

## Title:

Was Your Ovarian Cancer Misdiagnosed?

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## Summary:

Two Percent of All Female Newborns in the United States Are at Risk of Getting Ovarian Cancer

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## Article Body:

Two Percent of All Female Newborns in the United States Are at Risk of Getting Ovarian Cancer

As many as 30,000 U.S. women will be diagnosed with ovarian cancer this year. In 2006, between 15,000 and 16,000 women are likely to die from this silent killer. Ovarian cancer is the 5th leading cause of death among women, and it is responsible for about five percent of all cancer deaths. Chances are your doctor may have misdiagnosed you. That is often the case. A recent British study found 60 percent of all U.K. general practitioners had misdiagnosed their patients. Three-quarters of British doctors surveyed incorrectly assumed that symptoms only occurred in the late stages of ovarian cancer. Based upon that information, it should be no surprise that Britain has one of the lowest survival rates for ovarian cancer in the Western World - of 6,800 cases diagnosed each year, more than 4,600 die.

A similar discovery was made by University of California researchers, who announced last year, "Four in 10 women with ovarian cancer have symptoms that they tell their doctors about at least four months - and as long as one year - before they are diagnosed." According to their study of nearly 2,000 women with ovarian cancer, the researchers discovered physicians:

- First ordered abdominal imaging or performed gastrointestinal procedures

instead of the more appropriate pelvic imaging and/or CA-125 (a blood test that can detect ovarian cancer).

- Only 25 percent of patients, who reported ovarian cancer symptoms four or more months before diagnosis, were given pelvic imaging or had CA-125 blood tests.

Patients with early symptoms are frequently misdiagnosed. Abdominal imaging or diagnostic gastrointestinal studies are less likely to detect ovarian cancer. According to the American Cancer Society's website, "The most common symptom is back pain, followed by fatigue, bloating, constipation, abdominal pain and urinary urgency. These symptoms tend to occur very frequently and become more severe with time. Most women with ovarian cancer have at least two of these symptoms."

By the time a woman reaches the fourth stage of ovarian cancer, her first-line treatment is often Carboplatin, Paclitaxel and Cisplatin as the specific chemotherapy for ovarian cancer. In the first stage, cancer is contained inside one or both ovaries. By stage two, the cancer has spread into the fallopian tubes or other pelvic tissues, such as the bladder or rectum. When the cancer has spread outside the pelvis area into the abdominal cavity, especially when tumor growths are larger than two centimeters on the lining of the abdomen, then ovarian cancer has reached stage three. The fourth and final stage of ovarian cancer is reached when the cancer has spread into other body organs, such as the liver or lungs.

If detected early, survival rates can be as high as 90 percent. Detected in the advanced stage, the survival rate falls to between 30 and 40 percent. Various imaging tests such as computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and ultrasound studies can confirm whether a pelvic mass is present. A laparoscopy can help a doctor look at the ovaries and other pelvic tissue to in order to plan out a surgical procedure, or to determine the stage of the ovarian cancer. A biopsy, or tissue sampling, would confirm if there is cancer in your pelvic region, and would help determine how advanced it is. An elevated CA-125 blood test typically suggests the cancer has progressed to the advanced stage.

About 50 percent of ovarian cancer patients are already at an advanced stage by the time a correct diagnosis is made. Only 10 to 14 percent of women with advanced cancer are likely to survive more than five years.

### Evaluation of Therapies

While research shows drinking black (or green) tea or taking the herbal

supplement ginkgo biloba may be useful, as a preventative measure, or to reduce risk, a woman has few choices when her cancer has moved to the advanced stage. In the first stage, a woman faces surgical removal of the tumor, and possibly one or both ovaries, to increase her chances of survival. Beyond that, her choice is chemotherapy.

One major problem with chemotherapy is the side effects. The more advanced the cancer, the weaker one may be, reducing the survival rate potential. Survival rates have not changed very much over the past fifteen years. Chemotherapy can increase survival time by as much as 50 percent. But, quality of life suffers. The side effects and increased toxicity, accompanying chemotherapy, reduce how one spends the prolonged survival time.

Some of Paclitaxel's minor side effects, as reported by Medline Plus, may include nausea, vomiting, loss of appetite, change in taste, thinned or brittle hair, pain in the joints of the arms or legs, changes in the color of nails, and/or tingling in the hands or toes. More serious side effects may include mouth blistering or fatigue. Some alarming side effects could include unusual bleeding or bruising, dizziness, shortness of breath, severe exhaustion, chest pain, or difficulty swallowing. The most common side effect of Paclitaxel is a decrease of blood cells.

Carboplatin has its own list of side effects. It can reduce platelet production, which can interfere with your blood's ability to clot. You may become anemic, feeling tired or breathless. Nausea, vomiting, loss of appetite and a general feeling of weakness are common with this chemotherapeutic agent.

The latest breed of drugs, such as Eli Lilly's Gemzar, are hardly getting praise. On March 10th, the Food and Drug Administration (FDA) said it was skeptical of the benefits Eli Lilly's Gemzar, which was being used with Carboplatin to treat ovarian cancer patients. The FDA felt the 2.8 months increased survival time, provided by the Gemzar/Carboplatin combination failed to offset the treatment's increased toxicity.

In January, the New England Journal of Medicine reported on a remarkable new delivery system of chemotherapy, called the "intra-abdominal, or intraperitoneal, chemotherapy. Those who received the "belly bath" as it is now being called by the media can survive 16 months longer than those receiving intravenous chemotherapy. The major drawback is that 60 percent of the women in the study were unable to complete all six cycles of this chemotherapy. Those who did survived longer, but only two in every five women were able to advance to the end phase of the therapy.

One novel approach, now in Phase III trials at more than 60 research centers

across the United States, is OvaRex ® MAb, a murine monoclonal antibody, a type of biotech drug derived from mouse cells. It is being tested by highly regarded United Therapeutics, based in Silver Springs, Maryland. Their lead drug Remodulin, an injection which treats pulmonary arterial hypertension, is currently being marketed inside and outside the United States. More than \$32 million has been spent researching, and on the development of, OvaRex and may have it available on the market by 2008.

OvaRex was developed in Canada by a company called ViRexx Medical Corp, and first tested in that country. According to Dr. Lorne Tyrrell, Chief Executive of ViRexx, "The whole study has been set up with the FDA. This is a study where the drug has been given fast track approval and orphan drug status." Dr. Tyrrell is also on leave (until OvaRex become commercially available) as a Professor of Medical Microbiology and Immunology at the University of Alberta, and Director of the National Centre of Excellence for Viral Hepatitis Research.

OvaRex was tested in Canada, prior to the current Phase III trials in the U.S. "There have been a number of patients that have received OvaRex," said Dr. Tyrrell, "We've had really no adverse effects from these patients." Dr. Tyrrell explained the procedure, "After being injected intravenously, OvaRex binds to an antigen circulating in the blood." An antibody's general purpose is to neutralize an antigen. After an OvaRex injection, the murine monoclonal antibody binds to the CA-125 antigen.

In a way the body is tricked. But, the body is tricked in order to help "save" itself from the harmful antigen. When the OvaRex antibody is bound to the CA-125 antigen, the new combination is identified as a harmful unit. Before then, the antigen wanders through the body, without alerting the body's defense systems, the dendritic cells, to attack and destroy the harmful antigen. Because the body is trained to identify and zero in on a foreign protein, in this case a mouse protein, it alerts the dendritic cells. Until then, the dendritic cells "tolerate" the cancerous cells. The tolerance is what permits the cancer to spread throughout the body.

OvaRex seeks to break that tolerance. The murine monoclonal antibody is designed to target and bind exclusively to free floating CA-125 antigen. The dendritic cells refuse to tolerate the foreign protein. When the antibody binds with the free-floating antigen, the dendritic cells recognize the complex (antibody plus antigen) as being foreign and engulf the new unit. The dendritic cells break down the key proteins of this unit, presenting all parts on the cells surface. At the point, the body's killer T-Cells are alerted to fight the internal threat to the body. Once activated, the T-Cells will replicate and create more killer T-Cells. Any tumor cells expressing the CA-125 antigen is targeted for

destruction. The army of T-Cells move to attack the ovarian cancer tumor.

The principle behind OvaRex is to re-program the immune system to harness the body's defenses to prevent the growth and spread of the ovarian cancer. Will it cure ovarian cancer? "In most cases, it will be a delay," explained Dr. Tyrrell. "However, I think that, and everyone hopes that, often in some of these tumors, you're making incremental progress through careful clinical trials and adding new therapy. Each thing we do that improves the outcome when you start to look at the long term benefits of these, we hope that one day we will be able to cure this disease. We think this is a step. This has the potential to be an important step at helping to stimulate immune response to achieve a better outcome. Hopefully, one day we can improve that to where it is a cure."