CLINICAL TRIAL ABSTRACT

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Qualitative, interventional observational clinical study of plastic reconstruction of the human foreskin in circumcised patients by transplantation of decellularized tissue from the Emilia Romagna Regional Skin Bank

Foregen

Clinical Trial Abstract

Qualitative, interventional observational clinical study of plastic reconstruction of the human foreskin in circumcised patients by transplantation of decellularized tissue from the Emilia Romagna Regional (ERR) Skin Bank

Trial Start Date:	April 1st, 2023
Trial End Date:	March 30th, 2024
Trial Duration:	12 Months
Trial Location:	Italy
Trial Sponsor:	Foregen

Background and Rationale

Regenerative treatments are a new approach to modern medicine that allows for the regeneration of tissues and organs or, more often, parts of them. This is based on the design and production of laboratory scaffolds that, once transplanted in the recipient, are capable of mimicking the physiological functions performed by that organ or tissue. These therapies are primarily aimed at treating organs and tissues that are no longer functioning due to a pathology or because they have been subjected to an insult of an external nature that limits their functionality (surgery, accident, etc.). Today, with the help of other medical sciences, tissue engineering is making great strides in the regeneration of many tissues, including skin, tendons, bones, cartilage, and nerves.

Nevertheless, much remains to be clarified about the complex biological mechanisms underlying the regeneration of specific tissues and organs. The knowledge that has emerged over the years is that it is not enough to merely replace the missing “piece” in the complex biological machines that are our bodies. Instead, the regenerated organ or tissue must communicate with the local host cells and thus restore complete physiological function.

Specifically, the regeneration of the foreskin poses ethical, social, scientific, and medical challenges to tissue engineering, with the express goal of restoring full functionality to an organ with a highly complex structure and morphology. Few groups in the world

contend with the regeneration of this organ, either due to social or cultural taboos or a lack of ethical consideration of the serious social impact of the issue of circumcision. At the time of this writing, there are no known experimental studies or clinical trials in progress related to the complete regeneration of the foreskin.

Study Objectives

This study's objective is to reconstruct the foreskin in circumcised male patients, obtaining a vascularized and functional organ in the enrolled participants (n = 15) and the presence/absence of any adverse reactions related and correlated to the use of the transplanted decellularized tissue. Specifically, two endpoints are defined:

- **Primary Endpoint:** Plastic surgical reconstruction of the foreskin and regeneration of the complete functionality of the involved organ
- **Secondary Endpoint:** To evaluate the regenerative efficacy and absence of any adverse reactions related to the use of homologous decellularized tissue from the Emilia Romagna Regional (ERR) Skin Bank

Setting and Population under Study

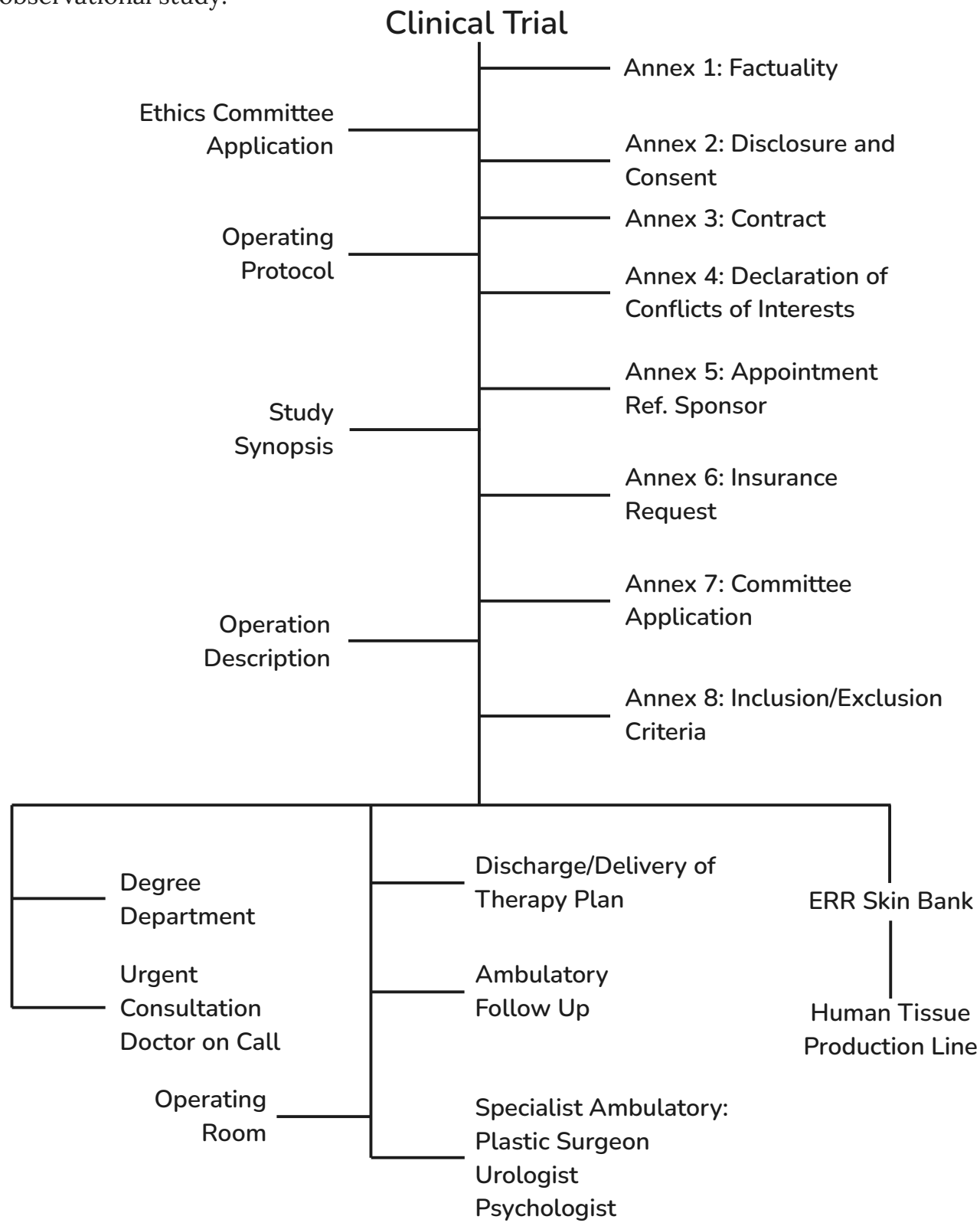
A total of 15 male patients who have expressed dissatisfaction with their circumcised status will be recruited for the study according to the following inclusion/exclusion criteria:

Inclusion/Exclusion Criteria

Inclusion criteria	Exclusion criteria
Age 18-64 years old	Concomitant diseases such as diabetes or heart and vascular diseases
Outcomes of circumcision with functional and/or urological damage	Psychiatric conditions, severe anxiety, severe depression, or other psychiatric conditions requiring drug treatment
Healthy patient	Presence of evident signs of septicemia and/or infection (e.g., ecchymosis, petechiae, or other) of the genital organ
	Positive test ascertained for viruses such as HIV, HBV, HCV

Study Design

This will be an internationally sponsored single-center qualitative interventional observational study:



Follow-up

All patients undergoing plastic and reconstructive surgery with decellularized tissue from the cell bank for transplantation purposes will be followed up over time to demonstrate the efficacy (or otherwise) of the procedure performed and its compliance with the objectives set. This is also done to detect any adverse reactions/events related and correlated to the specific biological products used (decellularized human tissues).

In the event that adverse events related and/or correlated to treatments of any nature are recorded, they will be immediately communicated to the ERR Skin Bank and to the relevant ethics committee, each within its own field of competence.

Follow-up Procedure

The follow-up procedure performed by the physician includes, for each enrolled patient:

- Clinical follow-up 15 days after surgery
- Clinical follow-up after 30, 60, and 90 days
- Clinical follow-up after 6 months
- Clinical follow-up after 12 months (last follow-up)
- Photographic documentation with digital camera
- Any other specialist follow-up examinations considered useful by the doctor for the purpose of the clinical evaluation of the case
- Self-assessment form provided by the physician to the patient at the end of treatment

Security Management

At the time of initial hospitalization and first follow up after 15 days, all participants will potentially be subjected to advanced medicalization and/or pharmacological treatment as determined by a post-surgical evaluation (anti-inflammatory drugs, painkillers, antibiotics, etc.) and prescribed for each specific case by the attending physician within the traditional methods.

Administrative Aspects

Study Funding

Foregen is the sponsor of the study and will cover its entire financing. This funding is regulated by a specific contract accepted and countersigned by the parties and filed with the administration of the Torrette Hospital of Ancona. A copy is also with the ethics committee that authorized the study.

Ethical Considerations

The study is in accordance with the principles of ethics and good clinical practice. The transplanted biological tissues will be provided by the ERR Skin Bank and certified and authorized by the National Transplant Center and *Istituto Superiore di Sanità* (last certification year 2021).

Acquisition of Informed Consent and Data Processing

Patients eligible for the study are evaluated and enrolled by the physician of the center responsible and involved in the study as a clinical investigator and/or sponsor. The patient is adequately informed about the study and provided with information material for himself and his personal physician, describing in detail what the patient will undergo and the possible risks inherent in this procedure.

Conflict of Interest

No conflicts of interest are present.

Responsibilities and Publication Policies

Role of the Sponsor and Investigators

The sponsor (Foregen) and the principal investigator (PI), who is also responsible for the study (Prof. Michele Riccio), have shared and promoted this study and undertake to follow the indications reported for the parts of its relevance. The sponsor will be sent all the data collected for the purpose of analysis and interpretation. At the end of the study, the PI will complete a conclusive scientific report, sending a copy to the sponsor.

Data Properties

The data is property of the sponsor, who guarantees its anonymity and the use provided by law.

Publishing Policies

Possible scientific publications and journals must be agreed upon by the parties and authors. Upon acceptance by all investigators, the data will be made available for publications and conferences once the study is completed.

Definition of Study Conclusion

The study will have an overall duration per patient of 12 months, including all the follow-ups, and will be concluded at the end of the final follow-up one year after surgery.

Data Management

All data will be collected by the plastic surgeon, ensuring anonymity and full compliance with the legislation on the privacy of personal data. This data will then be collected by the sponsor at the end of the study and stored in a password-protected database for final processing and statistical evaluation of results.