breast cancer trial fights recurrent cancer with light

AN EXPERIMENTAL TUMOR-FIGHTING DRUG THAT WORKS ONLY WHEN TRIGGERED BY LIGHT MIGHT ALLOW CLINICIANS TO LIMIT THEIR ATTACK TO CANCER CELLS, SPARING HEALTHY CELLS FROM ASSAULT.

By William A. Wells

Encouraged by early results, medical oncologists at Stanford are starting a new study targeting breast tumors with light. The light turns on an experimental tumor-destroying drug that remains inactive unless triggered by light.

Staff physician Alan Yuen, MD, and Robert Carlson, MD, associate professor of medicine (oncology), will conduct the phase II clinical trial with the help of Anne Favret, MD, a fellow in oncology. The new trial is aimed at helping women with recurrent breast cancer.

"Radiation and chemotherapy are very useful for treating breast cancer," notes Yuen, "but sometimes the cancer returns even after those treatments." The light treatment may offer an alternative in such cases, he says.

For each treatment in the study, patients receive the experimental drug, called lutetium texaphyrin (abbreviated lu-tex), which is preferentially taken up by the tumor cells. Why the drug homes specifically to tumors remains unclear, but researchers believe it hitches a ride on a protein that tumors consume in large quantities. A few hours later, doctors shine red light on the tumors. The light energy is captured by the drug and is then passed on to nearby oxygen molecules. These activated oxygen molecules can react with almost any molecule in their immediate vicinity. They damage cancer cells by scrambling the lipids that encase them and by chopping up proteins that do the cells' work.

Yuen announced the results of the phase I clinical trial with the light-activated drug last May at a meeting of the American Society for Clinical Oncology. That study, conducted at Stanford and two other medical centers, involved a total of 35 patients with a variety of cancers. The treatment turned out to be most successful for breast tumors, of which 45 percent disappeared completely after one treatment and a further 18 percent showed significant shrinkage. Eight breast cancer patients received a second treatment, which brought further improvements in four cases. The most common side effect was moderate local pain caused by activation of the drug during treatment, Yuen reported.

The research that laid the groundwork for the experimental treatment was conducted by Jonathan Sessler, who was cured of Hodgkin's disease at Stanford University Medical Center in the 1970s while pursuing graduate studies in the Department of Chemistry. Sessler went on the University of Texas at Austin, where he studied porphyrins — large, donut-shaped compounds that hold metal atoms at their central hole. (The best-known porphyrin is heme, which carries the blood's oxygen and gives red blood cells their color.) He came up with a molecule called texaphyrin — named after his new home state — that was big enough to hold a metal called lutetium. The combination of the porphyrin and the metal yielded lu-tex.

Richard Miller, MD, a clinical associate professor of medicine at Stanford, had treated Sessler in the 1970s and kept in touch with him in Texas. Convinced that lu-tex could improve on other light-activated drugs, Miller and Sessler founded Pharmacyclics Inc. to promote the new treatment. Miller, still on the voluntary clinical faculty, is now president and CEO of the Sunnyvale-based biotechnology firm.

The drug's advantage over other light-activated compounds, says Yuen, is that it is switched on by light of longer wavelengths. Short wavelengths are rapidly absorbed by flesh, so they cannot reach tumors that are more than a few millimeters beneath the skin surface. Red light, however, can penetrate deeper into tissue, which is why only red light emerges when a flashlight shines through a hand.

For the breast cancer patients in the study, the red light may reach as far as several centimeters into the tumor to activate the drug, says Yuen, who plans to begin recruiting study participants this fall.

Participants must not be currently undergoing radiation or chemotherapy, he says.

Pharmacyclics Inc. is supplying the lu-tex for the study and providing financial support. The study will be conducted in the General Clinical Research Center at Stanford, a research clinic funded by the National Institutes of Health. SM