

**Clinical trial results:
DPP4 inhibitors in Type 1 Diabetes****Summary**

EudraCT number	2012-002407-18
Trial protocol	GB
Global end of trial date	23 April 2014

Results information

Result version number	v1 (current)
This version publication date	22 June 2017
First version publication date	22 June 2017
Summary attachment (see zip file)	DPPIV inhibitors manuscript (saxagliptin therapy diabetes medicine.pdf)

Trial information**Trial identification**

Sponsor protocol code	2012DM07
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01922817
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor No: 2012DM07

Notes:

Sponsors

Sponsor organisation name	University of Dundee/NHS Tayside
Sponsor organisation address	Tayside Medical Science Centre, Dundee, United Kingdom, DD1 9SY
Public contact	Catrina Forde, University of Dundee, 44 01382 383890, c.forde@dundee.ac.uk
Scientific contact	Catrina Forde, University of Dundee, 44 01382 383890, c.forde@dundee.ac.uk
Sponsor organisation name	University of Dundee/NHS Tayside
Sponsor organisation address	Tayside Medical Science Centre, Dundee, United Kingdom, DD1 9SY
Public contact	Dr Catrina Forde, University of Dundee, 44 01382 383890, c.forde@dundee.ac.uk
Scientific contact	Dr Catrina Forde, University of Dundee, 44 01382 383890, c.forde@dundee.ac.uk

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	30 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2014
Global end of trial reached?	Yes
Global end of trial date	23 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The body secretes hormones such as adrenaline as a response to low blood sugars. Patients who have had insulin dependant diabetes for over 5 years rely heavily on adrenaline release, to produce symptoms, so that they can respond appropriately to low blood sugars. However, this response is blunted in those with Type 1 diabetes. Our question is whether the degree of this response can be increased by use of 3 months of the DPP4inhibitor, so that patients become better aware of hypoglycaemia.

Protection of trial subjects:

All patients notes were scrutinized thoroughly before enrolling on the trial, to ensure their suitability for the trial, and that they satisfied all inclusion and exclusion criteria.

Once they entered the trial, there was regular contact between PI and patient to ensure there were no emerging AEs. There was good training of all personnel, to ensure the hypoglycaemic clamp was performed safely.

Background therapy:

Type 1 diabetes patients to continue with their usual insulin regime.
IMP was saxagliptin 5mg once daily.

Evidence for comparator:

Comparator was Placebo (lactose filled hard gelatin capsules).

Actual start date of recruitment	03 September 2012
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	United Kingdom: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	14
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

September 2012 to July 2013

Recruited mainly from the diabetes clinics at Ninewells Hospital and from the SCI-Diabetes database.

Pre-assignment

Screening details:

Screening for eligibility carried out and signed off by the PI.

4 week run in period to optimize diabetes therapy prior to the start of the randomised treatment period.

Pre-assignment period milestones

Number of subjects started	14
Number of subjects completed	14

Period 1

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

Blinding implementation details:

Matched placebo

Arms

Arm title	Treatment arm 1
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Arm description:

12 weeks treatment followed by 2 week wash out followed by cross over to opposite treatment

Arm type	Experimental
Investigational medicinal product name	saxagliptin
Investigational medicinal product code	
Other name	Onglyza
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5mg once daily

Number of subjects in period 1	Treatment arm 1
Started	14
Completed	14

Period 2

Period 2 title	Treatment period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Treatment arm 1
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Arm description:

12 weeks treatment followed by 2 week wash out followed by cross over to opposite treatment

Arm type	Experimental
Investigational medicinal product name	saxagliptin
Investigational medicinal product code	
Other name	Onglyza
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5mg once daily

Number of subjects in period 2	Treatment arm 1
Started	14
Completed	14

Baseline characteristics

Reporting groups

Reporting group title	Treatment arm 1
Reporting group description: 12 weeks treatment followed by 2 week wash out followed by cross over to opposite treatment	

Reporting group values	Treatment arm 1	Total	
Number of subjects	14	14	
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)	14	14	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Age at consent			
Units: years			
arithmetic mean	45		
full range (min-max)	35 to 53	-	
Gender categorical			
Male or female			
Units: Subjects			
Female	6	6	
Male	8	8	

End points

End points reporting groups

Reporting group title	Treatment arm 1
Reporting group description:	
12 weeks treatment followed by 2 week wash out followed by cross over to opposite treatment	
Reporting group title	Treatment arm 1
Reporting group description:	
12 weeks treatment followed by 2 week wash out followed by cross over to opposite treatment	

Primary: Magnitude of epinephrine response at blood glucose of 2.5mmol/L

End point title	Magnitude of epinephrine response at blood glucose of 2.5mmol/L
End point description:	
End point type	Primary
End point timeframe:	
During clamp period	

End point values	Treatment arm 1	Treatment arm 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: pmol/L				
number (not applicable)	14	14		

Statistical analyses

Statistical analysis title	Paired T test
Statistical analysis description:	
Prior power calculations indicated that 12 participants were needed for a matched analysis, with 80% power to detect a difference in change of 450 pmol/l, with a standard deviation of 500 and a two-sided a value of 0.05. This difference in the adrenaline response was chosen based on previous published work	
Comparison groups	Treatment arm 1 v Treatment arm 1
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Median difference (final values)
Point estimate	450

Confidence interval	
level	95 %
sides	2-sided
lower limit	132
upper limit	767
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Consent to last study visit

Adverse event reporting additional description:

Recorded all AEs and SAEs but will not report on the common side effects of the drug such as upper respiratory/urinary tract infections, gastroenteritis, hypoglycaemia, headache, vomiting and rash.

Assessment type	Non-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	Saxagliptin
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Saxagliptin	Placebo	
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: 1 %

Non-serious adverse events	Saxagliptin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 14 (28.57%)	8 / 14 (57.14%)	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			

Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 14 (0.00%) 0	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	3 / 14 (21.43%) 3	
Musculoskeletal and connective tissue disorders Invertebral disc protrusion subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 14 (0.00%) 0	
Infections and infestations Influenza subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	3 / 14 (21.43%) 3	
Urinary tract infection bacterial subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	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

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26642301>