Personalised analysis of cell-free circulating tumour DNA for detection of molecular residual disease and recurrence in patients with head and neck squamous cell carcinoma: the LIONESS study

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Background & objectives

Early relapse and development of metastatic disease are some of the primary reasons for the poor prognosis of patients with head and neck squamous cell carcinoma (HNSCC). The recent advent of personalised assays capable of detecting circulating cell-free tumor DNA (ctDNA) has enabled detection of molecular residual disease (MRD) and recurrence following curative-intent therapy. We conducted LIONESS, a single-centre prospective cohort study to assess ctDNA in plasma and saliva from 77 patients with HNSCC receiving primary surgery with curative intent. Our objectives were to determine whether post-operative ctDNA detection can act as a biomarker for surgical tumour clearance and detection of MRD and to evaluate the potential of personalised ctDNA analysis for early molecular-level detection of relapse or prior to clinically confirmed recurrence.

Methods

Samples from 77 HNSCC patients (47% stage I/II, 53% stage III/IV; 94% p16-negative) were collected pre- and postoperatively and during clinical follow-up. Whole exome sequencing was performed on formalin-fixed paraffin-embedded tumour tissue to an average coverage of 250x. Tumour-specific variants for personalised assay design (RaDaR, NeoGenomics) were selected and used in the analysis of serial samples for evidence of MRD. Plasma ctDNA levels were correlated to tumour volumes from staging CT and other clinical parameters.

Results

In 550 longitudinal plasma and 84 saliva samples collected preoperatively and during clinical follow-up, ctDNA was detected at levels ranging from 18.4% estimated variant allele fraction (eVAF) to as low as 0.0005% eVAF. Increased plasma ctDNA levels were detected

postoperatively in cases with confirmed clinical recurrences (13/13) with lead times up to 508 days. All cases with detectable ctDNA prior to treatment which remained ctDNA-negative thereafter have not recurred to date. ctDNA was also detected in baseline saliva samples from patients with tumours of various anatomical locations.

Conclusion

The use of ctDNA measurements in this HNSCC patient cohort has significant potential to guide treatment decisions, improve disease outcome and potentially spare patients unnecessary, partially invasive interventions during clinical follow-up. Our work demonstrates the feasibility of personalised ctDNA assays for the detection of MRD postoperatively and for monitoring for early detection of relapse.