Abstract #2379

NCT03712566

Circulating tumor DNA kinetics in recurrent/metastatic Head and Neck Squamous Cell Cancer patients

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BACKGROUND

- Immuno-oncology agents (IO) have become a standard of care in the treatment of recurrent/metastatic head and neck squamous cell cancer (R/M HNSCC). However, only a subset of patients benefit with durable objective tumour responses.
- Liquid biopsy offers access to circulating tumor DNA (ctDNA). Currently data on ctDNA kinetics under treatment selection pressure is limited.
- Cancer Personalized Profiling by deep sequencing (CAPP-seq) is an ultra-sensitive next generation sequencing method used to quantify ctDNA.
- **Aim:** To characterize the clonal dynamics of serial ctDNA monitoring under the treatment selection pressure of systemic therapy in R/M HNSCC patients using a CAPP-seq SCC-optimized panel.

METHODS

- R/M HNSCC patients treated with either platinum-based chemotherapy (CT) or IO (defined as anti-PD1/L1 antibody +/- a second IO) underwent serial ctDNA collection pre-cycles 1/2/3 and upon disease progression, corresponding to timepoints (T) 1-4.
- Error-corrected sequencing using a SCC-optimised panel was applied at each available timepoint. After filtering out clonal hematopoiesis-associated mutations, mean variant allele frequency (VAF) was calculated per T.
- Median ctDNA abundance determined ctDNA groupings and changes were correlated with progression free survival (PFS) and overall survival (OS).

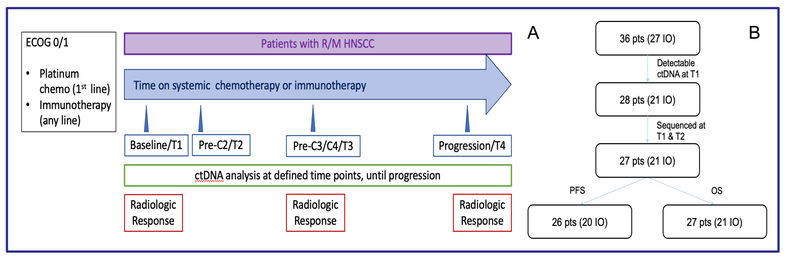

Figure 1. A) Study schema (NCT03712566) and B) patient samples included in workflow.

RESULTS

Table 1. Patient Characteristics (n=36).

Characteristics		N (%)
Median Age – years (range)		64 (20-82)
Gender	Male Female	24 (67) 12 (33)
ECOG PS	0 1	2 (6) 34 (94)
Smoking Hx	Current/Previous Never	26 (72) 10 (28)
Primary Site	Oral Cavity Oropharynx Larynx Pharynx	12 (33) 15 (42) 5 (14) 4 (11)
HPV status	Positive Negative	8 (22) 28 (78)
No. of metastatic sites	1-2 3+	30 (83) 6 (17)
Treatment	Platinum CT Immunotherapy	9 (25) 27 (75)

	IO Treated (n = 27)	CT Treated (n = 9)
CR/PR/SD ≥ 4cycles	8 (30%)	2 (22%)
PD/SD < 4cycles	19 (70%)	7 (78%)

Table 2. Clinical benefit rate/response at 4 cycles.

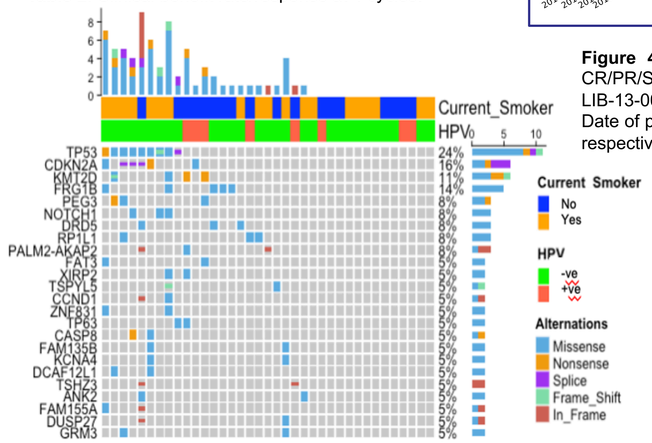

Figure 2. Oncoprint of somatic mutations at baseline. Twenty-eight patients (21 IO) had mutations detected.

- Median PFS and OS of entire cohort were 2.3 months (95% CI 0.7-11.2) and 6.9 months (95% CI 1.9-28) respectively.
- OS was significantly better in IO treated patients compared with CT treated patients, 6.1 vs 3.9 months (p = 0.01).

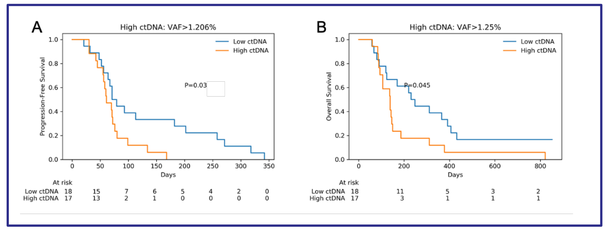

Figure 3. PFS/OS based on ctDNA abundance at baseline. Mean VAF was calculated per patient. Median VAF defined ctDNA group.

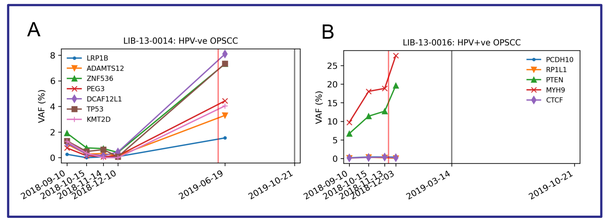

Figure 4. Individual patient mutation tracking. A) LIB-13-0014, CR/PR/SD≥4cycles; low baseline ctDNA that decreased at T2. B) LIB-13-0016, PD/SD<4 cycles; high baseline ctDNA that increased. Date of progression/death represented (red and black vertical lines, respectively).

CONCLUSIONS

- Low ctDNA abundance at baseline and non-persistence on treatment correlated with improved PFS and OS.
- Decrease in Δ VAF (T1-2) identified patients with longer OS, despite early radiological progression.
- Early changes in ctDNA after first treatment may help predict patient outcome beyond RECIST 1.1.

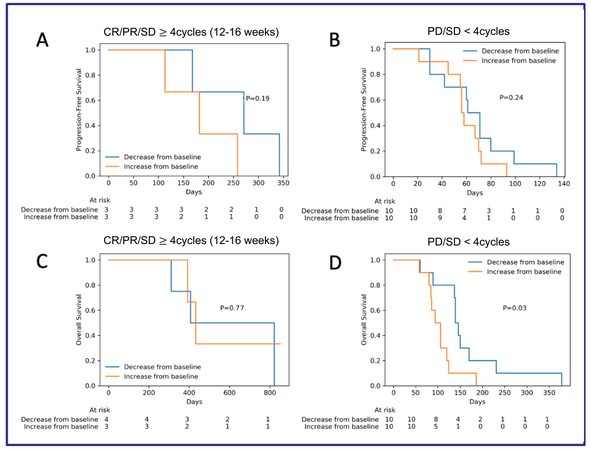

Figure 5. PFS/OS based on increased/decreased Δ VAF (change from T1-T2 where mean VAF at T1 is considered as baseline) and response to treatment at 4 cycles.

N=27	Δ VAF decrease T1-2	Δ VAF increase T1-2	HR (95% CI; p-value)
CR/PR/SD ≥4cycles	(A) n = 4 [4 IO] (mOS = 20.07 mo)	(B) n = 3 [3 IO] (mOS = 14.4 mo)	HR [A vs B] = 1.32 95% CI = 0.22–7.69 p = 0.77
PD/SD <4cycles	(C) n = 10 [8 IO] (mOS = 4.75 mo)	(D) n = 10 [6 IO] (mOS = 3.33 mo)	HR [C vs D] = 0.34 95% CI = 0.13–0.90) p = 0.03

Table 3. Decrease in Δ VAF (T1-2) identified patients with longer OS despite early radiological progression. mOS represents median OS.

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