



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/m ² 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 $\leq 6.4\%$ (≥ 39 and ≤ 46 mmol/mol) and reduced glucose clearance rate ≤ 360 ml/min/m ² 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>