Topic
dfNA

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Abstract
Analysis of cell-free tumour DNA, a liquid biopsy, is a promising biomarker for cancer. We have performed a proof-of principle study to test the applicability in the clinical setting, analysing copy number alterations (CNAs) in plasma and tumour tissue from 44 patients with gastro-oesophageal cancer.

DNA was isolated from blood plasma and a tissue sample from each patient. Array-CGH was applied to the tissue DNA. The cell-free plasma DNA was sequenced by low-coverage whole-genome sequencing using a clinical pipeline for non-invasive prenatal testing. WISECONDOR and ichorCNA, two bioinformatic tools, were used to process the output data and were compared to each other.

Cancer-associated CNAs could be seen in 59% (26/44) of the tissue biopsies. In the plasma samples, a targeted approach analysing 61 regions of special interest in gastro-oesophageal cancer detected cancer-associated CNAs with a z-score >5 in 11 patients. Broadening the analysis to a whole-genome view, 17/44 patients (39%) had cancer-associated CNAs using WISECONDOR and 13 (30%) using ichorCNA. Of the 26 patients with tissue-verified cancer-associated CNAs, 14 (54%) had corresponding CNAs in plasma. Potentially clinically actionable amplifications overlapping the genes *VEGFA, EGFR, ERBB2* and *FGFR2* were detected in the plasma from three patients.

We conclude that low-coverage whole-genome sequencing without prior knowledge of the tumour alterations could become a useful tool for cell-free tumour DNA analysis of total CNAs in plasma from patients with gastro-oesophageal cancer.