Medscape EDUCATION

The Significance of BRCA Mutations in Ovarian Cancer

Ovarian cancer starts in the ovaries, but it's not 1 disease. Every cancer has its own mutations. *Mutations* are changes to genes. They can affect cancer risk and how it responds to treatment. Many mutations are harmless, but some aren't. In ovarian cancer, screening for *BRCA* mutations can help guide prevention and treatment.

Up to 2 out of 3 women[1] with *BRCA* mutations will get ovarian cancer by the age of 75.

What are *BRCA* mutations?

BRCA mutations affect the *BRCA1* and *BRCA2* genes. These genes produce proteins that suppress tumors by helping cells repair damaged DNA. When harmful mutations are present, cells may not be able to repair the damage. As a result, the cells are more likely to have genetic alterations that can cause cancer.

But there is some good news: *BRCA1*- and *BRCA2*-related ovarian cancers often respond better to chemotherapy than other ovarian cancers. As a result, patients with these mutations tend to have better survival rates.

How would I get a *BRCA* mutation?

You can inherit a harmful *BRCA* mutation from your mother or your father. If one of your parents carries such a mutation in one of these genes, you have a 50% chance of having the mutation. Mutations that are inherited are also known as *germline mutations*.

In some cases, a *BRCA* mutation develops spontaneously. These are not passed down to other generations and only occur within the tumor cells. Such mutations are known as *somatic mutations*.

Does having an inherited *BRCA* mutation increase the risk of other cancers?

Inherited *BRCA* mutations can increase the risk of breast cancer. This includes male breast cancers and an aggressive form of breast cancer known as *triple-negative breast cancer*. *BRCA*-

related breast cancers are more likely to occur at a younger age (before age 50) and to affect both breasts.

BRCA mutations might also increase the risk of prostate cancer in men and pancreatic cancer in men and women. Researchers continue to study how *BRCA* mutations affect these and other cancers.

Did you know? Carriers of *BRCA* mutations have a 10% to 30%[2] chance of developing breast cancer in their opposite breast 10 years after their initial breast cancer diagnosis.

Should I be tested?

Certain factors can increase your chances of having a *BRCA* mutation. Testing is a good idea if you have:

- A family history of ovarian or breast cancer
- A personal history of ovarian or breast cancer
- Ashkenazi Jewish, French Canadian, European (particularly Norwegian, Swedish, Hungarian, Dutch, Icelandic),[3] or Mexican ancestry
- Limited information about your family history

Did you know? You're 3 times as likely to have a *BRCA* mutation if you don't know much about your family history.

How do you test for *BRCA* mutations?

Testing for germline *BRCA* mutations is noninvasive. Only a blood or saliva sample is required. *BRCA* testing may look for known harmful mutations in the *BRCA1* or *BRCA2* genes or check for all possible mutations in both genes. Your doctor will determine which test is best for you.

How would having these mutations affect me?

If you don't have cancer, your doctor can develop a prevention strategy. This might include monitoring, medications, or preventive procedures, such as removing your ovaries when you are done having children. Such interventions can decrease your risk of developing cancer and increase the likelihood of any cancer being caught early.

If you have cancer, knowing you have a *BRCA* mutation can help your doctor treat you more effectively. For example, cancer cells with *BRCA* mutations are known to be more sensitive to anticancer drugs that damage DNA, such as cisplatin, and if such drugs stop working, your

doctor can move to other lines of defense, such as poly (ADP-ribose) polymerase (PARP) inhibitors. You may also become eligible to participate in certain clinical trials.

What are PARP inhibitors?

PARP inhibitors are a new medication. They prevent PARP, a naturally occurring enzyme in the body, from repairing cancer cells once they've been damaged by chemotherapy, while sparing healthy cells. PARP inhibitors work especially well against *BRCA*-associated cancers because these tumors already have difficulty repairing damaged DNA.

Currently, PARP inhibitors are only approved for advanced ovarian cancers with a *BRCA* mutation.

Did you know? Less than 25% of patients with ovarian cancer know their germline *BRCA* status[4] despite the potential for expanded treatment options.

References

1. Cancer Research UK. Breast cancer genes. http://www.cancerresearchuk.org/about-cancer/type/breast-cancer/about/risks/breast-cancer-genes Updated July 25, 2014. Accessed March 15, 2015.

2. Susan G. Komen®. BRCA1 and BRCA2. http://ww5.komen.org/BreastCancer/BRCA1andBRCA2.html#ovariancancer Updated January 22, 2015. Accessed March 15, 2015.

3. National Cancer Institute. BRCA1 and BRCA2: cancer risk and genetic testing. http://www.cancer.gov/cancertopics/genetics/brca-fact-sheet Reviewed January 22, 2014. Accessed March 15, 2015.

4. Ray T. FDA approves first PARP inhibitor with Myriad's BRACAnalysis as CDx in advanced ovarian cancer. Genomeweb LLC. https://www.genomeweb.com/regulatory-news/fda-approves-first-parp-inhibitor-myriads-bracanalysis-cdx-advanced-ovarian-cancer. December 23, 2014. Accessed March 15, 2015.