



## Clinical trial results:

### A Prospective, Randomized, Open, Blinded Endpoint (PROBE), Clinical Trial to Assess The Renal and Humoral Effects of Sevelamer Carbonate in Patients with Chronic Kidney Disease and Residual Proteinuria Despite Best Available Treatment

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2012-005416-26    |
| Trial protocol           | IT                |
| Global end of trial date | 21 September 2015 |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 18 December 2019                                       |
| First version publication date    | 18 December 2019                                       |
| Summary attachment (see zip file) | Article (AJKD_The ANSWER Randomized Trial article.pdf) |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | ANSWER |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02464891 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Istituto di Ricerche Farmacologiche Mario Negri IRCCS   |
| Sponsor organisation address | via G.B. Camozzi, 3, Ranica BG, Italy, 24020  |
| Public contact               | Dep. Renal Medicine, Clinical Research Center for Rare Disease "Aldo & Cele Daccò", 0039 03545351, piero.ruggenenti@marionegri.it |
| Scientific contact           | Dep. Renal Medicine, Clinical Research Center for Rare Disease "Aldo & Cele Daccò", 0039 03545351, piero.ruggenenti@marionegri.it |

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                       | 27 September 2016 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 21 September 2015 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 21 September 2015 |
| Was the trial ended prematurely?                     | No                |

Notes:

---

**General information about the trial**

Main objective of the trial:

To assess the effect of 3-month Sevelamer carbonate therapy compared to standard therapy on 24 h urinary protein excretion in patients with Chronic Kidney Disease (CKD) and residual proteinuria despite optimized Renin Angiotensin System (RAS) inhibitor therapy:

Protection of trial subjects:

The study was conducted in conformance with Good Clinical Practice standards and applicable country regulations regarding ethical committee review, informed consent and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 18 November 2013 |
| 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 | Italy: 53 |
| Worldwide total number of subjects   | 53        |
| EEA total number of subjects         | 53        |

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)                      | 36 |
| From 65 to 84 years                       | 17 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

2 Italian centers (Clinical Research Center for Rare Diseases Aldo e Cele Daccò, Ranica, Bergamo, and Bianchi-Melacrino-Morelli Hospital, Nephrology Unit, Reggio Calabria) were activated respectively between November 2013 and December 2014.

### Pre-assignment

Screening details:

72 subjects were screened for inclusion in the study. 53 subjects were randomized. Of those not randomized, 9 did not meet inclusion criteria, 3 were lost to follow up and 7 declined to participate.

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | No      |
| <b>Arm title</b>             | Renvela |

Arm description:

Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level  $\leq 4$  or  $>4$  mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Renvela      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

1600 mg, 3 times per day during meals,

|                  |            |
|------------------|------------|
| <b>Arm title</b> | No Renvela |
|------------------|------------|

Arm description:

Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level  $\leq 4$  or  $>4$  mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily.

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| Number of subjects in period 1 | Renvela | No Renvela |
|--------------------------------|---------|------------|
| Started                        | 53      | 53         |
| Completed                      | 49      | 53         |
| Not completed                  | 4       | 0          |
| Adverse event, non-fatal       | 4       | -          |

## Period 2

|                              |                |
|------------------------------|----------------|
| Period 2 title               | Washout Period |
| Is this the baseline period? | No             |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

## Arms

|           |                |
|-----------|----------------|
| Arm title | Washout Period |
|-----------|----------------|

### Arm description:

Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level  $\leq 4$  or  $>4$  mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily.

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| Number of subjects in period 2 | Washout Period |
|--------------------------------|----------------|
| Started                        | 53             |
| Completed                      | 53             |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Treatment period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values       | Treatment period | Total |  |
|------------------------------|------------------|-------|--|
| Number of subjects           | 53               | 53    |  |
| Age categorical              |                  |       |  |
| Units: Subjects              |                  |       |  |
| Adults (18-64 years)         | 38               | 38    |  |
| From 65-84 years             | 15               | 15    |  |
| 85 years and over            | 0                | 0     |  |
| Age continuous               |                  |       |  |
| Units: years                 |                  |       |  |
| arithmetic mean              | 55               |       |  |
| standard deviation           | ± 17             | -     |  |
| Gender categorical           |                  |       |  |
| Units: Subjects              |                  |       |  |
| Female                       | 11               | 11    |  |
| Male                         | 42               | 42    |  |
| Body mass Index              |                  |       |  |
| Units: Kg/m2                 |                  |       |  |
| arithmetic mean              | 27               |       |  |
| standard deviation           | ± 4              | -     |  |
| Systolic Blood Pressure      |                  |       |  |
| Units: mm Hg                 |                  |       |  |
| arithmetic mean              | 128              |       |  |
| standard deviation           | ± 22             | -     |  |
| Diastolic Blood Pressure     |                  |       |  |
| Units: mm Hg                 |                  |       |  |
| arithmetic mean              | 73               |       |  |
| standard deviation           | ± 10             | -     |  |
| Pulse Rate                   |                  |       |  |
| Units: Beats/min             |                  |       |  |
| arithmetic mean              | 69               |       |  |
| standard deviation           | ± 11             | -     |  |
| Creatinine                   |                  |       |  |
| Units: mg/dl                 |                  |       |  |
| median                       | 1.6              |       |  |
| inter-quartile range (Q1-Q3) | 1 to 2.3         | -     |  |
| Phosphate                    |                  |       |  |
| Units: mg/dl                 |                  |       |  |
| arithmetic mean              | 3.8              |       |  |
| standard deviation           | ± 0.6            | -     |  |
| Calcium                      |                  |       |  |
| Units: mg/dl                 |                  |       |  |
| arithmetic mean              | 9.2              |       |  |
| standard deviation           | ± 0.4            | -     |  |

|   |                      |   |  |
|---|----------------------|---|--|
| PTH<br>Units: pg/dL<br>arithmetic mean<br>standard deviation  | 70<br>± 33           | - |  |
| Magnesium<br>Units: mg/dL<br>arithmetic mean<br>standard deviation  | 1.97<br>± 0.22       | - |  |
| Cholesterol<br>Units: mg/dL<br>arithmetic mean<br>standard deviation                                      | 181<br>± 38          | - |  |
| LDL cholestrol<br>Units: mg/dL<br>arithmetic mean<br>standard deviation                                   | 113<br>± 33          | - |  |
| Triglycerides<br>Units: mg/dL<br>median<br>inter-quartile range (Q1-Q3)                                   | 114<br>88 to 159     | - |  |
| Albumin<br>Units: g/dL<br>arithmetic mean<br>standard deviation   | 3.6<br>± 0.4         | - |  |
| Hemoglobin<br>Units: g/dL<br>arithmetic mean<br>standard deviation  | 12.9<br>± 1.8        | - |  |
| Urine Protein<br>Units: g/24 H<br>median<br>inter-quartile range (Q1-Q3)                                  | 1.54<br>0.97 to 2.59 | - |  |
| Urine Albumin<br>Units: µg/min<br>median<br>inter-quartile range (Q1-Q3)                                  | 829<br>481 to 1372   | - |  |
| mGFR<br>Units: mL/min/1.73m2<br>arithmetic mean<br>standard deviation                                     | 49.3<br>± 23.5       | - |  |
| Fractional Albumin clearance<br>Units: absolute value x 1000000<br>median<br>inter-quartile range (Q1-Q3) | 43<br>18 to 93       | - |  |

## End points

### End points reporting groups

|   |                |
|---|----------------|
| Reporting group title   | Renvela        |
| Reporting group description:<br>Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level $\leq 4$ or $>4$ mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily. |                |
| Reporting group title   | No Renvela     |
| Reporting group description:<br>Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level $\leq 4$ or $>4$ mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily. |                |
| Reporting group title   | Washout Period |
| Reporting group description:<br>Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level $\leq 4$ or $>4$ mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily. |                |

### Primary: Urinary protein 24 H

|   |                      |
|---|----------------------|
| End point title   | Urinary protein 24 H |
| End point description:  |                      |
| End point type  | Primary              |
| End point timeframe:<br>Changes in 24-hour proteinuria at the end of the 2 treatment periods with sevelamer or without sevelamer compared to each pretreatment period. Three consecutive 24-hour proteinuria measurements were obtained at each visit and the mean of the 3 samples |                      |

| End point values                      | Renvela            | No Renvela          |  |  |
|---------------------------------------|--------------------|---------------------|--|--|
| Subject group type                    | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed           | 49                 | 53                  |  |  |
| Units: g/24 H                         |                    |                     |  |  |
| median (inter-quartile range (Q1-Q3)) | 1.36 (0.77 to 2.6) | 1.48 (0.81 to 2.77) |  |  |

## Statistical analyses

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Change in Urine Proteine Excretion 24 H |
| Statistical analysis description:<br>changes in 24-hour proteinuria at the end of the 2 treatment periods with sevelamer or without sevelamer compared to each pretreatment period. Three consecutive 24-hour proteinuria measurements were obtained at each visit and the mean of the 3 samples was used. |   |
| Comparison groups  | Renvela v No Renvela                    |
| Number of subjects included in analysis  | 102                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority <sup>[1]</sup>              |
| P-value  | = 0.1 <sup>[2]</sup>                    |
| Method   | Wilcoxon (Mann-Whitney)                 |

Notes:

[1] - Wilcoxon signed rank test performed between pre-post treatment period.

[2] - P= 0.1 referred to Renvela vs non-Renvela period; differences between pre and post renvela treatment reported a p = 0.1; differences between pre and post non-renvela treatment reported a p = 0.5.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The adverse events will be reported during whole study up to 30 days after last dose of study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Renvela |
|-----------------------|---------|

Reporting group description:

Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level  $\leq 4$  or  $>4$  mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily.

|                       |            |
|-----------------------|------------|
| Reporting group title | No Renvela |
|-----------------------|------------|

Reporting group description:

Patients who met the selection criteria and were on maximal tolerated doses of ramipril and irbesartan were initially stratified according to serum phosphate level  $\leq 4$  or  $>4$  mg/dL. Each group was then randomly assigned to 1 of 2 treatment sequences: (1) 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times per day during meals, followed by a 1- month washout, and 3 months without sevelamer; or (2) 3 months without sevelamer, followed by a 1-month washout, and 3 months of treatment with sevelamer carbonate, 1,600 mg, 3 times daily.

| Serious adverse events  | Renvela        | No Renvela     |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events                   |                |                |  |
| subjects affected / exposed   | 2 / 53 (3.77%) | 2 / 53 (3.77%) |  |
| number of deaths (all causes)                                       | 0              | 0              |  |
| number of deaths resulting from adverse events                      | 0              | 0              |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |  |
| Colon adenoma   |                |                |  |
| subjects affected / exposed   | 0 / 53 (0.00%) | 1 / 53 (1.89%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications                      |                |                |  |
| Ankle fracture  |                |                |  |
| subjects affected / exposed   | 1 / 53 (1.89%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Nervous system disorders  |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Brain Hemorrhage                                |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Anal abscess                                    |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 53 (1.89%) |  |
| 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: 0 %

| <b>Non-serious adverse events</b>                     | Renvela          | No Renvela       |  |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 35 / 53 (66.04%) | 30 / 53 (56.60%) |  |
| Vascular disorders                                    |                  |                  |  |
| Hypotension   |                  |                  |  |
| subjects affected / exposed                           | 5 / 53 (9.43%)   | 7 / 53 (13.21%)  |  |
| occurrences (all)                                     | 5                | 8                |  |
| Claudicatio intermittens                              |                  |                  |  |
| subjects affected / exposed                           | 1 / 53 (1.89%)   | 0 / 53 (0.00%)   |  |
| occurrences (all)                                     | 1                | 0                |  |
| General disorders and administration site conditions  |                  |                  |  |
| legs edema  |                  |                  |  |
| subjects affected / exposed                           | 1 / 53 (1.89%)   | 0 / 53 (0.00%)   |  |
| occurrences (all)                                     | 1                | 0                |  |
| Immune system disorders                               |                  |                  |  |
| Allergic reaction                                     |                  |                  |  |
| subjects affected / exposed                           | 0 / 53 (0.00%)   | 1 / 53 (1.89%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Reproductive system and breast disorders              |                  |                  |  |
| Worsening symptoms of prostatic hypertrophy           |                  |                  |  |
| subjects affected / exposed                           | 1 / 53 (1.89%)   | 0 / 53 (0.00%)   |  |
| occurrences (all)                                     | 1                | 0                |  |
| Respiratory, thoracic and mediastinal disorders       |                  |                  |  |

|   |  |  |  |
|---|--|--|--|
| Common cold, cough, pharyngitis or<br>bronchitis<br>subjects affected / exposed<br>occurrences (all)  | 5 / 53 (9.43%)<br>5  | 7 / 53 (13.21%)<br>7   |  |
| Psychiatric disorders<br>Dysphoria<br>subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>1  | 0 / 53 (0.00%)<br>0  |  |
| Investigations<br>Increase of CPK levels<br>subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>1  | 0 / 53 (0.00%)<br>0  |  |
| Injury, poisoning and procedural<br>complications<br>Tendro tear, joint or traumatic pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 53 (1.89%)<br>1  | 4 / 53 (7.55%)<br>4  |  |
| Cardiac disorders<br>Sinus bradycardia<br>subjects affected / exposed<br>occurrences (all)<br><br>Ventricular, Supraventricular<br>extrasystoles<br>subjects affected / exposed<br>occurrences (all)<br><br>Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypertensive cardiopathy<br>subjects affected / exposed<br>occurrences (all) | 2 / 53 (3.77%)<br>2<br><br>1 / 53 (1.89%)<br>1<br><br>0 / 53 (0.00%)<br>0<br><br>0 / 53 (0.00%)<br>0 | 1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1 |  |
| Nervous system disorders<br>Syncope or dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Leg paresthesia   | 1 / 53 (1.89%)<br>1<br><br>0 / 53 (0.00%)<br>0   | 1 / 53 (1.89%)<br>2<br><br>1 / 53 (1.89%)<br>1   |  |

|  |  |  |  |
|--|--|--|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 53 (0.00%)<br>0  | 1 / 53 (1.89%)<br>1  |  |
| Blood and lymphatic system disorders<br>Anemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 53 (1.89%)<br>1  | 3 / 53 (5.66%)<br>3  |  |
| Ear and labyrinth disorders<br>Otitis media<br>subjects affected / exposed<br>occurrences (all)  | 0 / 53 (0.00%)<br>0  | 1 / 53 (1.89%)<br>1  |  |
| Eye disorders<br>Retinal exudates<br>subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>1  | 0 / 53 (0.00%)<br>0  |  |
| Gastrointestinal disorders<br>Gastroenteritis, diarrhea, abdominal<br>pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>lumbar pain or muscle pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all)<br><br>Meteorism<br>subjects affected / exposed<br>occurrences (all)<br><br>Pancreatic cyst<br>subjects affected / exposed<br>occurrences (all) | 7 / 53 (13.21%)<br>9<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1 | 2 / 53 (3.77%)<br>2<br><br>1 / 53 (1.89%)<br>1<br><br>1 / 53 (1.89%)<br>1<br><br>0 / 53 (0.00%)<br>0<br><br>0 / 53 (0.00%)<br>0<br><br>0 / 53 (0.00%)<br>0 |  |
| Skin and subcutaneous tissue disorders<br>Dermatitis and eczema  |  |  |  |

|   |                     |                     |  |
|---|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>1 | 1 / 53 (1.89%)<br>1 |  |
| Renal and urinary disorders<br>Urinary tract infection or dysuria<br>subjects affected / exposed<br>occurrences (all)         | 3 / 53 (5.66%)<br>3 | 0 / 53 (0.00%)<br>0 |  |
| Worsening of renal function<br>subjects affected / exposed<br>occurrences (all)   | 2 / 53 (3.77%)<br>2 | 1 / 53 (1.89%)<br>1 |  |
| Relapse of nephrotic syndrome<br>subjects affected / exposed<br>occurrences (all)   | 0 / 53 (0.00%)<br>0 | 2 / 53 (3.77%)<br>2 |  |
| Endocrine disorders<br>Thyroiditis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>1 | 1 / 53 (1.89%)<br>1 |  |
| Infections and infestations<br>Flulike syndrome or fever<br>(unspecified)<br>subjects affected / exposed<br>occurrences (all) | 2 / 53 (3.77%)<br>2 | 3 / 53 (5.66%)<br>4 |  |
| Dental infection, dental abscess or<br>toothache<br>subjects affected / exposed<br>occurrences (all)                          | 2 / 53 (3.77%)<br>2 | 1 / 53 (1.89%)<br>1 |  |
| Metabolism and nutrition disorders<br>Metabolic acidosis<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 53 (3.77%)<br>2 | 1 / 53 (1.89%)<br>1 |  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>1 | 0 / 53 (0.00%)<br>0 |  |
| Hypospermia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 53 (1.89%)<br>1 | 0 / 53 (0.00%)<br>0 |  |
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 53 (1.89%)<br>1 | 0 / 53 (0.00%)<br>0 |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Hyperkalaemia               |                |                |  |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 53 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Dyslipidemia                |                |                |  |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 53 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Vitamin D deficiency        |                |                |  |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 53 (1.89%) |  |
| occurrences (all)           | 0              | 1              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 05 February 2014 | The amendment makes the following changes without modifying the study design and without adding risk to patients:<br>1) possibility to include in the study |

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|  |
|--|
| Short treatment duration, lower pretreatment proteinuria than expected |
|--|

Notes:

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31027883>