# Association of preoperative TTMV-HPV DNA serologic testing with clinical presentation and demographics

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## Background

Human papilloma virus (HPV)-associated oropharyngeal squamous cell carcinoma (HPV OPSCC) has increased in prevalence over the last several decades, now comprising a significant portion of patients treated for head and neck cancer. Because patients with HPV OPSCC tend to have more favorable outcomes than those with HPV-negative OPSCC, focus has shifted to balancing treatment-related morbidity with cancer recurrence and mortality. Multiple ongoing trials are assessing the feasibility of therapy de-escalation for patients with HPV OPSCC, with no current consensus. Circulating tumor tissue modified viral (TTMV)-HPV DNA has emerged as a test that may be useful in both diagnosis and surveillance of HPV-associated cancers. However, it is not yet understood whether pre-treatment values are associated with clinical characteristics or outcomes, and how that association would influence treatment recommendations. One group recently found that among 110 patients, pre-treatment TTMV-HPV DNA values were associated with clinical N stage at the time of diagnosis – higher values correlated with higher nodal stage and undetectable levels more likely to be associated with clinically N0 disease. This project aims to further define the relationship between pretreatment TTMV-HPV DNA level and clinical characteristics.

## Methods

This is a retrospective review of adult patients treated for HPV OPSCC at a tertiary academic center from April 2020 to October 2022. All patients had plasma TTMV-HPV DNA measured before initiation of primary therapy using a commercially available test (NavDx®, Naveris Inc., Natick MA). Demographics, baseline comorbidities, tobacco/alcohol use history, clinical stage at

presentation and pathologic stage (if applicable) were evaluated for associations with pretreatment TTMV-HPV DNA level.

## Results

104 patients treated for HPV OPSCC or HPV-positive cancer of unknown primary had pretreatment TTMV-HPV DNA testing. Patients were mostly male (90.4%), with an average age of 63. A majority were never-smokers (54.9%) without history of alcohol abuse (85.4%). HPV status was determined with immunohistochemical p16 staining and/or HPV typing via polymerase chain reaction (PCR). HPV16 subtype was most common (94.2%), followed by HPV33 (4.7%) and HPV35 (1.2%). Positive pretreatment TTMV-HPV DNA values were found in 92% of patients. Median preoperative TTMV-HPV DNA level was 438.5 (IQR 51.5-1910.8) with overall range of 0-63,000. In univariate analysis, greater preoperative values were not associated with baseline demographics or clinical stage at presentation. TTMV-HPV DNA level tended to be lower in the 4 patients with unknown primary tumors, but this did not reach statistical significance (p=.063). Additionally, patients who underwent surgery alone had lower average pretreatment TTMV-HPV DNA levels, though this difference was not statistically significant. An assessment of the relationship between TTMV-HPV DNA level and nodal burden demonstrated no association (p=.292), as all patients in this cohort with a negative pretreatment TTMV-HPV DNA test were stage N1 or N2 at presentation. This result contrasts with recently reported findings by Rettig et al.

## Conclusion

Further research is needed to determine whether any consistent associations exist between preoperative TTMV-HPV DNA levels and disease status at presentation. If any associations are present, we will need to determine the utility of this test in appropriate treatment selection for our patients.