Novel combination therapy has similar response rates to chemotherapy for high-risk luminal B breast cancer

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Neoadjuvant treatment with the CDK4/6 inhibitor ribociclib (Kisqali) and the aromatase inhibitor letrozole (Femara) produced response rates similar to multi-agent chemotherapy in patients with high-risk luminal B breast cancer, according to results from the SOLTI-1402/CORALLEEN trial presented at the San Antonio Breast Cancer Symposium, held Dec. 10-14.

Data from this study are being published simultaneously in *The Lancet Oncology*.

"The current standard treatment for high-risk luminal B breast cancer is neoadjuvant chemotherapy, but this is associated with high levels of toxicity," said Joaquin Gavilá, MD, medical oncologist at the Instituto Valenciano de Oncologia in Valencia, Spain. Neoadjuvant endocrine therapy is an alternative to chemotherapy, but it has not shown high levels of efficacy for high-risk breast cancer, explained Gavilá. "Finding an effective alternative to multi-agent chemotherapy for patients with high-risk breast cancer is a priority," he added.

Previous studies showed that combining endocrine therapy with CDK4/6 inhibitors, drugs designed to prevent cancer cells from dividing, resulted in similar response rates to chemotherapy for metastatic breast cancers. "We already knew that the combination of endocrine therapy with CDK4/6 inhibitors was efficacious in advanced breast cancers, so we were interested in investigating the efficacy of this combination for high-risk, early-stage breast cancer," explained Gavilá.

In this study, the authors examined the efficacy of the CDK4/6 inhibitor ribociclib in combination with the aromatase inhibitor letrozole in patients with high-risk, luminal B, stage I to III operable breast cancer. The study enrolled 106 patients, who were randomly assigned 1:1 to receive either the ribociclib and letrozole combination or multi-agent chemotherapy as neoadjuvant treatment. The intention-to-treat analysis included 101 patients who had tissue samples available at the time of surgery.

At the time of surgery, 48 percent of the 49 patients in the ribociclib plus letrozole treatment arm had low risk of recurrence scores, as measured by PAM50, compared to 47.1 percent of the 52 patients treated with chemotherapy. Intrinsic subtype conversion to luminal A, which is a less aggressive subtype, occurred in 88 percent of patients in the ribociclib plus letrozole arm and in 84.3 percent of the chemotherapy arm. Rates of low residual cancer burden were 8 percent in the ribociclib plus letrozole arm and 11.8 percent in the chemotherapy arm. Rates of PEPI 0, another indicator of favorable prognosis, were 24 percent in the ribocliclib-letrozole arm and 17.6 percent in the chemotherapy arm.

Grade 3 and 4 toxicities were observed in 54.9 percent of patients in the ribociclib plus letrozole arm compared to 69.2 percent of patients in the chemotherapy arm.

"Our results indicate that neoadjuvant treatment with a combination of ribociclib and letrozole has similar clinical benefits as standard multi-agent chemotherapy, and with less toxicity," said Gavilá. "We believe that this combination is worth exploring as an alternative to chemotherapy for patients with high-risk luminal B breast cancer."

Gavilá cautioned that the results are preliminary and need to be confirmed in future clinical trials.

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