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Clopidogrel versus Aspirin in Chronic HEart failure

Submission date	Recruitment status	[ ] Prospectively registered
11/01/2012	Stopped	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
08/02/2012	Stopped	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
24/04/2019	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol
http://www.hta.ac.uk/2144

Contact information

Type(s)
Scientific

Contact name
Prof John Cleland

Contact details
Department of Cardiology
Daisy Building
Castle Hill Hospital
Castle Road
Cottingham
Hull
United Kingdom
HU16 5JQ
+44 (0)1482 761776
j.g.cleland@hull.ac.uk

Additional identifiers

EudraCT/CTIS number
2009-011637-27

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 08/53/36

Study information

Scientific Title
A randomised, open-label, study comparing the effects of aspirin and clopidogrel on outcomes in patients with chronic heart failure

Acronym
CACHE

Study objectives
Compared to clopidogrel, aspirin has an adverse effect on cardiovascular function in patients with heart failure leading to an increase in the symptoms of heart failure, reduced quality of life, an increase in hospitalisation and higher mortality.

Demonstrating whether such differences do or do not exist would be valuable and settle a substantial controversy in care, highlighted in international guidelines for the management of heart failure. The protocol designed to address this in a non-blinded, randomised controlled trial comparing aspirin and clopidogrel, conducted in 3,000 patients with heart failure over a period of approximately 5 years.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Northern & Yorkshire REC, 15/05/2012, ref: 10/H0903/13

Study design
Phase IV trial open-label interventional non-blinded randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Heart failure

Interventions
Clopidogrel vs aspirin both 75 mg/day per patient taken orally & daily.

This phase IV trial will compare the effects of prescribing aspirin 75 mg/day and clopidogrel 75 mg/day, primarily on all-cause mortality. Half of the patients will be randomised to each intervention. The investigator and the patient will know to which treatment the patient has been assigned. The duration of the study is determined by the event-rate although it could be stopped early for futility or because of a larger than anticipated treatment difference. The planned mean duration of follow-up is 3.8 years and some patients may be followed for more than five years before the required number of events has been attained. However, to allow for uncertainty we seek permission to follow patients for up to ten years.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Clopidogrel, aspirin

Primary outcome measure
All causes mortality

Secondary outcome measures
1. Cardiovascular death or hospitalisation for heart failure (time to first event)
2. Sudden death or a vascular event (myocardial infarction, stroke, peripheral embolism, requirement for angioplasty or vascular surgery) using a time to first event analysis
3. Total days lost to death or hospitalisation (all causes)
4. Quality-adjusted years alive (QALY) using repeated measurements of EQ5D
5. Cost per QALY

Overall study start date
11/02/2011

Completion date
31/08/2016

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Willing and able to provide written confirmation of informed consent
2. A clinical diagnosis of heart failure
3. Currently in sinus rhythm on clinical examination
4. Receiving diuretics for at least 6 weeks prior to inclusion
5. Patients must have a telephone
6. Patients must be willing to provide their personal contact details, those of their next of kin

and those of their general practitioner (GP) and hospital to the national coordinating office and be willing to be contacted by telephone by these staff.
7. Patients must be willing to have hospitalisation and other serious events tracked through mechanisms including:
7.1. In England:
7.1.1. The National Health Service (NHS) Central Register (NHSCR)
7.1.2. National Office of Statistics
7.2. In Scotland:
7.2.1. The Registrar Generals Office
7.2.2. NHS Information Statistics Division
8. If non-English speaking, patients must have a friend or relative who can translate or who have other access to translation

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
3000

Total final enrolment
87

Key exclusion criteria
1. Plasma (central lab) NT-proBNP <400pg/ml (47.3pmol/L) or MR-proANP <200pmol/L
2. Lack of an ECG within the previous 12 months documenting sinus rhythm. Patients who have had an episode of atrial fibrillation in the previous year may be enrolled provided the most recent ECG shows sinus rhythm and the treating doctor has decided not to prescribe anti-coagulants.
3. Severe valve disease in the investigators opinion (an echocardiogram report within the previous 12 months must be available)
4. Serum creatinine >250umol/L (local lab)
5. Intolerant of aspirin or clopidogrel or who have a contraindication to such treatment or who require anti-coagulation
6. Contraindications to aspirin or clopidogrel include:
6.1. Substantial, in the investigators opinion, bleeding from an uncorrected source within the previous year
6.2. Endoscopically proven peptic ulcer within the previous 3 months. Patients must be on treatment if peptic ulcer diagnosed in previous year
6.3. Haemorrhagic stroke within the previous 3 months
6.4. Known coagulation disorder (e.g. haemophilia)
6.5. Full blood count suggesting iron deficiency (patients may be enrolled in the study after the cause of iron deficiency is or has previously been investigated and treatment has been initiated) (local lab)
7. Platelet count <100,000 (local lab)
8. Scheduled procedure that would require discontinuation of study medication for > 2 weeks

(patient may be recruited after procedure)
9. History of uncontrolled seizures or high risks of falls
10. Regular use of non-steroidal anti-inflammatory agents > 3 times a week
11. Use of maintenance oral corticosteroids
12. Women of child-bearing potential or who are breast feeding
13. Patients with a history of asthma should not take part unless they have taken aspirin previously without ill-effect
14. Patients with an indication for oral anti-coagulation including:
14.1 Current or recent (within 12 months) atrial fibrillation or flutter (evidence of an ECG documenting sinus rhythm must be provided)
14.2. Prior embolic stroke
14.3. Mechanical prosthetic heart valve
15. Patients requiring dual anti-platelet therapy including:
15.1. Patients within 3 months of an acute coronary syndrome
15.2. Transient ischaemic attack or vascular procedure or within one year of receiving a drug eluting coronary stent
16. Patients likely to die of something other than heart failure or sudden (cardiac) death
17. Inability to walk without the physical assistance of another person (patients with walking aids are permitted)
18. Other patients deemed unlikely to comply with the protocol
19. Women who are at pregnant or who could become pregnant
20. Women of child-bearing age should be taking reliable contraception (tubal ligation or implanted contraceptive)
21. Inability to communicate in English

Date of first enrolment
11/02/2011

Date of final enrolment
31/08/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Castle Hill Hospital
Hull
United Kingdom
HU16 5JQ

Sponsor information

Organisation
Hull and East Yorkshire Hospitals NHS Trust (UK)

Sponsor details
Research and Development Department
Daisy Building
Castle Hill Hospital
Castle Road
Hull
England
United Kingdom
HU16 5JQ
+44 (0)1482 461882
priyai.parkinson@hey.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.hey.nhs.uk/

ROR
https://ror.org/01b11x021

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	02/09/2014	18/04/2019	Yes	No
HRA research summary			28/06/2023	No	No