# #3627: A novel, non-invasive, multimodal screening test for early detection of Precancerous Lesions and Colorectal Cancer using an artificial intelligence-based algorithm.

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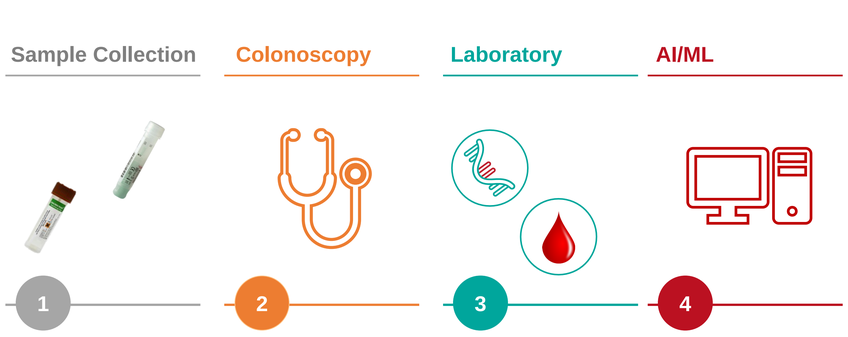
## BACKGROUND

- **Colorectal cancer (CRC)** ranks as the second leading cause of cancer-related mortality worldwide.
- **Detection** of early-stage CRC and in particular its **advanced precursor lesions (APLs)** are crucial for **successful treatment** and reduction in CRC-related mortality.
- Non-invasive methods for **early detection of CRC** are available but are limited by their sensitivity to detect APLs, the best in the low 40% sensitivity range.

## OBJECTIVES

Development of a novel and non-invasive stool-based approach that combines diagnostic biomarkers with a machine learning/artificial intelligence (ML/AI)-generated algorithm to improve diagnostic performance not only for the detection of CRC, but especially for APLs like advanced adenomas (AA).

## METHODS




- Stool sample collected in FIT tube
- Stool sample collected in DNA/RNA stabilization tube
- Stool samples from 690 subjects

- 9 clinical sites in Europe (COLOFUTURE)
- 21 clinical sites in the US (eAArly DETECT)
- Colonoscopy & pathology

- RNA extraction from stabilized stool samples
- Real-Time PCR for mRNA
- Quantification of human hemoglobin

- Biostatistical evaluation by AI/ML generated algorithm

## This multimodal screening test represents

- a **significantly improved** diagnostic approach
- a reliable test for **advanced precancerous lesion** and **early-stage CRC** detection
- a new and promising path for **CRC prevention** and an opportunity to **reduce CRC-related mortality**

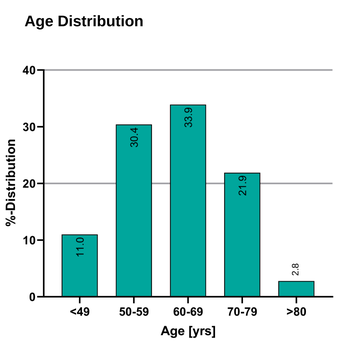


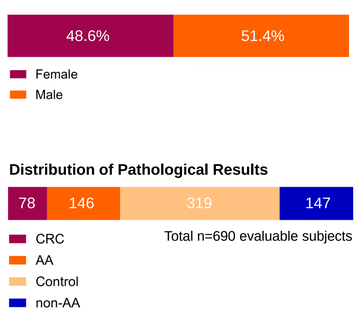
### Demographic Information

**537** EU subjects + **333** US subjects enrolled.

**9** EU study sites + **21** US study sites.

**690** evaluable data sets.

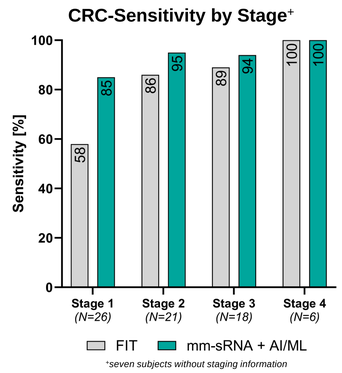


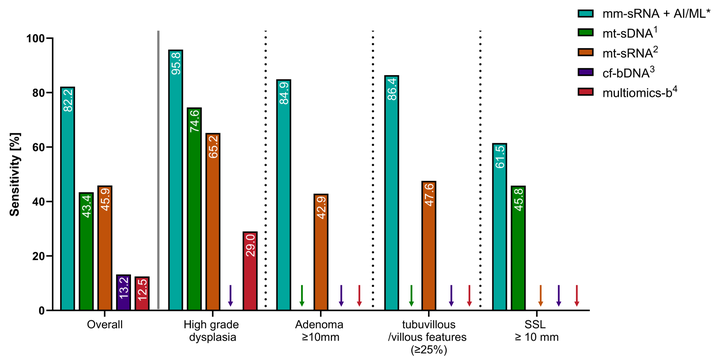

## RESULTS

### Clinical Performance

| Sensitivity (%) | |
|---|---|
| **CRC** (95% confidence interval) | **92.3%** (84.0-97.1) |
| **APL** (95% confidence interval) | **82.2%** (75.0-88.0) |
| **CRC + APL** (95% confidence interval) | **85.7%** (80.4-90.0) |
| **Specificity (%)** | |
| **Normal + non-AA** (95% confidence interval) | **90.1%** (87.1-92.7) |




### APL-Sensitivity by Pathological Group – Comparison to Other Approaches




*data generated in this study; [1]Imperiale et al. (2024): multitarget stool DNA test, [2]Barnell et al. (2023): multitarget stool RNA test; [3]Chung et al. (2024): cell-free DNA blood test, [4]PREEMPT CRC study, press release Freenome Holdings, Inc.: blood multiomics test
↓ data not reported.

**Compared to other approaches, the multimodal screening test allows improved early detection of advanced precancerous lesions and CRC**

## FUTURE DIRECTIONS FOR RESEARCH

- Validation of algorithm in an independent cohort
- Clinical validation in larger randomized screening cohort

*References:*
[1]*Imperiale TF, Porter K, Zella J, Gagrat ZD, Olson MC, Statz S, et al. Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening. N Engl J Med. 2024 Mar 14;390(11):984–93.*
[2]*Barnell EK, Wurtzler EM, La Rocca J, Fitzgerald T, Petrone J, Hao Y, et al. Multitarget Stool RNA Test for Colorectal Cancer Screening. JAMA. 2023 Nov 14;330(18):1760–8.*
[3]*Chung DC, Gray DM 2nd, Singh H, Issaka RB, Raymond VM, Eagle C, et al. A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening. N Engl J Med. 2024 Mar 14;390(11):973–83.*
[4]*press release Freenome Holdings, Inc.; Apr 02,2024; https://www.prnewswire.com/news-releases/freenome-announces-topline-results-for-preempt-crc-to-validate-the-first-version-of-its-blood-based-test-for-the-early-detection-of-colorectal-cancer-302105203.html*

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