Contact: Michele Rest
press@guardanthealth.com

Backgrounder: Guardant Reveal™ liquid biopsy test

The first blood-only liquid biopsy test for residual disease and recurrence monitoring, starting with early-stage colorectal cancer

For early-stage cancer patients and their oncologists, two fundamental questions remain after surgery: Does any cancer remain? What is the risk of the cancer returning? Guardant Reveal™ is the first liquid biopsy test that detects residual and recurrent disease in 7 days from a simple blood draw, helping to answer these questions by serving as a:

- ***Risk assessment tool** that identifies high-risk patients who are most likely to recur and may benefit most from adjuvant chemotherapy and active surveillance*
- ***Surveillance tool** that can be performed regularly to detect minimal residual disease (MRD) months earlier than current standard of care*

Incidence and mortality of colorectal cancer (CRC) today

- CRC remains the second leading cause of cancer death in the U.S.[1]
- Each year, roughly 150,000 people will be diagnosed with CRC in the U.S.[1]
- There are more than 1.5 million CRC survivors in the U.S.[1]
- The majority of CRC patients are diagnosed at an early stage (I to III)[2]
- Survival rates are improved when detected at earlier stages: 5-year survival rates for CRC are 80-90% at localized stage (stage I), 71% at regional stage (stage II and III), and only 14% at distant stage (stage IV)[3]
- The 5-year recurrence rate for early-stage CRC ranges from 10-30%[3], making recurrence monitoring critical

A clear unmet medical need exists given currently available risk assessment and surveillance tools

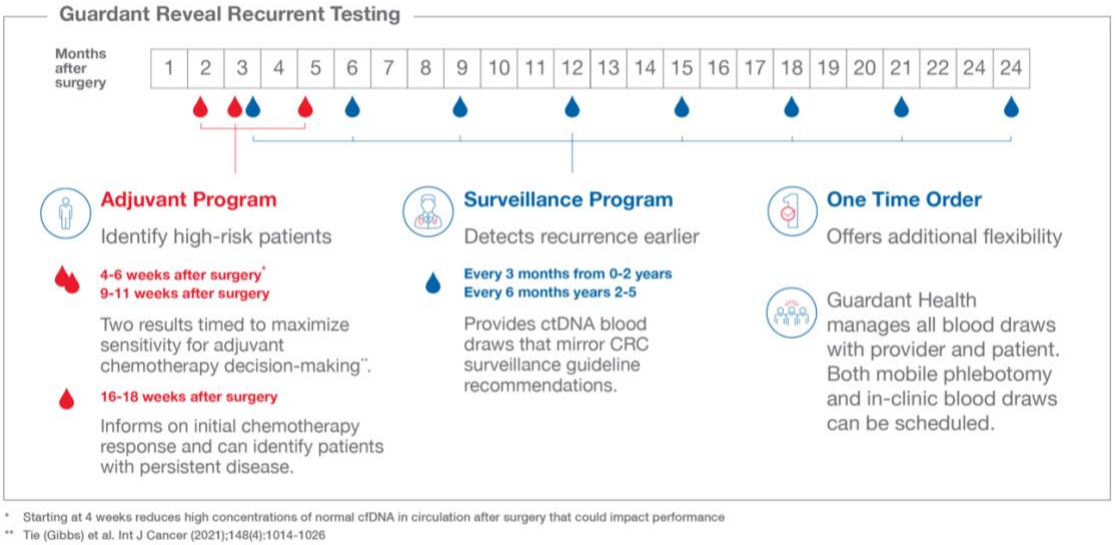
- Current clinicopathologic tools are limited in their ability to correctly identify patients at high risk of recurrence who may benefit most from adjuvant chemotherapy[4-8]
- Recent retrospective analysis shows that nearly 1 in 5 patients not selected to receive adjuvant chemotherapy have detectable circulating tumor DNA (ctDNA) 4 weeks after surgery[9], making them potential candidates for adjuvant chemotherapy
- Current standard of care for detection of early-stage CRC recurrence, carcinoembryonic antigen (CEA) protein tests, demonstrate low sensitivity and often miss recurrence[10]
- CT scans and MRI, while effective at detecting growing or new lesions, do not reliably detect recurrence early enough when the cancer may still be treated most effectively[11]

Introducing the Guardant Reveal test for residual and recurrent disease monitoring from a simple blood draw

The now commercially available liquid biopsy test allows oncologists to improve the management of early-stage CRC patients by quickly and conveniently detecting the presence of ctDNA from blood, without the need for tissue

- Circulating tumor DNA (ctDNA) outperforms standard-of-care CEA and all currently used clinicopathologic features at predicting risk for patients at high risk of recurrence
    - Most patients with ctDNA detected after surgery will eventually recur[9]
    - ctDNA predicts more high-risk patients than CEA and all current clinicopathological features[4-8]
    - Evidence suggests 20-30% of ctDNA+ patients may be treated effectively with adjuvant chemotherapy to prevent recurrence and have good outcomes[4-8]
    - The Guardant Reveal test shows 91% sensitivity[12] for correctly detecting ctDNA at different surveillance timepoints
- Innovative Guardant Reveal technology enables groundbreaking performance, speed, and ease of use
    - Interrogates two signals, genomic alterations and methylation, to achieve high sensitivity
    - Distinguishes between cancerous tumor and non-tumor signals without the need for tissue biopsy

  - Provides results in only 7 days for faster time to treatment and easier surveillance
  - Can be initiated at any time, as soon as 4 weeks after surgery
- Guardant Reveal improves the management of early-stage CRC for oncologists across multiple timepoints:



* Starting at 4 weeks reduces high concentrations of normal cfDNA in circulation after surgery that could impact performance
** Tie (Gibbs) et al. Int J Cancer (2021);148(4):1014-1026

The first indication for Guardant Reveal is early-stage CRC with additional cancer types to follow.

Transforming cancer care across the continuum through liquid biopsy

Guardant Health's vision is to transform cancer care across all stages of the disease through the power of blood. This includes for advanced cancer patients, early-stage patients, and asymptomatic people.

The company started in 2014 with the Guardant360® test for advanced cancer patients. It was the first-in-kind liquid biopsy to comprehensively sequence a patient's cancer to reveal actionable mutations for precision medicine treatment decisions. The blood test overcame challenges of tissue biopsy to enable faster, easier, more complete genomic testing, and in 2020 the Guardant360® CDx test became the first FDA-approved comprehensive liquid biopsy. Advanced cancer and the company's work with its Guardant360 test has laid the foundation, with each blood sample sequenced fueling progress toward earlier cancer management.

In 2021, the introduction of the Guardant Reveal™ test for residual disease and recurrence monitoring of early-stage cancer marks the next important step along the cancer care continuum. The innovative test holds the promise to transform management of early-stage cancer for millions of patients and survivors. Studies are currently underway to validate the clinical utility in practice of the Guardant Reveal test (COBRA Escalation Trial, ACT-III Escalation Trial, and PEGASUS De-Escalation Trial) as well as the LUNAR-2 test for early-stage CRC detection and screening (ECLIPSE Trial).

References:

1. www.cancer.org/cancer/colon-rectal-cancer/about/key-statistics.html Accessed online Feb 5, 2021.
2. Chakrabarti S, Peterson C, Sriram D, Amit Mahipal A, et al. Early stage colon cancer: Current treatment standards, evolving paradigms, and future directions. *World J Gastro Oncol*. 2020 Aug 15; 12(8): 808–832.
3. American Cancer Society: Colorectal Cancer Facts & Figured 2020-2022. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/colorectal-cancer-facts-and-figures/colorectal-cancer-facts-and-figures-2020-2022.pdf. Accessed online Feb 5, 2021.
4. Reinert T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. *JAMA Oncology*. 2019; 5 (8): 1125-1131.
5. Tie J, Wang Y, Tomasetti C, Li L, Springer S, et al. Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer. *Science Translational Medicine*. 2016; 8 (346): 346ra92.
6. Tie J, Cohen J, Wang Y, et al. Circulating Tumor DNA Analyses as Markers of Recurrence Risk and Benefit of Adjuvant Therapy for Stage III Colon Cancer. *JAMA Oncology*. 2019; 5(12): 1710-1717.
7. Peng J, Li Y, Mo S, Ma X, Hu X, Zhang L, et al. Prognostic value of circulating tumor DNA (ctDNA) detection during adjuvant chemotherapy in patients with stage III colorectal cancer: The interim report of a prospective, observational study. *Journal of Clinical Oncology*. 2020; 38, no.4_suppl.
8. Tarazona N, Gimeno-Valiente F, Gambardella V, et al. Targeted next-generation sequencing of circulating-tumor DNA for tracking minimal residual disease in localized colon cancer. *Annals of Oncology*. 2019; 30 (11): 1804-1812.
9. Parikh A, Van Seventer E, Marie Boland G, Hartwig A, Jaimovich A, Raymond V, et al. A plasma-only integrated genomic and epigenomic circulating tumor DNA (ctDNA) assay to inform recurrence risk in colorectal cancer (CRC). *Journal of Clinical Oncology*. May 2019:3602-3602.
10. Shinkins B, Nicholson B, Primrose J, et al. The diagnostic accuracy of a single CEA blood test in detecting colorectal cancer recurrence: Results from the FACS trial. PLoS One. 2017; 12(3): e0171810.
11. Young P, Womeldorph C, Johnson E. Early Detection of Colorectal Cancer Recurrence in Patients Undergoing Surgery with Curative Intent: Current Status and Challenges. *Journal of Cancer*. 2014; 5(4): 262–271.
12. Parikh A, Van Seventer E, Siravegna G, Hartwig A, et al. Minimal Residual Disease Detection using a Plasma-Only Circulating Tumor DNA Assay in Colorectal Cancer Patients. *Clinical Cancer Research*. April, 2021; 10.1158/1078-0432.CCR-21-0410.