: watch a video Q & A with Dr. Ron Natale at www.discoveringforlife.org/natale