



Clinical trial results: The Effect of Empagliflozin on Cardiac and Kidney Metabolism in Persons with Type 2 Diabetes

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-001779-22 |
| Trial protocol | DK |
| Global end of trial date | 19 December 2019 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 05 March 2021 |
| First version publication date | 05 March 2021 |
| Summary attachment (see zip file) | Summary and abstract (Abstract_EMA.pdf) |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | 04.2017 |
|-----------------------|---------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AUH |
| Sponsor organisation address | Palle Juul-Jensens blv. , Aarhus N, Denmark, 8200 |
| Public contact | Department of Endocrinology, Aarhus University Hospital, katrine.mj@rm.dk |
| Scientific contact | Department of Endocrinology, Aarhus University Hospital, katrine.mj@rm.dk |

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 July 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 December 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 December 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Empagliflozin is a sodium-glucose cotransporter 2 (SGLT-2) inhibitor, and is used in treatment of diabetes type 2. It is previously shown that SGLT-2 inhibitors have a remarkable protective effect on the heart by reducing death caused by cardiac diseases with 38%. The reasons for these effects are still unknown, but it is known that SGLT-2 treatment increase ketogenesis. We have in a previous study found that ketone body infusion shifts cardiac metabolism towards ketone body oxidation, which possibly increases cardiac efficiency. It is also shown that SGLT-2 inhibitors have reno protective effects. The aim of this study is to examine the effects of SGLT-2 treatment by:

- Examination of substrate metabolism in heart and kidney measured by PET.
- Examination of perfusion and total energy consumption in the heart and kidney measured by PET.
- Indirect calorimetry, bloodsamples, fat- and muscle biopsies, DXA-scan, measurement of arterial stiffness and oral glucose tolerance test.

Protection of trial subjects:

Interviews about side effects to treatment
GCP guidelines has been followed

Background therapy:

Metformin

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 05 September 2017 |
| 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 | Denmark: 13 |
| Worldwide total number of subjects | 13 |
| EEA total number of subjects | 13 |

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 | 0 |

| | |
|---------------------------|---|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 6 |
| From 65 to 84 years | 7 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited through advertisements in local press in the period between September 2017 - August 2019

Pre-assignment

Screening details:

- Age: 50-70 years
- Type 2 diabetes for > 1 år
- HbA1c: 48-75 mmol/mol
- Metformin treatment as only anti diabetic medicin

One-week walkout between study periods

23 volunteers were screened for inclusion. 13 participants were included. 1 withdraw consent due to claustrophobia during scans.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Placebo and intervention in crossover (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:

Encapsulation of medicine.

Randomization and encapsulation of medicine were handled by the hospital pharmacy.

Randomization code was given after finalising data analysis

Arms

| | |
|-----------|--------------------------|
| Arm title | Placebo and intervention |
|-----------|--------------------------|

Arm description:

13 patients were randomized to receive placebo and Jardiance 25 mg in a crossover design. Both placebo and Jardiance were encapsulated.

Comment: I found it necessary to choose the one arm design in this report. If I selected two arms, the number of participants were doubled.

| | |
|--|--------------------------|
| Arm type | Placebo and intervention |
| Investigational medicinal product name | Jardiance |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

25 mg once daily encapsulated

| Number of subjects in period 1 | Placebo and intervention |
|---------------------------------------|--------------------------|
| Started | 13 |
| Completed | 12 |
| Not completed | 1 |
| Consent withdrawn by subject | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Placebo and intervention in crossover |
|-----------------------|---------------------------------------|

Reporting group description: -

| Reporting group values | Placebo and intervention in crossover | Total | |
|---|---------------------------------------|-------|--|
| Number of subjects | 13 | 13 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 6 | 6 | |
| From 65-84 years | 7 | 7 | |
| Age continuous Units: years | | | |
| arithmetic mean | 62 | | |
| standard deviation | ± 6 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 3 | |
| Male | 10 | 10 | |
| Ischemic heart disease Units: Subjects | | | |
| Yes | 1 | 1 | |
| No | 12 | 12 | |
| HbA1c Units: mmol/mol | | | |
| arithmetic mean | 56.7 | | |
| standard deviation | ± 5.5 | - | |
| Diabetes duration Units: years | | | |
| arithmetic mean | 4.6 | | |
| standard deviation | ± 3.0 | - | |

End points

End points reporting groups

| | |
|---|--------------------------|
| Reporting group title | Placebo and intervention |
| Reporting group description: 13 patients were randomized to receive placebo and Jardiance 25 mg in a crossover design. Both placebo and Jardiance were encapsulated. | |
| Comment: I found it necessary to choose the one arm design in this report. If I selected two arms, the number of participants were doubled. | |

Primary: Cardiac uptake of free fatty acids

| | |
|---|---|
| End point title | Cardiac uptake of free fatty acids ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: After four weeks of treatment | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis are described in the attached article (more information)

| End point values | Placebo and intervention | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: umol/100g/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| Jardiance | 7.7 (± 3.7) | | | |
| Placebo | 8.2 (± 3.6) | | | |

| | |
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| Attachments (see zip file) | fig2_2_columns.pdf |
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Statistical analyses

No statistical analyses for this end point

Primary: Cardiac glucose uptake

| | |
|---|---------------------------------------|
| End point title | Cardiac glucose uptake ^[2] |
| End point description: | |
| End point type | Primary |
| End point timeframe: After four weeks of treatment | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis are described in the attached article (more information)

| End point values | Placebo and intervention | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: umol/100g/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| Jardiance | 0.6 (± 0.6) | | | |
| Placebo | 1.4 (± 0.6) | | | |

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| Attachments (see zip file) | fig2_2_columns.pdf |
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Statistical analyses

No statistical analyses for this end point

Primary: Cardiac oxygen consumption

| | |
|-------------------------------|---|
| End point title | Cardiac oxygen consumption ^[3] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| After four weeks of treatment | |

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis are described in the attached article (more information)

| End point values | Placebo and intervention | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: ml/100g/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| Jardiance | 8.8 (± 1.0) | | | |
| Placebo | 9.7 (± 1.4) | | | |

| | |
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| Attachments (see zip file) | fig3_2_columns.pdf |
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Statistical analyses

No statistical analyses for this end point

Primary: Myocardial perfusion in rest

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|-----------------|---|
| End point title | Myocardial perfusion in rest ^[4] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

After four weeks of treatment

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis are described in the attached article (more information)

| End point values | Placebo and intervention | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: ml/g/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| Jardiance | 0.74 (± 0.10) | | | |
| Placebo | 0.85 (± 0.10) | | | |

| | |
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| Attachments (see zip file) | fig3_2_columns.pdf |
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

09.10.2017 - 19.12.2019

Adverse event reporting additional description:

Weekly meetings with the participants with questions regarding adverse events.

Assessment type

Systematic

Dictionary used

Dictionary name

MedDRA

Dictionary version

10.0

Frequency threshold for reporting non-serious adverse events: 5 %

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 have been reported

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/33334875>