Clinical trial results:
Randomized, placebo controlled, crossover clinical study to analyse the effect of dapagliflozin on microvascular and macrovascular circulation and total body sodium content

Summary

EudraCT number	2013-004169-14
Trial protocol	DE
Global end of trial date	20 February 2015

Results information

Result version number	v1 (current)
This version publication date	28 July 2021
First version publication date	28 July 2021

Trial information

Trial identification

Sponsor protocol code	BMS-MB102-210

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Erlangen
Sponsor organisation address	Ulmenweg 4, Erlangen, Germany, 91054
Public contact	Clinical Research Centre, Medizinische Klinik 4, 0049 091318536245, roland.schmieder@uk-erlangen.de
Scientific contact	Clinical Research Centre, Medizinische Klinik 4, 0049 091318536245, roland.schmieder@uk-erlangen.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 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 February 2015
Global end of trial reached?	Yes
Global end of trial date	20 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of dapagliflozin on endothelial and microvascular function of the retinal circulation using Scanning-laser-Doppler-Flowmetry by assessing retinal capillary flow.

Protection of trial subjects:

All visits were performed including physical examination and measurement of glucose Levels (fasting blood glucose), safety laboratory markers - including biochemistry,
haematology and urinalysis - and vital signs (i.e. casual blood pressure and heart rate) as well as checking concomitant medication and assessment of adverse Events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2014
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: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from the University Outpatient Clinic, referring physicians, and advertisements in local newspapers.
After a first contact by phone eligible patients were invited to an interview and selected using a standardized questionnaire.

Pre-assignment

Screening details:

Female and male patients aged between 18 and 70 years with type 2 diabetes.
All eligible patients received respective advice and started to washout blood glucose lowering medication (if applicable) during the 4 weeks wash-out phase,
and had an additional Visit after 2 weeks (Visit -2).

Period 1

Period 1 title	Treatment Period 1 (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	Dapagliflozin

Arm description:

The study followed randomized cross-over-design, i.e. subjects underwent both treatment arms in randomized order for 6 weeks

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

Dosage and administration details:

10 mg once daily

Arm title	Placebo

Arm description:

The study followed randomized cross-over-design, i.e. subjects underwent both treatment arms in randomized order for 6 weeks

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

Dosage and administration details:

once daily

Number of subjects in period 1	Dapagliflozin	Placebo
Started	62	62
Completed	59	59
Not completed	3	3
Consent withdrawn by subject	1	1
Adverse event, non-fatal	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1

Reporting group description: -

Reporting group values	Treatment Period 1	Total	
Number of subjects	62	62	
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)	45	45	
From 65-84 years	17	17	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	23	23	
Male	39	39	

End points

End points reporting groups

Reporting group title	Dapagliflozin
Reporting group description:	
The study followed randomized cross-over-design, i.e. subjects underwent both treatment arms in randomized order for 6 weeks	
Reporting group title	Placebo
Reporting group description:	
The study followed randomized cross-over-design, i.e. subjects underwent both treatment arms in randomized order for 6 weeks	

Primary: the effect of dapagliflozin on endothelial and microvascular function of the retinal circulation

End point title	the effect of dapagliflozin on endothelial and microvascular function of the retinal circulation
End point description:	
using scanning-laser-doppler-Flowmetry by assessing retinal capillary flow (RCF)	
End point type	Primary
End point timeframe:	
6 weeks	

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: AU				
arithmetic mean (standard deviation)	308 (± 78)	318 (± 87)		

Statistical analyses

Statistical analysis title	effect of Dapagliflozin on retinal circulation
Comparison groups	Dapagliflozin v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	t-test, 2-sided
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	2.5

Secondary: effect of Dapagliflozin on central SBP

End point title	effect of Dapagliflozin on central SBP

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: mmHg				
arithmetic mean (standard deviation)	118 (± 12)	121 (± 13)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of Dapagliflozin on central pulse pressure

End point title	effect of Dapagliflozin on central pulse pressure

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: mmHg				
arithmetic mean (standard deviation)	40.9 (± 11)	43.9 (± 12)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of Dapagliflozin on central augmentation pressure

End point title	effect of Dapagliflozin on central augmentation pressure

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: mmHg				
arithmetic mean (standard deviation)	12.9 (± 6.0)	13.5 (± 6.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of dapagliflozin of RCF after flicker light exposure

End point title	effect of dapagliflozin of RCF after flicker light exposure

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: AU				
arithmetic mean (standard deviation)	344 (± 115)	352 (± 101)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of dapagliflozin on sodium conc Musc. triceps surae

End point title	effect of dapagliflozin on sodium conc Musc. triceps surae

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: AU				
arithmetic mean (standard deviation)	20.4 (± 3.7)	20.3 (± 3.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of Dapagliflozin on office SBP

End point title	effect of Dapagliflozin on office SBP

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: mmHg				
arithmetic mean (standard deviation)	126 (± 12)	129 (± 13)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of Dapagliflozin on fasting plasma glucose

End point title	effect of Dapagliflozin on fasting plasma glucose

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: mg/dl				
arithmetic mean (standard deviation)	114 (± 19)	134 (± 32)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of Dapagliflozin on postprandial plasma glucose

End point title	effect of Dapagliflozin on postprandial plasma glucose

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: mg/dl				
arithmetic mean (standard deviation)	135 (± 32)	154 (± 46)		

Statistical analyses

No statistical analyses for this end point

Secondary: effect of dapagliflozin on sodium conc skin

End point title	effect of dapagliflozin on sodium conc skin

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Dapagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: AU				
arithmetic mean (standard deviation)	22.7 (± 6.4)	23.3 (± 7.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In the course of the intire study , each adverse event had to be reported on an Adverse Event Case Report Form as soon as known, in general at the subsequent study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	all patients treated with IMP

Reporting group description: -

Serious adverse events	all patients treated with IMP		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 62 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	all patients treated with IMP		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 62 (100.00%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	8 / 62 (12.90%)		
occurrences (all)	8		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Diarrhoea			

subjects affected / exposed	6 / 62 (9.68%)		
occurrences (all)	6		
Flatulence			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Toothache			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 62 (9.68%)		
occurrences (all)	6		
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 62 (6.45%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Cystitis			
subjects affected / exposed	7 / 62 (11.29%)		
occurrences (all)	7		
Influenza			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	16 / 62 (25.81%)		
occurrences (all)	16		

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

None reported