A Multicenter, Phase III, Randomized, Placebo-Controlled Trial to Assess the Safety and Efficacy of MK-3102 Monotherapy in Subjects with Type 2 Diabetes Mellitus and Inadequate Glycemic Control

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The purpose of this study is: * To test the safety of the research study drug MK-3102.* To assess how well the research study drug MK-3102 lowers blood sugar levels (fasting plasma glucose [FPG], post meal glucose [PMG], and glycosylated hemoglobin...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON40348

Source
ToetsingOnline

Brief title
OMNEON-011

Condition

- Diabetic complications

Synonym
non-insulin-dependent diabetes, type 2 diabetes mellitus

Research involving

Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Merck

Intervention

Keyword: monotherapy, phase 3, type 2 diabetes mellitus

Outcome measures

Primary outcome

1) Objective: After 24 weeks, to assess the effect of treatment with MK-3102

compared with placebo on A1C.

2) To assess the safety and tolerability of MK-3102

Secondary outcome

1) Objective: After 24 weeks, to assess the effect of treatment with MK-3102

compared with placebo on 2-hour Post-Meal Glucose (PMG).

2) Objective: After 24 weeks, to assess the effect of treatment with MK-3102

compared with placebo on FPG.

3) Objective: After 54 weeks, to assess the effect of treatment with MK-3102 on

A1C, 2-hour PMG, and FPG.

4) Objective: After 24 weeks, and after 54 weeks, to assess the effect of

treatment with MK-3102 on proportion of subjects achieving an A1C goal (<6.5%,

<7.0%).

Study description

Background summary

MK-3102 is a novel dipeptidyl peptidase-IV (DPP-4) inhibitor that is in Phase III clinical development for the treatment of patients with T2DM. Unlike the presently marketed DPP-4 inhibitors, which are administered once- or twice-daily, MK-3102 has a half-life
that supports once-weekly dosing.

This is a research study to test a drug (MK-3102) that has not yet been approved for sale. MK 3102 is being developed as a once-weekly treatment for type 2 diabetes mellitus (T2DM), a condition wherein the patient*s blood sugar levels are abnormally high and the body cannot produce enough insulin.

This study will test MK-3102 in subjects with T2DM with poor blood sugar control on diet and exercise.
During this study, MK-3102 will be compared with placebo (look alike with no active ingredients, sometimes called a sugar pill). You may also receive other anti-diabetic drugs: metformin or glimepiride.

Study objective

The purpose of this study is:
* To test the safety of the research study drug MK-3102.
* To assess how well the research study drug MK-3102 lowers blood sugar levels (fasting plasma glucose [FPG], post meal glucose [PMG], and glycosylated hemoglobin A1C - a long term measure of blood sugar) as compared to placebo in subjects on diet and exercise who have poorly controlled blood sugar levels.

Study design

TRIAL DESIGN
This is a multicenter, double-blind, randomized, parallel-group trial (double-blind in Phase A and Phase B). The duration of the trial will be up to 65 weeks (with 12 visits) for each subject. This will include a 1-week screening period [Visits 1 to 2]; an 8-week diet/exercise and oral antihyperglycemic agent (AHA) *wash-off* (for subjects on oral AHAs) period [Visit 2 to Visit 3/Week -2]; a 2-week single-blind placebo run-in period [Visits 3 to 4]); a 24-week placebo-controlled, double-blind treatment period (Phase A); and 30-week active-controlled, double-blind treatment period (Phase B). Subjects with T2DM who are not on AHA medication (off for *12 weeks) at

Visit 1 and who meet all other enrollment criteria will directly enter into the 2-week single-blind placebo run-in period at a combined Visit 2/3 (since these subjects will go from Visit 1 to Visit 3/Week -2, the Visit 3/Week -2 visit will be referred to as a "combined" Visit 2/3/Week -2). For details on the run-in duration and visit schedule, see Section 2.4.3.
At Visit 4/Day 1, subjects who meet the trial enrollment criteria will enter Phase A of the double-blind treatment period, with randomization into 1 of 2 treatment groups (in a 1:1 ratio): MK-3102 25 mg q.w. or placebo.
After Visit 4/Day 1 and during Phase A, subjects not meeting progressively stricter protocol-specified glycemic thresholds will have glycemic rescue therapy initiated with open-label metformin.
At Visit 8/Week 24, subjects will complete Phase A and will enter Phase B of the double-blind treatment period. Subjects in the placebo treatment group who were not rescued with open-label metformin will be switched to blinded metformin (starting at 500 mg once daily with up-titration to 1000 mg b.i.d) in a blinded manner. Subjects in the MK-3102 treatment group who did not initiate rescue therapy in Phase A will continue to take the same dose of trial medication as provided in Phase A and initiate metformin placebo. Subjects who were previously rescued with open-label metformin in Phase A will continue in the trial on open-label metformin; blinded metformin will not be dispensed to these subjects. Subjects will complete Phase B at Visit 12/Week 54.
In Phase B, subjects meeting progressively stricter protocol-specified glycemic thresholds will have glycemic rescue therapy initiated with open-label glimepiride.
A telephone contact will be performed 21 days after the last dose of trial medication (either at trial completion or premature discontinuation from the trial medication) to assess for any serious adverse experiences (SAEs).
Subjects who are discontinued from trial medication for any reason other than withdrawal of consent will be followed for the duration of the trial by telephone contact and with clinic visit at key time points, as outlined in Section 2.4.3.12.

Intervention

MK-3102 or placebo 25 mg once weekly or metformine or glimepiride

Study burden and risks

MK-3102 is a structurally distinct and potent DPP-4 inhibitor, which is being developed for the treatment of T2DM. Unlike the presently marketed DPP-4 inhibitors, which are administered once- or twice-daily, MK-3102 has a t1/2 that supports once-weekly dosing.
Weekly dosing of an efficacious, well-tolerated, safe, oral agent that reduces pill burden has the potential to increase adherence to AHA therapy, which in turn may improve long-term outcomes. Such an agent would represent a welcome addition to the existing armamentarium

of oral agents for the treatment of T2DM and may help shape future treatment paradigms.

Monitoring of AE's ECG's, vital signs and lab safety tests will be performed to support patient safety and evaluation of the safety profile.

The risks and burden to the patient are thought to be in perspective to the treatment of the patient and the need to study new compounds with added benefits.

Contacts

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subject has T2DM and must be *18 years of age (for India: *18 and *65 years of age) on

the day of signing the informed consent form.;2. Subject meets one of the following criteria:;a. Subject is currently not on an AHA (off AHA therapies for *12 weeks) and has a Visit 1/Screening Visit A1C *7.0 (53 mmol/mol) and *10.0%.% (86 mmol/mol).;b. Subject is currently on a stable dose for > 12 weeks of a single AHA or low-dose dual oral AHA combination therapy (i.e., *50% maximum labeled dose of each agent [except thiazolidinediones (TZDs)]) and has a Visit 1/ Screening Visit A1C *6.5 (48 mmol/mol) and *9.0% (75 mmol/mol) AND based upon review of the subject's current diet, medical regimen, and Visit 1 A1C, subject is considered by the investigator to be likely to meet Visit 3/Week -2 inclusion criterion of A1C *7.0 (53 mmol/mol) and *10.0% (86 mmol/mol) AFTER the 8-week wash-off period prior to Visit 3/Week-2 (Visit 2/Week -10 to Visit 3/ Week -2).;3. Subject meets one of the following criteria:;a. Subject is a male;b. Subject is a female not of reproductive potential defined as one who has either ;* reached natural menopause (defined as *12 months of spontaneous amenorrhea in women >45 years of age, or *6 months of spontaneous amenorrhea with serum follicular stimulating hormone [FSH] levels in the postmenopausal range as determined by the laboratory), or ;* had a hysterectomy and/or bilateral oophorectomy, or had bilateral tubal ligation or occlusion at least 6 weeks prior to screening;c. Subject is a female of reproductive potential and agrees to:;* remain abstinent from heterosexual activity (if this form of birth control is accepted by local ;regulatory agencies and ethics review committees as the sole method of birth control), or;* agrees to use (or have their partner use) acceptable contraception to prevent pregnancy within the projected duration of the trial and for 21 days after the last dose of blinded study medication. Two methods of contraception will be used to avoid pregnancy. Acceptable combinations of methods include:;- use of one of the following double-barrier methods: diaphragm with spermicide and a condom, cervical cap and a condom, contraceptive sponge and a condom;- Use of hormonal contraception (any registered and marketed contraceptive agent that contains an estrogen and/or a progestational agent [including oral, subcutaneous, intrauterine and intramuscular agents, and cutaneous patch]) with one of the following: diaphragm with spermicide; cervical cap; contraceptive sponge; condom; vasectomy; or intrauterine device (IUD).;- Use of an IUD with one of the following: condom; diaphragm with spermicide; contraceptive sponge; vasectomy; or hormonal contraception (see above). ;- Vasectomy with one of the following: diaphragm with spermicide; cervical cap; contraceptive sponge; condom; IUD; or hormonal contraception (see above).;4. Subject understands the trial procedures, alternative treatments available, and risks involved with the trial, and voluntarily agrees to participate by giving written informed consent. The subject may also provide consent for Future Biomedical Research. However, the subject may participate in the main trial without participating in Future Biomedical Research.;5. Subject has an A1C of *7.0% (53 mmol/mol) and *10.0% (86 mmol/mol) within 2 weeks of Visit 3/Week -2.;6. Subject has 100% compliance with MK-3102 placebo treatment during the single-blind run-in period (as determined by site-performed capsule count).

Exclusion criteria

1.Subject has a history of type 1 diabetes mellitus or a history of ketoacidosis or is assessed by the investigator as possibly having type 1 diabetes confirmed with a C-peptide <0.7 ng/mL (0.23 nmol/L);2.has been treated with:;a.thiazolidinedione (TZD) within 4 months of

signing informed consent, or;b.GLP-1 receptor mimetic or agonist or DPP-4 inhibitors within 6 months of signing informed consent, or;c.insulin or sodium-glucose cotransporter (SGLT2) inhibitor within 12 weeks prior to signing informed consent;d.MK-3102 at any time prior to signing informed consent;3.has a history of hypersensitivity to a DPP-4 inhibitor;4.is currently participating in/has participated in another trial with an investigational compound or device within the prior 12 weeks of signing the informed consent and does not agree to refrain from participating in any other trial;5.has a history of intolerance,hypersensitivity or any contraindication to metformin (in Phase A),glimepiride or other sulfonyurea (in Phase B) based upon the label in the country of the investigational site;6.is on a weight loss program and is not in the maintenance phase;has been on a weight loss medication in the past 6 months;or has undergone bariatric surgery within 12 months prior to signing the informed consent.;7.has undergone a surgical procedure within 4 weeks prior to signing informed consent or has planned major surgery during the trial;8.Subject is on or likely to require treatment for *14 consecutive days or repeated courses of pharmacologic doses of corticosteroids;9.is currently being treated for hyperthyroidism or subject is on thyroid hormone therapy and has not been on a stable dose for at least 6 weeks;10.is currently on or likely to require treatment with a prohibited medication;11.is expecting to undergo hormonal therapy in preparation to donate eggs during the period of the trial,including 21 days following the last dose of blinded study medication;12.has a medical history of active liver disease,including chronic active hepatitis B or C,primary biliary cirrhosis, or symptomatic gallbladder disease;13.has HIV as assessed by medical history;14.has had new or worsening signs or symptoms of coronary heart disease or congestive heart failure within the past 3 months,or has any of the following disorders within the past 3 months:;a.Acute coronary syndrome ;b.Coronary artery intervention ;c.Stroke or transient ischemic neurological disorder;15.has poorly controlled hypertension defined as systolic blood pressure of *160 mm Hg or diastolic blood pressure of *90 mm Hg ;16.has a history of malignancy *5 years prior to signing informed consent except for adequately treated basal cell or squamous cell skin cancer,or in situ cervical cancer;17.has a clinically important hematological disorder;18.has exclusionary laboratory values (as per protocol);19.has a positive urine pregnancy test;20.is pregnant or breast-feeding,or is expecting to conceive during the trial,including 21 days following the last dose of blinded study medication;21.is a user of recreational or illicit drugs or has had a recent history of drug abuse;22.routinely consumes >2 alcoholic drinks per day or >14 alcoholic drinks per week,or engages in binge drinking;23.has a history or current evidence of any condition that makes participation not in the subject*s best interest;24.has donated blood products or has had phlebotomy of >300 mL within 8 weeks of signing informed consent, or intends to donate blood products within the projected duration of the trial OR subject has received, or is anticipated to receive,blood products within 12 weeks of signing informed consent or within duration of the trial;25.is unlikely to adhere to the trial procedures or is planning to relocate during the trial;26.has symptomatic hyperglycemia that requires immediate initiation,adjustment,or addition of antihyperglycemic therapy or has a fasting plasma glucose consistently ;27.has a clinically significant ECG abnormality which exposes the subject to risk by enrolling in the trial;28.has a fasting plasma glucose consistently;29.has poorly controlled hypertension defined as systolic blood pressure of *160 mm Hg or diastolic blood pressure of *90 mm Hg;30.is on lipid-lowering medication or thyroid replacement therapy,and has not been on a stable regimen for the 4 weeks (lipid-lowering medication),or 6 weeks (thyroid replacement therapy) prior to Visit 4/Day 1;31.has a positive urine pregnancy test;32.has a site-fasting-fingerstick glucose (FFSG) >260 mg/dL (>14.4

mmol/L);33.has developed a new medical condition/change in status of an established medical condition,developed a laboratory or ECG abnormality,or required a new treatment or medication during the pre-randomization period which meets any previously described trial exclusion criteria or which,in the opinion of the investigator,exposes the subject to risk by enrolling in the trial

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-06-2013
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MK-3102
Generic name:	nvt

Ethics review

Approved WMO

Date:	03-01-2013
Application type:	First submission

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-05-2013
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-11-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-09-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2012-003626-24-NL
CCMO	NL42827.058.12