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“FULLY AUTOMATED, PLASMA-BASED ANALYSIS OF CIRCULATING TUMOR DNA ON THE IDYLLA PLATFORM”

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INTRODUCTION: Non-invasive analysis of circulating tumor DNA (ctDNA) has been proposed as a powerful tool for rapid diagnosis and monitoring of cancer patients during personalized treatment.

RESULTS: We developed a novel, fully automated platform which allows ctDNA analysis using 1ml of EDTA plasma. The assay is performed using a disposable cartridge, which contains all reagents for fully integrated sample preparation, real time PCR and interpretation, and is processed on the Biocartis Idylla™ System.

The Idylla™ ctBRAF Mutation Assay detects BRAF mutations in ctDNA by allele-specific duplex PCR reactions, designed to detect the BRAF WT, V600E/E2/D and V600K/R/M mutations.

A linear correlation between Cq values reported by prototype Idylla™ assays and digital droplet PCR (ddPCR, Biorad) was established in clinical samples, allowing accurate and sensitive quantification of mutant DNA fragments in plasma with an analytical sensitivity down to 0.01%. Current turn-around time from plasma sample to result for the ctBRAF Mutation Assay (RUO) is below 90 minutes.

For KRAS & NRAS ctDNA mutation status, 21 KRAS mutations and 19 NRAS mutations respectively in exons 2, 3 and 4 are detected by allele-specific multiplex PCR reactions. The NRAS assay additionally analyses the EGFR S492R mutation which has been associated with cetuximab-resistance¹.

CONCLUSIONS: Analysis of extended RAS and BRAF mutations in ctDNA on the Idylla™ platform enables rapid and sensitive genotyping in plasma samples from patients with advanced cancers. The assessment of circulating BRAF and RAS mutations in plasma through the Idylla™ platform warrants further research for diagnostic and monitoring purposes in patients with advanced cancers.

¹ Montagut et al, Nature Med, 18, 2012