BRCA2 genetic mutation associated with improved survival, chemotherapy response in ovarian cancer

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Among women with a certain type of high-grade ovarian cancer, having BRCA2 genetic mutations, but not BRCA1, was associated with improved overall survival and improved response to chemotherapy, compared to women with BRCA wild-type (genetic type used as a reference to compare genetic mutations), according to a study in the October 12 issue of *JAMA*.

"Increased surveillance of BRCA1/2 germ line mutation carriers is a generally accepted strategy for detecting early ovarian cancer. Women with BRCA1 mutations have a 39 percent to 54 percent cumulative lifetime risk of developing ovarian cancer and women with BRCA2 mutations have an 11 percent to 23 percent risk," according to background information in the article. Conflicting data exist regarding the outcome of BRCA-deficient patients after ovarian cancer develops. Some researchers have found that ovarian cancer patients with BRCA1/2 germ line mutations have a more favorable clinical course, whereas others have shown the opposite. Also, most studies that have investigated the clinical features of BRCA1/2 mutation carriers lack detailed chemotherapy information.

Da Yang, Ph.D., of the University of Texas MD Anderson Cancer Center, Houston, and colleagues evaluated the association between BRCA1/2 deficiencies in ovarian cancer and patient overall survival (OS) and progression-free survival (PFS) rates and chemotherapy

response. The observational study included multidimensional genomics and clinical data on 316 high-grade serous (type of ovarian tumor) ovarian cancer cases that were made public between 2009 and 2010 via The Cancer Genome Atlas project. Patients with both types of mutations did not differ significantly from each other with respect to tumor stage, grade, or histologic type, but patients with BRCA1 mutations were younger at diagnosis (35 cases, average age, 56 years) than were those with wild-type BRCA (219 cases, average age, 62 years) or BRCA2 mutation (27 cases, average age, 61 years).

The researchers found that the 5-year survival rate of' BRCA2 mutation carriers was 61 percent, which was significantly higher than that of wild-type BRCA cases (25 percent). BRCA2 mutation carriers had significantly longer PFS durations than did wild-type BRCA carriers; no difference was found for BRCA1 mutation carriers. A direct comparison between BRCA1 and BRCA2 mutation carriers indicated significant difference in PFS: 44 percent of BRCA2-mutated cases remained progression free 3 years after surgical resection compared with only 22 percent of BRCA1-mutated cases.

"Moreover, BRCA2 mutations were associated with a significantly higher primary chemotherapy sensitivity rate (100 percent for BRCA2-mutated vs. 82 percent and 80 percent for BRCA wild-type and BRCA1-mutated cases, respectively) and longer platinum-free [a metal that is a component of some anticancer drugs used in chemotherapy] duration (median [midpoint] platinum-free duration, 18.0 months for BRCA2-mutated vs. 11.7 and 12.5 months for BRCA wild-type and BRCA1-mutated cases, respectively)," the authors write.

"… the discovery that BRCA1 and BRCA2 deficiencies are associated with differential effects on patient survival and chemotherapy response in ovarian cancer may have important implications for clinical prediction and trial design and sheds new light on the function of these 2 genes,"

the researchers write.

In an accompanying editorial, Victor R. Grann, M.D., M.P.H., and Ramon E. Parsons, M.D., Ph.D., of the Columbia University Medical Center, New York, comment on the findings of this study.

"The study by Yang et al provides a major advance in the understanding of the use of new treatments for ovarian cancer among patients with BRCA mutations by demonstrating a difference in the response among patients with BRCA1 and BRCA2 mutations diagnosed with ovarian cancer. Newer studies may support the use of poly (ADP-ribose) polymerase inhibitors for the treatment of such patients. Early studies among women with advanced breast cancer suggest some improvement—especially with platinum-based therapy and the use of neoadjuvant [administration of therapeutic agents before a main treatment] chemotherapy. The next step would be to enroll these patients in randomized clinical trials to test whether BRCA1 or BRCA2 mutation carriers respond differently with regard to ovarian cancer, as Yang et al suggest."

More information: *JAMA*. 2011;306[14]:1557-1565.

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