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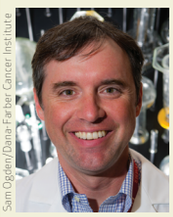
Sam Ogden/Dana-Farber Cancer Institute

James E. Bradner, MD, began his new role as president of the Novartis Institutes for BioMedical Research in Cambridge, MA, effective March 1. He succeeds Mark Fishman, MD, who retired after 13 years with Novartis.

Most recently, Bradner was a member of the faculty at Harvard Medical School in Boston, MA, and a hematologist in the Department of Medical Oncology at the nearby Dana-Farber Cancer Institute. His research focuses on creating molecules to control gene expression in cancer. For example, studies on the link between BET bromodomains and cancer led his lab to develop a first-in-class BET inhibitor called JQ1, which also has been shown to help prevent heart failure. In addition, he has worked to develop strategies to induce targeted protein degradation.

Panel Recommends Mammograms Start at 50

The U.S. Preventative Services Task Force (USPSTF) has issued its final recommendations on screening for breast cancer, concluding that women at average risk can wait until age 50 to begin routine biennial screenings (Ann Intern Med 2016;164:279–96). The decision to start screening between ages 40 and 49 should be individual, the panel said, based on personal risks, values, and preferences.

"We believe the science supports a range of individual choices for women, including starting screening anytime during their 40s or waiting until age 50," says Michael LeFevre, MD, MSPH, vice chair in the Department of Family and Community Medicine at the University of Missouri School of Medicine in Columbia and immediate past president of the USPSTF, who helped develop the recommendations. "These recommendations should empower women with the information they need to make decisions for themselves."

Despite the opposition and concerns expressed by many oncologists after the draft recommendations were issued last spring, the USPSTF stands by the same age guidelines it issued in 2009, with screening for women in their 40s remaining as a C level recommendation, meaning the panel is moderately certain that the net benefit is small. Typically, private insurers are required to cover only procedures graded A (high certainty of substantial net benefit) or B (moderate to high certainty of moderate to substantial net benefit) by the USPSTF, but in 2009 Congress approved—and recently extended—an exception for mammography for women ages 40 to 49.

Nonetheless, many oncologists are concerned that the updated recommendations will be used to justify future coverage limitations.

"If the government acts on these recommendations and insurers start denying annual mammograms, a lot of women will die unnecessarily," says Larry Norton, MD, a medical oncologist and deputy physician-in-chief for Breast Cancer Programs at Memorial Sloan Kettering Cancer Center in New York, NY. "I will continue to recommend that my patients get annual screenings starting at 40, but many women may decide against it if they won't get reimbursed."

The task force, an independent panel of nonfederal experts in evidence-based medicine, prevention, and primary care, reviewed randomized controlled trials and observational studies involving women ages 40 and older considered at average risk for breast cancer. It concluded that, while mammography screening reduces breast cancer mortality overall, that benefit is not as significant for women in their 40s compared with older women and must be weighed against the potential harms, including unnecessary testing and overtreatment.

"We looked hard for evidence that cancer treatment is less harmful when detected early versus later, and found very little to support that premise," says LeFevre. "On the opposite side of the equation, it is precisely those very early cancers which are most likely to be overdiagnosed, particularly the ductal carcinoma *in situ* or noninvasive cancers."

However, oncologists cannot predict at the time of diagnosis whether a tumor will lead to death if left untreated, says Norton. Most women would rather undergo treatment, even if it proves unnecessary, than risk a tumor going undetected at a potentially curable stage.

Norton notes that the task force based its recommendations on older studies that do not reflect advances in imaging technology. In addition, the group gives disproportionate weight to the potential harms caused by false-positive results, he says, including anxiety, repeat testing, and invasive follow-up procedures.

"The recommendations are based on a very subjective estimate of harm, which most often just means coming back to the office for another test," says Norton. "But the real bottom line is that if a woman 40 or older wants to minimize her chances of dying from breast cancer, she should get an annual mammogram." *–Janet Colwell* ■

Resensitizing Refractory ALK+ NSCLC: A Case Study

Drug resistance in ALK-positive non–small cell lung cancer (NSCLC), a known problem, can have unexpected twists. Researchers from Massachusetts General Hospital in Boston recently reported the case of a patient with advanced ALK-positive NSCLC, whose eventual relapse on the investigational ALK inhibitor lorlatinib (Pfizer) paradoxically restored her responsiveness to crizotinib (Xalkori; Pfizer) (N Engl J Med 2016;374:54–61).

The patient's treatment regimen began with crizotinib, followed by ceritinib (Zykadia; Novartis) and then lorlatinib. "When she stopped responding to crizotinib, we profiled her tumor and found an *ALK* mutation, C1156Y, which causes resistance by increasing ALK's kinase activity," says Alice Shaw, MD, PhD, a thoracic oncologist and the study's first author. "She didn't respond to ceritinib, but upon switching to lorlatinib, her response was quickly apparent."

Lorlatinib, which Shaw describes as "the newest next-generation ALK inhibitor, designed to overcome all known crizotinib-resistant mutations," reduced the patient's tumor burden by 41% in just 5 weeks. Unfortunately,

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