

Evaluating the Risk of Non-Colorectal Cancers in Individuals with a False Positive Blood-based Colorectal Cancer Screening Test

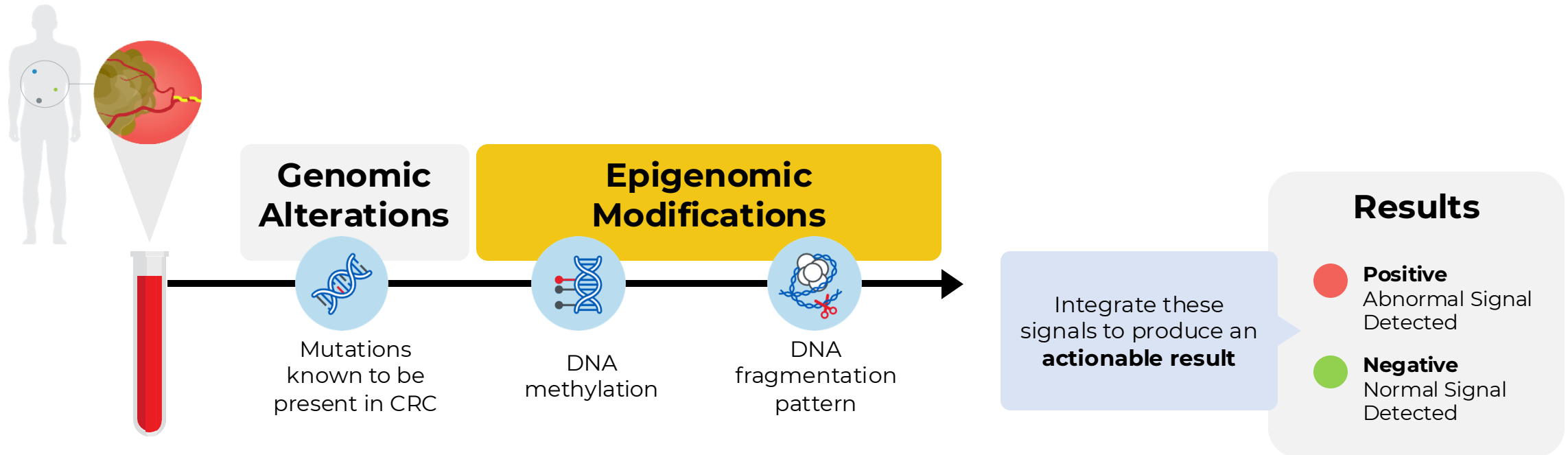
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Background

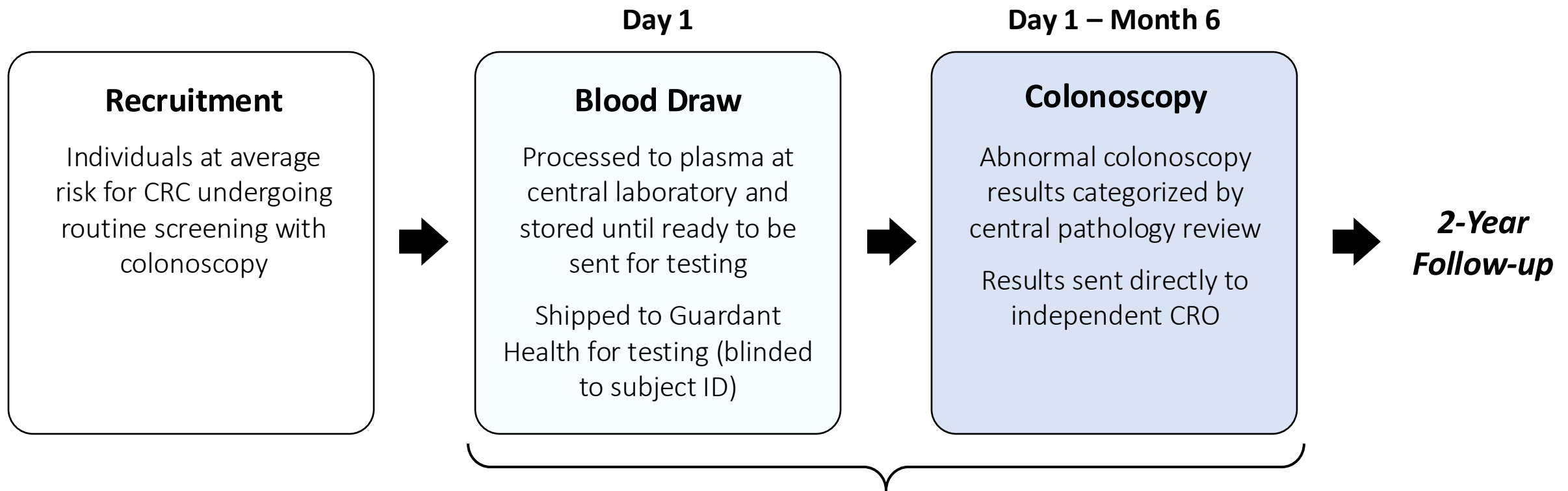
- Blood-based colorectal cancer (CRC) screening tests offer a non-invasive screening modality that can be completed at any healthcare encounter.
- Incorporating blood-based testing as a CRC screening option improves overall screening rates.^{1,2,3}
- It is uncertain whether additional follow-up is indicated to evaluate “false positive” blood-test results after a negative colonoscopy.
- To address this question, we report on the one-year clinical outcomes of individuals in the ECLIPSE study that evaluated the performance of the Shield cell-free DNA (cfDNA) assay for CRC screening.

Shield is a cfDNA blood-based CRC screening test¹



ECLIPSE: Prospective, US Based, Multi-Center Study of Shield Performance to Detect CRC¹

- Study enrolled participants from October 2019 – September 2022



ECLIPSE Enrolled Participants at Average Risk for CRC and Undergoing Routine Screening with Colonoscopy

Inclusion Criteria

- 45 – 84 years old
- Average risk for CRC
- Intended to undergo colonoscopy
- Consent to blood draw and colonoscopy within 60 days*
- Consent to follow-up for 2 years as per protocol

Exclusion Criteria

- History of cancer, inflammatory bowel disease
- Hereditary predisposition to CRC or history of CRC in first degree relative
- Colonoscopy within preceding 9 years
- Positive fecal immunochemical (FIT) or fecal occult blood test (HSgFOBT) within previous 6 months
- Completed mtsDNA or mSEPT9 testing within previous 3 years

ECLIPSE Enrolled 22,877 Study Participants From 265 Sites in United States

Clinical Validation Cohort

All enrolled participants allocated for clinical validation

N = 22,877

Selected Participants

Participants from all enrolled cohort randomly selected for clinical validation testing

N = 10,258

n = 10,179 Not selected through prespecified down-sampling
n = 2,440 Used for specificity interim futility analysis*

Evaluable Participants

Participants from clinical validation cohort with valid Shield & colonoscopy results and eligible for analysis

N = 7,861

n = 2,397 Not Evaluable

N = 65

**Colorectal
Cancer**

N = 1,116

**Advanced
Adenoma**

N = 6,680

**Non-Advanced
Neoplasia****

*4 subjects in interim futility analysis were determined to not meet I/E

**Non-advanced adenomas, non-neoplastic findings, and negative colonoscopy

ECLIPSE Study met the Co-Primary Objectives of CRC Sensitivity and Advanced Neoplasia Specificity¹

Study Objective	Performance Goal	Result
CRC Sensitivity	Lower-bound of 2-sided 95% CI > 65%	83.1% (72.2, 90.3)
Advanced Neoplasia Specificity	Lower-bound of 2-sided 95% CI > 85%	89.6% (88.8, 90.3)

1-Year Data Indicate the Rate of Non-CRC Malignancies Is Not Increased in False Positive Results

	Number of Results N	1-year Follow-Up	
		Follow-up Available N	Rate of non-CRC malignancies % (95% CI)
False Positives (Shield Positive and no CRC/AA at colonoscopy)	698	640 (92%)	0.8% (5/640) (0.3, 1.8)
True Negatives (Shield Negative and no CRC/AA at colonoscopy)	5,982	5,502 (92%)	0.9% (51/5,502) (0.7, 1.2)

Spectrum of Cancers Identified at 1 year follow-up

No post-colonoscopy colorectal cancers were diagnosed in either subgroup at 1 year of follow-up

False Positives (N = 5)

- Cholangiocarcinoma
- Bladder
- Esophageal Squamous
- Lung
- Prostate

True Negatives (N =51)

- Bladder
- Breast
- Cholangiocarcinoma
- Hematological
- Kidney
- Lung
- Melanoma
- Non-Melanoma Skin
- Prostate
- Thyroid
- Uterine

Conclusions

- In over 600 individuals evaluated in the ECLIPSE study, a “false positive” Shield test does not appear to correlate with an increased risk for non-colorectal malignancy at 1 year of follow-up.
- Clinical follow-up is ongoing and will continue to gather two-year cancer diagnoses in enrolled individuals.
- Current research seeks to understand if false positives are driven by underlying biological conditions that would be expected to remain positive on longitudinal testing.
- In individuals with a false positive Shield test, recommendations for repeat CRC screening should be guided by colonoscopy findings.

- Thank you
 - Healthy individuals who volunteered their participation in ECLIPSE.
 - Site investigators and study staff for their collaboration throughout the COVID pandemic
 - Guardant Health Clinical and Technology Development Teams
 - Co-authors and study team

- Questions?
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