MiR Scientific Validates Urine-Based Cancer Tests, Awaits NY State Approval

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NEW YORK – MiR Scientific is preparing to launch a suite of non-invasive microRNA-based cancer tests that it hopes can improve prostate and bladder cancers diagnoses and help guide clinical decision-making through other stages of the prostate cancer care continuum.

In support of its prostate cancer testing suite in particular, the firm recently published a comprehensive validation study describing the development of the three assays and reporting their sensitivity and specificity in a case-control training and validation cohort of about 1,400 samples.

Appearing last month in *The Journal of Urology*, the study reported that the company's miR Sentinel PCa Test (which distinguishes prostate cancer cases from non-cancer cases) showed 94 percent sensitivity and 92 percent specificity. The Sentinel CS Test (which stratifies confirmed cancer cases into low risk and intermediate/high risk subsets) showed 93 percent sensitivity and 90 percent specificity, and the Sentinel HG Test (also a prognostic subgrouping assay) demonstrated a sensitivity of 94 percent and specificity of 96 percent.

MiR Scientific's Chairman and CEO Sam Salman said that the company had been gearing up to start offering clinical tests this year as soon as it received approval from NY State's Clinical Laboratory Evaluation Program, but the emerging coronavirus pandemic is likely to now delay that certification.

"We were hoping for a much earlier timeline, but obviously everything's interrupted [in the current pandemic] … and as you can imagine, [CLEP operators] have their hands full for the next month or two," he said.

That said, he added, "we still plan on being in production and we [expect to] be able to produce up to a million tests initially per year ... split between these prostate cancer tests and bladder cancer … [hopefully starting] by the end of this year."

The company's cancer detection and classification approach relies on analysis of small non-coding RNAs (sncRNAs) including microRNAs and small nucleolar RNAs (snoRNAs) isolated from urinary exosomes.

For prostate cancer, the company has developed three unique miRNA signatures, which have been trained on case-control data to distinguish cancers from non-cancers; differentiate especially high-risk cases that require therapeutic intervention from low or intermediate-risk disease that can be monitored over time; and potentially to monitor these patients for signs of a tumor transitioning from low to intermediate or high risk.

In bladder cancer, the firm has also been able to glean a small non-coding RNA signature that indicates the presence of bladder cancer, again from urinary exosomes, which could help doctors decide which patients should receive cystoscopy when they present with symptoms, like blood in the urine, that are suspicious for a malignancy.

The approach works from a normal urine sample, with no requirement for digital rectal examination, something some other molecular assays being advanced in the prostate cancer space necessitate.

In their newly published prostate cancer study, researchers from MiR Scientific worked with collaborators at the Albany Medical College where the technology behind the assays was initially developed, as well as groups at Toronto's Princess Margaret Cancer Center and University Hospital Hamburg-Eppendorf's Martini Klinik.

The investigators divided a 1,400-patient cohort, separating out a 600-sample validation set designed to have equal numbers of cases and controls and, among the biopsy-positive cases, two thirds representing Grade Group 1-2 (low-risk) tumors and the other third made up of GG3-5 (high-risk) disease. The remaining 836 participants formed a training dataset.

According to the authors, the resulting Sentinel PCa Test incorporates the expression levels of 145 unique sncRNAs (85 miRNAs and 60 snoRNAs), the Sentinel CS Test utilizes 196 unique sncRNAs (130 miRNA and 66 snoRNAs), and the Sentinel HG Test examines 147 unique sncRNAs (122 miRNA and 25 snoRNAs).

Some of the targets, specifically 38 sncRNAs, overlap across all three tests, while another 89 miRNA and 9 snoRNAs are common to two of the three.

When the researchers trained the assays and then tested them in their 600-patient validation set, Sentinal PCa correctly classified 281 out of 300 positives and 275 out of 300 non-cancer controls.

The Sentinel CS test correctly classified 143/154 high-risk (GG2-5) patients and 132/146 low-risk (GG1) patients. Sentinel HG correctly classified 94/100 GG3-5 patients as high grade and 191/200 GG1-2 patients as not high grade

Importantly, Salman added, the firm's research has found no improvement in coupling its miRNA signatures with other biochemical markers like PSA, pathologic features, or clinical scoring nomograms.

According to Salman the performance and robustness that the now-published study represents should be sufficient to support its awaited laboratory approval.

Looking ahead to some of the other hurdles on the path to commercial success, he added that the company has also begun prospective clinical trials that will hopefully show that the tests' validity holds up when applied prospectively in their intended use population.

Both prospective trials (one for prostate cancer and the other for bladder cancer) are being undertaken across multiple centers, and the prostate trial, which is employing the Sentinel PCa and CS tests, is already actively recruiting. "We've already received specimens and are analyzing them," Salman said.

According to the trial listing, investigators aim to recruit 2,000 total participants between age 50 and age 80 with suspicion of prostate cancer, all of whom will have a core-needle biopsy performed and will provide urine samples for Sentinel tests. With results of the core needle biopsies serving as a "gold standard", participants will be designated as either "cancer-free" or having "clinically Insignificant" of "clinically significant" prostate cancer, and the performance of the MiR Sentinel tests will be established based on how closely they match those diagnoses.

According to Salman, one challenge for the MiR Scientific, like other precision oncology test developers, is that the "gold standard" that molecular testing hopes to improve upon isn't itself a perfect representation of cancer biology.

As such, the performance of tests like MiR Scientific's may actually be better than how it appears relative to the "gold standard" of pathologic cytology, which can be confounded by tumor heterogeneity, subjective interpretation, and other issues.

Although it hasn't listed any trials aimed at clinical utility, proving that its tests improve patient outcomes or healthcare efficiency will also be a significant future hurdle for the company once it gets up and running.

According to Salman, the company is preparing to take three concurrent approaches in this vein. "We have a team that is working [toward a] local coverage determination [from Medicare]," as well as looking into more generic test coding strategies, and into approaches to private payors based on health economic data, he said.

"We also have a team working on guideline development with the National Comprehensive Cancer Network, which informs all of that," he added. "These teams are very well along in terms of their work and positioning."