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The ‘Can Do Ramadan’ Study

Submission date
22/08/2016

Recruitment status
No longer recruiting

Registration date
16/09/2016

Overall study status
Completed

Last Edited
23/06/2020

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
There are over one billion Muslims in the world with the majority participating in Ramadan which is an integral part of Islamic identity. Muslims observing Ramadan are required to fast from sunrise to sunset during this holy month. During the summer season Ramadan can take place with the longest hours of daylight which has a greater impact and risk for people with diabetes who fast during this period. Although the Quran exempts “sick” people from the duty of fasting many Muslims with diabetes do not consider themselves to be sick and are keen to fast. The person with diabetes may not discuss fasting with their health care provider (HCP) if they are given generic advice not to fast due to diabetes. There is a lack of evidence available to help guide the management of people with diabetes who wish to observe Ramadan. One of the aims of this study is to determine the potential effects of fasting in people with diabetes on well-being and the management of this condition. Some known side-effects of fasting during Ramadan include low blood sugars (hypoglycaemia), high blood sugars (hyperglycaemia) and dehydration which may lead to hospitalisation. There have been significant advances in glucose lowering therapies in type 2 diabetes mellitus (T2DM) and their availability, thus offering a greater choice of therapies to people with diabetes with the potential for supporting safer fasting. Such therapies include the sodium-dependent glucose co-transporter-2 (SGLT2) inhibitors which increase glucose loss through the urine, resulting in lower blood glucose levels, improved diabetes control, weight loss and no hypoglycaemia risk. The present study will determine if the SGLT2 inhibitor Canagliflozin is effective in weight maintenance and improved diabetes control with less hypoglycaemic events compared with an established therapy (sulphonylureas, repaglinide or pioglitazone).

Who can participate?
Aged at least 25 and diagnosed with type 2 diabetes. Participants are also either treated with metformin alone (cohort 1) or metformin plus repaglinide, or a sulphonylurea or pioglitazone (cohort 2).

What does the study involve?
Participants are randomly allocated to one of four possible groups. Those in cohort 1 are treated with either Canagliflozin (Invokana™) or a second-line therapy (usually only given when the treatment of choice does not work) (repaglinide, or a sulphonylurea or pioglitazone). Those in cohort 2 either continue on their current treatment or switch to metformin and Canagliflozin (Invokana™). All participants are asked to visit the study centre at the start of the study (to be

allocated to a group), 3-4 weeks post-Ramadan, 12 weeks post-Ramadan and, if they are enrolled >3months before Ramadan, participants also have an additional visit before Ramadan begins. All participants are assessed to see whether they have maintained a healthy weight and whether their diabetes is well controlled throughout the duration of the study.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
University Hospitals of Leicester NHS Trust and Queen Elizabeth Hospital Birmingham (UK)

When is the study starting and how long is it expected to run for?
August 2016 to September 2017

Who is funding the study?
Janssen Pharmaceuticals

Who is the main contact?
Ms Natasha Wileman

Contact information

Type(s)
Public

Contact name
Ms Natasha Wileman

Contact details
Trial Manager
Leicester Diabetes Centre – Origin
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02694263

Clinical Trials Information System (CTIS)
2015-002104-91

Protocol serial number
31453

Study information

Scientific Title

A Randomised Controlled Trial for People with Established Type 2 Diabetes during Ramadan: Canagliflozin (Invokana™) vs. standard dual therapy regimen: The 'Can Do Ramadan' Study

Study objectives
This study is comparing the SGLT2 inhibitor Canagliflozin (Invokana TM) to sulphonylurea-based regimen, when used as an add-on therapy to metformin, on those achieving the double composite endpoint of a reduction in HbA1c (≥ 0.3%) and weight loss (≥1kg) 3-4 weeks post-Ramadan.

The primary objective is to achieve the double composite endpoint of a reduction in HbA1c (≥ 0.3%) and weight loss (≥1kg) between baseline and 3-4 weeks post-Ramadan.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands - Edgbaston Research Ethics Committee, 09/03/2016, ref: 16/WM/0009

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Drug

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Diabetes, Primary sub-specialty: Type 2; UKCRC code/ Disease: Metabolic and Endocrine/ Diabetes mellitus

Interventions
This is an open label randomised controlled trial with two cohorts:
1. Cohort 1 - Individuals on metformin monotherapy will be randomised (1:1) to either the addition of Canagliflozin (Invokana™) or second-line therapy (repaglinide, or a sulphonylurea or pioglitazone)
2. Cohort 2 - Individuals on dual therapy (metformin plus repaglinide, or a sulphonylurea or pioglitazone) will be randomised (1:1) to either continuation of their current therapy or to switch to metformin and Canagliflozin (Invokana™)

Randomisation will be stratified by site and entry therapy (monotherapy OR dual therapy which includes metformin plus pioglitazone or a sulphonylurea or repaglinide) Randomisation will not be carried out until after the baseline data have been collected.
The intervention group in Cohort 1 will be those randomised to metformin + Canagliflozin (Invokana™). The control group in Cohort 1 will be those randomised to receive metformin plus repaglinide, or a sulphonylurea or pioglitazone in line with current NICE guidance as the preferred second-line therapy after metformin.

The intervention group in Cohort 2 will be those randomised to switch to metformin plus Canagliflozin (Invokana™). The control group in Cohort 2 will be those who continue with their current medication.

There will be a minimum of three and a maximum of four participant visits depending upon when a participant is enrolled into the study. Specifically, each participant will have:
1. A baseline visit (pre-randomisation)
2. 3-4 weeks post-Ramadan
3. 12 weeks post-Ramadan
and, if they are enrolled >3months before Ramadan, participants will also attend visit (1a) which is a pre-Ramadan visit.

Participants will receive the intervention throughout the duration of the study.

Intervention Type
Other

Phase
Phase IV

Primary outcome(s)
Double composite endpoint of a change in HbA1c (≥ 0.3%) and weight loss (≥1kg) between baseline and 3-4 weeks post-Ramadan; Timepoint(s): baseline and 3-4 weeks post Ramadan

Key secondary outcome(s)
1. Triple composite endpoint of a reduction or maintenance of HbA1c, reduction in weight (≥ 1kg) and no hypoglycaemic events between baseline and 3-4 weeks post-Ramadan
2. Mean change in HbA1c level
3. Mean change in fructosamine
4. Mean change in body weight
5. Mean change in systolic blood pressure
6. Mean change in diastolic blood pressure
7. Mean changes in total cholesterol
8. Mean changes in HDL cholesterol
9. Mean change LDL cholesterol
10. Mean change in triglycerides
11. Mean change in treatment satisfaction (DTSQ)
12. Mean change in IPAQ score (self-reported activity levels)
13. Mean change in light, moderate, and vigorous intensity physical activity as determined by GENEActiv
14. Mean change in total volume of movement as determined by GENEActiv
15. Mean change in frequency of self-measured hypoglycaemic events recorded in glucose diaries and severe hypoglycaemic events
16. Median (IQR) number of self-measured hypoglycaemic episodes per patient
17. Median (IQR) number of severe hypoglycaemic episodes per patient
18. Incidence rate of self-measured hypoglycaemia per person year (incidence rate ratio (IRR))
19. Incident rate of severe hypoglycaemia per person year (IRR)
20. Number of hospital admissions between baseline and 3-4 weeks post-Ramadan
21. Changes to the type of dosage of medication, as recorded by healthcare professionals.These data will be obtained from electronic/paper hospital records before each study time point and confirmed at each study visit by the healthcare professional in the case report form

The following double composite outcomes will also be measured:
1. Double composite endpoint of weight loss and no severe hypoglycaemic events
2. Double composite endpoint of no weight gain and a reduction in number of self-measured

hypoglycaemic events +/- symptoms
3. Double composite endpoint of improved HbA1c and no severe hypoglycaemic events
4. Double composite endpoint of improved HbA1c and reduction in number of self-measured hypoglycaemic events
5. Double composite endpoint of no weight gain and improved HbA1c
6. Double composite endpoint of no weight gain and no severe hypoglycaemic events
7. Double composite endpoint of no weight gain and no self-measured hypoglycaemic events

In addition, the difference between treatment groups for the data will be calculated
1. Change in proportion of time spent in each glycaemic range calculated between treatment groups,
2. Incidence of FGM3.1 and FGM2.2 events
3. Change in the frequency of FGM3.1 and FGM2.2 events, and
4. Change in Mean Average Glucose Excursion (MAGE)

Unless otherwise stated, all assessed at the following timepoints: Pre-Ramadan anytime between August 2016- May 2017, 3-4 weeks post Ramadan - July 2017 and then 12 Weeks post Ramadan - September 2017 (last patient last visit)

Completion date
30/09/2017

Eligibility

Key inclusion criteria
1. Able, in the opinion of the Investigator, and willing to give informed consent
2. Age ≥ 25 years old
3. Established T2DM (≥ 3 months) on stable dose monotherapy (metformin only for ≥ 8 weeks prior to enrolment) OR stable dose dual therapy (metformin plus either repaglinide, a sulphonylurea or pioglitazone for ≥ 8 weeks prior to enrolment)
4. HbA1c between 7 – 10.5% (53 - 91mmol/mol) if on monotherapy OR between 6.5 - 9.5% (48 – 80mmol/mol) if on dual therapy at the screening visit
5. Individuals intending to fast for a minimum of 10 consecutive days during the holy month of Ramadan

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
25

Key exclusion criteria

1. Unable, in the opinion of the Investigator, and unable to provide informed consent
2. Aged ≤ 25 years old
3. Established T2DM (≤ 3 months) on medication for fewer than 8 weeks prior to enrolment
4. HbA1c ≤7 and ≥10.5% (if on monotherapy) and ≤6.5 and ≥9.5% (if on dual therapy)
5. Individuals not intending to fast for a minimum of 10 consecutive days during the holy month of Ramadan
6. Females of childbearing potential who are pregnant, breast-feeding or intend to become pregnant or are not using adequate contraceptive methods. The latter includes avoiding sex, hormonal prescription oral contraceptives, contraceptive injections, contraceptive patch, intrauterine device, double-barrier method (e.g., condoms, diaphragm, or cervical cap with spermicidal foam, cream, or gel), or male partner sterilization, consistent with local regulations regarding use of birth control methods for subjects participating in clinical trials, for the duration of their participation in the study, or not heterosexually active. Furthermore, subjects who are not heterosexually active at screening must agree to utilize a highly effective method of birth control if they become heterosexually active during their participation in the study. Women of childbearing potential must have a negative urine pregnancy test at baseline.
7. Suffer from terminal illness
8. Have renal disease that requires immunosuppressive therapy, dialysis or transplant
9. Have nephrotic syndrome or inflammatory renal disease
10. Have an estimated glomerular filtration rate (eGFR) <60ml/min/1.73m2 at screening
11. Have serum creatinine levels >132.6µmol/L for men or >123.8µmol/L for women
12. Impaired liver function (ALAT ≥ 2.5 times upper limit of normal)
13. Known Hepatitis B antigen or Hepatitis C antibody positive
14. Clinically significant active cardiovascular disease (including history of myocardial infarction, unstable angina,
previous revascularization procedure or cerebrovascular accident) within the past 6 months before screening
15. Have uncontrolled hypertension (defined as systolic blood pressure ≥180mm/Hg and diastolic ≥100mm/Hg in the supine position after >5minutes rest with confirmed compliance to antihypertensive medication)
16. Heart failure (NYHA class III and IV) at the discretion of the investigator
17. Previous history of recurrent major hypoglycaemia as judged by the study clinician
18. Known or suspected allergy to the study product
19. Receipt of any investigational drug within four weeks prior to this study
20. Has had previous treatment with a GLP-1 receptor agonist, DPP-IV inhibitor, insulin, or another SGLT2 inhibitor within 12 weeks of screening
21. Have severe and enduring mental health problems
22. Are not primarily responsible for their own care
23. Are receiving insulin therapy
24. Type 1 diabetes
25. Any contraindication to sulphonylureas, repaglinide and/or pioglitazone
26. Have severe irritable bowel disorder
27. Have hereditary glucose-galactose malabsorption
28. Have primary renal glycosuria
29. Patients who have participated in another study of an investigational medicinal product in the last 3 months

Date of first enrolment
15/08/2016

Date of final enrolment

30/09/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
Janssen Pharmaceuticals

Alternative Name(s)

Janssen Pharmaceutica NV, JANSSEN-CILAG NV, Janssen Belgium, Janssen, Janssen Pharmaceuticals

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Belgium

Results and Publications

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?
Basic results			23/06/2020	No	No
HRA research summary			28/06/2023	No	No