Embargoed for Release: 7:30 a.m. CT, Dec. 7, 2016

To interview Noah S. Kornblum, contact Julia Gunther at julia.gunther@aacr.org or 267-250-5441. For a photo of Kornblum, click here.

Adding Everolimus to Fulvestrant Improved Outcomes for Postmenopausal Patients With HR-positive Breast Cancer

SAN ANTONIO — Progression-free survival was more than doubled for patients with metastatic hormone receptor (HR)-positive, HER2-negative breast cancer resistant to aromatase inhibitor therapy by adding everolimus (Afinitor) to treatment with the endocrine therapeutic fulvestrant (Faslodex), according to data from the PrECOG 0102 phase II clinical trial presented at the 2016 San Antonio Breast Cancer Symposium, held Dec. 6–10.

"Endocrine therapy, often with an aromatase inhibitor, is the standard of care for most patients with HR-positive advanced breast cancer," said Noah S. Kornblum, MD, assistant professor of medicine at Albert Einstein College of Medicine and attending physician, medicine at Montefiore Einstein Center for Cancer Care. "However, over time, resistance to aromatase inhibitors develops and treating patients with aromatase inhibitor–resistant disease remains a challenge.

"Recent studies have shown that adding the mTOR inhibitor everolimus to exemestane [an aromatase inhibitor] and adding a CDK4/6 inhibitor to fulvestrant improves outcomes for patients," continued Kornblum. "Therefore, we were not surprised to find that the combination of everolimus and fulvestrant improved progression-free survival compared with fulvestrant alone.

"We have to resist temptation to immediately adopt a positive result of a novel combination from a small study into a new standard of care," concluded Kornblum. "It may one day be the case that everolimus and fulvestrant becomes a new approved therapy for metastatic HR-positive breast cancer, but caution is prudent until larger studies confirm our results."

The 130 postmenopausal women with HR-positive, HER2-negative metastatic breast cancer enrolled in the trial all received fulvestrant and were randomly assigned either everolimus or placebo.

Analysis conducted after 98 patients had disease progression showed that median progression-free survival was 10.4 months among patients assigned everolimus, compared with 5.1 months among those assigned placebo.

Grade 3/4 adverse events were more commonly experienced by those assigned everolimus: 53 percent of those assigned everolimus had a grade 3 adverse event compared with 23 percent of those assigned placebo. The most common grade 3/4 adverse events were hyperglycemia, stomatitis, hypertriglyceridedemia, lymphopenia, and pneumonitis.

"The rates of grade 3/4 adverse events in our study are very similar to those found in earlier studies evaluating combination therapies containing everolimus," said Kornblum. "It is important for patients and clinicians to be aware of these potential complications, to try to identify them early, and to learn ways to manage them. For example, recently we have learned that the use of prophylactic corticosteroid mouthwash could significantly reduce the risk of oral mucositis for some patients taking everolimus."

Kornblum explained that the main limitation of the study is that it was designed and conceived prior to the FDA approval of the CDK4/6 inhibitor palbociclib (Ibrance) as a treatment for metastatic HR-positive breast cancer. He noted that there were only two patients enrolled in the trial who had been treated with a CDK4/6 inhibitor and that it will be important to determine whether combination treatments that include everolimus will be active in such patients.

This study was funded by Novartis Pharmaceuticals. Kornblum declares no conflicts of interest.

Abstract Publication Number: S1-02
Title: PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in post-menopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy
Presentation: Wednesday, Dec. 7, General Session 1 – Hall 3, 9 a.m. CT

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