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STUDY FINDS THAT INHERITED BRCA-MUTATIONS IMPROVE TREATMENT RESPONSE AND SURVIVAL AMONG OVARIAN CANCER PATIENTS

LOS ANGELES, May 1, 2003 – In the last decade, much attention has focused on the gene abnormalities linked to certain diseases. Wide attention, for example, has focused on hereditary mutations of the BRCA genes, which can lead to the development of breast and ovarian cancer. But in recent years, researchers have also learned that ovarian cancer patients who inherit BRCA mutations may live longer than patients who do not. The reason for this survival advantage, however, has not been identified.

Now, researchers at Cedars-Sinai Medical Center have found that improved survival among patients with hereditary BRCA-associated ovarian cancer may result from a greater sensitivity and response to treatment with chemotherapy. Their findings are reported in the May 1st issue of the journal, *Cancer*, and may enable physicians to better plan treatment for their patients with BRCA-linked ovarian cancer.

“We found that advanced stage hereditary BRCA-associated ovarian cancer patients had a better response to platinum-based chemotherapy than patients without BRCA-mutations who had advanced disease,” said Ilana Cass, M.D., the principal investigator of the study and gynecologic oncologist at Cedars-Sinai Medical Center. “This may contribute to their improved prognosis.”

Evidence suggests that normal BRCA genes control cell growth and repair damage to DNA. But when defective, the genes fail to function properly and can lead to the development of breast or ovarian cancer. In fact, about 10 percent of invasive ovarian cancers are due to an inherited mutation in either the BRCA1 or BRCA2 genes. Ashkenazi Jewish women have the highest prevalence of these genes, with about two percent carrying mutations in BRCA1 or BRCA2. Of those women who carry mutations in BRCA genes, 16 to 44 percent develop ovarian cancer.

Although several studies have shown that patients with hereditary BRCA-associated ovarian cancers live longer, the basis for this survival advantage is unknown. Some research has suggested that longer survival may be due to a younger age at diagnosis, while other studies have suggested that hereditary BRCA-associated ovarian cancer patients respond better to chemotherapy.

To determine why hereditary BRCA mutations lead to better survival among ovarian cancer patients, the investigators examined the tumor characteristics, treatment responses and survival outcomes of Ashkenazi Jewish women with ovarian cancer who carry hereditary BRCA-mutations as compared to those who do not.

In the study, 71 Ashkenazi Jewish women with ovarian cancer underwent screening blood tests to determine whether inherited BRCA mutations were present. The investigators found that 34 patients, or almost half, carried BRCA mutations, with a higher proportion of patients carrying mutations in the BRCA1 gene.

“This finding was not surprising given that about 50 percent of Ashkenazi Jewish patients who have ovarian cancer are found to carry mutations in BRCA genes,” commented Dr. Cass.

The investigators also screened 54 of 71 available tumor specimens to determine whether there was a coexisting mutation in the *p53* gene which lead to an over-abundance of the *p53* protein in their tumor sample. *P53* mutations have been reported more frequently in patients with hereditary BRCA mutations, and may influence patient survival. They found that although *p53* was over-expressed in more of the hereditary BRCA-associated tumors and that these patients lived slightly longer than those without inherited BRCA mutations, the length of survival time did not prove to be statistically significant.

To determine whether patients with hereditary BRCA-associated ovarian cancer had a better response to chemotherapy, the investigators’ limited their analysis of patient survival and tumor response to patients with invasive, advanced stage ovarian cancer who were treated with combination platinum-based chemotherapy. Response to chemotherapy was defined by three criteria: a negative “second look” surgery, in which a second surgical procedure was performed following primary chemotherapy to check whether any residual cancer was present; a measurable reduction in tumor size; or no detectable disease found five years after diagnosis.

Their analysis revealed that 86 percent of patients with hereditary BRCA mutations had no recurrent disease at second look surgery as compared to 41 percent of patients with ovarian cancer but without BRCA-mutations. The average survival time among patients with advanced stage hereditary BRCA-associated ovarian cancer was 91 months as compared to 54 months. Further, hereditary BRCA-associated ovarian cancer patients remained free of disease for 49 months as compared to 19 months for patients without BRCA-associated disease.

“The significantly longer survival of patients with BRCA-associated ovarian cancers in our study, points to an enhanced tumor responsiveness to platinum-based chemotherapy, rather than less aggressive disease,” said Dr. Beth Karlan, senior author of the study and Director of the Women’s Cancer Research Institute at Cedars-Sinai. “Knowing how BRCA mutations increase response to treatment may lead to the development of targeted therapies or drugs that will improve survival for all women with ovarian cancer and point to novel means of cancer prevention.”

Cedars-Sinai Medical Center is one of the largest non-profit academic medical centers in the Western United States. For the fifth straight two-year period, Cedars-Sinai has been named Southern California’s gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthrough in biomedical research and superlative medical education. Named one of the 100 “Most Wired” hospitals in health care in 2001, the Medical Center ranks among the top 10 non-university hospitals in the nation for its research activities.

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