New Treatment Works Well for Women With Advanced Breast Cancer

The Food and Drug Administration grants priority review status to abemaciclib for HER2-negative breast cancer.

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A new type of treatment can hold off disease progression in women with advanced breast cancer that has relapsed or metastasized (spread beyond the breast), according to a study presented at the recent American Society of Clinical Oncology (ASCO) annual meeting in Chicago.

Abemaciclib, made by Eli Lilly, is a cyclindependent kinase inhibitor that blocks both CDK4 and CDK6. These proteins play a role in regulating cell division, and blocking them can slow the growth of cancer cells.

Breast cancer is classified according to the kind of receptors it expresses. A majority of breast tumors carry hormone receptors for estrogen or progesterone (known as HR-positive). Estrogen and progesterone encourage the growth of HR-positive breast cancer, and treatment usually includes hormone-blocking medications, also known as endocrine therapy. Other tumors express another receptor called HER2 (human epidermal growth factor receptor 2). Triple-negative breast cancer doesn't express any of these receptors.

At the ASCO meeting, George Sledge, MD, of Stanford University presented results from the MONARCH 2 study, which tested abemaciclib in combination with the estrogen blocker Faslodex (fulvestrant) in women with HR-positive/HER2-negative advanced breast cancer.

This Phase III trial enrolled 669 women in 19 countries with metastatic breast cancer who experienced relapse or disease progression after taking endocrine therapy but who had not used traditional chemotherapy. The median age was approximately 60 years, and over 80 percent were menopausal. More than half had their cancer spread to internal organs and a quarter had bone metastases.

Study participants were randomly assigned to receive abemaciclib by mouth twice daily plus Faslodex or else Faslodex plus a placebo. The starting dose of abemaciclib was reduced partway through the study (from 200 milligrams to 150 milligrams) because of side effects. Treatment continued until disease progression occurred, and more than half were still on therapy

at the time of this analysis.

Progression-free survival was significantly longer in the abemaciclib group. Women who took abemaciclib plus Faslodex were still alive without disease progression for a median of 16.4 months, compared with 9.3 months in the Faslodex plus placebo group. The median duration of response was 25.6 months in the placebo group but could not be determined in the abemaciclib group because most patients were still responding.

Women taking abemaciclib were also more likely to see their tumors shrink. The overall response rate—meaning partial or complete reduction in tumor size—was 35.2 percent in the abemaciclib group, compared with 16.1 percent in the placebo group. Complete response was uncommon but occurred more often in the abemaciclib group (3.1 percent vs. 0.4 percent, respectively). These are the highest response rates yet reported for breast cancer that does not respond to endocrine therapy, according to Sledge.

Most women in both treatment groups experienced some side effects, but severe adverse events were reported more often in the abemaciclib plus Faslodex group, compared with the Faslodex plus placebo group (60.5 percent vs. 22.8 percent, respectively). More abemaciclib recipients stopped treatment early because of side effects (15.9 percent vs. 3.1 percent).

The most notable side effect was diarrhea: 86.4 percent of participants had some diarrhea and 13.4 had severe diarrhea in the abemaciclib group, compared with 24.7 percent and 0.4 percent, respectively, in the placebo group. However, Sledge said diarrhea could be managed with antidiarrheal medications and severe diarrhea was uncommon after dose reduction. Women taking abemaciclib were also more likely to have severe neutropenia, or low white blood cell counts (26.5 percent vs. 1.7 percent).

Abemaciclib plus Faslodex "was an effective treatment for women with HR-positive/HER2-negative advanced breast cancer whose disease progressed on prior endocrine therapy," the researchers concluded.

Other research groups at the ASCO meeting presented promising findings from studies of two other CDK4/6 inhibitors in women with HR-positive/HER2-negative advanced breast cancer, Pfizer's Ibrance (palbociclib) and Novartis's Kisqali (ribociclib).

This month the Food and Drug Administration (FDA) gave abemaciclib priority review status. It is being considered both as monotherapy (used alone) for women who received prior endocrine therapy and chemotherapy, and in combination with Faslodex for women with disease progression after endocrine therapy.

In March, the FDA gave full approval to Ibrance (which had received accelerated approval in 2015) and Kisqali for HR-positive/HER2-negative advanced or metastatic breast cancer.

Commenting on the CDK4/6 breast cancer studies presented at the ASCO meeting, Ingrid Mayer,

MD, of Vanderbilt University Ingram Cancer Center, said it is too soon to tell whether this new class of drugs will prolong overall survival. But based on their good response rates to date—and the fact that they allow women to delay poorly tolerated chemotherapy—she suggested that clinicians should integrate CDK4/6 inhibitors into their practice.

To read an Eli Lilly press release about the MONARCH 2 results, click here.
