Drug helps fight breast tumors tied to 'cancer genes'

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A twice-daily pill could help some advanced breast cancer patients avoid

or delay follow-up sessions of chemotherapy, a new clinical trial reports.

The drug olaparib (Lynparza) reduced the chances of cancer progression by about 42 percent in women with breast cancer linked to BRCA1 and BRCA2 gene mutations, according to the study.

Olaparib delayed cancer progression by about three months. The drug also caused tumors to shrink in three out of five patients who received the medication, the researchers reported.

"Clearly the drug was more effective than traditional chemotherapy," said Dr. Len Lichtenfeld, deputy chief medical officer for the American Cancer Society.

"This is a group where a response is more difficult to obtain—a young group with a more aggressive form of cancer—and nonetheless we saw a close to 60 percent objective response rate," he said.

The study was funded by AstraZeneca, the maker of Lynparza.

Olaparib works by cutting off the avenues that malignant cancer cells use to stay alive, said lead researcher Dr. Mark Robson. He's a medical oncologist and clinic director of Clinical Genetics Service at Memorial Sloan Kettering Cancer Center in New York City.

The drug inhibits PARP, an enzyme that helps cells repair damaged DNA, Robson said.

Normal cells denied access to PARP will turn to the BRCA genes for help, since they also support the repair of damaged DNA, Robson said.

But that "backup capability" is not available to breast cancer cells in women with BRCA gene mutations, Robson said.

"When you inhibit PARP, the cell can't rescue itself," Robson said. "In theory, you should have a very targeted approach, one specifically directed at the cancers in people who have this particular inherited predisposition."

Olaparib already has been approved by the U.S. Food and Drug Administration for use in women with BRCA-related ovarian cancer. Robson and his colleagues figured that it also should be helpful in treating women with breast cancer linked to this genetic mutation.

The study included 302 patients who had breast cancer that had spread to other areas of their body (metastatic breast cancer). All of the women had an inherited BRCA mutation.

They were randomly assigned to either take olaparib twice a day or receive standard chemotherapy. All of the patients had received as many as two prior rounds of chemotherapy for their breast cancer. Women who had hormone receptor-positive cancer also had been given hormone therapy.

After 14 months of treatment, on average, people taking olaparib had a 42 percent lower risk of having their cancer progress compared with those who received another round of chemotherapy, Robson said.

The average time of cancer progression was about seven months with olaparib compared with 4.2 months with chemotherapy.

Tumors also shrank in about 60 percent of patients given olaparib. That compared with a 29 percent reduction for those on chemotherapy, the researchers said.

Severe side effects also were less common with olaparib. The drug's side effects bothered 37 percent of patients compared with half of those on

chemo. The drug's most common side effects were nausea and anemia.

"There were fewer patients who discontinued treatment because of toxicity compared to those who received chemotherapy," Robson said. "Generally it was pretty well tolerated."

Only about 3 percent of breast cancers occur in people with BRCA1 and BRCA2 mutations, the researchers said in background notes.

Despite this, the results are "quite exciting," said Dr. Julie Fasano, an assistant professor of hematology and medical oncology at the Icahn School of Medicine at Mount Sinai in New York City.

Olaparib could wind up being used early in the treatment of metastatic breast cancer as an alternative to chemotherapy, and future studies might find that the drug is effective against other forms of breast cancer, Fasano said.

"It may be a practice-changing study, in terms of being able to postpone IV chemotherapy and its associated side effects" like hair loss and low white blood cell counts, Fasano said.

Lichtenfeld noted that olaparib also places less burden on patients.

"It may be easier for women to take two pills a day rather than go in for regular chemotherapy," Lichtenfeld said. "Clearly, this is a treatment that will garner considerable interest.

The findings were scheduled to be presented Sunday at the American Society of Clinical Oncology's annual meeting, in Chicago. The study was also published June 4 in the *New England Journal of Medicine*.

More information: Len Lichtenfeld, M.D., deputy chief medical

officer, American Cancer Society; Mark Robson, M.D., medical oncologist and clinic director, Clinical Genetics Service, Memorial Sloan Kettering Cancer Center, New York City; Julie Fasano, M.D., assistant professor, hematology and medical oncology, Icahn School of Medicine at Mount Sinai, New York City; June 4, 2017 presentation, American Society of Clinical Oncology, Chicago

For more about BRCA mutations, visit the U.S. National Cancer Institute.