

# A randomised controlled trial to test whether active vitamin D can improve the clinical response to steroids in asthmatic patients

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| <b>Submission date</b><br>17/03/2009   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>07/05/2009 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>01/09/2014       | <b>Condition category</b><br>Respiratory          | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

Prof Chris Corrigan

### Contact details

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Protocol 08

# Study information

## Scientific Title

Does 1-alpha, 25-dihydroxyvitamin D3 (calcitriol) enhance corticosteroid activity in steroid refractory asthma? A randomised controlled trial

## Acronym

VitD1/08

## Study objectives

We hypothesise that the administration of the active form of vitamin D (calcitriol) improves the clinical response to systemic corticosteroid therapy in patients with moderate to severe asthma whose symptoms fail to improve on steroid therapy.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Guys Research Ethics Committee, 01/08/2008, ref: 08/H0804/84

## Study design

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 below to request a patient information sheet

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

Asthma

## Interventions

Screen visit 1:

Informed consent will be obtained before screening starts. Suitable subjects will undergo full assessment of their medical history (including a complete smoking history) and laboratory evaluation for safety haematology and biochemistry profile. Up to 100 ml of venous blood will also be drawn for ex-vivo experiments. Spirometry will be performed and the FEV1 and forced vital capacity (FVC) obtained. Reversibility would be assessed by giving the subject a short acting beta agonist and measuring the FEV1 pre- and 15 - 30 minutes post-bronchodilator. We will

measure fractional exhaled nitric oxide (FeNO) using an Aerocrine NIOX MINO® monitor following the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines. A peak flow meter and a diary card will be given to the subject to record morning and evening peak flows throughout the study. All these procedures are done in accordance with departmental Standard Operating Procedures.

Eligible subjects would be entered into the second part of the screening process. These subjects would be given prednisolone 40 mg/1.73 m<sup>2</sup>/day as a single dose in the morning for 14 days, to be taken at home.

#### Screen visit 2:

The subject's medical history and adverse events would be reviewed at the start of the screening visit 2. Spirometry will be performed and the FEV1 and FVC obtained. Subjects who demonstrate an increase of greater than 15% in the FEV1 when compared to baseline (screen visit 1) would be excluded. Subjects who are still eligible would be entered into the main part of the trial. We will repeat FeNO in exhaled air. Up to 100 ml of venous blood will be taken for safety haematology and biochemistry and for ex-vivo experiments.

#### Treatment visit day 1:

Following a 4-week washout period (from screen visit 2) participants would attend treatment visit day 1. The subjects' medical history and adverse events would be reviewed at the start of this visit. Up to 100 ml of venous blood would be taken for safety haematology and biochemistry and for ex-vivo experiments. Participants would be randomised to receive either calcitriol 0.25 mg twice daily or matching placebo. The first dose would be done under supervision. Subjects would be discharged following first dosing and would take the subsequent doses at home.

#### Treatment visit day 15:

On day 15 of treatment subjects would attend treatment visit day 15. Subjects are to withhold their day 15 treatment dose prior to attending. The subjects medical history and adverse events would be reviewed at the start of this visit. Prior to dosing up to 100 ml of venous blood would be taken for safety haematology and biochemistry and for ex-vivo experiments. Subject would perform spirometry and fraction of nitric oxide in exhaled air (FeNO) pre-dose. These would be done in accordance with departmental standard operating procedures. A standard Asthma Control Questionnaire (ACQ) would also be completed by the subject pre-dose.

FeNo measurements are highly correlated with eosinophilic airway inflammation; eosinophilic inflammation is correlated with response to steroid treatment. We will measure FeNO using a Aerocrine NIOX MINO® monitor, following the ATS/ERS guidelines.

Subjects who are still eligible to continue in the study would be commenced on prednisolone 40 mg/1.73 m<sup>2</sup>/day as a single dose for 14 days. The first dose of prednisolone and day 15 dose of treatment article would be done under supervision. Subjects would be discharged following dosing and would take subsequent doses of treatment and prednisolone at home.

#### Treatment visit day 28:

On day 28 of treatment subjects would attend treatment visit day 28. Subjects would have completed a 28-day dosing period of treatment article and a 14-day dosing period of prednisolone. The subject's medical history and adverse events would be reviewed at the start of this visit. Following this up to 100 ml of venous blood would be taken for safety haematology and biochemistry and for ex-vivo experiments. Subject would perform spirometry, and fraction of nitric oxide in exhaled air (FeNO). A standard Asthma Control Questionnaire (ACQ) would also be completed by the subject. A physical examination would also be performed.

Follow-up day 56:

After 1 month subjects will be interviewed either during a routine visit to the asthma clinic or via telephone call to check medical history and adverse events. Following all these procedures subjects would be discharged from the study.

## **Intervention Type**

Supplement

## **Phase**

Not Specified

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

Vitamin D3 supplementation

## **Primary outcome measure**

Change in FEV1 at baseline compared to the end of the treatment period.

## **Secondary outcome measures**

1. Level of the ex-vivo production of interleukin-10 (IL-10) and other surrogate biomarkers of outcome or drug effects/process by T-cells, measured at screen visit 1, screen visit 2, treatment visit day 1, treatment visit day 15 and treatment visit day 28
2. Serological markers of inflammation, measured at screen visit 1, screen visit 2, treatment visit day 1, treatment visit day 15 and treatment visit day 28
3. Fraction of nitric oxide in exhaled air, measured at screen visit 1, screen visit 2, treatment visit day 15 and treatment visit day 28
4. Asthma Control Questionnaire (ACQ) score, measured at treatment visit day 15 and treatment visit day 28

## **Overall study start date**

01/04/2009

## **Completion date**

30/09/2011

# **Eligibility**

## **Key inclusion criteria**

1. Male or female adults aged between 18 to 65 years
2. Documented history and typical symptoms of asthma for greater than or equal to 6 months prior to screening
3. Pre-bronchodilator forced expiratory volume in one second (FEV1) less than 70% predicted and greater than 15% reversibility to beta 2-agonist or diurnal peak flow variability of greater than 20%
4. Corticosteroid refractory asthma, as defined by a less than 15% improvement in FEV1 following a 14-day course of prednisolone 40 mg/1.73 m<sup>2</sup>/days 29 - 31
5. Written informed consent received

## **Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

80

**Key exclusion criteria**

1. Past or present disease, which, as judged by the investigator, may affect the study outcome (other than asthma, rhinitis or eczema)
2. Serum corrected calcium greater than 2.66 mmol/l
3. Clinically significant deviation from normal (physical examination or laboratory parameters) as judged by the investigator at the screening visit
4. Current smoker or an ex-smoker of less than 5 years with a greater than 5 pack year history
5. Pregnant or lactating females or those at risk of pregnancy (women of childbearing age may be offered a pregnancy test prior to recruitment)
6. History of a respiratory tract infection and/or exacerbation of asthma within 4 weeks of the screening visit requiring oral corticosteroid tablets
7. Participation in a study involving an investigational medicinal product in the previous 3 months or blood donation within the last year
8. Participants taking regular medications for diseases other than those for asthma or rhinitis
9. Current or previous allergen immunotherapy
10. Concomitant treatment with a thiazide diuretic or calcium supplement
11. Inability to understand or comply with the research protocol

**Date of first enrolment**

01/04/2009

**Date of final enrolment**

30/09/2011

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Department of Asthma, Allergy and Respiratory Allergy**

London

United Kingdom

SE1 9RT

# Sponsor information

## Organisation

Kings College London (UK)

## Sponsor details

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3rd floor Conybeare House  
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Great Maze Pond  
London  
England  
United Kingdom  
SE1 9RT

## Sponsor type

University/education

## Website

<http://www.kcl.ac.uk/>

## ROR

<https://ror.org/0220mzb33>

# Funder(s)

## Funder type

Charity

## Funder Name

Asthma UK (UK)

## Alternative Name(s)

Asthma UK, Asthma + Lung UK

## Funding Body Type

Private sector organisation

## Funding Body Subtype

Other non-profit organizations

## Location

United Kingdom

**Funder Name**

Friends of Guy's Hospital (UK)

## 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 provided at time of registration

**Study outputs**

| Output type                     | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a> | results | 01/06/2014   |            | Yes            | No              |