Ask an **Expert**

by **Christine Hensel Triantos**

What are PARP inhibitors, and how do they play a role in treating ovarian cancer?

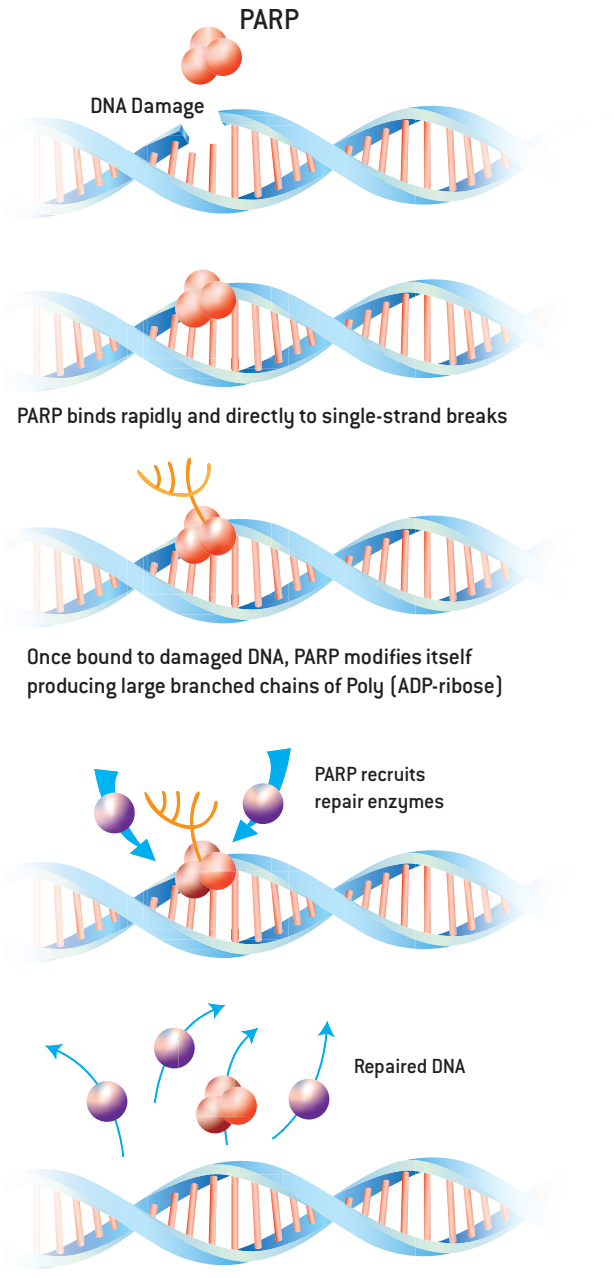
PARP inhibitors are relatively new "smart drugs" that target the DNA-repair pathways of cancer cells, potentially killing them off. Used to treat advanced and recurrent ovarian cancer in women with *BRCA* gene mutations as well as in women with high-grade serous tumors, PARP inhibitors might hold promise for treating other types of cancers as well, including some breast cancers.

Like healthy cells, cancer cells strive to correct DNA damage to stay alive, according to Ursula Matulonis, MD, medical director of the Gynecologic Oncology Program at the Susan F. Smith Center for Women's Cancers at Dana-Farber. If the DNA can't be repaired, the cells can die – which, in the case of cancer cells, is precisely the goal.

PARP (poly [ADP-ribose] polymerase) inhibitors work by blocking the repair of DNA breaks in some cancer cells. Some of the most vulnerable cells seem to be those in patients with *BRCA1* or *BRCA2* mutations, which hinder DNA repair. PARP inhibitors further impede the repair process.

Until recently, PARP inhibitor therapy was available only through clinical trials, including several at Dana-Farber, Dr. Matulonis explains. But in December 2014, the U.S. Food and Drug Administration approved the first PARP inhibitor, olaparib, for use in the treatment of advanced and recurrent ovarian cancer in women with *BRCA* gene mutations who had already received three or more courses of chemotherapy. Overall, the response of patients in studies of olaparib is considered to be an improvement over other therapies.

Olaparib (or Lynparza, as it's called commercially) is produced in pill form. Other PARP inhibitors are in the development pipeline, with extensive involvement of Susan F. Smith Center researchers. Dana-Farber patients have access to clinical trials involving PARP inhibitors, other targeted therapies, and various combinations of drugs (see page 18).



What advice would you give someone newly diagnosed with metastatic breast cancer?

Learning that your breast cancer has spread to distant organs is an understandably jolting experience. While metastatic (also called advanced, or stage IV) breast cancer is treatable, it is not yet curable. For most women, the diagnosis of a life-threatening disease presents steep emotional challenges as well as physical ones.

Though individual situations vary, it's not unusual for patients to live for years with metastatic breast cancer. "Increasingly, we are trying to manage metastatic breast cancer in ways people might associate with a chronic illness," says Eric P. Winer, MD, director of the Breast Oncology Program at the Susan F. Smith Center for Women's Cancers at Dana-Farber.

One of the first steps is to make sure you find the right health care providers. "You're going to have a pretty in-depth relationship with your doctors, nurses, and social workers, so find a team you're comfortable with," says Dr. Winer.

While managing side effects can be a challenge, women often tolerate chemotherapy for metastatic breast cancer better than chemotherapy for earlier stage cancer. "It's a little kinder and gentler," says Dr. Winer. Some drugs cause hair loss or low blood counts, but others do not. "Talk to your doctor about what treatment might be the most effective, and what side effects would be most tolerable," he says.

Feelings of fatigue and depression can also arise. It's important to rule out physical causes for fatigue, such as low thyroid function. Rather than immediately recommending medications for fatigue, Dr. Winer suggests trying light or moderate activity. "You've got to know when to push yourself and when to back off," he says. "Nothing makes people more tired than sitting around all the time."

As for depression, it's important to remember that emotional well-being is connected to physical well-being, so you might at times feel melancholy. "We don't have a mind and body that live in two separate states," says Dr. Winer. "The symptoms we have affect our emotions and psyche." In some cases, antidepressants can help. If you have concerns, talk with your oncologist.

If you are eligible for a clinical trial, consider taking part, Dr. Winer recommends, and remain optimistic. "The longer you live, the greater the chance there's going to be a new treatment for you," says Dr. Winer. "And that new treatment could be a game changer."

Eric Winer, MD, and his colleagues are helping women like Patricia Kartiganer live well with metastatic breast cancer.