A phase III randomised, double-blind, active-controlled parallel group efficacy and safety study of BI 10773 compared to glimepiride administered orally during 104 weeks with a 104-week extension period in patients with type 2 diabetes mellitus and insufficient glycaemic control despite metformin treatment

Published: 03-06-2010
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The objective of the current study is to investigate the efficacy, safety and tolerability of BI10773 (25mg once daily) compared to glimepriride (1-4mg daily) given for 104 weeks with a 104-week extention period in patients with type 2 diabetes...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON38357

Source
ToetsingOnline

Brief title
C-SCADE-7

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, Diabetes mellitus type 2

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim BV

Intervention

Keyword: BI 10773, Diabetes mellitus type 2, Glimepiride, SGLT-2 inhibitor

Outcome measures

Primary outcome

- Change from baseline in HbA1c after 52 weeks and 104 weeks of treatment.

Secondary outcome

- Change in body weight from baseline after 52 weeks and 104 weeks of treatment.

- Occurrence of confirmed syptomatic hypoglycaemic events during 52 weeks and

104 weeks of treatment.

- Changes in blood pressure (SBP and DBP) from baseline, after 52 weeks and 104

weeks of treatment.

Study description

Background summary

Diabetes Mellitus type 2 is a disease which is characterized by increased blood glucose levels. It is a condition that eventually causes damage in many organs and tissues, resulting in a marked decrease of life expectancy and quality of life. Therefore, treatment to maintain the blood glucose levels within normal ranges remains important.

There is no cure for Diabetes Mellitus type 2, but it can be treated by a diet,

excercise, several oral medications and insulin. Not all
medications are well tolerated and many compounds cause side-effects. BI 10773 is a SGLT-2 inhibitor that decreases reabsorption of glucose by the kidneys, resulting in excretion of this glucose by the urine. Previous studies have shown that this results in decreased plasmaglucose and HbA1c levels.

Study objective

The objective of the current study is to investigate the efficacy, safety and tolerability of BI10773 (25mg once daily) compared to glimepriride (1-4mg daily) given for 104 weeks with a 104-week extention period in patients with type 2 diabetes mellitus and insufficient glycaemic control despite metformin. The study is designed to show non-inferiority of BI 10773 to glimepiride.

Study design

About 1400 patients with Diabetes Mellitus type 2 will participate in this study worldwide . Half of them will receive treatment with
25 mg BI 10773 daily, the other half will receive treatment with glimepiride (1-4 mg daily).
The treatment will be add-on to the stable background treatment of metformin. The treatment period is preceded by a 2-week placebo run-in period, and concluded with a follow-up visit 4 weeks after study medication termination.

This is a randomized, double blind, double dummy, active controlled, parallel group, noninferiority study.

Intervention

At visit 2, the 2-week once-daily placebo run-in period starts.
At visit 3, patients are randomized to either once daily BI 10773 25 mg, or once daily glimepiride (uptitrated to a maximum of 4 mg daily).
Ratio BI 10773 : glimepiride = 1:1.

Study burden and risks

Assuming a treatment period of 104 weeks, this would at most be the following :
- Physical examination: visits 2, 10, 14, 18 and 22
- Urine sample: visits 1, 2, 3, 6, 8, 10, 12, 14, 16, 18, 20, 22 and 23
- Blood sample: all visits (PK sampling at visits 6 and 8)
- Vital signs: all visits
- Height (visit 1), weight and waist: visits 1, 3, 6, 8, 10, 12, 14, 16, 18, 20, 22 and 23
- Diet and excercise counselling: visits 2-21
- Diet dairy: 3 days prior to visits 2, 3, 6, 8, 10,12, 14, 16, 18, 20 and 22
- ECG: visits 3, 10, 14, 18 and 22

- Questionnaires EQ-5D and DTSQ: visits 3, 5, 8, 10, 12, 16, 18 and 22
- HBGM test: starting from visit 2 until the end of the study (during run-in and follow up at least once daily, otherwise at least once per week but preferably on a daily basis)

In addition, for patients who participate in the MTT substudy:
- MTT: visits 3, 8, 10, 14, 18, 22 and 23
- 8-point glusose test: prior to visits 3, 8, 10, 14, 18 and 22

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

(see paragraph 3.3.2 of the protocol for the complete list)
1. Diagnosis of type 2 diabetes mellitus prior to informed consent

2. Male and female patients on diet and exercise regimen who are pre-treated with immediate release metformin unchanged for 12 weeks prior to randomisation. Minimum dose for metformin: > <= 1500 mg/day or maximum tolerated dose (the investigator must have documented the reason why up-titration to ><= 1500 mg/day was not possible) or maximum dose according to local label.
3. HbA1c of *7.0% and * 10% at Visit 1
4. Age * 18yrs
5. BMI * 45 kg/m2 (Body Mass Index) at Visit 1
6. Signed and dated written informed consent by date of Visit 1 in accordance with GCP and local legislation

Exclusion criteria

(see paragraph 3.3.3 of the protocol for the complete list)
1. Uncontrolled hyperglycaemia with a glucose level >240 mg/dL (>13.3 mmol/L) after an overnight fast during placebo run-in and confirmed by a second measurement after an overnight fast using another device (not on the same day).
2. Any other antidiabetic drug within 12 weeks prior to randomisation except immediate release metformin
3. Acute coronary syndrome (non-STEMI, STEMI, unstable AP) Stroke or TIA within 3 months prior to informed consent.
4. Indication of liver disease, defined by serum levels of either ALT (SGPT), AST (SGOT), or alkaline phosphatase above 3 x upper limit of normal (ULN) as determined at Visit 1
5. Impaired renal function, defined as eGFR<60 ml/min (moderate to severe renal impairment using MDRD formula)
6. Bariatric surgery within the past two years and other gastrointestinal surgeries that induce chronic malabsorption
7. Medical history of cancer (except for basal cell carcinoma) and/or treatment for cancer within the last 5 years
8. Blood dyscrasias or any disorders causing haemolysis or unstable Red Blood Cell (e.g. malaria, babesiosis, haemolytic anaemia)
9. Contraindications including hypersensitivity known to metformin or sulfonylureas according to the local label
10. Treatment with anti-obesity drugs 3 months prior to informed consent or any other treatment at the time of screening (i.e. surgery, aggressive diet regimen, etc.) leading to unstable body weight
11. Current treatment with systemic steroids at time of informed consent or change in dosage of thyroid hormones within 6 weeks prior to informed consent or any other uncontrolled endocrine disorder except T2DM. (Treatment with local and inhaled steroids is allowed)
12. Pre-menopausal women (last menstruation * 1 year prior to informed consent) who:
- are nursing or pregnant or
- are of child-bearing potential and are not practising an acceptable method of birth control, or do not plan to continue using this method throughout the study and do not agree to

submit to periodic pregnancy testing during participation in the trial.
Acceptable methods of birth control include tubal ligation, transdermal patch, intra uterine devices/systems (IUDs/IUSs), oral, implantable or injectable contraceptives, sexual abstinence, (if acceptable by local authorities) double barrier method and vasectomised partner
13. Alcohol or drug abuse within the 3 months prior to informed consent that would interfere with trial participation or any ongoing condition leading to a decreased compliance to study procedures or study drug intake
14. Intake of an investigational drug in another trial within 30 days prior to intake of study medication in this trial.
15. Any other clinical condition that would jeopardize patients safety while participating in this clinical trial

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-12-2010
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amaryl
Generic name:	Glimepiride
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Nog niet bekend
Generic name:	Empagliflozin

Ethics review

Approved WMO Date:	03-06-2010
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	18-10-2010
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	10-11-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	01-12-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	21-12-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	30-12-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO	

Date:	20-01-2011
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	26-01-2011
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	02-03-2011
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	14-03-2011
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	19-05-2011
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	11-08-2011
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	22-05-2012
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen

	(Wijchen)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	18-10-2012
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	05-07-2013
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	23-01-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	19-06-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	03-07-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	06-11-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	18-08-2015

Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-016244-39-NL
ClinicalTrials.gov	NCT01167881
CCMO	NL32259.072.10

Study results

Date completed:	28-08-2015
Actual enrolment:	18

Summary results
Trial is onging in other countries