CDK4/6 Inhibitors Show Promise for Multiple Cancer Types

A study in mice suggests that therapies approved for breast cancer may also combat other types, including colorectal and stomach cancer.

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A study in mice found that cyclin-dependent kinase (CKD) inhibitors, such as Ibrance (palbociclib), Kisqali (ribociclib) and Verzenio (abemaciclib), appear to be effective at combating malignant tumor types beyond their approved breast cancer indication.

Michael J. Wick, PhD, director of preclinical research at South Texas Accelerated Research Therapeutics in San Antonio, presented findings from the study at the International Conference on Molecular Targets and Cancer Therapeutics, which was jointly sponsored by the American Association for Cancer Research, the National Cancer Institute and the European Organization for Research and Treatment of Cancer.

“The main goal of our study was to try to identify other tumor types that might benefit from CDK inhibition,” Wick said in a press release. “Many tumor types lack a robust standard-of-care option, and our results indicate that this class of drug may be efficacious in a variety of cancer types.”

The study investigated three medications approved by the Food and Drug Administration that inhibit cyclin-dependent kinases 4 and 6, known as CKD4/6 inhibitors. Ibrance, Kisqali and Verzenio are currently approved for the treatment of hormone receptor (HR)–positive, HER2-negative advanced or metastatic breast cancer, in combination with hormone therapy.

The study authors devised what are known as patient-derived xenograft (PDX) mouse models—in which tumor cells are grown in mice—of 100 types of cancer. The models were based on tumor samples from breast cancer patients who had all known subtypes of the diseases and had experienced the full spectrum of cancer treatment. These ranged from individuals who did not receive chemotherapy to those who were intensively treated for the malignancy.

The mouse models were deemed to be sensitive to the CKD4/6 inhibitors if the average tumor growth following treatment was no more than 20% of the growth of untreated control mouse models.

HR-positive PDX models derived from breast cancer patients who had not been treated with chemotherapy proved the most sensitive to CKD4/6 inhibitor treatment. Among the HR-positive models included in the study, there was differential sensitivity to the drugs in ESR1-mutant and PIK3CA-mutant breast cancers. Additionally, several HR-negative models of breast cancer also proved sensitive to the CKD4/6 inhibitors.

“The finding that HR-negative breast cancer could be sensitive to CDK inhibition is exciting, as it provides a rationale for further investigation of this class of drug beyond HR-positive breast cancers,” said Wick.

In further research on other solid tumors, the investigators found sensitivity to Ibrance in PDX models of stomach cancer (60% of models were sensitive), colon and rectal cancer (45%), kidney cancer (45%), melanoma (40%), head and neck cancer (35%), pancreatic cancer (30%), ovarian cancer (15%) and lung cancer (10%).

As for actual regression of tumors after treatment with Ibrance, the researchers saw partial responses in PDX models of ovarian, pancreatic, head and neck, kidney, and colon and rectal cancers as well as melanoma. One PDX model of lung cancer had a full response to the treatment.

More preclinical research is needed before such findings may be elevated to clinical trials of people with cancer.

“Based on our results, we believe that CDK inhibition may be a viable therapeutic option in a host of different cancer types, especially in combination with existing therapies,” said Wick. “We are actively investigating if the addition of clinically available drugs to CDK inhibitors can cause additive results in our PDX models.”

To read a press release about the study, click here.

Click here to see the full Targets conference program.

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