Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening[1,2]

Thomas F. Imperiale, MD; Kyle Porter, MAS; Julia Zella, PhD; Zubin D. Gagrat, BS; Marilyn C. Olson, PhD; Sandi Statz, MS; Jorge Garces, PhD; Philip T. Lavin, PhD; Humberto Aguilar, MD; Don Brinberg, MD; Charles Berkelhammer, MD; John B. Kisiel, MD; and Paul J. Limburg, MD for the BLUE-C Study Investigators

BLUE-C*

was a prospective, cross-sectional study that assessed the performance characteristics of the next-generation mt-sDNA test compared to FIT[1,†]

Enrolled >26,000 adults (>40 years old), across >180 clinical sites[1]

Demographics representative of today's US population[1,3]

The study was conducted between November 15, 2019, and January 5, 2023

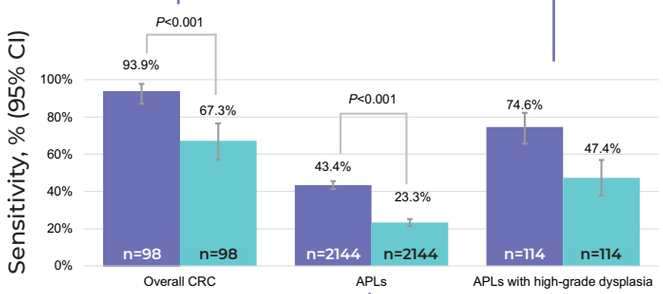
KEY HIGHLIGHTS

The next-generation mt-sDNA test had higher sensitivity than FIT† for all screening-relevant lesions; both had high specificity.

Sensitivity of the Next-generation mt-sDNA Test vs FIT†

CRC sensitivity: **93.9%** vs **67.3%** (*P*<0.001)

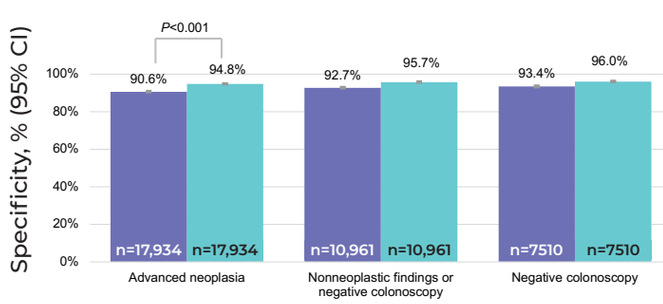
HGD sensitivity: **74.6%** vs **47.4%**



APL sensitivity: **43.4%** vs **23.3%** (*P*<0.001)

Specificity of the Next-generation mt-sDNA Test vs FIT†

CRC specificity (advanced neoplasia)‡: **90.6%** vs **94.8%** (*P*<0.001)



Prespecified outcomes were met

BLUE-C* STUDY DESIGN

STUDY DESIGN

Participants (N>26,000) were asymptomatic adults 40 years of age or older

mt-sDNA test and FIT† test performed on each stool sample

Participants also underwent screening colonoscopy (reference standard)

OUTCOMES

Primary outcomes

- Sensitivity of the test for CRC and specificity for advanced neoplasia (CRC or APLs)

Secondary outcomes

- Sensitivity for APLs,§ specificity for nonneoplastic findings or negative colonoscopy, and comparison of sensitivity for CRC and APLs between the mt-sDNA test and the commercial FIT†

Study limitations

- A relatively high proportion of persons who provided informed consent and were enrolled but whose samples could not be evaluated according to the protocol
- No direct comparison of the performance of the next-generation mt-sDNA test with the current version of the mt-sDNA test

Contains a new molecular panel of novel DNA markers and fecal hemoglobin for CRC screening in patients with average risk

Disclaimer: This technology is under development, and the features above describe current development goals. It has not been cleared or approved by the US Food and Drug Administration (FDA) or any other national regulatory authority.
*BLUE-C: Clinical Validation of An Optimized Multi-Target Stool DNA (mt-sDNA 2.0) Test, for Colorectal Cancer Screening.
†Polymedco OC-Auto® Micro 80 iFOB Test; positivity cutoff: hemoglobin >100 ng/mL.
‡Specificity for advanced neoplasia included all participants who did not have advanced neoplasia. Absence of advanced neoplasia was defined as all nonadvanced adenomas, nonneoplastic findings, and negative colonoscopy (categories 3 through 6 in the study-specific category scheme).
§Adenomas with high-grade dysplasia/carcinoma in situ of any size; adenomas with villous growth pattern (≥25%) of any size; adenomas ≥10 mm; sessile serrated lesions ≥10 mm; or hyperplastic polyps ≥10 mm.[2]
APL: advanced precancerous lesion; **CI:** confidence interval; **CRC:** colorectal cancer; **FDA:** Food and Drug Administration; **FIT:** fecal immunochemical test; **HGD:** high-grade dysplasia; **mt-sDNA:** multi-target stool DNA; **US:** United States.
1. Imperiale TF, et al. *N Engl J Med.* 2024;390(11):984-993. 2. Imperiale TF, et al. *N Engl J Med.* 2024;390(Suppl):S1-S46. 3. United States Census Bureau. QuickFacts United States—Population Estimates, July 1, 2023, (V2023). Accessed March 18, 2024.

Scan here for more resources on the BLUE-C* clinical trial on Exact Academy

EXACT SCIENCES

EXACT SCIENCES