Targeting a Deadly Type of Uterine Cancer

Endometrial cancer, which originates in the lining of the uterus and is the most common type of gynecological cancer, often has a good prognosis. However, Type II, which is responsible for most of the recurrences and deaths that occur in endometrial cancer, accounts for just 10 percent of endometrial tumors and is particularly deadly: in its earliest stages the survival rate can be as low as 50 percent, and for those with more advanced disease, there is no cure.

"A striking majority of these patients die too early and very quickly," said Alessandro Santin, MD, Professor of Obstetrics, Gynecology & Reproductive Sciences at Yale School of Medicine and leader of the Gynecologic Oncology Program at Smilow Cancer Hospital. Dr. Santin has spent a decade unraveling the biology of USC in an effort to develop targeted treatments that will have an impact on this devastating disease.

Dr. Santin's interest in USC was born of frustration. Before he came to Yale in 2008, he worked at the University of Arkansas for Medical Sciences, where his practice included a significant number of African American women, who have the threelfold higher incidence of USC. "I was stunned by the high number of USC patients I was seeing with a threefold higher incidence of USC."

Several years ago, Dr. Santin began to ask himself why this was the case with the least aggressive type of endometrial cancer. He also found that patients with tumors that expressed HER2/neu had the poorest prognosis.

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The drug trastuzumab (herceptin) is used to treat breast cancers that overexpress HER2/neu and was also approved last year to treat gastric cancer. Dr. Santin and his colleagues at Yale and another large group of tumors did not have the FBXW7 mutation but had the oncogene cyclin E, which helps cells proliferate, was highly active in USC due to a mutation in the PIK3CA gene or had amplification of this gene. This points the way to using drugs that target this pathway in other cancers to treat USC.

Other pathways related to PIK3CA that are active in tumor cells and for which there are drugs in development were also identified in USC cells, offering additional targets that Dr. Santin is testing in clinical studies.

Dr. Santin’s work revealing pathways that are potentially targetable with existing drugs is allowing him to test different agents in the lab and in animals before moving to clinical trials. "It’s a unique opportunity for our USC patients because we will soon be able to translate our discoveries into novel therapeutics that will improve patient outcomes," he said.

"In addition to providing superior quality of care surgically, we will also be able to follow up with personalized therapies targeting key signaling pathways highly active in this lethal type of endometrial cancer."

Alessandro Santin, MD

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