OHSU-led study shows promise for ovarian cancer

By Cliff Collins
For The Scribe

During the past two decades, progress in treatment options has been minimal for ovarian cancer, the second most common gynecologic cancer and the most common cause of death among women with a gynecologic cancer.

"There hasn't been [progress] in terms of real change in our thinking," said **Tanja Pejovic, MD, PhD**, a gynecologic oncologist at **Oregon Health & Science University's Knight Cancer Institute**. The same drugs have been used although their route of delivery changed, allowing some patients to live longer, she said.

But in terms of a different treatment paradigm, that has not happened, until possibly now.

Researchers led by OHSU scientists published a study in **PLoS One** in mid-January suggesting that a new class of drugs may be effective in treating a broad range of ovarian cancer patients. PLoS One is an international, peer-reviewed, online journal published by the Public Library of Science, a nonprofit organization.

The paper, titled "BRCAness Profile of Sporadic Ovarian Cancer Predicts Disease Recurrence," found that faulty proteins may prove significant in identifying new treatments.

Pejovic said "a constellation" of defective proteins suspected in causing a malfunction in the body's ability to repair its own DNA could be the link scientists need to prove that patients potentially can be treated with what are known as PARP inhibitors.

Up until now drugs that target the enzyme poly ADP ribose polymerase—or PARP—have been tested only on patients with the genetic mutations BRCA1 and BRCA2.

Pejovic said most medical research has focused on women who have BRCA1 or BRCA2, but 85 percent to 90 percent of all women with ovarian cancer do not have either of these genetic defects.

The OHSU study posits that proteins other than BRCA proteins also are responsible for driving the growth of ovarian cancer.

The study focused on proteins that are supposed to assist cells in repairing harmful breaks in DNA strands, a process called homologous recombination or HR.

"The consequences of defective HR are not understood in sporadic ovarian cancer, nor [has] the potential role of HR proteins other than BRCA1 and BRCA2 been clearly defined," the authors stated in the study. "However, it is clear that defects in HR and other DNA repair pathways are important to the effectiveness of current therapies."

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The authors hypothesize that a subset of sporadic ovarian carcinomas may harbor anomalies in HR pathways, and also that defects in HR or other DNA repair pathways could influence response rate and survival after chemotherapy.

Several forms of cancer are more dependent on PARP than regular cells for their growth, which means that targeting these enzymes when they go haywire is a potentially effective way to treat ovarian cancer.

PARP inhibitors have had limited use in trials, but "we think this class of drugs, combining these inhibitors with chemotherapy, may be beneficial," Pejovic said.

"If we are able to identify the proteins that differentiate these patients at risk for early recurrence, this would open up a new direction in ovarian cancer treatment," she said.

The study included 186 patients with advanced-stage nonhereditary cancer and found that 41 percent who had an early recurrence of the disease also had abnormal levels of the other proteins tracked. By contrast only 19.5 percent of patients who hadn't yet had a recurrence of the disease in three years had abnormal levels of these proteins.

She said the study's results provide evidence that further research into the role of multiple proteins is warranted.

Pejovic noted that OHSU has been among the first to examine these other proteins' role, and no center other than OHSU's has "looked exclusively"" at that angle as a potential for treatment.

Pejovic said she was "excited" over the prospects, which could change the dynamics of ovarian cancer treatment.

The study, which was supported by the **Sherie Hildreth Ovarian Cancer Foundation**, serves as an example of how OHSU is committed to customized—often called "personalized"—cancer treatment, Pejovic said.

Other researchers at the Knight Cancer Institute who contributed to the study were Weiya Z. Wysham, MD; Hong Li, MD; Laura Hays, PhD; Jay Wright; Nupur Pande, PhD; and Maureen Hoatlin, PhD.