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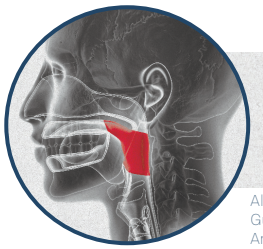
Optimizing HPV+ Cancer Care



Evolving Use of Circulating Tumor DNA for HPV+ Oropharyngeal Carcinoma: Consensus Recommendations From the California Head and Neck Consortium

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This paper presents the first set of professional recommendations for circulating tumor DNA (ctDNA) assays in HPV+ oropharyngeal squamous cell carcinoma, as defined and presented by the California Head and Neck Consortium. The Consortium notes that ctDNA assays are positioned to transform current disease surveillance paradigms, but there is a lack of guidance on their implementation and use.

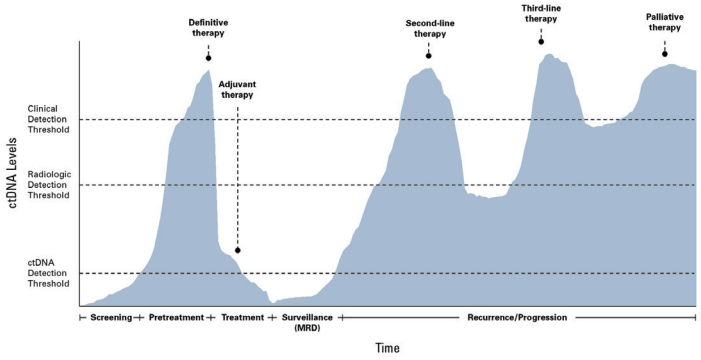
Thirty-three physicians from a cross-section of 15 institutions, including academic medical centers, integrated managed care systems, county hospitals, VA hospitals, community care centers, and private practice, delivered 33 statements across 5 subject domains. A hybrid Delphi approach was used to determine consensus over iterative rounds of feedback, with each statement achieving Strong Consensus, Consensus, No Consensus, or Rejected.

Key Takeaway

> The NavDx® test is the most clinically utilized ctHPVDNA assay. ctHPVDNA assays are now supported by expert consensus as a valuable adjunct to standard diagnostic and surveillance modalities in HPV+ OPSCC. The consortium recommended longitudinal, serial testing should be performed, rather than testing at a single post-treatment time point. However, treatment decisions (e.g., de-escalation) should remain confined to clinical trials and require additional investigation.

General Domain

ctHPVDNA assays exhibit higher specificity and sensitivity than conventional surveillance tools. While these assays are yet to demonstrate improved outcomes, the Consortium rejected the idea that detection of MRD will likely not affect outcomes, and said:



- Since surgical salvage is associated with better overall survival, earlier identification of locoregional recurrence should improve outcomes. Additionally, since oligometastatic disease is potentially curable with ablation (e.g., SBRT), earlier identification of distant recurrence should improve outcomes.
- ctHPVDNA should be incorporated into clinical trials evaluating treatment response and outcome and that large-scale, prospective randomized controlled trials are necessary to validate ctHPVDNA's role in HPV+ oropharyngeal cancer management.
- There was no consensus that ctHPVDNA is useful for all HPV-mediated head and neck cancers, including sinonasal and larynx.
- There was consensus that ctHPVDNA will likely increase costs associated with diagnosis, treatment, and surveillance.

Screening / Early Diagnosis

The Consortium recommends **against** using ctHPVDNA to screen the general population. There is strong consensus that doing so will artificially inflate outcomes through lead-time bias, whereby survival time appears extended irrespective of whether a patient truly lives longer. Further, ctHPVDNA without clinical or radiographic evidence of disease often increases patient distress.

Pre-Treatment

ctHPVDNA can confirm an HPV+ etiology in an oropharynx cancer diagnosis, in cases with indeterminate biopsies or occult primary cancers.

Obtaining baseline/pretreatment ctHPVDNA levels is important in order to use testing for post-treatment surveillance. There was no consensus on whether testing should be incorporated into the surveillance regimens of patients without baseline/pretreatment levels.

ctHPVDNA Should **Not** Be Used for:

Treatment Decisions: No consensus was reached on whether ctHPVDNA should be used to help guide management decisions for treatment intensification or deintensification. The Consortium recommends that treatment decisions not be made outside of an established clinical protocol at this time.

Disease Burden & Prognosis: The Consortium rejected the idea that baseline/pretreatment ctHPVDNA levels correlate with disease burden and prognosis and/or that in recurrence, quantitative ctHPVDNA levels correlate with disease burden (local, regional, distant) and prognosis.

Measurement of Treatment Response

In the M1 setting, ctHPVDNA levels during therapy offer earlier assessment of response compared to traditional imaging, enabling faster pivots to alternative regimens.

The Consortium rejected the idea that, during definitive treatment, changes in ctHPVDNA levels can be used to adapt therapeutic intensity (eg, radiation dose, number of cycles of chemotherapy).

They also rejected the idea that, during maintenance systemic therapy (eg, immunotherapy), negative ctHPVDNA results guide when to stop treatment.

Surveillance

The consortium achieved strong consensus that the recommended time to check the first post-treatment ctHPVDNA is 3 months; testing improves time to detection of cancer recurrence compared to conventional surveillance tools; ctHPVDNA levels are clinically or meaningfully useful to identify recurrence after treatment; testing should supplement conventional surveillance tools, rather than reducing or replacing them; and that longitudinal, serial testing should be performed, rather than testing at a single post-treatment time point.

If a Test is Positive:

- A single positive test should lead to immediate clinical exam and imaging.
- No consensus was reached on whether a single positive test should lead to repeat testing for confirmation.
- For patients with a single positive post-treatment test with no clinical or radiographic evidence of disease, the best time to repeat testing is 1 month.
- In patients with persistent ctHPVDNA levels after treatment, more intense imaging surveillance should be undertaken.

Testing Cadence:

- The recommended testing cadence after treatment, in conjunction with conventional surveillance, is q3mo (years 1-2) and q6mo (years 3-5; match routine surveillance visits).
- The Consortium reached consensus that testing is not recommended after year 5.
- Testing cadence should be more frequent for higher-stage cancers.

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