



## Clinical trial results:

### Randomized, controlled interventional trial to investigate the efficacy of amiloride for the treatment of edema in human nephrotic syndrome

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2019-002607-18 |
| Trial protocol           | DE             |
| Global end of trial date | 30 April 2023  |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 27 June 2024   |
| First version publication date    | 27 June 2024   |
| Summary attachment (see zip file) | Publication (Schork_Acta Physiologica_2024_Amiloride vs furosemide for treatemnt of edema in NS.pdf) |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | AmiloridNS-01 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05079789 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | University Hospital Tuebingen  |
| Sponsor organisation address | Geissweg 3, Tuebingen, Germany, 72076  |
| Public contact               | Secretary's office Dep. Int.Med. IV, Univerity Hospital Tuebingen, +49 707129 83172, |
| Scientific contact           | Secretary's office Dep. Int.Med. IV, Univerity Hospital Tuebingen, +49 707129 83172, |

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                       | 02 February 2024 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 30 April 2023    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 30 April 2023    |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

Objective of the study is to prove the efficacy and superiority of amiloride for reduction of edema and overhydration in human nephrotic syndrome in comparison to standard medication with furosemide.

Protection of trial subjects:

No further follow up is necessary for this Phase IIIB study after completion of the follow up period according to the study protocol.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 08 June 2020 |
| 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)                      | 17 |
| From 65 to 84 years                       | 3  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 20 |
| Number of subjects completed | 20 |

### Period 1

|                              |                           |
|------------------------------|---------------------------|
| Period 1 title               | Period 1 (overall period) |
| Is this the baseline period? | Yes                       |
| Allocation method            | Randomised - controlled   |
| Blinding used                | Not blinded               |

### Arms

|  |              |
|--|--------------|
| Are arms mutually exclusive?           | Yes          |
| <b>Arm title</b>                       | Amiloride    |
| Arm description: -                     |              |
| Arm type                               | Experimental |
| Investigational medicinal product name | Amiloride    |
| Investigational medicinal product code |              |
| Other name                             | Modamide®    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

initial dose 5 mg once daily, maximum dose 15 mg once daily

|  |                   |
|--|-------------------|
| <b>Arm title</b>                       | Furosemide        |
| Arm description: -                     |                   |
| Arm type                               | Active comparator |
| Investigational medicinal product name | Furosemide        |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Tablet            |
| Routes of administration               | Oral use          |

Dosage and administration details:

initial dose 40 mg once daily, maximum dose 120 mg once daily

| <b>Number of subjects in period 1</b> | Amiloride | Furosemide |
|---------------------------------------|-----------|------------|
| Started                               | 10        | 10         |
| Completed                             | 10        | 10         |

## Baseline characteristics

## End points

### End points reporting groups

|                                |            |
|--------------------------------|------------|
| Reporting group title          | Amiloride  |
| Reporting group description: - |            |
| Reporting group title          | Furosemide |
| Reporting group description: - |            |

### Primary: Primary end point: decrease of overhydration (OH) at day 8

|   |  |
|---|--|
| End point title   | Primary end point: decrease of overhydration (OH) at day 8 |
| End point description:<br>decrease of overhydration (OH) at day 8 |  |
| End point type  | Primary  |
| End point timeframe:<br>8 days                                    |  |

| End point values                      | Amiloride         | Furosemide        |  |  |
|---------------------------------------|-------------------|-------------------|--|--|
| Subject group type                    | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed           | 10                | 10                |  |  |
| Units: % of extracellular water (ECW) |                   |                   |  |  |
| median (inter-quartile range (Q1-Q3)) | 1.95 (0.8 to 6.4) | 5.15 (0.9 to 8.3) |  |  |

### Statistical analyses

|   |                              |
|---|------------------------------|
| Statistical analysis title              | Analysis of primary endpoint |
| Comparison groups                       | Amiloride v Furosemide       |
| Number of subjects included in analysis | 20                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.38                       |
| Method                                  | t-test, 1-sided              |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

23 days for every subject.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |       |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

|                    |            |
|--------------------|------------|
| Dictionary version | 2012/C 302 |
|--------------------|------------|

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Amiloride |
|-----------------------|-----------|

Reporting group description: -

|                       |            |
|-----------------------|------------|
| Reporting group title | Furosemide |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events  | Amiloride       | Furosemide      |  |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events                         |                 |                 |  |
| subjects affected / exposed   | 1 / 10 (10.00%) | 4 / 10 (40.00%) |  |
| number of deaths (all causes)   | 0               | 0               |  |
| number of deaths resulting from adverse events                            | 0               | 0               |  |
| Surgical and medical procedures   |                 |                 |  |
| delayed discharge from hospital due to macrohematuria after kidney biopsy |                 |                 |  |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all                           | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0           |  |
| Cardiac disorders   |                 |                 |  |
| myocardial infarction   |                 |                 |  |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all                           | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0           |  |
| pericardial effusion with in-hospital monitoring                          |                 |                 |  |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all                           | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders  |                 |                 |  |
| abdominal pain with diarrhea with in-hospital treatment                   |                 |                 |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Renal and urinary disorders                     |                |                 |  |
| AKI stage 2 with in-hospital treatment          |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Amiloride       | Furosemide        |  |
|---|-----------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                 |                   |  |
| subjects affected / exposed                           | 9 / 10 (90.00%) | 10 / 10 (100.00%) |  |
| Surgical and medical procedures                       |                 |                   |  |
| planned hospitalization for kidney biopsy             |                 |                   |  |
| subjects affected / exposed                           | 2 / 10 (20.00%) | 3 / 10 (30.00%)   |  |
| occurrences (all)                                     | 2               | 3                 |  |
| Nervous system disorders                              |                 |                   |  |
| dizziness   |                 |                   |  |
| subjects affected / exposed                           | 0 / 10 (0.00%)  | 1 / 10 (10.00%)   |  |
| occurrences (all)                                     | 0               | 1                 |  |
| headache  |                 |                   |  |
| subjects affected / exposed                           | 0 / 10 (0.00%)  | 1 / 10 (10.00%)   |  |
| occurrences (all)                                     | 0               | 1                 |  |
| Gastrointestinal disorders                            |                 |                   |  |
| nausea  |                 |                   |  |
| subjects affected / exposed                           | 2 / 10 (20.00%) | 0 / 10 (0.00%)    |  |
| occurrences (all)                                     | 2               | 0                 |  |
| Respiratory, thoracic and mediastinal disorders       |                 |                   |  |
| epistaxis   |                 |                   |  |
| subjects affected / exposed                           | 1 / 10 (10.00%) | 1 / 10 (10.00%)   |  |
| occurrences (all)                                     | 1               | 1                 |  |
| Hepatobiliary disorders                               |                 |                   |  |



|  |  |  |  |
|--|--|--|--|
| elevated liver enzymes<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0                              | 1 / 10 (10.00%)<br>1                           |  |
| Skin and subcutaneous tissue disorders<br>rash<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0                              | 1 / 10 (10.00%)<br>1                           |  |
| Renal and urinary disorders<br>urinary infection<br>subjects affected / exposed<br>occurrences (all)<br><br>hypervolemia (worsening)<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1<br><br>1 / 10 (10.00%)<br>1 | 0 / 10 (0.00%)<br>0<br><br>0 / 10 (0.00%)<br>0 |  |
| Musculoskeletal and connective tissue disorders<br>cramps of legs and hands<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0                              | 1 / 10 (10.00%)<br>1                           |  |
| Infections and infestations<br>SARS CoV 2 infection<br>subjects affected / exposed<br>occurrences (all)  | 2 / 10 (20.00%)<br>2                             | 1 / 10 (10.00%)<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