Colorectal Cancer Screening: Where Does the Shield Liquid Biopsy Fit In?

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In July, the Food and Drug Administration (FDA) approved the first blood test to use as primary screening for people at average risk for colon cancer.

Called Shield, the test looks for the presence of specific changes to DNA floating freely in the blood, called cell-free DNA, that indicate the presence of a tumor or precancerous growths in the colon.

The approval was based on findings from a study that involved nearly 8,000 people, in which the test detected colorectal cancers in more than 83% of the participants found to have colorectal cancer on colonoscopy. But its sensitivity for detecting precancerous growths in the colon was much lower, only about 13%.

Finding these precancerous lesions, called adenomatous polyps, is a strength of colonoscopy, because the clinician performing the procedure can also remove them during the same procedure, said Asad Umar, D.V.M., Ph.D., of NCI's Division of Cancer Prevention, who was not involved in the study. In this sense, Dr. Umar added, colonoscopy can also help prevent colon cancer.

Although some experts said they are excited about the prospect of the Shield test to screen for colorectal cancer, they also cautioned that it's unclear where the test fits in within the current screening paradigm for the disease, which includes other noninvasive screening options.

"Having a simple blood test for colorectal cancer that could be added to a routine medical visit is a major step toward closing the screening gap," said Dr. Umar, referring to the fact that nearly one-third of people who are eligible for colorectal cancer screening don't get screened. "But there are still important questions about how this test will perform among other available options."

Those uncertainties include factors like how often people need to be tested and the cost of the test. But ultimately, Dr. Umar stressed, the most critical question to answer is if this test "has an impact on preventing colon cancer deaths."

Entering the colorectal cancer screening landscape

The U.S. Preventive Services Task Force recommends that people aged 45 to 75 who are at average risk for colorectal cancer should get screened for the disease regularly. How often they should be screened varies by screening test. For example, with colonoscopy, if the initial test is negative, people can wait 10 years to get screened again. Tests that use stool samples, by comparison, must be repeated every 1 to 3 years.

Rates of colorectal cancer screening are among the highest of the cancers for which screening is recommended. Even so, according to recent data, 30% of eligible adults are not up to date with any type of recommended colorectal cancer screening, and the disease remains the second leading cause of cancer deaths in the United States.

Colonoscopy is considered the gold standard and is by far the most common screening method for colorectal cancer in the United States. But colonoscopy is invasive, with a risk, albeit low, of damage to the colon and is time-consuming, requiring a full day of preparation that many people find unpleasant. Colonoscopy also involves sedation and logistical considerations, including the need for a ride home after the procedure.

Another FDA-approved screening test, the fecal immunochemical test (FIT), works by detecting blood in stool samples people can collect at home. One type of FIT test, (sDNA-FIT or Cologuard), can also detect genetic changes linked to colorectal cancer.

Neither the FIT test nor the Cologuard test is as accurate as colonoscopy. And when the results of these tests are positive, people still have to have a colonoscopy to find and remove any potential growths or cancer. Both tests, however, are more convenient and less expensive than colonoscopy.

Developing blood-based cancer screening tests has been an active area of research, with researchers and device companies developing different ways of identifying clues in cell-free DNA that can potentially detect cancer early.

Cell-free DNA is the basis of the Shield test and uses the same type of technology that is used in some of the so-called multi-cancer detection tests that have been developed and are being investigated in large studies, including the NCI-funded Vanguard Study.

Shield demonstrates strong sensitivity for cancer, but not precancers

FDA based its approval on data from a large study called ECLIPSE, results of which were published earlier this year.

The study—funded by Guardant Health, the test's manufacturer—enrolled about 23,000 people undergoing routine colorectal cancer screening by colonoscopy. Of these, a random selection of about 10,000 participants provided a blood sample for the study prior to colonoscopy, and the

researchers were able to compare blood test results with colonoscopy results in nearly 8,000 participants.

Overall, in addition to its 83% sensitivity for identifying colorectal cancers and 13% of advanced precancerous polyps found by colonoscopy, the Shield test had a specificity of 90%. This means that among those who did not have cancer or advanced precancerous polyps, 90% had a negative result on the test. To be useful in screening, Dr. Umar said, a test must be both highly sensitive and highly specific.

“These numbers are on target for our performance goals of an effective cancer screening test and are in the range of [those from] other noninvasive colorectal cancer screening tests,” said Daniel Chung, M.D., a gastroenterologist at Massachusetts General Hospital, who led the ECLIPSE study.

The test’s sensitivity for detecting precancerous polyps was lower than that of colonoscopy, Dr. Chung noted. But if people who aren’t staying up to date with current screening recommendations are willing to use the blood test, he continued, “we would see higher rates of screening in the population as a whole and that could have a significant impact.”

Will the Shield test encourage more people to get screened?

In an NEJM editorial that accompanied the study’s results, John M. Carethers, M.D., of UC San Diego, agreed.

“Because the assay uses blood, thus avoiding the collection of stool, it may easily be prescribed and sent from any caregiver’s office as part of a standard blood draw, thus potentially increasing the use of colorectal cancer screening in multiple diverse populations,” Dr. Carethers wrote.

But in practice, the Shield test shares the same extra—and critical—step that stool tests require, he pointed out: if somebody has a positive result, meaning cancer or precancer may be present, they still have to get a colonoscopy.

And too often, studies have shown, that follow-up step doesn’t happen. The lack of follow-through after a positive FIT test can have significant consequences, with one study, for example, showing that those who didn’t have a follow-up colonoscopy were twice as likely to die from colorectal cancer as those who did.

Although many people may be more inclined to use a blood-based tests over a time-consuming colonoscopy or collecting stool for a FIT test, he noted, like Dr. Umar, that factors such as the test’s cost and how often it needs to be performed, will ultimately determine its impact in reducing colorectal cancer incidence and deaths.

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