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Colorectal Cancer Detection Data from CellMax Life Bodes Well for Planned FDA Bid

Jan 19, 2023 | Molika Ashford

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NEW YORK – Cancer screening firm CellMax Life shared new data this week from a multi-site prospective study of its blood-based colorectal cancer detection assay, FirstSight.

The results, while unpublished, are notably positive, especially regarding the assay's sensitivity for detecting advanced adenomas, dysplastic precursor nodules at a high risk of transforming into malignant colorectal cancer.

Investigators led by Shai Friedland, a gastroenterologist at Stanford Medicine, are presenting the results this week at the American Society of Clinical Oncology's Gastrointestinal Cancer Symposium. In a cohort of about 1,000 patients, the researchers calculated that the FirstSight test showed 92 percent sensitivity for colorectal cancer and 55 percent sensitivity for advanced adenomas at 91 percent specificity.

Buoyed by the results, the company is now building a follow-up trial intended to support a premarket approval application to the US Food and Drug Administration. Based on earlier data, the FDA issued FirstSight a Breakthrough Device designation in 2021.

Most of CellMax's prominent competitors, which include Guardant Health and Exact Sciences, have focused their test development on cancer-associated methylation patterns in circulating cell-free DNA. CellMax instead based its test on a proprietary platform for the isolation of circulating epithelial cells.

Since then, it has updated the assay to also include circulating tumor DNA mutations and methylation, but the company has said that the cell-based aspect remains especially crucial for adenoma detection.

While 55 percent sensitivity for advanced adenoma may not appear to represent strong performance, it is competitive with the current leader in stool-based CRC screening, Exact Sciences' Cologuard, and trounces the blood-based screening market's first entrant, Guardant Health's Guardant Shield. In a release of data from its own 20,000-plus-patient prospective trial last December, Guardant reported 83 percent sensitivity for colorectal cancer but only 13 percent sensitivity for advance adenomas at 90 percent specificity.

Most of the subjects in CellMax's new study were followed prospectively — the FirstSight test was used prior to any diagnosis of colorectal cancer or adenoma and the test result was compared to findings from subsequent standard-of-care colonoscopy screening. Overall, 11 patients were diagnosed with colorectal cancer (2 stage I, 3 stage II, 6 stage III) and 93 patients with advanced adenomas among the 954 prospective recruits.

To power the study appropriately, the investigators had to then add 84 case-control samples from patients with known colorectal cancer and adenoma diagnoses. As such, the 92 percent and 55 percent sensitivity results don't fully reflect an intended use population.

However, Friedland and his colleagues also calculated sensitivity for the 954 intended-use, average-risk screening patients, which came out at 100 percent for colorectal cancers and about 56 percent for advanced adenomas.

"What we were trying to do is to make sure that this study … is going to be a good predictor of what's going to happen in the [future] PMA trial without actually running the large PMA trial," explained CellMax CEO Atul Sharan. Because of the low prevalence of colorectal cancer in asymptomatic individuals, there would be no way to see enough cases in a prospective cohort of this size, so in order to get the appropriate statistical significance researchers had to seed the study with additional positives.

Friedland also highlighted that staging information was available for 68 of 76 colorectal cancers in the study cohort. Breaking down by stage, the assay showed 100 percent sensitivity for stage I tumors and 96 percent sensitivity for stage II disease. For the adenomas considered at the highest risk of becoming cancers, lesions with so-called high-grade dysplasia, villous growth, or serrated features, FirstSight detected between 60 and 100 percent.

"The terminology is very traditional in colonoscopy of what an advanced adenoma is, but it's a little too loose in the sense of a lot of these … are just a tiny bit bigger than a regular adenoma," Friedland said. "As you get into the more worrisome lesions — the very large lesions, the lesions with high grade dysplasia — we think we're going to do substantially better than even the very good results that we have already."

Friedland also led a previous single-center prospective study of the FirstSight assay, which was presented in 2020. In that study, the test detected 100 percent of cancers and 75.5 percent of advanced adenomas.

According to Sharan, because of the structure of this study, with detection of both non-advanced adenomas and colonoscopy-negatives considered negative, sensitivity can take a hit compared to case-control studies where a flood of disease-negatives may artificially boost advanced adenoma detection numbers.

Located at the time in Taiwan, Sharan said CellMax had initially planned to market laboratory-developed tests in "semi-regulated markets overseas." But positive reception to the first meeting presentation on FirstSight, at the 2018 ASCO GI meeting, led the company to change strategy, refocusing on bringing this single test through the US regulatory process.

"We've basically streamlined, everything else is gone," Sharan said.

CellMax is now working on building out its planned premarket approval study. The plan is to have an intermediate endpoint for advanced adenoma, which should be achievable more quickly due to the higher prevalence of these precursors relative to cancer.

There will then be an end-of-study endpoint of advanced neoplasia detection: advanced adenomas and colorectal cancers.

Sharan said the approach takes advantage of the "regulatory optionality" provided by the relatively higher prevalence of advanced adenomas. For this intermediate endpoint, about 3,000 patients will probably provide enough power to read out results. Cancers will take a much larger cohort — about 13,500 individuals in his estimation.

If the company can maintain the performance levels demonstrated in the newly presented trial in this larger study and gain FDA approval it will be poised for an accelerated path to reimbursement under a

national coverage determination finalized by the US Centers for Medicare and Medicaid Services in 2021, in anticipation of the rise of tests like FirstSight.

Under that NCD, CMS will provide coverage for FDA authorized blood-based CRC screening tests in average-risk, asymptomatic patients between 50 and 85 years old — as long as the test used has proven sensitivity greater than or equal to 74 percent and specificity greater than or equal to 90 percent in the detection of colorectal cancer.

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