Personalized circulating tumor DNA (ctDNA) analysis in patients with recurrent/metastatic Head & Neck Squamous Cell Cancer (R/M HNSCC)

Kirsty Taylor[1], Jinfeng Zou[2], Marcos Magalhaes[1], Karen Howarth[3], Giovanni Marsico[3], Samantha Terrell[3], Greg Jones[3], Charlene Knape[3], Tim Forshew[3], Marc Oliva[1], Anna Spreafico[1], Aaron R. Hansen[1], Simon S. McDade[4], Vicky M. Coyle[4], Mark Lawler[4], Elena Elimova[1], Scott V. Bratman[5], Lillian L. Siu[1]

[1]Division of Medical Oncology & Haematology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [2]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [3]INIVATA, Babraham Research Park, Cambridge, United Kingdom, [4]Patrick G. Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, Northern Ireland, [5]Department of Radiation Oncology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

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BACKGROUND

- Immuno-oncology agents (IO) have become standard-of-care in the treatment of R/M HNSCC, but only a subset of patients (pts) benefit.
- Highly sensitive quantification of plasma circulating tumor DNA (ctDNA) may permit real time assessment of disease under selective pressures of treatment.

Aim: To characterize the clonal dynamics of serial ctDNA monitoring under the treatment selection pressure of systemic therapy in R/M HNSCC pts using a highly sensitive personalized panel.

METHODS

- R/M HNSCC pts treated with platinum-based chemotherapy (CT) or IO (anti-PD1/L1 +/- second IO) underwent serial ctDNA collection pre-cycles 1/2/3 and at disease progression, corresponding to timepoints (T) 1-4. T1 was considered baseline. Figure 1.
- Whole exome sequencing of pt tumor tissue identified patient specific somatic variants which were used as targets for RaDaR®, a personalized multiplexed PCR-based NGS assay.
- Matched buffy coat DNA was sequenced to filter germline mutations and identify confounding CHIP.
- RaDaR was applied at each available T, an estimated variant allele frequency (eVAF) was calculated and correlated with progression free- (PFS) and overall- survival (OS).

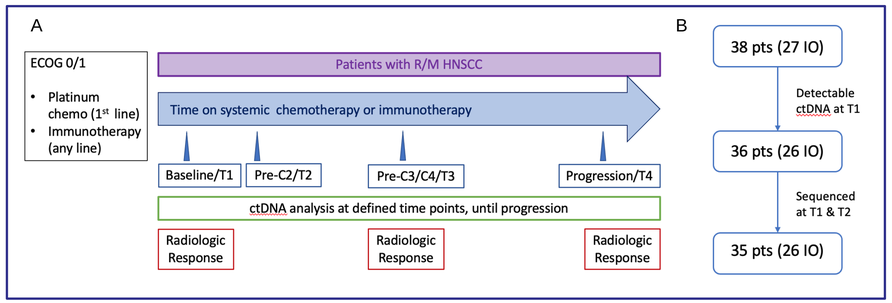

Figure 1. A) Study schema (NCT03712566) and B) patient samples included in workflow.

- Findings were compared against prior (ESMO 2021, Abstract #2379) data generated using a fixed 580 gene CAPP-seq (CAncer Personalized Profiling by deep Sequencing) panel designed specifically against squamous cell carcinoma.

REFERENCES

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RESULTS

- RaDaR panels targeted a median of 48 variants (17-50).
- ctDNA was detected in 35/38 (92%) patients at baseline, with median eVAF 0.345% (range 0.0004% - 43.37%).

Characteristics		N (%)
Median Age – years (range)		62 (20-84)
Gender	Male Female	27 (77) 8 (23)
ECOG PS	0 1	2 (6) 33 (94)
Smoking Hx	Current/Previous Never	24 (69) 11 (31)
HPV status	Positive Negative	9 (26) 26 (74)
No. of metastatic sites	1-2 3+	29 (83) 6 (17)
Treatment	Platinum CT Immunotherapy	9 (26) 26 (74)

Table 1. Patient Characteristics (n=35).

- Median PFS and OS, for 35 included pts, was 2.57 mo (95% CI 0.48 - 4.66) and 8.37 mo (95% CI 5.42 - 11.32) respectively.
- For IO treated pts (2nd line and PD-L1 unselected), median PFS was 2.45 mo (95% CI 0 - 5.18) and median OS 7.38 mo (95% CI 3.84 - 10.93).

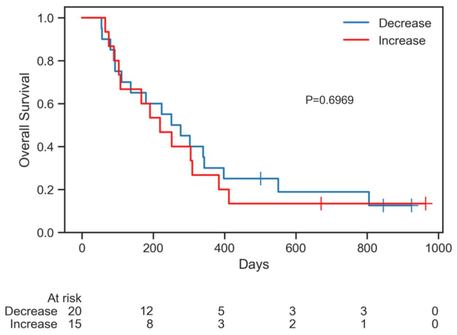

Figure 2. A numerical but non-significant trend was seen in median OS for pts with a decrease vs. increase in Δ eVAF (T1 to 2), 8.8 mo vs 7.3 mo (HR = 0.87 (0.42, 1.79)).

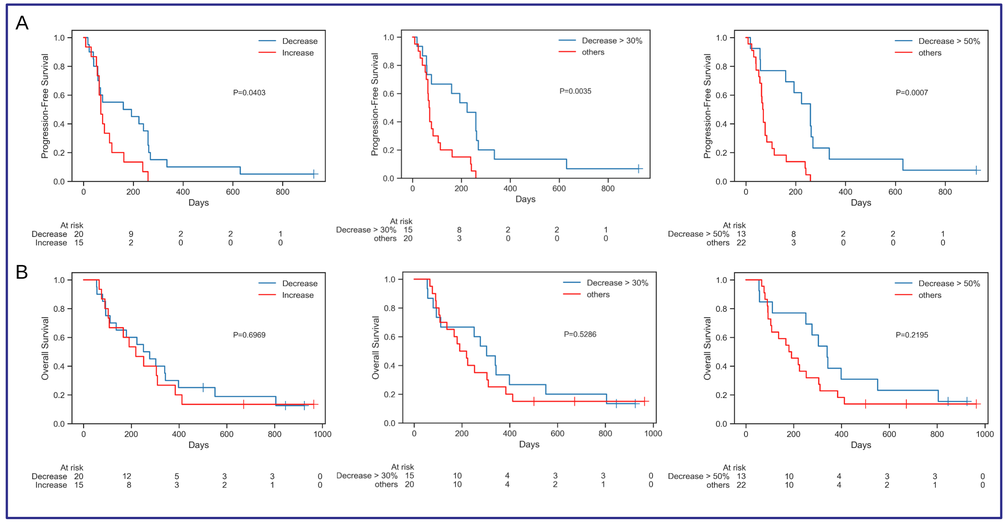

Figure 3. A decrease in Δ eVAF from T1 to T2, by >30%, or >50% identified pts with improved PFS (A) for all patients: with HR 0.45 (0.21, 0.96) p = 0.04, 0.31 (0.14, 0.70) p < 0.01, and 0.23 (0.10, 0.56) p < 0.01, respectively. (B) for the 26 IO pts, with HR 0.40 (0.16, 1.03) p = 0.06, 0.19 (0.05, 0.66) p < 0.01, and 0.06 (0.01, 0.47) p < 0.01, respectively.

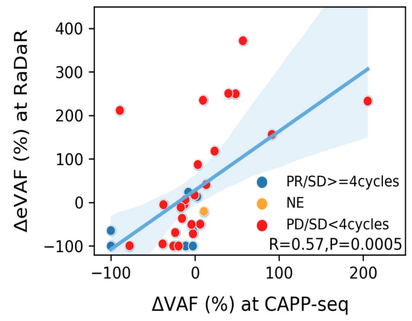

Figure 4. For 33 pts with a T2 sample, a comparison of Δ ctDNA levels, based on personalized RaDaR vs. CAPP-seq assays, from T1 to T2 demonstrated a correlation coefficient of R = 0.57, P < 0.01. PR: Partial Response; SD: Stable Disease; NE: Not Evaluable; PD: Progressive Disease

CONCLUSIONS

- In pts with R/M HNSCC, a decrease in ctDNA eVAF after first treatment correlated with improved PFS.
- There was a significant correlation between fixed CAPP-seq and personalized RaDaR assays when comparing Δ in ctDNA levels.

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Correspondence to: ktaylor13@qub.ac.uk