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HPV-SEQ NGS Assay

Ultra-sensitive liquid biopsy solution for the detection and quantification of circulating HPV 16 and HPV 18 DNA

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HPV 16 and HPV 18

Cell-free HPV DNA represents a promising surrogate of disease burden in patients with HPV-driven cancers

According to the CDC, approximately 36,000 cancer cases diagnosed each year are attributable to human papillomavirus (HPV).[1] Of the oncogenic HPV subtypes, HPV 16 and HPV 18 are the two most common high-risk HPV strains, and persistent infections are driving an increasing prevalence of HPV-associated cancers, including cervical, anal, and head and neck cancers.[2]

Cell-free HPV DNA (cfHPV-DNA) represents a promising surrogate of disease burden in patients with HPV-driven cancers. Research demonstrates that dynamic changes in HPV DNA levels correlate with treatment response.

Recently, clinical investigators have explored new strategies for cancer treatment de-escalation in an effort to optimize oncologic control as well as minimize over-treatment and unnecessary side-effects. Others are investigating the potential of cfHPV-DNA as a noninvasive biomarker for use in surveillance for cancer recurrence.

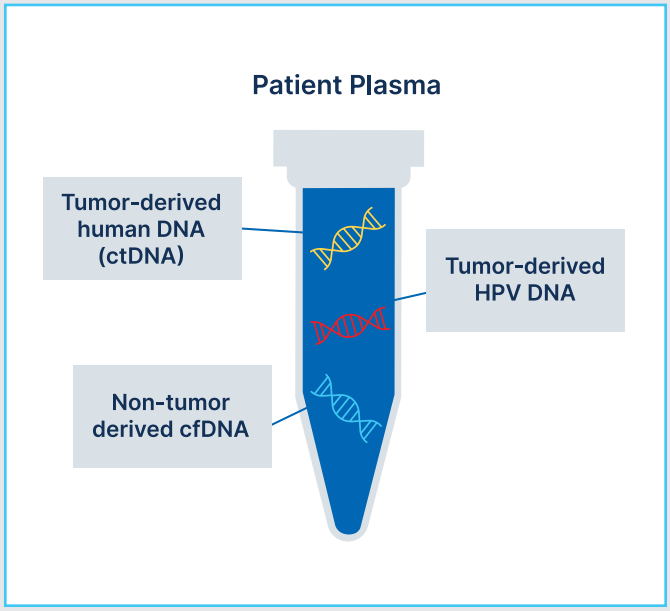
HPV-SEQ

Applying ultra-sensitive technology to detect and quantify circulating HPV DNA, HPV-SEQ is an innovative and exciting step forward in the development of more targeted approaches when managing HPV-associated cancers. Using the Plasma-Safe-SeqS NGS platform, cfHPV-DNA can be interrogated alongside tumor-derived mutations present in plasma (ctDNA).

HPV-SEQ is a clinical grade, ultra-sensitive liquid biopsy solution for the detection and quantification of circulating HPV 16 and HPV 18 DNA in patients with cancers caused by HPV infection.

Harnessing opportunity: cfHPV-DNA as a noninvasive biomarker for HPV-associated cancers

- Dynamic changes in HPV DNA levels have been shown to correlate with treatment response.
- Longitudinal HPV DNA monitoring may demonstrate utility for surveillance of cancer recurrence after curative-intent therapy.
- Using the Plasma-Safe-SeqS NGS platform, cfHPV-DNA can be interrogated alongside tumor-derived mutations present in plasma (ctDNA).
- Ultra-sensitive detection of cfHPV-DNA may enable more informed therapeutic approaches for management of HPV-driven cancers.



HPV-SEQ achieves ultra-sensitive detection and accurate quantification of HPV 16 and HPV 18 through a unique, proprietary method to better detect clinically meaningful changes.

HPV-SEQ enables highly sensitive, quantitative monitoring of cfHPV-DNA that facilitates noninvasive, precise evaluation of therapy response and tracking of disease burden during and after treatment.

Data demonstrates that patients with certain HPV-positive cancers have a favorable prognosis, which has led to interest in treatment de-escalation. By measuring cfHPV-DNA levels as a surrogate for tumor burden, clinicians may opt to modify, or de-escalate, treatment to avoid unnecessary toxicity and side-effects.

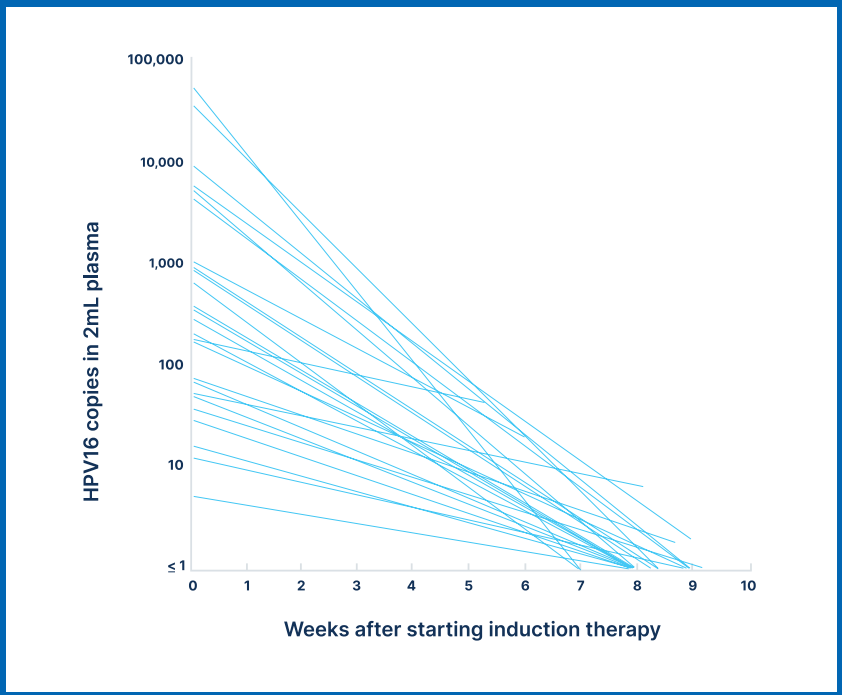
Treatment response[3]

HPV-SEQ has been employed to evaluate dynamic changes in circulating HPV alongside patients' radiographic assessment of therapy response to evaluate future utility in guiding treatment de-escalation strategies.

Longitudinal plasma samples were tested from patients with locoregional HPV+ oropharyngeal cancer treated in the OPTIMA 2 (NCT03107182) trial, a de-escalation protocol of induction chemoimmunotherapy followed by risk and response-adaptive treatment. HPV-SEQ showed robust quantitative detection of HPV 16 and HPV 18 across a broad dynamic range over five orders of magnitude. Importantly, there was high correlation between changes in patients' cfHPV-DNA levels and radiographic response following induction therapy.

The reliable and consistent sensitivity of HPV-SEQ, and its correlation to radiographic response, can bolster confident therapeutic decision-making for HPV-associated cancers. Prospective studies are underway to further evaluate the kinetics of cfHPV-DNA as a predictor of response to therapy in order to more precisely guide the management of patients with HPV-associated cancer.

DYNAMIC CHANGES IN PATIENTS' CFHPV-DNA LEVELS IN RESPONSE TO INDUCTION THERAPY[3]



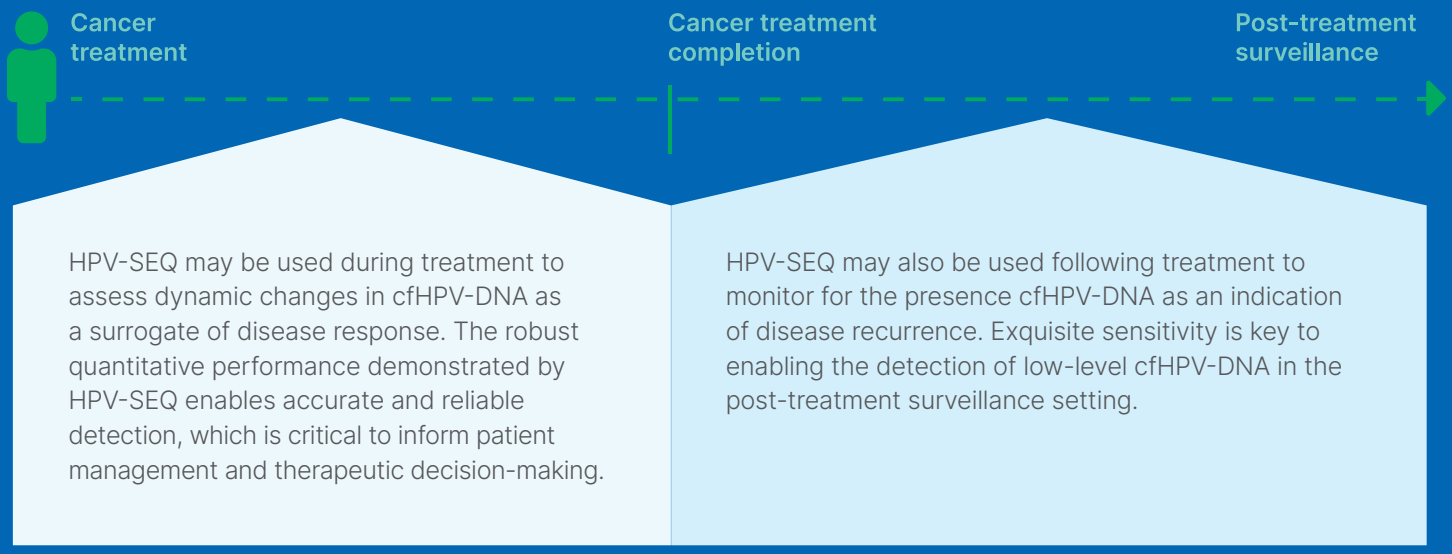
- Data displayed in the graph to the left represents changes in cfHPV-DNA levels from 25 patients undergoing induction therapy in the OPTIMA 2 trial.
- Plasma samples were collected from patients prior to induction therapy and 6-9 weeks after beginning therapy.
- Decreases in cfHPV-DNA levels were consistent with tumor response (determined radiographically post-therapy) observed in 24/25 (96%) patients.

Disease surveillance

Demonstrating ultra-sensitive detection of cfHPV-DNA, HPV-SEQ may also be employed as a surveillance tool to monitor patients for recurrence of disease following treatment for certain HPV-driven tumors.

In particular, patients with HPV-positive oropharyngeal squamous cell carcinoma (OPSCC) experience a more favorable prognosis than those with HPV-negative disease. Still, as many as one in four patients will ultimately develop disease recurrence, usually in the first two years following treatment, but in some cases up to five years or more.[4] Implementing HPV-SEQ for longitudinal monitoring of dynamic changes in HPV-DNA offers a more-informed approach to patient management over the surveillance period.

HPV-related cancer patient journey



Technology advantages

HPV-SEQ offers numerous advantages to biopharmaceutical sponsors exploring noninvasive solutions in the discovery and development of HPV cancer therapies:

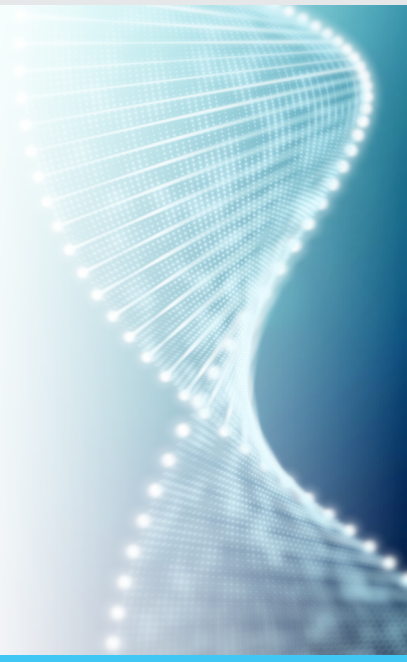
- Demonstrates **high analytical sensitivity**, with the ability to reliably and consistently detect low levels of HPV 16 and HPV 18 DNA.
- Exhibits **quantitative detection** of HPV DNA across a broad dynamic range, enabling **high-resolution molecular monitoring** for superior correlation with therapeutic benefit.
- Displays **low quantitative variability**.
- Demonstrates **low level of background signal** (<0.04 copies per sample across 20 healthy donor samples), indicating **high specificity**.[3]

Sample requirements and processing time

Sample specification
2×10mL tubes of whole blood

Pre-analytical sample handling
Sysmex Inostics' validated shipping kits and temperature loggers ensure sample stability

Result turnaround time
7 – 10 business days



HPV-SEQ for clinical development and patient management

Sysmex Inostics cfHPV-DNA and somatic mutation detection solutions represent a promising step forward for clinical development of novel therapeutic and patient management approaches for HPV-related cancers. HPV-SEQ is CLIA-validated and available to support clinical trials through the Sysmex Inostics turnkey testing service in its CLIA lab located in Baltimore, MD.

Have a question about HPV-SEQ?

Please email info@sysmex-inostics.com or visit www.sysmex-inostics.com/contact-us.

REFERENCES

1 US Centers for Disease Control. HPV and Cancer https://www.cdc.gov/cancer/hpv/statistics/cases.htm, accessed 7/7/2021.

2 Van Dyne, E.A. et al. (2018) Trends in Human Papillomavirus–Associated Cancers — United States, 1999–2015. MMWR Morb Mortal Wkly Rep. 67:918–24.

3 Sloane, H. et al. (2021) Ultra-sensitive detection and quantification of HPV DNA in the plasma of patients with oropharyngeal squamous cell carcinoma (OPSCC) enrolled in the OPTIMA 2 treatment de-escalation trial. J Clin Oncol. 39:15_suppl, 6048.

4 Chera, B.S. et al. (2020) Plasma Circulating Tumor HPV DNA for the Surveillance of Cancer Recurrence in HPV-Associated Oropharyngeal Cancer. J Clin Oncol. 38 (10), 1050-58.

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