

Liquid biopsy identifies mutations in colorectal cancer undetected in tissue biopsy

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An international, randomized, phase III study has analyzed the DNA of 503 patients with metastatic colorectal cancer by liquid biopsy (BEAMing platform) to detect KRAS, PIK3CA and BRAF gene mutations in tumors. These patients, who had previously received different treatment lines, were administered either the multi-kinase inhibitor regorafenib or placebo. Regorafenib is an inhibitor of several proteins involved in oncogenesis and tumor angiogenesis.

The results of the trial were twofold: liquid biopsy effectively unmasked different [tumor](#)-related mutations. More specifically, in a subgroup of 41 [patients](#) who had previously received anti-EGFR therapy, it was revealed that they had acquired KRAS mutations during the course of their disease. Such accurate information is difficult to obtain using [tissue biopsy](#) which could, in the absence of this data, lead to a selection of therapy which may not be the most appropriate for these patients. Moreover, the study concludes that regorafenib is effective in patients with KRAS and PIK3CA mutations.

"This is the first large clinical trial to compare liquid versus conventional tissue biopsy data, and the results show the former (BEAMing technology) obtain more data on tumor mutation throughout the course of the disease, enabling us to better target therapy to the specificities of patient's tumor; this could have a considerable impact on clinical practice, as novel applications of this technology could be further investigated and developed", says Josep Tabernero, Head of the Medical Oncology Department of Hospital Universitario Vall d'Hebron, Director

of VHIO, and Co-Director of the study.

The majority of clinical studies published on the use of DNA in blood to determine tumor genotype, have only enrolled a relatively small number of patients which limits the significance of the findings as well as the ability to research possible correlations between genotype and clinical outcome. Furthermore, most studies evaluated a single gene (such as KRAS) and used technologies that are not commercially available. The importance of the CORRECT trial is that it involved a large number of patients, providing correlative analyses that showed clinical benefits of regorafenib in all the subgroups in which mutations had been identified.

Liquid biopsy: facilitating analysis of mutations and improved selection of targeted therapies tailored to the specificities of each patient's tumor

Tumor genotype plays an important role in drug resistance in patients with [metastatic colorectal cancer](#), but the genotype obtained at diagnosis can vary after different treatment lines. Therefore, DNA analysis using liquid biopsy has clear advantages over DNA analysis with tissue biopsy and is rapidly gaining importance and momentum in the oncology field.

Liquid biopsy, also known as a blood-based biomarker test, is a fast, simple method for detecting RAS (KRAS and NRAS) mutation status in tumors, as it only requires a blood test rather than a tissue biopsy or surgical procedure. Further, it also provides mutation status results in a matter of days, helping to determine the most specific, targeted treatment in each case. It represents one more important step in realizing the true promise of precision medicine in oncology - the main focus behind research at VHIO which aims to both advance and deliver targeted therapies tailored to the particularities of each tumor for an increasing number of patients.

Although there are still some important questions that will need to be resolved concerning liquid biopsy, for example, the possibility that not all tumors release enough DNA into the blood for it to be detected, as well as the difficulty of assigning a particular genotype for each particular tumor in patients with multiple metastases, the CORRECT study shows that liquid biopsy could become an essential tool in [clinical practice](#).

Provided by Vall d'Hebron Institute of Oncology

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