Clinical Genomics Building Clinical Utility Evidence for Colorectal Cancer Recurrence Assay

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NEW YORK (GenomeWeb) – Molecular diagnostic firm Clinical Genomics is in the midst of a clinical study to build clinical utility for Colvera, its blood-based epigenetic assay for colorectal cancer recurrence, and aims to apply for Medicare local coverage determination for the test later this year.

The study, called the Colvera North American Validation Trial (NOVA), specifically aims to further develop clinical evidence for Colvera by comparing it to paired carcinoembryonic antigen (CEA) testing in subjects who have undergone treatment for CRC and are in remission.

"We have been working on detecting epigenetic changes based on methylation to provide a mutational-agnostic solution" Clinical Genomics Chief Innovation Officer Lawrence LaPointe explained. He noted that the firm has previously published peer-reviewed papers that highlight the tool's utility.

Colvera has been commercially available out of Clinical Genomics' CLIA-certified, CAP-accredited laboratory in Bridgewater, NJ since late 2016. The test directly detects circulating tumor DNA (ctDNA) in a person's bloodstream.

The overall process begins with oncologists sending two tubes of a patient's whole blood to Clinical Genomics' lab, where technicians prepare a plasma fraction to conduct a PCR assay for two methylated genes — BCAT1 and IKZF1 — that are epigenetically silenced in the cancer process and persist through the late stage. Clinical Genomics then sends a detailed report with the assay results back to the oncologist.

According to LaPointe, the report informs the physician if Colvera has detected evidence of ctDNA. In addition, clinicians can request an expanded reporting option that includes the amount of ctDNA present in the specimen. LaPointe noted that the company can provide recurrence results in a couple of days, and an expanded report in about two weeks.

In a study presented at the American Society of Clinical Oncology conference earlier this month, researchers from Clinical Genomics and Flinders University in Australia compared Colvera's ability to monitor CRC recurrence with the CEA assay, marketed by DiaSorin.

The researchers collected blood samples from 144 CRC patients at a single timepoint closest to confirming their recurrence status using CEA and Colvera. The team then performed radiological imaging to determine the clinical status of recurrence.

Including 50 recurrence and 94 non-recurrence patients in the analysis, the researchers found that CEA had a 32 percent clinical sensitivity and 96 percent clinical specificity for recurrence using the manufacturer's recommended detection limit cutoff, while Colvera had a clinical sensitivity of 66 percent and a clinical specificity of between about 90 percent and 98 percent depending on the detection cutoff used.

According to the study authors, 14 of the 47 patients with recurrence were positive for both tests, while the ctDNA test detected an additional 18 cases that were CEA negative. In contrast, the researchers identified one case that was only CEA positive.

In addition, the authors noted that the ctDNA test was positive up to 11 months before confirmation of recurrence while no CEA test was positive more than six months before recurrence confirmation. As such, they concluded that the methylated ctDNA is more sensitive for detecting CRC recurrence up to five months earlier than the CEA test.

Clinical Genomics began its NOVA clinical trial earlier this year. The trial is currently being conducted in concert with about 20 different private investigators across roughly 40 different academic groups including the Baylor College of Medicine, the University Hospitals Cleveland Medical Center, Cedars-Sinai, Indiana University, and Penn Medicine Princeton Health. LaPointe said the study will collect whole blood samples from about 600 patients, with the intent to demonstrate the "clinical utility of Colvera for detecting CRC recurrence in comparison to paired CEA testing.

According to LaPointe, the researchers expect to publish the study's results by the end of 2019 or early next year.

Clinical Genomics CEO Betsy Hanna noted that the firm is currently working with 10 mostly private, regional payors for clinical reimbursement for its tests including groups such as Fortified Provider Network and Multiplan. She also said that Clinical Genomics' target price for Colvera has remained at $450.

"We're just doing some early work on testing the value proposition, price points, and getting some early experience and working with payers on how they view the reimbursement and use of the test," Hanna explained. This work will help the company "build our knowledgebase and expand once we get full reimbursement," she added.

Clinical Genomics is currently able to offer its assay as an LDT in all US states except for New York. Hanna said that the firm filed for New York state approval in late 2018 and expects to have approval by the end of this year.

Rather than seeking 510(k) approval from the US Food and Drug Administration for Colvera, LaPointe said that the firm will keep the assay as an LDT.

Although many other companies and groups are developing blood-based assays for CRC detection, LaPointe said that Colvera is the only solution other than CEA for CRC recurrence monitoring. He also noted that Colvera uses qPCR, which is much more cost-effective than sequencing, which is the methodology of choice for many newer tests under development.

As part of its marketing efforts around Colvera in the US, Clinical Genomics has established relationships with US CRC physicians, surgeons, and oncologists.

"We've had over 200 physicians who've tried the test, and some that tell us that they've replaced the current standard of care and they're using Colvera exclusively," Hanna said. "But again, it's a modest effort right now, and it's really about getting the right partnerships and understanding the clinical [results] and building that early clinical support to build into reimbursement."

According to Hanna, the firm has performed over 2,000 tests on blood samples collected from its clinical partners.

Hekmat Hakiman, a colorectal surgeon from Gilbert, Arizona, was an early adopter of Colvera, and has a paid consulting relationship with Clinical Genomics. He has been

applying Colvera in his clinical practice to assess the adequacy of resections and monitor the disease after CRC surgery in 20 to 30 patients since early 2018.

In addition to testing for CRC before surgery, Hakiman uses Colvera to track the presence of the disease in his patients every two to three months post-operation.

He cited Colvera's "very high specificity" as a positive aspect of the test. "While it is still early in our series of patients, other studies show that [Colvera] can be a [tool] for early recurrence," he said.

At the same time, Hakiman hopes that the firm improves the assay's sensitivity and noted one instance in which a patient with known CRC was reported to be negative with the Colvera test.

"Regarding negative Colvera tests with known malignancies, I think we need more studies to identify which subset of patients fall into that category," Hakiman said. "As we know, the test is not 100 percent accurate and cannot direct all colorectal cancers. "As there is more research and studies, we can start to delineate what [patient] subsets would be a better candidate for testing. With larger studies in a larger group of patients, we should be able to start answering those questions."

Despite the test's current limited utility, he wants to see Colvera expanded to other malignancies like pancreatic cancer, since he argued that early detection would help save even more lives.