Clinical trial results:
A Randomized, Double-Blind, Placebo-controlled, Single-center Phase 1 Inpatient Pilot Study to Explore the Safety and Efficacy of DAPAglifozin as Add-on to day and night closed-loop control using the DreaMed Substance Administration Device Software in Adolescent and Adult Subjects with Type 1 Diabetes mellitus

Summary

EudraCT number	2016-002212-41
Trial protocol	DE
Global end of trial date	19 December 2017

Results information

Result version number	v1 (current)
This version publication date	29 March 2022
First version publication date	29 March 2022
Summary attachment (see zip file)	CSR Synopsis (CSR_DAPA_Dream_17DEC 2019_synopsis_final.pdf) Report (FINAL STUDY REPORT_DAPA_Dream_17DEC 2019.docx)

Trial information

Trial identification

Sponsor protocol code	ESR-15-11453

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Stiftung Hannoversche Kinderheilanstalt
Sponsor organisation address	Janusz-Korczak-Allee12, Hannover, Germany, 30173
Public contact	Deputy Principal Investigator, Stiftung Hannoversche Kinderheilanstalt, Kinder - und Jugendkrankenhaus AUF DER BULT, , 0049 51181153344, biester@hka.de
Scientific contact	Deputy Principal Investigator, Stiftung Hannoversche Kinderheilanstalt, 0049 51181153344, biester@hka.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	18 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the pilot study is to collect clinical data of a single-dose of 10mg dapagliflozin as add-on to night and day closed-loop control using the DreaMed Algorithm on the time within glucose range 70-180 mg/dl (3.9-10mmol/l) [%] for the ensuing 24 hours with two oral mixed-meals.

Protection of trial subjects:

Close monitoring of patients onsite and remotely.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2017
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: 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)	15
Adults (18-64 years)	15
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

31 did receive treatment, one subject discontinued, 30 completed the study

Pre-assignment

Screening details:

34 subjects were screened

Period 1

Period 1 title	Overall trial (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?	No
Arm title	Sequence 1

Arm description:

dapa - Placebo

Arm type	Sequence
Investigational medicinal product name	Forxiga
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg x 2

Arm title	Sequence 2

Arm description:

Placebo - Dapa

Arm type	Sequence

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Sequence 1	Sequence 2
Started	30	30
Completed	30	30

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	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)	15	15	
Adults (18-64 years)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Males and females were screened.			
Units: Subjects			
Female	19	19	
Male	11	11	

Subject analysis sets	
Subject analysis set title	Dapagliflozin
Subject analysis set type	Per protocol
Subject analysis set description: Time in glucose range 70-180 mg/dL	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Tine in glucose range 70-180 mg/dL	

Reporting group values	Dapagliflozin	Placebo	
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)	15	15	

Adults (18-64 years)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Males and females were screened.			
Units: Subjects			
Female	19	19	
Male	11	11	

End points

End points reporting groups

Reporting group title	Sequence 1
Reporting group description: dapa - Placebo	
Reporting group title	Sequence 2
Reporting group description: Placebo - Dapa	
Subject analysis set title	Dapagliflozin
Subject analysis set type	Per protocol
Subject analysis set description: Time in glucose range 70-180 mg/dL	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Tine in glucose range 70-180 mg/dL	

Primary: Time within glucose range 70-180 mg/dl

End point title	Time within glucose range 70-180 mg/dl
End point description: Time within glucose range 70-180 mg/dl (3.9-10mmol/l) [%] during night and day closed-loop control using the DreaMed automated insulin delivery with two oral mixed-meals after oral administration of 10mg dapagliflozin	
End point type	Primary
End point timeframe: 24 hours	

End point values	Dapagliflozin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: percentage				
arithmetic mean (standard deviation)	68 (± 6)	50 (± 13)		

Statistical analyses

Statistical analysis title	t-test
Statistical analysis description: one sided	
Comparison groups	Placebo v Dapagliflozin

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)

Secondary: insulin dose reduction

End point title	insulin dose reduction

End point description:

To investigate the degree of insulin dose reduction during the DreaMed automated insulin delivery 24 hours after a single dose of 10mg dapagliflozin in patients with type 1 diabetes

End point type	Secondary

End point timeframe:

24 hours

End point values	Dapagliflozin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: IU				
arithmetic mean (standard deviation)	40 (± 13)	31 (± 10)		

Statistical analyses

No statistical analyses for this end point

Secondary: on urinary glucose excretion

End point title	on urinary glucose excretion

End point description:

To investigate the effect on urinary glucose excretion

End point type	Secondary

End point timeframe:

24 hours

End point values	Dapagliflozin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: mg/dL				
arithmetic mean (standard deviation)	149 (± 42)	49 (± 23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post prandial insulin need

End point title	Post prandial insulin need
End point description: To investigate if dapagliflozin influences postprandial insulin need.	
End point type	Secondary
End point timeframe: post prandial	

End point values	Dapagliflozin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: IU/kg/24h				
arithmetic mean (standard deviation)	0.425 (± 0.09)	0.57 (± 0.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: ßhydroxybutyrate levels

End point title	ßhydroxybutyrate levels
End point description: To investigate if dapagliflozin is associated with elevated ßhydroxybutyrate levels.	
End point type	Secondary
End point timeframe: 24 hours	

End point values	Dapagliflozin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: mmol/L				
arithmetic mean (confidence interval 95%)	0.29 (0.28 to 0.31)	0.16 (0.15 to 0.18)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 72 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23
Reporting groups	
Reporting group title	Dapagliflozin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

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

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

Non-serious adverse events	Dapagliflozin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 30 (16.67%)	7 / 30 (23.33%)	
Investigations			
Blood bilirubin			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			

subjects affected / exposed	3 / 30 (10.00%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	2 / 30 (6.67%)	4 / 30 (13.33%)	
occurrences (all)	2	4	
Otitis media			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Periodentitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2016	Double dose of dapagliflozin: Dapagliflozin dose was increased from 1x10mg to 2x10mg over a period of 2 days (10mg/day) due to short term efficacy of Dapagliflozin.
13 March 2017	02 Informed Consent Form (ICF) on visit 1: The written consent can occur on visit 1 since patients and parents (where applicable) were already informed about the study before screening visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/3321711