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Mechanisms of action of hypoglycemic drugs in nonalcoholic fatty liver disease (NAFLD)

Submission date
30/11/2013

Recruitment status
No longer recruiting

Registration date
16/12/2013

Overall study status
Completed

Last Edited
13/02/2017

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
Nonalcoholic fatty liver disease (NAFLD) has attracted considerable attention as a cause of type 2 diabetes. Although no full-scale survey has been conducted in Japan, it is highly expected that the number of patients with NAFLD will increase rapidly with the advancing westernization of eating habits.

Who can participate?
Participants are diabetic males, aged 40-70 years, who are previously untreated for type 2 diabetes (T2DM).

What does the study involve?
Participants will be classified into two groups based on the presence or absence of NAFLD. The participants with NAFLD will be randomly allocated to one of four groups and treated with pioglitazone, metformin or sitagliptin, or a non-antidiabetic drug (non-OAD), for 6 months. In the non-OAD group, participants are provided with dietary and exercise guidance. The participants in the non-NAFLD group will be referred to their respective attending physicians as outpatients for the treatment of diabetes.

What are the possible benefits and risks of participating?
Participants will receive information on their body composition and blood pressure. Possible risks would be adverse effects from antidiabetic drugs. Although computed tomography (CT) poses no significant risk associated with the use of contrast medium, patients may be exposed to some (permissible) dose of radiation.

Where is the study run from?
Second Department of Internal Medicine, Ryukyus University Hospital (Japan)

When is the study starting and how long is it expected to run for?
August 2010 to December 2012

Who is funding the study?
University of the Ryukyus (Japan)

Who is the main contact?
Dr Kouichi Yabiku

Contact information

Type(s)
Scientific

Contact name
Dr Kouichi Yabiku

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Mechanisms of action of hypoglycemic drugs in nonalcoholic fatty liver disease (NAFLD): elucidation of its association with 'inflammation'

Study objectives
Several oral antidiabetic drugs (OADs) will be effective treatments for NAFLD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Faculty of Medicine at the University of the Ryukyus, 09/03/2010, No. 122

Study design
Randomized parallel group 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 to request a patient information sheet

Health condition(s) or problem(s) studied
Nonalcoholic fatty liver disease, type 2 diabetes

Interventions
Patients are divided into NAFLD and non-NAFLD groups by abdominal ultrasound.

The patients with NAFLD will be then randomly allocated to receive either pioglitazone (30 mg /day), metformin (1 g/day), sitagliptin (50 mg/day) or a non-antidiabetic drug (non-OAD). In the non-OAD group, all subjects are provided with dietary and exercise guidance. Abdominal CT is performed before and after the trial, and changes in NAFLD activity are evaluated.

The patients in the non-NAFLD group are referred to their respective attending physicians as outpatients for the treatment of diabetes, and those in the above monotherapy groups or non-antidiabetic drug group similarly undergo abdominal CT and blood tests before and after the trial.

All subjects are provided with dietary and exercise guidance once a month during the study (6 months).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Pioglitazone, metformin, sitagliptin

Primary outcome measure
Differences between baseline and end-of-treatment liver to spleen (L/S) ratios determined by CT and physical findings (blood pressure, body mass index and waist circumference) will be measured in each group.
Blood samples will be obtained to measure concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT), cholinesterase, fasting plasma glucose, fasting insulin, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, non-esterified fatty acids (NEFA), high-sensitivity C-reactive protein (hsCRP), soluble tumor necrosis factor receptors 1 (sTNFR-1), and 2 (sTNFR-2), high-molecular-weight (HMW) adiponectin, and ferritin.

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/08/2010

Completion date
27/12/2012

Eligibility

Key inclusion criteria
1. Diabetic males aged 40-70 years
2. Previously untreated for type 2 diabetes (T2DM)
3. Body mass index (BMI) >25 kg/m2
4. Glycated hemoglobin (HbA1c) of 6.4-7.9% (National Glycohemoglobin Standardization Program units)
5. Fasting plasma glucose of 126-261 mg/dl

Participant type(s)
Patient

Age group
Adult

Sex
Male

Target number of participants
800

Key exclusion criteria
1. Patients with mental disorders, including alcohol dependence, or with such a history
2. Patients with pancreatitis
3. Patients with malignant diseases
4. Patients with viral hepatitis
5. Patients who have participated in any clinical study or trial within 6 months
6. Patients experiencing a weight gain or loss of 1 kg or more within 3 months before the start of the trial
7. Patients deemed ineligible for the trial

Date of first enrolment
01/08/2010

Date of final enrolment
27/12/2012

Locations

Countries of recruitment
Japan

Study participating centre
207 Uehara Nishihara-cho
Nakagami-gun
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903-0215

Sponsor information

Organisation
University of Ryukyus (Japan)

Sponsor details
207 Uehara Nishihara-cho
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Sponsor type
University/education

ROR
https://ror.org/02z1n9q24

Funder(s)

Funder type
University/education

Funder Name
University of Ryukyus (Japan)

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?
Results article	results	01/03/2017		Yes	No