

STUDY PROTOCOL

Narrow Band Imaging versus Artificial Intelligence for Colonic Surveillance in Inflammatory Bowel Disease: a Prospective, Randomized, Crossover Study

The CLEAR-IBD Trial (Colorectal Lesion Evaluation Assisted by Real-time AI in Inflammatory Bowel Disease)

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Approving body: Comité de Ética de la Investigación con Medicamentos (CEIm), Hospital Universitari Vall d'Hebron, Barcelona, Spain

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Protocol Summary

Title	Narrow Band Imaging versus Artificial Intelligence for Colonic Surveillance in Inflammatory Bowel Disease: a Prospective, Randomized, Crossover Study (CLEAR-IBD)
Design	Unicentric, two-arm, open-label, randomized, crossover clinical trial
Population	Adult patients with long-standing colonic ulcerative colitis or Crohn's disease undergoing colorectal cancer surveillance colonoscopy
Interventions	Colonoscopy with computer-aided detection (CADe; ENDO-AID, Olympus) versus narrow-band imaging (NBI), performed sequentially in randomized order during the same procedure
Primary outcome	Per-lesion neoplasia miss rate (NMR)
Main secondary outcome	Per-patient neoplasia miss rate (NMR)
Sample size	60 evaluable patients (pragmatic estimate, accounting for an anticipated 20% dropout)
Recruitment period	January 2025 to March 2026
Sponsor	Societat Catalana de Digestologia

1. Background and Rationale

Patients with inflammatory bowel disease (IBD) remain at increased risk of colorectal cancer (CRC) compared with the general population, underscoring the importance of regular endoscopic surveillance. Colonoscopic surveillance has been shown to reduce both CRC incidence and CRC-related mortality; however, adherence to recommended surveillance modalities and intervals remains low in routine practice.

Although most guidelines recommend high-definition dye-based chromoendoscopy as the surveillance technique of choice, its uptake remains limited due to training requirements, additional procedure time, and cost. As a result, several guidelines continue to consider virtual chromoendoscopy techniques, including narrow-band imaging (NBI), and high-definition white-light endoscopy as acceptable alternatives.

Computer-aided detection (CADe) systems based on artificial intelligence (AI) have demonstrated meaningful improvements in adenoma and polyp detection in non-IBD populations. However, most convolutional neural network-based algorithms underlying these systems have been trained on datasets that largely excluded patients with IBD.

Consequently, the real-world performance of currently available non-IBD-trained CADe systems for detecting colitis-associated dysplasia remains unknown.

Existing evidence evaluating AI performance in IBD has relied mainly on retrospective analyses of still-image datasets, without assessing real-time performance against validated comparators such as chromoendoscopy or NBI in a prospective clinical setting. A direct, prospective comparison is therefore needed to determine whether a commercially available, non-IBD-trained CADe system can perform comparably to an established imaging technique for dysplasia detection in patients with long-standing colonic IBD.

2. Objectives

2.1 Primary Objective

To compare the neoplasia miss rate (NMR), assessed in a per-lesion analysis, between a non-IBD-trained CADe system (ENDO-AID CADe, Olympus) and narrow-band imaging (NBI) in patients with IBD undergoing surveillance colonoscopy.

2.2 Secondary Objectives

- To compare the NMR between CADe and NBI in a per-patient analysis.
- To compare withdrawal times between the two techniques.
- To assess the impact of histological inflammatory activity on neoplasia detection.
- To characterize and compare the lesions detected by each technique according to histology, morphology (Paris classification), size, and anatomical location.

3. Study Design

This is a unicentric, two-arm, open-label, randomized, crossover clinical trial conducted at the IBD Clinic of the Gastroenterology Department, Vall d'Hebron University Hospital, Barcelona, Spain.

Each participant undergoes a single colonoscopy in which the entire colon is examined twice, consecutively, by two different endoscopists using the two study techniques (CADe and NBI) in randomized order. This design allows each patient to act as their own control, minimizing confounding due to between-patient variability.

4. Study Population

4.1 Inclusion Criteria

- Age ≥ 18 years.
- Diagnosis of ulcerative colitis (UC) or colonic Crohn's disease (CD) of at least 8 years' duration, scheduled for endoscopic colorectal cancer surveillance according to ECCO guidelines.

- Patients with concomitant primary sclerosing cholangitis (PSC) are eligible for screening colonoscopy regardless of disease duration.

4.2 Exclusion Criteria

- Inadequate bowel preparation, defined as a Boston Bowel Preparation Scale (BBPS) score < 6.
- Presence of any degree of active endoscopic inflammation at the time of the procedure.
- Technical reasons preventing completion of colonoscopy, such as a critical stenosis.

Patients are not excluded based on the presence of inflammatory activity identified on histological specimens.

5. Study Procedures and Interventions

5.1 Endoscopic Examination

Each participant is examined on the same day by two endoscopists with expertise in IBD endoscopic surveillance, who alternate consecutively between the two techniques.

1. Endoscopist 1 examines the entire colon using either AI (ENDO-AID CADe System, Olympus, Tokyo, Japan) or NBI, according to the randomization sequence. Before lesion assessment, endoscopic remission is confirmed using the Mayo endoscopic score (UC) or the Simple Endoscopic Score for Crohn's Disease (SES-CD) for CD, requiring a score of 0.
2. Lesions identified by Endoscopist 1 are documented and managed accordingly (resection or biopsy).
3. Endoscopist 2, blinded to the findings of Endoscopist 1, re-examines the entire colon using the alternate technique, documents any additional findings, and manages any lesions missed during the first examination.

Both endoscopists perform an equal number of examinations with NBI and AI as the first or second technique. High-definition endoscopes and the same processor (Olympus CF-HQ190L, EVIS X1) are used for all procedures.

5.2 Lesion Assessment and Histology

All lesions resected or biopsied using either technique, regardless of whether detection occurred during the first or second examination, are documented and endoscopically categorized using the Paris classification. Location and size are recorded. Tissue specimens are assessed by pathologists with expertise in IBD as part of standard care. Adenocarcinoma, serrated adenoma, tubular adenoma, and any dysplasia are classified as neoplastic lesions. Biopsies are systematically obtained from previously identified colitic segments in all patients to assess the impact of histological inflammatory activity on neoplasia detection.

5.3 Withdrawal Time

Withdrawal time, defined as the time between the start of inspection at the cecum and the end of the procedure, is recorded separately for each technique and for each examination order (first vs. second).

6. Randomization and Blinding

Patients are consecutively allocated in a 1:1 alternating sequence to either the “NBI first followed by AI” arm or the “AI first followed by NBI” arm. Allocation is performed prior to the procedure by Endoscopist 1.

Blinding of endoscopists to the study technique is not feasible owing to the nature of the intervention (the AI overlay is visible on screen). However, Endoscopist 2 remains blinded to the findings of the first examination.

7. Study Outcomes

7.1 Primary Outcome

Per-lesion neoplasia miss rate (NMR): the number of neoplastic lesions missed during the first examination and subsequently detected during the second examination, divided by the total number of neoplastic lesions detected across both examinations.

7.2 Main Secondary Outcome

Per-patient neoplasia miss rate (NMR): the number of patients with at least one neoplastic lesion missed during the first examination and detected during the second examination, divided by the total number of unique patients with at least one neoplastic lesion detected across both examinations.

7.3 Other Secondary Outcomes

- Withdrawal time, overall and stratified by examination order (first vs. second).
- Impact of histological inflammatory activity on neoplasia detection.
- Characteristics of neoplastic and non-neoplastic lesions (histology, Paris classification, size, and anatomical location) according to detection technique.

8. Data Collection

The following patient and disease characteristics are collected for all participants: age, sex, IBD type, age at diagnosis, disease location and behavior (Montreal classification for CD; extent for UC), presence of perianal disease, presence of primary sclerosing cholangitis, current and past medication, personal history of dysplasia, previous IBD-related surgery, and time elapsed since the last surveillance colonoscopy.

Procedural data collected include the randomization arm, the order of techniques, all detected lesions (with technique, endoscopist, morphology, size, and location), histological findings, withdrawal times, and any procedure-related complications.

9. Sample Size and Statistical Analysis

9.1 Sample Size

Given the absence of prior data on AI-assisted CAdE performance in IBD surveillance colonoscopy, the sample size was pragmatically set at 60 evaluable patients, based on previously published crossover studies comparing dye-based chromoendoscopy and NBI in this population. A 20% dropout rate was anticipated to account for incomplete explorations, withdrawal of informed consent, and suboptimal bowel preparation; recruitment was therefore planned for approximately 72 patients.

9.2 Statistical Analysis

Results are expressed as median (interquartile range) unless otherwise specified. Statistical tests are selected according to data type and unit of analysis:

- For the primary outcome and main secondary outcome, lesion-level detection (paired binary outcomes) is compared using the McNemar test, while per-patient dysplastic lesion counts (paired non-normally distributed data) are compared using the Wilcoxon signed-rank test.
- As most lesions are sampled immediately upon detection, only missed or unresected lesions can be identified during the second examination, precluding fully paired analyses; individual lesions are therefore treated as statistically independent observations for these comparisons.
- Quantitative variables are compared using Student's t-test or the Mann–Whitney U test, as appropriate.
- Proportions are compared using the χ^2 test or Fisher's exact test.
- A Bonferroni correction is applied for multiple comparisons, specifically for analyses of lesion location and histology.

All p-values are two-sided, and $p < 0.05$ is considered statistically significant. Analyses are performed using SPSS version 16 (SPSS Inc., Chicago, IL).

10. Ethical and Regulatory Considerations

This protocol was approved by the Drug Research Ethics Committee (Comité de Ética de la Investigación con Medicamentos) of Hospital Universitari Vall d'Hebron under code PR(AG)237/2023. All participants provide written informed consent prior to enrolment. The study is conducted in accordance with the principles of the Declaration of Helsinki and applicable national and institutional regulations governing clinical research.

10.1 Patient and Public Involvement

No patients or members of the public were involved in the design, conduct, reporting, or dissemination plans of this research.

10.2 Data Management and Availability

Study data are collected and stored in accordance with institutional data protection policies. The dataset underlying the study results will be made available upon reasonable request to the corresponding author.

11. Safety and Procedure Complications

Any immediate or delayed procedure-related complications (e.g., bleeding, perforation) are recorded for each participant and reported according to institutional protocols for adverse event monitoring during endoscopic procedures.

12. Funding and Disclosures

This work is supported by the Societat Catalana de Digestologia through the Ajut per a la Iniciació a la Recerca grant. The funder has no role in the study design, data collection, data analysis, interpretation of data, writing of the manuscript, or the decision to submit the manuscript for publication.

The investigators declare no conflicts of interest relevant to this study.

13. Study Timeline

Milestone	Period
Ethics committee approval	Prior to recruitment (code PR(AG)237/2023)
Patient recruitment and procedures	January 2025 – March 2026
Data analysis	Following completion of recruitment
Reporting and dissemination	Following data analysis

Abbreviations

- AI – Artificial Intelligence
- BBPS – Boston Bowel Preparation Scale
- CAdE – Computer-Aided Detection
- CD – Crohn's Disease
- CRC – Colorectal Cancer
- HDWLE – High-Definition White-Light Endoscopy
- IBD – Inflammatory Bowel Disease
- NBI – Narrow-Band Imaging
- NMR – Neoplasia Miss Rate
- PSC – Primary Sclerosing Cholangitis
- SES-CD – Simple Endoscopic Score for Crohn's Disease
- UC – Ulcerative Colitis