NEWS RELEASE

Signatera™ in Head and Neck Cancer: Three New Publications Demonstrate Strong Clinical Performance and Actionability

2026-11-04

Findings show Signatera's predictive and prognostic abilities in a cancer that carries recurrence rates of up to 60%, along with excellent performance of the test in both HPV-positive and HPV-negative subtypes

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced three peer-reviewed publications in npj Precision Oncology, JAMA Otolaryngology, and Advances in Radiation Oncology, highlighting the performance of its Signatera test in head and neck squamous cell carcinoma (HNSCC).

HNSCC carries recurrence rates of up to 60% depending on stage, and traditional surveillance modalities (e.g., imaging) are limited by high rates of false-positive results and low sensitivity.1-3 Human papillomavirus (HPV) can be a major driver of HNSCC and defines two distinct forms of the disease, HPV-positive (HPV+) and HPV-negative (HPV-).

npj Precision Oncology

In an institutional cohort study, patients were prospectively tested with Signatera after curative-intent surgical resection. Key findings included:

- Predictive benefit: Post-operative, pre-adjuvant Signatera-status was predictive of adjuvant chemotherapy benefit in mucosal HNSCC. Among Signatera-positive patients, chemotherapy was associated with a 35% absolute reduction in 2-year locoregional recurrence (28.6% vs. 63.3% without). Signatera-negative patients

saw no difference in disease-free survival (DFS), locoregional recurrence, and distant metastases, regardless of adjuvant chemotherapy treatment.
- Outperformed high-risk factors: Signatera outperformed clinicopathologic risk factors for prognostication of disease free survival risk.

JAMA Otolaryngology

In this study of 168 patients, Signatera was evaluated in the pre-treatment and surveillance settings, with the following key findings:

- High baseline detection of molecular residual disease (MRD): 92.2% of pre-treatment samples were Signatera-positive.
- Strong MRD performance across HPV+ and HPV- patients: Serial Signatera testing showed 95.2% sensitivity and 99.4% negative predictive value, with 100% specificity and 100% positive predictive value in the surveillance setting.

Advances in Radiation Oncology

In a retrospective analysis of 97 patients with stage 1-4 HNSCC, key findings on Signatera's clinical utility during post-definitive treatment surveillance included:

- Advance detection of recurrence over imaging: Serial Signatera testing detected recurrence by a median of 4.3 months before radiographic progression, with 91.7% sensitivity and 96.4% specificity.
- Excellent MRD performance across HPV+ and HPV- subtypes: Signatera achieved 100% sensitivity in HPV+ patients, outperforming TTMV-HPV DNA assays commonly used to detect recurrence in this patient population. 4
- Multivariate analysis: Signatera-positivity was the only independent predictor of progression-free survival in a multivariate analysis, outperforming clinical stage, p16 status, and tumor location.

"Head and neck cancer is difficult to treat and carries high recurrence rates, underscoring the importance of catching relapse as early as possible," said Michael Krainock, MD, PhD, MBA, Medical Director, Oncology, Natera. "Collectively, these new studies demonstrate Signatera's ability to detect recurrence well in advance of clinical signs and predict which patients were likely to benefit from adjuvant chemotherapy."

References

1. Hulse K, Hurley R, Lowit A, Maguire R, Paterson C, Douglas CM. Patient-reported symptoms in the detection of head and neck cancer recurrence: a systematic review. Front Oncol. 2025;15:1632592
2. NCCN Clinical Practice Guidelines in Oncology. Head and Neck Cancers. V2.2026
3. Isles, M.G., McConkey, C. and Mehanna, H.M. (2008), A systematic review and meta-analysis of the role of positron

emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy. Clinical Otolaryngology, 33: 210-222. **https://doi.org/10.1111/j.1749-4486.2008.01688.x**.
4. Ferrandino RM, Chen S, Kappauf C, et al. Performance of Liquid Biopsy for Diagnosis and Surveillance of Human Papillomavirus–Associated Oropharyngeal Cancer. JAMA Otolaryngol Head Neck Surg. 2023;149(11):971–977. doi:10.1001/jamaoto.2023.1937

About Natera

Natera is a global leader in cell-free DNA and precision medicine, dedicated to oncology, women's health, and organ health. We aim to make personalized genetic testing and diagnostics part of the standard-of-care to protect health and inform earlier, more targeted interventions that help lead to longer, healthier lives. Natera's tests are supported by more than 400 peer-reviewed publications that demonstrate excellent performance. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas, San Carlos, California, and Boulder, Colorado. For more information, visit **www.natera.com**.

Forward-Looking Statements

All statements other than statements of historical facts contained in this press release are forward-looking statements and are not a representation that Natera's plans, estimates, or expectations will be achieved. These forward-looking statements represent Natera's expectations as of the date of this press release, and Natera disclaims any obligation to update the forward-looking statements. These forward-looking statements are subject to known and unknown risks and uncertainties that may cause actual results to differ materially, including with respect to whether the results of clinical or other studies will support the use of our product offerings, the impact of results of such studies, our expectations of the reliability, accuracy, and performance of our tests, or of the benefits of our tests and product offerings to patients, providers, and payers. Additional risks and uncertainties are discussed in greater detail in "Risk Factors" in Natera's recent filings on Forms 10-K and 10-Q, and in other filings Natera makes with the SEC from time to time. These documents are available at **www.natera.com/investors** and **www.sec.gov**.

Investor Relations: Mike Brophy, CFO, Natera, Inc., **investor@natera.com**
Media: Lesley Bogdanow, VP of Corporate Communications, Natera, Inc., **pr@natera.com**

Source: Natera, Inc.