

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

<b>Submission date</b> 30/11/2013	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/12/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 13/02/2017	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> 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

**Contact details**  
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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/m<sup>2</sup>
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

Japan

903-0215

## **Sponsor information**

**Organisation**

University of Ryukyus (Japan)

**Sponsor details**

207 Uehara Nishihara-cho

Nakagami-gun

Japan

903-0215

**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?
<a href="#">Results article</a>	results	01/03/2017		Yes	No