

Doctors In-Depth

full length interview

Ovarian Cancer
Eric T. Fung, M.D., Ph.D.
Chief Scientific Officer, Vermillion

Eric T. Fung, M.D., Ph.D., senior vice president and chief scientific officer, Vermillion Inc., talks about the new OVA1™ test to diagnose ovarian cancer...

How prevalent is ovarian cancer?

Dr. Eric Fung: Ovarian cancer is more common than people think. It's known as a silent killer because it's difficult to diagnose. What's even less well known is that ovarian masses are actually very common. We believe that there are up to a million women who each year are found to have ovarian masses who face a difficult decision of whether or not to have surgery to remove that mass.

Do more women die of ovarian cancer than breast cancer?

Dr. Fung: No, I think more women still die of breast cancer than of ovarian cancer because breast cancer is more common, but, in fact, if you look at the percent death rate so to speak, there's a higher death rate from ovarian cancer. Each year, there are 22,000 new cases of ovarian cancer, but about 14,000 women die from ovarian cancer each year, so the death rate from ovarian cancer is higher.

Why is it so hard to diagnose?

Dr. Fung: Ovarian cancer, as we said, is known as the silent killer, and that's because the symptoms you typically associate with ovarian cancer are very non-descript. It can be bloating, constipation, a sense of fullness, and those are obviously very non-specific. Additionally, the ovaries are tucked away in the back of the pelvis, so they tend not to provide sort of physical findings that are easy to detect.

Another reason is that we haven't had tools that have really allowed us to help assess ovarian masses and help us assess the likelihood that they're cancerous, and to refer women to special surgeons, such as gynecologic oncologists. This is really an unmet clinical need that OVA1 can fulfill and the key reason why we at Vermillion developed the OVA1 test.

I want to note that the OVA1™ test should not be used without an independent clinical/radiological evaluation and is not intended to be a screening test or to determine whether a patient should proceed to surgery. OVA1 is indicated for women who are over age 18, have an ovarian mass for which surgery is planned, and who have not yet referred to an oncologist.

How do you currently determine if there's a mass?

Dr. Fung: The most common methodology to identify a mass is typically a transvaginal ultrasound. It does describe some features that can help a physician try to understand whether or not it's likely to be malignant. There has been a blood test that has been used, although the FDA has not cleared that blood test for assessing a mass, but it is traditionally the only test that has been available for over 20 years. That's called CA125. But together CA125 and ultrasound miss a lot of these cancers, and OVA1 has been shown in clinical study to identify more cancers than the traditional methodologies.

Currently, when you find a mass, what is the course of action?

Dr. Fung: Of course, each case is specific to the clinical characteristics that surround it, and not all masses need to be removed. Some of the clinical characteristics that will help drive these decisions include whether or not the patient is pre or post-menopausal and what the ultrasound characteristics of that mass are. Ovarian masses can be broadly divided into persistent and what we call physiologic. The physiologic ones, as the name sounds like, can come and go. Part of the process may be to determine whether the mass is persistent or not, and that would be a watchful waiting period, so to speak. At the end of the day, a certain number of masses do need to be surgically removed, and that's a situation where a physician would really like to know whether that mass is likely to be cancer or not.

How does OVA1 work?

Dr. Fung: OVA1 is the first and only FDA cleared test to help physicians assess, prior to surgery, the likelihood that a mass is malignant. If the OVA1 test score comes back showing a high score, it will heighten the concern that there might be cancer and allow the physician to make a decision as to whether to refer the patient on to a special surgeon, typically called a gynecologic oncologist, who has a lot of experience taking out ovarian cancer. Studies have shown that gynecologic oncologists who do this surgery for ovarian cancer can experience better outcomes for their patients for this deadly disease.

In addition, by directly referring a woman to the gynecologic oncologist for her surgery, this can avoid duplicate surgeries that might otherwise be done. For example, we know a patient, Cindy Hastings who unfortunately had to experience this process of double surgery because the initial suggestion was not malignancy. Cancer was found and removed in that first surgery, but she had to be referred to a specialist surgeon for a second surgery to stage the cancer, to determine how invasive it was – a necessary step for treatment.

What does OVA1 find in the blood?

Dr. Fung: OVA1 detects five proteins in a blood specimen. It measures those five proteins. The science of OVA1 is that there's this special mathematical equation that's used to look at the relationship between these five proteins and provide a single numerical score back to the physician, and that single numerical score can be interpreted by the physician to help assess the likelihood that the mass is cancerous or not.

Is there one certain protein that means the mass is cancerous, or is it a combination?

Dr. Fung: It is a combination, and in fact, that's really the science of OVA1 and the thousands of clinical trial samples that were used helped us to develop this mathematical equation that allows us to look at the relationship between these five proteins. This is really a clear advance over what had been available to physicians before, who relied on a single protein, CA125. Unfortunately, CA125 can detect only about 80 percent of cancers.

What are the five proteins?

Dr. Fung: OVA1 incorporates five proteins. They are CA125, beta-2 microglobulin, transferrin, apolipoprotein A1, and transthyretin.

In the double blind clinical trial study, how difficult was it to determine which ovarian masses were cancerous?

Dr. Fung: The double blind clinical study was done at 27 sites around the country. It incorporated over 500 women with ovarian masses, and importantly, the comparison was whether a clinician, using all the tools available to him or her, could determine whether the mass was cancerous or not. Using clinical assessment, the physicians were able to identify 72 percent of the ovarian cancers. Had OVA1 been available, and if the physician had been able to use clinical assessment along with OVA1, they would have identified 92 percent of

those ovarian cancers. This 20 percent improvement in ovarian cancer detection rate is a clear benefit of OVA1 for both patients and physicians.

Is it just a simple blood test?

Dr. Fung: The way this would be done would be that a physician who sees a mass and is concerned about the presence of cancer would order the OVA1 test, which is available through Quest Diagnostics. The patient would get a blood draw, and that blood would be sent to Quest Diagnostics where the five proteins would be measured and the mathematical equation performed. The physician would receive a report back from Quest Diagnostics several days later with the OVA1 score.

You mentioned a patient, Cindy, earlier. Is she someone who would have benefited from OVA1?

Dr. Fung: She might have benefited from this test. It, unfortunately, was not available at the time, but she is a patient who had the exact characteristics that OVA1 might have helped in the sense that she had an ovarian mass, surgery was planned and the physician was worried about the presence of cancer. Cindy told us that she even got a second opinion from a specialist who evaluated the mass and the consensus prior to surgery was that it was not cancer, and this was because the traditional methodologies, including CA125, as just discussed, did not indicate that it was likely to be cancer. Her initial surgery was done by the generalist, and when cancer was found, she needed to go to the specialist for a second surgery.

How important is it for women to avoid two surgeries?

Dr. Fung: The pain, the cost, and the emotional trauma of having to go through two surgeries are things that we all want to avoid. Additionally, we do know that women who have cancer who are operated on by these special surgeons benefit from extended survival time and even a better chance of outright cure. This is really why we would like to see more women with ovarian cancer referred to the specialist for surgery.

Today, only about a third of women with ovarian cancer are operated on by the specialist for their initial surgery, which means the other two-thirds are likely to be operated on by a general surgeon or a general gynecologist. Of course, we do know about the survival benefit of having had that initial operation by the specialist, so this is the kind of situation where we believe OVA1 will benefit the patient and physicians.

In terms of survival, how important is it to catch ovarian cancer early?

Dr. Fung: The survival rate for late stage ovarian cancer is around 50 percent, and the survival for stage 1 ovarian cancer is over 90 percent, so you can really see the benefit of detecting ovarian cancer in its earliest stages. Currently, only 20 percent of ovarian cancer is detected in stage I.

END OF INTERVIEW

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The OVA1™ Test is a qualitative serum test that combines the results of five immunoassays into a single numerical result. It is indicated for women who are over age 18, have an ovarian adnexal mass for which surgery is planned, and who have not yet been referred to an oncologist. The OVA1™ Test is an aid to further assess the likelihood that malignancy is present when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not intended as a screening or stand-alone diagnostic assay.

Vermillion Inc. developed and owns the trademark to OVA1. Quest Diagnostics offers OVA1 testing nationally.

For more information on OVA1, visit www.QuestDiagnostics.com.

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