

# STAG: effect of the drug AZD4017 on bone density in post-menopausal women

<b>Submission date</b> 20/05/2015	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 20/05/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 07/12/2022	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

As people age, their bones naturally become less dense in minerals, but for some people this can lead to osteoporosis, an advanced stage of a condition that leads to brittle bones that break (fracture) easily. It is often seen in women who have been through the menopause, or people who are at risk of osteoporosis due to various health or lifestyle factors. In older people, osteoporosis is often diagnosed following a minor fall which has led to a bone fracture. The bones most often fractured are those of the hips and spine, and these injuries cause problems for millions of people around the world (9 million every year) as a result of pain, hospital admissions, lack of independence at home or the need to move into sheltered/nursing home care. There are some similarities between the bones of older people and the bones of people taking steroid medications. This is because steroids reduce bone mineral density. A new drug called AZD4017 has been developed to reduce the level of steroids that are naturally produced by the body in local tissues; it may help to reduce the loss of bone mineral density that occurs as people age. The aim of this study is to look at the effect of AZD4017 on bones in women diagnosed with osteopaenia, a condition where some bone density has been lost but it has not yet progressed to the stage of osteoporosis.

### Who can participate?

Women aged 50 and over diagnosed with osteopaenia

### What does the study involve?

Participants are randomly allocated into one of two groups. Those in group 1 (intervention group) are given the drug AZD4017 to take for 90 days. Those in group 2 (control group) are given a placebo (dummy tablet with no drug in it) to take for 90 days. Participants have 5 visits to the clinic while taking the drug, and another 3 months later. Participants have blood tests and scans to check the effect of AZD4017 on bones, and urine tests to make sure that steroid production in the tissues is reduced in response to the drug. Participants also have muscle tests (walk, stand and grip tests) to see if blocking steroid production improves muscle strength.

What are the possible benefits and risks of participating?

AZD4017 has the potential to be developed into an effective treatment for patients with osteoporosis and high fracture risk. The participants involved in this study are not at high risk of fracture, and as such, are unlikely to gain any direct benefits.

Where is the study run from?

1. Northern General Hospital (UK)
2. Chapel Allerton Hospital (UK)

When is the study starting and how long is it expected to run for?

May 2015 to December 2017

Who is funding the study?

Medical Research Council (MRC) (UK)

Who is the main contact?

Dr L Flanagan

## Contact information

### Type(s)

Scientific

### Contact name

Dr Louise Flanagan

### Contact details

Clinical Trials Research Unit  
Leeds Institute of Clinical Trials Research  
University of Leeds  
Leeds  
United Kingdom  
LS2 9JT

## Additional identifiers

### EudraCT/CTIS number

2013-003387-32

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

15665

## Study information

### Scientific Title

Phase II study of the impact of AZD4017, a selective 11 $\beta$ HSD1 inhibitor, on biochemical markers of bone turnover in post-menopausal osteopaenia

**Study objectives**

The drug AZD4017, which reduces steroid production in tissue, may reverse some of the bone changes that are seen with aging and improve muscle strength.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Multicentre Research Ethics Committee (MREC), 11/11/2013, ref: 13/SC/0523

**Study design**

Randomised interventional treatment study

**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 below to request a patient information sheet

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

Osteoporosis

**Interventions**

Participants will take AZD4017, a selective 11 $\beta$ -HSD1 inhibitor, for 90 days. Control group participants will take a placebo (dummy tablet with no drug in it) for 90 days.

**Intervention Type**

Drug

**Phase**

Phase II

**Drug/device/biological/vaccine name(s)**

AZD4017

**Primary outcome measure**

Change from baseline in serum osteocalcin after 90 days.

### **Secondary outcome measures**

1. Change from baseline in serum  $\beta$ CTx after 90 days
2. Change in bone density, microstructure and strength after 180 days
3. Change in bone remodelling after 90 days
4. Change in muscle strength after 90 days

### **Overall study start date**

29/05/2015

### **Completion date**

30/04/2016

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 21/06/2017:

1. Provision of informed consent prior to any study specific procedures
2. Aged >50 and post-menopausal based on amenorrhoea for >12 months
3. Documented presence of osteopenia (BMD T-score at lumbar spine and/or total hip of less than or equal to -1 and greater than -2.5) as measured by DXA
4. Placebo treatment for the duration of the study must not be considered detrimental to the study participant
5. Must be able to understand the patient information sheet and consent form and comply with study requirements

Previous inclusion criteria:

1. Provision of informed consent prior to any study specific procedures
2. Aged >50 and postmenopausal based on amenorrhoea for >12 months
3. Documented presence of osteopaenia (bone density T-score at lumbar spine or hip of less than -1 and greater than -2.5 by Dual-energy X-ray Absorptiometry (DXA) criteria)
4. Placebo treatment for the duration of the study must not be considered detrimental to the study subject
5. Must be able to understand the patient information sheet and consent form and comply with study requirements

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Sex**

Female

### **Target number of participants**

Planned Sample Size: 100; UK Sample Size: 100

### **Total final enrolment**

## Key exclusion criteria

Current exclusion criteria as of 21/06/2017:

Bone-related exclusion criteria:

1. Clinical or biochemical evidence of secondary causes of bone loss (screening tests to include but are not restricted to: normal serum sodium, potassium, urea, creatinine (eGFR at >60 mls/min), LFTs, ALP, TFTs; free T4 and TSH), FBC and ESR (<40mm/hr))
2. Vitamin D deficiency (defined as a 25-OH vitamin D level of <20nmol/L)
3. The current or recent use (within the last 2 years) of medication likely to have an impact on bone (oestrogens, aromatase inhibitors, bisphosphonates, fluoride, denosumab, strontium ranelate, anti-convulsants; and oral, inhaled or nasal glucocorticoids). Participants already on calcium/vitamin D supplementation will be asked to continue this for the duration of the study. Those with a 25-OH vitamin D level of 20-50nmol/L at screening will be supplemented prior to inclusion. Medications will be reviewed at the screening visit
4. Bilateral fractures of the radius and/or tibia

General exclusion criteria:

1. Women of child-bearing potential (WOCBP). Note: WOCBP include any female who has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or is not postmenopausal (defined as amenorrhea  $\geq$  12 consecutive months or women on hormone replacement therapy with documented serum follicle stimulating hormone level >35 mIU/mL)
2. Have an estimated glomerular filtration rate (eGFR) calculated by the Modification of Diet in Renal Disease (GFR calculation) using theMDRD equation of <60ml/min/1.73m<sup>2</sup>
3. Have any endocrine disorder that would merit therapy according to national guidelines. The only exception to this is patients with hypothyroidism on treatment with thyroid function tests within normal parameters for a minimum of 3 months
4. Suspicion of, or known Gilbert's disease
5. CK >2 x ULN on 2 consecutive measurements
6. ALT and/or AST > 1.5\*ULN
7. ALP > ULN
8. Bilirubin (total) > 1.5\*ULN
9. Participant is, at the time of signing the informed consent, a user of recreational or illicit drugs (including marijuana) or has had a recent history (within the last year) of drug or alcohol abuse or dependence, on questioning or clinical history
10. Have uncontrolled systemic hypertension (BP >150/90) on 3 successive measurements on the morning of the screening visit. Note: Participants with controlled hypertension (BP of 150/90 or better on same treatment for 3 months) may be included, and should continue on the same anti hypertensive medication for the duration of the study. Thus, if hypertension is identified at screening and the hypertension is then treated and remains controlled for 3 months, then the patient may enter screening again
11. Are receiving systemic (including vaginal/rectal) or inhaled glucocorticoid treatment at the time of the screening visit. Note: Topical (skin) application of mild, over-the-counter topical steroid containing medication to small localised areas of the skin is permitted
12. Are taking probenecid at the time of the screening visit
13. Have any screening laboratory abnormality which is outside the local reference ranges specified in the Investigator Site File that, in the investigator's judgement, is considered to be clinically significant
14. History of any clinically significant disease or disorder which, in the opinion of the investigator, may either put the participant at risk because of participation in the study, or

influence the results of the participant's ability to participate in the study. Specifically, a diagnosis of any inflammatory disorder that might reasonably need treatment with glucocorticoids during the course of the study, should be considered for exclusion

15. History or presence of any significant gastrointestinal, hepatic, or renal disease or any other condition known to interfere with absorption, distribution, metabolism, or excretion of drugs
16. Any clinically significant illness, medical/surgical procedure or trauma within 4 weeks of the first administration of IMP as judged by the investigator
17. Have known hypersensitivity or intolerance to 11 $\beta$ -HSD1 antagonists or to AZD4017
18. Have been involved in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
19. Have participated in any other clinical study within 1 month prior to the screening visit
20. Previous randomisation for treatment in the present study

Previous exclusion criteria:

Bone-related exclusion criteria:

1. Clinical or biochemical evidence of secondary causes of bone loss
2. 25-OH vitamin D level <20nmol/L
3. The current or recent use (within 2 years) of medication likely to have an impact on bone (oestrogens, aromatase inhibitors, bisphosphonates, fluoride, denosumab, strontium ranelate, anti-convulsants, teriparatide; and oral, inhaled or nasal glucocorticoids). Patients already on calcium/vitamin D supplementation will continue this for the study. Those with a 25-OH vitamin D level of 2050nmol/L at screening will be supplemented prior to inclusion

General exclusion criteria:

1. Women of child-bearing potential
2. eGFR calculated by MDRD equation <60ml/min/1.73m<sup>2</sup>
3. Any endocrine disorder, e.g. thyroid dysfunction
4. Suspicion of or known Gilbert's disease
5. CK > twice upper limit normal on 2 consecutive measurements
6. Liver transaminases > upper limit normal
7. Alkaline phosphatase > upper limit normal
8. Bilirubin (total) > upper limit normal
9. User of recreational or illicit drugs (including marijuana) or has had a recent history (within the last year) of drug or alcohol abuse or dependence
10. Uncontrolled systemic hypertension (BP >150/90); on 3 successive measurements on the morning of the screening visit
11. Systemic (including vaginal/rectal) or inhaled glucocorticoid treatment at the time of the screening visit
12. Probenicid therapy at the time of the screening visit
13. Any screening laboratory abnormality that, in the investigator's judgement, is considered to be clinically significant
14. History of any clinically significant disease or disorder which, in the opinion of the investigator, may either put the subject at risk because of participation in the study, or influence the results of the subject's ability to participate in the study. Specifically, a diagnosis of any inflammatory disorder that might reasonably need treatment with glucocorticoids during the course of the study
15. History of any other condition known to interfere with absorption, distribution, metabolism, or excretion of drugs
16. Any clinically significant illness, medical/surgical procedure or trauma within 4 weeks of the first administration of IP as judged by the investigator
17. Hypersensitivity or intolerance to 11 $\beta$ -HSD1 antagonists or to AZD4017

- 18. Involvement in the planning and/or conduct of the study
- 19. Participation in any other clinical study within 1 month prior to the screening visit
- 20. Previous randomisation for treatment in the present study

**Date of first enrolment**

29/05/2015

**Date of final enrolment**

01/12/2017

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Northern General Hospital**

Herries Road

Sheffield

United Kingdom

S5 7AU

**Study participating centre**

**Chapel Allerton Hospital**

Chapeltown Road

Leeds

United Kingdom

LS7 4SA

## **Sponsor information**

**Organisation**

University of Leeds

**Sponsor details**

School of Medicine

The Worsley Medical & Dental Building

Clarendon Way

Leeds

England  
United Kingdom  
LS2 9NL

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/024mrx33>

## **Funder(s)**

**Funder type**

Research council

**Funder Name**

Medical Research Council

**Alternative Name(s)**

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**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**

The datasets generated during and/or analysed during the current study will be available upon request from [ctr-stag@leeds.ac.uk](mailto:ctr-stag@leeds.ac.uk) dependent upon the planned usage, any trial contractual obligations, and the participant consent given.

**IPD sharing plan summary**

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Abstract results</a>		21/08/2020	23/04/2021	No	No
<a href="#">Results article</a>		16/06/2022	07/12/2022	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No