## Main

*Note: This record shows only 22 elements of the WHO Trial Registration Data Set. To view changes that have been made to the source record, or for additional information about this trial, click on the URL below to go to the source record in the primary register.*

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| **Register:** | ISRCTN |
| **Last refreshed on:** | 31 October 2022 |
| **Main ID:** | ISRCTN74621291 |
| **Date of registration:** | 18/10/2017 |
| **Prospective Registration:** | Yes |
| **Primary sponsor:** | University of Leeds |
| **Public title:** | A study looking at the effects of blocking stress hormone activation on skin function and wound healing in patients with type 2 diabetes |
| **Scientific title:** | GC-SHealD (Glucocorticoids and Skin Healing in Diabetes) :A double-blind, randomized, placebo-controlled phase II pilot trial investigating efficacy, safety and feasibility of 11ß-hydroxysteroid dehydrogenase type 1 inhibition by AZD4017 to improve skin function and wound healing in patients with type 2 diabetes |
| **Date of first enrolment:** | 06/04/2018 |
| **Target sample size:** | 30 |
| **Recruitment status:** | Completed |
| **URL:** | https://www.isrctn.com/ISRCTN74621291 |
| **Study type:** | Interventional |
| **Study design:** | Randomised; Interventional; Design type: Treatment, Process of Care, Drug (Treatment) |
| **Phase:** | Phase II |

### Countries of recruitment

England United Kingdom

### Contacts

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| **Affiliation:** | | **Affiliation:** |

### Key inclusion & exclusion criteria

Inclusion criteria:
1. Able and willing to consent
2. T2DM with HbA1c =11% (=97 mmol/mol) at screening while taking standard therapy at a stable dose for =10 weeks
3. Aged 18 and older

Exclusion criteria:
1. Women of child-bearing potential
2. Active leg/foot ulceration
3. Clinically relevant acute ECG anomalies
4. Uncontrolled hypertension
5. Endocrine disorder (other than T2DM), including type 1 or secondary diabetes (except treated hypothyroidism)
6.Gilbert's disease
7. Alanine aminotransferase and/or aspartate aminotransferase and/or alkaline phosphatase >1.5x ULN
8. Bilirubin >1.5x ULN
9. eGFR <45 ml/min/m2
10. CK >2x ULN
11. Drug abuse within the last year
12. Any GC treatment within 3 months of screening
13. Anti-coagulant medication
14. Probenecid therapy
15. Medical/surgical procedure or trauma during IMP administration or one week after IMP cessation (excluding skin biopsies)
16. Involvement in trial planning and/or conduct
17. Participation in other clinical study within 1 month
18. Deemed inappropriate to participate by the trial team

Age minimum:
Age maximum:
Gender: Both

### Health Condition(s) or Problem(s) studied

Specialty: Diabetes, Primary sub-specialty: Type 2; UKCRC code/ Disease: Metabolic and Endocrine/ Diabetes mellitus, Skin/ Other disorders of the skin and subcutaneous tissue Nutritional, Metabolic, Endocrine
Diabetes mellitus

### Intervention(s)

This study aims to conduct a double-blind, randomised, parallel group, placebo-controlled phase II pilot trial of 35 days' duration with 400mg oral AZD4017 twice daily (n=15) or placebo (n=15) in patients with type 2 diabetes mellitus. Participants are followed up for 7 days after treatment cessation.

Taking part does affect routine diabetes treatment or access to care. The study involves 8 hospital visits. Patients receive either tablets containing the test drug or tablets which do not contain the test drug (dummy). These are given in a random way and neither patients nor the research team will know which tablets were provided until the end of the study. The tablets containing the drug AZD4017 blocks the enzyme to lower cortisol levels. AZD4017 has already been studied in human volunteers and is safe and well tolerated at the dose and duration in this study. Participants are asked to attend a short screening visit to check heart function, blood pressure and blood tests. Participants who pass screening will be enrolled into the trial.

They are asked to provide two 24 hour urine samples, four blood samples and five skin biopsies (two at one visit and three at another visit). Skin biopsies are taken from the arm after numbing the area with an injection. They are smaller than a ballpoint pen lid hole, do not require stitches and will not leave a noticeable scar. Participants are also measured for skin thickness, water loss, water content and nerve function using pain-free probes. Weight, height, blood pressure, waist and hip circumference are also recorded.

**Primary Outcome(s)**

11ß-HSD1 activity in skin measured by evaluating conversion of radiolabelled 11ß-HSD1 substrate (cortisone) to 11ß-HSD1 product (cortisol) at baseline and day 28.

**Secondary Outcome(s)**

1. Systemic 11ß-HSD1 activity is measured by evaluating tetrahydrocortisol to tetrahydrocortisone urinary metabolites ratios at baseline and day 35
2. AZD4017 in plasma and skin is measured by pharmacokinetic analysis at day 28
3. Adverse Event-related participant withdrawals (safety) will be measured by reviewing patient notes at day 42
4. Clinical evaluation of biopsy site (safety) will be measured by reviewing the patient notes at days 2, 7, 28, 30, 35 and 42
5. Body mass index (safety) will be measured as body weight (in kilograms to the nearest 100 grams) divided by the square of the body height (in metres to the nearest centimetre) at baseline and day 35
6. Waist-hip ratio (safety) will be measured as waist measurement (to the nearest cm) divided by hip measurement (to the nearest cm) at baseline and day 35
7. Blood pressure (safety) will be measured systolic (maximum) pressure over diastolic (minimum) pressure at baseline, day 35 and day 42
8. Blood tests (safety) will be conducted for HbA1c, lipids (total and high density lipoprotein cholesterol and triglycerides), full blood count, liver function (alanine and aspartate aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase, albumin and bilirubin), estimated glomerular filtration rate, kidney function (sodium, potassium, urea and creatinine), adrenal function (testosterone and dehydroepiandrosterone sulphate) and thyroid function (thyroid stimulating hormone and free thyroxine) at baseline and days, 7, 28, 35 and 42
9. Adverse event reporting (safety) will be measured by reviewing the patient notes at baseline and days 2, 7, 28, 30, 35 and 42
10. Sudomotor nerve function (skin function) will be conducted using a Sudoscan device at baseline and day 35
11. Skin hydration (skin function) will be measured using a Corneometer CM 825 device at baseline and day 35
12. Epidermal barrier function (skin function) will be measured by evaluating trans-epidermal water loss (TEWL) using a Tewameter TM 300 device at baseline and day 35
13. Epidermal barrier integrity (skin function) will be measured by evaluating the number of D-Squame tape strips required to induce barrier disruption (TEWL of 40-50 g/h/m2) at baseline and day 28
14. Epidermal barrier recovery (skin function) will be measured by evaluating TEWL after barrier disruption at baseline and days 2, 7, 28, 30 and 35
15. Skin thickness (skin function) will be measured by Optical Coherence Tomography imaging at baseline and day 35
16. Wound healing (skin function) will be measured by Optical Coherence Tomography imaging of biopsy wounds at days 2, 7, 30 and 35
17. Skin RNA-seq gene expression profiling (skin function) will be measured by RNA extraction and Next Generation Sequencing of mRNA at baseline and day 28
18. Feasibility will be measured by evaluating eligibility, recruitment, consent, randomization, adherence, retention and data completeness captured using Logs, Informed Consent Forms, Pharmacy Records and Diary Cards at the end of the study

**Secondary ID(s)**

NCT03313297

2017-001351-31

34599

**Source(s) of Monetary Support**

Medical Research Council

**Secondary Sponsor(s)**

**Ethics review**

Status:
Approval date:
Contact:
North West - Greater Manchester Central Research Ethics Committee, 10/08/2017, ref: 17/NW/0283

**Results**

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| **Results available:** | |
| **Date Posted:** | |
| **Date Completed:** | 21/05/2019 |
| **URL:** | |

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