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	Prospectively registered		
		[] Protocol		
Registration date	Overall study status	[] Statistical analysis plan		
12/02/2018	Completed	[X] Results		
Last Edited 11/06/2019	Condition category Nutritional, Metabolic, Endocrine	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 info@pedoendo.gr

Contact information

Type(s) Scientific

Contact name Dr Dimitrios Papadimitriou

ORCID ID http://orcid.org/0000-0002-6083-3560

Contact details 58, av. Kifisias Marousi, Athens Greece 15125 +30 (0)2103638536 info@pedoendo.gr

Additional identifiers

EudraCT/CTIS number Nil known

IRAS number

ClinicalTrials.gov number Nil known

Secondary identifying numbers 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 minipuberty 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

Secondary study design Non randomised study

Study setting(s) Other

Study type(s) Treatment

Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet

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 measure

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

Secondary outcome measures

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

Overall study start date 01/01/2009

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

Age group Neonate

Sex Male

Target number of participants 10

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 Marousi Greece 15125

Sponsor information

Organisation Athens Medical Center

Sponsor details

5-7, Distomou str Marousi Greece 15125 +30 (0)2106198100 info@iatriko.gr

Sponsor type Hospital/treatment centre

ROR https://ror.org/03078rq26

Funder(s)

Funder type

Other

Funder Name

Investigator initiated and funded

Results and Publications

Publication and dissemination plan

55th Annual Meeting of the European Society of Paediatric Endocrinology, Abstract No. 1158, Title Replacement of male minipuberty. Presentation INVITED PROGRAMME SPEAKER

ICE/ENDO 2014, CHICAGO, U.S., ORAL PRESENTATION LB-OR01-1: Successful 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®).

Abstract presenting the followed protocol has already been published: Horm Res Paediatr 2016; 86(suppl 1):1-556 https://doi.org/10.1159/000449142 page 121

Planning to publish the trial in NEJM or other major journal until 2019.

Intention to publish date

01/12/2018

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