

Using two drugs in combination at the start of drug treatment for type 2 diabetes vs using a single drug

Submission date 10/05/2017	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 11/05/2017	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 11/05/2017	Condition category Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Type 2 diabetes mellitus (T2DM) is a long term condition where a person is unable to control their blood sugar (glucose) levels as they do not produce enough insulin to function properly (insulin deficiency), or that the body's cells don't react to insulin as they should do (insulin resistance). According to the 2015 International Diabetes Federation estimates, there are 35.4 Million people with type 2 diabetes mellitus in the MENA (Middle East and North Africa) region with an estimated rise to up to 72.1 million by 2040. Diabetes-related deaths stand at a staggering 342,000 during 2015, with over half of all deaths from diabetes in the region occurring in people under 60. A major issue that is dealt with by diabetologists, especially with patients with a rural background, is poor compliance with medication and dietary advice. Furthermore, the characteristics of the diabetic Asian population are unique, in the sense that as compared to western counterparts, Asians tend to have lower BMIs, a younger onset of type 2 diabetes, a high carbohydrate diet, high blood sugar levels after meals, and a more marked problem with insulin production. Standard treatment for T2DM involves treatment with a drug called metformin. DPP4 inhibitor is another drug which helps the body to produce more insulin. The aim of this study is to assess blood sugar control in newly diabetic patients treated with DPP4 inhibitor and metformin to treatment with metformin alone.

Who can participate?

Adults who have been newly diagnosed with T2DM.

What does the study involve?

Participants are randomly allocated to receive either a single initial drug (as current guidelines recommend), or a combination of two drugs (in a single pill). They are then monitored at intervals of three months, as is the standard procedure for people with type 2 diabetes, and blood tests are performed at the regular intervals to assess their blood sugar control. If, at any of their scheduled visits, it was found that their diabetes control was not up to standard, an additional drug is added after thorough patient education. Visits thereafter are at the scheduled

three month intervals, or earlier if the patient desires. A line of communication always remains open, allowing the patients direct access to their doctors. Participants attend regular clinic appointments over a period of five years to assess how well they are managing their diabetes.

What are the possible benefits and risks of participating?

The direct benefits were availability of the drugs with no cost to the patient, scheduled visits with consultants, and direct access to a doctor if and when desired by the patient. Since no new drugs are being tested, and the treatment being used is well established, there were no unforeseen risks to the participants other than those normally encountered by diabetics taking regular medication.

Where is the study run from?

Pakistan Institute of Medical Sciences (Pakistan)

When is the study starting and how long is it expected to run for?

June 2009 to July 2016

Who is funding the study?

Investigator initiated and funded (Pakistan)

Who is the main contact?

1. Dr Mohammad Ali Arif (public)
2. Professor Rauf Niazi (scientific)

Contact information

Type(s)

Public

Contact name

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Additional identifiers

Protocol serial number

U1111-1196-4371

Study information

Scientific Title

Intensified treatment at the onset of diagnosis of type 2 diabetes mellitus in drug naive patients in the asian population

Acronym

INTRON

Study objectives

The use of initial combination therapy with a DPP4 inhibitor plus metformin is superior to metformin monotherapy with sequential add on treatment in achieving and maintaining an HbA1c of <7%.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics Committee of the Pakistan Institute of Medical Sciences, 19/01/2010, ref: EC/PIMS-2010/0119-03-Intron

Study design

Open labelled prospective randomised clinical trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Type 2 diabetes mellitus

Interventions

Participants are randomised to one of six groups using covariate adaptive randomization.

1. MHD2 Group: Metformin 1000mg twice daily
2. MHD255 Group: Metformin 850mg thrice daily
3. SMHD Group: (Sitagliptin 50mg plus metformin 1000mg) twice daily
4. SMLD Group: (Sitagliptin 50mg plus Metformin 500mg) twice daily

5. VMHD Group: (Vildagliptin 50mg plus Metformin 1000mg) twice daily
6. VMLD Group: (Vildagliptin 50mg plus Metformin 500mg) twice daily

After the first visit, patients are evaluated at week two followed by an interval thereafter of 12 weeks up to 5 years. A complete physical examination was conducted at baseline, along with anthropometric measurements (weight and height) and baseline laboratory parameters (serum creatinine, ALT and fasting lipid profile). Vital signs, fasting and random blood glucose and lab investigations are repeated at each visit along with documentation of any adverse effects (AE).

Patients are instructed regarding the use of home blood glucose monitoring along with once weekly documentation of fasting plasma glucose (after a 12 hour fast) and random plasma glucose prior to the evening meal. SMBG (self-monitoring of blood glucose) could be performed at any point in time if the patient experiences symptoms of hypoglycaemia.

Intervention Type

Drug

Phase

Not Applicable

Primary outcome(s)

Glycated Haemoglobin is measured at baseline, 3, 6, 9, and 18 months, 2, 3, and 5 years using a standardized laboratory assay for HbA1c. The reduction in HbA1c is calculated by subtracting the former measurements from the latter.

Key secondary outcome(s)

1. Percentage of patients achieving and maintaining the target HbA1c of <7% is assessed from the documented HbA1c measured at baseline, 3, 6, 9, and 18 months, 2, 3, and 5 years
2. Need for additional therapy is assessed by the treating physician based on the laboratory parameters highlighted above and was documented on the patients file along with the choice of the add on agent at any point within the study period
3. Hypoglycaemia, if suspected, is checked by the patient using a glucometer and the recording reading was documented in mg/dL at any point within the study period
4. Weight is measured using a digital weighing scale at the clinic at baseline, 3, 6, 9, and 18 months, 2, 3, and 5 years

Completion date

06/07/2016

Eligibility

Key inclusion criteria

1. Newly diagnosed patients with type 2 diabetes
2. Had not received any prior medication for diabetes
3. Aged 18 – 80 years
4. Asian ethnicity (Pakistani population)

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria

1. Previous history of ischaemic heart disease
2. Previous history of stroke or other cerebrovascular disease
3. Previous history of chronic kidney disease

Date of first enrolment

19/01/2010

Date of final enrolment

19/01/2011

Locations

Countries of recruitment

Pakistan

Study participating centre

Pakistan Institute of Medical Sciences

Ibn-e-Sina Rd

Islamabad

Pakistan

44000

Sponsor information

Organisation

Pakistan Institute of Medical Sciences

ROR

<https://ror.org/0358b9334>

Funder(s)

Funder type

Other

Funder Name

Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from mohammad_ali_arif@hotmail.com or ali.arif@shifa.com.pk

IPD sharing plan summary

Available on request