NEWS RELEASE

Two Publications Highlight Clinical Utility of Signatera™ in Anal and Rectal Cancers

2026-03-16

New findings show that Signatera status can help identify high-risk patients and inform non-operative management and surveillance strategies

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced two peer-reviewed publications highlighting the clinical utility of Signatera, its personalized, tumor-informed circulating tumor DNA (ctDNA) assay, in anal squamous cell carcinoma (ASCC) and locally advanced rectal cancer (LARC).

ASCC: publication in **Nature Communications**

A recently published study evaluated 84 patients with ASCC to assess whether serial Signatera testing may offer a dynamic, treatment-responsive biomarker to further stratify recurrence risk and inform surveillance and treatment. Key findings include:

- Signatera-status was strongly correlated with clinical outcomes. Patients who were Signatera-negative at baseline or cleared ctDNA during chemoradiotherapy (CRT) had favorable outcomes, including 100% one-year overall survival and progression-free survival, and 0% one-year local regional failure. Patients who remained ctDNA-positive after CRT had poorer outcomes (63% OS, 44% PFS, 39% locoregional failure at one year).
- In 100% of recurrent cases, Signatera-positivity preceded clinical and/or radiographic recurrence highlighting ctDNA's potential as an early indicator of relapse.

LARC: publication in **Cancers**

Another recent study evaluated 220 patients with LARC treated with neoadjuvant therapy (NAT) followed by non-operative management (NOM) (n=72) or surgery (n=148). The study examined how Signatera status after NAT may inform patient selection for organ-preserving NOM versus surgery and guide intensified surveillance strategies. Key findings include:

- Signatera identified post-NAT patients at high risk of relapse requiring surgical intervention. Signatera-positive NOM patients were at 4.6x higher risk of regrowth requiring surgery (HR 4.62; p=0.003), even among those with a complete or near-complete clinical response.
- Post-operative Signatera negativity was associated with excellent clinical outcomes. Signatera-negative patients (HR:15, p=0.001) experienced a relapse rate of 11.5% compared to 88.0% among Signatera-positive patients (p<0.0001).

“Together, these publications address key questions about monitoring treatment response and recurrence risk in anal and rectal cancers,” said Alexey Aleshin, M.D., MBA, corporate chief medical officer and general manager of oncology at Natera. “By providing earlier insight into molecular residual disease, Signatera can support more individualized surveillance and treatment decisions.”

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, and San Carlos, California, and through Foresight Diagnostics, its subsidiary, operates an ISO 27001-certified and CAP-accredited laboratory certified under CLIA in 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**.

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Source: Natera, Inc.