NEWS RELEASE

Signatera™ Monitoring During First-Line Immunotherapy Showed ctDNA Clearance is Associated with Long-Term Survival Across Four Metastatic Cancers

2026-11-05

New data at SITC includes real-world analysis highlighting that Signatera can inform immunotherapy duration and optimize treatment

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced it will present important new Signatera data at the Society for Immunotherapy of Cancer (SITC) Annual Meeting, taking place November 4–8 in Phoenix, Arizona.

Immune checkpoint inhibitors (ICIs) have transformed treatment for many metastatic cancers, and some patients achieve durable disease control.1 However, it remains challenging for clinicians to determine how long to continue therapy, since imaging alone is prone to error and cannot show whether disease has cleared at the molecular level.2,3 As a result, treatment duration remains an open question, particularly for patients who achieve a durable clinical response.

A real-world analysis at SITC studied outcomes of 424 patients treated with first-line immunotherapy across stage IV melanoma, renal cell carcinoma, microsatellite instability-high (MSI-H) colorectal cancer (CRC), and non-small cell lung cancer (NSCLC). The Signatera test was used to identify complete molecular responders (CMRs), defined as patients with two consecutive negative results. Findings showed:

- Improved survival in Signatera MRD-negative patients: CMRs had a 36-month overall survival (OS) of 93.2% vs.

77.9% in all other patients (HR 0.24; P=0.0003).

- Favorable survival across tumor types: At 36 months, OS in CMRs ranged from 83.1% (NSCLC) to 100% (MSI-H CRC).
- No significant survival difference with early ICI discontinuation: OS for CMRs who remained on IO was 93.5% vs. those who stopped (89.4%) (P=0.42).

"For patients with metastatic cancer who achieve a durable response, deciding how long to continue immunotherapy is one of the most difficult clinical decisions," said Meghan J. Mooradian, MD, Cutaneous Medical Oncology, Mass General Brigham Cancer Institute, and lead author of the study. "Because imaging alone may not fully capture whether disease has been completely cleared, our findings support further investigation of molecular response as a biomarker to help personalize treatment duration and identify patients who may discontinue therapy early."

"Melanoma, kidney, lung, and colorectal cancers differ biologically, yet sustained Signatera negativity was associated with favorable survival in each," said Alexey Aleshin, MD, Corporate Chief Medical Officer and General Manager, Oncology, Natera. "These data support the role of Signatera in identifying exceptional ICI responders who may be able to de-escalate treatment."

References

1. Wolchok JD, et al. Final, 10-Year Outcomes with Nivolumab plus Ipilimumab in Advanced Melanoma. N Engl J Med 2025;392:11-22.
2. Steimle AK, et al. Circulating Tumor DNA (ctDNA) Clearance After Immune Checkpoint Inhibition (ICI) with Radiotherapy (RT) as a Prognostic Biomarker for Advanced Melanoma. Cancers 2026;18(18):3032.
3. Anagnostou V, et al. Immuno-oncology trial endpoints: Capturing clinically meaningful activity. Clin Cancer Res 2017;23(17):4959-69.

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.