NEWS RELEASE

Signatera™ MRD Outperformed AMERK Testing in Predicting Merkel Cell Carcinoma Recurrence in JAMA Dermatology Study

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Signatera outperformed AMERK, the current standard of care for prognosis and recurrence monitoring, across sensitivity, positive and negative predictive value, and lead time to recurrence

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced the publication of results from a prospective, multicenter study in Merkel cell carcinoma (MCC) **published** in JAMA Dermatology. The study evaluated the Signatera test against the Merkel cell polyomavirus antibody test (AMERK), finding Signatera to be a significantly stronger predictor of recurrence that also detected relapse earlier.

MCC is a rare but aggressive skin cancer that recurs in approximately 40% of patients.1 Despite its severity, clinicians have lacked a reliable, universal biomarker to guide surveillance. The AMERK test has been a widely used monitoring tool, but its utility is limited: it can only be used in the roughly 50% of MCC patients whose tumors are virus-positive, and its accuracy diminishes after immunotherapy exposure or multiple recurrences.2-3 Signatera's clinical validation has been **published** across all MCC patients, irrespective of viral status, leading to inclusion in NCCN Guidelines as a recommendation for surveillance monitoring.

This published study is a retrospective analysis of a prospective, multicenter, head-to-head comparison of Signatera and AMERK testing in 169 patients with MCC. Key findings include:

- Superior predictive power: The Signatera test was a significantly stronger predictor of recurrence than AMERK

(HR difference = 6.6; $p < 0.001$), with higher hazard ratios, higher positive predictive value (PPV), and higher negative predictive value (NPV).

- Higher Sensitivity: Signatera detected recurrence more frequently than AMERK with a sensitivity of 90% vs 55%, respectively.
- Longer Lead Time: In patients where recurrence was detected by both tests, Signatera detected recurrence earlier than AMERK with a median lead time of 5.1 months vs. 2.1 months, respectively.

"For years, AMERK had been our best available tool, but its inability to function in virus-negative patients and after immunotherapy has been a recognized limitation," said Lisa Zaba, M.D., Ph.D., associate professor of dermatology and director of the Merkel cell carcinoma multidisciplinary clinic at the Stanford University School of Medicine, and corresponding author of the study. "These data demonstrate that Signatera can give clinicians a more precise and earlier signal across all patients, enabling more proactive management of this challenging disease."

"Signatera MRD testing outperformed AMERK across every key measure in this study — sensitivity, hazard ratios, predictive values, and lead time to detection," said Alexey Aleshin, M.D., MBA, corporate chief medical officer and general manager, oncology, at Natera. "Signatera was shown to be a more universally reliable biomarker for MCC surveillance, particularly because it retains its accuracy in both virus-positive and virus-negative disease and after exposure to immunotherapy."

References

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2. Paulson KG, Lewis CW, Redman MW, et al. Viral oncoprotein antibodies as a marker for recurrence of Merkel cell carcinoma: a prospective validation study. Cancer. 2017;123(8):1464-1474. doi: **10.1002/cncr.30475**
3. Miller DM, Shalhout SZ, Wright KM, et al. The prognostic value of the Merkel cell polyomavirus serum antibody test: a dual institutional observational study. Cancer. 2024;130(15):2670-2682. doi: **10.1002/cncr.35314**

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 our 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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