Clinical trial results:
MaasFlex: A Double-Blind, Randomized, Phase IV, Mechanistic, Placebo-Controlled, Cross-Over, Single-Center Study to Evaluate the Effects of 2 Weeks Dapagliflozin Treatment on Nocturnal Substrate Oxidation, Glucose Metabolism and Muscle Mitochondrial Function in Individuals with Impaired Glucose Homeostasis

Summary

EudraCT number	2018-003283-31
Trial protocol	NL
Global end of trial date	07 July 2021

Results information

Result version number	v1 (current)
This version publication date	13 December 2023
First version publication date	13 December 2023

Trial information

Trial identification

Sponsor protocol code	NL67170.068.18

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03721874
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	maastricht university
Sponsor organisation address	universiteitssingel 50, maastricht, Netherlands,
Public contact	Project leader, Maastricht University, +31 433881502, p.schrauwen@maastrichtuniversity.nl
Scientific contact	Project leader, Maastricht University, +31 433881502, p.schrauwen@maastrichtuniversity.nl

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	09 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2021
Global end of trial reached?	Yes
Global end of trial date	07 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to examine the effects of dapagliflozin on nocturnal substrate oxidation in overweight or obese subjects with disrupted glucose homeostasis but without T2D.

Protection of trial subjects:

The Ethics Committee of Maastricht University Medical Center approved the study, which was registered at clinicaltrials.gov (NCT03721874) and conducted conform the declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2019
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	Netherlands: 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 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)	4
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment of participants will be done in the vicinity of Maastricht by means of posters in public spaces (supermarkets, hospital, pharmacy, general practitioners) and advertisements in local newspapers and on the internet.

Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:

Inclusion criteria:
– Provision of signed and dated informed consent prior to any study specific procedures.
– Men aged ≥ 40 and ≤ 75 years and post-menopausal women (defined as at least 1 year post cessation of menses) aged ≥ 50 and ≤ 75 years.
– BMI ≥ 27 and ≤ 38 kg/m2.
– Sedentary lifestyle (no

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	placebo

Arm description: -

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

Dosage and administration details:

1 tablet per day

Arm title	dapagliflozin

Arm description: -

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/day in the morning (orally).

Number of subjects in period 1	placebo	dapagliflozin
Started	14	14
Completed	14	14

Baseline characteristics

Reporting groups	
Reporting group title	overall period

Reporting group description:

Male and female individuals between 40 – 75 years and BMI of 27 – 38 kg/m2 without T2DM were eligible for participation. Moreover, the eligible participants should have a sedentary lifestyle and an impaired glucose homeostasis based on one or a combination of criteria including impaired fasting glucose, impaired glucose tolerance, HbA1c ≥ 5.7 and ≤ 6.4% (≥39 and ≤46 mmol/mol) and reduced glucose clearance rate ≤ 360 ml/min/m2 indicating insulin resistance calculated by the Oral Glucose Insulin Sensitivity (OGIS) model.

Reporting group values	overall period	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)	4	4	
From 65-84 years	10	10	
85 years and over	0	0	
Age continuous Units: years			
geometric mean	66.3		
standard deviation	± 6.2	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	8	8	

End points

End points reporting groups	
Reporting group title	placebo
Reporting group description: -	
Reporting group title	dapagliflozin
Reporting group description: -	

Primary: nocturnal fat oxidation	
End point title	nocturnal fat oxidation
End point description:	
End point type	Primary
End point timeframe: 14 days	

End point values	placebo	dapagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: g/day				
geometric mean (standard deviation)	79.2 (± 4.2)	89.5 (± 4.8)		

Statistical analyses

Statistical analysis title	cross over comparison
Comparison groups	placebo v dapagliflozin
Number of subjects included in analysis	28
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: 24h fat oxidation	
End point title	24h fat oxidation
End point description:	
End point type	Primary
End point timeframe: 14 days of treatment vs placebo	

End point values	placebo	dapagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: g/day				
geometric mean (standard deviation)	124.3 (± 6)	136.1 (± 7.6)		

Statistical analyses

Statistical analysis title	comparision placebo vs dapagliflozin
Comparison groups	placebo v dapagliflozin
Number of subjects included in analysis	28
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 30-4-2019 until 15-07-2001	
Adverse event reporting additional description: no adverse events	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	toetsingonline
Dictionary version	1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: no adverse events occurred in this small, experimental intervention

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/36592688