

**Abstract Title:** *Prognostic Significance of Post-Treatment Circulating Tumor DNA as a Marker of Minimal Residual Disease Following Curative-Intent Therapy in Head and Neck Malignancies: A Systematic Review*

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**Introduction:**

Circulating tumor DNA (ctDNA) has emerged as a potential biomarker for detecting minimal residual disease (MRD) following curative-intent treatment. Although post-treatment ctDNA has demonstrated prognostic value in other malignancies, its role across the diverse spectrum of head and neck malignancies remains incompletely characterized. This systematic review aims to evaluate the association between detectable post-treatment ctDNA and oncologic outcomes following curative-intent therapy for head and neck malignancies.

**Methods:**

A systematic literature search was conducted using PubMed and Embase to identify studies evaluating post-treatment blood-based ctDNA in patients with head and neck malignancies treated with curative intent. The search encompassed squamous and nonsquamous head and neck malignancies and included both virus-associated ctDNA, including circulating HPV DNA, and virus-agnostic ctDNA assays. Eligible studies must evaluate ctDNA following definitive treatment and report oncologic outcomes. Studies evaluating both pre- and post-treatment ctDNA are eligible when post-treatment results are reported separately; studies evaluating pre-treatment ctDNA alone are excluded. The search yielded 11,039 records, of which 2,591 duplicates were removed, leaving 8,448 unique records for title and abstract screening. Screening by three independent reviewers is currently ongoing. Following study selection, data will be extracted regarding tumor type, treatment modality, ctDNA assay methodology, timing of post-treatment sampling, and oncologic outcomes, including recurrence and progression-free survival. Planned subgroup analyses will evaluate clinically relevant sources of heterogeneity, including HPV association and ctDNA assay characteristics.

**Results:**

At the time of abstract submission, 541 unique records had completed title and abstract screening by independent reviewers. Of these, 501 were excluded and 40 advanced for full-text eligibility assessment. Remaining screening is ongoing. Full-text review and subsequent data extraction

will identify studies meeting predefined eligibility criteria for post-treatment ctDNA assessment following curative-intent therapy.

**Conclusion:**

This systematic review will characterize the prognostic significance of post-treatment ctDNA as a marker of MRD across head and neck malignancies. By focusing specifically on ctDNA obtained following curative-intent therapy, this review seeks to clarify its potential utility for post-treatment risk stratification and surveillance and to identify areas requiring further investigation.