CLINICAL TRIAL PROTOCOL

Evaluation of Fecal Multi-Target Biomarker Detection in Gastrointestinal Cancer Screening: A Multicenter Prospective Observational Cohort Study

Evaluation of Fecal Multi-Target Biomarker Detection in Gastrointestinal Cancer Screening

SPONSOR

The First Affiliated Hospital of Air Force Medical University

National Clinical Research Center for Digestive Diseases

Lead Institution: The First Affiliated Hospital of Air Force Medical University

Principal Investigator: Nie Yongzhan

Participating Institutions:
Wuxi People's Hospital | The 960th Hospital of PLA
The First Affiliated Hospital of Dalian Medical University | Qingdao Municipal Hospital
Zhaoqing Gaoyao District People's Hospital | Yixing Fifth People's Hospital
Zhaoqing First People's Hospital | Gansu Wuwei Tumor Hospital
Yanchi County People's Hospital | Yanting County Tumor Hospital

Study Period: January 1, 2026 – December 31, 2027

Protocol Version: V1.0

Version Date: December 25, 2025

CONFIDENTIAL

The information contained in this document is confidential and may be disclosed only as required by applicable laws and regulations. Under all circumstances, all personnel who have access to this document shall be informed that the contents of this document are confidential and shall not be disclosed. This confidentiality agreement also applies to any other unpublished or non-public information provided to you.

PROTOCOL SYNOPSIS

Full Title	Evaluation of Fecal Multi-Target Biomarker Detection in Gastrointestinal Cancer Screening: A Multicenter Prospective Observational Cohort Study
Short Title	Evaluation of Fecal Multi-Target Biomarker Detection in Gastrointestinal Cancer Screening
Objective	To construct and evaluate the sensitivity and specificity of fecal multi-target biomarkers for gastrointestinal cancer screening.
Study Reagents	Qualitative fecal occult blood detection reagent and ultra-sensitive quantitative fecal immunochemical test (FIT) reagent, used to detect trace levels of human hemoglobin (Hb) in feces. Fecal samples will also be used for novel biomarker exploration.
Study Design	This trial is a multicenter, prospective, observational study.
Estimated Number of Subjects	5,000 subjects
Estimated Number of Study Centers	Currently 10 participating research centers nationwide
Primary Endpoint	Sensitivity and specificity of fecal multi-target biomarker detection for upper and lower gastrointestinal cancer screening, compared with endoscopic examination combined with pathological biopsy as the gold standard.
Secondary Endpoints	Sensitivity and specificity of fecal multi-target biomarker detection for upper and lower gastrointestinal cancer screening.
Follow-up Plan	Annual follow-up conducted through telephone callbacks, review of medical insurance reimbursement records, and linkage of screening population information with cancer registry and death registry data.
Key Inclusion Criteria	1. Age ≥18 years at enrollment; 2. Planned to undergo upper and lower gastrointestinal endoscopic screening; 3. Agree to a two-year follow-up period as per the protocol; 4. Willing and able to sign informed consent.
Key Exclusion Criteria	1. Gastrointestinal endoscopic screening within 1 year; 2. History of any type of gastrointestinal malignancy; 3. Severe comorbidities that reduce screening benefit, such as severe pulmonary, renal, hepatic, cardiovascular/cerebrovascular, or hematological diseases; 4. Other conditions assessed by physicians as posing excessive risk for endoscopic screening (e.g., hemodynamic instability) or no benefit (short life expectancy); 5. Pregnant or lactating women.

Primary Statistical Hypothesis	Based on a diagnostic trial design (gold standard: endoscopic examination), with an expected gastrointestinal cancer detection rate of 2.0%, sample size was calculated for the sensitivity and specificity of combined fecal multi-target biomarker detection. Referencing prior research, target values were set (sensitivity 85%, specificity 80%), and the final enrollment was determined to be 5,000 cases.

TABLE OF CONTENTS

1. Research Background

2. Research Content

3. Research Objectives

4. Study Design

5. Study Population

5.1 Inclusion Criteria

5.2 Exclusion Criteria

6. Study Endpoints

6.1 Primary Outcome Measures

6.2 Secondary Outcome Measures

7. Proposed Research Protocol

7.1 Study Design and Methodological Steps

7.1.1 Research Support and Organizational Structure

7.1.2 Screening Site Selection and Setup

7.1.3 Screening Population Invitation Plan

7.1.4 Screening Implementation Methods and Procedures

7.2 Statistical Considerations and Sample Size Calculation

7.2.1 Analysis Population

7.2.2 Sample Size Calculation

7.2.3 Statistical Analysis

8. Data Management

9. Screening Process Indicators and Quality Control

9.1 Screening Process Indicators

9.2 Screening Process and Quality Control

10. Safety Justification and Risk Contingency Plan

10.1 Recruitment Process

10.2 Withdrawal and Termination Criteria

10.3 Clinical Research Project Risk Contingency Plan

11. Ethical Requirements

11.1 Ethics Committee

11.2 Informed Consent

1. Research Background

In recent years, the disease burden of gastrointestinal cancer in China has been extremely heavy. The incidence of upper gastrointestinal cancers (esophageal cancer and gastric cancer) remains high, while the incidence of colorectal cancer continues to rise. These have become the major types of malignant tumors threatening the life and health of the Chinese population, imposing tremendous pressure on patient families and the social healthcare system. Early diagnosis and treatment are key measures to reduce gastrointestinal cancer mortality and improve patient prognosis. They are also one of the core tasks explicitly defined by the National Center for Digestive Diseases, and represent an important public health need for improving the health of the entire population. Within the gastrointestinal cancer screening technology system, fecal immunochemical testing (FIT) has become an important non-invasive method for colorectal cancer screening due to its advantages of being non-invasive, convenient, and having high compliance. Compared with the traditional guaiac-based chemical fecal occult blood test (gFOBT), FIT offers higher sensitivity and specificity, and is less affected by external factors such as diet and medications, significantly improving screening efficacy. In particular, ultra-sensitive quantitative FIT has achieved a technological breakthrough by significantly lowering the detection limit to 2 ng/mL, enabling precise capture of ultra-trace bleeding caused by adenomas and other precancerous lesions and early tumors. This achieves "dual control" over colorectal cancer and its precancerous lesions, providing more reliable technical support for early intervention. Notably, clinical studies have suggested that among patients with positive results on traditional qualitative FIT but no lower gastrointestinal lesions found on colonoscopy, the incidence of upper gastrointestinal cancer is significantly higher than in FIT-negative populations. This phenomenon indicates that ultra-sensitive quantitative FIT may possess potential value for combined screening of upper and lower gastrointestinal cancers. However, systematic research data on the use of ultra-sensitive quantitative FIT for combined screening of upper and lower gastrointestinal tumors is currently scarce both domestically and internationally, unable to provide sufficient evidence-based medical support for clinical practice. This study was designed precisely based on this clinical need and research gap. Through scientific validation of the efficacy of ultra-sensitive quantitative FIT in combined screening, it is expected to optimize gastrointestinal cancer screening strategies, improve overall screening efficiency, and reduce the risk of missed diagnoses. It has clear clinical significance and public health value, and its conduct is fully justified in terms of ethics and necessity. Novel biomarker detection will also be performed to explore the clinical application value of multi-target detection.

2. Research Content

This study is a multicenter, observational study. Subjects planning to undergo gastroscopy and colonoscopy will be enrolled. Prior to endoscopic examination, an epidemiological survey will be completed, and fecal samples will be collected for qualitative FIT, quantitative FIT, and novel biomarker detection, followed by completion of endoscopic examination. After completion of baseline endoscopic screening, all enrolled subjects will undergo 2 years of follow-up. The primary endpoint is the sensitivity and specificity for gastrointestinal cancer screening.

3. Research Objectives

The primary objective is to evaluate the application value of fecal multi-target biomarker detection in combined screening for upper and lower gastrointestinal tumors, and to establish precise stratified management strategies for the population, with high-risk patients immediately referred for endoscopic examination. In addition, the remaining samples after detection will be used for exploration of other gastrointestinal cancer screening biomarkers.

4. Study Design

This study employs a prospective, multicenter, observational trial design. Subjects planning to undergo gastrointestinal endoscopic screening will be enrolled. Prior to endoscopic examination, an epidemiological survey will be completed, and fecal samples will be collected for fecal multi-target biomarker detection, followed by completion of endoscopic examination. After completion of baseline endoscopic screening, active and passive combined follow-up will be conducted through telephone callbacks, review of medical insurance reimbursement records, and linkage of screening population information with cancer registry and death registry data. The primary endpoint is the sensitivity and specificity of fecal multi-target biomarker detection for gastrointestinal cancer screening.

5. Study Population

For individuals aged over 18 years, invitation to participate in the screening trial will be extended. For those willing to participate in screening, the assessment results of inclusion and exclusion criteria in Sections 5.1 and 5.2 will be documented in detail.

5.1 Inclusion Criteria

1) Age >18 years at enrollment;

2) Planned to undergo gastroscopy and colonoscopy;

3) Agree to a two-year follow-up period as per the protocol;

4) Willing and able to sign informed consent.

5.2 Exclusion Criteria

1) Gastrointestinal endoscopic screening within 1 year;

2) History of any type of gastrointestinal malignancy;

3) Severe comorbidities that reduce screening benefit, such as severe pulmonary disease, renal disease, hepatic disease, cardiovascular/cerebrovascular disease, and hematological diseases, etc.;

4) Other conditions assessed by physicians as posing excessive risk for endoscopic screening (e.g., hemodynamic instability) or no benefit (short life expectancy);

5) Pregnant or lactating women.

6. Study Endpoints

6.1 Primary Outcome Measures

Sensitivity and specificity of fecal multi-target biomarker detection for gastrointestinal cancer screening, compared with endoscopic examination combined with pathological biopsy as the gold standard.

6.2 Secondary Outcome Measures

Secondary outcome measures include:

1) Sensitivity and specificity of fecal multi-target biomarker detection for upper gastrointestinal cancer screening;

2) Sensitivity and specificity of fecal multi-target biomarker detection for esophageal cancer screening;

3) Sensitivity and specificity of fecal multi-target biomarker detection for gastric cancer screening;

4) Sensitivity and specificity of fecal multi-target biomarker detection for colorectal cancer screening;

5) Sensitivity and specificity of fecal multi-target biomarker detection for screening of esophageal mucosal high-grade intraepithelial neoplasia and early esophageal cancer;

6) Sensitivity and specificity of fecal multi-target biomarker detection for screening of gastric mucosal high-grade intraepithelial neoplasia and early gastric cancer;

7) Sensitivity and specificity of fecal multi-target biomarker detection for screening of intestinal mucosal high-grade intraepithelial neoplasia and early colorectal cancer;

8) Endoscopic screening complications, mainly including possible bleeding, perforation, infection, cardiovascular/cerebrovascular-related complications, aspiration, or screening-related death, etc.

7. Proposed Research Protocol

7.1 Study Design and Methodological Steps

This study is a multicenter, observational study. Subjects planning to undergo gastrointestinal endoscopic examination will be enrolled. Prior to endoscopic examination, an epidemiological survey will be completed, and fecal samples will be collected for fecal multi-target biomarker detection, followed by completion of endoscopic examination. After completion of baseline endoscopic screening, all enrolled subjects will undergo 2 years of follow-up. The primary endpoint is the sensitivity and specificity of fecal multi-target biomarker detection for gastrointestinal cancer screening.

7.1.1 Research Support and Organizational Structure

This study is an investigator-initiated clinical trial. It is supported by China's Major Special Project on "Prevention and Treatment Research of Cancer, Cardiovascular and Cerebrovascular, Respiratory, and Metabolic Diseases." The Study Steering Committee (Nie Yongzhan, Pan Yanglin, Shang Lei) is responsible for the overall concept, design, and execution of the study, and ensures the scientific integrity and medical ethics of the research. The Steering Committee will hold regular meetings to ensure effective management and execution of the study, including data acquisition, safety, analysis, and reporting. This study follows the ethical principles outlined in the Declaration of Helsinki and has applied for ethical review by the Ethics Committee of Xijing Hospital.

7.1.2 Screening Site Selection and Setup

The selection of screening sites for this project has been carefully considered to enhance population representativeness and regional coverage balance: the layout of screening sites covers northern, eastern, central, western, and southern China, reflecting nationwide sample representativeness. A total of 5,000 subjects are planned for enrollment.

7.1.3 Screening Population Invitation Plan

For community-based screening populations, collaboration will be established with local health departments and hospital physical examination centers, utilizing provided lists of eligible screening populations to extend screening invitations. Recruitment of hospital-based patients will primarily take place at physical examination centers, outpatient clinics, and endoscopy centers, with face-to-face recruitment.

7.1.4 Screening Implementation Methods and Procedures

For individuals aged 18 years and older who are planning to undergo endoscopic examination, invitation and assessment will be conducted. For those who meet the inclusion and exclusion criteria, enrollment will be invited. First, an epidemiological survey will be completed, and fecal samples will be collected for qualitative FIT, quantitative FIT, and novel biomarker detection, followed by completion of

endoscopic examination. After completion of baseline endoscopic screening, active and passive combined follow-up will be conducted through telephone callbacks, review of medical insurance reimbursement records, and linkage of screening population information with cancer registry and death registry data.

1) Preliminary Publicity and Gastrointestinal Health Knowledge Popularization

- Conduct extensive publicity through government-coordinated broadcasting, units, communities, and other media institutions;
- Organize hospital, community, or village committee staff to participate in gastrointestinal health and cancer prevention science popularization;
- Prepare promotional materials and develop publicity plans.

2) Population Pre-screening

For community-based screening populations, plans are to collaborate with local health management departments to obtain household registration information of individuals aged 18 years and older at the screening site. Those meeting the pre-screening criteria will be recruited by telephone. Recruitment of hospital-based patients will primarily take place at physical examination centers, outpatient clinics, and endoscopy centers, with face-to-face recruitment. When they have fully understood the study and are willing to participate, the following assessments should be conducted to determine whether the patient is eligible to join this study; at the same time, this portion of the assessment will serve as the patient's baseline data and be completely recorded in the Case Report Form (CRF):

a) Demographic baseline characteristics: including age, sex, household registration, etc.;

b) Current health status: including diet, swallowing, abdominal symptoms, bowel movements, etc.;

c) Past medical history and medication use history: including history of esophageal disease, gastric disease, cardiovascular/cerebrovascular disease, anticoagulant medication use, etc.

3) Final Confirmation

If a subject withdraws informed consent or fails to meet the inclusion/exclusion criteria, they will be defined as a screening failure. These patients will be excluded and will not undergo epidemiological investigation or blood testing.

4) Informed Consent

After confirming that the subject meets the inclusion/exclusion criteria, the patient will be asked whether they voluntarily participate in this trial, and the Informed Consent Form (ICF) will be signed. All relevant information about this study is summarized in the ICF, which consists of subject information and the informed consent document. The investigator shall fully explain to the subject the research background of this trial, as well as the benefits and risks related to the subject during the trial process. At the same time, the subject should be informed that additional assessments are necessary to ensure their

eligibility. Informed consent may be signed by the subject or their legally authorized representative. The investigator must obtain the informed consent form before conducting relevant research for this trial. Patients who fail to sign the informed consent form will not be eligible to participate in the trial. Enrolled subjects will retain a copy of the signed informed consent form. The investigator must ensure that the informed consent process is conducted in accordance with the requirements of the Ethics Committee and specific national regulations, and guarantee that subjects may withdraw from the study at any time for any reason. Informed consent must inform subjects that they may receive follow-up telephone calls within 2 years to collect supplementary clinical database information.

5) Living Conditions and Health Survey

Enrolled patients will undergo an epidemiological survey according to the "Living Conditions and Health Survey Form," with a survey duration of approximately 5-10 minutes per person. After completion of the epidemiological survey, endoscopic examination will be arranged. Each screening site hospital will determine the number of subjects for each screening session and develop a survey and blood collection schedule based on the inclusion/exclusion criteria. Different survey methods will be arranged according to the number of people and their characteristics for each survey session, such as hospital-based centralized surveys, door-to-door surveys, etc.

6) Fecal Collection and Fecal Multi-Target Biomarker Detection

- The screening site will determine the number of fecal collections and develop a fecal collection plan according to the screening schedule. It is recommended to arrange community personnel to participate in the organization together; other required personnel include blood collection nurses, registration staff, security personnel, etc.;
- Fecal specimens will be collected, separated, aliquoted, and stored by designated personnel arranged by each participating institution;
- FIT detection of fecal samples will be performed by designated personnel (at the participating institution or Xijing Hospital), and in principle, detection should be completed within 1 week after fecal collection. Detection of other novel biomarkers will be conducted centrally.

7) Endoscopic Examination Arrangement

- Endoscopic examination can be arranged immediately after fecal collection, without waiting for test results;
- The pathology department of the hospital performing endoscopic examination is responsible for preparation and HE staining of esophageal and gastric tissue specimens. Pathologists from participating institutions may assist screening site pathologists in pathological result interpretation and report preparation;
- Each screening site hospital will decide whether to perform anesthetized endoscopic examination based on its own conditions and the screening subjects' preferences.

8) Positive Case Management Recommendations

Participants meeting the following criteria will be classified as positive cases: high-grade intraepithelial neoplasia of the esophageal or gastric mucosa, advanced colorectal adenoma, esophageal cancer, gastric cancer, or colorectal cancer. Corresponding treatment plans will be recommended for these patients. High-grade intraepithelial neoplasia or intramucosal carcinoma is recommended to be treated by endoscopic mucosal resection or endoscopic submucosal dissection. Treatment methods for submucosal carcinoma and invasive carcinoma include surgery, radiotherapy, and chemotherapy, etc.

9) Follow-up Period

All residents aged 18 years and older who have signed informed consent, regardless of whether they participated in the questionnaire survey or screening, will be followed up using both passive and active methods. Passive follow-up will link patient identity information with data from cancer registries, medical insurance databases, and clinical visit records to identify new cancer cases and deaths. Active follow-up will be conducted by local public health staff from each group through telephone calls or home visits to collect information on the status of the participating population and medical visit information. For patients with gastrointestinal high-grade intraepithelial neoplasia and gastrointestinal cancer, detailed investigations will be conducted to obtain accurate diagnosis and treatment information.

7.2 Statistical Considerations and Sample Size Calculation

7.2.1 Analysis Population

Data analysis will be conducted in the per-protocol set, consisting of all subjects who signed the informed consent form and complied with the trial protocol as planned, including those who underwent epidemiological survey, fecal multi-target biomarker detection, and endoscopic examination. If a subject ultimately fails to undergo endoscopic examination as scheduled, they will be excluded. Analysis of the primary endpoint and all secondary endpoints will be conducted within the per-protocol set.

7.2.2 Sample Size Calculation

Based on a diagnostic trial design (gold standard: endoscopic examination), with an expected gastrointestinal cancer detection rate of 2.0%, sample size was calculated for the sensitivity and specificity of combined fecal multi-target biomarker detection. Referencing prior research, target values were set (sensitivity 85%, specificity 80%), and the final enrollment was determined to be 5,000 cases.

7.2.3 Statistical Analysis

All reported P values are two-sided, with no correction for multiple comparisons. A P value less than 0.05 or a 95% confidence interval (CI) for rates less than or greater than 1 is considered statistically significant.

1. Baseline Characteristics

The report will include the following characteristics: sex, age, ethnicity, marital status, education, body mass index, smoking, alcohol consumption, and family history of cancer, etc. Continuous variables will be expressed as median and interquartile range, and categorical variables will be reported as counts and percentages.

2. Efficacy Evaluation

Outliers and missing data will be verified and processed to ensure the integrity of the Per-Protocol Set (PPS) and Safety Set (SS). The primary analysis of this trial will be conducted according to the per-protocol set principle. Mean, standard deviation, and disease detection rate of baseline characteristics (age, sex distribution) will be calculated, with data visualization presented through histograms, box plots, etc. A multivariate Logistic regression model will be used to evaluate the screening efficacy of quantitative FIT detection, with ROC curves constructed to calculate sensitivity, specificity, and AUC. Center effects will be addressed through random intercept mixed models or stratified analysis. For subgroup analysis of esophageal/gastric/colorectal cancer, stratified Logistic regression will be used to adjust for confounding factors such as sex and Helicobacter pylori infection status. Comparison of efficacy among various screening combinations will be performed using the DeLong test for AUC difference analysis. Screening complication incidence will be described as frequency and percentage, with inter-group differences analyzed using the chi-square test or Fisher's exact test.

3. Cost-Effectiveness Assessment

When conducting health economic evaluation, a Markov model will be developed to simulate the natural progression of gastrointestinal cancer, and economic evaluation indicators such as Quality-Adjusted Life Years (QALYs) and Incremental Cost-Effectiveness Ratios (ICERs) will be calculated. Analysis results will be reported according to the Consolidated Health Economic Evaluation Reporting Standards.

The statistical management personnel of this trial will complete the analysis using the latest version of SAS or R software.

8. Data Management

All research centers are required to record participant information, including epidemiological surveys and risk assessments, endoscopic examination results, pathological diagnosis results, and any subsequent treatment information. All epidemiological data and health economic data from questionnaires will be collected by trained interviewers. Endoscopists and pathologists will collect endoscopic screening and pathological data based on corresponding diagnostic results. Follow-up results for cancer patients and all-cause mortality will be collected by health visitors. All data will be submitted to the Xijing Hospital Coordinating Center through the web-based management system for review and centralized review. All data will be treated as protected health information and securely stored in the encrypted database of Xijing Hospital. Paper charts will also be properly stored in locked filing cabinets. Access to raw data will be limited to the principal investigator and data management personnel. Data managers, entry clerks, and the principal investigator will have passwords to access the database. Data entry personnel will only have the right to enter data and view their own entered data for a limited time. Only data managers have the authority to modify entered data. Any inconsistencies will be carefully reviewed and corrected based on written records.

9. Screening Process Indicators and Quality Control

9.1 Screening Process Indicators

1) Number of Screenings Completed (Number of Participants)

Target Population: Individuals aged 18 years and older who meet the conditions for endoscopic screening and have not undergone gastrointestinal endoscopic screening within the past year.

Target Number: At least 5,000 people are expected to be completed within approximately 1 year.

2) Endoscopic Examination Completion Rate

Endoscopic Examination Time: Within 2 months from the date of consent to screening enrollment.

Endoscopic Examination Completion Rate: Number of subjects who completed endoscopic examination / Total number of subjects who signed informed consent. The expected proportion of completed endoscopic examinations is not less than 95%.

3) Screening Population Follow-up Completion Rate

Follow-up Population: All screening subjects who signed informed consent and completed the epidemiological risk factor survey.

Follow-up Completion Rate: Number of follow-ups completed through telephone, death registry records, and cancer registry system archives / Total number of screening subjects who completed the epidemiological risk factor survey.

9.2 Screening Process and Quality Control

(1) After screening initiation, each participating center is required to report to the project lead institution on a monthly basis regarding the number of screened individuals, cancer cases, follow-up information, etc. This information will be discussed at project meetings.

(2) Once enrolled subjects have completed fecal collection, screening institutions must complete fecal multi-target biomarker detection within 1 month, fill out test result notification forms, and return these forms to the screening center to facilitate tracking of these cases.

(3) Each participating institution is responsible for monitoring screening and high-risk case follow-up in each township, and will hold coordination meetings with Xijing Hospital physicians on a monthly basis, inviting experts and scholars to discuss project execution progress and content.

(4) Organize expert consensus meetings to develop screening service models, establish standard procedures for case collection, referral, and diagnosis, to ensure consistency in screening quality and promote the extension of this policy to other screening counties and cities.

(5) The sponsor has ethical, legal, and scientific obligations to carefully track this trial study in accordance with the provisions of the trial protocol.

(6) Data Monitoring Committee: A Data Monitoring Committee will be established to ensure that all conclusions in the clinical trial are derived from raw data, and corresponding data management measures will be implemented during the clinical trial and data processing phases to ensure data authenticity, accuracy, and reliability.

(7) Data Audit: The quality assurance department of the sponsor institution may conduct audits of the trial at clinical research institutions. Audits include: reagent supply, required trial documents, records of the informed consent process, and consistency between case report forms and source documents, etc.

10. Safety Justification and Risk Contingency Plan

10.1 Recruitment Process (Including Recruitment Procedures, Initiation Time, and Expected Number of Recruits)

This study primarily determines whether screened individuals are eligible to join this study through investigator assessment of inclusion/exclusion criteria. Investigators may screen subjects based on the examination/treatment practices of each center, on the basis of completing the requirements of this study protocol. The study plans to initiate patient recruitment in January 2026.

10.2 Withdrawal and Termination Criteria

1) Screening of a subject shall be terminated when any of the following conditions occur, and the reason for terminating the screening trial must be clearly described in the subject's source documents and case report form:

a. The patient withdraws the informed consent form;

b. The patient cannot tolerate adverse reactions from study examinations;

c. As determined by the investigator, the patient is no longer suitable to continue the trial due to adverse events (AE) or abnormal laboratory test values;

d. As determined by the investigator, the patient has developed serious concurrent diseases that necessitate termination of the trial;

e. Considering the patient's best interests, the investigator believes that the best option is to terminate the screening trial;

f. The investigator believes there is serious protocol deviation (subject does not meet inclusion/exclusion criteria; unable to follow study procedures and examination requirements; excessively low examination compliance; use of prohibited medications, etc.);

g. Any other situation determined by the investigator, including serious adverse events (SAE) that threaten the subject's health.

2) Sponsor-requested termination (e.g., due to funding reasons, management reasons, etc.)

3) Administrative authority revocation of the trial

In the event of the above situations, the sponsor shall promptly inform investigators at each research center, clinical pharmacology trial institutions, and ethics committees.

10.3 Clinical Research Project Risk Contingency Plan

Possible risks; measures to minimize risks within possible limits; risks and protections for special populations (women, children, elderly, etc.).

1) Possible Risks

The primary potential risk of this trial originates from endoscopic screening, with complications including possible bleeding, perforation, infection, cardiovascular/cerebrovascular-related complications, aspiration, or screening-related death, etc.

2) Measures to Minimize Risks Within Possible Limits

The research team has extensive clinical experience in subject management and has established a strict adverse event reporting system in this study to maximize the reduction of subject risk. During the trial period, the investigator will conduct close follow-up of all enrolled patients, and provide comprehensive management including lifestyle improvement, gastrointestinal cancer warning symptoms, and timely medical visit screening through face-to-face and telephone visits to minimize the risks of patients participating in the clinical trial. At the same time, close monitoring will be conducted for each subject to determine whether screening-related adverse events have occurred. If an event meets the criteria for a serious adverse event, it shall be immediately reported in the case report form without delay; and within at least 3 days, the investigator shall clarify the relationship between this adverse event and the screening procedure and screening laboratory tests/examinations. All serious adverse events will be tracked and followed up until the event is resolved (with or without sequelae) or the chronic disease reaches a stable state.

3) Special Population Protection

Before enrollment in this study, the investigator shall fully explain to the subject the research background of this trial, as well as the benefits and risks related to the subject during the trial process, ask whether the patient voluntarily participates in this trial, and sign the Informed Consent Form (ICF). The ICF shall be signed by the subject or their legally authorized representative. The investigator must obtain the informed consent form before conducting relevant research for this trial. In addition, this study does not involve minors under 18 years of age; female patients who are pregnant or lactating (premenopausal women must undergo pregnancy testing within 7 days prior to enrollment in this trial).

11. Ethical Requirements

This clinical trial will be conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP).

11.1 Ethics Committee

Before the clinical trial begins, the clinical trial protocol must be reviewed and approved by the Ethics Committee, and implementation may only proceed after the approval opinion is signed. During the clinical trial, any modifications to the clinical trial protocol and informed consent form must be approved by the Ethics Committee before execution.

11.2 Informed Consent

All subjects participating in this clinical trial will be provided with an informed consent form describing this study, along with sufficient information to enable the subject to make an informed decision regarding whether to participate in this study. This informed consent form will be submitted to the Ethics Committee for review and approval together with the clinical trial process documents. After the Ethics Committee approves the informed consent form, the subject must sign this approved version of the informed consent form before entering any clinical trial procedure. The informed consent form must be signed by the subject themselves or their legal representative, and collected by the professional designated by the investigator for this study.