Does the ALDOsterone:RENin ratio predict the efficacy of spironolactone over bendroflumethiazide in hypertension?

Submission date	Recruitment status	Prospectively registered		
21/03/2007	No longer recruiting	[X] Protocol		
Registration date	Overall study status	Statistical analysis plan		
13/04/2007	Completed	[X] Results		
Last Edited	Condition category	[] Individual participant data		
28/09/2018	Circulatory System			

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Prof Thomas MacDonald

Contact details

Level 7
Hypertension Research Centre
Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY
+44 (0)1382 632852
t.m.macdonald@dundee.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Study information

Scientific Title

Does the ALDOsterone:RENin ratio predict the efficacy of spironolactone over bendroflumethiazide in hypertension?

Acronym

RENALDO

Study objectives

Primary objective:

To test the hypothesis that the aldosterone:renin ratio predicts the antihypertensive response to spironolactone, specifically that the effect of spironolactone 50 mg is greater than that of bendroflumethiazide 2.5 mg in hypertensive subjects with high aldosterone:renin ratios.

Secondary objectives: to determine whether -

- 1. Bendroflumethiazide induces adverse metabolic abnormalities, especially in subjects with high aldosterone:renin ratios
- 2. Baseline renin measurement predicts the antihypertensive response to spironolactone and/or bendroflumethiazide

Ethics approval required

Old ethics approval format

Ethics approval(s)

The main study and sub-studies have ethical approval from Tayside Committee on Medical Research Ethics and West Ethics Committee on the 20th June 2002 (ref: 2006/01).

Study design

A double-blind, randomised, crossover, controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Hypertension/cardiovascular diseases

Interventions

120 hypertensive subjects are randomised to 12 weeks treatment with spironolactone 50 mg once daily and 12 weeks treatment with bendroflumethiazide 2.5 mg once daily. The two treatment periods are separated by a two-week washout period.

Investigators and subjects do not know the order of the treatment periods, which is according to a computer generated randomisation list. Randomisation is stratified by aldosterone:renin ratio to include equal numbers of subjects with high and low aldosterone:renin ratios. This is necessary as in an unselected population, only 15% of subjects will have an aldosterone:renin ratio greater than 750.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Spironolactone, bendroflumethiazide

Primary outcome measure

The primary endpoint is the difference in mean 24-hour blood ambulatory pressure recorded at the end of each 12-week treatment period.

Secondary outcome measures

Secondary endpoints include the differences between the following measurements taken at the end of each 12-week treatment period:

- 1. Mean daytime ambulatory blood pressure
- 2. Mean night time ambulatory blood pressure
- 3. Mean clinic blood pressure defined as mean of mean clinic BPs on both penultimate and final days of treatment periods
- 4. Clinical biochemistry measurements of plasma potassium (K+), magnesium (Mg2+), creatinine, triglycerides, cholesterol and High Density Lipoprotein (HDL) cholesterol

Overall study start date

01/08/2002

Completion date

01/02/2006

Eligibility

Key inclusion criteria

- 1. Mild-to-moderate hypertension with daytime mean Ambulatory Blood Pressure Monitoring (ABPM) systolic Blood Pressure (BP) greater than 140 mmHg
- 2. Either untreated or on stable treatment for at least two weeks
- 3. Either:
- a. aldosterone:renin ratio greater than 750 and plasma aldosterone greater than 250 pmol/l, or

- b. aldosterone:renin ratio less than 300 and plasma renin activity less than 10 ng/ml/h
- 4. No clinically significant abnormalities on screening laboratory results
- 5. Written informed consent

Participant type(s)

Patient

Age group

Not Specified

Sex

Not Specified

Target number of participants

120

Key exclusion criteria

- 1. Females of child-bearing potential not using reliable contraception
- 2. Subjects on more than four classes of anti-hypertensive drugs at screening
- 3. Secondary hypertension other than hyperaldosteronism
- 4. Addisons disease
- 5. Severe or malignant hypertension
- 6. Subjects who take and are unable to discontinue taking a thiazide diuretic or potassium sparing diuretic
- 7. Serum potassium less than 3.3 or greater than 5 mmol/l two weeks after discontinuing diuretics
- 8. Serum creatinine greater than 160 µmol/l
- 9. Subjects intolerant of spironolactone or thiazide diuretics
- 10. Subjects who have taken spironolactone or potassium canrenoate in the previous three months
- 11. Previous Myocardial Infarction (MI) or Cardiovascular Accident (CVA)
- 12. Chronic Heart Failure (CHF)
- 13. Any condition that would:
- a. interfere with the ability to provide informed consent
- b. place at increased risk
- c. confound interpretation of results

Date of first enrolment

01/08/2002

Date of final enrolment

01/02/2006

Locations

Countries of recruitment

Scotland

United Kingdom

Study participating centre

Level 7

Dundee United Kingdom DD1 9SY

Sponsor information

Organisation

Ninewells Hospital & Medical School (UK)

Sponsor details

c/o Dr Harikrishnan Parthasarathy, Specialist Registrar Dundee Scotland United Kingdom DD1 9SY

_

krishnankala@hotmail.com

Sponsor type

Hospital/treatment centre

ROR

https://ror.org/039c6rk82

Funder(s)

Funder type

Government

Funder Name

Chief Scientist Office, Scottish Executive Health Department (UK) (ref: BA-01-25)

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 summaryNot provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	09/05/2007		Yes	No
Results article	results	01/01/2010		Yes	No