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EARLY DETECTION AND DIAGNOSIS (CIRCULATING DNA)

1P Application of liquid biopsies in metastatic gastrointestinal cancer to identify candidate therapeutic targets

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Background: Next-generation sequencing (NGS) of cell-free tumor DNA (ctDNA) has great potential for liquid biopsy in cancer diagnostics and to identify patients with actionable genomic alteration. This study, a prospective longitudinal study, focused in a cohort of metastatic cancer patients without standard effective active antineoplastic medical treatment options to establish the rate of patients with actionable genomic alteration and the rate of patients accessing medical treatment. The final objective was to determine the clinical performance based on non-invasive tumor sequencing.

Methods: We collected plasma of 10 metastatic gastrointestinal patients with known status of the RAS genes and microsatellites instability in tumor tissue. CtDNA was extracted from plasma and genomic alterations were analyzed by Guardant 360 (Guardant Health, Biosequence, OncoDNA), a next generation sequencing panel. This panel consists of 73 cancer related genes and is able to identify different types of genomic alterations. Informed consent was obtained from all patients.

Results: We were able to identify 78 somatic mutations in total resulting in a median number of eight somatic mutations per patient. The most common altered genes are well known tumor suppressor and oncogenes like TP53, APC, KRAS, MYC andEGFR. At least one actionable alteration in plasma cfDNA were detected in eight from the 10 patients (80%) but the proportion of patients for which a genomic identified recommended therapy was available to effectively initiate the treatment were only 37,5% (3/8). In these patients, the identification of alterations like c-MET amplification, FGFR1 amplification or PIK3CA c.1633G>A (p.E545K) mutation, involved in clinically actionable pathways, allowed the selection of a specific therapy. For the rest of cases the main causes of non-access to medical treatment associated with a specific mutation were, among others, the advanced pre-treated patient and clinical trial logistical access difficulties.

Conclusions: Our findings confirm the percentage of cases with potentially druggable aberrations is similar to other studies using this strategy and emphasizes their clinical value to identify candidate therapeutic targets.

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