Trial Description

Title

Biomarkers in Cardiology (BIC) -8: The effect of integrating the biomarker Copeptin into the process of managing patients with suspected ACS

Trial Acronym

BIC-8

URL of the trial

[---]*

Brief Summary in Lay Language

Acute chest pain is commonly known to be the classic sign of a heart attack. Of the many patients which visit the Emergency Department because of chest pain, less than half do actually suffer from an acute heart attack or an acute narrowing of their coronary arteries, which - in an extreme case causes - the heart attack or myocardial infarction. In some patients the acute heart attack can be diagnosed immediately, either because of typical changes in their ECG or because of increased levels of the laboratory value Troponin in their blood. Troponin is currently the most important marker to diagnose acute coronary artery disease. Unfortunately we see a lot of patients with suspected acute coronary artery disease who do not show any ECG or Troponin changes. These patients pose a major problem in emergency medicine as they need to precautionally be admitted to a chest pain unit and started on medical treatment until a second Troponin test after 6-9 hours is available.

We investigate a newly discovered biomarker, Copeptin. Copeptin has shown excellent results in clinical trials assessing its use in various acute diseases. There are two important trials showing the diagnostic use of Copeptin in patients with suspected acute coronary artery disease.

This trial compares two processes of managing patients with suspected acute coronary syndrome (ACS). Main Hypothesis: Patients with suspected ACS who test negative for Troponin and negative for Copeptin at their initial presentation to the ED can safely be discharged (interventional process). They will not experience more major cardiac adverse events than patients who were managed by standard practise (control process).

We want to test Copeptin in patients with suspected acute coronary artery disease in whom the ECG is unspecific and the initial Troponin test is negative. Further patient care will be based on the Copeptin result. Patients with a negative Copeptin will be discharged into the ambulant care of resident cardiologists. Copeptin positive patients will be managed according to standard guidelines for the management of patients with ACS.

Brief Summary in Scientific Language

The management of patients with suspected Non-ST elevation acute coronary syndrome (NSTEACS) can be time-consuming and expensive. Often patients need to be hospitalized for precautionary medical treatment and serial Troponin testing
Copeptin is a newly discovered biomarker which reflects the body's individual stress level. In acute myocardial infarction (AMI) Copeptin levels increase early after the onset of symptoms. In patients with suspected ACS Copeptin levels were significantly higher in patients with AMI than in patients with other diagnoses. Copeptin in conjunction with Troponin T was particularly useful as a rule-out marker of AMI.

This is a randomized controlled diagnostic trial to quantify the benefit of integrating Copeptin into the management process of patients with NSTEACS and a negative baseline Troponin I test result in the Chest Pain Unit (CPU). Patient management will depend on Copeptin rather than serial Troponin results. Patients will be randomized in either a standard group (management according to current guidelines on managing patients with ACS, Copeptin will be tested, but result will not be revealed to treating personnel) or an interventionell group (Copeptin testing, further management dependent on Copeptin result).

In this interventionell group, patients with a negative baseline Copeptin will be discharged into the ambulant care of co-operating resident cardiologists. Patients with a positive Copeptin result will be treated as by standard care (like patients in the control group).

We will assess the efficacy and safety of the new process as compared to the standard process. Secondary endpoints will assess patient satisfaction and length of hospital stay. Our study design will not only assess the diagnostic use but also the clinical relevance of Copeptin testing in the ED/CPU.

Consecutive N-STEACS patients of the Chest Pain Unit with a negative Troponin I at admission will be invited to participate. Troponin I is tested as part of the standard management of patients with suspected acute coronary syndrome on a point of care test device (POCT).

Patients who give their written informed consent will then be randomized into one of two study arms (experimental and standard management) where further management depends on their Copeptin result at admission.

Organizational Data

- DRKS-ID: DRKS00000276
- Date of Registration in DRKS: 2010/11/17
- Date of Registration in Partner Registry or other Primary Registry: 2011/10/25
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: EA2/085/10, Ethik-Kommission der Charité - Universitätsmedizin Berlin-

Secondary IDs

- Universal Trial Number (UTN): U1111-1118-1665
- Primary Registry-ID: NCT01498731 (ClinicalTrials.gov PRS)

Health condition or Problem studied
ICD10: I20 - Angina pectoris
ICD10: I20-I25 - Ischaemic heart diseases

Interventions/Observational Groups

Arm 1: Experimental Arm:
Patients who test negative for Copeptin at admission will be considered low-risk and will be discharged home without further interventions. To secure the patients safety they will be transferred into our co-operating network of resident cardiologists using the software "Praxis-connect" i.e. these patients will be discharged with an electronically booked appointment to see a cardiologist preferably the next day (but latest within the next three days). In case of any findings suggestive of acute coronary syndrome or worsening of the patient's condition, the patient will immediately be re-admitted to our Emergency Room.
Patients who test positive for Copeptin will be treated as by standard practise.

Arm 2: Control Arm:
Patients will be managed as by standard practice abiding current guidelines for the management of patients with suspected ACS.

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Randomized controlled trial
- Blinding: [---]*
- Who is blinded: [---]*
- Control: Other
- Purpose: Diagnostic
- Assignment: Parallel
- Phase: N/A
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): [---]*

Primary Outcome

Safety effectivity endpoint: Proportion of MACE (all- cause death or survived sudden cardiac arrest, myocardial infarction, re-hospitalisation for acute coronary syndrome, acute unplanned PCI, coronary artery bypass grafting (CABG) and documented life-threatening arrhythmias (VF, VT, AV-block III)) within 30 days Copeptin vs. Control arm (non-inferiority).

Secondary Outcome

Efficiency endpoint of proportion of patients in whom coronary angiography is performed copeptin vs. control arm.
Proportion of patients requiring PCI due to their findings in cardiac catheterization copeptin vs. control arm. (Assessment of Copeptin as a rule-in marker)

Further secondary endpoints evaluate efficacy, safety, cost effectiveness and patient satisfaction of the new process including length of stay in the hospital.

All-cause death, survived sudden cardiac arrest, myocardial infarction, re-hospitalisation for acute coronary syndrome, acute unplanned PCI, coronary artery bypass grafting (CABG) and documented life-threatening arrhythmias (VF, VT, AV-block III) at 30 and 90 days.

Countries of recruitment

- DE Germany
- AT Austria
- CH Switzerland

Locations of Recruitment

- University Medical Center Charité - Universitätsmedizin Berlin, Berlin
- University Medical Center Abteilung Innere Medizin III - Kardiologie, Angiologie und Pneumologie, Heidelberg
- Medical Center Kerckhoff-Klinik - Abteilung für Kardiologie, Bad Nauheim
- University Medical Center Klinik und Poliklinik für Allgemeine und Interventionelle Kardiologie, Hamburg
- Medical Center <style fontName='DejaVu Sans' isBold='true'>Wilhelminenspital, 3. Medizinische Abteilung, Kardiologie & Internistische Notaufnahme, Wien</style>
- University Medical Center Universitätsspital Basel, Klinik für Kardiologie, Basel

Recruitment

- Planned/Actual: Actual
- (Anticipated or Actual) Date of First Enrollment: 2011/04/13
- Target Sample Size: 892
- Monocenter/Multicenter trial: Multicenter trial
- National/International: International

Inclusion Criteria

- Gender: Both, male and female
- Minimum Age: 18 Years
- Maximum Age: no maximum age

Additional Inclusion Criteria
Admission to the Emergency Department with symptoms consistent with ACS:
- Typical chest pain (with or without ECG-changes, but no ST-elevation) suggestive of unstable angina or non-ST-elevated myocardial infarction (NSTEMI)
- Troponin negative at admission according to the current clinical practice
Patient willing and able to give written informed consent

### Exclusion criteria

- Patients with ST-elevation myocardial infarction (STEMI)
- Continuing chest pain or recurrent episodes of chest pain under therapy
- High-risk patients with suspected ACS who need to be hospitalized for reasons independent of their initial troponin result
- Patients who need to be hospitalized for other medical reasons
- Patients in need of urgent life-saving interventions
- Patients under 18 years of age
- Patients with a life expectancy < 6 months
- Patients with any condition that leads the treating physician to not consider the patient eligible for the trial

### Addresses

#### Primary Sponsor
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Sources of Monetary or Material Support

- Commercial (pharmaceutical industry, medical engineering industry, etc.)
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Status

- Recruitment Status: Recruiting complete, follow-up complete
- Study Closing (LPLV): 2013/06/24

Trial Publications, Results and other documents

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* 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.

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