# 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)<br>Dapalost 0-52 weeks (Dapalost 0-52 weels CTR Part 2 Final 2017-03-21.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | D1690L00016 |

**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 |

Arm description:

Placebo

| | |
|---|---|
| Arm type | Placebo |

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: Effecacy of dapagliflozin

| | |
|---|---|
| End point title | Effecacy 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: 2015-02-01-206-02-08 | |

| 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<br>Dapalost 0-52 weels CTR Part 2 Final 2017-03-21.pdf |

### 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 measuremen | |
| 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Not applicable |

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: