



Src kinase (pdb/1CC-BY/5A/3.0)

The crystal structure of the Abl1 kinase domain (blue) is shown in complex with dasatinib (in red).

aromatase inhibitor, and dasatinib to fulvestrant (Faslodex; AstraZeneca), an estrogen antagonist, did not show any benefit in PFS for women with metastatic breast cancer. However, those trials were conducted in women whose cancers had become resistant to aromatase inhibitor therapy. Paul says the improvement in PFS in this trial suggests that dasatinib might be effective if it were added initially to aromatase inhibitor therapy.

One next step is to find markers of Src activity. “Before you invest a lot of money in a phase III trial, it would be nice to have some markers to look at so we can select out patients who aren’t likely to benefit,” Paul says. Bristol-Myers Squibb is investigating several possible markers of Src activity, he adds. ■

High-Risk Women Should Have BRCA Testing

The U.S. Preventive Services Task Force (USPSTF) has updated its recommendations on *BRCA* mutation testing, essentially reaffirming its 2005 position that the tests be limited to high-risk women.

Published online December 24 in the *Annals of Internal Medicine*, the guidelines recommend that testing for mutations in *BRCA1* and *BRCA2* be limited to women who have a family history of breast, ovarian, tubal, or peritoneal cancer, and who first receive screening and genetic counseling. They recommend against routine genetic counseling or testing.

“We do provide better guidance” in the new document, says Virginia Moyer, MD, MPH, chair of the USPSTF, “while making it clear that more than 90% of women do *not* need this test.”

BRCA testing is inherently complex due to the many possible mutations. Certain mutations increase breast cancer risk by as much as 85%, while others have a moderate, low, or unknown impact.

“This is not a simple positive or negative test like some other population-based screenings,” says Moyer. Having a negative *BRCA* test does not rule out other genetic risks, and having a positive test can be misleading. “If a patient has a *BRCA* mutation, there is often no way to tell if it’s likely to lead to cancer without background information about that patient’s family,” notes Moyer.

To select candidates for testing, the USPSTF recommends that physicians screen women using one of several familial risk-stratification tools. Women deemed high-risk during screening are advised to meet with a health professional trained to provide genetic counseling and interpret test results, to determine if *BRCA* testing is appropriate and discuss potential harms of false-positive or inconclusive results.

“Regrettably, many women act on uninformative results by opting for interventions such as chemoprevention or surgery to remove breasts or ovaries,” says Moyer. “This is why genetic counseling is recommended.”

The guidelines apply to asymptomatic women who have not already been diagnosed with a *BRCA*-related cancer. Not including patients with previous diagnoses, critics say, could hinder their chances of having tests covered by insurance and put them at further risk.

“We did not evaluate the science required to make a recommendation for women who have a previous cancer diagnosis,” says Moyer. “This does not imply that these women should not be tested; they should talk with their physicians.” ■

NOTED

- **Ludwig Cancer Research of New York, NY, gave \$540 million to fund cancer research** at the six U.S. Ludwig Centers, which are located at Harvard University, Johns Hopkins University, the Massachusetts Institute of Technology, Memorial Sloan-Kettering Cancer Institute, Stanford University, and the University of Chicago.
- **Pfizer and The University of Texas MD Anderson Cancer Center in Houston announced that they will collaborate to develop immune-based approaches to cancer treatment.** The 3-year agreement is designed to help speed progress on immune-based treatments and to more efficiently identify and exploit new combination therapies, as well as biomarkers to guide and monitor treatment.
- Researchers estimate that **tobacco control efforts in the United States have prevented about 8 million premature deaths**, with those people each gaining about 20 years of life on average (JAMA 2014;311:164–71). According to a second study, although the percentage of the population that smokes daily has decreased, the number of cigarette smokers worldwide has increased due to population growth (JAMA 2014;311:183–92).
- In a review published in the *New England Journal of Medicine*, **researchers wrote that tripling taxes on cigarettes worldwide would reduce the number smokers by one third and prevent 200 million premature deaths** from lung cancer and other diseases in this century (N Engl J Med 2014;370:60–8).
- The city council in **New York City, NY, voted to expand its ban on indoor smoking to include e-cigarettes**, battery-operated devices that deliver nicotine vapor to users. Several states, including Arkansas, New Jersey, North Dakota, and Utah, have already added e-cigarettes to their indoor smoking bans.
- **The success rate for competing research project grant (RPG) applications submitted to the NIH fell from 17.6% in fiscal year (FY) 2012 to 16.8% in FY2013**, blogged Sally Rockey, PhD, the deputy director for Extramural Research at NIH (<http://nexus.od.nih.gov/all/2013/12/18/>). In FY2013, NIH received 49,581 RPG applications, of which 8,310 were awarded, compared with 51,313 applications and 9,032 awards in FY2012.

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