Approximately 10% of all pregnancies experience mal nutrition of the fetus resulting in intrauterine growth restriction (IUGR). IUGR is the most important cause of perinatal mortality and morbidity. Impaired placental function determined by insufficient transformation of the uterine arteries and mal-perfusion of the placenta is the leading cause of IUGR. So far, there is no treatment option for pregnancies complicated by IUGR and the clinical management is restricted to close monitoring, assessing for the optimal time point of delivery of the fetus threatened by intrauterine death. In a small study at our University Hospital we could demonstrate a risk reduction of 38% for the development of IUGR and IUGR or death by giving the organic nitrate pentaerithrityl-tetranitrate (PETN) to patients recognized at risk for IUGR by impaired uterine artery Doppler at mid gestation (Schleussner, 2014). To confirm these results this bigger study, a prospective randomized placebo controlled double-blinded multicentre trial, was now initiated.
weeks of gestation. The composite endpoint of severe IUGR (< birth weight below the 3rd centile) and intrauterine or neonatal death was defined as primary efficacy endpoint. and perinatal death. Key secondary endpoints are development of IUGR (defined by birth weight < 10th percentile), severe IUGR (< birth weight below the 3rd centile), intrauterine or neonatal death, placental abruption and preterm birth.

Organizational Data

- DRKS-ID: DRKS00011374
- Date of Registration in DRKS: 2017/06/29
- Date of Registration in Partner Registry or other Primary Registry: 2018/09/14
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: 5085-02/17, Ethikkommission der Friedrich-Schiller-Universität Jena an der Medizinischen Fakultät

Secondary IDs

- EudraCT-No. (for studies acc. to Drug Law): 2016-004396-51
- Primary Registry-ID: NCT03669185 (clinicaltrials.gov)

Health condition or Problem studied

- MedDRA: 10016505: Intrauterine growth retardation
- ICD10: P05 - Slow fetal growth and fetal malnutrition

Interventions/Observational Groups

- Arm 1: Pentalong® 50 mg (Pentaeritrithyl tetranitrate/PETN), 2 x daily 1 tablet; intake max. 133 days
- Arm 2: Placebo, 2 x daily 1 tablet; intake max. 133 days

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [--]*
- Allocation: Randomized controlled trial
- Blinding: [--]*
Study Type: **Interventional**

Allocation: **Randomized controlled trial**

Who is blinded: patient/subject, investigator/therapist

- Control: **Placebo**
- Purpose: **Prevention**
- Assignment: **Parallel**
- Phase: **IIIb**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

**Primary Outcome**

This trial investigates the efficacy and safety of PETN to reduce the incidence of intrauterine growth restriction (IUGR), perinatal death and accompanied preterm delivery in women with insufficient placental development and uterine perfusion identified by pathological artery Doppler at 19+0 to 22+6 weeks of gestation.

**Secondary Outcome**

1. severe morbidity and mortality as a combined result of severe IUGR (birth weight below the 3rd or 5th percentile) or perinatal death or premature abruption of placenta
2. percentage of children with birth weight below the 3rd, 5th or 10th percentile
3. development of an IUGR, which necessitates delivery before 30 and 34 week of gestation
4. rate of infants who have to be transferred to the intensive care unit in the paediatric clinic
5. rate of infants, who require a breathing, suffer intraventricular cerebral haemorrhage (grade II - IV) or develop necrotizing enterocolitis
6. premature births below accomplished 34 and 37 week of gestation

**Countries of recruitment**

- **DE Germany**

**Locations of Recruitment**

- University Medical Center **Klinik für Geburtsmedizin, Jena**
University Medical Center Zentrum für Geburtshilfe und Frauenheilkunde, Bonn
Medical Center Charité, Klinik für Geburtsmedizin, Berlin
Medical Center Krankenhaus St. Elisabeth und St. Babara, Klinik für Frauenheilkunde und Geburtshilfe, Halle Saale
University Medical Center MHH, Klinik für Geburtshilfe und Pränatalmedizin, Hannover
University Medical Center Klinik für Gynäkologie und Geburtshilfe, Kiel
University Medical Center Abteilung für Geburtsmedizin, Leipzig
Medical Center Städtisches Klinikum München GmbH Klinikum Harlaching Frauenklinik, München
University Medical Center Universitäts-Frauenklinik, Tübingen
University Medical Center Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, Dresden
University Medical Center Klinik und Poliklinik für Geburtshilfe und Pränatalmedizin, Halle Saale
University Medical Center Universitätsklinik für Frauenheilkunde und Geburtshilfe, Ulm
University Medical Center Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, München
Medical Center Vivantes - Netzwerk für Gesundheit GmbH, Klinikum Neukölln, Klinik für Geburtsmedizin, Berlin

**Recruitment**

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2017/08/15**
- Target Sample Size: **324**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

**Inclusion Criteria**

- Gender: **Female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

**Additional Inclusion Criteria**

1. abnormal uterine artery Doppler at 19+0 to 22+6 weeks of gestation, defined by a mean pulsatility index (PI) greater than 1.6; 2. singleton pregnancy; 3. age≥= 18 years ; 4. informed consent
Exclusion criteria

- known fetal chromosomal or suspected major structural defects at time of enrollment;
- premature rupture of membranes at time of enrollment;
- maternal disease defined as contraindication for intake of PETN;
- anamnestic known insensitivity to Pentalong® or its ingredients or to medications with similar chemical structure;
- participation of the patient in another clinical trial (parallel or within the waiting period of a previous clinical trial);
- multiple pregnancy

Addresses

- **Primary Sponsor**
  
  Friedrich-Schiller-Universität Jena, vertreten durch Dekan der Medizinischen Fakultät
  Bachstraße 18
  07743 Jena
  Germany

  Telephone: [---]*
  Fax: [---]*
  E-mail: [---]*
  URL: [---]*

- **Contact for Scientific Queries**
  
  Universitätsklinikum Jena, Klinik für Geburtsmedizin
  Ms. PD Dr. med. habil. Tanja Groten
  Am Klinikum 1
  07747 Jena
  Germany

  Telephone: +49 (0) 3641 9329207
  Fax:
  E-mail: PETN at med.uni-jena.de
  URL: [---]*

- **Contact for Public Queries**
  
  Universitätsklinikum Jena, Klinik für Geburtsmedizin
  Ms. PD Dr. med. habil. Tanja Groten
  Am Klinikum 1
  07747 Jena
  Germany

  Telephone: 03641 9329207
  Fax: [---]*
  E-mail: PETN at med.uni-jena.de
  URL: [---]*
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.)

  Deutsche Forschungsgemeinschaft
  Kennedyallee 40
  53175 Bonn
  Germany

  Telephone: [---]*
  Fax: [---]*
  E-mail: [---]*
  URL: www.dfg.de

Status

- Recruitment Status: Recruiting ongoing
- Study Closing (LPLV): [---]*

Trial Publications, Results and other documents

- trial protocol (mandatory for transfer to Studybox) PETN_Prüfplan_20181211

* 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.