Sysmex Inostics GmbH

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Sysmex Inostics' SafeSEQ ER+/HER2- breast cancer panel demonstrates equivalent sensitivity to OncoBEAM(TM) enhanced digital PCR technology for detection of mutations in circulating tumor DNA

Hamburg/Baltimore (ots) -

Recent data presented by Dr. Hope S. Rugo from the University of California San Francisco on behalf of investigators in the Translational Breast Cancer Research Consortium at the American Association of Cancer Research 2019 meeting in Atlanta, Georgia demonstrate how Sysmex Inostics' novel SafeSEQ ER+/HER2- breast cancer panel can detect clinically relevant mutations in circulating tumor DNA (ctDNA) from patients with metastatic breast cancer with sensitivity equivalent to Sysmex's highly clinically validated OncoBEAM liquid biopsy testing. Patients in this study received two different dose levels of palbociclib, a CDK4/6 inhibitor, in combination with either fulvestrant or tamoxifen. In addition to tissue-based retinoblastoma protein phosphorylation and Ki67 expression levels, mutations detected in ctDNA were evaluated to determine correlation with response. Overall, the results indicated that the presence of a PIK3CA mutation in plasma was associated with worse outcome, while the presence of ESR1 mutations in ctDNA did not appear to impact response to therapy.

Sixty-nine patients were evaluated by the SafeSEQ panel, of whom 52 (75%) had a mutation in ctDNA affecting PIK3CA, ESR1, TP53, ERBB2, AKT1, or KRAS. Consistent with observed mutation rates for this breast cancer subtype, 27 (39%) patients had a mutation in PIK3CA. Additionally, 24 (35%) patients had mutation affecting ESR1, which agrees with the expected mutation rate for this gene for patients who have received aromatase inhibitor therapy. For patients with a PIK3CA mutation, the median progression free survival (PFS) was 2.3 months, versus 9.7 months for patients who did not. However, there was no significant difference in PFS for patients with an ESR1 mutation versus ESR1-wildtype patients, which is consistent with previous studies that demonstrated the efficacy of palbociclib in combination with hormone therapy regardless of ESR1 mutation status.

In addition to SafeSEQ testing, 35 patients had sufficient plasma available for matched analysis using Sysmex Inostics OncoBEAM breast cancer panel which is highly clinically validated for ultra-sensitive detection of mutations affecting PIK3CA, AKT1, and ESR1 (limit of detection 0.04% mutant allele frequency, MAF). A total of 54 positive calls across these three genes were successfully detected by both assays (100% positive percent agreement), of which 22 (41%) were below 1% MAF, and 5 (9%) were below 0.1% MAF for the OncoBEAM reference method. Given numerous published studies which have demonstrated decreased reliability of blood-based "pan-cancer" next-generation sequencing tests below 1% MAF, the robust accuracy at low allelic frequencies observed for SafeSEQ in this study demonstrates the advantages of highly focused panels for defined clinical intended uses. SafeSEQ's ability to deliver ultra-sensitive blood-based detection of mutations in ctDNA is due to its foundational technology which was specifically developed and optimized for the detection of rare mutant molecules, an essential capability for clinical ctDNA analysis.

Interestingly, for the 35 patients tested with both SafeSEQ and OncoBEAM, the median MAF for AKT1 and PIK3CA mutations detected by both tests was approximately 10%, while the median MAF for ESR1 mutations was below 1%. "The ability to evaluate mutations in blood in patients with advanced hormone receptor positive breast cancer profoundly impacts our ability to understand both response and resistance and will allow delivery of more effective therapy", commented Hope Rugo, the lead investigator for this trial. Dr. Rugo noted that "a highly sensitive blood-based assay is even more important now given recent positive data with a PI3K inhibitor in patients with known mutations in this pathway, particularly given the difficulty in obtaining tumor biopsies in this disease." Dr. Ben Park, a senior investigator in the study commented, "Given the rising interest in ESR1 mutation detection in plasma for various clinical applications including possible therapeutic targets as well as molecular monitoring of minimal residual disease for recurrence, highly sensitive liquid biopsy tests capable of reliable detection at ultra-low frequency are now more important than ever."

Presentation Details

Rugo, H.S. et al. (2019, April). Palbociclib in combination with fulvestrant or tamoxifen as treatment for hormone receptor positive metastatic breast cancer with prior chemotherapy for advanced disease (TBCRC 035): A Phase II study with pharmacodynamic markers. Presented at the American Association of Cancer Research annual conference, Atlanta, Georgia.

This work was supported by Pfizer and the Translational Breast Cancer Research Consortium.

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 mutation detection in oncology utilizing highly sensitive technologies such as OncoBEAM(TM) and SafeSEQ. 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 pharmaceutical companies, advancing their efforts to bring the most effective personalized cancer therapies to global markets.

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 as kit products in EU.

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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