



NEWS RELEASE

Signatera™ MRD Test Predicted Overall Survival Benefit from Chemotherapy in Resected Metastatic Colorectal Cancer

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Newly published study shows Signatera MRD-positive patients lived longer with adjuvant chemotherapy, while MRD-negative patients saw no significant benefit

First predictive data for overall survival from GALAXY trial in patients with oligo-metastatic CRC in the liver

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced the **publication** of new data in JAMA Oncology, evaluating the utility of Signatera, its personalized molecular residual disease (MRD) test, in patients with resected colorectal liver metastases (CRLM). The data was also presented as an oral presentation at the 2026 European Society for Medical Oncology Gastrointestinal (ESMO GI) Congress.

The liver is the most common site of distant metastasis in colorectal cancer, and CRLM is a major cause of cancer-related mortality.^{1,2} In patients where curative-intent surgery is possible, the benefit of adjuvant chemotherapy (ACT) has been a point of debate and uncertainty.³ MRD status has previously been shown to predict a disease free survival (DFS) benefit from ACT, but not an overall survival (OS) benefit. This is the first dataset in a large cohort to show MRD test prediction of OS from ACT in this population.

The JAMA paper included 298 patients from the GALAXY trial, the prospective, observational arm of CIRCULATE-Japan. Outcomes were evaluated according to MRD status and whether patients received ACT, with a median follow-up of 43 months. Key findings included:

- Signatera identified patients who derive a significant survival benefit from ACT. Among MRD-positive patients who underwent surgery without neoadjuvant chemotherapy, ACT was associated with improved DFS and OS compared to observation (OS: adjusted HR, 0.27; P=0.03; 48-month OS, 65.3% vs. 32.9%; DFS: adjusted HR, 0.07; P<0.0001). MRD-negative patients had favorable outcomes, with no observed survival benefit from ACT.
- Post-surgical MRD status was strongly prognostic. MRD positivity 2–10 weeks after surgery was associated with significantly worse DFS and OS, including those who received neoadjuvant chemotherapy before surgery (DFS: HR, 4.82; P<0.0001; OS: HR, 9.43; P<0.001), and those who did not (DFS: HR, 4.14; P<0.0001; OS: HR, 9.13; P<0.0001).

“For patients with colorectal liver metastases, the benefit of ACT after curative-intent surgery has remained uncertain,” said Kozo Kataoka, M.D., Ph.D., division of lower GI, department of gastroenterological surgery, Hyogo Medical University, and senior author of the study. “Importantly, this is the largest analysis to show that post-surgical MRD status may help identify which patients benefit from ACT in patients who underwent upfront surgery.”

“This analysis adds important overall survival data in resected colorectal liver metastases, a setting where clinicians have historically had limited tools to determine who is most likely to benefit from ACT,” said Adham Jurdi, M.D., senior medical director of oncology at Natera. “It further reinforces how Signatera can help tailor treatment to each patient.”

References

1. Adam R, de Gramont A, Figueras J, Kokudo N, Kunstlinger F, Loyer E, et al. Managing synchronous liver metastases from colorectal cancer: a multidisciplinary international consensus. *Cancer Treat Rev*. 2015;41(9):729-41.
2. Filho AM, Laversanne M, Ferlay J, Colombet M, Piñeros M, Znaor A, et al. The GLOBOCAN 2022 cancer estimates: Data sources, methods, and a snapshot of the cancer burden worldwide. *Int J Cancer*. 2025;156(7):1336-46.
3. Adam R, Kitano Y. Multidisciplinary approach of liver metastases from colorectal cancer. *Ann Gastroenterol Surg*. 2019;3(1):50-6.

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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