AZIENDA OSPEDALIERA UNIVERSITARIA MEYER IRCCS

Determina del Dirigente n. 419 del 06-11-2024

Proposta n. 1110 del 2024

Oggetto: AUTORIZZAZIONE ALLA CONDUZIONE DELLO STUDIO OSSERVAZIONALE NON-PROFIT DENOMINATO “CURRENT OUTCOMES OF TOTAL COLONIC AGANGLIONOSIS IN EUROPE”, CODICE PROT. HDRETROSPECTIVEERNICA - APPROVAZIONE SCHEMA DI ACCORDO CON L’HOSPITAL DISTRICT OF HELSINKI AND USIMAA (HUS)

Dirigente: FERRIGNO MARIANGELA

Struttura Dirigente: CONVENZIONI E AFFARI GENERALI

AZIENDA OSPEDALIERA UNIVERSITARIA MEYER I.R.C.C.S.
Istituto di Ricovero e Cura a Carattere Scientifico
Viale Pieraccini, 24 - 50139 FIRENZE
C.F. P.Iva 02175680483

DISPOSIZIONE DIRIGENZIALE

Oggetto	Studio osservazionale
Contenuto	AUTORIZZAZIONE ALLA CONDUZIONE DELLO STUDIO OSSERVAZIONALE NON-PROFIT DENOMINATO "CURRENT OUTCOMES OF TOTAL COLONIC AGANGLIONOSIS IN EUROPE", CODICE PROT. HDRETROSPECTIVEERNICA - APPROVAZIONE SCHEMA DI ACCORDO CON L'HOSPITAL DISTRICT OF HELSINKI AND USIMAA (HUS)

Struttura	CONVENZIONI E AFFARI GENERALI
Dirigente Proponente	MARIANGELA FERRIGNO
Responsabile del procedimento	ALESSIO FABBIANO
Immediatamente Esecutiva	SI

Conti Economici			
Spesa prevista	**Conto Economico**	**Codice Conto**	**Anno Bilancio**

Estremi relativi ai principali documenti contenuti nel fascicolo		
Allegato	**N° di pag.**	**Oggetto**
1	10	Schema accordo

"documento firmato digitalmente"

IL RESPONSABILE S.O.S.D. CONVENZIONI E AFFARI GENERALI
(Dr.ssa Mariangela Ferrigno)

Richiamati:

- il Decreto Legislativo n. 502 del 30.12.1992 e successive modifiche ed integrazioni, recante "*Riordino della disciplina in materia sanitaria, a norma dell'art.1 della legge 23 ottobre 1992, n. 421*";
- il Decreto Legge n. 75 del 22 .06.2023, così come modificato dalla Legge n. 112 del 10.08.2023, recante "*Disposizioni urgenti in materia di organizzazione delle pubbliche amministrazioni, di agricoltura, di sport, di lavoro e per l'organizzazione del Giubileo della Chiesa cattolica per l'anno 2025"* ed in particolare l'art. 8-bis, contenente "*Disposizioni in materia di dirigenza sanitaria, amministrativa, professionale e tecnica del Servizio sanitario nazionale*";
- la Legge Regionale Toscana n. 40 del 24.02.2005 e successive modifiche ed integrazioni, di "*Disciplina del Servizio Sanitario Regionale*";
- la Legge Regionale Toscana n. 12 del 16.03.2023 e successive modifiche ed integrazioni "*Disposizioni in materia di istituti di ricovero e cura a carattere scientifico pubblici. Modifiche alla l.r. 40/2005*" con la quale si è proceduto alla disciplina degli istituti di ricovero e cura a carattere scientifico di diritto pubblico ed in particolare l'art. 13 con il quale sono state dettate le "*Disposizioni transitorie per il passaggio da Azienda Ospedaliero Universitaria Meyer ad Azienda Ospedaliera Universitaria Meyer IRCCS…*";

Dato atto che**:**

- con deliberazione del Direttore Generale n. 443 del 23.09.2022 l'A.O.U. Meyer ha disposto la presa d'atto del Decreto del Ministero della Salute del 02.08.2022, pubblicato nella Gazzetta Ufficiale n. 200 del 27.08.2022, con cui l'Azienda Ospedaliero Universitaria Meyer è stata riconosciuta Istituto di Ricovero e Cura a Carattere Scientifico (I.R.C.C.S.), per la disciplina di pediatria;
- con deliberazione del Direttore Generale n. 286 del 09.05.2024 è stato adottato ai sensi dell'art. 50 novies comma 3 della L.R.T. 40/2005 e s.m.i., a seguito dei pareri favorevoli della Giunta Regionale e del Ministero della Salute, il Regolamento di organizzazione e funzionamento dell'A.O.U. Meyer I.R.C.C.S.;
- con deliberazione del Direttore Generale n. 296 del 10.05.2024 è stato approvato il nuovo assetto organizzativo dell'A.O.U. Meyer I.R.C.C.S. il cui organigramma ha decorrenza dal 01.07.2024;

Richiamata la deliberazione del Direttore Generale n. 551 del 02.10.2024 con la quale si è provveduto, a seguito delle azioni di sistematizzazione dell'organizzazione aziendale, alla declaratoria delle funzioni attribuite e/o delegate dal Direttore Generale ai singoli Dirigenti Responsabili delle Strutture Aziendali, anche ai fini dell'individuazione delle competenze nell'adozione degli atti amministrativi;

Dato atto che il Responsabile della S.O.S.D. Convenzioni e Affari Generali, Dr.ssa Mariangela Ferrigno, con riferimento alla presente procedura, attesta la regolarità amministrativa e la legittimità dell'atto;

Considerata la richiesta da parte del promotore Hospital district of Helsinki and Uusimaa (HUS), un ospedale pubblico con sede in Finlandia, per la conduzione dello studio osservazionale non-profit denominato "Current outcomes of total colonic aganglionosis in Europe", codice prot. HDretrospectiveERNICA, presso la SOC Chirurgia Pediatrica Ricostruttiva e Rigenerativa intestinale, sotto la responsabilità del Dr. Riccardo Coletta;

Atteso che lo studio si configura come multicentrico e che il promotore ha proposto un Accordo per la conduzione dello studio medesimo;

Preso atto che il Comitato Etico Regione Toscana - Pediatrico, nella seduta del 10.09.2024, ha esaminato e approvato il protocollo relativo allo studio in oggetto;

Verificato che dal presente atto non derivano oneri economici a carico dell'AOU Meyer IRCCS;

Ritenuto, pertanto, di prendere atto del parere favorevole espresso dal Comitato Etico Regione Toscana - Pediatrico, di autorizzare lo studio in oggetto e di approvare lo schema di Accordo da stipulare con l'Hospital district of Helsinki and Uusimaa (HUS), per la disciplina delle condizioni normative ed operative dello studio medesimo secondo lo schema che, allegato N. 1 al presente atto, ne forma parte integrante e sostanziale;

Considerato che il Responsabile del Procedimento, individuato ai sensi della Legge n. 241/1990 nella persona del Dr. Alessio Fabbiano sottoscrivendo l'atto attesta che lo stesso, a seguito dell'istruttoria effettuata, nella forma e nella sostanza è legittimo;

DISPONE

Per quanto esposto in narrativa che espressamente si richiama,

1. Di prendere atto del parere favorevole all'esecuzione dello studio in oggetto espresso dal Comitato Etico Regione Toscana - Pediatrico nella seduta del 10.09.2024.

2. Di autorizzare lo svolgimento dello studio di cui al punto precedente presso la SOC Chirurgia Pediatrica Ricostruttiva e Rigenerativa intestinale.

3. Di approvare lo schema di Accordo per la conduzione dello studio da stipulare con l'Hospital district of Helsinki and Uusimaa (HUS) che, allegato N. 1 al presente atto, ne forma parte integrante e sostanziale.

4. Di dare atto che il Dr. Riccardo Coletta risulta essere il Responsabile dello studio di cui trattasi.

5. Di precisare che dal presente atto non derivano oneri economici a carico dell'AOU Meyer IRCCS.

6. Di trasmettere il presente atto al Collegio Sindacale ai sensi dell'art. 42, comma 2, della L.R.T. n. 40/2005 contemporaneamente all'inoltro all'albo di pubblicità degli atti di questa A.O.U. Meyer I.R.C.C.S.

IL RESPONSABILE S.O.S.D. CONVENZIONI E AFFARI GENERALI
(Dr.ssa Mariangela Ferrigno)

DATA TRANSFER AGREEMENT

PARTIES

This agreement on the transfer of data ("**Agreement**") is signed between HUS and the Provider:

1. **HUS Group**, the joint authority for Helsinki and Uusimaa (hereinafter referred to as "**Recipient**")
   Stenbäckinkatu 9, P.O. Box 200, FI-00029 Helsinki, Finland
   Business ID 1567535-0

and

2. **Meyer Children's Hospital IRCCS** (hereinafter referred to as "**Provider**"), having its registered office at Viale Gaetano Pieraccini 24, 50139 Firenze, Italy, VAT/tax code 02175680483

Hereinafter 1. and 2. are jointly referred to as the "**Parties**" and individually as a "**Party**".

1 DEFINITIONS

Affiliated entity	Shall mean any legal entity 1) directly or indirectly controlled by a Party, 2) directly or indirectly controlling a Party, or 3) under direct or indirect common control with a Party of another legal entity. Control herein refers to a legal entity owning or holding fifty (50) percent or more of the share capital and/or the legal entity being entitled to elect or appoint directors or persons performing similar functions.
"Confidential Information"	Any and all research, technical, financial, business or commercial information, data, products, know-how, substances or material disclosed or made available by Provider, which: (i) Is specified as Confidential Information of a Party in this Agreement; (ii) If in written or other tangible form, is clearly marked as "Proprietary" or "Confidential" or with a similar marking; (iii) If disclosed orally, visually or in other intangible form, is at the time of disclosure identified as confidential and confirmed in writing to be "Confidential" within fourteen (14) days of such disclosure; or (iv) in the absence of such marking or written confirmation, is of confidential nature as evident from its contents or the circumstances surrounding the disclosure. Confidential Information also includes all copies, reproductions, photographs, images, records, and extracts of such information, as well as all notes and summaries prepared by Recipient from the Confidential Information. Confidential Information shall not include any information which: (a) is in the public domain at the time of disclosure or later becomes part of the public domain through no breach of this Agreement by Recipient; (b) was known to Recipient prior to disclosure by Provider as proven by Recipient; (c) is disclosed without confidentiality obligations to Provider by a third party who did not obtain such confidential information, directly or indirectly, from Provider; (d) was independently developed by Recipient without use of Provider's Confidential Information as proven by the Recipient; or (e) is approved for disclosure by a prior written authorization by Provider. Confidential Information shall not be deemed to be within the foregoing exceptions on the grounds only that: (a) the general principle is public knowledge or known to the Receiving Party unless the particular practice is not itself public knowledge or so known; or (b) it constitutes a combination of or can be drawn from information which is public knowledge or known to the Receiving Party unless the combination itself, its principle and mode of operation and method of use is also public knowledge or known to the Receiving Party. This Agreement shall not restrict the Recipient from complying with a lawfully issued governmental order or legal requirement to produce or disclose Confidential Information,

	provided however, that the Recipient, if legally possible, promptly notifies Provider in order to enable Provider to oppose such an order or obtain a protective order and that the Recipient cooperates fully with Provider in any such proceeding. If the Recipient is thereafter required to disclose Confidential Information, both Parties will endeavour to agree to mutually satisfactory means to disclose such information.
"Data Controller" **"Joint Controller"**	"**Data Controller**" is as defined in GDPR Article 4(7). "**Joint Controller**" is as defined in GDPR Article 26.
"Data Protection Laws" / **"GDPR" /**	All applicable legislation concerning the protection of Personal Data that apply partly or fully to the Parties, including but not limited to the following: (a) the General Data Protection Regulation (EU) 2016/679 ("**GDPR**"); (b) the Finnish Data Protection Act (1050/2018) and all other Finnish data protection legislation as it applies to the Parties; (c) the Finnish Act on the Secondary Use of Health and Social Data (522/2019) ("**Secondary Use Act**"); (d) The Finnish Biobank Act (688/2012) ("**Biobank Act**"); (e) The Italian Personal Data Protection Code (Legislative Decree No. 196 of 30 June 2003) as amended by Legislative Decree No. 101 of 10 August 2018; and (f) Any other data protection legislation applicable to Personal Data, as well as the binding orders of data protection authorities. For clarity, the aforementioned Data Protection Laws are understood to include any amendments and modifications made thereto from time to time as well as any possible future legislative measures that substitute(s) and/or repeal the one or more of the Data Protection Laws.
"Intellectual Property Rights"	All statutory protection forms of intellectual property anywhere in the world, including without limitation patents, utility models, design rights, copyright, trademarks, trade secrets, integrated circuit rights and applications for any of the above.
"Invention"	Any subject matter that is, to the best of knowledge of the Party having ownership thereof, eligible for patent protection anywhere in the world under any legislation and created, invented, or generated from the activities conducted in the course of the Research which is defined in the Section 3.
"Personal Data"	"**Personal Data**" is as defined in GDPR Article 4(1) and elsewhere in the Data Protection Laws.
"Provider" / **"Recipient"**	"**Provider**" means Meyer Children's Hospital IRCCS, with registered office at Viale Gaetano Pieraccini 24, 50139 Firenze, Italy, which is a Party and/or its Affiliate that discloses its Confidential Information, Background or Material to another Party and/or its Affiliate, with the receiving Party thereof constituting the "**Recipient**".
Provider's Investigator	The Provider's Investigator is Dr Riccardo Coletta of the Paediatric Surgery Department
Project	The research project sponsored by HUS and entitled "**Current outcomes of total colonic aganglionosis in Europe**", study prot. HDretrospectiveERNICA.

2 TRANSFER OF PERSONAL DATA

PROVIDER is in possession of certain personal data from medical records ("**Personal Data**"), which will be retrospectively collected as anonymized data by the PROVIDER's Investigator and analyzed within the framework of the Project of the Recipient. PROVIDER, through its Investigator, collaborates with the Recipient for the specific Project. HUS is the controller of the Personal Data received from the PROVIDER and processed at its facilities for the purposes of the Project; the Provider is the controller with respect of the Personal Data processed at its facilities for the purposes of the Project.

The Parties wish the Recipient to be able to analyze the Personal Data in the Project and the PROVIDER agrees to make the mentioned Personal Data available to the Recipient for the Project purposes. A Party shall carry out the work related to the Project using reasonable skill, care and diligence as well as professional personnel.

PROVIDER undertakes to assist the Recipient with the transfer of the Personal Data specified in Attachment 1 for the purposes of the Project.
The Personal Data for the Project is provided in anonymized form and uploaded onto a RedCap database for data collection. The Provider's Investigator will retain no code related to the Personal Data so that an individual cannot directly be identified.

All rights and title to the transferred Personal Data remain with the PROVIDER.

3 PERMITTED USE

The Recipient represents and warrants to use the provided Personal Data solely as described in this Agreement and in accordance with all applicable laws, regulations, policies, guidelines, ethical standards and under all circumstances solely in accordance with the research subject's written consent.

The Recipient cannot transfer, assign or sublicense its rights or obligations under this Agreement to any third party without the prior written permission of PROVIDER.

PROVIDER has the right to prevent, interrupt or discontinue any processing of the Personal Data if PROVIDER determines that such processing of the Personal Data is not or would not be in accordance with the Data Protection Laws, or if the Subject has revoked their consent, or if PROVIDER is issued a cease order by a valid governmental or regional authority. In such situation, the PROVIDER shall not be liable for any claims or damages which may result from such a decision.

PROVIDER makes no representations that the use does not infringe any rights of third parties and makes no representation and gives no warranty or undertaking, in relation to the Personal Data. As examples, but without limiting the foregoing, PROVIDER gives no warranty: i) that it owns all necessary property and other rights in the Personal Data and that their use will not infringe any patent, copyright, trade mark or other right owned by any third party; or ii) that the Personal Data is of merchantable or satisfactory quality or fit for any particular purpose, has been developed with reasonable care and skill.

4 ACCESS TO THE PERSONAL DATA

The Recipient agrees to ensure that only those persons involved in the Project have access to and the use of the Personal Data for the Project.

The Recipient shall take all reasonable measures to secure the safety and confidentiality of the Personal Data, any derivatives and data and for that purpose, but without limitation, shall ensure that all research personnel are similarly bound by appropriate undertakings contained in the contracts under which such research personnel are employed or render services to the Recipient, or otherwise as appropriate in the circumstances.

5 SECURITY FOR MATERIALS

All information and material provided by PROVIDER to the Recipient that is not publicly available constitutes Confidential Information of PROVIDER. The confidentiality provisions of this Agreement expressly supersede and replace any pre-existing agreements between the Parties concerning the subject matter of this Agreement, with such pre-existing agreements expiring on the Effective Date and being supplanted by the provisions included herein.

As part of the collaboration of the Parties contemplated herein, PROVIDER may disclose its Confidential Information to Recipient, with such disclosures being governed by the provisions of this Section.

Recipient shall:

(a) treat all the Confidential Information disclosed by PROVIDER as strictly confidential;

(b) protect the secrecy of PROVIDER's Confidential Information and refrain from disclosure and unauthorized use of PROVIDER's Confidential Information;
(c) not publish, disclose or transfer PROVIDER's Confidential Information to any third party without the prior written authorisation of PROVIDER, unless otherwise expressly agreed in this Agreement;
(d) not use PROVIDER's Confidential Information for any purpose other than for the purposes contemplated in this Agreement, unless given prior written authorization by; and
(e) not use PROVIDER's Confidential Information for any purpose or in any manner that would constitute a violation of any laws or regulations applicable to either PROVIDER or Recipient.

In fulfilling these obligations, Recipient undertakes to protect PROVIDER's Confidential Information by using at least the equivalent measures as those by which Recipient protects its own information of a similar nature, however not less than reasonable measures.

The Recipient ensures that any materials is protected from unauthorized use and of theft.

The Recipient acknowledges that it under no circumstances shall use the Personal Data transferred under this Agreement to identify individuals or to contact any individual whose Personal Data it has dealt with. If the Recipient becomes aware of any unauthorized use or disclosure of the use of Material, the Recipient undertakes to contact PROVIDER without delay.

6 RESULTS AND PUBLICATIONS

The Parties agree that all Intellectual Property Rights, the results and the Inventions, of the Project shall belong to HUS. The Provider agrees to report all the results and Inventions to HUS under confidentiality.

The Provider shall not publish the results arising from the use of the Personal Data in seminars, conferences and scientific publications etc. without the prior written consent of HUS.

7 INDEMNITY

A Party shall be liable towards another Party for the damage that the first Party has caused by act or omission and whether willfully or due to negligence that constitutes a breach of this Agreement. A Party is liable for the acts and omissions of its Affiliates, employees, representatives, agents and consultants as if they were its own. A Party shall not be liable towards another Party for any indirect, incidental or consequential damage nor losses such as, but not limited to, loss of profit, revenue or contracts; reduction or interruption in production or turnover; other loss arising because Results cannot be used as intended; inability to secure intended required research related permits; losses or damages because a contract with a third party is breached; loss due to damage to property other than Results; or other similar loss that is difficult to foresee; except if directly caused by the breach of the confidentiality obligations. The total aggregated liability of a Party towards the other Party is limited to three hundred thousand (300 000) Euro

The limitations of liability specified in above shall not be applied:
(a) if the Party caused the damage willfully or by gross negligence;
(a) in any matters relating to the Data Protection Laws or the processing of Personal Data, for which the liability is determined solely in accordance with the breach of Personal Data as regulated by the Data Protection Laws.

PROVIDER is not responsible for the Recipient´s use of the Personal Data and in case of loss, damage or liability which may arise from or in connection with this Agreement or the equivalent in case of storage or transport of the Personal Data to the Recipient.

Each Party shall indemnify, defend, and hold harmless the other Party and their respective Representatives (the "Indemnitees"), from and against any and all third party damages, claims, threatened claims, damages, losses, suits, proceedings, liabilities, costs (including reasonable legal expenses, costs of litigation and reasonable attorney's fees), or judgments, of any kind ("Losses") to the extent arising out of or relating to, directly or indirectly, the gross negligence, recklessness, or wrongful intentional acts or omissions of such Party or its representatives, in connection with the performance of obligations or exercise of rights under this Agreement; except for third party Losses to the extent attributable to any Indemnitee having committed an act or acts of gross negligence, recklessness, or wrongful intentional acts or omissions.

The Recipient agrees to indemnify and hold harmless PROVIDER and its employees, whether in contract, delict or otherwise, against any loss, claim, and damage caused as a result of the use, keeping, storage or transport of the Personal Data or the consequences of their use under this Agreement – including but not limited to i) injury to the Recipient and/or its employees and third parties; ii) infringement of third party intellectual property rights and iii) use of the Personal Data within or outside the scope of this Agreement.

8 TERM AND TERMINATION OF THIS AGREEMENT

This Agreement shall enter into force on the last date of signature hereof and shall remain in force for three (3) years or until research under the research Project has been completed, whichever occurs first.

This Agreement may be terminated by either party for any justified reason, by giving the other party thirty (30) day´s written notice.

PROVIDER has the right to terminate this Agreement with immediate effect if the Recipient is in breach of its obligations under this Agreement or is bankrupt or under liquidation.

All confidentiality and other obligations of a continuing nature contained herein shall remain in force and shall survive this Agreement notwithstanding its termination as aforesaid.

9 TERMINATION OF USAGE OF THE DATA

The Recipient agrees on expiry of this Agreement to stop the use of the Personal Data.

The Recipient also agrees to return or destroy the Personal Data and any copies of coded Personal Data obtained by Recipient as instructed by PROVIDER, when the research according to the research Project is complete, or within thirty (30) days after termination or expiration of this Agreement, whichever occurs first. The Personal Data will be stored by the Recipient for 3 years since the end of the Project, which is estimated to last until 31.12.2026.

The Recipient shall however have the right to retain such copies as are required to comply with applicable laws, rules and regulations.

10 OTHER

No provision of this Agreement may be amended or modified, except by written instrument duly executed by the Parties.

All communications concerning this Agreement shall be in writing and shall be delivered to the address indicated below, unless party has specifically been notified by the other party of another address for this purpose.

Message is delivered in person, by mail or e-mail. A receipt shall always be provided for each received message.

Any event, which is beyond the reasonable control of the Party in question and prevents or renders the performance of that Party's obligations unreasonably difficult within the time specified, is considered force majeure. Such events include, but are not limited to, war, insurrection, natural disaster, interruption in the general energy supply, fire, pandemic, epidemic, strike, embargo, material restriction imposed by the government budget or by the government or the activities of a Party, or other equally significant and uncommon reasons beyond a Party's control (collectively "Force Majeure"). A Party shall not be responsible for any defects or delays caused to another Party nor for any delays or damages by its Representatives and subcontractor that are due to Force Majeure. The affected Party shall take all necessary measures in order to reduce to a minimum and mitigate the effect of any delay caused by the Force Majeure event. In order to invoke Force Majeure, a Party shall without undue delay inform the commencement or the cessation of the Force Majeure in writing to the other Parties' and submit to the other Parties reasonable proof of the nature of such event of Force Majeure and its effect upon the time of performance of the said Party's obligations under this Agreement.

11 APPLICABLE LAW AND DISPUTES

This Agreement shall be governed by and construed in accordance with the laws of the defendant without regard to its conflict of laws rules.

Any dispute, controversy or claim arising out of or in connection with this Agreement shall be resolved amicably. In case an amicable resolution is not agreed upon within 30 days, a Party may take the dispute to be finally settled by the court of competent jurisdiction of the defendant.

AGREEMENT DOCUMENTS

ATTACHMENTS

ATTACHMENT 1: PERSONAL DATA

ATTACHMENT 2: RESEARCH PROJECT TO BE CONDUCTED

This Agreement may be executed in counterparts, each and every one of which shall be deemed an original and all of which together shall constitute one and the same instrument. Parties may execute the Agreement in Adobe Portable Document Format (PDF) sent by electronic mail to the Parties' contact persons or as otherwise agreed between the Parties. PDF signatures of authorised signatories of the Parties shall be deemed to be original signatures, shall be valid and binding upon the Parties, and, upon delivery, shall constitute due execution of the Agreement.

***** *** *****

[signature page follows]

RECIPIENT: HUS Group, the joint authority for Helsinki and Uusimaa

____/___.2024

_____ _____

[Mikko Seppänen],

HUS, Head Physician of Research, Children and Adolescents

Chief Physician, Rare Disease Center

PROVIDER:

____/____.2024

_____

Mariangela Ferrigno

Contracts and General Affairs Dept. Manager

For acceptance and acknowledgement

____/____.2024

_____

Riccardo Coletta

Provider's Investigator

ATTACHMENT 1

Description of *Personal Data* to be transferred: diagnosis, length of aganglionosis, surgical treatment, surgical complications, nutritional data, mortality, other anomalies, genetic diagnosis of Hirschsprung's disease, need for intestinal transplantation.

All data sets are identified by a numerical code generated by REDCap; Subject-identifiable data are not available to Recipient.

ATTACHMENT 2: RESEARCH TO BE CONDUCTED

Research Plan:

Current outcomes of total colonic aganglionosis in Europe

First investigator: Annika Mutanen

Principal investigator: Mikko Pakarinen

Participating centers: The study will be proposed to all full and affiliated ERNICA members

Background

Hirschsprung disease (HD) is a rare, incidence of 1:5000-10000 at birth, congenital anomaly of the enteric nervous system leading to aganglionosis involving rectum with variable length of proximal extension. Total colonic aganglionosis (TCA) occurs in around 8% of cases leading to low numbers of cases per center. TCA is the most severe form of HD associated with variable management practices, high complication rates and unsatisfactory outcomes. Currently available studies on management and long-term outcomes of TCA at the European level are scarce, limiting the ability to make strong recommendations regarding management of TCA patients. Large collaborative multi-center studies with precise anatomic definitions of the site of aganglionosis and surgical management are needed to address management in relation to long-term outcomes and complications.

Aims

This observational cross-sectional study aims to address the current number of patients followed-up, management strategies and outcomes of TCA in European Reference Network (ERNICA) centers.

Patients and methods

Design

This is a retrospective multicenter cross-sectional study including all patients diagnosed with total colonic aganglionosis (TCA) who are currently alive and under follow up in the participating ERNICA centers. TCA is defined as histopathologically confirmed aganglionosis of the entire colon with or without extension of aganglionosis into the small bowel managed by colectomy and small intestinal pull-through surgery or enterostomy formation. Patients with a shorter aganglionosis will be excluded. All ERNICA centers treating TCA patients are invited to participate. Based on the available incidence data, around 100-200 patients will be included. Each participating center will obtain local institutional review board approval.

Inclusion criteria

- All patients diagnosed with TCA irrespective of the length of small intestinal extension of aganglionosis, who are currently under follow up in the participating ERNICA centers are included. Patients of all ages without limitations may be included if the patient is under follow up in the participating center.
- All included patients have TCA diagnosis is confirmed by histopathology.
- TCA patients who have received intestinal transplantation will be included. Follow up data for transplanted patients is collected at the latest follow-up visit before transplantation. In addition, age at transplantation will be recorded.

Exclusion criteria

- Deceased patients (only the number of deceased patients during the inclusion period is recorded)
- Patients who have unreliable diagnosis of Hirschsprung's or of its extension
- No follow up data available
- Patients with rectosigmoid- or long-segment Hirschsprung's disease

Data collection

The participating investigators will retrospectively collect anonymized data from medical records or local TCA registries using a preformed data collection sheet (see attachments 1 and 2). A RedCap database is used for data collection. Helsinki Children's hospital will serve as the primary researcher and will merge the locally data from all participating centers.

Epidemiology and outcome measures

The epidemiological and follow up data will include patient demographics (age at latest follow up, sex, family history of Hirschsprung's disease, other anomalies, length of aganglionosis), surgical management (type off pull through, presence of stoma), and surgical complications.

Main outcome measures are survival, duration of parenteral nutrition, bowel and/or infectious problems (i.e., enterocolitis, IBD-like intestinal lesions, need for intersphincteric botox injections).

Data analysis

The first investigator will merge locally collected data, perform statistical data analysis and write the first draft of the manuscript. The manuscript draft will be circulated to all co-authors and modified accordingly. Before submitting the manuscript for review, all authors must approve the final version of the manuscript.

Ethics

There are no ethical concerns, as all data are collected retrospectively and patients are not approached.

Authorship

The study results will be presented in international scientific meetings and published in international peer-reviewed journals. All publications will be done under ERNICA collaboration. From each participating center, one or two researchers may be included as co-authors.

Detailed specification of *the purposes* for personal data may be used:

The personal data will be used for an observational cross-sectional study aiming to address the current number of total colon aganglionosis (TCA) patients followed-up, management strategies and outcomes of TCA in European Reference Network (ERNICA) centers. In HUS (recipient) the data will be collected and analyzed in Department of Pediatric Surgery.

All data sets are identified by a numerical code; Subject-identifiable data are not available to recipient.