Groupe d'Etude Thérapeutique des Affections Inflammatoires du tube Digestif

Clinical Study Protocol

SECURITY

Evaluation of a remote monitoring application in the follow-up of patients with active Inflammatory Bowel Diseases.

The SECURITY trial

GETAID-2023-02

IdRCB Number: 2024-A01751-46

EC Protocol Version: V3 02/03/2026

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SIGNATURE PAGE

Main sponsor: Groupe d'Etude Thérapeutique des Affections Inflammatoires Digestives (GETAID)

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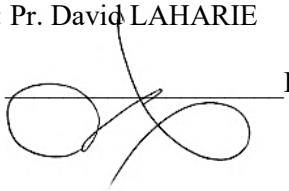
Signature  Date 02/03/2026

Coordinator Investigator: Pr Xavier TRETON

Signature  Date 02/03/2026

Site Investigator

I will conduct the trial in compliance with GCP, with the relevant regulatory requirement(s) and with the protocol agreed to by the sponsor and given approval/favorable opinion by the IRB/IEC; I agree to comply with procedure for data recording/reporting, especially to report all SAEs to GETAID and, if applicable to my National Sponsor within 24H of awareness. I agree to allow and facilitate monitoring, auditing and inspection and to retain the trial related essential documents until the sponsor informs me/institution these documents are no longer needed.

I will conduct this trial according to the timelines provided.

I understand that all information concerning the study supplied to me by GETAID in connection with this trial and not previously published is considered confidential information.

I agree that documents and other data pertinent to this trial are property of GETAID.

I understand that any changes in the protocol must be approved in writing by GETAID and the IRB/IEC and local competent authorities before implementation.

By my signature below, I hereby attest that I have read, understood and agree to abide by all conditions, instructions and restrictions contained in the protocol.

Investigator

Name

_____Signature _____ Date

TABLE OF PROTOCOL VERSIONS

Reference	Version	Date	EC approval date	RA approval date	Status
MS3	3	02/03/2026			
MS2	2	05/06/2025	04/08/2025	12/08/2025	
Initial protocol RFI ANSM	1.3	18/11/2024	09/10/2024	28/11/2024	Initial application
Initial protocol RFI CPP	1.2	17/09/2024	09/10/2024	On going	Initial application
Initial protocol	1.1	17/09/2024	On going	On going	Initial application

SYNOPSIS

Title	Evaluation of a remote monitoring application in the follow-up of patients with active Inflammatory Bowel Diseases, the SECURITY trial
Sponsor	GETAID 50, rue Richer, 75009 Paris, France
Protocol number	GETAID 2023-02
IdRCB number	2024-A01751-46
Principal investigator	Pr Xavier Treton Institut des MICI 23-25 Bd Victor Hugo, Neuilly-sur-Seine, France Tél : Mail : xavier.treton@institutdesmici.fr
Protocol version	Version 3 du 02/03/2026
Medical device description	MedicWise, the SEMEIA remote monitoring application configured for IBD
Medical device technical caracteristics and considerations	The MedicWise application allows the patient to complete PROs and functional disability (IBDdisk) questionnaires. It also allows, without any intervention from the patient, but after obtaining their consent, to retrieve the biological results of routine examinations, as well as all the care consumed (explorations, medicines collected in pharmacy, etc...). A working group made up of GI physicians and IBD nurses defined the specific algorithm to generate alerts to the healthcare team, in the event of a medical event relevant to the care pathway of the patient with IBD, likely to lead to an adapted therapeutic intervention. In this way, we hope to demonstrate that patients equipped with this remote monitoring tool, MedicWise®, specifically configured for IBD, will have an optimized care pathway, with a positive influence on disease control, and the time spent in remission.
Rationale / background	Telemonitoring is of definite theoretical interest for patients suffering from chronic diseases and could help to improve monitoring of treatment efficacy and tolerance, and hence remission and quality of life. Reimbursement is now planned in France for devices that have demonstrated a positive effect on patient intake. However, available studies testing different tools in IBD have shown no significant improvement in disease control or quality of life. Nevertheless, major secondary endpoints such as reduced hospitalization, complications and healthcare costs have been demonstrated. Several biases have been identified to explain these disappointing results, such as the heterogeneity of the tools/applications tested, methodological limitations concerning the main objective and technological limitations of the tools evaluated. We propose here to evaluate the impact of a tight remote monitoring through digital tool on disease control, in patients with active IBD,

	thanks to the MedicWise platform. The technology of the MedicWise solution enables the automatic collection of a wide range of biological and healthcare consumption data, thus limiting the need for patient input. MedicWise has obtained the CE label and is already used and reimbursed in France in other chronic diseases. The SECURITY trial proposes to evaluate the impact of a tight remote monitoring through digital tool on time spent in remission. Improvement of IBD related disability is also a major secondary objective of the study. It also has the following secondary objectives to analyze the impact of this tool on the organization of care teams caring for patients with IBD.
Study objectives	**Main objective:** To evaluate whether tight control through remote monitoring device improves disease activity compare to standard of care in patients with active Inflammatory Bowel Disease (IBD). **Secondary Objectives:** • To evaluate the IBD related disability in patients with active IBD • To evaluate the quality of life in patients with active IBD • To evaluate the proportion of patients in symptomatic remission at M6 and M12 • To evaluate the correlation between S-IBDQ and IBD-Disk variations • To compare the number of consultations between the two groups (number of physical consultations and teleconsultations) • To evaluate the compliance • To compare the proportion of disease related complications • To evaluate the satisfaction of patients to be monitored with telemonitoring • To evaluate the satisfaction and the gain of time for the care team performing remote monitoring
Study endpoint	Main assessment criteria: **Percentage of cumulative time spent in symptomatic remission within 12 months** Time spent in symptomatic remission defined by (PRO2): - MC: abdominal pain ≤ 1 and stool frequency ≤ 3 defined clinical remission in CD, both not worsening compared from inclusion - UC: absence of rectal bleeding (score 0) and stool frequency score ≤ 1, both not worsening compared with inclusion Key secondary assessment criteria: • Average value of IBD disk change from baseline over 12 months (M3, M6, M9 and M12) • Clinical remission according to PRO2 at M12 • • Average value of S-IBDQ change from baseline over 12 months (M4 and M12)

	• number of complications (, hospitalizations, surgeries) over 12 months • Time spend per day in out patient management at M12 • Medication and care compliance/consumption over 12 months • <u>Other secondary assessment criteria</u>: • Absolute change in IBD Disk value between inclusion and M12 and absolute change in S-IBDQ value between inclusion and M12 • Clinical remission according to PRO2 at M6 • Number of hospitalizations over 12 months • Patient satisfaction questionnaire at M12 • Care team satisfaction questionnaire at M12
Study design	Multicenter randomized controlled trial comparing two strategies to following-up patients with active IBD **<u>Active arm</u>**: alerts activated, **<u>Control arm</u>**: alerts disabled • Both arms are equipped with the application, data are collected via the application and telemonitoring with alerts to the care team are activated in the active telemonitoring arm. • Data are collected in both arms at baseline, M3, M6, M9 and M12 • Each center defines who handles alerts internally (physicians, IBD nurses, others, etc.) according to its internal organization. The application does not impose an internal operation. • the alert thresholds are identical and fixed for all centers during the study. Within the framework of the study, alerts are defined according to the study's modalities but cannot be modified by the centers. • Participating sites will have to tagg on the platform each action taken in response to the alerts to validate Randomization will be stratified by centers and by diseases (Crohn and UC) with unbalanced blocks of randomization
Population	Adult patients with active IBD (Crohn's disease (CD), ulcerative colitis (UC)) with indication for modification of medical treatment
Inclusion / exclusion criteria	<u>Inclusion criteria</u>*:* • CD/UC patients with a validated diagnosis • Patients age > 18 years • IBD with clinical signs of PRO2 activity leading to modification of medical treatment: introduction of a new treatment, or change of dose or addition of a treatment (corticoids, ASA, IS, biotherapy (a 4 week induction phase is authorized • Patients willing and able to participate in the collection of data via SEMEIA App on their smartphone

	• Patients agreeing to participate for 12 months Exclusion criteria: • Patients with an inability to use a smartphone and email • Patients < 18 years old • Digestive surgery expected within 3 months • Pregnancy at baseline • Patients with an history of sub-total colectomy, coloproctectomy, digestive ostomy, extensive or multiple intestinal resections with sequelae of diarrhoea, short bowel syndrome. • Patients who have had recent digestive surgery (ileal resection < 6 months) • Patients scheduled for digestive surgery within 3 months. • Patients with any other uncontrolled somatic or psychiatric pathology • Patients enrolled in a trial with an investigational treatment
Number of patients	290 patients
Study procedure	Duration of participation per patient: 12 months • **Protocol visits**: inclusion, M4 and M12. At each visit the following data will be collected: clinical examination, S-IBDQ questionnaire, safety and treatment compliance • **Data collection from the app:** For the whole duration of the study, the following data will be collected with the App in both arms: PRO, Scores/ IBDisk/treatment consummation, biology, medical event at M0, M3, M6, M9 and M12 (alerts will be generated only in the active telemonitoring arm). The app will push e-Questionnaire to each patient (PRO; scores, IBD disk) and will pull other related clinical data directly from the patient personal medical file (“mon espace santé”) • Patients in both arms will be notified by the application or the SEMEIA platform in the event of incomplete data filling at M0,3,6,9 and 12 • Events of interest (declaration of flare up, extra-intestinal symptom, new treatment, complication…) will be collected via the application and verified during protocol visits for **the active arm** In the event of an alert received by the team via the application (active arm), or directly by the patient (control arm), the medical team will choose the mode with which it will interact with the patient (message, teleconsultation, consultation face-to-face) and will collect the data from this visit/emergency contact in the CRF In case of alert according to the investigators clinical decision the following actions could be taken : - No treatment adjustment or modification - Treatment optimization - Treatment modification Others medical intervention

Trial population size and Statistical analysis	Sample size calculation: By considering the following assumptions for the percentages of patients in remission as a function of time in the patient groups: - Control arm: 30% at 1 month, 40% at 3 months, 50% at 9 months and 60% at 12 months - Monitored arm: 30% at 1 month, 50% at 3 months, 60% at 9 months and 75% at 12 months (these assumptions are based on PI's IBD unit personal data). From these percentages we calculated by simulations the probability that a patient in the Monitored arm has a time spent in remission larger than a patient in control arm. This p value was equal to 0.61 corresponding to an effect size equal to 0.4. Then we introduced this value in the formula proposed by Noether G (Noether, G. E. (1987). Sample Size Determination for Some Common Nonparametric Tests. Journal of the American Statistical Association, 82(398), 645–647) to calculate sample size for Mann-Whitney test. We found that a sample size of n=145 patients randomized per group will provide 90% power to demonstrate a difference in time spent in remission by Mann-Whitney test at 5% two-sided alpha risk. Statistics Main analysis will use the intention to treat population. Additional per protocol analysis will be performed to discuss the impact of the monitoring in absence of major protocol violations. If percentages of missing values are higher than 5% they will be inputed using Monte Carlo Markov Chain methods. In addition since it cannot be excluded that missing values will not be at random (MAR), sensitivity analyses for hypothesis of MNAR missing values will be performed using the delta-adjusted pattern imputation implemented in the MNAR Statement of PROC MI from SAS 9.4. (details of the procedures will be provided in the SAP) Primary criterion will be analyzed by Mann-Whitney test. Secondary criteria corresponding to IBD and IBDQ measurements will be analyzed by ANCOVA using baseline value as covariate. Normalizing transformations or rank analyses will be used if necessary. Satisfaction and other questionnaires will be analyzed by Mann-Whitney tests. Counts of events will be analyzed by Poisson regression. Correlation between SIBDQ and IBDisk values will be studied by Spearman's nonparametric correlation test. Management of alpha risk. In order to take into account multiplicity for secondary criteria, we will use a hierarchical method of test for the following secondary criteria that will be analyzed in the following order.

	• Average value of IBD disk change from baseline over 12 months • PR02 at M12 • Average value of S-IBDQ change from baseline over 12 months • number of complications (AE/SAE, hospitalizations, surgeries) over 12 months • Time spend per day in outpatient management (questionnaire at M6 and M12) • Medication and care compliance/consumption over 12 months A p value will be reported for the nth criterion of the list only if the p value for the test of the (n-1)th criterion of the list is <0.05 (two-sided). Otherwise only difference between group and associated 95% two-sided confidence interval will be reported. Other secondary criteria will be considered as exploratory and only difference between group and associated 95% two-sided confidence interval will be reported.
Inform consent procedure	Patients will be informed orally and in writing by a research investigator by means of an information note, and their explicit consent will be obtained. No procedure specific to the protocol may be undertaken before the patient has been informed and consent has been obtained. In accordance with the French Data Protection Act (Loi Informatique et Liberté), patients will be informed of their right of access, opposition and rectification of data recorded during this research.
Safety assessment	Only serious and non-serious adverse events (possibly related to treatment) AND occurring during the period from the signing of informed consent to the end of patient follow-up in the study will be reported.
Study duration	Inclusion period: 18 months Patient follow-up: 12 months Total study duration: 30 months Estimated start date: April 2025 Estimated end date:Octobre 2027

SECURITY

Evaluation of a remote monitoring application in the follow-up of patients with active inflammatory bowel diseases (IBD)

SECURITY's objectives: To evaluate whether a remote monitoring device (SEMEIA) improves disease activity (ie symptomatic remission) in patients with active Inflammatory Bowel Disease (IBD).

*** Activated alerts = the healthcare professional receives targeted alerts (PRO2 value, biological result, patient's declarative questionnaire on a possible relapse, etc.) --> the patient is then contacted to assess his or her state of health and adapt the treatment if necessary.**

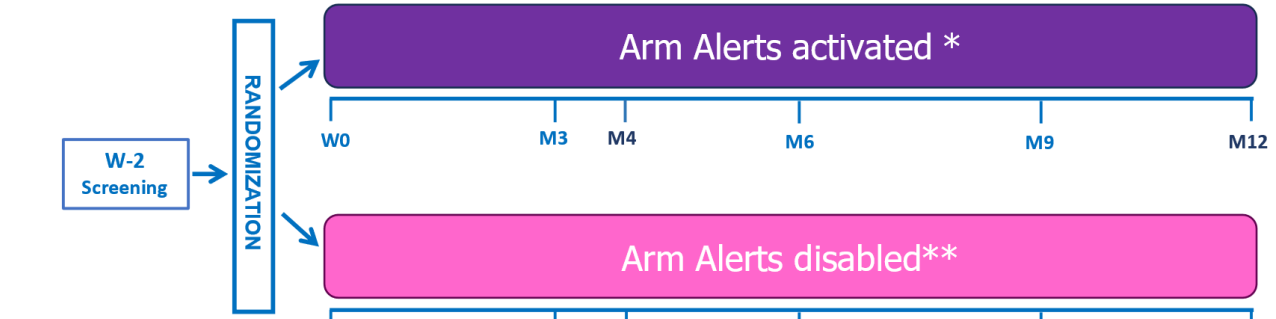
**** Inactivated alerts = all data are collected in the application, but none are transmitted to the healthcare professional. The patient will be assessed at M4 and M12.**

NB: in the event of an emergency, the patient should consult the emergency department or his or her doctor, as per usual practice.

Patients with IBD: Crohn's or UC
- ✓ Age >18 years
- ✓ IBD with clinical signs of activity:
  - ➢ PRO2

Leading to modification of medical treatment:
- ➢ introduction of a new treatment
- ➢ change of dose
- ➢ Addition of a treatment: corticoids, ASA, IS, biotherapy

- ✓ Equipped with a smartphone.
- ✓ Patients agreeing to participate for 52 weeks.



W-2 screening: Consent signed, clinical examination, questionnaires.

W0 randomisation 1:1 randomization to either alerts on or alerts off arm.

* Screening and randomization visits can be carried out on the same day.

M4 and M12 visits (on-site or téléconsultation, depending on practice)
M3, M6, M9 and M12: PRO2 / IBD disk completed via the SEMEIA l'application

LIST OF ABBREVIATIONS

AE	Adverse Event
ANCOVA	covariance analysis
ASA	Amino salicylates
CD	Crohn's Disease
DO	Drop out
DSMB	Data and Safety Monitoring Board
e-CRF	Electronic Case Report Form
ePRO	Electronic Patient Reported Outcomes
GCP	Good Clinical Practice
GETAID	Group d'Etude Thérapeutique dans les Affections Inflammatoires Digestives
IBD	Inflammatory Bowel Disease
IBDQ	Inflammatory Bowel Disease Questionnaire
ICH	International Conference on Harmonization
ICF	Informed Consent Form
IS	Immunossupressants
IRB/IEC	Independent Review Board/ Independent Ethics Committee
ITT	Intent To Treat
MH	Mucosal Healing
PP	Per Protocol
PGA	Physician Global Assessment
PRO	Patient Reported Outcomes
QoL	Quality of life
SES-CD	Simplified endoscopy score for Crohn's disease
S-IBDQ	Short Inflammatory Bowel Disease Questionnaire
SoC	Standard of Care
RCT	randomized controlled trials
RSF	Rectosigmoidoscopy
SAE	Serious Adverse Event
SUSAR	Suspected Unexpexted Serious Adverse Reaction
UC	Ulcerative Colitis
UCEIS	Ulcerative Colitis Endoscopic Index of Severity
VAS	Visual Analogue Scale

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1 BACKGROUND AND STUDY RATIONALE

Digital health technologies can overcome the physical and time limitations of traditional face-to-face encounters through remote monitoring of disease activity, increasing access to health care providers via mobile technologies, and enhance patient participation through individualized alerts and action plans[1].

With the rapid technological advances, digital health tools and telemedicine (defined as diagnosis, treatment, and monitoring of disease by means of the internet, mobile phone applications, and wearable devices) can potentially provide an opportunity for highvalue care by improving efficiency in health care delivery[2].

Multiple trials on the development and implementation of multidimensional digital health technologies and telemedicine have variably impacted clinical outcomes, remote disease monitoring, IBD-related quality of life (QoL), and health care utilization. Telemonitoring is of definite theoretical interest for patients suffering from chronic diseases and could help to improve monitoring of treatment efficacy and tolerance, and hence remission and quality of life. Reimbursement is now planned in France for devices that have demonstrated a positive effect on patient intake. However, the studies testing different tools in IBD have shown no significant improvement in disease control or in Qol.

In a systematic review of 14 RCTs comparing different digital health technologies vs standard of care (SoC) in patients with IBD, digital health technologies did not result in lower rates of disease relapses compared with SoC [3]. However, relapse rates were comparable to patients who received routine face-to-face encounters, suggesting that digital health technologies may offer a safe and effective complimentary mechanism for chronic care management. Digital health interventions were associated with lower burden of health care utilization, primarily driven by lower rates of office visits, without any higher risk of unplanned hospitalizations, emergency department visits, surgeries, and/or corticosteroid use compared with SoC. Because IBDs are chronic conditions, patients often require lifelong therapy, which may make treatment adherence difficult. Based on results from 2 large, multicenter RCTs in Europe (myIBDcoach and Constant-care), web-based technologies were associated with significantly higher rates of treatment adherence compared with SoC [4,5]. The largest clinical trial with a telemonitoring program to date was performed with the Dutch web myIBDcoach (http://www.mijnibdcoach.nl)[6]. This web allows distance monitoring of disease activity, treatment adherence and side effects, as well as nutritional status, smoking habits, QoL, fatigue, stress, anxiety and depression. As other platforms, it provides educational elements to improve empowerment. In a clinical trial including 909 patients with different disease characteristics, the use of this system reduced outpatient visits and hospitalizations compared to standard care after 12 months of follow-up [6] .

Furthermore, in studies that evaluated the impact of digital health technologies on health care costs, 3 studies demonstrated significant cost savings with web-based interventions or telephone consultations compared with face-to-face clinic visits [7,5,8].

Although there were generally positive results associated with the use of digital health technologies, adherence to these technologies was a concern as studies reported high rates of attrition during follow-up in patients who received these interventions, which suggests fatigability with long-term use.

Nevertheless, major secondary endpoints such as reduced hospitalization, complications and healthcare costs have been demonstrated. Several biases have been identified to explain these disappointing results, such as the heterogeneity of the tools/applications tested, methodological limitations concerning the main objective and technological limitations of the tools evaluated[3].

We propose here to evaluate the impact of a tight remote monitoring through digital tool on disease control in patients with active IBD, thanks to the MedicWise platform. The technology of the MedicWise solution enables the automatic collection of a wide range of biological and healthcare consumption data, thus limiting the need for patient input. MedicWise has obtained the CE label and is already used and reimbursed in France in other chronic diseases.

Functional disability measured by the IBD disk, a validated tool, makes it possible to assess key items of QoL but other aspects of daily life[9]. This visual tool is very suitable for digital monitoring of the overall impact of IBD on patients' daily lives. It allows an overall quantitative measurement of disability, but also an analysis in 10 items, some of which are common to established Qol scores, and other items are complementary. Thus, the criteria evaluated in the SECURITY study are different from previous trials in this field, while evaluating the impact of telemonitoring on the duration of time spent in symptomatic remission and on overall disability on daily life. The application also allows to collect data concerning the recovery of patients' major treatments in pharmacies and therefore an objective monitoring of therapeutic compliance, which in the available studies has only been declarative.

The SECURITY trial aim is to evaluate the impact of a tight remote monitoring through digital tool on time spent in remission , Improvement of IBD related disability is also a major secondary objective of the study. It also has the following secondary objectives to analyze the impact of this tool on the organization of care teams caring for patients with IBD

2 STUDY OBJECTIVES

2.1 Primary objective

2.2 To evaluate whether tight control through remote monitoring device improves disease activity compared to standard of care in patients with active Inflammatory Bowel Disease (IBD).Secondary objectives

- To evaluate the IBD related disability in patients with active IBD
- To evaluate the quality of life in patients with active IBD
- To evaluate the proportion of patients in symptomatic remission at M6 and M12
- To evaluate the correlation between S-IBDQ and IBD-Disk variations
- To compare the number of consultations between the two groups (number of physical consultations and teleconsultations)
- To evaluate the treatment compliance
- To compare the proportion of disease related complications
- To evaluate the satisfaction of patients to be monitored with telemonitoring
- To evaluate the satisfaction and the gain of time for the care team performing remote monitoring

3 TRIAL END POINTS

3.1 Primary end point

Percentage of cumulative time spent in symptomatic remission within 12 months

Time spent in symptomatic remission over 12 months defined by (PRO2):

- CD : abdominal pain ≤ 1 and stool frequency ≤ 3 defined clinical remission in CD, both not worsening compared from inclusion
- UC: absence of rectal bleeding (score 0) and stool frequency ≤ 1, both not worsening compared with inclusion

3.2 Secondary end points

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Key secondary assessment criteria:

1. Average value of IBD disk change from baseline over 12 months (M3, M6, M9 and M12)
2. Clinical remission according to PRO2 at M12
3. Average value of S-IBDQ change from baseline over 12 months (M4 and M12)
4. Number of complications (hospitalizations, surgeries..) over 12 months
5. Time spent per day in outpatient management at M12

6. Medication and care compliance/consumption over 12 months

Other secondary assessment criteria:

- Absolute change in IBD Disk value between inclusion and M12 and absolute change in S-IBDQ value between inclusion and M12
- Clinical remission according to PRO2 at M6
- Number of hospitalizations over 12 months
- Patient satisfaction questionnaire at M12
- Care team satisfaction questionnaire at M12

4 STUDY POPULATION

4.1 Number of participants

290 patients to be enrolled in GETAID centers

4.2 Criteria to be checked at selection visit

4.2.1 Inclusion criteria

- CD/UC patients with a validated diagnosis
- Patients age > 18 years
- IBD with clinical signs of PRO2 activity leading to modification of medical treatment: introduction of a new treatment or change of dose or addition of a treatment (corticoids, ASA, IS, biotherapy). PRO2 activity is defined by:
  - CD: abdominal pain ≥ 2 and stool frequency ≥ 4
  - UC: rectal bleeding ≥ 1 and stool frequency ≥ 2
- Patients equipped with a smartphone and agreeing to use it for the purpose of the study.Patients agreeing to participate for 12 months

4.2.2 Non selection criteria

The patients should not present any of the following criteria:

- Patients with an inability to use a smartphone and email
- Patients < 18 years old
- Pregnancy at baseline
- Patients with an history of sub-total colectomy, coloproctectomy, digestive ostomy, extensive or multiple intestinal resections with sequelae of diarrhoea, short bowel syndrome.

- Patients who have had recent digestive surgery (ileal resection < 6 months)
- Patients scheduled for digestive surgery within 3 months.
- Patients with any other uncontrolled somatic or psychiatric pathology
- Patients enrolled in a trial with an investigational treatment

5 DEFINITION OF THE INVESTIGATION

5.1 Medical device: MedicWise telemonitoring tool

SEMEIA's MedicWise is a CE label's class IIa remote monitoring software intended for healthcare professionals and patients with chronic diseases. It collects, stores, and compares clinical and biological data to alert rules defined according to the patient's profile and pathology to alert practitioners in the event of non-compliance with these rules. Data comes from connected devices, manual entry and secure data flows from computerized patient records. The tool was first developed in nephrology for monitoring patients who have had a kidney transplant, treated with immunosuppressants and anti-rejection drugs. All intended use, this tool is already used by several clinical teams for the monitoring of more than 12,000 patients with a chronic disease. It collects information on health status via questionnaires that patients complete themselves. MedicWise also allows the automatic recovery, without patient intervention, of biological parameters and current care consumption reimbursed by the French health care insurance (explorations, medicines collected in pharmacy, etc...). An algorithm considering the clinical and biological data generates relevant alerts which are transmitted to the healthcare team via the platform.

In addition, the SEMEIA platform has a team of specialized and trained nurses who equip and train patients in the use of the tool and who monitor that the alerts transmitted via the platform to the care teams are properly processed.

5.2 Investigational process

The GETAID study group wanted to scientifically evaluate whether remote monitoring was relevant and effective for patients with IBD. After analyzing the telemonitoring tools currently available, we considered that MedicWise was suitable for IBD for the following reasons: 1-The tool is currently used in kidney transplant patients, sharing with patients with IBD the chronic nature of the disease, the need to resort to heavy treatments at home with a similar tolerance profile, 2- MedicWise allows monitoring based on data retrieved automatically, the filling of data by patients themself is limited, 3-MedicWise can be configured to IBD and allows the alert definition algorithm to be adapted specifically, and 4-MedicWise makes it possible to identify lack of compliance in the event of failure to deliver treatments in pharmacies and to generate an alert.

The MedicWise application developed by SEMEIA has been customized for IBD by a working group made up by gastroenterologists who are experts in IBD and representative of different modes of practice (university hospitals, general hospitals and private medicine), and IBD nurses from the national MICIDEC association. PROs and functional disability (IBDdisk) questionnaires were defined so that patients regularly (every 3 months) provide information on the status of their disease with a limited list of queries and so that they can declare a relevant medical event (flare-up, complication, extra digestive manifestation, adverse effect, pregnancy, etc.). The working group defined the specific algorithm to generate alerts to the healthcare team, in the event of a medical event relevant to the care pathway of the patient with IBD, likely to lead to an adapted therapeutic intervention. The nature of the alerts, as well as their thresholds, have been validated by an independent panel of healthcare professionals.

Our aim is to investigate if patients using remote monitoring follow-up thanks to the MedicWise platform specifically configured for IBD (brand name DigetsWise®), will have an optimized care pathway, with a positive influence on disease control, and the time spent in symptomatic remission.

For this, after randomization, patients included in two arms will be equipped with the MedicWise application. Data will be collected through MedicWise application in both arms at baseline, M3, M6, M9 and M12.

Alerts to the care team will be activated in only one arm: the active telemonitoring arm.

Each center will be free to define who handles alerts internally (physicians, IBD nurses, others, etc.) according to its own organization. The participation to the SECURITY study will not impose internal operations changes.

The alerts nature and thresholds will be frozen and identical for all centers during the study. Within the framework of the study, alerts are defined according to the study's modalities, but cannot be modified by the centers. Participating sites will have no obligation to respond to alerts.

Patients will be informed that the MedicWise application is not a device for managing urgent medical situations, and that they will have to, in both arms of the study, call the usual emergency services in this case, where to go to a usual emergency structure.

6 STUDY DESIGN

The study is a multicenter randomized controlled open labelled trial comparing two strategies to following-up patients with active IBD.

This study is based on the impact of a tight remote monitoring through digital tool on disease control in patients with active IBD using the MedicWise platform

MedicWise is a health data collection and processing online tool, which offers an innovative approach to remote patient monitoring without overburdening patients and healthcare teams. This tool is designed

to facilitate the medical practice of health professionals, to optimize the medical time available, to have a complete and up-to-date medical file, to reinforce remote management and, ultimately, to improve the quality of care offered to patients.

In both arms, patients are equipped with the MedicWise application configurated for IBD, clinical data and patients' reported outcome (such as PRO2 and IBD Disk and automatic data collection: use of other conventional treatments, patient healthcare costs can be partly reconstructed by healthcare reimbursement data and consumptions/routine biology parameters) are collected via the application.

In the **active arm** (telemonitoring), patients will be trained by local CRA teams and the SEMEIA platform to use the MedicWise tool and to complete the disease status questionaries in case of any medical event. Only in this arm, the MedicWise device will generate alerts to the local team according to an IBD specifically designed algorithm. The alert thresholds are identical and fixed for all centers during the study. Within the framework of the study, alerts are defined according to the study's modalities but cannot be modified by the centers. Each center defines who handles alerts internally (physicians, IBD nurses, others, etc.) according to its internal organization. The local care team will choose the mode with which it will interact with the patient (message, teleconsultation, consultation face-to-face). The study protocol does not enforce to change usual internal operations in each participating centers and they will to tagg on the platform each action taken in response to the alerts to validate. In case of alert according to the investigators clinical decision the following actions could be taken :

- No treatment adjustment or modification
- Treatment optimization
- Treatment modification
- Others medical intervention

In the **control arm** (deactivated alerts), the MedicWise device will be used by the patients to fulfill the PRO2/IBD Disk questionaries and to collect automatically health data. No alerts will be provided to the local care team, and the patients will be invited to contact the local care team in case of medical event, according to usual communication channels established in the local center (phone call, email, visit…).

Randomization rules: A 1:1 randomization is planned. To limit potential bias linked to centers sizes and specific organizations, the randomization will be stratified by centers. To balance also disease types, the randomization will also be stratified by diseases (CD and UC). Randomization with random block size will be used.

Patients will be informed that the MedicWise device is not dedicated to managing emergent medical situations and complications, and in such cases, patients must call emergency units and services directly.

Patients will be followed-up for an observational period of 12 months with last visit at M12.

7 STUDY FLOWCHART

PERIOD (WEEK/MONTH)	W-2	W0	M3	M4[6]	M6	M9	M12[6]
Site visits[1]	Screening VS	Randomization V1		V2			End of study V3
Signature of Consent Form	X						
Inclusion/ exclusion	X						
Randomization		X					
Vitals/ physical exam	X	X		X			X
Patient education and MedicWise training[2]		X					
Telemonitoring for **Active arm**		◆	→	→	→	→	→
PRO2 score[3]		X	X		X	X	X
S-IBDQ[4]		X		X			X
IBDdisk[3]		X	X		X	X	X
Patient adhesion		X		X			
Number of contacts / consultations / hospitalizations				X			X
Adverse events		X		X			
Time spends per day in outpatient management[5]		X		X			X

1- Each visit shall be carried out at the end of the relevant time period ± 14 days.
2- Installation & training will be done by Semeia for the **active arm**
3- PRO2 and IBDdisk will be collected directly from patients using MedicWise® tool
4- S-IBDQ will be collected during the on-site visit and collected on the eCRF tool
5- Only for sites willing to participate
6- This visit can be performed on-site (face to face visit) or remotely (teleconsultation)

8 DESCRIPTION OF THE STUDY VISITS

8.1 VS (W-2) Screening visit

The screening visit will take place after the decision by the investigator to introduce a new biologic treatment to the patient. During the screening visit, the investigator informs the participant and answers all questions regarding the purpose, nature of the constraints, foreseeable risks and the expected benefits of the research. The investigator also specifies the participant's rights in the context of a study and checks the eligibility criteria. The investigating doctor then gives a copy of the information note and the consent form to the participant. After this information session, the participant has a reflection period. The randomization can be done on the same day if the patient has had sufficient time to think and all of his questions have been answered appropriately and a signed informed consent will be obtained prior to entry into the trial for each patient having made a positive decision to participate. The investigator must confirm that the patient meets all inclusion criteria and none of the non-inclusion criteria

- Inclusion/ exclusion criteria
- Presentation of the study information note and consent form to the patient

8.2 V1 (W0) Randomization visit / could be coupled with screening visit

The investigator collects the inform consent form signed by both parties (patient and investigator). After performing the clinical evaluation, the investigational team can perform the randomization via the eCRF and present the MedicWise telemonitoring tool to the patient.

If the patient is randomized in the **Active Arm**, a meeting with the SEMEIA team and the patient has to be setting up quickly to be trained to report medical events via MedicWise.

After the randomization the patient will have to:

- Download the MedicWise app on patient’s cell phone and/or laptop and be trained by the sites' CRAs if he was randomized in the **Control arm** and/or by the SEMEIA platform team if he was randomized in the **Active Arm**.
- Complete the baseline data collection (PRO2, IBD disk) using MedicWise telemonitoring tool (all patients).

For all patients the following assessment has to be done by the investigational team to fill the eCRF:

- Medical history
- Treatments
- Disease activity assessment
- S-IBDQ

8.3 V2 (Month 4 +/- 2 weeks)

The visit must be performed by an investigator of the study. This visit can be performed on-site (face to face visit) or remotely (teleconsultation). During the visit, the following assessment has to be done to fill the eCRF:

- Collection of relevant medical events and explorations (endoscopy, imaging, biology)
- Complications and adverse event
- Disease activity assessments
- Treatments
- S-IBDQ
- Check the data collection by patients on the MedicWise app. (PRO2, IBD disk)

8.4 V3 (Month 12 +/- 2 weeks) End of study visit

The visit must be performed by an investigator of the study. This visit can be performed on-site (face to face visit) or remotely (teleconsultation). During the visit, the following assessment has to be done to fill the eCRF:

- Collection of relevant medical events and explorations (endoscopy, imaging, biology)
- Complications and adverse event
- Disease activity assessments
- End of study assessment
- Treatments
- S-IBDQ
- Check the data collection by patients on the MedicWise app. (PRO2, IBD disk)

8.5 eQuestionnaire: M0-M3-M6-M9-M12

MedicWise will push e-Questionnaire to each patient (PRO2, IBD disk). Patients in both arms will be notified by the application in the event of incomplete data filling at M0, 3, 6, 9 and 12. The window to fill-in the data in the app. will be open during a maximum period of 14 days.

The SEMEIA team will regularly send a report to each site, to inform the investigational team, any delays in completion to follow up patients if necessary to avoid missing data.

8.6 MedicWise telemonitoring tool:

MedicWise will pull other related clinical data directly from the patient personal medical file (“mon espace santé”) to collect treatments consumption, routine biology data, emergency explorations for all patients and generate appropriate alerts only for patients enrolled in the “**Active arm**”.

Patients in the **Active arm** can use MedicWise® app. at any time to report a medical event to the care team, who will choose whether to respond according to their own rules. Patients in the control arm will contact their care team using the usual channels available at each center.

8.7 Concomitant medications

All approved treatments are permitted in the trial according to physician choice and current guidelines.

9 END OF STUDY

The end of study is defined as the last participant's last visit.

The Investigators and/or the trial steering committee, DSMB and/or the co-sponsor(s) have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the Ethic Committee and Regulatory Authority within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow up is arranged for all participants involved.

A summary report of the study will be provided to the IRB and Regulatory Authority and will be publicly available within 1 year of the end of the study in accordance to the European DM Regulation 2017/745 and MDCG 2020-10/1,

9.1 Removal of Subjects from Therapy or Assessment

In accordance with the Declaration of Helsinki and ICH Clinical Guidelines, subjects will be free to withdraw from the study at any time if they wish so, for any reason specified or unspecified.

9.1.1 Criteria to withdraw subject from the trial

- Screen failure
- Consent withdrawn
- Lost to follow up
- Protocol violation
- Investigators decision

9.1.1.1 Type and timing of data to be collected from withdrawn subject

When possible the following information or part of it should be collected from patients withdrawing study.

- Demographics
- If applicable sentry selection criteria not met
- Cause of study withdrawal if not screen failure
  - Consent withdrawn

- Lost to follow up
- Protocol violation
- Investigators decision

9.1.1.2 Patient replacement

No patient replacement procedure is applied in this study

9.1.1.3 Follow up for withdrawn patients

Adverse events up to one month after study withdrawal should be reported to study sponsor.

Study subject participation can be discontinued due to:

- Withdrawal of subject consent, or loss to follow-up, or inability to remain under medical observation including post study examination,
- Non-compliance or major deviation from the protocol, where, in the opinion of the Investigator, continuation of the study would not be in the interest of the subject,
- SAE occurrence,
- Any other situation where, in the opinion of the Investigator, continuation of the study would not be in the interest of the subject,
- Study termination by GETAID.

The reason for withdrawal will have to be recorded in the eCRF for all withdrawn subjects.

The CRF must be completed up to the time of drop out. The premature termination form in the CRF must be completed for all dropouts.

All data, including any information collected from MedicWise® app. from any withdrawn subject, has to be included in the final report. These data will only be evaluated if both the Sponsor and the Investigator agree that it is valid to do so.

Subjects withdrawn because of adverse experiences will undergo a physical examination and laboratory tests planned at the follow-up visit. A follow-up of AEs will also be undertaken for withdrawn subjects.

9.2 Continuation of telemonitoring following the end of study

At the end of the study, patients and care teams will have the option to continue telemonitoring using the MedicWise application, in accordance with the software's EC certificate.

10 STATISTICS

10.1 Sample size calculation

By considering the following assumptions for the percentages of patients in remission as a function of time in the patient groups:

- Control arm: 30% at 1 month, 40% at 3 months, 50% at 9 months and 60% at 12 months
- Monitored arm: 30% at 1 month, 50% at 3 months, 60% at 9 months and 75% at 12 months (these assumptions are based on investigators personal data).

From these percentages we calculated by simulations the probability that a patient in the Monitored arm has a time spent in remission larger than a patient in control arm. This p value was equal to 0.61 corresponding to an effect size equal to 0.4. Then we introduced this value in the formula proposed by Noether G (Noether, G. E. (1987). Sample Size Determination for Some Common Nonparametric Tests. Journal of the American Statistical Association, 82(398), 645–647) to calculate sample size for Mann-Whitney test. We found that a sample size of n=145 patients randomized per group will provide 90% power to demonstrate a difference in time spent in remission by Mann-Whitney test at 5% two-sided alpha risk.

10.2 Randomization

Randomization will be performed centrally, using the eCRF support tool Cleanweb® provided by Telemedecine Techonlogies. It will be performed once all eligibility criteria have been checked. The randomization will be stratified by centers. To balance also disease types, the randomization will also be stratified by diseases (CD and UC). Unbalanced blocks of randomization will be applied.

10.3 Statistical Analysis

10.3.1 Analyses populations

10.3.1.1 Intention-to-treat (ITT) population

The intention-to-treat (ITT) population will include all randomized patients. Patients will be analyzed according to the group determined by their randomization, and not by the strategy actually followed.

In the case of a major protocol deviation (as per 'ICH 6 Essential Trial Documentation'), such as lack of informed consent, subjects will be excluded from the ITT population in the efficacy. Patients who will withdraw their consent during the trial will be analyzed until the time of withdraw.

10.3.1.2 Full Analysis Set (FAS) Population

Not adapted in this study randomizing strategy

10.3.1.3 Per Protocol Population

The per-protocol (PP) population will include all patients in the ITT population who have no major violations.

All violations of the protocol will be classified as major/minor in a blinded manner by a specific committee before data-base freezing.

A priori defined major violations are:

- Non respect of the inclusion/exclusion criteria
- No answers to ePRO
- Non respect of the randomization arm
- Non respect of the modalities of the strategy recommended by the protocol (i.e no answer to alert by the center, technical problem at the level of the platform, use of the app by the patient less than 15% of that anticipated)
- Early End of the study.

Main analysis will use the intention to treat population. Additional per protocol analysis will be performed to discuss the impact of the monitoring in absence of major protocol violations.

For the primary criterion, if percentages of missing values are higher than 5% they will be imputed using Monte Carlo Markov Chain methods. In addition since it cannot be excluded that missing values will not be at random (MAR), sensitivity analyses for hypothesis of MNAR missing values will be performed using the delta-adjusted pattern imputation implemented in the MNAR Statement of PROC MI from SAS 9.4. (details of the procedures will be provided in the SAP)

No imputation will be performed for missing data on secondary criteria (complete cases analysis).

- Primary criterion will be analyzed by Mann-Whitney test.
- Secondary criteria corresponding to IBD and IBDQ measurements will be analyzed by ANCOVA using baseline value as covariate. Normalizing transformations or rank analyses will be used if necessary.
- Satisfaction and other questionnaires will be analyzed by Mann-Whitney tests
- Counts of events will be analyzed by Poisson regression.
- Correlation between SIBDQ and IBDisk values will be studied by Spearman's non parametric correlation test.

Management of alpha risk.

In order to take into account multiplicity for secondary criteria, we will use a hierarchical method of test for the following secondary criteria that will be analyzed in the following order.

- Average value of IBD disk change from baseline over 12 months
- PR02 at M12
- Average value of S-IBDQ change from baseline over 12 months
- Number of complications (, hospitalizations, surgeries) over 12 months
- Time spend per day in outpatient management (questionnaire at M6 and M12)
- Medication and care compliance/consumption over 12 months

A p value will be reported for the n^{th} criterion of the list only if the p value for the test of the $(n-1)^{th}$ criterion of the list is <0.05 (two-sided). Otherwise only difference between group and associated 95% two-sided confidence interval will be reported.

Other secondary criteria will be considered as exploratory and only difference between group and associated 95% two-sided confidence interval will be reported.

10.4 Interim analysis

An interim analysis is planned when 50% of patients have reached the primary endpoint for sample size reassessment if necessary.

Based on promising zone approach (Mehta and Pocock (2011)): if the conditional power is ≥ 80% (favorable zone), continue with original sample size; if the conditional power is 50% ≤ CP < 80% (promising zone), sample size will be increased to achieve a conditional power of 80% with the maximum sample size caped at n=200 patients/group; if the conditional power is <50% (unfavorable zone), then the trial will continue with the initial planned sample size. No Type I error rate adjustment is needed since the sample size is only to be increased when the interim results are promising (Chen, DeMets, Lan, 2004)

10.5 Data Collection

All data will be collected in an electronic case report form (eCRF). The Statistical Centre will perform data collection, data quality control and statistical analysis.

The CRFs will be prepared by Cleanweb® and will be reviewed by the Biostatistics and the Data Management units approved by the GETAID.

If applicable all data recorded on subject diary of the clinical phase of the study will be recorded directly and legibly in black ink and reported in the eCRF by the study coordinator present on each investigational site.

For patients randomized in the **Active arm**, clinical data (biology, ePRO) collected by MedicWise® will be uploaded directly in the eCRF, thanks to regular extractions transmitted by SEMEIA to the study coordinator and investigators.

10.5.1 Data Monitoring

As described in the Monitoring Plan, the complete eCRFs sets will be received and reviewed by the Monitor to check protocol adherence and to detect any data inconsistency or discrepancy. Once corrections made and signed by the investigator and monitor data will be and all the requested modifications will be traced on Data Clarification Forms. Subject diary data will be reviewed by the study site to check protocol adherence and to detect any data inconsistency or discrepancy.

Once monitored, the eCRF forms will be locked and any requested changes will be tracked in the data clarification forms.

10.5.2 Database set-up

The GETAID data management system and standard libraries are used to set up the database and design the screens.

10.5.3 Data Handling Manual

A Data Handling Manual is edited. This document contains the annotated CRF, the data validation plan (list of rules to be applied to validate the data) and the database structure.

This document is provided by the data management unit to Sponsor for approval before starting the double data entry process if any.

10.5.3.1 Data Validation

Automatic checks and listings are designed and performed according to the data validation plan. In case of missing values, out of range values, data inconsistencies or values that fail logical checks, Data Clarification Forms (queries) will be edited and forwarded to the Investigator for clarification. Inconsistencies found to be correct are documented on Data Clarification Form. Modifications performed on electronic study data are also fully tracked.

10.5.3.2 Data Coding

AEs will be coded using MedDRA terminology. The medical coding will be performed by a Data Manager and reviewed by the Investigator before being submitted to the Sponsor for approval.

10.5.3.3 Database Lock

Once all queries validated, the database will be locked so that no more change will be possible on the frozen data.

11 SAFETY ASSESSMENTS

11.1 Definition

According to article R1123-46 of the French public health code, the European DM regulation 2017/745 and MDCG 2020-10/1

11.1.1 Adverse event

Any adverse event, unintended illness or injury, or any clinically relevant untoward sign, including an abnormal laboratory result, in participants, users or other persons, as part of a clinical investigation, whether or not related to the medical device(s) of a clinical investigation.

For users or other patient, this is limited to events related to the investigational medical device.

Note:

- This definition includes both expected and unexpected events.
- This definition includes events occurring during a clinical investigation related to the investigational device, comparator or procedures involved.

11.1.2 Serious adverse event (SAE)

If an adverse event meets any of the following criteria, it is regarded as SAE and should be reported within 24 hours of the site being made aware of the serious adverse event to the GETAID and the national Sponsor:

- death;
- a serious deterioration in the participant's state of health, resulting in:
  - a life-threatening illness or injury;
  - permanent impairment of an anatomical structure or function;
  - hospitalization or prolongation of hospitalization of the patient;
  - medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment of an anatomical structure or function;
  - a chronic illness;
- fetal suffering, fetal death, congenital physical or mental impairment or congenital malformation;

The term SAE includes any device malfunction that could have resulted in a serious adverse event in the absence of appropriate measures or intervention, or if circumstances had been less favorable.

Refer to paragraph 11.2.2 for SAE not requiring immediate notification to the sponsor and events of special interest.

11.1.3 Device deficiency

Any defect in the identity, quality, durability, reliability, safety or performance of a device under investigation, including any malfunction, error of use or defect in the information provided by the manufacturer.

11.1.4 Causal relationship

The causal relationship between the use of the medical device (including the medical/surgical procedure) and the occurrence of each adverse event must be assessed and classified. The above explanations also apply to serious adverse events occurring in the comparator group.

To harmonize reporting, each SAE will be classified according to four different levels of causality:

11.1.4.1 Unrelated:

The causal relationship with the device, comparator or procedures can be excluded when :

- the event has no temporal relationship with the use of the investigational device or the procedures related to the application of the investigational device;
- the serious adverse event does not follow a mechanism of action known to the medical device (if previously known) and is biologically implausible;
- stopping use of the medical device, or reducing the activation/exposure level where clinically possible, and re-using it (or increasing the activation/exposure level), has no impact on the serious adverse event;
- the event involves a body site or organ that cannot be affected by the device or procedure;
- the serious adverse event can be attributed to another cause (for example, an underlying or concomitant disease/clinical condition, an effect of another device, drug, treatment or other risk factors);
- the event does not depend on a false result given by the investigational device used for diagnosis, if applicable;

To establish the absence of a link, all the criteria listed above may not be met at the same time, depending on the type of device/procedure and the serious adverse event.

11.1.4.2 Possible:

The causal relationship with the use of the investigational device or comparator, or the relationship with the procedures, is weak but cannot be totally excluded. Alternative causes are also possible (e.g., an underlying or concomitant disease/clinical condition and/or an effect of another device, drug or treatment). Cases where the link cannot be assessed, or where no information has been obtained, should also be classified as far as possible.

11.1.4.3 Probable:

The causal relationship with the use of the investigational device or comparator, or the relationship with the procedures, seems relevant and/or the event cannot be reasonably explained by another cause.

11.1.4.4 Causal link (certain)

An adverse event that is evaluated with a possible, probable or certain causal relationship is considered an effect.

11.1.5 Serious unexpected adverse reaction

A serious undesirable effect considered unexpected if its nature, incidence, severity or evolution is not identified in the current risk assessment document.

11.1.6 Immediate notification of Serious Adverse Events (SAEs) to the sponsor

The investigator assesses each adverse event/defect in terms of its seriousness.

The investigator must notify the sponsor immediately, and at the latest within 3 calendar days of becoming aware of the event, of all serious adverse events occurring in the trial, and of any device malfunction that could have resulted in a serious adverse event in the absence of appropriate measures or intervention, or if circumstances had been less favorable, with the exception of those identified in the protocol as not requiring immediate notification (paragraph 11.2.2).

This initial notification is the subject of a report and must be followed by one or more additional detailed reports within 8 days of the first notification.

The investigator validates the SAE notification form, dates it, and sends it by e-mail via the eCRF to GETAID, as soon as he/she has the 4 minimum elements required to notify an SAE:

- A notifier
- A subject
- An experimental device (if applicable)
- A serious adverse event

SERIOUS ADVERSE EVENTS MUST BE REPORTED TO:

GETAID Central Office

50 rue Richer, 75009 PARIS FRANCE

Tel: + 33 (0) 9 72 57 61 60 Fax: +33 1 84 10 85 45

sae@getaid.org

The investigator must document the event to the full extent possible (using copies of laboratory results, test reports or hospitalization records documenting the serious event, including relevant negative results, without omitting to anonymize these documents and record the patient's number and code), the medical diagnosis and establish a causal link between the serious adverse event and the medical device(s) and the procedure used to implement it.

The investigator must follow the patient who has had a SAE until it is resolved, stabilized at a level deemed acceptable by the investigator, or returned to its previous state, even if the patient has left the trial, and inform the sponsor by completing the eCRF and sending it by e-mail to sae@getaid.org (fill in the FU [Follow Up] section with name, date and signature on the eCRF).

11.2 Restriction of AEs/SAEs, reporting period for AEs and adverse events of particular interest

11.2.1 Events of particular interest:

Certain events require special monitoring and will be notified as a serious AE even if they do not meet the severity criteria (at the request of the sponsor, the Independent Monitoring Committee, a pharmaceutical company or the competent authorities):

- Device failure causing an SAE
- Device malfunction that could have led to a serious adverse event in the absence of appropriate measures

11.2.2 Restriction of adverse events in the CRF:

In view of the medical device studied, the following adverse events will not be collected in the adverse events section of the CRF, nor notified as an SAE to the sponsor with the SAE notification form.

11.3 Sponsor's responsibilities

According to the Art. 80 of the MDR: The sponsor of a clinical investigation conducted in France records and notifies the safety data mentioned below whether they occur in the clinical investigation in France, in the EU, or in a third country outside the EU.

11.3.1 Events to be recorded

The sponsor records the following data ie adverse events, serious adverse events and device deficiency (defined in section 11.1), which have been transmitted to them by the investigator without delay and no later than within 3 calendar days of awareness:

a) any adverse event defined in the protocol as critical for the evaluation of the clinical investigation results;

b) any serious adverse event;

c) any device deficiency that could have led to a serious adverse event in the absence of appropriate measures or intervention, or if the circumstances had been less favorable; d) any new information regarding an event referred to in points a) to c).

11.3.2 Event to be reported to the competent authorities

In accordance with article R1123-55 of the CSP, the European DM Regulation 2017/745 and MDCG 2020-10/1, the sponsor must report the following "reportable events" to the competent authorities:

a) any serious adverse event with a proven or reasonably foreseeable causal relationship with:

- the medical device under investigation,
- or the comparator medical device,
- or the preceding investigation procedure;

b) any defect of a medical device that could have led to a serious adverse event in the absence of appropriate measures or intervention, or if the circumstances had been less favorable;

c) any new information regarding an event referred to in points a) and b).

Notification begins once the clinical investigation is duly authorized, even if the first participant has not yet been included in France.

All events and defects mentioned in thissection that have resulted in death or an imminent risk of death, serious injury or illness, and that require rapid corrective action for participants/patients, users, or other persons, or any new information related to these events:

- Without delay (immediately), and no later than 2 calendar days from the day the sponsor became aware of the event to be reported or new information regarding an already reported event.

Other events and defects mentioned in section 4 or any new information/updates concerning them:

- Without delay (immediately), and no later than 7 calendar days from the day the sponsor became aware of the event to be reported or new information regarding an already reported event.

12 BENEFIT/RISK

Security is a study classified IC DM 4.4 according to the European DM Regulation 2017/745 and MDCG 2020-10/1 in terms of risk. The goal here is to evaluate the contribution of a remote monitoring tool (MedicWise®) to the care pathway for patients with IBD. Patients will be treated as part of routine care in both arms of the study and will have the paraclinical examinations

necessary for their follow-up and care following physician (investigators) indications. We anticipate that there will be no risk of adverse events linked to the digital tool (MedicWise®) tested in the study. The remote monitoring tool tested in the SECURITY study is not dedicated to emergency situations. Patients will be informed that in the event of a medical emergency, they should contact their healthcare facility or an emergency department directly. In addition, in the event of a technical failure in the transmission of alerts in the active telemonitoring arm, patients will still be able to contact their healthcare team through the usual communications channels. Furthermore, pejorative medical events (disease flare-up, drug intolerance, complications of the disease from treatments, etc.) will be collected in both arms since they are part of the events of interest used to evaluate the main objective or secondary objectives of the study.

13 ORGANIZATIONAL, LEGAL AND GENERAL CONSIDERATIONS

13.1 Ethical Conduct of the Study

The trial will be carried out in accordance with the Declaration of Helsinki (Edinburgh, 2000) completed by Notes of Clarification to articles 29 (Washington, 2002) and 30 (Tokyo, 2004) respectively, and revised in 2008 (Sixth version Seoul). The trial will also be conducted in compliance with the protocol, the ICH Guidelines for Good Clinical Practice (ICH E6), the European DM Regulation 2017/745 and MDCG 2020-10/1, and the applicable local country laws/regulations.

Written favorable approval will be obtained from an Independent Ethic Committee (IEC) and the Competent Authority (CA) will be notified prior to the study being implemented.

The study will be conducted in accordance with International Guidelines on Good Clinical Practices (GCP) and Standard Operating Procedures (SOP) for clinical investigation and documentation in force at GETAID.

The study will be monitored by a monitor designed by the GETAID who will regularly check compliance with the protocol, will compare selected key data in the CRF with its source data, and will verify the medical device management and Informed Consent.

13.2 Submission to Ethics Committee and Health Authorities

This protocol complies with the French regulations. Approval by the national Ethics Committee and Competent Authority notification will be required before study start. According the local regulatory requirements:

- It is the Investigators' responsibility or the Sponsor's responsibility to obtain and maintain written approval of the final Study protocol, including the Patient Information and Informed Consent, from the appropriate Ethics Committee.

- It is the Investigators' responsibility or the Sponsor's responsibility to notify the Independent Ethics Committee (IEC) about any amendments to these documents. In case the protocol amendment changes the scope of the study or increases the risks of the study patients, the investigator or sponsor should wait for approval of this amendment by the Independent Ethics Committee before implementing the protocol amendment. The written approval and the approved versions of the documents and a list of the Ethics Committee members, their titles and occupations should be sent to the responsible study personnel at GETAID. The written approval should identify the study and document the date of review. The Investigators and the sponsor should file all correspondences with the Ethics Committee in the Site Investigator's File and Trial Master File, respectively.
- It is the investigator's responsibility or the Sponsor's responsibility to issue a final report to the Ethics Committee within 12 months after completion, termination or discontinuation of the study.

13.3 Compliance with Good Clinical Practices (GCP)

This clinical investigation will be conducted in accordance with Good Clinical Practices (GCP) as defined by standard ISO 14155:2020 and Regulation (EU) 2017/745 on medical devices. The study protocol, data collection procedures, and analyses will be designed to ensure the protection of the rights, safety, and well-being of the subjects participating in the study. All data will be recorded and presented in a manner that ensures their reliability and integrity, in compliance with current regulatory and ethical requirements.

13.4 Emergency procedures

The GETAID accepts the right of the Investigator to deviate from the protocol in an emergency when necessary to safeguard the life or the wellbeing of a study patient. The Investigator must inform the study personnel responsible at GETAID of any emergency deviations and justification for the deviation as quickly as possible after the episode, in any event no later than 24 hours after the emergency. According to the local regulatory requirements, the investigator or the sponsor must inform the Ethics Committees of any emergency deviations and justification for the deviation in the local regulatory timelines.

13.5 Study protocol amendment and study extension

Without a common agreement between all the investigators, national sponsors or the global sponsor GETAID, no alteration or modification of this protocol will be considered valid. In case of such an agreement the planned modifications will be subjected to an amendment linked with the protocol. Any protocol amendment must be notified by the coordinator to the Ethics Committees and Regulatory Authorities.

13.6 Study documents

Prior to initiation, the investigator will supply sponsor representatives with a copy of his personal curriculum vitæ, together with those of his co-investigators. He will commit himself to respect the protocol, local regulations, Helsinki Declaration terms, ICH and Good Clinical Practices.

The sponsor representatives will be supplied with a dated and signed copy of the latest study drug information (e.g SmPC, IB, …).

13.7 Patient information and patient informed consent form

Voluntary written Informed Consent Form (ICF) must be obtained from each subject prior to performing any study related procedures in compliance with the recommendations of the Declaration of Helsinki and ICH guidelines. Subject should not be screened or treated until the subject has signed an approved ICF written in a language that is understandable to the subject.

Each subject should be given both verbal and written information describing the nature and duration of the clinical study. The ICF should be signed and personally dated in 2 originals by the subject and the person who conducted the informed consent discussion. The Investigator, or the attending physician, will explain the nature, purpose and risks of the study. The subject will be informed that he has the right to withdraw at any time from the study, without giving reasons. In this condition, the subject will also be informed that he will not receive any indemnity according to applicable regulations. The informed consent process should take place under conditions where the subject has adequate time to consider the risks and benefits associated with his participation in the study.

The Investigator is responsible for assuring the appropriate content of the ICF and that informed consent is obtained from each subject in accordance with all applicable regulations and guidelines. The ICF will be reviewed and approved by the Sponsor, and then submitted to the IEC.

Each subject should receive one original of the signed and dated written ICF and any other information provided to the subject.

The second original of the signed and dated ICF should be retained in the Investigator's file. The Investigator should maintain a log of all subjects who sign the ICF.

13.8 Data transcription

All data will be collected in an electronic case report form Cleanweb® provided by Telemedecine technologies. At each clinical visit, the treating physician will complete the electronic CRF with clinical observations regarding disease activity, disease complications, and adverse events. Patients will complete every 3 months ePRO (PRO2 and IBD-Disk) with the MedicWise® tool on their smartphone or tablet. For patients in the **active arm,** MedicWise will pull other related clinical data directly from the patient

personal medical file ("mon espace santé") *ie*. treatments consumption, routine biology data, emergency explorations and uploaded in the eCRF at the end of the study.

At the end of the study, all data collected in the participating centers will be centralized and the complete data set of the study will be analyzed by the principal investigators and the statisticians.

13.9 Monitoring procedures

The CRA will perform data review on an ongoing basis for completeness and quality control and will perform data source validation according to the monitoring plan. The investigator and co-investigators agree to welcome at regular intervals the GETAID monitors. After every visit, monitors will write a visit report and send a letter to the center to address issues requiring follow up.

Investigators and institutions involved in the study will permit trial related monitoring and audits on behalf of the sponsor, IRB review, and regulatory inspection(s). In the event of an audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

13.10 Responsibilities

GETAID is the main study sponsor. In accordance with the French regulations GETAID signed an insurance policy with the SHAM group covering civil liability for potential damages that could happen to any subject involved in this research in France under agreement No 127.047.

National Sponsor shall secure and maintain at their own expense in full force and effect through the performance of the Study (and following termination of the Study to cover any claims arising from the Study) insurance coverage in amounts appropriate to the conduct of the Study and in conformance with applicable legal and regulatory requirements as well as comprehensive and professional liability insurance of reasonable policy limits for their own country.

All the information concerning the patients will be anonymized

14 AUTHORSHIP RULES

The GETAID publication charter will apply to the publication of any related study results.

15 STORAGE

The data concerning the study will be stored for 25 years after the end of the study by the investigator.

A copy of these data will also be stored for 25 years by the GETAID offices.

16 FINAL STATEMENT

GETAID owns all data. No use and no transmission to a third party will be made possible without its prior consent.

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ANNEXES

17 ANNEX 1- S-IBDQ

Le SIBDQ est une version plus courte de l'IBDQ, avec seulement 10 questions. Les scores SIBDQ peuvent aller de 10 (qualité de vie très altérée) à 70 (qualité de vie normale).

les questions du Short Inflammatory Bowel Disease Questionnaire (SIBDQ) en français :

1. Pendant la semaine dernière, avez-vous souffert de douleurs abdominales, de crampes ou de ballonnements ?
2. Pendant la semaine dernière, avez-vous eu des nausées ou des vomissements ?
3. Pendant la semaine dernière, avez-vous éprouvé de la fatigue, une sensation de faiblesse ou d'épuisement ?
4. Pendant la semaine dernière, avez-vous eu des diarrhées ?
5. Pendant la semaine dernière, avez-vous eu des douleurs anales ?
6. Pendant la semaine dernière, avez-vous eu des saignements rectaux ?
7. Pendant la semaine dernière, avez-vous évité de manger ou de boire parce que cela provoque des symptômes ?
8. Pendant la semaine dernière, avez-vous évité les activités sociales ou professionnelles parce que cela provoque des symptômes ?
9. Pendant la semaine dernière, avez-vous éprouvé des inquiétudes ou des inconvénients liés au traitement ?
10. Dans l'ensemble, comment évaluez-vous votre état de santé pendant la semaine dernière ?

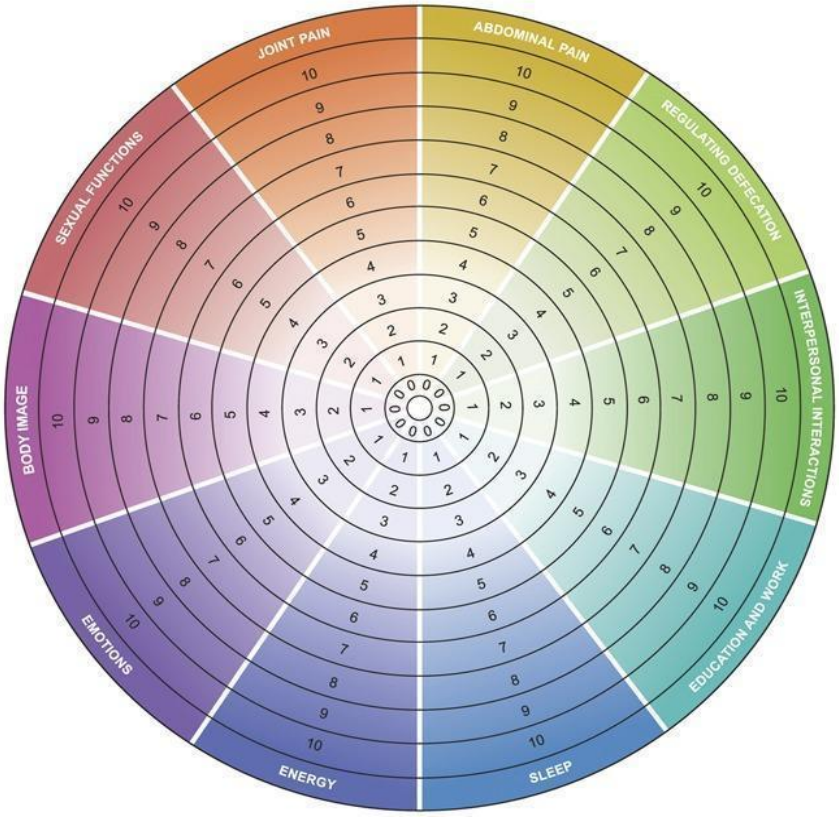
Chaque question est évaluée sur une échelle de 7 points, allant de 1 (symptômes graves) à 7 (absence de symptômes). Le score total du SIBDQ est calculé en additionnant les réponses à chaque question, avec un score maximal de 70 et un score minimal de 10.

18 ANNEX 2: IBD-DISK

For each of the ten statements below, score your level of agreement on a scale of 0 to 10. Circle your scores on the coloured disc.

Absolutely disagree					Neither agree or disagree					Absolutely agree
0	1	2	3	4	5	6	7	8	9	10

In the last week, because of my Crohn's disease or ulcerative colitis...	
Abdominal pain	...I have had aches or pains in my stomach or abdomen
Regulating defecation	...I have had difficulty coordinating and managing defecation, including choosing and getting to an appropriate place for defecation and cleaning myself afterwards
Interpersonal interactions	...I have had difficulty with personal relationships and/or difficulty participating in the community
Education and work	...I have had difficulty with school or studying activities, and/or difficulty with work or household activities
Sleep	...I have had difficulty sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning
Energy	...I have not felt rested and refreshed during the day, and have felt tired and without energy
Emotions	...I have felt sad, low or depressed, and/or worried or anxious
Body image	...I have not liked the way my body or body parts look
Sexual functions	...I have had difficulty with the mental and/or physical aspects of sex
Joint pain	...I have had pains in the joints of my body



19 ANNEX 3: PRO2

For UC:

STOOL FREQUENCY:

Mean number of smooth or liquid stools per day during the last 7 days :

0: Normal

1: 1-2 stools/day more than normal

2: 3-4 stools/day more than normal

3: 5 or more stools/day more than normal

RECTAL BLEEDING:

Evaluation of rectal bleeding during the last 7 days:

0: None

1: Visible blood with stool less than half the time

2: Visible blood with stool half of the time or more

3: Passing blood alone

For CD:

STOOL FREQUENCY:

Mean number of smooth or liquid stools per day during the last 7 days :

0: Normal

1: 1-2 stools/day more than normal

2: 3-4 stools/day more than normal

3: 5 or more stools/day more than normal

ABDOMINAL PAIN:

Evaluation of mean abdominal pain intensity during the last 7 days:

0: None

1: mild

2: moderate

3: severe