Clinical trial results:
Study of the Effect of Vildagliptin versus Dapagliflozin on Glucagon Response to Mixed Meal in Metformin-treated Subjects with Type 2 Diabetes

Summary

EudraCT number	2015-001334-21
Trial protocol	SE
Global end of trial date	13 March 2018

Results information

Result version number	v1 (current)
This version publication date	10 March 2021
First version publication date	10 March 2021
Summary attachment (see zip file)	2015-001334-21 Results (EudraCT 2015-001334-21 results.pdf)

Trial information

Trial identification

Sponsor protocol code	350A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02475070
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lund university
Sponsor organisation address	Sölvegatan 19, Lund, Sweden, 22184
Public contact	Bo Ahrén, Lund university, 46 462220758, Bo.Ahren@med.lu.se
Scientific contact	Bo Ahrén, Lund university, 46 462220758, Bo.Ahren@med.lu.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	15 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2017
Global end of trial reached?	Yes
Global end of trial date	13 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effects of vildagliptin versus dapagliflozin on glucagon response to mixed meal ingestion in metformin-treated patients with type 2 diabetes

Protection of trial subjects:

Subjects with type 2 diabetes

Background therapy:

Metformin

Evidence for comparator:

Vildagliptin versus Dapagliflozin

Actual start date of recruitment	01 September 2015
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: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	20
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

28 subjects were recruited through hospitals

Pre-assignment

Screening details:

Subjects were examined by physician and lab tests were taken

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, Monitor, Data analyst

Blinding implementation details:

Patients received vildagliptin or dapagliflozin first, then dapagliflozin or vildagliptin. Randomization and blinding were handled by the University hospital pharamcist.

Arms

Are arms mutually exclusive?	Yes
Arm title	Vildagliptin

Arm description:

Vildagliptin 50mg twice daily for two weeks followed by a meal test. This was followed by a 4 weeks wash-out period followed by two week treatment with Dapagliflozin 10 mg once daily followed by a meal test.

Arm type	Active comparator
Investigational medicinal product name	Vildagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg twice daily

Arm title	Dapagliflozin

Arm description:

Dapagliflozin 10 mg once daily for two weeks followed by a meal test. This was followed by a 4 weeks wash-out period followed by two week treatment with Vildagliptin 50 mg twice daily followed by a meal test.

Arm type	Active comparator
Investigational medicinal product name	Dapagliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg once daily

Number of subjects in period 1	Vildagliptin	Dapagliflozin
Started	14	14
Completed	14	14

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	28	28	
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)	20	20	
From 65-84 years	8	8	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	63.2		
standard deviation	± 7.2	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	20	20	
HbA1c Units: mmol/mol			
arithmetic mean	50.4		
standard deviation	± 6.7	-	
BMI Units: kg/m2			
arithmetic mean	30.7		
standard deviation	± 5.6	-	
Diabetes duration Units: Years			
arithmetic mean	5.8		
standard deviation	± 3.0	-	

End points

End points reporting groups

Reporting group title	Vildagliptin
Reporting group description:	
Vildagliptin 50mg twice daily for two weeks followed by a meal test. This was followed by a 4 weeks wash-out period followed by two week treatment with Dapagliflozin 10 mg once daily followed by a meal test.	
Reporting group title	Dapagliflozin
Reporting group description:	
Dapagliflozin 10 mg once daily for two weeks followed by a meal test. This was followed by a 4 weeks wash-out period followed by two week treatment with Vildagliptin 50 mg twice daily followed by a meal test.	

Primary: Glucagon response to mixed meal

End point title	Glucagon response to mixed meal
End point description:	
Area under the glucagon curve (AUC) for glucagon after mixed meal ingestion	
End point type	Primary
End point timeframe:	
4 hours	

End point values	Vildagliptin	Dapagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: nmol/l min				
arithmetic mean (standard error)	32.1 (± 2.3)	37.5 (± 2.7)		

Statistical analyses

Statistical analysis title	t-test
Statistical analysis description:	
t-test for mean between the groups	
Comparison groups	Vildagliptin v Dapagliflozin
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	t-test, 2-sided
Parameter estimate	Median difference (final values)

Secondary: Fasting glucagon

End point title	Fasting glucagon

End point description:

Fasting glucagon after two weeks of treatment with either vildagliptin or dapagliflozin

End point type	Secondary

End point timeframe:

Two weeks

End point values	Vildagliptin	Dapagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: pmol/L				
arithmetic mean (standard error)	35.6 (± 2.5)	39.4 (± 3.4)		

Statistical analyses

Statistical analysis title	t-test

Statistical analysis description:

t-test of difference in means

Comparison groups	Vildagliptin v Dapagliflozin
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.032
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Two weeks	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21
Reporting groups	
Reporting group title	Vildagliptin
Reporting group description: -	
Reporting group title	Dapagliflozin
Reporting group description: -	

Serious adverse events	Vildagliptin	Dapagliflozin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (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	Vildagliptin	Dapagliflozin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 14 (28.57%)	3 / 14 (21.43%)	
Nervous system disorders			
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Infections and infestations			
Common cold			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 14 (7.14%) 1	

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.

None reported

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29498469