**Study title:**

**Study Acronym:**

**EudraCT N°:**

**Protocol version: Date:**

**Sponsor:** Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD)

Confidential

The information provided in this document is strictly confidential and is intended solely for the guidance of the clinical investigation. Reproduction or disclosure of this document - whether in part or in full - to parties not associated with the clinical investigation or its use for any other purpose without the prior written consent of the sponsor is not permitted.

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| --- | --- | --- | --- |
| Study synopsis | | | |
| **Study title** |  | | |
| **Sponsor** | Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD) | | |
| **Principal Investigator** |  | | |
| **EudraCT N.** |  | | |
| **Protocol Version and Date** |  | **Phase** |  |
| **Background and rationale** |  | | |
| **Study objectives** |  | | |
| **Study design** |  | | |
| **Study popolation** |  | | |
| **Methodology** |  | | |
| **Statistical plan** |  | | |
| **Ethical considerations** |  | | |
| **Study timeline** | Project start date: Completion date of patients’ enrollment: Data collection completion date: Data analysis: Presentation of the scientific report: | | |

|  |  |
| --- | --- |
| **Roles and responsibilities**  **Principal Investigator**  **Sponsor:** | Name  Phone:  Fax:  e-mail:  Phone:  Fax:  e-mail: |
| **Study Coordinator:** | Name Surname  Phone:  Fax:  e-mail: |
| **Steering Committee:** |  |
| **Trial Manager:** | Name Surname  Phone:  Fax:  e-mail: |
| **Statistician:** | Name Surname  Phone:  Fax:  e-mail: |

**Notification in case of Serious Adverse Events:** Name Surname

Phone:

Fax:

e-mail:

**Authorizations and Signatures**

***Study Title***

**AGREEMENT**

**This document is confidential and belongs to the IgIBD.**

**The information is confidential and is to be used only in connection with matters authorized by the Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD), and no part of it is to be disclosed to others without prior written permission from the IG-IBD.**

**This document, however, can be made known to the designated Ethics Committee, or representatives authorized by the Investigator or the Health Authority provided that they are bound to its confidentiality.**

**The Principal Investigator’s signature below confirms his agreement to this protocol and provides the necessary guarantees that:**

**1.This study will be conducted following all the clauses of the protocol and in accordance with the Helsinki declaration (Edinburgh 2000 with Explanatory note paragraph 29 from Washington 2002 and paragraph 30 from Tokyo 2004) and current legislation regarding clinical studies.**

**2. No partial or final data (written or verbal) will be published without prior agreement between the Investigator and the IgIBD**

**PRINCIPAL INVESTIGATOR SIGNATURE**

**Printed name:**

**Institution:**

**Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date** XX.XX.XXXX

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Informed consent NON CONFONDERE, neanche nella terminologia, IL CONSENSO INFORMATO AL TRATTAMENTO SANITARIO CON QUELLO AL TRATTAMENTO DEI DATI PERSONALI (art. 7, Reg. 679/2016: “If the data subject's consent is given in the context of a written declaration which also concerns other matters, the request for consent shall be presented in a manner which is clearly distinguishable from the other matters, in an intelligible and easily accessible form, using clear and plain language (…)” 11

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# INTRODUCTION

## Background and rationale

*Breve revisione della letteratura (corredata da riferimenti bibliografici).*

*È fondamentale sostenere adeguatamente i presupposti dello studio. Il razionale deve mettere in evidenza le carenze conoscitive sull’argomento oggetto dello studio seguendo un filo logico che indichi come queste possano essere superate e che porti a concludere con l’ipotesi/le ipotesi del progetto (è comunque meglio indicare una ipotesi globale più ampia che tante più piccole)*

# Study design

*Definire il* ***disegno dello studio****: multicentrico, retrospettivo o prospettico, controllato o non controllato, aperto o in cieco, randomizzato o non randomizzato, osservazionale o interventistico, etc*.

## Primary objective

*Descrivere lo scopo principale per cui lo studio verrà condotto e le caratteristiche generali della popolazione che verrà analizzata (se sono presenti eventuali sottogruppi vanno specificati i criteri secondo cui vengono distinti i pazienti)*

## Secondary objectives

*Descrivere gli obiettivi secondari per cui lo studio verrà condotto e le caratteristiche generali della popolazione che verrà analizzata*

## Primary Endpoint

*Inserire la variabile che rappresenta la misura dell’obiettivo primario (e.g. morte, ospedalizzazione, effetto avverso ad un farmaco etc.).*

## Secondary Endpoints

*Inserire le variabili che misurano gli obiettivi secondari. I singoli* ***parametri e variabili*** *che verranno indagati durante lo studio devono essere elencati in maniera ordinata e precisa indicando anche gli strumenti, i tempi e i dettagli tecnici con cui i dati verranno acquisiti*

*Specificare la tempistica dei controlli a cui i soggetti in studio verranno sottoposti: valutazione basale ed eventuali follow up oppure strategia di trattamento, comparazione con farmaci già pre-esistenti, dose e posologia richiesti in caso di studio farmacologico. Questa sezione può essere corredata da grafici e flow chart che rendano più immediata l’interpretazione della strategia dello studio.*

# Methods: Participants, interventions and outcomes

## Eligibility criteria

## Inclusion criteria

*Elencare in maniera dettagliata i* ***criteri di inclusione*** *(compresa l’età e il sesso dei soggetti, nel caso in cui voglia essere ristretta ad una determinata fascia o genere)*

## Exclusion criteria

*Elencare i* ***criteri di esclusione*** *dallo studio per garantire che i soggetti che verranno analizzati siano selezionati in maniera corretta e i bias vengano ridotti più possibile.*

## Study design description

*Descrivere in maniera esaustiva come verrà condotto lo studio, come verranno arruolati e seguiti i pazienti.. In particolare specificare ( se possibile):*

1. *Trattamenti per ogni gruppo incluse modalità e tempistiche di somministrazione*
2. *Criteri per sospendere o modificare i trattamenti assegnati ad un determinato partecipante (es.modificare la dose del farmaco in seguito ad eventi avversi, in conseguenza ad un miglioramento o peggioramento della malattia)*
3. *Strategie per migliorare l’aderenza ai trattamenti previsti dal protocollo e procedure per monitorare l’aderenza (es restituzione di compresse, test di laboratorio)*
4. *Assistenza e trattamenti sanitari concomitanti e rilevanti permessi/non consentiti durante il trial*

***Outcome***

*Outcome primario, outcome secondari e altri outcome, con indicazione della variabile di misurazione specifica (es. pressione sistolica), di metrica dell’analisi (es., modifica dei dati basali, valore finale, tempo all’evento), del metodo di aggregazione (es. mediana, proporzione) e il timing di rilevazione per ciascun outcome. è fortemente raccomandata la spiegazione della rilevanza clinica degli outcome di efficacia e di sicurezza selezionati .*

***Participant timeline***

*Pianificazione delle tempistiche di arruolamento, erogazione degli interventi (compresi i periodi di run-in e washout), valutazioni e visite per i partecipanti. E’ fortemente raccomandato l’uso di un diagramma ( figura).*

***Sample size***

*Stima del numero di partecipanti necessari per raggiungere gli obiettivi dello studio. Si dovrà giustificare la numerosità del campione sulla base di un calcolo statistico basato sull’incidenza o prevalenza della patologia in esame, della frequenza di utilizzo di un determinato farmaco etc., sulla risposta attesa, indicando valori di α e potenza dello studio, indicando eventualmente anche se si richiede un numero massimo o minimo di soggetti reclutati presso ciascun centro in caso di studi multicentrici*

***Recruitment***

*Strategie finalizzate ad ottenere un adeguato arruolamento dei partecipanti al fine di raggiungere le dimensioni del campione stimate*

# Methods: Assignment of interventions (PER I TRIAL CONTROLLATI)

# *Allocation*

***Sequence generation***

*Metodo di generazione della sequenza di allocazione (es. numeri casuali generati da un computer) e lista di ogni eventuale variabile utilizzata per la stratificazione.*

***Allocation concealment mechanism***

*Meccanismo di implementazione della sequenza di allocazione (es. telefono centralizzato; sequenza numerica di buste opache e sigillate), con la descrizione di ogni eventuale step finalizzato a mantenere occultata la sequenza sino all’assegnazione dei trattamenti*

***Implementation***

*Chi genera la sequenza di allocazione, chi arruola i partecipanti e chi assegna i partecipanti ai trattamenti*

***Blinding (masking)***

*Chi è in cieco dopo l’assegnazione dei trattamenti (es. partecipanti , professionisti sanitari, valutatori dell’esito, chi analizza i datu ) e relative modalità*

*Se il trial è in cieco, indicazione delle circostanze in cui è permesso interrompere il blinding e procedura per rivelare l’intervento assegnato a un partecipante durante il trial*

# Methods: Data collection, management and analysis

# *Data collection methods*

1. Azioni pianificate per la valutazione e la raccolta degli outcome, dei dati basali e di altri dati del trial, incluso ogni eventuale processo correlato per promuovere la qualità dei dati (es. misure duplicate, training dei valutatori) e una descrizione degli strumenti dello studio (es. questionari, test di laboratorio) con indicazione della loro affidabilità e validità, se note.
2. Azioni pianificate per sostenere la permanenza dei partecipanti nel trial e per completare il follow-up, incluso un elenco completo degli outcome da raccogliere per i partecipanti che escono dallo studio o deviano dai protocolli di trattamento

The processing of the patient’s data, that is any operation or set of operations which is performed on personal data or on sets of personal data (such as collection, recording, organisation, structuring, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, restriction, erasure or destruction), will be carried out mainly with electronic and IT tools, in compliance with EU Regulation 2016/679. The same data will be entered in the General Register on the platform provided by IBISmed.

The personal data the patient provide from the time of signing the informed consent form and for the entire duration of the Project will be collected and processed, within the limits of the law and the consents provided by the patient, in a lawful manner, according to correctness, in compliance with the principle of relevance and non-excess and with the utmost confidentiality, and will not be subject to automated decision-making processes.

In particular, the data concerning the patient will be processed by the Data Controller and/or the Data Processors, therefore, recorded, organized, processed and stored, also through other subjects explicitly authorized by the Data Controller and/or the Data Processors themselves, ~~and/or by~~ like employees, collaborators, auxiliaries or professionals, also external. ~~-~~ In compliance with the roles assigned ~~to each subject~~ and for the only necessary time ~~-~~, each subject is appointed for this purpose ~~appointed~~ as Data Processors or as Authorized Subjects; in particular, the Authorized Subjects, adequately trained in order to the purposes and methods of treatment, are authorised to process personal data under the direct authority of the Controller or Processor. The list of service providers on behalf of the Data Controller, and for this purpose appointed as Data Processors, is available to the patient at \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [address and DPO references not yet appointed; pending, indicate the references of the Data Processor; this list is also contained in the Register of Treatment activities, viewable on request, not yet available]. At the time of uploading the patient’s data on the platform by the doctor who will follow the project, the system will assign the patient a progressive code, which will be kept separately from the other data collected so that only the doctor and the subjects expressly authorized by the owner will be able to connect this code to the patient’s name, thus allowing the patient’s identification. BISOGNA DEFINIRE LA TERMINOLOGIA, USANDO SEMPRE LO STESSO TERMINE PER EVITARE CONFUSIONE: NEL REGOLAMENTO IN LINGUA INGLESE QUELLO CHE NOI CHIAMIAMO “TITOLARE” NON E’ “OWNER”, MA “CONTROLLER”, TERMINE CHE VOI INFATTI USATE CORRETTAMENTE IN ALTRE PARTI DEL TESTO. E’ PREFERIBILE USARE SEMPRE “CONTROLLER”, MAGARI PREVEDENDO NELLA PREMESSA CHE IL “OWNER” E “PROMOTER” COINCIDONO CON IL “DATA CONTROLLER”.

When two or more Data Controllers jointly determine the purposes and means of processing, they shall be Joint Controllers. They determine in a transparent manner their respective responsibilities for compliance with the obligations under the UE Regulation, in particular as regards the exercising of the rights of the data subject and their respective duties to provide the information referred to in Articles 13 and 14, by means of an arrangement between them unless, and in so far as, the respective responsibilities of the Controllers are determined by Union or Member State law to which the Controllers are subject. The arrangement designates a contact point for data subjects and duly reflects the respective roles and relationships of the joint controllers vis-à-vis the data subjects. The essence of the arrangement is made available to the patient/data subject. Irrespective of the terms of the arrangement, the patient/data subject may exercise his or her rights in respect of and against each of the Controllers.

The patient’s participation in the Project implies that, in accordance with the legislation on clinical trials of medicinal products, the staff of the Promoter/Owner of the Study or of external companies that perform monitoring and verification of the Study on behalf of the former, the Ethics Committee and the Italian health authorities, will be able to know the data concerning the patient, also contained in the patient’s clinical documentation, in such a way as to guarantee the patient’s confidentiality, unless otherwise required by law.

The patient’s data may be disclosed, even though their making available or consultation, only in strictly anonymous form, for example through scientific publications, statistics and scientific conferences. If after the conclusion of the Project it should be necessary to match the anonymous data, uploaded on the platform, to the patient’s name, the Owner can proceed - with the patient’s consent - only where and to the extent that this is indispensable in order to carry out further research, connected and not connected with those of this Project.

All data processing operations are carried out in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, in such a way as to guarantee the integrity, confidentiality and availability of personal data, using appropriate technical or organisational measures such as:\_\_\_\_\_\_\_\_\_\_\_ ~~adopting all the necessary technical and organizational measures~~ ~~and, in particular, the following security measures~~: XXXX

The Data Controller provides the patient/data subject with all of the following information:

1. (a) the identity and the contact details of the Controller and, where applicable, of the Controller's representative;
2. (b) the contact details of the data protection officer, where applicable;
3. (c) the purposes of the processing for which the personal data are intended as well as the legal basis for the processing;
4. d) where the processing is based on point (f) of Article 6(1), the legitimate interests pursued by the controller or by a third party;
5. (e) the recipients or categories of recipients of the personal data, if any;
6. (f) where applicable, the fact that the controller intends to transfer personal data to a third country or international organization.

***Data management and protection***

Azioni pianificate per l’inserimento, la codifica, la sicurezza e l’archiviazione dei dati , incluso ogni eventuale processo correlato per promuovere la qualità dei dati (es. doppio inserimento dei dati ; check di range per i valori dei dati ).

The processing of the patient’s personal data, that is any information relating to an identified or identifiable natural person (‘data subject’); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person, is carried out by the Data Controller with free, specific, informed, expressed and unequivocal consent.

The patient’s participation in the Project and, therefore, the provision of the patient’s data, are optional; failure to provide, however, will make it impossible to participate. The processing of the patient’s personal data is, therefore, carried out by the Data Controller only upon the expression of the patient’s specific and explicit consent, in accordance with the provisions of art. 9, paragraph 2, lett. a), EU Regulation 2016/679.

The consent can be revoked at any time.

# *Statistical methods*

*Descrivere brevemente i metodi statistici da applicare per l’analisi dei dati utilizzati per analizzare l’outcome primario e quelli secondari.*

# Methods: Monitoring

# Data monitoring

1. Composizione del Data monitoring committee (DMC) ; sintesi del suo ruolo e struttura del reporting; dichiarazione di indipendenza dallo sponsor e dei conflitti d’interesse. Se non è previsto alcun comitato di monitoraggio dei dati , riportare le motivazioni.
2. Descrizione di ogni eventuale analisi ad interim e delle linee guida per l’interruzione del trial, indicando chi è autorizzato ad accedere ai risultati intermedi e chi prenderà la decisione finale d’interrompere lo studio.

# Advers event

Azioni pianificate per la raccolta, valutazione, reporting e gestione delle segnalazioni degli eventi avversi.

# Auditing

Frequenza e procedure per e effetuare l’audit sulla conduzione del trial, se previsto, specificando da chi e come verrà svolto (es. piano di monitoraggio)

# Ethical considerations

The study investigator will ensure that this study is conducted in full conformance with the principles of the “Declaration of Helsinki” (as amended in Tokyo, Venice, Hong Kong, South Africa and Edimburgh) or with the laws and regulations of the country in which the research is conducted, whichever affords the greater protection to the individual.

Studies conducted in EU countries must fully adhere to the principles outlined in “Guideline for Good Clinical Practice” ICH Tripartite Guideline (January 1997) and in “Integrated addendum to Good Clinical Practice (GCP)" (December 2016) or with local law if it affords greater protection to the subject.

The protocol and its annexes are subject to review and approval by the relevant Independent Ethics Committee(s) (“IEC”).

## Informed consent

## NON CONFONDERE, neanche nella terminologia, IL CONSENSO INFORMATO AL TRATTAMENTO SANITARIO CON QUELLO AL TRATTAMENTO DEI DATI PERSONALI (art. 7, Reg. 679/2016: “If the data subject's consent is given in the context of a written declaration which also concerns other matters, the request for consent shall be presented in a manner which is clearly distinguishable from the other matters, in an intelligible and easily accessible form, using clear and plain language (…)”

## Informed consent

All patients will be informed of the aims of the study, the possible adverse events, the procedures and possible hazards to which he/she will be exposed. An example of a patient informed consent statement is given as an appendix to this protocol.

It will be emphasized that the participation is voluntary and that the patient is allowed to refuse further participation in the protocol whenever he/she wants. This will not prejudice the patient’s subsequent care. Documented informed consent must be obtained for all patients included in the study before they are registered or randomized at the Data Center. This must be done in accordance with the national and local regulatory requirements.

A copy of Informed consent has been attached to this Protocol Template.

**CONSENT OF THE DATA SUBJECT.**

If the patient/data subject decides to participate in the Project the legal base for the processing is the explicit consent, freely given, specific, informed and unambiguous. The patient’s participation in the Project and, therefore, the provision of the patient’s data, are optional; failure to provide, however, will make it impossible topartecipate.

A copy of ~~Informed consent~~ the patient/data subject’s consent ~~should be~~ has been attached to this Protocol Template.

# Conflict of Interest

Any investigator and/or research staff member who has a conflict of interest with this study (such as patent ownership, royalties, or financial gain greater than the minimum allowable by their institution) will be asked to fully disclose the nature of the conflict of interest.

# Data ownership

According to the ICH Guidelines on Good Clinical Practice the sponsor of the study will be the owner of the data resulting therefrom. However, all centers and investigators participating in the study should be made aware of such circumstance and invited not to disseminate information or data without the Institution’s prior express consent. IN QUESTO CASO “OWNER” SI RIFERISCE, MI SEMBRA DI CAPIRE, AI DIRITTI DI PROPRIETA’ INTELLETTUALE SUI RISULTATI DELLO STUDIO; TECNICAMENTE E’ CORRETTO, MA AL FINE DI EVITARE AMBIGUITà SI POTREBBE SPECIFICARE.

# Publication Policy

After completion of the study, the project coordinator will prepare a draft manuscript containing final results of the study on the basis of the statistical analysis. The manuscript will be derived to the co-authors for comments and after revision will be sent to a major scientific journal.

All publications, abstracts, presentations, manuscripts and slides including data from the present study will be submitted to and reviewed by the Study Coordinator for coordination and homogeneity purposes. The timing of publications (in the event several Centers should be participating in the Study) will be set according to the MoH’s Decree of May 12, 2006, since investigators cannot be precluded from or limited in publishing the results of their studies.

The Study Coordinator will be the first or the senior Author and the Corresponding Author of the relevant publications. The Authors’ list will include all the investigators (up to the maximum required by the Journal to whom the article will be submitted) in a decreasing order of patients included into the final analysis for the primary outcome.

# Study timeline

***Submission date:***

***Enrollment start date:***

***Enrollment end date:***

***Statistical analysis:***

***Final report:***

# Annexes

Annex 1: Informed consent form

Annex 3: Privacy Protection Form

Annex 4: Letter to the GP

Annex 5: Case Report Form

# References