Recurrent low-grade carcinoma of the ovary less responsive to chemo than more common ovarian cancers

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Tampa, Fla.- Recurrent low-grade serous carcinoma, a rare type of ovarian cancer, is less sensitive to chemotherapy and therefore more difficult to treat than more common high-grade ovarian cancers, according to researchers from The University of Texas M. D. Anderson Cancer Center. The findings were reported at the Society of Gynecologic Oncologists 39th Annual Meeting on Women's Cancers.

The retrospective study is the first to analyze how women with low-grade tumors respond to chemotherapy in recurrent setting and confirms clinical impressions that the tumors are chemoresistant, said lead author David M. Gershenson, M.D., professor and chair of the Department of Gynecologic Oncology at M. D. Anderson. Previous studies have shown similar tumor resistance in newly diagnosed patients, and there is currently no standard of care for women facing the disease.

The results support a growing body of research that shows low-grade ovarian tumors behave differently than their high-grade counterparts, genetically and clinically. "In order to make meaningful advances in treatment, women with low-grade ovarian tumors must not be grouped together with those with more common ovarian tumors. They require unique consideration and more targeted treatment options for a better chance of survival," Gershenson said.

Gershenson and his colleagues identified all patients treated for recurrent

low-grade serous carcinoma of the ovary seen at M. D. Anderson from 1990 through 2007 using databases from the Department of Gynecologic Oncology. Out of 52 patients with sufficient clinical information with which to assess response to one or more of 98 different chemotherapy regimens, the overall response rate was only 4 percent. Specifically, researchers found:

-- Among 24 patients who received carboplatin for platinum-sensitive disease, there were two partial responses and one complete response.
-- Of 11 patients who received a taxane/platinum combination for platinum-sensitive disease, no objective responses were observed.
-- In the entire platinum-sensitive cohort, the overall response rate was only 6 percent.
-- No response was observed in women with platinum-resistant disease to standard chemotherapy agents such as liposomal doxorubicin; topotecan; hexamethylmelamine; oral VP-16; xeloda and gemcitabine. One patient had a partial response to paclitaxel. The overall response rate in this subgroup was 2 percent.
-- Sixty-one (62 percent) of the regimens stabilized the disease from 8 to 79 weeks, with a median of 22 weeks.
-- In 18 instances of stable disease, CA125 levels decreased by 50 percent or more.

Gershenson said that these results compared unfavorably to findings from trials of more common ovarian cancers. "It is unclear whether the high rate of stable disease is more reflective of tumor biology of low-grade serous carcinoma of the ovary or of the therapy regimen administered. However, since these tumors do not respond to conventional types of chemotherapies, new agents to treat these tumors must be identified and tested," said Gershenson.

One area to explore further is hormonal therapy, a treatment that has been shown to have some activity against low-grade serous carcinoma,

he said. A detailed analysis of the M.D. Anderson experience with hormonal therapy is planned in the near future.

Low-grade serous carcinoma represents about ten percent of all serous ovarian cancers. The disease is characterized by a young age at diagnosis - an average of 42 years old, versus more common ovarian cancers, which are generally diagnosed at about 60 years old. In addition, the median overall survival of women with low-grade serous carcinomas is much longer than that of patient with high-grade ovarian cancers-82+ months versus 50-67 months in various reported series.

Two-Tier Grading System Advances Better Treatment Options

Histologic grade has been shown to be one of the most important prognostic factors in ovarian serous carcinoma cases. However, no universal grading system exists. Over the last 15 years, researchers at M. D. Anderson have developed a two-tier grading system for serous carcinoma of the ovary (low and high), based on knowledge that this type of epithelial ovarian cancer comprises not one homogenous group of tumors but rather two distinct phenotypes.

Historically, a three-tier grading system to classify tumors has been used, but there has been no precise mechanism to define the thresholds between the grades, particularly grades two and three. Consequently, there were variations in designating how ovarian tumors should be classified and ultimately, treated.

Rare Ovarian Tumors Receive Increasing Attention

The study of rare cancers, such as low-grade serous carcinoma of the ovary, brings inherent challenges, including the limited number of cases

to examine, difficulty in obtaining tissue samples, low funding, and the small pool of investigators working on research, according to Gershenson.

Recognizing the need for more research, the Gynecologic Oncology Group, a National Cancer Institute-funded cooperative group, recently established a rare tumor committee that has initiated a separate series of clinical trials for recurrent low-grade serous carcinoma as well as for other rare ovarian cancers.

Gershenson said that changing the design of clinical trials to segregate patients is key. "In addition to providing direct benefits to patients and their families, the study of rare tumors can also uncover information about the etiology, biology, and treatment of more common cancers."

Source: University of Texas M. D. Anderson Cancer Center