PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Potential influence of coagulation inhibition on the perception of fear or aggressiveness

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

As part of the diagnosed cardiovascular disease is planned for the patient to begin a preventive anticoagulant therapy with dabigatran. This is to protect against the development of blood clots, so that no stroke or occlusion of a blood vessel (embolism / thrombosis) occurs.
Previous results from basic research indicate that the coagulation system plays an important role not only in the bloodstream but also in the brain. It is believed that the coagulation system is involved in the regulation of behavior and mental well-being. However, it has not yet been further investigated whether such mechanisms actually play a role in humans. Anticoagulant therapy could also

Brief Summary in Scientific Language

The main side effect of the anticoagulant is the risk of bleeding. Neuronal side effects are not described - except for the rare but then serious risk of intracranial hemorrhage. There is a possibility that the anticoagulants may actually have no neuro-psychological side effects, or that they may have not been sufficiently considered. It is also conceivable that corresponding neuro-psychiatric side effects only occur in the case of the DOACs, since this group of substances inhibits for the first time highly selectively specific single clotting proteases and thus disturbs the physiological balance, and DOACs (direct oral anticoagulants) may pass through the blood-brain barrier due to the small size.
Animal experimental work proves that altered activation of the coagulation system changes the behavior of the mice. It could e.g. an increased anxiety behavior, coupled with increased aggressiveness, is demonstrated in mice having a partial (95%) loss of function of the endogenous anticoagulant thrombomodulin-protein C system.
This would mean that anticoagulant therapy may also change patient behavior. Due to the well-described effects of thrombin on cells of the CNS (central nervous system), the central importance of thrombin for the regulation of coagulation and the clinical availability of a thrombin-specific DOAC (dabigatran) is initially focused on this substance.
In order to further investigate this human hypothesis generated in the animal

Do you plan to share individual participant data with other researchers?

No

Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00017043**
- Date of Registration in DRKS: **2019/03/28**
- 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.: **150/18 , Ethikkommission der Medizinischen Fakultät der Otto-von-Guericke-Universität Magdeburg**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1230-6228**

Health condition or Problem studied

- ICD10: **I48 - Atrial fibrillation and flutter**

Interventions/Observational Groups

- Arm 1: **Treatment arm:**
  Naturalistic longitudinal examination of approximately 25 adult patients consecutively admitted at one year's hospital admission to the thrombus inhibitor dabigatran (Pradaxa®) at one of the approved indications (e.g., atrial fibrillation, thrombosis, pulmonary embolism) at the Department of Cardiology.
  1. Educating patients about the anonymised documentation and scientific analysis of the sociodemographic data, the cardiological assessment, as well as the questionnaires regarding mental illness, anxiety and aggressiveness.
  2. Documentation
  • Recording mode (elective, self-initiated, emergency department, Psych KG), recording time
  • Neuropsychiatric / Cardiovascular (Prae-) Diseases
  • concomitant diseases,
  • Familly history
  • alcohol, nicotine and drug use,
  • medication
  • Social history (e.g., relationship status, educational background, currently working).

- Initial: General medical history, physical examination, if necessary, laboratory examinations (creatinine / GFR, small blood count, quick-value / INR, nt-proBNP, D-dimer) as indicated for the indication and testing of contraindications / recommended precautions for the administration of Dabigatran are required; Additionally it is planned:
• creation of an ECG; with VHF also LZ-ECG
• Blood pressure measurement
• 6-minute walk test
• Assignment of the patient to a functional performance class (NYHA, EHRA, WHO)
• Acquiring echocardiography, if not collected anyway
• Pulmonary embolism: original PESI score, classification into high-risk or low-risk PE (if not collected anyway?)
• Thrombosis: elevation, whether index event, extension of aortic femoral or iliac vein TVT risk factors (surgery, hospitalization, plaster, birth)
• QOL questionnaire (SF-36)
- Follow-up assessments after 4 weeks and 4 months: General medical history, physical examination, laboratory examinations if necessary (creatinine / GFR, small blood count, quick value / INR, nt-proBNP, D-dimer, thrombin-antithrombin complex / TAT) as required for the indication and testing of contraindications / recommended precautions for the administration of dabigatran. Additionally it is planned:
• EKG; at VHF LZ-ECG
• RR measurement
• 6-minute walk test
• Assignment of the patient to a functional performance class
• QOL questionnaire
• Possible reason for termination anticoagulation
4. Psychometric Assessment
Screening for previously known / manifest mental disorders: Diagnostic short interview for mental disorders / Mini-DIPS (external assessment by Dipl. Psych. Scholz)

■ Arm 2: **Control group:**
matched for age, gender, body mass index and smoking: patients who, after clarifying questionable cardiac arrhythmia in the long-term ECG, e.g. only harmless extrasystoles were found that require no further drug or pacemaker treatment.
1. Clarification of the control patients on the anonymized documentation and scientific analysis of the sociodemographic data, the cardiological assessment, as well as the below-mentioned questionnaires regarding mental illness, anxiety and aggressiveness.
2. Documentation
• Recording mode (elective, self-initiated, emergency department, Psych KG), recording time
• Neuropsychiatric / Cardiovascular (Vor) Diseases
• In addition to diseases,
• Family History
• alcohol, nicotine and drug use,
• medication
• Social history (e.g., relationship status, educational background, currently working).
• results of the cardiological / psychometric assessment (s.u.)
3. Internal cardiological assessment
- Initial: General medical history, physical examination, if necessary, laboratory examinations (creatinine / GFR, small blood count, quick-value / INR, nt-

• 6-minute walk test
• Assignment of the patient to a functional performance class (NYHA, EHRA, WHO)
• Acquiring echocardiography, if not collected anyway
• Pulmonary embolism: original PESI score, classification into high-risk or low-risk PE (if not collected anyway?)
• Thrombosis: elevation, whether index event, extension of aortic femoral or iliac vein TVT risk factors (surgery, hospitalization, plaster, birth)
• QOL questionnaire (SF-36)
- Follow-up assessments after 4 weeks and 4 months: General medical history, physical examination, laboratory examinations if necessary (creatinine / GFR, small blood count, quick value / INR, nt-proBNP, D-dimer, thrombin-antithrombin complex / TAT) as required for the indication and testing of contraindications / recommended precautions for the administration of dabigatran. Additionally it is planned:
• EKG; at VHF LZ-ECG
• RR measurement
• 6-minute walk test
• Assignment of the patient to a functional performance class
• QOL questionnaire
• Possible reason for termination anticoagulation
4. Psychometric Assessment
Screening for previously known / manifest mental disorders: Diagnostic short interview for mental disorders / Mini-DIPS (external assessment by Dipl. Psych. Scholz)
Examination of anxiety: Hamilton anxiety scale / HAM-A (external assessment

- Arm 3: **Atrial fibrillation, fear perception, aggressiveness, anticoagulant, NOAC**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Non-randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Control group receives no treatment**
- Purpose: **Diagnostic**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

- Treatment arm:

Change in timidity under anticoagulant therapy: Hamilton anxiety scale / HAM-A

- control group:

Change in timidity under anticoagulant therapy: Hamilton anxiety scale / HAM-A

-exploratory analysis

Secondary Outcome

Altering Anxiety with Anticoagulant Therapy: State Trait Anger Expression Inventory / STAXI

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Universitätsklinik für Kardiologie und Angiologie,**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2018/11/01**
- Target Sample Size: **25**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **80 Years**

Additional Inclusion Criteria

Treatment group: Patients receiving dabigatran under one of the approved indications, e.g. non-valvular atrial fibrillation, thrombosis, pulmonary embolism or control group: Patients who, after clarifying questionable cardiac arrhythmias, do not require further drug or pacemaker treatment

Exclusion criteria

a) contraindications for dabigatran, e.g. Hypersensitivity to the active substance or to any of the excipients, severe renal insufficiency (creatinine clearance [CrCl] <30 ml / min), acute clinically relevant bleeding, organ damage increasing the risk of bleeding, spontaneous or pharmacological limitation of haemostasis, severe

administered ketoconazole, cyclosporin, itraconazole or tacrolimus; Pat. With artificial heart valves.
b) Severe infections, trauma, tumors or terminal diseases that affect the brain.
c) Lack of consent.

Addresses

- **Primary Sponsor**

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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 ongoing**
- Reason, if "Recruitment stopped after recruiting started" or "Recruiting withdrawn before recruting started": **[---]***
- Reason, if Reason for Recruiting Stop "Other": **[---]***
- Study Closing (LPLV): **[---]***
- Number of Participants in Germany after Recruiting complete: **[---]***
- Total Number of Participants (all Sites worldwide) after Recruiting complete: **[---]***

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.*