Nature Reviews Clinical Oncology | Published online 19 Sep 2017; doi:10.1038/nrclinonc.2017.154

COLORECTAL CANCER

Liquid biopsy provides highly sensitive detection of *RAS* mutations

Analysis of circulating tumour DNA (ctDNA) in blood samples has the potential to provide a more-complete indication of tumour heterogeneity than analyses of biopsy samples; however, prospective data confirming this potential are currently limited. Now, findings from a phase II study involving patients with metastatic colorectal cancer (mCRC) receiving the EGFR inhibitory antibody panitumumab confirms the superior sensitivity of this type of liquid biopsy analysis.

A total of 74 patients with *KRAS* exon 2 wild-type mCRC received at least one dose of panitumumab; primary tumour material was collected before treatment, and, when possible, upon progression, in addition to blood samples. Beads, emulsion, amplification, magnetics (BEAMing) analyses of liquid biopsy samples revealed the emergence of *RAS* mutations on progression in 36.7% of samples, but in only 9.5% of paired tumour biopsy samples. The superiority of ctDNA analysis for the detection of emergent *RAS* mutations was then confirmed in a subset of 14 patients with paired tumour-tissue and plasma samples: 7.1% of patients had emergent *RAS* mutations detected in tissue samples, while 57.1% had similar mutations detected in ctDNA. Of note, patients who developed these mutations during treatment had similar outcomes to those with wild-type *RAS* on recurrence; however, in selected patients, an exploratory longitudinal analysis of *RAS*-mutation levels during treatment showed higher *RAS* mutational burdens were correlated with a higher tumour burden.

The findings of this prospective study demonstrate that liquid biopsy is more sensitive than traditional approaches in the detection of mutations that emerge during treatment; nevertheless, emergent *RAS* mutations are not associated with inferior outcomes.

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ORIGINAL ARTICLE Siena, S. *et al.* Dynamic molecular analysis and clinical correlates of tumor evolution within a phase 2 trial of panitumumab-based therapy in metastatic colorectal cancer. *Ann. Oncol.* http://dx.doi.org/10.1093/annonc/mdx504 (2017)