Preliminary results of the Liquid BIOpsy for MiNimal RESidual DiSease Detection in Head and Neck Squamous Cell Carcinoma (LIONESS) study

LMU KLINIKUM
Klinik und Poliklinik für Hals-Nasen-Ohrenheilkunde

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susanne.flach@med.uni-muenchen.de

HNO LMU

Susanne Flach[1], Karen Howarth[3], Sophie Hackinger[3], Christodoulos Pipinikas[3], Kirsten McLay[3], Giovanni Marsico[3], Christoph Walz[2], Olivier Gires[1], Martin Canis[1], Philipp Baumeister[1]

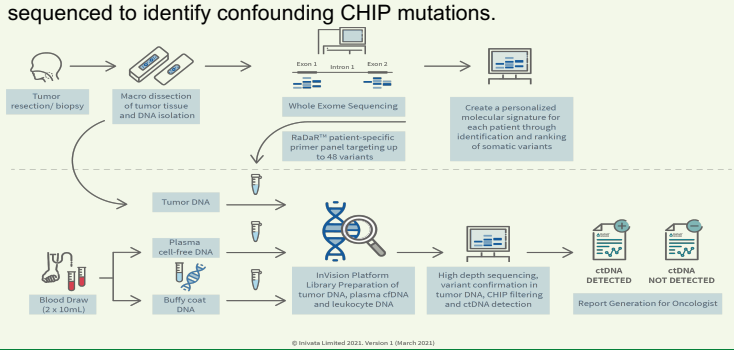
[1]Department of Otorhinolaryngology, Head and Neck Surgery, LMU Klinikum, Marchioninistrasse 15, 81377 Munich, Germany, [2]Institute of Pathology, Faculty of Medicine, LMU Munich, Germany, [3]Inivata, Babraham Research Park, Cambridge, United Kingdom

INTRODUCTION

- Head and neck squamous cell carcinoma (HNSCC) remains a substantial burden to global health with 5-year survival of <50%. Despite improvements in treatments for HNSCC, many patients develop recurrences.
- Cell-free circulating tumor DNA (ctDNA) is an emerging biomarker but has not yet been studied sufficiently for HNSCC. The detection of ctDNA as a marker of minimal residual disease following curative-intent treatment holds promise for identifying patients at an increased risk of relapse, who may benefit from adjuvant radio(chemo)therapy or closer monitoring with repeat resection, if needed.
- Here, we use RaDaR™, a personalised ctDNA assay, to detect ctDNA in pre- and post-operative plasma samples collected from the LIONESS study, a single-centre prospective experimental evidence-generating cohort study, conducted at the Hospital of the University of Munich.

METHODS & RaDaR™ WORKFLOW

- We analysed ctDNA in 17 patients with p16-negative HNSCC (stages III-IVB) who received primary surgical treatment with curative intent at the Hospital of the University of Munich, Germany.
- Plasma samples were collected 1-4 days pre-operatively (T0), 2-7 days post-operatively (T2), before start of adjuvant therapy (if any) and at follow-up visits (T3-T10). Whole exome sequencing was performed on formalin-fixed paraffin-embedded tumour tissue to a median depth of 250x.
- For each patient, up to 52 tumour-specific variants for RaDaR™ assay design were selected to analyse serial plasma samples for evidence of minimal residual disease or recurrence. Variants were verified by deep sequencing of tumour tissue DNA and matched buffy coat DNA was sequenced to identify confounding CHIP mutations.



RESULTS & DISCUSSION

Characteristics	Patients (n=17)
Stage	**Age, Median (Range)**
Stage III (n=8)	67 (55-78)
Stage IV (n=9)	60 (48-76)
Sex	
Male	13 (76.5%)
Female	4 (23.5%)

Tumour characteristics	
Location	
Oral cavity	5 (27.8%)
Oropharynx	2 (11.1%)
Larynx	7 (38.9%)
Hypopharynx	4 (22.2%)
Second primary tumour	1 (5.9%)

Table 1: Patient demographics of HNSCC patients enrolled in the LIONESS study to date.

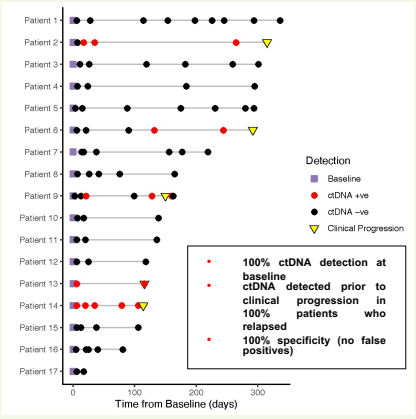


Figure 1: Longitudinal monitoring of serial plasma samples from 17 patients, indicating when ctDNA was detected and whether the patient subsequently relapsed.

In all cases with clinical recurrence to date (5/5), ctDNA was detected prior to clinical progression, with lead times ranging from 108 to 298 days.

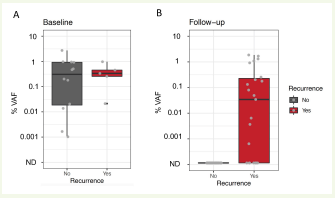


Figure 2: A: ctDNA levels in baseline samples taken prior to surgery ranged from 0.001% to 2.737% estimated variant allele frequency (% VAF).
B: In post-surgery samples, ctDNA could be detected at levels as low as 0.0006% VAF, with levels below 0.01% VAF in 20% of ctDNA positive samples.

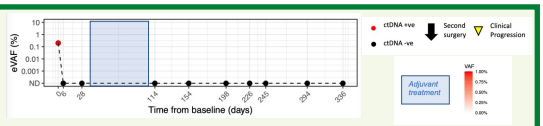


Figure 3: Longitudinal monitoring of ctDNA from a patient where no clinical progression was observed. Plasma was taken at various time points, including pre-operatively (day 0) and post-operatively (day 6 to day 336).

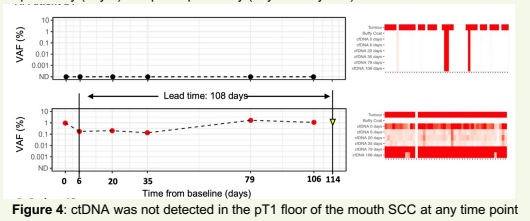


Figure 4: ctDNA was not detected in the pT1 floor of the mouth SCC at any time point for this patient (top panel) but was detected at all time points pre- and post-operatively in the second primary pT4a laryngeal SCC (bottom panel), with a lead time of 108 days from ctDNA detection to clinical progression. Heat maps on the right, each column representing a different variant, each row a different sample type.

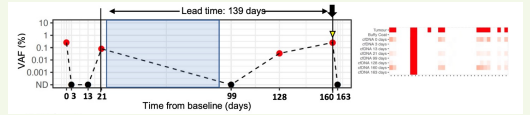


Figure 5: ctDNA detected before surgery, but not 3 or 13 days post-op. ctDNA detected 21 days post-op, which decreased after completion of adjuvant treatment only to rise again by day 128, prior to clinical progression. ctDNA levels were undetectable following a second surgical intervention at 160 days after the first surgery. Heat map as in Fig. 4.

CONCLUSION

This study illustrates the potential of ctDNA as a biomarker for detection of minimal residual disease as well monitoring of recurrence in patients with HNSCC and demonstrates the feasibility of personalised ctDNA assays for detection of disease post-treatment and with consequences for further therapy planning. Early detection of relapse using ctDNA could indicate patient populations where earlier therapeutic intervention may be beneficial.

Acknowledgements

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