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Sysmex Inostics' OncoBEAM shows superior performance in mutation detection for HCC

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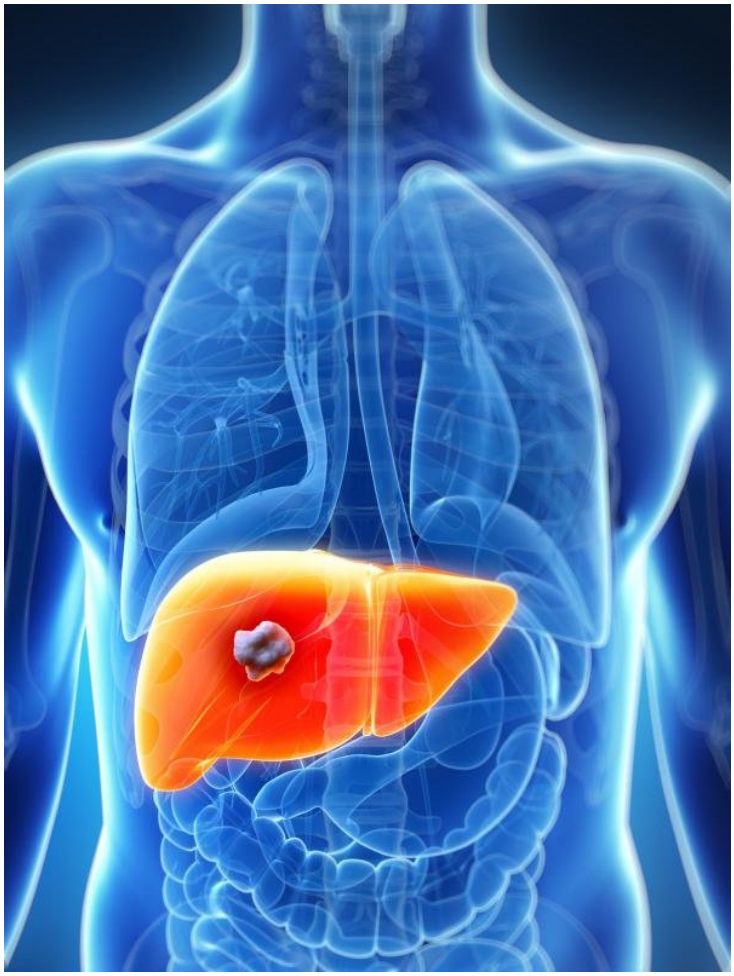

Data recently published in *Clinical Cancer Research* demonstrate the advantages of using an ultra-high sensitivity test for detection of mutations which may predict therapeutic efficacy for hepatocellular carcinoma (HCC). Sysmex Inostics' OncoBEAM technology, a highly clinically validated technology for circulating tumor DNA (ctDNA) analysis, was used to determine *RAS* mutational status across a total of 1,318 patients screened for two phase II studies which evaluated the efficacy of refametinib monotherapy, and refametinib plus sorafenib in patients with *RAS*-mutant unresectable or metastatic HCC.

Building on evidence from a prior phase II clinical trial which showed that HCC patients whose tumors had a *RAS* mutation exhibited a robust clinical response in comparison with patients who were wild-type for *RAS*, investigators planned a prospective cohort to evaluate *RAS* mutation status at the time of enrollment.

Patients were enrolled from 80 study centers in 21 countries across Asia, Europe, and the USA. A primary challenge of enrollment across the world is that patients with advanced or metastatic HCC do not typically undergo tissue biopsy due considerable risk of complications; therefore, molecular testing is not routinely performed in this cancer. Further confounding enrollment is the low prevalence of *RAS* mutations in patients with HCC, estimated to be 5%.

To overcome these challenges, investigators utilized OncoBEAM to screen patient plasma for *RAS* mutations, as plasma testing can overcome the need for a tumor biopsy procedure and deliver tumor mutational status via a blood draw. Similar to other previously published studies across various cancer types, OncoBEAM testing enabled investigators to obtain information they would not otherwise receive in order to inform eligibility for inclusion in these HCC studies.

Not only was OncoBEAM able to successfully detect *RAS* mutations across this patient population at a rate consistent with the expected *RAS* mutation rate for HCC via a simple, minimally-invasive blood draw, but for a subset of patients who were also tested using a broad, next-generation sequencing (NGS)-based method, OncoBEAM demonstrated superior detection for low frequency *RAS* mutations. Out of 27 patients determined to be *RAS*-positive by OncoBEAM who were also tested using NGS, *RAS* mutation status was only confirmed in 12 patients (44.4%). The limited detection with NGS was most likely due to the order of magnitude difference in the limit of detection between the two assays (0.1% for NGS versus 0.02% for OncoBEAM). In fact, the overall *RAS* mutation rate of the HCC patients screened with OncoBEAM in these trials was 4.4%, which matched very closely with previous reports in this population (5%).

Screening across a greater breadth of genomic targets via NGS can sometimes reveal additional biomarker information which may inform future research. For these two HCC phase II studies, NGS testing revealed that outside of *KRAS* and *NRAS* the most frequently mutated region was the *TERT* promoter, followed by *TP53* and *CTNNB1*. However, actionable mutations in genes other than RAS were rare, occurring in less than 10% of the patients tested with NGS.

These HCC clinical studies highlight the utility of focused testing with an assay like OncoBEAM: ultra-high sensitivity detection of rare mutant molecules may provide benefits for patient welfare, and can ensure the most time and cost-effective approach to screening and enrollment for biomarker-driven trials when the biomarker relationship to disease and therapeutic strategy has been established.