Small Study: Antiepileptics Interfere With OCs

BY HEIDI SPLETE

FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF NEUROLOGY

TORONTO — A standard dose of the antiepileptic drug carbamazepine allowed ovulation and the potential for pregnancy in women using low-dose birth control pills in a small randomized, double-blind study of healthy women without epilepsy.

The key clinical implication of the findings is that women using antiepileptic drugs who wish to avoid pregnancy should take additional birth control measures, according to Dr. Anne Davis of Columbia University in New York.

"We were very surprised to see that half of the women who took the [carbamazepine] ovulated," placing them at an obvious increased risk for pregnancy, Dr. Davis said in an interview.

VITALS

Major Finding: Half of healthy women taking the antiepileptic carbamazepine ovulated despite taking a low-dose oral contraceptive.

Data Source: A randomized, double-blind crossover study of 24 healthy women aged 18-35 years.

Disclosures: Dr. Davis has received personal compensation from Bayer Pharmaceuticals and Schering Plough for participating on their advisory boards.

Clinicians have suspected that oral contraceptives are not fully effective in women who take antiepileptic medications, Dr. Davis and colleagues said in a poster.

But case reports of breakthrough bleeding in epileptic patients were not enough to establish a causal relationship between the antiepileptic drug carbamazepine and the loss of effectiveness from low-dose oral contraceptives, the researchers said.

In this study, the researchers randomized 24 women, aged 18-35 years, with regular menstrual cycles to receive a low-dose birth control pill containing 20 mcg of ethinyl estradiol and 100 mcg of levonorgestrel for 4 months. In addition, the women took either 600 mg of carbamazepine or a matching placebo daily for 2 months.

Breakthrough bleeding was more frequent in the carbamazepine group, with a median of 7 bleeding days, compared with zero bleeding days in the placebo group.

At least 3 days of breakthrough bleeding occurred in 8 of 10 carbamazepine cycles, compared with 2 of 10 placebo cycles.

In addition, progesterone levels greater than 3 ng/mL (suggestive of ovulation) occurred in five of the carbamazepine cycles, compared with one of the placebo cycles.

Three women in the carbamazepine group showed increased levels of progesterone during week 1 of a cycle, immediately after the placebo pills in the oral contraceptive pack, they said.

The differences between the groups fell short of statistical significance, in part because only 10 of the 24 women completed the entire study.

Of the women initially randomized, two in the carbamazepine group and one in the placebo group did not take the drug.

Five women in the carbamazepine group discontinued due to reversible side effects, and three women in the placebo group discontinued for reasons unrelated to the medication.

One patient in the placebo group discontinued due to an adverse event, and samples were lost for one patient in each group, leaving four carbamazepine patients and six placebo patients in the final analysis.

Despite the study's small size, the results show that the known pharmacokinetic effect of carbamazepine on contraceptive steroids has a clinically significant effect, Dr. Davis said.

"If a woman is taking carbamazepine, and she needs birth control, a low-dose pill is not going to be effective," Dr. Davis said.

"I think the next question is to figure out what will be effective for women in that situation," she said. ■

Bevacizumab Plus Chemo Ups Ovarian Cancer Survival

BY NEIL OSTERWEIL

AMERICAN SOCIETY OF CLINICAL ONCOLOGY 2010 ANNUAL MEETING

CHICAGO — Progression-free survival in women with advanced ovarian or related female reproductive tract cancers was increased by nearly 4 months when they received frontline therapy with standard chemotherapy and concurrent bevacizumab followed by maintenance with bevacizumab alone, reported investigators from the Gynecologic Oncology Group's GOG-0218 trial.

In a randomized, placebo-controlled, phase III trial, the addition of bevacizumab (Avastin) to chemotherapy with carboplatin and paclitaxel followed by bevacizumab monotherapy resulted in a median progression-free survival (PFS) of 14.1 months, compared with 10.3 months for women on standard chemotherapy and placebo (hazard ratio 0.717, *P* less than .0001), reported lead investigator Dr. Robert A. Burger of the Fox Chase Cancer Center in Philadelphia.

VITALS

Major Finding: There was a 3.8-month increase in progression-free survival in women with advanced ovarian and related cancers who received bevacizumab as an adjunct and follow-on to standard chemotherapy.

Data Source: GOG-0218 trial.

Disclosures: Dr. Burger has served as an advisor/consultant to Genentech Inc. Dr. Eisenhauer reports no relevant disclosures.

But bevacizumab was effective only when used both as an adjunct to chemotherapy and as maintenance therapy: Women who received the angiogenesis inhibitor with chemotherapy but got a placebo during the maintenance phase had a median progression-free survival of 11.2 months, which was not significantly better than that of women who received chemotherapy and placebo only (HR 0.98, *P*=.16), Dr. Burger said.

"Bevacizumab is the first molecular-targeted and first antiangiogenic agent to demonstrate benefit in this population, and bevacizumab combined with chemotherapy followed by bevacizumab maintenance should be considered as one standard option for women with this disease," said Dr. Burger.

That recommendation may be a bit premature, however, because the data so far show an effect of bevacizumab on only progression-free survival and not on overall survival, and "we cannot infer that a progression-free survival gain will mean an overall survival gain," commented Dr. Elizabeth A Eisenhauer, the invited discussant.

"A progression-free survival gain of only 3.8 months may not be meaningful to patients. We need the mature overall survival and quality-of-life results, and ideally the results of the other frontline trial of bevacizumab in this disease, ICON-7, to understand the full story of the impact of this advance," said Dr. Eisenhauer of the National Cancer Institute of Canada.

GOG-0218 investigators enrolled 1,873 women with stage III or IV epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer.

Each group received the CT regimen, consisting of 22 3-week cycles, with the first 6 cycles consisting of intravenous paclitaxel 175 mg/m^2 plus carboplatin at an area under the curve of 6 mg/mL per minute. One group also received concurrent placebo followed by maintenance placebo, a second received concurrent bevacizumab plus maintenance placebo, and the third received concurrent bevacizumab and bevacizumab maintenance. ■