Sysmex Inostics GmbH

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Sysmex Inostics' updated SafeSEQ Breast Cancer Panel advances novel clinical uses of ctDNA through quantitative testing

Maryland (ots) -

Building on the ultra-high sensitivity SafeSEQ Breast Cancer Panel circulating tumor DNA (ctDNA) test launched at the American Association of Cancer Research 2019 annual meeting, Sysmex Inostics has updated the test to provide additional key information for investigation of the validity of ctDNA for molecular monitoring and recurrence surveillance for breast cancer patients who are receiving novel therapies.

In addition to a high detection rate even for patients with very low frequency mutations, the SafeSEQ Breast Cancer Panel has now also demonstrated the ability to delineate true changes in the level of ctDNA from random sampling or technical variation. This is in contrast to other liquid biopsy methods which report mutations detected along with the ratio of mutant molecules to wildtype molecules (mutant allele frequency, MAF), but are unable to relate changes in MAF to changes in the disease status of the patient with confidence. For instance, clinical data presented at San Antonio Breast Cancer Symposium (SABCS) demonstrated the importance of accurate detection of ctDNA with SafeSEQ testing to monitor tumor response in breast cancer patients receiving neoadjuvant treatment.

As a highly refined clinical development diagnostic, the SafeSEQ breast cancer panel has demonstrated exquisite sensitivity for detecting mutations in *ESR1, which* are known to arise in patients with estrogen receptor-positive breast cancer who have progressed on adjuvant hormone therapy. Extensive *ESR1* ctDNA testing by Sysmex Inostics' OncoBEAM enhanced digital PCR has shown that these mutations occur at very low frequencies in circulation. Patients who are receiving an investigational *ESR1*-directed therapy as part of a clinical trial may exhibit an *ESR1* mutation well below 1% MAF at baseline which could then decrease further, sometimes below 0.1% MAF, several months after initiation of therapy. Using a traditional qualitative ctDNA next generation sequencing-based test would not only make detection of these low-frequency mutations difficult, but it would also not be possible to determine whether this reduction in MAF represents a true decrease in ctDNA that could reflect a clinical response. This is because the reduction in MAF may result from an increase in wildtype DNA rather than a decrease in tumor-derived DNA, and the magnitude of change in MAF may be within the range of random variation that is inherent to the assay. Quantitative ctDNA detection is also important for other clinical applications such as monitoring tumor response for patients receiving neoadjuvant treatment as illustrated by SafeSEQ data presented at the recent San Antonio Breast Cancer Symposium, Poster P6-10-05.

The updated SafeSEQ Breast Cancer Panel can overcome these challenges by determining whether the change in the absolute number of *ESR1* mutant molecules detected at each timepoint, irrespective of the wildtype background, is sufficient to suggest a true biological cause such as a clinical response. This ability for true quantitative mutation detection is based on a rigorous linearity validation study and is especially important given the increasing interest in ctDNA-based monitoring and surveillance to support rapid advancements in therapies for breast cancer patients.

"Without quantitatively measuring ctDNA in a way that is specific for the patient's disease and instead employing qualitative methods based on mutant allele frequency that have traditionally been used for tissue analysis, you're neglecting some of the unique aspects of ctDNA testing that can make it an extremely powerful tool for clinical development," noted Matt Ryder, Sysmex's Associate Director of Biomarkers & Companion Diagnostics. "We are confident that the SafeSEQ Breast Cancer Panel is now one of the most informative tests available to support development of novel therapies for breast cancer, and we look forward to helping our pharma partners explore the clinical validity of ctDNA-based therapeutic monitoring and recurrence surveillance."

The updated SafeSEQ Breast Cancer Panel is available now for use as a clinical trial assay in Sysmex Inostics' Baltimore-based CLIA laboratory.

About Sysmex Inostics

Sysmex Inostics, a subsidiary of Sysmex Corporation, is a molecular diagnostic company that is a pioneer in blood-based cell-free tumor DNA (ctDNA) mutation detection in oncology utilizing highly sensitive technologies such as OncoBEAM(TM) (digital PCR) and SafeSEQ (NGS). These technologies were initially developed by experts at the Johns Hopkins School of Medicine over a decade ago and this deep expertise in ctDNA analysis extends to the core of Sysmex Inostics' capabilities for technology development and implementation.

With more than 10 years of experience in liquid biopsy Sysmex Inostics is a trusted partner to leading biopharmaceutical companies, advancing their efforts to bring the most effective personalized cancer therapies to global markets, from discovery through companion diagnostics.

Sysmex Inostics' OncoBEAM(TM) and SafeSEQ services are readily available to support clinical trials and research in oncology. In

addition, OncoBEAM(TM) tests are available through a CLIA-certified laboratory for routine clinical analysis as well as distributed kit products in the EU and Asia Pacific.

Sysmex Inostics' headquarters and GCP Service Laboratory are located in Hamburg Germany; Sysmex Inostics' CLIA-certified and GCP Clinical Laboratory is located in Baltimore, Maryland. For more information refer to www.sysmex-inostics.com or email info@sysmex-inostics.com.

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