Drug Monitor

CLEOPATRA Study and MBC

Trastuzumab, an anti-human epidermal growth factor receptor 2 (HER2) monoclonal antibody treatment, prolongs survival among women with HER2-positive metastatic breast cancer (MBC), but the disease usually progresses. So findings from the Clinical Evaluation of Pertuzumab and Trastuzumab (CLEOPATRA) study, although preliminary, are encouraging: Combining trastuzumab with a similar-yet-different treatment, pertuzumab, significantly adds to progression-free survival, with no increase in cardiac toxic effects.

The CLEOPATRA Study Group conducted a double-blind, phase 3 trial of 808 patients with HER2-positive MBC at 204 centers in 25 countries. The patients who had not received chemotherapy or biologic therapy for their metastatic disease were randomly assigned to receive placebo plus trastuzumab plus docetaxel or pertuzumab plus trastuzumab plus docetaxel as first-line treatment until the disease progressed or the patient developed adverse effects that could not be effectively managed. Each patient in the control group had a median of 15 study-treatment cycles (range 1 to 50); the pertuzumab group had 18 per patient (range 1 to 56). The median duration of study treatment was estimated to be 11.8 months and 18.1 months, respectively. Dose reductions were not permitted for placebo, pertuzumab, or trastuzumab. Patients in each group received docetaxel for a median of 8 cycles. The median dose intensity of docetaxel was 24.8 mg/m^2 per week in the control group and 24.6 mg/m^2 per week in the pertuzumab group.

Adding pertuzumab extended median progression-free survival by 6 months—to 18.5 months, compared with 12.4 months in the control group. Among 88 patients who had received adjuvant or neoadjuvant chemotherapy with trastuzumab, median progression-free survival was 10.4 months in the control group and 16.9 months in the pertuzumab group. Among 288 patients who had received adjuvant or neoadjuvant chemotherapy without trastuzumab, median progression-free survival was 12.6 months in the control group, compared with 21.6 months in the pertuzumab group. More patients died in the control group: 96 vs 69. The objective response rate was 69% in the control group compared with 80.2% in the pertuzumab group—a difference of nearly 11 percentage points.

The safety profile was similar in both groups. However, left ventricular systolic dysfunction was reported twice as often in the control group (8.3% vs 4.4%); febrile neutropenia and grade 3+ diarrhea were more common in the pertuzumab patients.

The researchers note that the survival data are not yet mature—although they found a strong trend toward prolonged survival with the combination/complementary treatment, the result is "exploratory." The final analysis is scheduled for 2013.

Source: *N Engl J Med.* 2012;366(2):109-119. doi: 10.1056/NEJMoa1113216.

Diabetes Drug Helps With Weight Loss

An incretin mimetic used to treat diabetes may also be an effective weight loss drug for people without diabetes, according to a study at the Beth Israel Deaconess Medical Center in Boston, Massachusetts. In the study of 41 obese women, subjects treated with exenatide, a glucagon-like peptide (GLP)-1, lost an average 2.5 kg.

The 35-week crossover study included two 16-week treatment periods separated by a 3-week washout period. Women with type 1 or type 2 diabetes were excluded (although 24% of participants were prediabetic at enrollment), as were those who had uncontrolled hypertension or dyslipidemia, those who had been treated with anti-obesity medication within 1 year, those who had a history of bariatric surgery, or those who had previously been on exenatide. The subjects reported a stable weight within 6 months of the screening visit and, as a whole, had well-controlled cardiovascular risk factors.

Participants injected 5 µg of exenatide or placebo before breakfast and supper. After 2 weeks, they increased their doses to 10 µg twice daily. The women were weighed at study visits every 2 weeks. Glycemic status was also measured at the beginning and end of each treatment period.

Four months of exenatide treatment resulted in significant weight loss: 2.49 kg (2.7% decrease in body weight) compared with 0.43 kg gained during placebo treatment. Weight loss was significant after 2 weeks of exenatide; the difference persisted throughout the treatment period.

The most common adverse effect was nausea: More than half the women reported 1 or more episodes of nausea during exenatide treatment compared with 21% during placebo treatment. Two women dropped out of exenatide treatment due to nausea.

The researchers say this study is the first to report on stratified weight loss in response to exenatide treatment in obese, nondiabetic individuals.

Source: *Diabetes Care.* 2012;35(1):4-11. doi: 10.2337/dc11-0931.

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