



## Clinical trial results:

### The effects of SGLT2-inhibition in patients with non-diabetic chronic kidney disease on renal hemodynamics, kidney function and vasoactive hormones

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2019-004467-50   |
| Trial protocol           | DK               |
| Global end of trial date | 22 December 2022 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 22 February 2025 |
| First version publication date | 22 February 2025 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | SFN-3-2019 |
|-----------------------|------------|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | University Clinic of Nephrology and Hypertension, Regional Hospital Holstebro  |
| Sponsor organisation address | Hospitalparken 15, Herning, Denmark, 7400  |
| Public contact               | Steffen Flindt Nielsen, University Clinic of Nephrology and Hypertension, Regional Hospital Holstebro, 0045 78436588, steffen.nielsen@midt.rm.dk |
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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:

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**Results analysis stage**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 22 December 2022 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 22 December 2022 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 22 December 2022 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

To examine the effects of SGLT2-inhibition versus placebo on renal hemodynamics in patients with non-diabetic chronic kidney disease

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 March 2021 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 21 |
| Worldwide total number of subjects   | 21          |
| EEA total number of subjects         | 21          |

Notes:

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**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)                      | 9  |
| From 65 to 84 years                       | 12 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 21 |
| Number of subjects completed | 21 |

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Empagliflozin   |
| Is this the baseline period? | No  |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Investigator, Monitor, Data analyst, Carer, Subject, Assessor |

### Arms

|  |               |
|--|---------------|
| Arm title                              | Empagliflozin |
| Arm description: -                     |               |
| Arm type                               | Experimental  |
| Investigational medicinal product name | Empagliflozin |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Tablet        |
| Routes of administration               | Oral use      |

Dosage and administration details:

10 mg x 1 day

| Number of subjects in period 1 | Empagliflozin |
|--------------------------------|---------------|
| Started                        | 21            |
| Completed                      | 16            |
| Not completed                  | 5             |
| Consent withdrawn by subject   | 3             |
| Adverse event, non-fatal       | 1             |
| non-compliance                 | 1             |

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**Period 2**

|                              |   |
|------------------------------|---|
| Period 2 title               | Placebo   |
| Is this the baseline period? | Yes <sup>[1]</sup>  |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

**Arms**

|  |          |
|--|----------|
| <b>Arm title</b>                       | 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 x 1 day

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: It is a cross over design, where placebo is the "baseline"

|   |         |
|---|---------|
| <b>Number of subjects in period 2<sup>[2]</sup></b> | Placebo |
| Started   | 16      |
| Completed   | 16      |

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Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: see above

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Reporting group values                                | Placebo | Total |  |
|---|---------|-------|--|
| Number of subjects                                    | 16      | 16    |  |
| Age categorical                                       |         |       |  |
| Units: Subjects                                       |         |       |  |
| In utero  |         | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) |         | 0     |  |
| Newborns (0-27 days)                                  |         | 0     |  |
| Infants and toddlers (28 days-23<br>months)           |         | 0     |  |
| Children (2-11 years)                                 |         | 0     |  |
| Adolescents (12-17 years)                             |         | 0     |  |
| Adults (18-64 years)                                  |         | 0     |  |
| From 65-84 years                                      |         | 0     |  |
| 85 years and over                                     |         | 0     |  |
| Age continuous  |         |       |  |
| Units: years  |         |       |  |
| arithmetic mean                                       | 66.9    |       |  |
| standard deviation                                    | ± 8.2   | -     |  |
| Gender categorical                                    |         |       |  |
| Units: Subjects                                       |         |       |  |
| Female  | 7       | 7     |  |
| Male  | 9       | 9     |  |

## End points

### End points reporting groups

|                                |               |
|--------------------------------|---------------|
| Reporting group title          | Empagliflozin |
| Reporting group description: - |               |
| Reporting group title          | Placebo       |
| Reporting group description: - |               |

### Primary: Renal Blood flow

|                                     |                  |
|-------------------------------------|------------------|
| End point title                     | Renal Blood flow |
| End point description:              |                  |
| End point type                      | Primary          |
| End point timeframe:                |                  |
| at the end of each treatment period |                  |

| End point values                              | Empagliflozin       | Placebo             |  |  |
|---|---------------------|---------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                   | 16                  | 16                  |  |  |
| Units: ml/min/ccm                             |                     |                     |  |  |
| geometric mean (inter-quartile range (Q1-Q3)) | 1.17 (0.96 to 1.34) | 1.18 (0.99 to 1.42) |  |  |

### Statistical analyses

|   |                         |
|---|-------------------------|
| Statistical analysis title              | paired t-test           |
| Comparison groups                       | Empagliflozin v Placebo |
| Number of subjects included in analysis | 32                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.72                  |
| Method                                  | t-test, 2-sided         |

### Secondary: GFR

|                                     |           |
|-------------------------------------|-----------|
| End point title                     | GFR       |
| End point description:              |           |
| End point type                      | Secondary |
| End point timeframe:                |           |
| at the end of each treatment period |           |

| End point values                              | Empagliflozin       | Placebo             |  |  |
|---|---------------------|---------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                   | 16                  | 16                  |  |  |
| Units: ml/min/1.73m2                          |                     |                     |  |  |
| geometric mean (inter-quartile range (Q1-Q3)) | 30.1 (21.9 to 42.6) | 33.8 (25.7 to 47.1) |  |  |

### Statistical analyses

|   |                         |
|---|-------------------------|
| Statistical analysis title              | paired t-test           |
| Comparison groups                       | Empagliflozin v Placebo |
| Number of subjects included in analysis | 32                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.018                 |
| Method                                  | t-test, 2-sided         |

### Secondary: RVR

|                           |           |
|---------------------------|-----------|
| End point title           | RVR       |
| End point description:    |           |
| End point type            | Secondary |
| End point timeframe:      |           |
| at the end of each period |           |

| End point values                              | Empagliflozin       | Placebo             |  |  |
|---|---------------------|---------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                   | 16                  | 16                  |  |  |
| Units: mmHg/ml/min                            |                     |                     |  |  |
| geometric mean (inter-quartile range (Q1-Q3)) | 0.42 (0.29 to 0.59) | 0.43 (0.30 to 0.56) |  |  |

### Statistical analyses

|                            |                         |
|----------------------------|-------------------------|
| Statistical analysis title | paired t-test           |
| Comparison groups          | Empagliflozin v Placebo |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 32              |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.67          |
| Method                                  | t-test, 2-sided |

### Secondary: systolic blood pressure

|   |                         |
|---|-------------------------|
| End point title                                   | systolic blood pressure |
| End point description:                            |                         |
| End point type                                    | Secondary               |
| End point timeframe:<br>at the end of each period |                         |

| End point values                     | Empagliflozin   | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 16              | 16              |  |  |
| Units: mmHg                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 122 (± 13)      | 126 (± 12)      |  |  |

### Statistical analyses

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>       | paired t-test           |
| Comparison groups                       | Empagliflozin v Placebo |
| Number of subjects included in analysis | 32                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.07                  |
| Method                                  | t-test, 2-sided         |

### Secondary: diastolic blood pressure

|   |                          |
|---|--------------------------|
| End point title   | diastolic blood pressure |
| End point description:                                      |                          |
| End point type  | Secondary                |
| End point timeframe:<br>at the end of each treatment period |                          |



| End point values                     | Empagliflozin   | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 16              | 16              |  |  |
| Units: mmHg                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 77 (± 10)       | 79 (± 9)        |  |  |

### Statistical analyses

| Statistical analysis title              | paired t-test           |
|---|-------------------------|
| Comparison groups                       | Empagliflozin v Placebo |
| Number of subjects included in analysis | 32                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.1                   |
| Method                                  | t-test, 2-sided         |

### Secondary: TVR

|                           |           |
|---------------------------|-----------|
| End point title           | TVR       |
| End point description:    |           |
| End point type            | Secondary |
| End point timeframe:      |           |
| at the end of each period |           |

| End point values                     | Empagliflozin   | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 16              | 16              |  |  |
| Units: dyn*s/m5                      |                 |                 |  |  |
| arithmetic mean (standard deviation) | 1678 (± 136)    | 1721 (± 136)    |  |  |

### Statistical analyses

| Statistical analysis title              | paired t-test           |
|---|-------------------------|
| Comparison groups                       | Empagliflozin v Placebo |
| Number of subjects included in analysis | 32                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.03                  |
| Method                                  | t-test, 2-sided         |

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**Secondary: heart rate**

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|                 |            |
|-----------------|------------|
| End point title | heart rate |
|-----------------|------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

at the end of each period

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| End point values                     | Empagliflozin   | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 16              | 16              |  |  |
| Units: min-1                         |                 |                 |  |  |
| arithmetic mean (standard deviation) | 68 (± 8)        | 69 (± 9)        |  |  |

**Statistical analyses**

|   |                         |
|---|-------------------------|
| Statistical analysis title              | paired t-test           |
| Comparison groups                       | Empagliflozin v Placebo |
| Number of subjects included in analysis | 32                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.37                  |
| Method                                  | t-test, 2-sided         |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from beginning of trial to LPLV+1 Week

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | total trial |
|-----------------------|-------------|

Reporting group description:

total trial

| Serious adverse events                            | total trial    |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 21 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    |                |  |  |

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

| Non-serious adverse events                            | total trial                               |  |  |
|---|---|--|--|
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 8 / 21 (38.10%)                           |  |  |
| Cardiac disorders                                     |   |  |  |
| Hypotension   |   |  |  |
| subjects affected / exposed                           | 2 / 21 (9.52%)                            |  |  |
| occurrences (all)                                     | 2   |  |  |
| General disorders and administration site conditions  |   |  |  |
| Dehydration   |   |  |  |
| subjects affected / exposed                           | 1 / 21 (4.76%)                            |  |  |
| occurrences (all)                                     | 1   |  |  |
| Febrile infection                                     |   |  |  |
| subjects affected / exposed                           | 1 / 21 (4.76%)                            |  |  |
| occurrences (all)                                     | 1   |  |  |
| Vasodilatation  | Additional description: Vasovagal episode |  |  |

|  |   |  |  |
|--|---|--|--|
| subjects affected / exposed<br>occurrences (all)   | 2 / 21 (9.52%)<br>2   |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 1 / 21 (4.76%)<br>1   |  |  |
| Renal and urinary disorders<br>Renal injury<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)         | 1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1                    |  |  |
| Musculoskeletal and connective tissue disorders<br>Pain  | Additional description: 3 hours of pain under the right curvature |  |  |
| subjects affected / exposed<br>occurrences (all)   | 1 / 21 (4.76%)<br>1   |  |  |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Erysipelas<br>subjects affected / exposed<br>occurrences (all) | 1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1                    |  |  |
| Metabolism and nutrition disorders<br>Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 21 (4.76%)<br>1   |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39810756>