Clinical trial results:
A phase IIa, dose-finding, double-blind, placebo-controlled, double-dummy, randomized, eightfold cross-over study to investigate the glucose lowering effects of dextromethorphan alone or in combination with sitagliptin in subjects with type 2 diabetes mellitus (T2DM) after an oral glucose tolerance test

Summary

EudraCT number	2013-003356-21
Trial protocol	DE
Global end of trial date	01 April 2014

Results information

Result version number	v1 (current)
This version publication date	19 February 2020
First version publication date	19 February 2020
Summary attachment (see zip file)	Publication to DXM2 (DXM2_manuscript_DiabCare_04_4_15_clean.pdf)

Trial information

Trial identification

Sponsor protocol code	00/0648-DXM2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01936025
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Profil Institut für Stoffwechselforschung GmbH
Sponsor organisation address	Hellersbergstr. 9, Neuss, Germany, 41460
Public contact	Regulatory Affairs, Profil Institut für Stoffwechselforschung GmbH, +49 21314018411, regulatory@profil.com
Scientific contact	Regulatory Affairs, Profil Institut für Stoffwechselforschung GmbH, +49 21314018411, regulatory@profil.com

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	04 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 April 2014
Global end of trial reached?	Yes
Global end of trial date	01 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

First primary objective:
to find the lowest dose of DXM that, compared to placebo, exerts BG lowering effects related to an OGTT

Second primary objective:
to demonstrate whether the administration of DXM on top of sitagliptin exerts additive BG lowering effects related to an OGTT as compared to sitagliptin alone and DXM alone.

Protection of trial subjects:

While the risk for hypoglycemia might theoretically increase related to an OGTT and treatment with DXM and sitagliptin, subjects will be under tight blood glucose control for several hours post-dosing and will not be discharged unless they will have lunch and their blood glucose is stable. The in-house stay will be prolonged at the discretion of the investigator and according to the individual situation in case of side-effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2013
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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	8
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment occured in one trial site

Pre-assignment

Screening details:

Eligible subjects were male individuals with a diagnosis of T2DM according to ADA criteria at least 4 months prior to screening and on a stable regimen of metformin monotherapy, for at least 3 months, 20 subjects completed the clinical trial.

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

Arms

Are arms mutually exclusive?	No
Arm title	DXM30

Arm description:

Treatment with 30 mg Dextromethorphan

Arm type	Experimental
Investigational medicinal product name	Dextromethorphan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

single dose: 1 capsule DXM 30 mg (+ 2 capsules DXM placebo + 1 tablet sita placebo)

Investigational medicinal product name	Sita Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

single dose: 1 tablet sita placebo (+ 1 capsule DXM 30 mg + 2 capsules DXM placebo)

Investigational medicinal product name	DXM Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

single dose: 2 capsules DXM placebo (+ 1 capsule DXM 30 mg + 1 tablet sita placebo)

Arm title	Sitagliptin

Arm description:

Treatment with 100 mg Sitagliptin

Arm type	Active comparator

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 100 mg sita (+ 3 capsules DXM placebo)

Investigational medicinal product name	DXM Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 3 capsules DXM placebo (+ 100 mg sita)

Arm title	DXM 30/Sita

Arm description:
Treatment with 30 mg Dextrometorphan and 100 mg Sitagliptin

Arm type	Experimental
Investigational medicinal product name	Dextromethorphan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 1 capsule DXM 30 mg (+ 2 capsules DXM placebo + 100 mg sita)

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 100 mg sita (+ 1 capsule DXM 30 mg + 2 capsules DXM placebo)

Investigational medicinal product name	DXM Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 2 capsules DXM placebo (+ 1 capsule DXM 30 mg + 100 mg sita)

Arm title	DXM60

Arm description:
Treatment with 60 mg Dextromethorphan

Arm type	Experimental
Investigational medicinal product name	Dextromethorphan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 2 capsules DXM 30 mg (+ 1 capsule DXM placebo + 1 tablet sita placebo)

Investigational medicinal product name	DXM Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 1 capsule DXM placebo (+ 2 capsules DXM 30 mg + 1 tablet sita placebo)

Investigational medicinal product name	Sita Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 1 tablet sita placebo (+ 2 capsules DXM 30 mg + 1 capsule DXM placebo)

Arm title	DXM90

Arm description:
Treatment with 90 mg Dextromethorphan

Arm type	Experimental
Investigational medicinal product name	Dextromethorphan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 3 capsules DXM 30 mg (+ 1 tablet sita placebo)

Investigational medicinal product name	Sita Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 1 tablet sita placebo (+ 3 capsules DXM 30 mg)

Arm title	DXM 60/Sita

Arm description:
Treatment with 60 mg Dextrometorphan and 100 mg Sitagliptin

Arm type	Experimental
Investigational medicinal product name	Dextromethorphan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 2 capsules DXM 30 mg (1 capsule DXM placebo + 100 mg sita)

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 100 mg sita (+ 2 capsules DXM 30 mg + 1 capsule DXM placebo)

Investigational medicinal product name	DXM Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 1 capsule DXM placebo (+ 2 capsules DXM 30 mg + 100 mg sita)

Arm title	DXM 90/Sita

Arm description:
Treatment with 90 mg Dextrometorphan and 100 mg Sitagliptin

Arm type	Experimental
Investigational medicinal product name	Dextromethorphan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 3 capsules DXM 30 mg (+ 100 mg sita)

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 100 mg sita (+ 3 capsules DXM 30 mg)

Arm title	Placebo

Arm description:
Placebo treatment only

Arm type	Placebo
Investigational medicinal product name	DXM Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
single dose: 3 capsules DXM placebo (+ 1 tablet sita placebo)

Investigational medicinal product name	Sita Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
single dose: 1 tablet sita placebo (+ 3 capsules DXM placebo)

Number of subjects in period 1	DXM30	Sitagliptin	DXM 30/Sita
Started	20	20	20
Completed	20	20	20

Number of subjects in period 1	DXM60	DXM90	DXM 60/Sita
Started	20	20	20
Completed	20	20	20

Number of subjects in period 1	DXM 90/Sita	Placebo
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
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)	8	8	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	63.1		
standard deviation	± 7.1	-	
Gender categorical Units: Subjects			
Male	20	20	

End points

End points reporting groups	
Reporting group title	DXM30
Reporting group description: Treatment with 30 mg Dextromethorphan	
Reporting group title	Sitagliptin
Reporting group description: Treatment with 100 mg Sitagliptin	
Reporting group title	DXM 30/Sita
Reporting group description: Treatment with 30 mg Dextrometorphan and 100 mg Sitagliptin	
Reporting group title	DXM60
Reporting group description: Treatment with 60 mg Dextromethorphan	
Reporting group title	DXM90
Reporting group description: Treatment with 90 mg Dextromethorphan	
Reporting group title	DXM 60/Sita
Reporting group description: Treatment with 60 mg Dextrometorphan and 100 mg Sitagliptin	
Reporting group title	DXM 90/Sita
Reporting group description: Treatment with 90 mg Dextrometorphan and 100 mg Sitagliptin	
Reporting group title	Placebo
Reporting group description: Placebo treatment only	

Primary: AUCBG(1-3h)	
End point title	AUCBG(1-3h)
End point description:	
End point type	Primary
End point timeframe: 1-3h	

End point values	DXM30	Sitagliptin	DXM 30/Sita	DXM60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	20	20
Units: mg/dl/h				
arithmetic mean (standard deviation)	430.2 (± 64.2)	412.4 (± 74.3)	393.2 (± 77.9)	425.2 (± 78.0)

End point values	DXM90	DXM 60/Sita	DXM 90/Sita	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	20	20
Units: mg/dl/h				
arithmetic mean (standard deviation)	433.4 (± 76.2)	393.3 (± 73.1)	391.0 (± 92.2)	444.7 (± 69.3)

Statistical analyses

Statistical analysis title	PD analysis DMX vs Placebo
Statistical analysis description: DMX 30, 60 or 90 vs placebo	
Comparison groups	DXM30 v Placebo v DXM90 v DXM60
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Mixed models analysis

Statistical analysis title	PD analysis Sita vs Placebo
Comparison groups	Placebo v Sitagliptin
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Statistical analysis title	PD analysis DXM/Sita vs Placebo
Statistical analysis description: 30, 60 or 90mg DMX + 100mg Sita vs placebo	
Comparison groups	Placebo v DXM 30/Sita v DXM 60/Sita v DXM 90/Sita
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis

Statistical analysis title	PD analysis DMX30,60/Sita vs DXM30,60
Statistical analysis description: 30 or 60 mg DXM + 100 mg Sita vs 30 or 60 mg DXM	
Comparison groups	DXM30 v DXM 30/Sita v DXM60 v DXM 60/Sita

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Statistical analysis title	PD analysis DMX90/Sita vs DXM90
Statistical analysis description: 90 mg DXM + 100 mg Sita vs 90 mg DXM	
Comparison groups	DXM90 v DXM 90/Sita
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	as reported
Dictionary version	n/a
Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)		
Vascular disorders			
Painful lymphnode swellings under both armpits			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Headache			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Husky voice			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Respiratory, thoracic and mediastinal disorders Creaky sounds right basal lung and upper bronchi right and left subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Cutaneous abscess on the back subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 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