The Utility of Liquid Biopsy for Diagnosis and Surveillance of Non-Oropharyngeal HPV+ Head and Neck Squamous Cell Carcinoma

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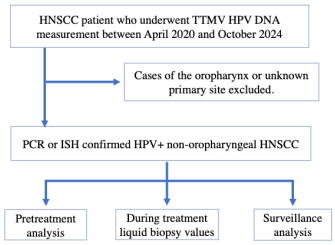
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BACKGROUND

- The application of tumor tissue-modified viral (TTMV) HPV DNA measurement for head and neck squamous cell carcinoma (HNSCC) has primarily been studied in oropharyngeal disease.
- The utility of the liquid biopsy measurement in HPV-associated non-oropharyngeal HNSCC remains largely unexplored.
- TTMV DNA measurements for 4 non-oropharyngeal head and neck subsites are studied, specifically the oral cavity, nasopharynx / nasal cavity, hypopharynx, and larynx
- Three clinical settings are assessed
  - 1) Pre-treatment measurement after biopsy confirmation
  - 2) During radiation +/- chemotherapy primary treatment
  - 3) Post-treatment surveillance

METHODS

Study population



*Surveillance measurements were considered true positives if a recurrence was detected via imaging or tissue biopsy within 3 months of a positive TTMV HPV DNA test.

Study Metrics

Diagnostic cohort
- Sensitivity

During treatment cohort
- TTMV HPV DNA values at each measurement during treatment

Surveillance cohort
- Sensitivity
- Specificity

CONCLUSION

- While HPV status is not prognostic in non-oropharyngeal HNSCC, tissue-agnostic liquid biopsy testing for HPV-positive confirmed cases may serve as a reliable biomarker in the pretreatment, during treatment, and surveillance settings
- Of the 4 non-oropharyngeal subsites assessed, only the nasopharynx / nasal cavity portended false negatives in any of the 3 analyses
- Pretreatment PCR / ISH testing for HPV with non-oropharyngeal head and neck cancer biopsies may be worthwhile to track disease progression via TTMV HPV DNA testing for HPV+ cases

RESULTS

Table 1. Cohort demographics and treatment modalities

	Non-oropharyngeal HNSCC subsite			
Characteristic	**Hypopharynx N = 4**	**Larynx N = 4**	**NP/Nasal cavity N = 13**	**Oral Cavity N = 2**
Age at diagnosis	66 (63, 70)	49 (38, 62)	66 (60, 78)	69 (67, 72)
Gender (male %)	4 (100%)	2 (50%)	7 (54%)	2 (100%)
Smoking history				
Never	2 (50%)	3 (75%)	4 (31%)	0 (0%)
Former	2 (50%)	1 (25%)	8 (62%)	2 (100%)
Active	0 (0%)	0 (0%)	1 (7.7%)	0 (0%)
p16+	3 (100%)	4 (100%)	12 (92%)	2 (100%)
HPV testing modality				
ISH	1 (25%)	0 (0%)	0 (0%)	0 (0%)
PCR	3 (75%)	4 (100%)	13 (100%)	2 (100%)
Treatment modality				
Non-surgical	4 (100%)	3 (75%)	3 (23%)	1 (50%)
Surgical	0 (0%)	1 (25%)	10 (77%)	1 (50%)
Recurrence	2 (50%)	0 (0%)	6 (46%)	1 (50%)
Follow up (years)	3.4 (2.1, 4.9)	0.9 (0.4, 2.4)	1.1 (0.7, 2.7)	1.4 (1.1, 1.7)

NP: nasopharynx; ISH: in situ hybridization; PCR: polymerase chain reaction

Table 2. Pretreatment analysis

	Hypopharynx n = 2	**Larynx n = 2**	**NP/NC n = 7**	**Oral cavity n = 0**	***Total n = 11***
TP	2	2	4	-	*8*
FN	0	0	3	-	*3*
Sensitivity	100%	100%	57%	-	*73%*

TP: true positive; FN: false negative; NP/NC: nasopharynx/ nasal cavity

Table 3. Liquid biopsy values during treatment

	TTMV HPV+ fragments / mL				
Pt #: Subsite	**Pre-Tx**	**During Tx 1**	**During Tx 2**	**During Tx 3**	**During Tx 4**
1: NP/NC	10480	0	0	-	-
2: NP/NC	254	21	0	-	-
3: NP/NC	-	0	-	-	-
4: NP/NC	-	32	22	★ 30	0
5: NP/NC	300	0	-	-	-
6: HP	36	53	0	0	-
7: Larynx	273	41	-	-	-
8: Larynx	-	0	-	-	-

TTMV: tumor-tissue modified viral; Tx: treatment; HP: Hypopharynx; NP/NC: nasopharynx / nasal cavity
★ Disease progression identified on imaging (no progression identified for the other pts during treatment)

Table 4. Surveillance analysis

Subsite	**Hypopharynx n = 1**	**Larynx n = 1**	**NP/NC n = 9**	**Oral cavity n = 4**	***Total n = 13***
TP	4	0	3	1	*8*
FN	0	0	1	0	*1*
TN	0	1	7	1	*8*
FP	0	0	0	0	*0*
Sensitivity	100%	100%	75%	100%	*89%*
Specificity	-	100%	100%	100%	*100%*

TP: true positive; FN: false negative; TN: true negative; FP: false positive; NP/NC: nasopharynx/ nasal cavity