Clinical trial results:
A 24 week monocentric prospective randomized, placebo-controlled trial to evaluate Efficacy of combination of Exenatide and Dapagliflozin compared to Dapagliflozin and Placebo and its effects on hepatic, myocardial and pancreatic fat distribution in patients with uncontrolled type 2 diabetes mellitus.

Summary

EudraCT number	2016-000574-38
Trial protocol	AT
Global end of trial date	27 November 2019

Results information

Result version number	v1 (current)
This version publication date	03 March 2021
First version publication date	03 March 2021
Summary attachment (see zip file)	Diabetes_Obesity_ and_Metabolism_2021 (dom.14319-1.pdf)

Trial information

Trial identification

Sponsor protocol code	ESR-15-10882

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03007329
WHO universal trial number (UTN)	U1111-1179-3250

Notes:

Sponsors

Sponsor organisation name	Medical University Vienna
Sponsor organisation address	Spitalgasse 23, Wien, Austria, 1090
Public contact	Medical University Vienna, Medical University Vienna, +43 140400 21260, juergen.harreiter@meduniwien.ac.at
Scientific contact	Medical University Vienna, Medical University Vienna, +43 140400 21260, juergen.harreiter@meduniwien.ac.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	01 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to investigate the effects on hepatic lipid content reduction of combination therapy with dapagliflozin (10mg daily) and exenatide (2mg weekly) compared to dapagliflozin (10mg daily) and placebo given for 24 weeks in patients with type 2 diabetes mellitus and insufficient glycaemic control.

Protection of trial subjects:

not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 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	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)	18
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

recruitment was conducted between June 2017 to May 2019. In total 7 study visits were conducted during the study, which was a screening visit (week -4 to 0) followed by the randomization visit at baseline (week 0), study visits at 4,8,16,24 weeks and a follow-up visit at week 28.

Pre-assignment

Screening details:

Screening woindow was 4 weeks, in these 4 weeks all necessary examinations were performed.
In total 563 were screened/prescreened of whom 533 were excluded.

- Not meeting inclusion criteria (n=481)
- Declined to participate (n=52)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	placebo

Arm description:

placebo + dapagliflozin 10mg once daily

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

Dosage and administration details:

10mg once daily

Arm title	combined treatment

Arm description:

exenatide 2mg + dapagliflozin 10mg

Arm type	Active comparator
Investigational medicinal product name	dapagliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10mg once daily

Investigational medicinal product name	exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
2mg once weekly

Number of subjects in period 1	placebo	combined treatment
Started	14	16
Completed	13	16
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	placebo
Reporting group description: placebo + dapagliflozin 10mg once daily	
Reporting group title	combined treatment
Reporting group description: exenatide 2mg + dapagliflozin 10mg	

Reporting group values	placebo	combined treatment	Total
Number of subjects	14	16	30
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	11	18
From 65-84 years	7	5	12
85 years and over	0	0	0
18	0	0	0
12	0	0	0
Age continuous Units: years			
arithmetic mean	60.9	59.4	
standard deviation	± 7.4	± 8.5	-
Gender categorical Units: Subjects			
Female	4	6	10
Male	10	10	20
liver fat content Units: 12.85 %			
arithmetic mean	13.17	12.85	
standard deviation	± 8.91	± 9.26	-

End points

End points reporting groups	
Reporting group title	placebo
Reporting group description: placebo + dapagliflozin 10mg once daily	
Reporting group title	combined treatment
Reporting group description: exenatide 2mg + dapagliflozin 10mg	

Primary: liver fat content	
End point title	liver fat content
End point description:	
End point type	Primary
End point timeframe: 24 weeks	

End point values	placebo	combined treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	16		
Units: percentage				
arithmetic mean (standard deviation)	9.30 (± 8.43)	8.43 (± 8.00)		

Statistical analyses

Statistical analysis title	statistical analysis
Comparison groups	placebo v combined treatment
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: screening - to follow up visit after 28 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	placebo
Reporting group description: placebo + dapagliflozin 10mg once daily	
Reporting group title	combined treatment
Reporting group description: exenatide 2mg + dapagliflozin 10mg	

Serious adverse events	placebo	combined treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Otitis media acute			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	placebo	combined treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 14 (85.71%)	12 / 16 (75.00%)	
Gastrointestinal disorders			
Gastroinestinal Side Effects			
subjects affected / exposed	1 / 14 (7.14%)	4 / 16 (25.00%)	
occurrences (all)	1	4	
Skin and subcutaneous tissue disorders			
Skin reaction			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Pain			
subjects affected / exposed	8 / 14 (57.14%)	2 / 16 (12.50%)	
occurrences (all)	8	2	
Infections and infestations			
Mycosis			
subjects affected / exposed	2 / 14 (14.29%)	5 / 16 (31.25%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2018	Inclusion criteria were adapted: inclusion criteria was changed from HbA1c 7.0-11.0% to 6.5-11.0%.

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/33464703