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Backgrounder: FDA-Approved Guardant360® CDx

Guardant360® CDx liquid biopsy is helping to bring the promise of precision oncology to more advanced cancer patients

Comprehensive genomic profiling (CGP), also known as biomarker testing, genotyping, or tumor profiling, is a test that looks at the DNA of a patient's tumor to identify its genomic alterations. Knowing these alterations, for example an EGFR *mutation in a lung cancer patient, enables doctors to match a patient with the right precision medicine, which can significantly extend survival compared to chemotherapy alone.[1-7] However, due to the challenges of traditional tissue biopsy, many patients today are not receiving CGP before starting treatment.*

Reliance on traditional tissue biopsy has created a state of emergency when it comes to CGP

Doctors want the best treatment fast for their patients, and waiting for tissue biopsy results, which may take many weeks or longer, can delay treatment. Doctors also may not be informed of the latest guidelines and treatment options. As a result, CGP is tragically underperformed for advanced cancer patients today:

- 80% of patients with advanced non-small cell lung cancer[8] and 60% of patients with advanced colon cancer do not receive guideline-recommended CGP[9]
- 50% of patients with prostate cancer and 33% with breast cancer have bone-only metastases, making tissue biopsies difficult[10]

Guardant360® liquid biopsy overcomes the challenges of tissue biopsy to help widen adoption of CGP

Many doctors forgo CGP and rush to prescribe chemotherapy or immunotherapy, which is not always right, due to the inherent challenges that tissue biopsies present:

- Requires significant tissue, more than may be available
- Repeated biopsies can expose patients to potential adverse events[11]
- Results can take many weeks or longer, and can be incomplete
- Staff burden requires coordination with multiple care team members

Guardant360® liquid biopsy overcomes these challenges across all advanced solid cancers:

- Non-invasive and faster results in only 7 days (instead of many weeks or longer)
- Enables complete genomic profiling for 3x more patients than tissue*
- Trusted by 9,000+ oncologists in more than 150,000 tests to date
- Clinically validated with more than 200 peer-reviewed publications
- Broadly covered by Medicare and many private payers, representing 200 million+ lives

With FDA approval, Guardant360 CDx liquid biopsy presents a potential new standard for CGP

Guardant360 CDx is now FDA approved for tumor mutation profiling, or CGP, in advanced cancer patients across all solid cancers, and for use as a companion diagnostic to identify non-small cell lung cancer (NSCLC) patients who may benefit from Tagrisso® (osimertinib), RYBREVANT™ (amivantamab-vmjw), and LUMAKRAS™ (sotorasib). The test is also being pursued as a companion diagnostic for investigational products in development by other collaborators in addition to AstraZeneca, Janssen, and Amgen, including Daiichi Sankyo, Inc. and Radius Health, Inc.

The FDA approval of Guardant360 CDx is an important milestone, demonstrating the value liquid biopsy brings to oncologists and, more importantly, the patients they treat. The ease of the Guardant360 CDx blood test together with approval of the FDA is expected to help widen adoption of CGP and enable more patients to receive potentially life-changing precision medicines. FDA approval also marks a milestone for Guardant Health in our mission to conquer cancer with data. Since our inception, we've been dedicated to unlocking the potential of liquid biopsy to transform cancer care at all stages of the disease.

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Guardant360 CDx helps inform the rapidly growing number of targeted therapies for patients

Targeted therapies that can be informed by the Guardant360 CDx test are already approved for use in many cancers including lung, breast, colorectal, and prostate. This growing number of approved targeted therapies and those in development demonstrates the increasing importance of CGP and precision oncology for advanced cancer patients:

Cancer	Guideline-recommended biomarkers	FDA-approved matched targeted therapy	Opportunities in clinical practice
Non-small cell lung	*EGFR, ROS1, ALK, BRAF, NTRK1, MET, RET, ERBB2, KRAS*	*EGFR, ROS1, ALK, BRAF, NTRK1, KRAS G12C*	21% of advanced NSCLC patients have alterations associated with currently FDA-approved drugs[12] and now with additional approvals this number is even higher
Breast	*PIK3CA, ERBB2 (HER2), BRCA1/2*	*PIK3CA, ERBB2 (HER2), BRCA1/2, NTRK1*, MSI	40% of HER2 negative patients have *PIK3CA* mutation[13]
Colorectal	MSI, *KRAS, NRAS, BRAF, NTRK1, ERBB2*	MSI, *BRAF, NTRK1*	72% of patients who receive anti-EGFR therapy did not have guideline-aligned *RAS* and *BRAF* testing to determine eligibility for that treatment[9]
Prostate	MSI, *BRCA1/2*	MSI, *BRCA1/2, NTRK1*	Emerging data suggests 15-25% of patients with advanced prostate cancer have BRCA1/2 alterations and may benefit from PARP inhibitors[14]

Guardant Health is leading the way for liquid biopsy to help patients across the cancer care continuum

In 2014, we introduced 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. Our test overcame the challenges of tissue biopsy to allow for faster, easier CGP. In 2019, a landmark head-to-head prospective study demonstrated Guardant360's high concordance with tissue testing and consistent results with numerous other studies.

Advanced cancer, and our work with Guardant360, is the foundation of our efforts so far, and we are now poised to transform cancer management in earlier stage cancers. Each Guardant360 blood sample we sequence contributes to real-world data that fuels this progress. For cancer survivors, our Guardant Reveal™ blood test detects residual and recurrent disease in early-stage cancer patients, starting with colorectal cancer, to help inform adjuvant treatment decisions and monitor recurrence. For asymptomatic people, our LUNAR-2 blood test aims to realize our vision of detecting cancer early, starting with early-stage colorectal cancer where an unmet medical need exists. Studies are underway to validate the clinical utility of our LUNAR-2 assays in clinical practice.

References:

1. Shaw AT, Riely GJ, Bang Y-J, et al. Crizotinib in ROS1-rearranged advanced non-small-cell lung cancer (NSCLC): updated results, including overall survival, from PROFILE 1001. *Annals of Oncology*. 2019;30(7):1121-1126.
2. Ramalingam SS, Gray JE, Ohe Y, et al. Osimertinib vs comparator EGFR-TKI as first-line treatment for EGFRm advanced NSCLC (FLAURA): Final overall survival analysis. *Annals of Oncology* 2019;30(5):v851-v934.
3. Garon EB, Hellmann MD, Costa EC, et al. Five-year long-term overall survival for patients with advanced NSCLC treated with pembrolizumab: Results from KEYNOTE-001. *J Clin Oncol*. 2019;37(28):2518-2527.
4. Camidge DR, Dziadziuszko R, Peters S, et al. Updated Efficacy and Safety Data and Impact of the EML4-ALK Fusion Variant on the Efficacy of Alectinib in Untreated ALK-Positive Advanced Non–Small Cell Lung Cancer in the Global Phase III ALEX Study. *J Thorac Oncol*. 2019;14(7):1233-1243.
5. https://www.hcp.novartis.com/products/tafinlar-mekinist/metastatic-nsclc/efficacy/ Accessed online Jan. 10, 2020.
6. Gadgeel SM, Garassino MC, Esteban E, et al. KEYNOTE-189: Updated OS and progression after the next line of therapy (PFS2) with pembrolizumab (pembro) plus chemo with pemetrexed and platinum vs placebo plus chemo for metastatic nonsquamous NSCLC. *J Clin Oncol*. 2019;37(suppl; abstr 9013).
7. Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. *N Engl J Med*. 2006;14;355(24):2542-2550.
8. Leighl NB, Page RD, Raymond VM, et al. Clinical Utility of Comprehensive Cell-Free DNA Analysis to Identify Genomic Biomarkers in Patients with Newly Diagnosed Metastatic Non-Small Cell Lung Cancer. *Clin Cancer Res*. 2019;25(15)4691-4700.
9. Gutierrez ME, Price KS, Lanman RB, et al. Genomic Profiling for KRAS, NRAS, BRAF, Microsatellite Instability (MSI) and Mismatch Repair Deficiency (dMMR) among Patients with Metastatic Colon Cancer. *JCO Precision Oncology*. December 2019; 3:PO.19.00274.
10. Halabi S, Kelly W, Ma H, Zhou H, Solomon N, Lanman RB, et al. Meta-Analysis Evaluating the Impact of Site of Metastasis on Overall Survival in Men With Castration-Resistant Prostate Cancer. *J Clin Oncol*. 2016; 10.1200/JCO.2015.65.7270.
11. Odegaard JI, Vincent JJ, Mortimer S, et al: Validation of a plasma-based comprehensive cancer genotyping assay utilizing orthogonal tissue- and plasma-based methodologies. *Clin Cancer Res* 24:3539-3549, 2018
12. Campbell JD, Alexandrov A, Kim J, et al. Distinct patterns of somatic genome alterations in lung adenocarcinomas and squamous cell carcinomas. Nature Genetics. 2016;48(6):607-616.
13. Moynahan M, Chen D, He W, Sung P, Samoila A, et al. Correlation between PIK3CA mutations in cell-free DNA and everolimus efficacy in HR +, HER2 - advanced breast cancer: results from BOLERO-2. *Br J Cancer*. 2017 Mar 14;116(6):726-730.
14. Swift S, Lang S, White H, Misso K, Kleijnen J, et al. Effect of DNA damage response mutations on prostate cancer prognosis: a systematic review. *Future Oncology*. 2019; VOL. 15, NO. 28.
*For alterations with FDA-approved therapies