Topics cfNA (Circulating free nucleic acid)

Name (s) Joseph Zouein, Hampig Raphaël Kourie

Institution / Organization Saint Joseph University of Beirut, Faculty of Medicine.

Address Damascus Street

City Beirut

Country Lebanon

Email address josephzouein98@gmail.com

Telephone contact +96171166604

The relevance of liquid biopsy for KRAS/NRAS/BRAF baseline testing, and monitoring at disease progression, in metastatic colorectal cancer (NEORAS)

Background: The detection of the RAS status in metastatic colorectal cancer (mCRC) is an important predictive biomarker for response to anti-EGFR therapies. However, the appearance of mutations during therapy may be responsible for acquired resistance in primary RAS wild type disease. It is important to monitor RAS mutational status in mCRC before treatment and at disease progression.

Methods: NEORAS is a phase IV prospective, observational, uncontrolled, non-comparative, non-randomized, open label pilot study. RAS/BRAF status will be tested at baseline using tissue and liquid biopsy, and upon progression using liquid biopsies alone using an Idylla/Biocartis device. Primary endpoints are the comparison of the RAS status based on liquid biopsy with the RAS status based on tissue biopsy prior to start of first line treatment in patients with mCRC and the evaluation the RAS status based on liquid biopsy at disease progression in patients with initially RAS mutant, mCRC. The secondary endpoint was the evaluation of the RAS status based on liquid biopsy at progression in initially RAS wild type mCRC patients.

Results: As of the data cutoff date of October 5, 2021, 60 patients were recruited. All of the patients have undergone the liquid biopsy at baseline including 17 patients who had a liquid biopsy on progression. Concordance in RAS status between liquid and solid biopsies was seen in 71.67% (95% CI, 59.23%-81.49%). Among the 41 patients who had hepatic metastases concordance between solid and liquid biopsies was 70.73% (95% CI, 55.52 – 82.39 %). Among the 17 patients who had had a second liquid biopsy on progression, 12 patients had concurring results with the liquid biopsy at baseline and 15 patients had concurring results with the solid biopsy. There was no association between the presence of hepatic metastasis and the concordance of the liquid and solid biopsies at baseline.

Conclusion: The sensitivity of detection of the RAS status using liquid biopsy remains low in comparison with the RAS status detected on solid biopsies. RAS mutations at disease progression were mostly concordant with results at baseline.