Trial Description

Title

Comparison of clinical and metabolic effects of testosterone and estrogens in adult gonadectomized patients with 46,XY DSD due to complete androgen insensitivity syndrome (CAIS)

Trial Acronym

CAIS-Study

URL of the trial

http://www.uksh.de/kinderhormonzentrum-luebeck/Forschung/CAIS_Studie-p-24.html

Brief Summary in Lay Language

In 46, XY women with CAIS the male chromosome set induces the development of an inner male genitalia (testicles). Due to androgen resistance the external genitailia is female. The patients perceive themselves in a female gender role. Based on the assumption that the gonads carry a higher risk for malignacy they mostly have been removed. As a consequence these women have been substituted with estradiol. Under this treatment patients complained of a decrease of well- being and sexual lifequality. In self-induced experiments patients probed testosteron as an alternative substitution and reported an enhancement of psychological and sexual lifequality. In our study we will compare the two medications in patients with CAIS.

Brief Summary in Scientific Language

Complete androgen insensitivity syndrome (CAIS) is characterized as a completely female external phenotype in 46,XY individuals despite high endogenous testosterone secretion via the intact testes due to mutation of the androgen receptor (AR). After gonadectomy patients recieve estrogens as hormone substitution. However, after gonadectomy, many patients have voiced severe complains about lack of self-esteem, libido and overall well-being. Therefore, we propose a study comparing the endocrine profiles of patients with proven CAIS with the arbitrary conventional treatment with estradiol compared to an experimental treatment with testosterone, both applied transdermally. We hypothesize that testosterone treatment will improve quality of life and well-being because of different expected profiles of estrogen and androgen levels in these patients. As control parameters, we will determine blood parameters that are affected in a secondary fashion by sex steroids. Quality of life and psychological well-being will be assessed in a standardized fashion at all investigation time

Organizational Data

- DRKS-ID: **DRKS00003136**

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- Date of Registration in DRKS: **2011/10/11**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **11-066 , Ethik-Kommission Universität zu Lübeck Medizinische Fakultät des Universitätsklinikums Schleswig-Holstein**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2010-021790-37**
- BfArM-No.: **4037571**

Health condition or Problem studied

- ICD10: **E34.5 - Androgen resistance syndrome**
- ICD10: **[---]* - [---]***

Interventions/Observational Groups

- Arm 1: **Testogel Bayer/ BESINS Bruessels**
(testosterone 50mg/ 5g gel) gel application, daily administration of 50mg testosterone for the duration of six months (shoulder/ upper arm)
Matching placebo-application in combination with Gynokadin medication testosterone daily for also six months after cross-over.
- Arm 2: **Gynokadin dosage gel from Dr. KADE/ BESINS**
(estradiol 0,6mg/g gel)) , daily administration of 1,5 mg estradiol for the duration of six months (shoulder/ upper arm)
Matching placebo-application in combination with testosterone medication daily for also six months after cross-over .

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**

Study Type: **Interventional**

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Who is blinded: **[---]***

Control: **Active control (effective treament of control group)**

- Purpose: **Treatment**
- Assignment: **Crossover**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

Primary objective: To detect differences in the effects of testosterone versus estrogen treatment on quality of life and mental health/psychological well being in patients with complete androgen insensitivity at seven visit dates (after 0, 2, 5, 8, 11, 14, 17 treatment months).
measuring instrument: psychological sum scale of the SF-36-questionnaire (= Short Form Health Survey)

Secondary Outcome

Secondary objectives: To compare the levels of testosterone and estradiol, as well as other sex steroid metabolites between both treatments and to determine steroid extraction profiles and levels of SHBG, Insulin, Cholesterol (total, HDL, LDL), Triglycerides, Hematocrit, Haemoglobin in serum or EDTA-blood respectively, as control parameters and to investigate the correlations with quality of life and hormones (measured through questionnaires: physical Sumscale SF-36= = Short Form Health Survey, FSFI-d =Female Sexual Function Index, BSI = Body Symptom Inventory).
Furthermore we will include functional analysis of the androgen receptor regarding residual activity in correlation to hormone levels.
Rate of side effects will be measured in both treatment arms.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2011/11/07**
- Target Sample Size: **30**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Female**
- Minimum Age: **18 Years**
- Maximum Age: **55 Years**

Additional Inclusion Criteria

Postpubertal adult patient with complete androgen insensitivity syndrome classified as either Sinnecker Type 5A or 5B (1)
Mutation of the androgen receptor gene proved
Gonadectomy at least 1 year before entering the study

Exclusion criteria

1. Disorder of Sex Development other than complete androgen insensitivity syndrome
2. Steroid medication other than study trial medication
3. Gonads in situ
4. Disorder of liver function
5. Chronic skin disease
6. Serious chronic disorders affected by sex steroid medication
7. Malignant disorders
8. Severe psychiatric disorders
9. Porphyria
10. previous venous thromboembolism or arterial embolism
11. hypersensitivity versus active substance or auxiliary substances of study medication
12. participation in other clinical trial in the foregone 4 weeks, individual decision of the principal investigator possible
13. any circumstances that arise doubts that the trial is reasonable for the individual patient or circumstances that hinder a protocol conform conduct

Addresses

- **Primary Sponsor**

  Universitätsklinikum Schleswig-Holstein, Campus Lübeck, kaufmännischer Vorstand
  Mr. Peter Pansegrau

Primary Sponsor

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Sources of Monetary or Material Support

■ **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

Bundesministerium für Bildung und Forschung Dienstsitz Bonn
Heinemannstr. 2

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URL: **www.bmbf.de**

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2016/01/31**

Trial Publications, Results and other documents

- Paper **Birnbaum, W., L. Marshall, R. Werner, A. Kulle, P. M. Holterhus, K. Rall, B. Kohler, A. Richter-Unruh, M. F. Hartmann, S. A. Wudy, M. K. Auer, A. Lux, S. Kropf and O. Hiort (2018). "Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome: a multicentre, randomised, double-dummy, double-blind crossover trial." Lancet Diabetes Endocrinol. DOI: 10.1016/S2213-8587(18)30197-9.**

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*