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Replacement of male mini puberty in neonates and children with micropenis and/or cryptorchidism due to hypogonadotropic hypogonadism

Submission date
09/02/2018

Recruitment status
No longer recruiting

Registration date
12/02/2018

Overall study status
Completed

Last Edited
11/06/2019

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Male hypogonadotropic hypogonadism is a condition where a lack of hormones can result in micropenis and bilateral cryptorchidism (where the testes do not descend from the abdomen to the scrotum). Micropenis has been traditionally successfully treated with hormone replacement, usually with 3 monthly injections of testosterone, but bilateral cryptorchidism requires surgery - usually twice. The aim of this study is to find out whether daily injections of LH and FSH hormones (Pergoveris®) can successfully treat bilateral cryptorchidism, repair micropenis, and reinstate normal growth.

Who can participate?
Male babies/ infants with bilateral cryptorchidism and micropenis

What does the study involve?
Participants are treated for 3 months with daily injections of Pergoveris®. Parents are trained to perform the injections. Penile length, testicular volume and position, and hormone levels are monitored before, during and at the end of treatment. Ultrasound examination of the testes is performed before and after the end of treatment.

What are the possible benefits and risks of participating?
The treatment may repair micropenis and bilateral cryptorchidism. It is non-invasive, costs less than two surgical operations, is feasible to perform at home by the parents, and preserves future fertility. Based on early results, it is safe with no side effects.

Where is the study run from?
Athens Medical Center (Greece)

When is the study starting and how long is it expected to run for?
January 2009 to December 2020

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Dimitrios Papadimitriou
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
17/2009

Study information

Scientific Title
Treatment of neonatal micropenis and bilateral cryptorchidism due to hypogonadotropic hypogonadism (HH) with 3-month daily subcutaneous injections of the commercially available recombinant FSH plus recombinant LH preparation (Pergoveris®)

Acronym
REplacement of MAle mini Puberty (REMAP)

Study objectives

Hormonal replacement in boys with congenital HH remains a challenge in pediatric endocrinology. Micropenis has been traditionally successfully treated, usually with 3 monthly injections of 50 mg of testosterone enanthate in the post-neonatal period or in early infancy, but when bilateral cryptorchidism coincides, surgical intervention - usually needed twice - is required. Even after a successful surgery, the hypoplastic testes with the deficient proliferation of immature Sertoli cells before and during puberty, due mainly to the lack of the male mini-puberty in the neonatal period as well as the subsequent midinfancy surge in pulsatile gonadotropin secretion, are condemned in azoospermia and the boys in infertility later in their adult life.

The aim of this study is to investigate whether early postnatal daily injections of the commercially available recombinant LH plus FSH preparation (Pergoveris®) could mimic the physiological male mini puberty and successfully resolve bilateral cryptorchidism, repair micropenis, reinstate normal growth in the post neonatal period and restore the responses of the Leydig and Sertoli cells to normal.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Athens Medical Center Scientific Board and Ethics Committee, 01/05/2009, No 17/2009

Study design
Non-randomised study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hypogonadotropic hypogonadism in neonates and infants

Interventions
Neonates or infants all with micropenis and/or bilateral cryptorchidism with absence of neonatal male mini-puberty will be treated for 3 months with daily subcutaneous injections of Pergoveris® (recombinant LH 75 IU and FSH 150 IU), followed monthly. Parents are trained to perform the injections at home. Penile length, testicular volume and position, LH, FSH, Testosterone, AMH and Inhibine b are monitored before, during and at the completion of treatment. Ultrasound examination of the testes by a pediatric radiologist is performed before and after completion of therapy.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Pergoveris (rLH 75IU/FSH 150 IU)

Primary outcome(s)
Measured at baseline and 1 – 2 – 3 months after initiation of therapy:
1. Stretched penile length measured with a ruler
2. Testicular volume measured with a Prader Orchidometer
3. Ultrasound measurements of the testes recorded by an experienced Pediatric Radiologist

Key secondary outcome(s))
Height velocity and body measurements recorded and analysed by Growth Analyser ver 3.1 at baseline and 1 – 2 – 3 months after initiation of therapy

Completion date
31/12/2020

Eligibility

Key inclusion criteria
Male neonates and infants with micropenis and/or cryptorchidism with hypogonadotropic hypogonadism

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
Male

Total final enrolment
10

Key exclusion criteria
Gonadal dysgenesis, partial androgen resistance, 5-a reductase deficiency

Date of first enrolment
01/06/2009

Date of final enrolment
31/05/2019

Locations

Countries of recruitment
Greece

Study participating centre
Athens Medical Center
Department of Pediatric-Adolescent Endocrinology & Diabetes
58 av. Kifisias
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Sponsor information

Organisation
Athens Medical Center

ROR
https://ror.org/03078rq26

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
All data at study completion will be available in Excel format on demand only by scientists or journal reviewers etc. Data will be hopefully but not necessarily published as supplementary material to the main publication of REMAP study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2019	11/06/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes