THE CIRCULATING CELL-FREE GENOME ATLAS STUDY

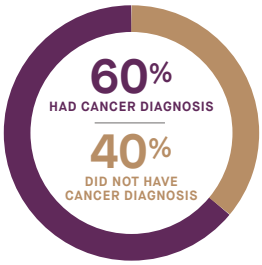
Developing a single blood test for the early detection of multiple deadly cancer types is a challenging endeavor for many reasons, including complex cancer biology.

GRAIL is developing technology to attempt to overcome these challenges using the power of next-generation sequencing, machine learning, and data science. Through a robust and rigorous clinical study program, which includes our foundational study, the Circulating Cell-free Genome Atlas (CCGA) study, we are working to make a multi-cancer early detection blood test a reality.

About CCGA

CCGA is a prospectively designed, observational, longitudinal, case-controlled study designed to develop and validate a blood test for the early detection of cancer

- Enrollment completed in Feb. 2019: **15,254** participants enrolled from **142** sites in the United States and Canada
- Approximately **60%** of participants had cancer at the time of enrollment (newly diagnosed and had not yet received treatment), and **40%** did not have a known cancer diagnosis



- Included **>50 CANCER TYPES**
- Cancer and non-cancer groups were similar with respect to age, sex, race/ethnicity, and BMI

All participants followed for 5+ years to collect clinical outcomes

CCGA consists of three pre-specified sub-studies:

Initial CCGA Sub-Study: **DISCOVERY** (COMPLETED)

We took a comprehensive approach and evaluated three prototype next-generation sequencing blood tests and their ability to detect hallmarks of cancer: mutations, chromosome changes, and DNA methylation changes.

PURPOSE: Served as proof-of-concept and evaluated different approaches for a multi-cancer early detection test

SIZE: ~2,800 participants; multiple deadly tumor types represented in cohort, many of which are unscreened

RESULTS

- Demonstrated feasibility of using cell-free DNA (cfDNA) to detect cancer in the blood
- Strong signal was detected for multiple deadly cancer types across all three blood tests. Methylation was selected for further development because it outperformed the other two approaches
- Showed that a very low false positive rate is possible

The first sub-study demonstrated that a cfDNA-based blood test detected multiple cancers across all stages, including at early stages when treatment may be more effective

Second CCGA Sub-Study: **TRAINING/INITIAL VALIDATION** (COMPLETED)

Based on our initial assessment in the first sub-study, we selected targeted methylation as our preferred approach to move forward in the development of our test as it outperformed the other two approaches.

PURPOSE: Trained selected targeted methylation assay and conducted initial validation of this test; demonstrated tissue of origin determination (where in the body the cancer is located)

SIZE: **~6,600** participants

RESULTS

Results from the second sub-study provided initial validation of the ability of GRAIL's test to detect more than 50 cancer types, including at early stages, with a very low false positive rate and high accuracy in determining the tissue of origin

INITIAL DATA (ASCO 2019)

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FULL TRAINING DATA (ESMO 2019)

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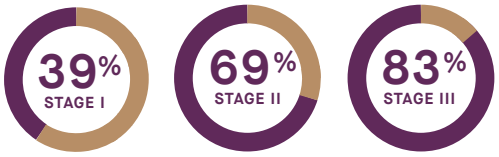
INDEPENDENT VALIDATION DATA (ASCO BREAKTHROUGH 2019)

- **67.3% DETECTION RATE** for pre-specified cancer types across stages I-III



(All results reported at 99.3% specificity)

- Tissue of origin result provided for **96%** of all cancers detected; test returned accurate result in **93%** of these cases

Full sub-study results: Liu MC, Oxnard GR, Klein EA, Swanton C, Seiden MV, on behalf of the CCGA Consortium. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. *Annals of Oncology*.

Third CCGA Sub-Study: **VALIDATION** (ONGOING)

PURPOSE: Confirm performance in an additional independent validation set and help support commercial launch

SIZE: Target **~5,000** participants

Data to be presented at future medical meetings