NEWS RELEASE

Natera Announces New Study Highlighting the Benefits of Signatera's Unique Method of Quantifying ctDNA

12/21/2023

Pan-cancer study showed MTM/mL dynamics were more predictive of therapy response than mVAF dynamics, with an observed hazard ratio nearly 2x higher

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced a new study published in Molecular Oncology comparing the performance of mean tumor molecules per milliliter (MTM/mL) against mean variant allele frequency (mVAF) for measuring circulating tumor DNA (ctDNA), using Signatera™, Natera's personalized and tumor-informed molecular residual disease (MRD) test. The full study can be found **here**.

To date, mVAF and MTM/mL are the two main metrics that have been used to quantify ctDNA levels in the blood. Unlike mVAF, which is a fraction that can be confounded by changes in total background cfDNA, MTM/mL takes into account total cfDNA as well as plasma volume. The premise is that MTM/mL is therefore more representative of a patient's true disease burden, a hypothesis that was validated in this study.

The study analyzed ctDNA data generated in 55,183 ctDNA-positive samples from 23,543 patients who underwent testing with Signatera for various cancer diagnoses, and it reported the correlation between MTM/mL and mVAF, as well as the correlations of each with patient outcomes.

Key findings include:

- Among the 18,426 patients with longitudinal ctDNA measurements, 13.3% had discordant ctDNA trajectories (increase/decrease) when calculated using MTM/mL versus mVAF.
- In patients with stage IV disease receiving immunotherapy (N=51), ctDNA dynamics measured in MTM/mL were more predictive of therapy response than those measured in mVAF, with a hazard ratio (HR) nearly 2x higher (MTM/mL HR 16, p<0.0001; mVAF HR 8.8, p<0.0001).
- In a case study of a patient with metastatic triple-negative breast cancer, disease progression during systemic therapy was reflected in increasing MTM/mL values, while mVAF levels remained stable.

“We are pleased to see the publication of these important findings, in which MTM/mL provided a more accurate measure of ctDNA than mVAF, particularly for patients undergoing active therapy which can impact the levels of background cfDNA,” said Minetta Liu, M.D., chief medical officer of oncology at Natera. “Clinicians need tools to enable reliable predictions of therapy response and clinical outcomes. As the only MRD test that uses MTM/mL, this study supports the utility of Signatera for ctDNA quantification, to measure treatment response at critical time points and inform decisions on how patients are managed.”

About Signatera

Signatera is a personalized, tumor-informed, molecular residual disease test for patients previously diagnosed with cancer. Custom-built for each individual, Signatera uses circulating tumor DNA to detect and quantify cancer left in the body, identify recurrence earlier than standard of care tools, and help optimize treatment decisions. The test is available for clinical and research use and is covered by Medicare for patients with colorectal cancer, breast cancer (stage IIb and higher) and muscle invasive bladder cancer, as well as for immunotherapy monitoring of any solid tumor. Signatera has been clinically validated across multiple cancer types and indications, with published evidence in more than 50 peer-reviewed papers.

About Natera

Natera™ is a global leader in cell-free DNA testing, 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 validated by more than 180 peer-reviewed publications that demonstrate high accuracy. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas and San Carlos, California. 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.