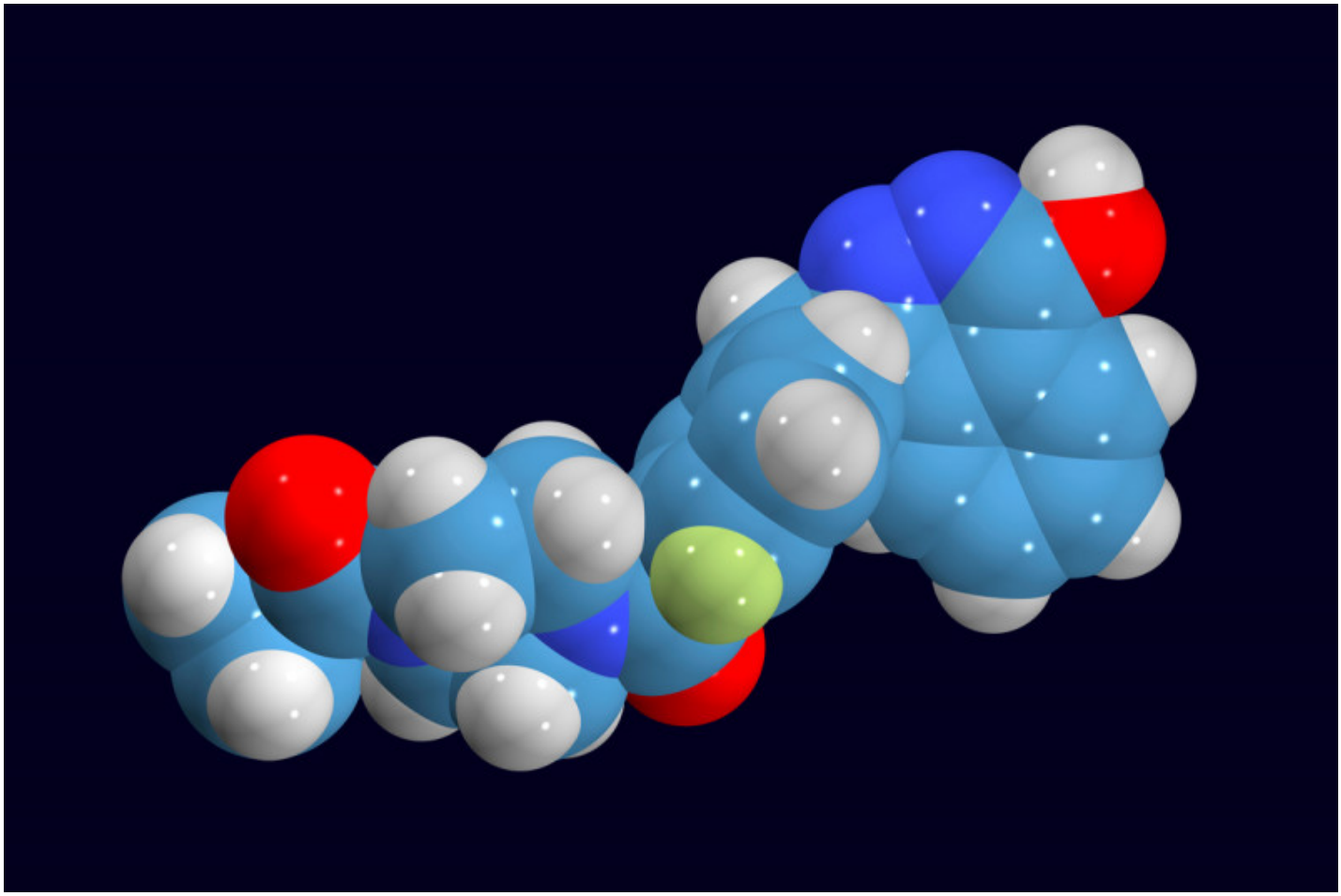
The Latest on Genetic Testing for BRCA Mutations in Breast Cancer

By Julie Grisham, **Wednesday, February 21, 2018**



Olaparib (shown above) is the first drug in the class called PARP inhibitors to be FDA approved for treating breast cancer. (Science Source/Dr. Tim Evans)

Summary

In this interview, Mark Robson, Chief of the Breast Medicine Service at Memorial Sloan Kettering, discusses olaparib, the latest drug approved for breast cancer, and how genetic testing can lead to new targeted therapies.

Last month, the US Food and Drug Administration approved **olaparib (Lynparza®)** for people who have certain types of **breast cancer** that has spread and who have been previously treated with chemotherapy. Olaparib was the first drug in a class called PARP inhibitors to be approved for breast cancer.

Medical oncologist **Mark Robson** headed the first multicenter phase III clinical trial of this drug for breast cancer. Results from that study, which were **reported** at the American Society of Clinical Oncology meeting last summer, led to the drug's approval.

Dr. Robson, who was named Chief of Memorial Sloan Kettering's **Breast Medicine Service** in November 2017, was recently part of a **panel discussion** held at New York City's 92nd Street Y entitled "Knowledge Is Power: Understanding and Managing BRCA-Related Cancer Risk." We spoke with him about what this drug approval means for people with breast cancer, as well as its implications for expanding the use of genetic testing for BRCA mutations.

How do we know whether someone's cancer is caused by a BRCA mutation?

At MSK, everyone with advanced cancer is offered the opportunity to undergo testing with **MSK-IMPACT™**. In addition to looking for cancer mutations in the tumor itself, this test can scan the normal tissue for cancer mutations, if the patient agrees. Because BRCA mutations are carried in the germline, meaning all the cells in the body, they show up with this test.

Mark Robson, medical oncologist and geneticist

There are other tests for inherited BRCA mutations that are available through a number of companies. But we don't recommend taking these tests unless you speak with a genetic counselor.

Based on your findings, who do you think should get BRCA testing?

Now that olaparib is an approved therapy, I would recommend that anyone with advanced breast cancer get the BRCA test. It can help guide their treatment, and it may allow them to avoid getting chemotherapy for a longer period. Olaparib is taken at home as a pill, and it has relatively few side effects.

People with earlier-stage breast cancer as well as other forms of cancer that have been associated with BRCA mutations may want to consider getting tested if their personal or family history suggests they might be carrying a BRCA mutation. That is best determined through a consultation with a genetic counselor. Knowing that they have a mutation can help them plan ways to reduce their risk of developing another cancer. It also might tell them if there is a clinical trial that might help them.

These are genes that are inherited and run in families. Because of that, close relatives of people who are known to have BRCA mutations should strongly consider talking to a genetic counselor and getting tested.

Some people have suggested that because BRCA mutations are more common in people of Ashkenazi Jewish descent, the use of this test should be expanded to include this whole group. There is certainly the potential to benefit, since many people with mutations don't have a family history that would prompt them to get tested. But there are also possible risks if people aren't prepared to learn that they have a mutation. There are a number of studies that are trying to find the best way to get this information to people who want it. One of them is the **BFOR study,** which is being led by **Kenneth Offit** of the **Clinical Genetics Service** here at MSK.

How would a BRCA mutation affect my options for drug therapies?

PARP inhibitors work by blocking enzymes called poly (ADP-ribose) polymerases, or PARPs for short. Members of this family of enzymes help repair breaks in DNA. If DNA cannot be repaired, cells cannot divide and will die. An emerging strategy in cancer therapy has been to block the repair role of PARPs. Normal cells can overcome this type of attack, but certain cancer cells cannot.

In particular, mutations in the genes *BRCA1* and *BRCA2* are connected with the inability to repair this kind of damage. This weakness makes cancers linked to BRCA mutations good candidates for these drugs.

Hereditary Cancer & Genetics

If you have a family history of cancer, the Clinical Genetics Service at Memorial Sloan Kettering can help you to understand your risk for disease.

Learn more

Besides breast cancer, what other cancers are BRCA mutations linked to?

BRCA mutations have been known to be associated with breast cancer and **ovarian cancer** for more than two decades. More recent studies have shown that they are also linked to many cases of **advanced prostate cancer**, as well as **pancreatic cancer**.

Olaparib was previously approved for treating BRCA-associated ovarian cancer. There are two other PARP inhibitors approved for ovarian cancer as well. Clinical trials at MSK and many other centers are looking at expanding PARP drugs to all cancers that are associated with BRCA mutations.

You have been studying BRCA for a long time. Is there anything that's surprised you about recent developments?

It's been an incredibly exciting and interesting time to be involved in this field. When the **Human Genome Project** was completed in 2003, there were all these theoretical ideas of how genetic information could be applied to human health. But none of them were very practical.

The ways that we are beginning to use genetic information now are what we always hoped we would be able to do, even though at that time we couldn't envision the details. So I would not say that I'm surprised, even though I couldn't have predicted exactly what we'd be doing today.

We have reached the place we're at in this field because of investments in fundamental research. It's been a privilege to help turn promise into reality.

Comments

> Commenting is disabled for this blog post.

Diane M Ashton

Mar 28, 2019 • 2:03 AM
I would like to submit my MSKCC Clinical Genetics Family History Questionnaire on line however the web address printed on the form doesn't work (unable to distinguish lowercase L from upper case i). Can the link be emailed to me. Thank you

Memorial Sloan Kettering

Mar 28, 2019 • 8:49 AM
Dear Diane, we recommend that you call the Clinical Genetics Service at **646-888-4050**. Thank you for your comment.

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