A Phase III, 3-Arm, Randomized, Double-Blind, Placebo-Controlled, Multi-Centre Study to Investigate the Impact of Diamyd® on the Progression of Diabetes in Patients Newly Diagnosed with Type 1 Diabetes Mellitus.

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

Summary

ID

NL-OMON33991

Source
ToetsingOnline

Brief title
D/P3/07/4

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Autoimmune disorders

Synonym
diabetes mellitus type I; diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Diamyd Therapeutics
Source(s) of monetary or material Support: Diamyd Therapeutics;Stockholm;Zweden

Intervention

Keyword: beta-cell preservation, placebo-controlled, type 1 diabetes mellitus

Outcome measures

Primary outcome

The change from baseline (Visit 2) to Month 15 (Visit 6) in C-peptide (AUCmean

0-120 min) during an MMTT.

Secondary outcome

• Hemoglobin A1c (HbA1c), change between baseline and subsequent visits

• Exogenous insulin dose per kg body weight and 24 hours, change between

baseline and subsequent

visits

• Number of self-reported episodes of hypoglycemia

• Fasting C-peptide, change between baseline and subsequent visits

• C-peptide AUCmean 0-120 min during MMTT, change between baseline and

subsequent visits

• C-peptide measured at 30, 60, 90, and 120 minutes during MMTT

• Maximum C-peptide during MMTT, change between baseline and subsequent visits

• Proportion of patients with a stimulated maximum C-peptide level above 0.2

nmol/L

+ safety variables as observation of reactions at the injection site, GAD65Ab

titer, occurrence of

adverse events (AEs), findings from: laboratory measurements, vital signs,

neurological assessments, and limited physical

examination.

Study description

Background summary

Type 1 diabetes (T1D) belongs to the group of medical disorders classified as *autoimmune* due to a pathologic feature involving an inappropriate immunological recognition of the body*s own tissues. This abnormal immune response, in the case of T1D, results in the destruction of insulin-secreting pancreatic beta cells which in turn leads to a lifelong dependence on exogenous insulin treatment. Although the use of insulin has dramatically improved the survival of patients with T1D, insulin does not represent a cure as individuals with the disorder, even if well managed, display marked increases in the frequency of life-altering (e.g., blindness, limb amputation) and even life-threatening complications including hypoglycemic unawareness and accelerated macrovascular disease. The severity of these complications makes the development of a therapy allowing for beta cell preservation of great urgency for patients and caregivers. The underlying basis of autoimmune diabetes involves a *pro-inflammatory* T-cell response against insulin-secreting beta cells that is sufficient to cause their destruction and result in insufficient production of endogenous insulin. Diamyd therapy aims at intervening in this destructive process by modulating the immune system in a discrete, antigen-specific fashion to prevent the destruction of beta cells and reduce or abolish dependence on insulin treatment.

Study objective

The primary objective is to evaluate the efficacy of i) a prime-and-boost regimen with 20 µg Diamyd and ii) a prime-and-boost regimen with 20 µg Diamyd, followed by 2 additional single doses with 20 µg Diamyd, compared to placebo with respect to
preserving insulin secretion. This will be evaluated by the change from baseline (Visit 2) to Month 15 (Visit 6) in C-peptide area under the curve mean 0-120 minutes (AUCmean 0- 120 min) during an MMTT.

Study design

This study is a 3-arm, randomized, double-blind, placebo-controlled, multicenter, clinical trial. All groups will continue to receive intensive diabetes management through their personal physician/diabetes team. Patients will receive 2 subcutaneous injections with 20 µg Diamyd in a prime-and-boost regimen, followed by 2 additional single doses with Diamyd 20µg, or 2 injections with 20 µg Diamyd in a prime-and-boost regimen, followed by 2 additional single doses with placebo, or placebo alone, depending on to which treatment arm they are randomized.
Total duration of the study is 30 months (15 months blinded period with study medication and 15 months follow-up)

Intervention

Each patient will receive four injections (Day 1, Day 30, Day 90 and Day 270)

Study burden and risks

Each patient receives 4 injections and has to remain in the study centre for observation for at least 1 hour after each injection. At 6 visits a MMTT is performed to measure the function of the beta cells. At each visit blood samples are taken and for menarchal females a pregnancy test. The patient keeps a diary during the study in which possible adverse events and hypoglycemia periods are noted. Every day of the 4 days before a visit, the patient must call the centre to report their daily use of insuline. At 7 visits the patient should arrive fasting. At 8 visits a physical examination is carried out and at 5 visits a neurological exam.
The total study (two-and-a-half years) will mean 1-2 additional visit for the patient in comparison with the visit frequency during standard diabetes care. However the visits will last half an hour - two hours longer. Standard diabetes care will be given during the study. No adverse events from the study medication are expected. The burden for the patient during the visits has been tried to keep as low as possible a.o. by using painkilling cream before the needle stick and by using a catheter for blood sampling.

Contacts

Public
Diamyd Therapeutics

Linnégatan 89B, plan 5
SE-11523 Stockholm
Zweden
Scientific
Diamyd Therapeutics

Linnégatan 89B, plan 5
SE-11523 Stockholm
Zweden

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. Male and female patients between 10 and 20 years of age
2. Insulin dependent type 1 diabetes mellitus diagnosed within the previous 3 months at time of screening
3. Fasting C-peptide level at time of screening above 0.1 nmol/L
4. Elevated GAD65 antibodies (GADA) at time of screening
5. Menarchal females must agree to avoid pregnancy and have a negative urine pregnancy test
6. Patients must agree to using adequate contraception, if sexually active, until 1 year after the last study drug administration
7. Must be willing to comply with intensive diabetes management
8. Written informed consent obtained from the patient and/or patient*s parents or legal acceptable representative(s) according to local regulations.

Exclusion criteria

1. Previous or current treatment with immunosuppressant therapy (although topical or inhaled steroids are accepted)
2. Treatment with any oral or injected anti-diabetic medications other than insulin
3. A history of anemia or significantly abnormal hematology results at screening
4. A history of epilepsy, head trauma or cerebrovascular accident, or clinical

features of continuous motor unit activity in proximal muscles
5. Clinically significant history of acute reaction to vaccines or other drugs in the past
6. Treatment with any vaccine within 1 month prior to planned first Diamyd dose or planned treatment with vaccine up to 2 months after the last injection with Diamyd, excluding the influenza vaccine
7. Participation in other clinical trials with a new chemical entity within the previous 3 months
8. Inability or unwillingness to comply with the provisions of this protocol
9. A history of alcohol or drug abuse
10. A significant illness other than diabetes within 2 weeks prior to first dosing
11. Known human immunodeficiency virus (HIV) or hepatitis
12. Females who are lactating or pregnant (for females who have started menstruating the possibility of pregnancy must be excluded by urine βHCG onsite within 24 hours prior to the investigational product administration)
13. Males or females not willing to use adequate contraception, if sexually active, until 1 year after the last study drug administration
14. Presence of associated serious disease or condition, including active skin infections that preclude subcutaneous injection, which in the opinion of the investigator makes the patient non-eligible for the study.

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):	17-10-2008
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Diamyd
Generic name:	Diamyd

Ethics review

Approved WMO Date:	10-07-2008
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	19-08-2008
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	11-03-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	25-03-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	02-02-2011
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	25-02-2011
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

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	EUCTR2007-002728-13-NL
CCMO	NL23850.003.08