Everolimus Approved for HR-Positive Breast Cancer

For women with hormone receptor (HR)-positive breast cancer, the go-to therapy for the last decade has been endocrine therapy. However, increasing numbers of women are developing resistance to hormone therapy. Among potential mechanisms for this resistance is overactivation of the mTOR pathway, which regulates cell growth, proliferation, motility, and survival, and is overactive in many forms of cancer.

In July, the U.S. Food and Drug Administration approved the mTOR inhibitor everolimus (Afinitor; Novartis) for the treatment of postmenopausal women with advanced HR-positive, HER2-negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.

The decision followed the phase III BOLERO-2 trial, reported in December 2011 and involving 724 postmenopausal women with advanced HR-positive breast cancer. The trial indicated that treatment with everolimus and exemestane extended median progression-free survival to 7.8 months, compared with 3.2 months for exemestane alone. “This was the first large randomized study suggesting that we may be able to overcome endocrine therapy resistance,” says Ben Ho Park, MD, PhD, associate professor of oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, who was not involved in the study.

Without a way to test for mTOR pathway activation, as clinicians do for HER2-positive breast cancer to guide treatment, “we need to be clinically astute,” comments Andrew Seidman, MD, a medical oncologist at Memorial Sloan-Kettering Cancer Center, who also was not involved in the study. “The patients prescribed this drug combination should resemble those in the trial.”

“The long-term challenge is to figure out how to predict who will respond to this combination versus another,” says Park.

Everolimus also has been approved for treating renal cell carcinomas, but it is a first-generation mTOR inhibitor. “It’s not 100% specific to the target and has off-target effects,” says Park. “The toxicity profile is not insignificant.” For patients, agrees Seidman, this drug combination is “often a transition into a world of more toxicity.”

Second-generation mTOR inhibitors now in development may improve efficacy and decrease toxicity. “I don’t think anyone thinks that this is the definitive drug that’s going to overcome all hormone therapeutic-resistant cancers, but it is a step in the right direction,” says Park.

University of Kansas Earns NCI Center Designation

The University of Kansas Cancer Center (KUCC) in Kansas City was named a National Cancer Institute (NCI)–designated cancer center in July, a distinction currently held by just 67 institutions in the United States that exhibit scientific excellence and integrate diverse approaches to cancer research.

Cancer patients in the region now will have access to treatments and clinical trials only available at NCI-designated centers. In addition, KUCC will receive about $7 million from the NCI over the next 5 years, will be able to apply for other federal grants set aside for NCI-designated centers, and can make a stronger case for attracting additional research dollars from private organizations. Private money will be used to fund pilot research projects, purchase advanced technology, and recruit top-notch investigators.

To bolster its application to the NCI, KUCC renovated 170,000 square feet of existing space for basic science research and, separately, 82,000 square feet of space in a building donated for clinical research.

The designation “can have a game-changing effect on the institution,” says KUCC Director Roy Jensen, MD, adding that civic and political leaders embraced the idea of applying for the NCI designation. “It was an opportunity to ‘do good’ and enhance the local economy.”

Hundreds of millions of dollars in philanthropic gifts and money from state and local coffers—including more than $107 million from private
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