Title:
Stimulating the Body's Defenses to Fight Ovarian Cancer

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Summary:
OvaRex® MAb is a monoclonal antibody – a biotech drug – designed to help the patient's immune system recognize and more effectively fight ovarian cancer. OvaRex® MAb is given during the 'watchful waiting' period, following successful front-line therapy. It may become recognized as the most significant advance in ovarian cancer treatment since the use of chemotherapy to treat this illness.

Keywords:
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Article Body:
Comediennes such as Gilda Radner and Madeline Kahn, Oscar-winning actresses like Loretta Young and Sandy Dennis, singers Laura Nyro and Dinah Shore, actor Pierce Brosnan's wife Cassandra Harris, actress Jessica Tandy, former Connecticut governor Ella Grasso, and Martin Luther King's wife Coretta Scott King all died of ovarian cancer. It's not just celebrities, politicians or movie stars, who are stricken with ovarian cancer. One in every 55 U.S. women is at risk for ovarian cancer. The American Cancer Society estimates about 22,000 new cases of ovarian cancer will be diagnosed. More than 16,000 women will die because the symptoms are often subtle, and her doctor did not recognize the symptoms soon enough. It is the leading cause of death from gynecologic malignancies, and the fifth leading cause of cancer deaths among women.

Silent and undetected, this cancer often spreads beyond the ovary or ovaries into the abdominal cavity, or by the final stage, into other body organs such as the liver or lungs. Family doctors often fail to properly diagnose "The Silent Killer" until it is too late. Last August, University of California Davis researchers reported 40 percent of women told their doctors about their symptoms for as long as a year before they were correctly diagnosed. A British survey discovered 75 percent of family doctors believed symptoms are only present during the advanced stages of the cancer. By the time women are diagnosed for ovarian cancer, 40 to 50 percent of the patients are in the advanced stage, where there is little hope for survival.

Less than one-half the women diagnosed with ovarian cancer will live five years.

About 10 to 14 percent live beyond five years after their diagnosis. Their choices have been limited, mainly reserved to variations of chemotherapy drugs or a new way to delivery the drug. The general public is often unaware of the side effects ovarian cancer patients suffer during chemotherapy. In mid March, the U.S. Food and Drug Administration criticized the safety profile of Eli Lilly's Gemzar for ovarian cancer patients, saying the 2.8 months increased survival seen in studies of patients taking the drug wasn't enough to offset the treatment's increased toxicity which included anemia, neutropenia (a blood disorder) and thrombocytopenia (reduced platelets in the blood). Presently used first-line treatments for ovarian cancer patients include Cisplatin, with associated side effects such as nerve, kidney and/or ear damage, Carboplatin (side effects: nerve damage in the arms and/or legs, joint pain, and/or thrombocytopenia), Paclitaxel (neurotoxicity), or Melphalan, with side effects which include irreversible bone marrow failure, bone marrow suppression).

A woman stricken with ovarian cancer faces first surgery, then chemotherapy. Recent widespread press heralding a new development in treating ovarian cancer, intra-abdominal or intraperitoneal chemotherapy, is just that: more chemotherapy. The "belly bath," as it has been nicknamed by some television reporters, it has been highly praised because the treatment can extend life by about 16 months more than "regular" chemotherapy. The results were first published in the prestigious New England Journal of Medicine in December 2005. Most news reports failed to mention that only 40 percent of the women treated with the belly bath were able to complete all six cycles. Why? The therapy relies upon infusions of Paclitaxel and Cisplatin (see side effects in the previous paragraph). According to Dr. Robert Edwards, research director of the Magee-Women's Gynecologic Cancer in Pittsburgh, "Many women don't feel well enough to work for the duration of the intra-abdominal (therapy)." Some patients, such as Cindy Pakalnis of Marshall (Pennsylvania) have called the treatments "grueling."

The unsolved problem of chemotherapy is the reduction in the "quality of life." While some life extension has been proven, the patient's life deteriorates. Many patients struggle with balancing the loss in quality of life with the rigors of the therapy. Researchers are actively pursuing new directions that may some day provide new hope for the ovarian cancer patient. A University of Minnesota research study has suggested the use of thalidomide, which would be used in conjunction with chemotherapy, as a prospective means of increasing the likelihood of remission. Minnesota cancer researcher Dr. Levi Downs explained, "It prevents the tumor from making new blood vessels. Without new blood vessels, the tumor can't sufficiently feed new cells, so the cancer can't grow." His randomized trial was small with only 65 patients (only 28 took thalidomide), and more testing will certainly be required.

New Hope for Ovarian Cancer Patients?

One promising technology that has been developed over the past decade is OvaRex® MAb. It was developed by ViRexx Medical Corp., an Edmonton-based company, which trades on the American Stock Exchange (ticker symbol: REX) and on the Toronto Stock Exchange (ticker symbol: VIR). Now licensed to Unither Pharmaceuticals, a wholly owned subsidiary of United Therapeutics (NASDAQ: UTHR), OvaRex® MAb is currently undergoing two identical Phase III trials at about 64 research centers across the United States. One trial has completed enrollment, according to a mid December news release issued by ViRexx Medical Corp.

We spoke with ViRexx Medical Corp's Chief Executive Officer, Dr. Tyrrell who was the Dean of the Faculty of Medicine and Dentistry at the University of Alberta and the Director of the Glaxo Heritage Research Institute. "OvaRex® MAb is our lead candidate for the treatment of ovarian cancer, and is an intravenous infusion of a monoclonal antibody," he said. Monoclonal antibodies are a new breed of biotech drugs that are extremely specific; that is, each antibody binds to only one particular antigen. In the case of OvaRex® MAb, it is a monoclonal antibody that binds specifically to the CA-125 antigen. Dr. Tyrrell added, "The treatment doesn't take long, and is given every 4 weeks for the first 3 injections, and then once every 3 months until the patient relapses".

Dr. Tyrrell talked about the current Phase III studies, "The trials are ongoing. All of the patients have successfully completed their surgery and front-line chemotherapy and are now in what we call the 'watchful waiting' period. It is in this phase that we treat the patients with OvaRex® MAb with the hopes of increasing the time to disease relapse." He explained the recurrence rate is very high in the stage III / IV late forms of ovarian cancer, with a time to relapse of about 10.4 months. Patients who have turned to OvaRex hope to delay that relapse. Tyrrell noted, "In the original study, the average time to relapse was delayed by about 14 months. If we can achieve that difference or better in the current Phase III trials, it would be a major advance for the treatment of ovarian cancer." He expects an analysis of the current OvaRex® MAb studies to be completed by the second or third quarter of 2007.

What makes OvaRex® MAb different from other immunotherapeutic treatments is, instead of attacking the body's cancerous cells directly, the monoclonal antibody targets the cancerous antigen in circulation. Some believe it helps retrain the body's immune system to fight the ovarian cancer cells. The mechanism that reportedly has made OvaRex® MAb effective is how it alerts the body to recognize and fight the CA-125.

ViRexx has addressed the "tolerance problem" a body suffers when it has become

inflicted with a malignant tumor. The hypothesis behind the tolerance issue is that the body fails to recognize the CA-125 antigen as harmful. Introducing a foreign antibody, in this case the mouse antibody against CA125, the body's defense systems are awakened to the ovarian cancer cells. This begins a chain reaction alerting the immune system to battle the invading antibody CA125 complex. The body's defense systems are reprogrammed to attack the CA-125 antigen and seek to destroy it. Along with that destruction comes the attempt of the immune response to eliminate the cancerous cells from the body.

As with many pioneering scientific breakthroughs, serendipity is what lies behind the OvaRex® MAb story. As one technology was being developed, another – the murine monoclonal antibody treatment for ovarian cancer – came about by accident. We talked to its inventor, Dr. Antoine Noujaim, about the biotech drug's roots. "It came out of the imaging technology," the Professor Emeritus of the University of Alberta explained. In the early 1980s, biotech companies, such as Immunomedics and Cytomedics were researching tumors and using antibodies to image the tumors so they could be evaluated in a cancer patient's body. "I worked with Dr. Mike Longenecker and we established a company called Biomira (Toronto: BRA) in 1984," Dr. Noujaim recalled. "We had a number of targets and then needed to make specific antibodies." Part of his effort was to target certain cancers, such as prostate, breast and ovarian cancer.

"We developed antibodies against a mucin, which is really a glycopeptide," explained Dr. Noujaim. "It's a peptide that has a lot of sugars on it present in the ascitis fluid from ovarian cancer patients." That is how Dr. Noujaim and his team developed the very early antibody which is now used for OvaRex® MAb. "We sent some of these antibodies to Professor Richard Baum in Germany for imaging of ovarian cancer patients," Noujaim remembered. "Dr. Baum phoned back, after some time, and told me, 'The patients I was imaging here had advanced ovarian cancer and some of them seem to have done quite well after we gave them a couple of shots (of the B43.13 antibody, the clinical name for OvaRex® MAb) to image the tumor.' I thought he was joking with me."

This is serendipity at work as Dr. Noujaim explained to us. "Richard was imaging patients that were in the last stages of the disease," he pointed out. Monoclonal antibodies can be used as diagnostic agents in oncology, when they are radiolabeled with a marker that can be imaged by external detectors. "These patients had maybe four or five months to live. All of a sudden, a year later and they're still around." Baum urged Noujaim to investigate this further. Dr. Noujaim recalls him saying, "Something is happening here. I've seen hundreds of patients, but nothing like this." From this encouragement, Noujaim began formulating the potential mechanism of how this monoclonal antibody would work. His sharp mind chased the puzzling questions raised by Dr. Baum's observations.

At this point of his recollections, Noujaim got excited, "Through sheer serendipity, we were using murine antibodies, not humanized antibodies. We were using foreign antibodies, a small amount of foreign antibodies." How in the world did Noujaim know to use murine (mouse) antibodies? "Because that was the easiest way to do the imaging at the time," he replied. "Before you make a chimeric (something derived from two different animal species) antibody, you start with a murine one. If that one works, you humanize the antibody." From this research, Noujaim founded a company called AltaRex, which was taken public in 1995. "We raised about $30 million and expanded the program."

The serious effort to develop the antibodies began in 1996. Having conducted trials in Canada and Europe, it was a "massive undertaking" Noujaim told us. "We had over 500 patients injected with the murine monoclonal antibody." He extrapolated beyond OvaRex® MAb, saying, "We've proven completely the mechanism of action on this, how it works. It is so unique it may apply to all of the other antibodies we have." Noujaim believes it can apply to breast, ovarian, prostate and pancreatic cancer. Indeed, BrevaRex® MAb for breast cancer and multiple myeloma patients has completed Phase 1 trials, and ProstaRex® MAb for prostate cancer patients is at the pre-clinical stage.

"Our studies to date may show that vaccines may slow the growth of the tumor with a very good safety profile," concluded Dr. Noujaim. Then he added something which bears investigating further, "There is the very original (ovarian cancer) patient who was injected in 1987. She's in Germany, and according to Dr. Baum she was still alive a year ago." That's nearly nine years later! "It's a matter of great pride for me that some people who received OvaRex® MAb are alive today," he said.

While the company has licensed, under a royalty agreement, the OvaRex® MAb technology to United Therapeutics, through that company's subsidiary, Unither Pharmaceuticals, ViRexx has retained rights to most member nations of the European Union and certain other countries. Key ones include France, the United Kingdom and the Benelux countries. ViRexx has also established strategic relationships with Dompé Farmaceutici, Medison Pharma, Ltd. and Genesis Pharma S.A. for certain European and Middle-East Countries.