# Impact of EECP-treatment (Enhanced External Counterpulsation) on myocardial adaptive arteriogenesis in patients suffering from stable symptomatic coronary heart disease

Submission date	Recruitment status	<ul><li>Prospectively registered</li></ul>
11/10/2007	No longer recruiting	Protocol
Registration date	Overall study status	Statistical analysis plan
18/12/2007	Completed	Results
Last Edited	Condition category	Individual participant data
20/10/2008	Circulatory System	<ul><li>Record updated in last year</li></ul>

## Plain English summary of protocol

Not provided at time of registration

# Contact information

# Type(s)

Scientific

#### Contact name

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# Additional identifiers

**Protocol serial number** N/A

# Study information

#### Scientific Title

#### Acronym

Art.Net. 2 Trial

#### Study objectives

Please note that as of 20/10/2008 this record was updated due to the addition of a control arm to this pilot study. All changes can be found in the relevant field with the above update date. Please also note that Sweden was removed from the country of recruitment section, and the target number of participants was amended from 20 participants to 21 participants.

#### Main hypothesis:

To determine wether the application of 35 hours of Enhanced External Counterpulsation (EECP) in patients suffering from significant coronary artery disease leads to an improvement of myocardial perfusion and whether this improvement is due to recruitment and proliferation of collateral arteries. Assessment through invasive (Collateral Flow Index [CFIp], Fractional Flow Reserve [FFR]) and non-invasive methods (Cardiac Magnetic Resonance [CMR]). No change of the Collateral Flow Index is expected in the control group (added 20/10/2008).

#### Secondary hypothesis:

- 1. EECP improves systolic and/or diastolic ventricular dysfunction
- 2. Several plasma markers of arteriogenesis and angiogenesis are elevated during and after the intervention. The vascular endothelial function is improved after the course of EECP as assessed by the adaptation of endothelial plasma markers

## Ethics approval required

Old ethics approval format

# Ethics approval(s)

Approval received from the Ethics Committee of Charite - Berlin Medical University (Universitaetsmedizin Berlin) in September 2006 (ref: EA3/009/06). Ethical addendum for the control group received on the 25th September 2008.

## Study design

A phase I (pilot-study), intention to treat, prospective, non-randomised, controlled, multicentre, proof-of-concept study

# Primary study design

Interventional

# Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Coronary artery disease/arteriogenesis/endothelial function

#### **Interventions**

Current information as of 20/10/2008:

The EECP course consists of 35 1-hour sessions of therapy over 7 weeks. The therapy takes place in outpatient clinics. Patients in the control group visit the outpatient clinic three times per week

and undertake weekly nutrition advice, diagnostic tests (twice exercise bicycle test, twice heart rate and blood-pressure monitoring, ultrasound diagnsotics) and an optimization of the medical treatment over the period of 7 weeks. In the control group as well as in the EECP group before and after treatment a coronary angiography and measurement of fractional flow reserve as well collateral flow index is performed. In the second coronary angiography - depending on the result of the FFR measurement and myocardial ischaemic tests - Percutaneous Coronary Intervention (PCI) is done or not.

Initial information at time of registration:

The EECP course consists of 35 1-hour sessions of therapy over 7 weeks. The therapy takes place in outpatient clinics. Before and after 35 hours EECP-treatment a coronary angiography and measurement of fractional flow reserve as well collateral flow index is performed. In the second coronary angiography - depending on the result of the FFR measurement and myocardial ischaemic tests - Percutaneous Coronary Intervention (PCI) is done or not.

#### **Intervention Type**

Other

#### Phase

Phase I

#### Primary outcome(s)

Changes in CFIp and FFR indexes evaluated at baseline and after the 7 weeks therapy.

#### Key secondary outcome(s))

- 1. Changes in CMR perfusion at rest and under adenosine. Quantitative assessment (ml/min/g of myocardium)
- 2. Changes in the Ejection Fraction (EF) assessed through CMR and echocardiography
- 3. Changes in the Canadian Cardiovascular Society (CCS) classification of the angina pectoris and in the New York Heart Association (NYHA) classification of the heart failure
- 4. Treadmill test for ischaemic signs
- 5. Changes in the plasma levels of pro-arteriogenic and pro-angiogenic markers
- 6. Changes in the plasma levels of several markers of the endothelial function

The endpoints 1, 2, 3, 5, 6 are evaluated at baseline, after 2 weeks of therapy, after 7 weeks (end of EECP) and 6 months after the therapy. Point 4 is assessed at baseline and after 7 weeks.

#### Completion date

31/12/2008

# **Eligibility**

#### Key inclusion criteria

- 1. Patients of both genders
- 2. Age greater than 30 to less than 80 years
- 3. Suffering from stable coronary vessel disease for more than 3 months
- 4. With an angiographically diagnosed haemodynamic significant stenosis of at least one epicardial vessel
- 5. An objective positive test for stress-induced ischaemic imaging and pathological Fractional Flow Reserve (FFR less than 0.8)

#### Participant type(s)

Patient

#### Healthy volunteers allowed

No

#### Age group

Adult

#### Sex

All

#### Key exclusion criteria

- 1. Unstable angina
- 2. After aorto-coronary bypass grafting
- 3. No previous Q-wave infarction in the area assessed for coronary collaterals
- 4. Non-ischaemic left ventricle dysfunction Ejection Fraction (EF) less than 35%, fluid overload
- 5. Tricuspid and aortic valve insufficiency greater than grade II and aortic valve stenosis greater than grade II
- 6. Relevant stenosis of the aorta abdominalis or aorta thoracica, coarctatio aortae
- 7. Symptomatic angiopathy of the lower limb (neuropathy, vasculitis, symptomatic Peripheral Arterial Disease [PAD] ankle pressure less than 80 mmHg)
- 8. Chronic venous insufficiency grade greater than III, symptomatic varicosis, thrombosis, occlusion of vena cava inferior, phlebitis
- 9. Evident lesions at the lower extremity (ulcera, big scar, etc.)
- 10. Diabetic retinopathy
- 11. Anticoagulation International Normalised Ratio (INR) greater than 3 or less and bleeding symptoms, disturbed homeostasis
- 12. Orthopaedic disease (hip. knee)
- 13. Severe systemic disease
- 14. Severe hypertension greater than 180 mmHg
- 15. Status post cerebral bleeding
- 16. Pregnancy
- 17. Mental retardation or dementia
- 18. Severe kinking of coronary vessels
- 19. Atrial fibrillation
- 20. Pacemaker (PM)/Implantable Cardioverter Defibrillator (ICD), metal valve
- 21. Acute renal insufficiency, progressive renal insufficiency, chronic renal insufficiency cut off creatinine 2 mg/dl

#### Date of first enrolment

01/11/2007

#### Date of final enrolment

31/12/2008

# Locations

#### Countries of recruitment

Germany

Study participating centre HELIOS Klinikum Berlin Berlin Germany 13125

# Sponsor information

#### Organisation

Charite - University Medicine Berlin (Charite - Universitatsmedizin Berlin) (Germany)

#### **ROR**

https://ror.org/001w7jn25

# Funder(s)

## Funder type

Hospital/treatment centre

#### **Funder Name**

Center of Cardiovascular Research (Germany)

# **Results and Publications**

Individual participant data (IPD) sharing plan

# IPD sharing plan summary

Not provided at time of registration