



Clinical trial results:

A 24-week, single centre, randomized, parallel-group, double-blind, placebo controlled Phase II study to evaluate the efficacy on body weight of dapagliflozin 10 mg once daily in combination with exenatide 2mg once weekly in obese non-diabetic subjects

Summary

EudraCT number	2014-003432-39
Trial protocol	SE
Global end of trial date	14 March 2016

Results information

Result version number	v1 (current)
This version publication date	07 August 2020
First version publication date	07 August 2020
Summary attachment (see zip file)	Dapalost 0-24weeks (Dapalost 0-24 weeks CTR Part 1 final 2017-01-11.pdf) Dapalost 0-52 weeks (Dapalost 0-52 weeks CTR Part 2 Final 2017-03-21.pdf)

Trial information

Trial identification

Sponsor protocol code	D1690L00016
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Uppsala university
Sponsor organisation address	Akademiska sjukhuset , Uppsala, Sweden, 751 85
Public contact	Jan Eriksson, Dept of Medical Sciences, Clinical Diabetes and Metabolism, Uppsala University, 0046 18611 4419, jan.eriksson@medsci.uu.se
Scientific contact	Jan Eriksson, Dept of Medical Sciences, Clinical Diabetes and Metabolism, Uppsala University, 0046 18611 4419, jan.eriksson@medsci.uu.se

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	11 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 March 2016
Global end of trial reached?	Yes
Global end of trial date	14 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of dapagliflozin 10 mg once daily and exenatide 2 mg once weekly in combination compared to placebo on body weight after 24 weeks of treatment in obese subjects (by measuring change in body weight (kg) from baseline to 24 weeks)

Protection of trial subjects:

Safety • Clinical laboratory tests (clinical chemistry, haematology) were performed at screening and weeks 12, 24 and 52. Urinalysis was performed at screening. • Creatinine clearance was assessed at screening and weeks 12, 24 and 52. • Vital signs were assessed at screening, randomization and weeks 4, 8, 12, 24, 38 and 52. • Incidence and type of adverse events (AEs) and serious adverse events (SAEs). AE reporting started at screening and continued throughout the entire treatment period until week 24 or up to week 52 for subjects participating in the extension study. At each visit, subjects were asked for the occurrence of AEs since the last visit at the clinic. Subjects were specifically asked about the occurrence of symptoms related to hypoglycaemia (e.g. fatigue, dizziness, tremor, palpitations, sweating).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	43
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Via add in news paper

Pre-assignment

Screening details:

3.1 Inclusion criteria

For inclusion in the study subjects should fulfil the following criteria:

- 1) Provision of signed informed consent prior to any study specific procedures.
- 2) Female and/or male aged 18 to 70 years with body mass index (BMI) (measured as body weight (kg)/(height (m))²) 30 to 45 kg/m².
- 3) Female subjects must meet all o

Pre-assignment period milestones

Number of subjects started	50
Number of subjects completed	50

Period 1

Period 1 title	w 24
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Active substance

Arm description:

Efficacy of dapagliflozin 10 mg once daily and exenatide 2 mg once weekly in combination

Arm type	Active comparator
Investigational medicinal product name	Dapagliflozine, Exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for suspension for injection, Tablet
Routes of administration	Oral use, Subcutaneous use

Dosage and administration details:

Dapagliflozine 10 mg, Exenatide 2 mg

Arm title	Placebo
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Arm description:

Placebo

Arm type	Placebo
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Active substance	Placebo
Started	25	25
Completed	23	20
Not completed	2	5
Not applicable	2	5

Period 2

Period 2 title	w 52
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Active
Arm description:	
Dapagliflozine 10 mg and exenatide 2 mg	
Arm type	Active
No investigational medicinal product assigned in this arm	

Number of subjects in period 2^[1]	Active
Started	38
Completed	33
Not completed	5
Not applicable	5

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The actual number for period 2 is 38 subjects started and 33 subjects completed the study.

Baseline characteristics

Reporting groups

Reporting group title	Active substance
Reporting group description: Efficacy of dapagliflozin 10 mg once daily and exenatide 2 mg once weekly in combination	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	Active substance	Placebo	Total
Number of subjects	25	25	50
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
age 18-70y			
Units: years			
median	0	0	
standard deviation	± 0	± 0	-
Gender categorical			
Units: Subjects			
Female	15	15	30
Male	10	10	20

End points

End points reporting groups

Reporting group title	Active substance
Reporting group description: Efficacy of dapagliflozin 10 mg once daily and exenatide 2 mg once weekly in combination	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Active
Reporting group description: Dapagliflozine 10 mg and exenatide 2 mg	

Primary: Efficacy of dapagliflozin

End point title	Efficacy of dapagliflozin
End point description: To assess the efficacy of dapagliflozin 10 mg once daily and exenatide 2 mg once weekly in combination when compared to placebo on body weight after 24 weeks of treatment in obese subjects	
End point type	Primary
End point timeframe: 2015-02-01-2016-02-08	

End point values	Active substance	Active	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	38	25	
Units: kg	23	20	33	

Attachments (see zip file)	Dapalost 0-24 weeks CTR Part 1 final 2017-01-11.pdf Dapalost 0-52 weeks CTR Part 2 Final 2017-03-21.pdf
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Statistical analyses

Statistical analysis title	Analysis of efficacy variables
Statistical analysis description: In this Phase IIa study, all efficacy variables will be assessed at a 2-sided 0.050 significance level. It is unnecessary to control for multiplicity of endpoints in this proof-of-concept setting. The change in body weight from baseline up to Week 24 will be analysed by a longitudinal repeated measures mixed model including treatment, week, treatment-by-week interaction and gender as well as the continuous fixed covariate of baseline body weight measurement	
Comparison groups	Active substance v Active v Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	> 0.01
Method	Not applicable

Notes:

[1] - longitudinal repeated measures

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2015-02-01-2016-03-01

Adverse event reporting additional description:

Overviews of AEs, including intensity, relationship to IP (causality), SAEs and AEs leading to withdrawal, are presented by treatment group, from baseline to week 24 in Table 69, from week 24 to week 52 in Table 70 and from baseline to week 52 in Table 233 (Section 14.3.2.1). All 38 subjects (100.0%) that participated in the extension study, report

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18
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Reporting groups

Reporting group title	Not applicable
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Reporting group description: -

Serious adverse events	Not applicable		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 50 (8.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Head trauma			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Quinckes edema			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal hemmorage			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal adenocarcinoma			

subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Not applicable		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 50 (76.00%)		
Infections and infestations			
Infection			
subjects affected / exposed	22 / 50 (44.00%)		
occurrences (all)	22		
Metabolism and nutrition disorders			
Nutr disorders			
subjects affected / exposed	16 / 50 (32.00%)		
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

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

No

Notes: