Clinical trial results:
Glycemic control with GlucoTab using an ultra-long acting insulin analogue in non-critically ill patients with type 2 diabetes at the general ward

Summary

EudraCT number	2015-003669-27
Trial protocol	AT
Global end of trial date	12 October 2016

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	GlucoTab_U300

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Graz, Department of Internal Medicine, Division of Endocrinology and Diabetology
Sponsor organisation address	Auenbruggerplatz 15, Graz, Austria, 8010
Public contact	Julia Mader, Medical University of Graz/Department of Internal Medicine/Division of Endocrinology and Diabetology, 43 31638580254, julia.mader@medunigraz.at
Scientific contact	Julia Mader, Medical University of Graz/Department of Internal Medicine/Division of Endocrinology and Diabetology, +43 31638512383, julia.mader@medunigraz.at

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	30 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 October 2016
Global end of trial reached?	Yes
Global end of trial date	12 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of the GlucoTab system for glycemic management using insulin glargine U300 in non-critically ill patients with type 2 diabetes at the general ward

Protection of trial subjects:

This study was conducted in full accordance with the principles of the "Declaration of Helsinki" (as amended in Tokyo, Venice, Hong Kong, Somerset West, and Edinburgh) and with the laws and regulations of the respective European countries.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2016
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	Austria: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	9
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

It was the responsibility of the investigator to obtain oral and written informed consent prior to any study-related procedures. In obtaining and documenting informed consent, the investigator complied with applicable regulatory documents and adhered to the ICH GCP guideline and to the requirements in the Declaration of Helsinki.

Pre-assignment

Screening details:

This study included patients with type 2 diabetes mellitus or newly diagnosed hyperglycemia, both male and female, treated initially with oral agents, non-insulin injected antidiabetic medicine, insulin, diet or any combination of the four, and who were hospitalized for any condition at the Medical University of Graz.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	GlucoTab U300

Arm description:

.Glinide, sulfonylureas and glitazones were stopped. Metformin, SGLT2-inhibitors, GLP-1 analoga and DPP-4-inhibitors were continued according local standard procedures. Insulin therapy was adjusted according to the GlucoTab® system with incorporated software algorithm.
Participants were treated with the GlucoTab® and its REACTION-Algorithm for basal bolus therapy using insulin glargine U300 and insulin glulisine. The algorithm had been tested previously using insulin glargine and had shown to safely establish glycemic control.
Insulin therapy prescription for every following 24 hours was suggested once daily by the GlucoTab® system taking previous insulin doses, glucose readings, patient age, renal function and insulin sensitivity into account. The goal of the GlucoTab® system is to maintain fasting and pre-meal glucose concentrations between 70-140 mg/dL.

Arm type	Experimental
Investigational medicinal product name	Toujeo 300 Einheiten/ml-Injektionslösung in einem Fertigpen
Investigational medicinal product code	ATC-Code: A10A E04
Other name	Toujeo, Sanofi-Aventis (insuline glargine U300)
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

According to GlucoTab®, insulin therapy was initiated at a daily dose of 0.5 units/kg. Half of this dose was administered as long acting once daily (glargine U300) and the other half as short acting insulin (glulisine) before meals. A bedtime glucose >180 mg/dL was not corrected by GlucoTab®. The initial total daily dose was reduced to 0.3 units/kg in patients ≥70 years of age and/or serum creatinine ≥ 2.0 mg/dL. In case the patient was already on insulin therapy it was possible to pre-set the doses manually.

Investigational medicinal product name	Apidra Solostar 100 Einheiten/ml-Injektionslösung in einem Fertigpen
Investigational medicinal product code	A10A
Other name	Apidra, Sanofi Aventis (Insulin glulisine)
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

According to GlucoTab®, insulin therapy was initiated at a daily dose of 0.5 units/kg. Half of this dose was administered as long acting once daily (glargine U300) and the other half as short acting insulin (glulisine) before meals. A bedtime glucose >180 mg/dL was not corrected by GlucoTab®. The initial total daily dose was reduced to 0.3 units/kg in patients ≥70 years of age and/or serum creatinine ≥ 2.0

mg/dL. In case the patient was already on insulin therapy it was possible to pre-set the doses manually.

Number of subjects in period 1	GlucoTab U300
Started	30
Completed	30

Baseline characteristics

Reporting groups	
Reporting group title	GlucoTab U300

Reporting group description:

.Glinide, sulfonylureas and glitazones were stopped. Metformin, SGLT2-inhibitors, GLP-1 analoga and DPP-4-inhibitors were continued according local standard procedures. Insulin therapy was adjusted according to the GlucoTab® system with incorporated software algorithm.
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Reporting group values	GlucoTab U300	Total	
Number of subjects	30	30	
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)	9	9	
From 65-84 years	21	21	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	67.3		
standard deviation	± 11.1	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	18	18	
HbA1c Units: mmol/mol			
arithmetic mean	78.7		
standard deviation	± 26.1	-	
Serum creatinine Units: mg/dL			
arithmetic mean	1.3		
standard deviation	± 0.5	-	

End points

End points reporting groups

Reporting group title	GlucoTab U300

Reporting group description:

.Glinide, sulfonylureas and glitazones were stopped. Metformin, SGLT2-inhibitors, GLP-1 analoga and DPP-4-inhibitors were continued according local standard procedures. Insulin therapy was adjusted according to the GlucoTab® system with incorporated software algorithm.
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Primary: Mean percentage of blood glucose measurements restricted to blood glucose values measured ≥ 24 hours after start of therapy in the target range 70 to 140 mg/dL

End point title	Mean percentage of blood glucose measurements restricted to blood glucose values measured ≥ 24 hours after start of therapy in the target range 70 to 140 mg/dL[1]

End point description:

End point type	Primary

End point timeframe:

whole study duration ≥ 24 hours after start of therapy

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: All parameters were analysed by descriptive and explorative statistical methods. No hypotheses were tested. The primary endpoint was "the mean percentage of blood glucose measurements lying in the target range from 70 to 140 mg/dL."

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage				
arithmetic mean (standard deviation)	51.5 (± 26.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall mean BG values

End point title	Overall mean BG values

End point description:

End point type	Secondary

End point timeframe:
whole study duration

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: mg/dl				
arithmetic mean (standard deviation)				
Overall daily BG	154 (± 26.7)			
Overall pre-breakfast BG	143 (± 30.1)			
Overall pre-lunch BG	170 (± 42.7)			
Overall pre-dinner BG	156 (± 30)			
Overall bedtime BG	146 (± 29.1)			
Pre-enrolment BG	189 (± 57.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: BG measurements in different ranges (percentage)

End point title	BG measurements in different ranges (percentage)

End point description:

End point type	Secondary

End point timeframe:
whole study duration

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage				
number (not applicable)				
0-<40 mg/dL	0.1			
40-<60 mg/dL	0.3			
40-<70 mg/dL	0.8			
70-<100 mg/dL	13.8			
100-140 mg/dL	37.7			
>140-<180 mg/dL	24.9			
180-<300 mg/dL	21			
>=300 mg/dL	1.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Missed BG measurements and insulin injections

End point title	Missed BG measurements and insulin injections

End point description:

End point type	Secondary

End point timeframe:

whole study duration except first and last study day

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage				
number (not applicable)				
missed BG measurements	0.9			
missed bolus insulin injections	1.3			
missed basal insulin injections	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall mean numbers

End point title	Overall mean numbers

End point description:

Suggested dose: Insulin dose suggested by the first step of the algorithm before applying the sliding-scale correction
Correction dose: Insulin dose added (or subtracted) by the second step of the algorithm
Calculated dose: Insulin dose finally calculated by the algorithm
Dose correction by user: Difference between calculated insulin by the algorithm and insulin dose finally administered
Injected dose: Insulin dose finally administered

End point type	Secondary

End point timeframe:

whole study duration

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number				
arithmetic mean (standard deviation)				
Number of BG measurements	4 (± 0.2)			
Number of pre-meal bolus injections	2.8 (± 0.5)			
Number of standard bolus injections	3.1 (± 0.8)			
Number of standard basal injections	1 (± 0)			
Injected bolus insulin dose (U)	34.9 (± 19.9)			
Calculated bolus insulin dose (U)	35.1 (± 19.6)			
Suggested bolus insulin dose (U)	27.1 (± 20.5)			
Bolus correction by the algorithm (U)	8 (± 8.9)			
Bolus correction by the user (U)	-0.2 (± 1.4)			
Injected basal insulin dose (U)	29 (± 21)			
Suggested basal insulin dose (U)	29 (± 21)			
Corrective basal insulin dose by the user (U)	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Basal and bolus insulin dose corrections (percentage)

End point title	Basal and bolus insulin dose corrections (percentage)

End point description:

End point type	Secondary

End point timeframe:

whole study duration except day 1

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage				
number (not applicable)				
Basal corrections by the user	4.5			
Bolus corrections by the user	5.6			
Bolus morning corrections by the user	4.9			
Bolus noon corrections by the user	4.4			
Bolus evening corrections by the user	6.7			
Bolus bedtime corrections by the user	6.4			

Total daily insulin dose corrections	4.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Health-care professional adherence to suggested insulin doses

End point title	Health-care professional adherence to suggested insulin doses

End point description:

End point type	Secondary

End point timeframe:

whole study duration after day 1

End point values	GlucoTab U300			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage				
number (not applicable)				
physician adherence to total daily dose suggestion	97.3			
physician adherence with basal insulin doses	99.1			
adherence for bolus insulin doses by nurses	95.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed during the whole study duration

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	GlucoTab U300

Reporting group description:

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Serious adverse events	GlucoTab U300		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	GlucoTab U300		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)		
Vascular disorders			
Peripheral artery disease left popliteal artery and left common iliac artery			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Diabetic foot			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Peripheral artery disease			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Subacute stroke			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Surgical and medical procedures			
Post-OP intraabdominal-organizing-hematoma			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Cardiac disorders			
Hypotension			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Collapse			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Coronary artery disease (2 vessels)			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Coronary artery disease (1 vessel)			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Nervous system disorders			
Diabetic neuropathy			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Acute onset of headache			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Hypokalaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

Ear and labyrinth disorders Cerumen obturans right ear subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1		
Eye disorders Papilledema subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1		
Gastrointestinal disorders Intestinal wall thickening subjects affected / exposed occurrences (all) 3 Polyps of the colon subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Ileus/Subileus subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Hepatobiliary disorders Liver enzyme elevation and steatosis hepatis subjects affected / exposed occurrences (all) Gallstone disease subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Skin and subcutaneous tissue disorders Balanitis candida subjects affected / exposed occurrences (all) Drug eruption	 1 / 30 (3.33%) 1		

subjects affected / exposed occurrences (all) Vaginitis due to candida infection subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Renal and urinary disorders Urinary tract infection subjects affected / exposed occurrences (all) Renal cyst subjects affected / exposed occurrences (all) Detoriation of kidney insufficiency subjects affected / exposed occurrences (all)	 3 / 30 (10.00%) 3 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Endocrine disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1		
Musculoskeletal and connective tissue disorders Fracture of the bridge of the nose subjects affected / exposed occurrences (all) Lumbar disk herniation subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

limited number of patients; no randomization; study was only performed at one clinical ward

Notes: