



## Clinical trial results:

### A Randomized, Double Blind, Placebo-controlled, Parallel Group, Multicentre, Phase 2a Study to Assess Target Engagement, Safety and Tolerability of AZD4831 in Patients with Heart Failure with Preserved Ejection Fraction (HFpEF)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-002895-42 |
| Trial protocol           | SE DK FI NL    |
| Global end of trial date | 07 May 2020    |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 23 May 2021  |
| First version publication date | 23 May 2021  |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D6580C00003 |
|-----------------------|-------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                        |
|------------------------------|----------------------------------------------------------------------------------------|
| Sponsor organisation name    | AstraZeneca                                                                            |
| Sponsor organisation address | Astraallén, Södertälje, Sweden, 15185                                                  |
| Public contact               | Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact           | Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com   |

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                       | 26 November 2020 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 15 March 2020    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 07 May 2020      |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of AZD4831 (an MPO inhibitor) on TE, by measuring MPO specific activity in plasma following ex vivo stimulation of fresh blood samples with zymosan, in patients with HFpEF. The study objectives also included evaluation of the safety and tolerability of AZD4831 in patients with HFpEF, and the incidence of Grade 3 maculopapular rash (maculopapular rash is an identified risk for AZD4831), and to assess the effect of AZD4831 on CFVR (as a measure of myocardial microvascular function) and 6MWD, in addition to assessing the PK of AZD4831 after repeated dosing.

Protection of trial subjects:

Visit 4 and 6 may be performed as telephone contacts with the patient, if judged appropriate by investigator.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 11 December 2018 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety           |
| Long term follow-up duration                              | 4 Months         |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Denmark: 5       |
| Country: Number of subjects enrolled | Netherlands: 3   |
| Country: Number of subjects enrolled | United States: 1 |
| Country: Number of subjects enrolled | Finland: 8       |
| Country: Number of subjects enrolled | Sweden: 24       |
| Worldwide total number of subjects   | 41               |
| EEA total number of subjects         | 40               |

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)                     | 2  |
| From 65 to 84 years                      | 38 |
| 85 years and over                        | 1  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects may enter a screening period up to 28 days prior to randomization.

### Period 1

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Period 1 title               | Overall Study (overall period)                                |
| Is this the baseline period? | Yes                                                           |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind                                                  |
| Roles blinded                | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |         |
|------------------|---------|
| <b>Arm title</b> | AZD4831 |
|------------------|---------|

Arm description:

AZD4831 tablets taken orally for for 90 days.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | AZD4831            |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Once daily

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Placebo tablets taken orally for 90 days.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Placebo            |
| Investigational medicinal product name | Placebo            |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Once daily

| Number of subjects in period 1      | AZD4831 | Placebo |
|-------------------------------------|---------|---------|
| Started                             | 27      | 14      |
| Completed                           | 24      | 9       |
| Not completed                       | 3       | 5       |
| Subject meets exclusion criteria    | -       | 1       |
| Dosing discontinued due to COVID-19 | 3       | 3       |

|                   |   |   |
|-------------------|---|---|
| Lost to follow-up | - | 1 |
|-------------------|---|---|

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | AZD4831 |
|-----------------------|---------|

Reporting group description:

AZD4831 tablets taken orally for 90 days.

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

Reporting group description:

Placebo tablets taken orally for 90 days.

| Reporting group values                    | AZD4831 | Placebo | Total |
|-------------------------------------------|---------|---------|-------|
| Number of subjects                        | 27      | 14      | 41    |
| Age categorical                           |         |         |       |
| Units: Subjects                           |         |         |       |
| Adults (18-64 years)                      | 1       | 1       | 2     |
| From 65-84 years                          | 25      | 13      | 38    |
| 85 years and over                         | 1       | 0       | 1     |
| Age Continuous                            |         |         |       |
| Units: years                              |         |         |       |
| arithmetic mean                           | 74.8    | 73.5    |       |
| standard deviation                        | ± 6.61  | ± 6.99  | -     |
| Sex: Female, Male                         |         |         |       |
| Units: participants                       |         |         |       |
| Female                                    | 12      | 7       | 19    |
| Male                                      | 15      | 7       | 22    |
| Race (NIH/OMB)                            |         |         |       |
| Units: Subjects                           |         |         |       |
| American Indian or Alaska Native          | 0       | 0       | 0     |
| Asian                                     | 0       | 0       | 0     |
| Native Hawaiian or Other Pacific Islander | 0       | 0       | 0     |
| Black or African American                 | 0       | 1       | 1     |
| White                                     | 27      | 13      | 40    |
| More than one race                        | 0       | 0       | 0     |
| Unknown or Not Reported                   | 0       | 0       | 0     |
| Ethnicity (NIH/OMB)                       |         |         |       |
| Units: Subjects                           |         |         |       |
| Hispanic or Latino                        | 0       | 0       | 0     |
| Not Hispanic or Latino                    | 27      | 14      | 41    |
| Unknown or Not Reported                   | 0       | 0       | 0     |
| Country                                   |         |         |       |
| Units: Subjects                           |         |         |       |
| Denmark                                   | 3       | 2       | 5     |
| Netherlands                               | 2       | 1       | 3     |
| USA                                       | 0       | 1       | 1     |
| Finland                                   | 5       | 3       | 8     |
| Sweden                                    | 17      | 7       | 24    |

## End points

### End points reporting groups

|                                                                               |         |
|-------------------------------------------------------------------------------|---------|
| Reporting group title                                                         | AZD4831 |
| Reporting group description:<br>AZD4831 tablets taken orally for for 90 days. |         |
| Reporting group title                                                         | Placebo |
| Reporting group description:<br>Placebo tablets taken orally for 90 days.     |         |

### Primary: The change from baseline in MPO activity in % after AZD4831 treatment.

|                                                                                            |                                                                        |
|--------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| End point title                                                                            | The change from baseline in MPO activity in % after AZD4831 treatment. |
| End point description:<br>To compare the effect of AZD4831 to placebo on target engagement |                                                                        |
| End point type                                                                             | Primary                                                                |
| End point timeframe:<br>Measurements on day 0, 10, 30 and 90.                              |                                                                        |

| End point values                             | AZD4831                | Placebo                |  |  |
|----------------------------------------------|------------------------|------------------------|--|--|
| Subject group type                           | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed                  | 20                     | 14                     |  |  |
| Units: Ratio                                 |                        |                        |  |  |
| least squares mean (confidence interval 95%) | 0.547 (0.379 to 0.790) | 2.177 (1.168 to 4.058) |  |  |

### Statistical analyses

|                                         |                                                   |
|-----------------------------------------|---------------------------------------------------|
| Statistical analysis title              | Relative change from baseline to end of treatment |
| Comparison groups                       | AZD4831 v Placebo                                 |
| Number of subjects included in analysis | 34                                                |
| Analysis specification                  | Pre-specified                                     |
| Analysis type                           | superiority                                       |
| P-value                                 | < 0.001                                           |
| Method                                  | Mixed models analysis                             |
| Parameter estimate                      | Least Square Means Ratio                          |
| Point estimate                          | 0.25                                              |
| Confidence interval                     |                                                   |
| level                                   | 95 %                                              |
| sides                                   | 2-sided                                           |
| lower limit                             | 0.12                                              |
| upper limit                             | 0.52                                              |

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**Secondary: Change from baseline in CFVR measured in the mid-distal segment of the left anterior descending (LAD) coronary artery under adenosine infusion measured by Transthoracic Doppler Echocardiography (TDE).**

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|                 |                                                                                                                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in CFVR measured in the mid-distal segment of the left anterior descending (LAD) coronary artery under adenosine infusion measured by Transthoracic Doppler Echocardiography (TDE). |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

To compare the effect of AZD4831 to placebo on coronary flow velocity reserve (CFVR)

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

End point timeframe:

Measurement on day 0 and 90.

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| End point values                             | AZD4831                | Placebo                |  |  |
|----------------------------------------------|------------------------|------------------------|--|--|
| Subject group type                           | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed                  | 18                     | 5                      |  |  |
| Units: Ratio                                 |                        |                        |  |  |
| least squares mean (confidence interval 95%) | 0.975 (0.835 to 1.138) | 1.002 (0.747 to 1.344) |  |  |

**Statistical analyses**

|                                         |                                                   |
|-----------------------------------------|---------------------------------------------------|
| <b>Statistical analysis title</b>       | Relative change from baseline to end of treatment |
| Comparison groups                       | AZD4831 v Placebo                                 |
| Number of subjects included in analysis | 23                                                |
| Analysis specification                  | Pre-specified                                     |
| Analysis type                           | superiority                                       |
| P-value                                 | = 0.568                                           |
| Method                                  | ANCOVA                                            |
| Parameter estimate                      | Least Square Means Ratio                          |
| Point estimate                          | 0.97                                              |
| Confidence interval                     |                                                   |
| level                                   | 95 %                                              |
| sides                                   | 1-sided                                           |
| lower limit                             | 0.74                                              |

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**Secondary: Change from baseline in Walking distance**

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|                 |                                          |
|-----------------|------------------------------------------|
| End point title | Change from baseline in Walking distance |
|-----------------|------------------------------------------|

End point description:

To compare the effect of AZD4831 to placebo on 6 minutes walking test (6MWT)

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

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End point timeframe:

Measurement on day 0, 30 and 90.

| <b>End point values</b>                      | AZD4831             | Placebo              |  |  |
|----------------------------------------------|---------------------|----------------------|--|--|
| Subject group type                           | Reporting group     | Reporting group      |  |  |
| Number of subjects analysed                  | 23                  | 11                   |  |  |
| Units: Meters                                |                     |                      |  |  |
| least squares mean (confidence interval 95%) | 47.4 (20.3 to 74.5) | 25.6 (-19.8 to 71.1) |  |  |

### Statistical analyses

| <b>Statistical analysis title</b>       | Change from baseline to end of treatment |
|-----------------------------------------|------------------------------------------|
| Comparison groups                       | AZD4831 v Placebo                        |
| Number of subjects included in analysis | 34                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.407                                  |
| Method                                  | Mixed models analysis                    |
| Parameter estimate                      | Mean difference (final values)           |
| Point estimate                          | 21.8                                     |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -30.5                                    |
| upper limit                             | 74.1                                     |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events will be collected from the time of the first dose throughout the treatment period and including the follow-up period. Serious Adverse Events will be recorded from the time of signing the informed consent form.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 23.0   |

### Reporting groups

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

Reporting group description:

Placebo tablets taken orally for 90 days.

|                       |         |
|-----------------------|---------|
| Reporting group title | AZD4831 |
|-----------------------|---------|

Reporting group description:

AZD4831 tablets taken orally for for 90 days.

| Serious adverse events                            | Placebo         | AZD4831        |  |
|---------------------------------------------------|-----------------|----------------|--|
| Total subjects affected by serious adverse events |                 |                |  |
| subjects affected / exposed                       | 2 / 14 (14.29%) | 2 / 27 (7.41%) |  |
| number of deaths (all causes)                     | 0               | 0              |  |
| number of deaths resulting from adverse events    |                 |                |  |
| Surgical and medical procedures                   |                 |                |  |
| Hospitalisation                                   |                 |                |  |
| subjects affected / exposed                       | 1 / 14 (7.14%)  | 0 / 27 (0.00%) |  |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Nervous system disorders                          |                 |                |  |
| Syncope                                           |                 |                |  |
| subjects affected / exposed                       | 1 / 14 (7.14%)  | 1 / 27 (3.70%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Transient ischaemic attack                        |                 |                |  |
| subjects affected / exposed                       | 0 / 14 (0.00%)  | 1 / 27 (3.70%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Infections and infestations                       |                 |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Pyelonephritis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| <b>Non-serious adverse events</b>                     | Placebo         | AZD4831          |  |
|-------------------------------------------------------|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events |                 |                  |  |
| subjects affected / exposed                           | 9 / 14 (64.29%) | 21 / 27 (77.78%) |  |
| Vascular disorders                                    |                 |                  |  |
| Bleeding varicose vein                                |                 |                  |  |
| subjects affected / exposed                           | 0 / 14 (0.00%)  | 1 / 27 (3.70%)   |  |
| occurrences (all)                                     | 0               | 2                |  |
| Peripheral coldness                                   |                 |                  |  |
| subjects affected / exposed                           | 1 / 14 (7.14%)  | 0 / 27 (0.00%)   |  |
| occurrences (all)                                     | 1               | 0                |  |
| Surgical and medical procedures                       |                 |                  |  |
| Hospitalisation                                       |                 |                  |  |
| subjects affected / exposed                           | 1 / 14 (7.14%)  | 0 / 27 (0.00%)   |  |
| occurrences (all)                                     | 1               | 0                |  |
| General disorders and administration site conditions  |                 |                  |  |
| Chest pain                                            |                 |                  |  |
| subjects affected / exposed                           | 0 / 14 (0.00%)  | 1 / 27 (3.70%)   |  |
| occurrences (all)                                     | 0               | 1                |  |
| Fatigue                                               |                 |                  |  |
| subjects affected / exposed                           | 0 / 14 (0.00%)  | 2 / 27 (7.41%)   |  |
| occurrences (all)                                     | 0               | 2                |  |
| Infusion site oedema                                  |                 |                  |  |
| subjects affected / exposed                           | 0 / 14 (0.00%)  | 1 / 27 (3.70%)   |  |
| occurrences (all)                                     | 0               | 1                |  |
| Pyrexia                                               |                 |                  |  |
| subjects affected / exposed                           | 0 / 14 (0.00%)  | 2 / 27 (7.41%)   |  |
| occurrences (all)                                     | 0               | 2                |  |
| Respiratory, thoracic and mediastinal disorders       |                 |                  |  |

|                                                |                |                |  |
|------------------------------------------------|----------------|----------------|--|
| Cough                                          |                |                |  |
| subjects affected / exposed                    | 1 / 14 (7.14%) | 1 / 27 (3.70%) |  |
| occurrences (all)                              | 1              | 1              |  |
| Dyspnoea                                       |                |                |  |
| subjects affected / exposed                    | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences (all)                              | 1              | 0              |  |
| Epistaxis                                      |                |                |  |
| subjects affected / exposed                    | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                              | 0              | 1              |  |
| Oropharyngeal pain                             |                |                |  |
| subjects affected / exposed                    | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                              | 0              | 1              |  |
| Rhinorrhoea                                    |                |                |  |
| subjects affected / exposed                    | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences (all)                              | 1              | 0              |  |
| Investigations                                 |                |                |  |
| Blood urea increased                           |                |                |  |
| subjects affected / exposed                    | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences (all)                              | 1              | 0              |  |
| Prostatic specific antigen increased           |                |                |  |
| subjects affected / exposed                    | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences (all)                              | 1              | 0              |  |
| Troponin T increased                           |                |                |  |
| subjects affected / exposed                    | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences (all)                              | 1              | 0              |  |
| Injury, poisoning and procedural complications |                |                |  |
| Contusion                                      |                |                |  |
| subjects affected / exposed                    | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                              | 0              | 1              |  |
| Head injury                                    |                |                |  |
| subjects affected / exposed                    | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                              | 0              | 1              |  |
| Scratch                                        |                |                |  |
| subjects affected / exposed                    | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                              | 0              | 1              |  |
| Subcutaneous haematoma                         |                |                |  |

|                                                                                             |                     |                      |  |
|---------------------------------------------------------------------------------------------|---------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                            | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Cardiac disorders<br>Bradycardia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 1 / 14 (7.14%)<br>1 | 3 / 27 (11.11%)<br>3 |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Syncope<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 14 (7.14%)<br>1 | 1 / 27 (3.70%)<br>1  |  |
| Transient ischaemic attack<br>subjects affected / exposed<br>occurrences (all)              | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Ear and labyrinth disorders<br>Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Eye disorders<br>Blindness<br>subjects affected / exposed<br>occurrences (all)              | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 2 / 27 (7.41%)<br>2  |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 14 (7.14%)<br>1 | 0 / 27 (0.00%)<br>0  |  |

|                                                                                                                   |                     |                      |  |
|-------------------------------------------------------------------------------------------------------------------|---------------------|----------------------|--|
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                                        | 0 / 14 (0.00%)<br>0 | 2 / 27 (7.41%)<br>2  |  |
| Plicated tongue<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Skin and subcutaneous tissue disorders<br>Dermatitis allergic<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                      | 1 / 14 (7.14%)<br>1 | 3 / 27 (11.11%)<br>3 |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 14 (7.14%)<br>1 | 0 / 27 (0.00%)<br>0  |  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 14 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1  |  |
| Musculoskeletal stiffness<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 14 (7.14%)<br>1 | 0 / 27 (0.00%)<br>0  |  |
| Infections and infestations<br>Gingivitis<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 14 (7.14%)<br>1 | 0 / 27 (0.00%)<br>0  |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                                                     | 1 / 14 (7.14%)<br>1 | 1 / 27 (3.70%)<br>1  |  |

|                                    |                |                |  |
|------------------------------------|----------------|----------------|--|
| Nasopharyngitis                    |                |                |  |
| subjects affected / exposed        | 0 / 14 (0.00%) | 2 / 27 (7.41%) |  |
| occurrences (all)                  | 0              | 2              |  |
| Pyelonephritis                     |                |                |  |
| subjects affected / exposed        | 1 / 14 (7.14%) | 0 / 27 (0.00%) |  |
| occurrences (all)                  | 1              | 0              |  |
| Respiratory tract infection        |                |                |  |
| subjects affected / exposed        | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Urinary tract infection            |                |                |  |
| subjects affected / exposed        | 0 / 14 (0.00%) | 1 / 27 (3.70%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Metabolism and nutrition disorders |                |                |  |
| Gout                               |                |                |  |
| subjects affected / exposed        | 0 / 14 (0.00%) | 2 / 27 (7.41%) |  |
| occurrences (all)                  | 0              | 4              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                      |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| 09 January 2020 | Exclusion criteria 1 is updated to decrease eGFR from 45 to 30 ml/min/1.73m <sup>2</sup> , at screening visit. |

Notes:

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### 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.

Due to premature study termination, the statistical assumptions for the study design according to the protocol could not be fulfilled, therefore, no statistical conclusions can be made based efficacy objectives.

Notes: