Multi-modal blood-based colorectal cancer screening is a viable colorectal cancer screening option – a prospective study

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DDW2022
Digestive Disease Week®
MAY 21-24 | SAN DIEGO, CA
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Disclosures

Paloma Peinado

Research funding from Guardant Health.
Speaking fees from Merck and Lilly.
Background

1. Despite the availability of multiple colorectal cancer (CRC) screening options, about one-third of individuals are not up to date with CRC screening\(^1,2\)
   - Screening adherence rates have remained below the 80% target set forth by leading health care organizations

2. A blood-based CRC screening test with optimized sensitivity and specificity may improve screening adherence\(^3\)

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Background: Blood-based CRC screening test

- Retrospective studies of a multimodal blood-based test in individuals with early-stage CRC have yielded promising results:
  - In a previously reported case-cohort study, this blood-based test demonstrated 91% CRC sensitivity at 94% specificity\(^1\)
  - However, no prospective studies in screened populations have been completed
  - We aimed to evaluate the performance of this blood-based colorectal neoplasia test in a prospective study of individuals presenting for colonoscopy

Methods: Clinical Cohort

**Exclusion:**
- History of any malignancy, including CRC
- Colonoscopy in last 9 years
- Known Hereditary Predisposition to CRC

**Real world, prospective, observational study of adults undergoing colonoscopy at one of four hospitals in Spain**
- Enrollment target: n = 600 individuals

**Colonoscopy results** categorized based on most advanced finding:
- Colorectal Cancer
- Advanced Adenoma
- Non-advanced adenoma/negative colonoscopy
- Not evaluable

**Primary analysis:** Correlate blood-based test results with colonoscopy findings:
- Colorectal cancer
- Non-advanced adenoma/negative

Age 45 – 84 years
Undergoing colonoscopy

Consent to research permitting use of medical records and to provide a blood sample

Whole blood sample collected prior to colonoscopy
Cohort Demographics

At the time of analysis, 93% (n=557) of individuals had a complete colonoscopy and a blood sample analyzed.

### Demographics (N = 557)

<table>
<thead>
<tr>
<th>Biological Sex</th>
<th>Number of Subjects</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>269</td>
<td>48.3%</td>
</tr>
<tr>
<td>Female</td>
<td>288</td>
<td>51.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Median (range)</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 - 49</td>
<td>116</td>
<td>20.8%</td>
</tr>
<tr>
<td>50 - 64</td>
<td>338</td>
<td>60.7%</td>
</tr>
<tr>
<td>65 - 74</td>
<td>79</td>
<td>14.2%</td>
</tr>
<tr>
<td>75+</td>
<td>24</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

### Colorectal Cancer Findings

<table>
<thead>
<tr>
<th>Findings</th>
<th>Number</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal Cancer</td>
<td>8</td>
<td>1.4%</td>
</tr>
<tr>
<td>Advanced Adenoma</td>
<td>41</td>
<td>7.4%</td>
</tr>
<tr>
<td>Non-AA / Negative</td>
<td>508</td>
<td>91.2%</td>
</tr>
</tbody>
</table>

### Indication for Colonoscopy

- Positive Family History: 11%
- Screening: 33%
- Symptomatic: 49%
- Positive FIT/FOBT: 6%
- Other: 1%

AA: advanced adenoma; FIT: fecal immunohistochemical test; FOBT: fecal occult blood test
At 90% Specificity, CRC sensitivity was 100%

- No differences in sensitivity or specificity based on the indication for colonoscopy.
- Specificity did not differ when restricting the analysis to only those with negative colonoscopy (excluding the non-advanced adenoma).

<table>
<thead>
<tr>
<th>CRC Stage</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1 / 1</td>
</tr>
<tr>
<td>II</td>
<td>3 / 3</td>
</tr>
<tr>
<td>III</td>
<td>2 / 2</td>
</tr>
<tr>
<td>IV</td>
<td>2 / 2</td>
</tr>
<tr>
<td>Overall</td>
<td>8 / 8</td>
</tr>
</tbody>
</table>

N = 508 (95% CI: 87-92%)
N = 8 (95% CI: 68-100%)

CI: Confidence Interval
Results: Sensitivity and Specificity

At 90% Specificity, CRC sensitivity was 100%

- Specificity: N = 508 (95% CI: 87-92%)
- CRC Sensitivity: N = 8 (95% CI: 68-100%)

At 95% Specificity, CRC sensitivity was 88%

- Specificity: N = 508 (95% CI: 93-96%)
- CRC Sensitivity: N = 8 (95% CI: 53-98%)

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<td>2 / 2</td>
</tr>
<tr>
<td>Overall</td>
<td>7 / 8</td>
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Strengths:
• Prospective study conducted at multiple institutions
• “All-comers” population
• First prospective evaluation of this blood-based test in individuals undergoing colonoscopy

Limitations:
• Given this is a real-world analysis, referral patterns were based on national guidance in Spain, leading to a higher proportion of individuals presenting with “symptomatic” disease
• Few cases limit ability for subgroup analyses
Conclusions:

• In this **real-world, prospective study of individuals eligible for colonoscopy**, sensitivity and specificity of the multi-modal blood-based test reaches **thresholds consistent with available stool-based screening options**.

• Analysis of the full cohort is ongoing, as is one-year clinical follow-up.

• The reported performance, combined with a more acceptable mode of testing suggests that **this multi-modal blood-based test may be a viable CRC screening option**.

• An updated version of this multi-modal test has been validated for clinical use and is undergoing further clinical validation (**ECLIPSE; NCT04136002**).
Acknowledgements

• Healthy individuals undergoing CRC screening who consented to this research
• Study teams at HM Hospitales
• Collaborators at Guardant Health

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