Biofidelity Highlights Consistency, Accessibility of Lung Cancer Mutation Assay

Apr 12, 2024 | Forest Ray
Premium

NEW YORK – Cancer molecular diagnostics company Biofidelity this week presented the results of three studies the American Association for Cancer Research (AACR) annual meeting showcasing the consistency, reproducibility, and superiority in certain sample types of its ASPYRE-Lung cancer mutation detection assay compared to next-generation sequencing (NGS).

The Cambridge, UK -based company, which recently completed a $24 million financing round, currently markets its assay as a lab-developed test in the US through its North Carolina CLIA lab, but hopes to eventually garner regulatory approval in both the US and Europe in hopes of achieving wide distribution in clinical labs.

In addition, while the company is currently focused on demonstrating the value of its assay for treatment guidance in lung cancer, it plans to expand to other cancer types and into applications such as early disease detection and minimal residual disease monitoring.

"We see Biofidelity as a full, end-to-end solution in oncology," said Biofidelity CEO Barnaby Balmforth. "That's where we're ultimately going."

In a late-breaking abstract presented as a poster on Monday, the firm showed that ASPYRE-Lung could successfully "rescue" samples that failed quality control checks for NGS because of poor sample or DNA quality.

In that study, Biofidelity analyzed 26 non-small cell lung carcinoma (NSCLC) samples that had passed NGS QC and 94 that had failed, despite having sufficient clinical material, and for which genomic biomarker data were unavailable.

The ASPYRE-Lung assay showed complete concordance with the 26 samples that had passed NGS QC, while enabling Biofidelity to obtain actionable information from 92 of the 94 samples that had previously failed, each of which contained a detectable NSCLC variant.

Balmforth said that ASPYRE-Lung's underlying technology makes it less susceptible to problems involving DNA damage and otherwise poor-quality samples.

"ASPYRE-Lung uses an amplification-based approach rather than a sequencing-based approach," Balmforth said, which makes it much more robust when used with poor-quality samples.

ASPYRE-Lung can detect 114 mutations relevant to NSCLC across 11 genes using a method called pyrophosphorolysis, which runs on standard real-time PCR systems and involves a high concentration of pyrophosphate ions that drive enzymatic DNA polymerization in reverse, resulting in the digestion of one strand of double-stranded DNA. The reaction's high precision stems from being almost entirely inhibited by the presence of even a single mismatched nucleotide pair.

Min-Han Tan, founder and CEO of molecular diagnostics firm Lucence, complimented the study in an email, saying that the data provided looked sound and calling it a reasonable comparison to what is currently the gold standard for a cancer tissue profiling centralized service. "The next question commercial [*in vitro* diagnostics] customers will ask is then a comparison to other targeted amplification assays," he said.

Tan added that while the reported coverage of 114 variants in 11 genes is more limited than NGS, which spans additional actionable variants, ASPYRE-Lung appears to constitute an "excellent" bridge in settings where NGS may be less accessible due to cost and training issues.

Biofidelity presented a second study at AACR, which assessed how easy it was to set up ASPYRE-Lung at different sites as well as the agreement between results obtained at each site.

The assay was set up at the University of Pennsylvania, the Medical College of Wisconsin, and at Biofidelity's CLIA-certified lab in Morrisville, North Carolina. Results showed high concordance of ASPYRE-Lung and NGS across different types of clinical samples and sample preparation methods. The data also showed high reproducibility between sites, with 75 of 77 samples returning the same result across all three sites and identical positive variant calls in 98 percent of cases.

Of particular interest, Balmforth said, "was that some of the samples we used are really challenging to analyze."

These included fine needle aspirates, pleural effusions, and peritoneal fluid.

"One of the really unique things about our approach is the liquid and the tissue tests [use] the same workflow — it's the same test," Balmforth said. "The only difference is the extraction of the DNA."

Additionally, Balmforth added, "you can run a mixture of [liquid] biopsy and tissue biopsy samples in the same instrument, in a single test, which I think is helpful."

For example, Barnaby said, separate tests are currently used for analysis of tissue and liquid biopsy samples, which requires a lab to implement and validate two different workflows using two different sets of reagents and two different instruments. Running a mixture of sample types through the same instrument at the same time could simplify testing, while making it more accessible, reducing the challenges of batching samples prior to analysis, as well as costs, staff requirements, and bioinformatics.

Finally, Biofidelity presented a validation study assessing ASPYRE-Lung's limit of detection, specificity, analytical accuracy, and precision in variant-positive and variant-negative FFPE lung tissue samples.

Results showed a specificity of 100 percent and a high sensitivity with respect to variant allele frequency, gene fusion copies, and MET exon 14 skipping, a mutation present in about 3 percent of NSCLC cases. ASPYRE-Lung's analytical accuracy was concordant with NGS, and results were replicable across operators, reagent lots, runs, and real-time PCR instruments.

Since ASPYRE-Lung requires only a real-time PCR system, which are widely available and relatively cheap, it can offer significant cost savings over NGS, though Barnaby declined to provide the exact cost of an assay.

"We're talking about hundreds of dollars versus thousands of dollars," he said.

Balmforth also said that ASPYRE-Lung's turnaround time of two days from sample receipt to result addresses the issue of "very, very slow" turnaround times in the centralized lab model.

"It's really crippling hospital systems," he said.

Biofidelity launched ASPYRE-Lung late last year as a single-site clinical LDT through its North Carolina-based CLIA laboratory. The company commercially launched the assay reagents shortly thereafter for research use only to enable other laboratories to implement testing for genomic variants locally.

One past criticism of pyrophosphorolysis-based amplification is that the method struggles with certain complex nucleic acid sequences, limiting its use.

Balmforth said, however, that Biofidelity has "substantially" improved the technology and is not finding sequences for which the assay doesn't work.

"A lot of our work over the last year has been around getting the product and manufacturing to the highest possible quality standards," he said.