Clinical trial results:
Randomized double blind parallel design study comparing risk of nocturnal hypoglycemia and critical arrhythmias with sitagliptin versus glimepiride in patients with type 2 diabetes insufficiently controlled with metformin monotherapy

Summary

EudraCT number	2014-003792-34
Trial protocol	DE
Global end of trial date	24 January 2017

Results information

Result version number	v1 (current)
This version publication date	06 June 2024
First version publication date	06 June 2024

Trial information

Trial identification

Sponsor protocol code	DIA-2-REDESIGN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02373865
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GWT-TUD GmbH
Sponsor organisation address	Freiberger Str. 33, Dresden, Germany, 01067
Public contact	Katja Reichardt, GWT-TUD GmbH, 0049 35125933188, katja.reichardt@gwtonline.de
Scientific contact	Katja Reichardt, GWT-TUD GmbH, 0049 35125933188, katja.reichardt@gwtonline.de

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	20 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 January 2017
Global end of trial reached?	Yes
Global end of trial date	24 January 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Hypoglycemic episodes (HE) and time spent below critical values are the primary objectives of this study. We will calculate overall episodes/time (5 days) and nocturnal episodes.

Protection of trial subjects:

The conduct of this trial was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also carried out in keeping with applicable local law(s) and regulation(s).
Both IMPs were used in the authorized therapeutic indication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2015
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	Germany: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	2

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at one study site in Germany. Of originally planned 68 patients only 4 patients could be included into the trial.

Pre-assignment

Screening details:

The inclusion and exclusion criteria were yielding to an impeded recruitment of patients. Thus, in the time period between the start of the clinical trial in March 2015 (Approval of BfArM) and the premature termination at Jan 24, 2017 (09/2015 – 12/2015) only 4 patients could be recruited and medicated.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group

Arm description:

Patients received Sitagliptin 100 mg (qd) + Glimepiride Placebo (qd) (titrated up to 6 mg) for the duration of 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	Januvia®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin was continuously administered at a dose of 100 mg once daily (each 24 h)

Investigational medicinal product name	Glimepiride-Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard + tablet
Routes of administration	Oral use

Dosage and administration details:

The starting dose is 1 mg glimepiride-placebo per day titrated up to 6 mg per day.
Oral administration, shortly before or during a meal
tablets encapsulated in capsules for blinding

Arm title	Control group

Arm description:

Patients will receive Glimepiride 1 mg (qd) (titrated up to 6 mg) + Sitagliptin Placebo 100 mg (qd) for the duration of 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard + tablet
Routes of administration	Oral use

Dosage and administration details:

The starting dose is 1 mg glimepiride per day titrated up to 6 mg glimepiride per day.
Oral administration, shortly before or during a meal
tablets encapsulated in capsules for blinding

Investigational medicinal product name	Sitagliptin-Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin-placebo was continuously administered at a dose of 100 mg once daily (each 24 h)

Number of subjects in period 1	Treatment group	Control group
Started	2	2
Completed	2	2

Baseline characteristics

Reporting groups

Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	4	4	
Age categorical 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)	2	2	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	4	4	

End points

End points reporting groups

Reporting group title	Treatment group
Reporting group description:	
Patients received Sitagliptin 100 mg (qd) + Glimepiride Placebo (qd) (titrated up to 6 mg) for the duration of 12 weeks.	
Reporting group title	Control group
Reporting group description:	
Patients will receive Glimepiride 1 mg (qd) (titrated up to 6 mg) + Sitagliptin Placebo 100 mg (qd) for the duration of 12 weeks.	

Primary: Hypoglycemic episodes

End point title	Hypoglycemic episodes[1]
End point description:	
Primary command variables of the trial were the number hypoglycemic episodes per patient and the overall duration of hypoglycemia (time of interstitial glucose below 3,1 mmol/l, according to CGMS iPro" Continuous Glucose Reporter, measured over 5 days). Total duration of hypoglycemic episodes were calculated (5 days) including nocturnal episodes. Night was defined as: 10 pm - 06 am.	
End point type	Primary
End point timeframe:	
5 days	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Given the low number of only 4 patients at this time point, a reliable conclusion cannot be drawn. All included patients showed an improvement of HbA1C during the trial, which was leading at the end of the treatment to an HbA1C of 1,25 % average.

End point values	Treatment group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: percent				
number (not applicable)	1.5	1.0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 12 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: During the analyzed period of time no serious adverse events could were occurring. 1 patient showed once symptoms of a hypoglycemia with a blood sugar value of 4,2 mmol/l in combination with a slight tachycardia. Again the low number of patients and the shortened period of examination do not allow any reliable evaluation of issues relevant for safety. Additional risk factor could not be identified upon the given results and informations.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 March 2015	Specification of inclusion criteria; Specification of visit schedule and addition of ECG evaluation as well as patient diary; Specification of screening failure definition; Specification of treatment description; Specification of CGM recordings and blood glucose measurement as well as test meal description; Specification of glimepiride titration (dose adaption); Addition of unblinding procedures

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early termination on 16.01.2017 due to immense delay in patient recruitment (difficult inclusion and exclusion profile); increase in the study costs due to conditions imposed on the investigational product

Notes: