Trial Description

Title

A single-center, randomized, open-label cross-over study to investigate the drug-drug interaction of trimethoprim and metformin in healthy volunteers

Trial Acronym

KPE22

URL of the trial

[---]*

Brief Summary in Lay Language

Main purpose of the study is the examination of occurrence and extent of the drug interaction between the drugs trimethoprim and metformin.

Background: Trimethoprim is an antibiotic that is used mainly in therapy of urinary tract infection. Metformin is a drug that is used for treatment of so called adult onset diabetes. Both metformin and trimethoprim are frequently used drugs, and trimethoprim possibly influences the behaviour (drug concentrations and effect) of metformin in the body.

Potential participants: Healthy adult male and female subjects.

Outcomes: The effect of trimethoprim on concentrations of metformin in blood and urine and therewith on the effects of metformin shall be investigated.

The hypothesis is: We suspect that trimethoprim influences the concentrations of metformin in blood and urin and therewith the therapeutic effects of metformin. Possibly, the extent of this interaction may be influenced by the genes. This means, that the extent of the interaction may vary from person to person depending on the genes.

Brief Summary in Scientific Language

Both metformin and trimethoprim are frequently used drugs. We hypothesize that trimethoprim influences both pharmacokinetics and pharmacodynamics of metformin. Furthermore, we hypothesize that the extent of this interaction is influenced by genetic variants.

Organizational Data

- DRKS-ID: **DRKS00004349**
- Date of Registration in DRKS: **2012/08/28**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

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- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **86_12 , Ethik-Kommission der Friedrich-Alexander-Universität Erlangen-Nürnberg**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2012-000500-15**
- BfArM-No.: **4038173**

Health condition or Problem studied

- ICD10: **E11 - Non-insulin-dependent diabetes mellitus**

Interventions/Observational Groups

- Arm 1: **Period 1: Metformin, 850 mg p.o., once daily for 2 days; Glucose syrup, 75 g glucose p.o., once daily for 2 days**

  Period 2: Metformin, 850 mg p.o., once daily for 2 days; Glucose syrup, 75 g glucose p.o., once daily for 2 days; trimethoprim, 200 mg p.o., twice daily for 5 days

  Duration of wash-out period: at least 7, maximal 56 days
- Arm 2: **Period 1: Metformin, 850 mg p.o., once daily for 2 days; Glucose syrup, 75 g glucose p.o., once daily for 2 days; trimethoprim, 200 mg p.o., twice daily for 5 days**

  Period 2: Metformin, 850 mg p.o., once daily for 2 days; Glucose syrup, 75 g glucose p.o., once daily for 2 days

  Duration of wash-out period: at least 7, maximal 56 days

Characteristics

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

Study Type: **Interventional**

Study Type Non-Interventional: **[---]***

Allocation: **Randomized controlled trial**

- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Other**
- Assignment: **Crossover**
- Phase: **I**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

Primary Outcome

Primary pharmacokinetic outcome: The area under the metformin plasma concentration time curve, analysed by LC/MS/MS. Time points of measurements: pre-dose until 24 hours after the second intake of metformin in each period.

Primary pharmacodynamic outcome: The area under the plasma glucose concentration time curve in the oral glucose tolerance test. Time points of measurements: pre-dose until 5 hours after intake of glucose syrup.

Secondary Outcome

- Other kinetic and dynamic parameters of metformin and trimethoprim in blood and urine (e.g., the area under the concentration time curve for other time intervals, the maximal concentrations, the fraction excreted in the urine, the renal, extrarenal and secretory clearance, the time of maximal concentration)
- The effect of genetic variants on metformin and trimethoprim concentrations and on endogenous substances in blood and urine, e.g., lactate
- Gender aspects of the analyses

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- other **Institut für Experimentelle und Klinische Pharmakologie und Toxikologie, Erlangen**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2012/09/07**
- Target Sample Size: **24**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **60 Years**

Additional Inclusion Criteria

- Healthy male or female
- No clinically relevant findings at screening
- body mass index between 18 and 30 kg/m²
- willing to use contraceptive measures

Exclusion criteria

- Clinically relevant deviation of laboratory parameters at screening
- Pathologic deviations in the hemogram at screening
- Fasted plasma glucose of 100 mg/dl or higher at screening
- Anamnestically known glucose malabsorption
- Simultaneous participation in another clinical study according to the German Drug Law
- Use of other medication within 14 days before study start (except for hormonal contraceptives)
- smoking of 5 or more cigarettes per day
- Dependency of alcohol, illegal drugs or medication
- Current, relevant disease or relevant physiologic change
- Blood loss of 200 ml blood or more within 4 weeks before study start
- Contraindication for the use of one of the investigational drugs
- Pregnancy or lactation
- No capacity to consent
- dependence on one of the investigators

Addresses

- **Primary Sponsor**

  Friedrich-Alexander-Universität Erlangen-Nürnberg
  Mr. Prof. Dr. med. Dr. h.c. Jürgen Schüttler
  Krankenhausstraße 12

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Sources of Monetary or Material Support

■ **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting stopped after recruiting started**
- Study Closing (LPLV): **2014/02/27**

Trial Publications, Results and other documents

** 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.*