



VIRUS THERAPY

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No cancer diagnosis is good news, but ovarian cancer can be particularly unsettling since more than eighty percent of patients are diagnosed with the disease after it has already spread. Despite several effective treatments for this type of cancer, most women whose cancer has spread to distant locations in their bodies, or whose tumors return after treatment, find themselves in a tough battle for survival.

In my eight years as a practicing gynecologic oncologist, I have been continually frustrated that recurrent ovarian cancer remains incurable. It's difficult to deliver bad news to these patients, particularly after they undergo a failed regimen of chemotherapy and all its side effects. "Isn't there anything else we can try?" is a question I hear all the time.

Each year nearly 22,000 American women are diagnosed with ovarian cancer. Despite all the progress we've made in treating ovarian and other cancers, close to 16,000 women die from ovarian cancer every year.

My practice at the James Cancer Hospital at The Ohio State University is currently testing a new treatment for women whose ovarian cancer has recurred or progressed either during or shortly after chemotherapy treatment. The treatment, Reolysin, is an entirely new agent in the war on ovarian cancer or, for that matter, on any type of cancer: Reolysin happens to be a live, infectious virus.

But before getting into the specifics of how we came to use a virus to treat cancer, it would be useful to provide a bit of background on ovarian cancer and its treatment.

Conventional Treatments

Most women with suspected ovarian cancers undergo surgery to remove the main tumor and to confirm that it originated in the ovaries. Once ovarian cancer is confirmed by examining a slice of the tumor under a microscope, the surgeon typically removes the woman's ovaries, uterus, fallopian tubes, and sometimes other nearby tissues. Depending on the stage of the cancer, some women will subsequently receive chemotherapy.

First-line chemotherapy for ovarian cancer is comprised of platinum-based drugs (carboplatin or cisplatin), often in combination with a taxane (paclitaxel). New combinations of drugs are helping women live cancer-free longer than at any time in the past. Most women respond well to these drugs, which is good news. Unfortunately, in many patients the cancer returns.

If the patient had responded initially to a chemotherapy regimen, most physicians (including me) will try the same drug or combination of drugs again. If it worked once, it is most likely to work again. But once the tumor returns it is not considered curable.

If the treatment used initially fails to shrink the tumor during the second round of therapy, an oncologist may try any of the half-dozen other chemotherapy agents approved specifically for ovarian cancer, or even prescribe drugs normally used for other cancers. The goal of therapy for recurrent ovarian cancer thus shifts from curing the disease to improving quality of life by slowing or stopping tumor growth. I have many patients who are still in remission after many years of being treated in this way.

Hope Out of Despair

For women whose tumors fail to respond at this stage, one potential and interesting treatment option may be a clinical trial.

A clinical trial is a specialized human study of an experimental drug performed under carefully controlled conditions. Pharmaceutical companies, hospitals, and government institutions use clinical trials to evaluate new treatments and to investigate the optimal use of already-approved drugs.

Participation in a clinical trial can be fulfilling and beneficial to patients in many ways. Participants in clinical trials receive the best evaluation and care available, usually from highly trained physician-researchers. While no study will promise a long-term remission or even prolonged survival, those outcomes do occur in patients treated in clinical trials.

In addition to direct benefits, study patients can take satisfaction in the knowledge that they are advancing medical science, and in so doing may help not only themselves, but other patients with their disease.

Virtually every important medicine on the market today, including all cancer drugs, was tested extensively in clinical trials. Taxane chemotherapy agents, which are part of the standard of care for first-line ovarian cancer treatment, were first tested during the 1980s and 1990s and have greatly extended the lives of millions of cancer patients, including those with ovarian cancer.

The Reolysin Study

Our clinic is currently testing one of the most interesting, and potentially promising,

cancer therapies to emerge in many years. The treatment, Reolysin, consists of a virus that attacks tumor cells while leaving normal cells unscathed. The treatment is being developed by Oncolytics Biotech, a Canadian biotechnology company.

Virus therapy works by exploiting a genetic mutation inside cancer cells that does not exist in normal cells. The mutation allows the virus to enter tumor cells and produce thousands of copies of itself. Eventually, the cancer cells burst, releasing the virus particles, which in turn will infect other cancer cells. To date, 270 patients with various forms of cancer have been treated with Reolysin in various trials in Canada, the U.S. and the U.K.

Side effects of oncolytic virus treatment are extremely mild compared with those of chemotherapy or radiation. Some patients report a combination of mild, flu-like symptoms, low-grade fever, and a feeling of fullness in the abdomen (more on that in a minute). Side effects usually resolve rapidly. Several of my patients have commented that the side effects of Reolysin therapy have been much less severe than those of chemotherapy. In our clinic, no patient has had to drop out of a Reolysin study due to side effects.

Women in the Reolysin study receive the virus intravenously for five consecutive days. On two of those days patients also receive an infusion of Reolysin into their abdomens (hence the feeling of fullness mentioned above). The treatment cycle is repeated every 28 days as long as the patient continues without undue side effects.

Several ovarian cancer studies suggest greater effectiveness with chemotherapy agents when the drugs are administered into the abdomen as well as intravenously. Researchers believe this effect is due to the drug being in closer contact with the cancer. Based on these findings, the National Cancer Institute, under whose auspices we are conducting this study, was interested in testing if abdominal administration could improve outcomes with virus therapy as well.

Reolysin is currently under investigation in ten U.S. and U.K clinical trials for a variety of cancers, including tumors of the lung, head and neck, bone or soft tissue, colon, skin, and ovaries. In some trials, as in the ovarian cancer trial, Reolysin is administered alone; in others patients receive it along with chemotherapy. So far, reported results have been extremely encouraging, with many patients seeing their cancers stabilize or shrink significantly.

The appeal of Reolysin is that unlike chemotherapy, which affects many different cells, the oncolytic virus kills only cancer cells. Normal cells, such as hair follicles and intestinal cells, are undisturbed, so patients do not lose their hair or appetite. Compared with conventional chemotherapy and radiation, this alone is a huge step forward.

Experience has shown that oncolytic viruses are not only well tolerated, but offer hope for cancer patients who otherwise have limited options. Oncolytic viral therapy is a welcome addition to the fight against ovarian cancer.

Women with cancers of the fallopian tube, ovaries, or the abdominal cavity who are interested in entering the ovarian cancer study at the James Cancer Hospital at The Ohio State University should call (614) 293-3873 or visit their website, www.jamesline.com

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