Clinical trial results:
The DIAMOND for the Treatment of Type 2 Diabetes: Can Blood Triglycerides level be the predictor for therapy efficiency?

Summary

EudraCT number	2013-001003-36
Trial protocol	AT IT
Global end of trial date	17 June 2016

Results information

Result version number	v1 (current)
This version publication date	02 January 2020
First version publication date	02 January 2020
Summary attachment (see zip file)	The DIAMOND® for the Treatment of Type 2 Diabetes: Can blood Triglycerides level be the predictor for therapy efficiency? A Multicentre, Prospective, Semi-randomized Study (End Report 04-02-19.pdf)

Trial information

Trial identification

Sponsor protocol code	MC-CP-TAN2012-60

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Metacure/Hobart
Sponsor organisation address	Route de Meyrin, Geneva, Switzerland, 1203
Public contact	Dr. Ricardo Aviv, Metacure Ltd, ricardoa@metacure.com
Scientific contact	Dr. Ricardo Aviv, Metacure Ltd, 43 6647966285, ricardoa@metacure.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were: (1) to evaluate the efficacy of gastric stimulation (GCM) using the DIAMOND System in the improvement of glycemic control measured by changes in HbA1c. (2) Examine the relationship between blood TG levels and the GCM efficacy for mechanistic purpose. (3) The effects of GCM on weight loss and associated co-morbid conditions

Protection of trial subjects:

Enrolled subjects did not experience pain as part of the treatment. Diabetes type 2 remained under anti oral medication.

Background therapy:

All patients received oral antidiabetes medications and the GCM, an electrical current applied to the stomach during meals to enhance gastric contractility and thereby increase the sensation of satiety during the emal, help reduce weight and better control hunger.

Evidence for comparator:

This was a study where subjects were divided in two groups according to their level of triglycerides: normal (low) or High triglycerdides. Subjects in the high triglycreide group were further randomized and divided into two furthr groups in a double blind fashion to placebo or Fenofibrate, a drug known to lower trigylerides.

Actual start date of recruitment	21 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Serbia: 26
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 27
Country: Number of subjects enrolled	Greece: 1
Worldwide total number of subjects	59
EEA total number of subjects	33

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	45
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Note that out of the 105 patients who signed the inform consent only 59 were implanted and entered the study phase.
First patient recruited 21 Oct 2013 First patient implanted: 6 Nov 2013 Last patient implanted 17 Jun 2016 Last patient completed 17 June 2018

Pre-assignment

Screening details:

The protocol had a screening failure rate of 45% . Of a total of 59 implanted subjects 27 subjects were implanted in 5 sites throughout Poland, 26 in two sites in Serbia, 5 subjects were implanted in one site in Italy, and one patient was implanted in Greece. The most common cause for failure was appropriate glycemic control

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Baseline

Arm description:

patients kept their oral anti diabetes medication

Arm type	baseline evaluations
Investigational medicinal product name	No Diamond implant on baseline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Not mentioned

Dosage and administration details:

permanent

Number of subjects in period 1	Baseline
Started	59
Completed	59

Period 2

Period 2 title	Diamond treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Normal Triglyceride

Arm description:

Patients with normal TG levels were compared to the High TG level groups

Arm type	Active comparator
Investigational medicinal product name	Diamond
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Active from week 1

Arm title	High TG Fenofibrate

Arm description:

Patients with Hight TG were randomized to Fenofibrate or placebo. Patients with Fenofibrate were exected to lower the TG levels, and thus behave like low Normal TG level group

Arm type	Active comparator
Investigational medicinal product name	Diamond
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Active from week 1

Arm title	High Triglyceride Placebo

Arm description:

Patients eith High TG randomized to placebo received only the Diamond treatment and were expected to have the least efficacy on glycemic control

Arm type	Placebo
Investigational medicinal product name	Diamond
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Active from week 1

Number of subjects in period 2	Normal Triglyceride	High TG Fenofibrate	High Triglyceride Placebo
Started	21	21	17
Completed	21	21	17

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	59	59	
Age categorical			
All subjects were adults of 18 years old or more			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	45	45	
From 65-84 years	14	14	
85 years and over	0	0	
adults > 18 years old	0	0	
Age continuous			
Units: years			
arithmetic mean	52.32		
standard deviation	± 7.68	-	
Gender categorical			
All genderes could participate			
Units: Subjects			
Female	34	34	
Male	25	25	

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description:	
patients kept their oral anti diabetes medication	
Reporting group title	Normal Triglyceride
Reporting group description:	
Patients with normal TG levels were compared to the High TG level groups	
Reporting group title	High TG Fenofibrate
Reporting group description:	
Patients with Hight TG were randomized to Fenofibrate or placebo. Patients with Fenofibrate were exected to lower the TG levels, and thus behave like low Normal TG level group	
Reporting group title	High Triglyceride Placebo
Reporting group description:	
Patients eith High TG randomized to placebo received only the Diamond treatment and were expected to have the least efficacy on glycemic control	
Subject analysis set title	Normal TG
Subject analysis set type	Per protocol
Subject analysis set description:	
Only 1 subject did not have data at the last visit	
Subject analysis set title	High TG Fenofibrate
Subject analysis set type	Per protocol
Subject analysis set description:	
3 subjects did not have data t the last visit	
Subject analysis set title	High TG Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
all 17 subjects havd data at the last visit	

Primary: to evaluate the efficacy of gastric stimulation (GCM) using the DIAMOND System in the improvement of glycemic control measured by changes in HbA1c.

End point title	to evaluate the efficacy of gastric stimulation (GCM) using the DIAMOND System in the improvement of glycemic control measured by changes in HbA1c.
End point description:	
End point type	Primary
End point timeframe:	
baseline vs 12 month	

End point values	Normal Triglyceride	High TG Fenofibrate	High Triglyceride Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	17	
Units: percent volume/volume				
arithmetic mean (confidence interval 0.05%)	7.32 (6.7 to 8.1)	7.39 (6.7 to 8.1)	8.07 (7.8 to 8.4)	

Statistical analyses

Statistical analysis title	t-test

Statistical analysis description:

The analysis compared ends of period measurements, specifically, the null hypothesis that there is no difference in HbA1c between baseline and 12 months post implant as tested by a two-sided 0.05 level test using a t-statistic.

Comparison groups	Normal Triglyceride v High Triglyceride Placebo v High TG Fenofibrate
Number of subjects included in analysis	55
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	1.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

A total of 68 Adverse Events were recorded in 28 subjects. 58 AE (85.2%) were considered unrelated to device function or implant procedure and included 2 SAE, 3 AE of documented hypoglycemia, 3 events of suspected hypoglycemia and one hyperglycemic event.

Adverse event reporting additional description:

2 SAE: a,intracerebral hemorrhage occurring 2 month after the implant and b, hospitalization after suspicion of breast cancer. A patient had a fatal car accident. 3 subjects had in 39.7% of the AE (7, 9 and 11 AE each); all other subjects reported AE frequency:1 event (13 subjects), 2 events (7 subjects), 3 events (2 subjects) 4 events (2 events)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	group 1

Reporting group description: -

Serious adverse events	group 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 59 (1.69%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Vascular disorders			
Stroke in evolution			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	group 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 59 (1.69%)		
Surgical and medical procedures			
Wound complication			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2014	The formal written approval by the EC and all relevant correspondence pertaining to this submission have been filed in the Trial Master Files. Slight revisions to the protocol addressed guiding Ethics Committee requests as new sites were incorporated. These changes maintained however, the same endpoints, enrollment criteria and methods:
05 May 2015	A second revision Rev 02c, dated 5 May 2015 was approved to reflect newly appointed sites in Australia (no patient was eventually enrolled). This version allowed the study period to start in March 2015 and continuing until successful enrollment of 65 patients with a 30% dropout. The version had additional information on risks associated with Fenofibrate, the drug used to lower Triglycerides in High TG patients randomized to Triglyceride (lowering) treatment group.
01 April 2016	A Ver 01 of the protocol was released the 1st April 2016, changing the name to MC CP TAN2016 – 60. The Rev 1 version allowed the study to run from April 2016 to April 2018, changed the amount of implanted subjects to at least 40. It also added references to recent studies with the DIAMOND system, and allowed for potential use of the DIAMOND II device (not implemented eventually). This version widened the scope of the Triglyceride effect on the DIAMOND treatment through the randomization into treatment and placebo controlled data on patients enrolled to the high TG group.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported