



## Clinical trial results:

**A multicenter, open-label post authorization safety study to evaluate the effect of LysaKare infusion on serum potassium levels in GEP-NET subjects eligible for Lutathera treatment**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2019-004073-76   |
| Trial protocol           | NL IT PL         |
| Global end of trial date | 18 November 2023 |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 10 February 2025  |
| First version publication date | 25 November 2024  |
| Version creation reason        | • Correction of full data set<br>updated endpoint # 8 and Adverse Event description |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CAAA001A12401 |
|-----------------------|---------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04524442 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharma, AG   |
| Sponsor organisation address | CH 4002, Basel, Switzerland,  |
| Public contact               | Clinical Disclosure Office, Novartis Pharma, AG, 41<br>613241111, novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma, AG, 41<br>613241111, novartis.email@novartis.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                       | 18 November 2023 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 18 November 2023 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To assess the effect of LysaKare administration on serum potassium concentrations in GEP-NET subjects eligible for Lutathera treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial. Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd>.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 25 January 2021 |
| 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 | United Kingdom: 9 |
| Country: Number of subjects enrolled | Italy: 4          |
| Country: Number of subjects enrolled | Netherlands: 8    |
| Country: Number of subjects enrolled | Poland: 21        |
| Worldwide total number of subjects   | 42                |
| EEA total number of subjects         | 33                |

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) | 29 |
| From 65 to 84 years  | 13 |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 42 participants were enrolled in 7 centers in 4 countries.

### Pre-assignment

Screening details:

The study schedule for each participant consisted of a screening period followed by an infusion day with an optional overnight in-clinic stay, and a follow-up call.

### Period 1

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

### Arms

|           |         |
|-----------|---------|
| Arm title | GEP-NET |
|-----------|---------|

Arm description:

One dose of arginine/lysine solution administered intravenously over a 4-hour period

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | LysaKare              |
| Investigational medicinal product code |                       |
| Other name                             | 2.5% Lys-Arg solution |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

The study treatment was a 1000 mL solution of LysaKare (2.5% Lys-Arg solution for infusion), administered intravenously over a 4-hour period (infusion rate: 250 mL/h). Only 1 infusion was administered in the treatment phase of the study.

| Number of subjects in period 1           | GEP-NET |
|--|---------|
| Started                                  | 42      |
| Treated                                  | 41      |
| Not treated                              | 1       |
| Post-trtment f/u ph-48 hrs post-infusion | 40      |
| Completed                                | 41      |
| Not completed                            | 1       |
| Subject Decision                         | 1       |

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | GEP-NET |
|-----------------------|---------|

Reporting group description:

One dose of arginine/lysine solution administered intravenously over a 4-hour period

| Reporting group values   | GEP-NET | Total |  |
|--|---------|-------|--|
| Number of subjects   | 42      | 42    |  |
| Age categorical  |         |       |  |
| Units: Subjects  |         |       |  |
| Adults (18-64 years)   | 29      | 29    |  |
| From 65-84 years   | 13      | 13    |  |
| Age Continuous   |         |       |  |
| Mean age reported is from 41 subjects who received study treatment, and not from 42 subjects who were enrolled in the study. |         |       |  |
| Units: years   |         |       |  |
| arithmetic mean  | 57.7    |       |  |
| standard deviation   | ± 9.46  | -     |  |
| Sex: Female, Male  |         |       |  |
| Units: Participants  |         |       |  |
| Female   | 20      | 20    |  |
| Male   | 22      | 22    |  |
| Race/Ethnicity, Customized   |         |       |  |
| Units: Subjects  |         |       |  |
| White  | 39      | 39    |  |
| Black or African American  | 3       | 3     |  |

## End points

### End points reporting groups

|  |         |
|--|---------|
| Reporting group title  | GEP-NET |
| Reporting group description:   |         |
| One dose of arginine/lysine solution administered intravenously over a 4-hour period |         |

### Primary: Mean change from baseline in serum potassium levels over 24 hours

|                 |  |
|-----------------|--|
| End point title | Mean change from baseline in serum potassium levels over 24 hours <sup>[1]</sup> |
|-----------------|--|

End point description:

Serum potassium levels at each collection time point will be measured at local laboratories of study sites using validated methods. The potassium concentration results will be summarized descriptively and will include mean change, maximum change, time to the maximum change, and the overall dynamics of the potassium concentration curve during and after the arginine/lysine infusion.

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

End point timeframe:

Day 0/Infusion Day (Hour 0, Hour 2, Hour 4, Hour 6, Hour 8, Hour 12, Hour 24)

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

| End point values                     | GEP-NET           |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 25 <sup>[2]</sup> |  |  |  |
| Units: mmol/L                        |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| Pre-dose (hour 0)                    | 4.3 (± 0.397)     |  |  |  |
| Change from Baseline (BL) to Hour 2  | 0.25 (± 0.452)    |  |  |  |
| Change from Baseline (BL) to Hour 4  | 0.60 (± 0.666)    |  |  |  |
| Change from Baseline (BL) to Hour 6  | 0.49 (± 0.602)    |  |  |  |
| Change from Baseline (BL) to Hour 8  | 0.38 (± 0.487)    |  |  |  |
| Change from Baseline (BL) to Hour 12 | 0.24 (± 0.557)    |  |  |  |
| Change from Baseline (BL) to Hour 24 | 0.07 (± 0.396)    |  |  |  |

Notes:

[2] - Evaluable Set had 25 subjects who had pre-dose & at least 1 post-dose serum potassium measurement

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with treatment Adverse Events (AEs) & Serious Adverse Events (SAEs)

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with treatment Adverse Events (AEs) & Serious Adverse Events (SAEs) |
|-----------------|--|

End point description:

Safety measured by the percentage of participants with treatment emergent adverse events (starting from the signing of the ICF until the end of the follow-up call (48 hours after infusion).

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

End point timeframe:

Day 0/Infusion Day up to 48 hours post infusion

| End point values                              | GEP-NET           |  |  |  |
|---|-------------------|--|--|--|
| Subject group type                            | Reporting group   |  |  |  |
| Number of subjects analysed                   | 41 <sup>[3]</sup> |  |  |  |
| Units: Participants                           |                   |  |  |  |
| Adverse Event (AEs)                           | 11                |  |  |  |
| Treatment-related AEs                         | 6                 |  |  |  |
| Serious Adverse Events (SAEs)                 | 0                 |  |  |  |
| Fatal SAEs                                    | 0                 |  |  |  |
| AEs leading to discontinuation                | 0                 |  |  |  |
| AEs leading to Interruption                   | 0                 |  |  |  |
| AEs requiring additional therapy              | 5                 |  |  |  |
| Treatment related AEs req. additional therapy | 3                 |  |  |  |

Notes:

[3] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Notable Changes in vital signs

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Notable Changes in vital signs |
|-----------------|--|

End point description:

Safety measured by the notable post-baseline changes in vital signs: (systolic blood pressure, diastolic blood pressure, pulse rate & weight) compared to baseline.

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

End point timeframe:

Day 0/Infusion Day (0, 2, 4, 6, 8, 12 and 24 hours)

| End point values   | GEP-NET           |  |  |  |
|--|-------------------|--|--|--|
| Subject group type   | Reporting group   |  |  |  |
| Number of subjects analysed                                    | 41 <sup>[4]</sup> |  |  |  |
| Units: Participants  |                   |  |  |  |
| SBP(mmHg): $\geq 180$ with increase from baseline of $\geq 20$ | 0                 |  |  |  |
| SBP(mmHg): $\leq 90$ with decrease from baseline of $\geq 20$  | 0                 |  |  |  |
| DBP(mmHg): $\geq 105$ with increase from baseline of $\geq 15$ | 0                 |  |  |  |
| DBP(mmHg): $\leq 50$ with decrease from baseline of $\geq 15$  | 0                 |  |  |  |
| Pulse rate (bpm): $\geq 100$ & $>25\%$ increase from BL        | 0                 |  |  |  |

|   |   |  |  |  |
|---|---|--|--|--|
| Pulse rate (bpm): $\leq 50$ & $> 25\%$ decrease from BL | 0 |  |  |  |
| Weight (kg): increase $\geq 10\%$ from Baseline         | 0 |  |  |  |
| Weight (kg): decrease $> 10\%$ from Baseline            | 0 |  |  |  |

Notes:

[4] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Notable Changes in electrocardiogram (ECG)

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Notable Changes in electrocardiogram (ECG) |
|-----------------|--|

End point description:

Safety measured by the notable post-baseline changes in ECG values compared to baseline PR, QRS, QT, QTcF, and RR intervals were obtained from 12-lead ECGs for each subject during the study

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

End point timeframe:

Day 0/Infusion Day (0, 4, 8 and 24 hours)

| End point values                                    | GEP-NET           |  |  |  |
|---|-------------------|--|--|--|
| Subject group type                                  | Reporting group   |  |  |  |
| Number of subjects analysed                         | 41 <sup>[5]</sup> |  |  |  |
| Units: Participants                                 |                   |  |  |  |
| QTcF (ms): Increase $>30$ to $\leq 60$ ms           | 7                 |  |  |  |
| QTcF (ms): Increase $>60$ ms                        | 0                 |  |  |  |
| QTcF (ms): New $>450$ to $\leq 480$ ms (n = 39)     | 7                 |  |  |  |
| QTcF (ms): New $>480$ to $\leq 500$ ms              | 0                 |  |  |  |
| QTcF (ms): New $>500$ ms                            | 0                 |  |  |  |
| QT (ms): Increase $>30$ to $\leq 60$ ms             | 9                 |  |  |  |
| QT (ms): Increase $>60$ ms                          | 2                 |  |  |  |
| QT (ms): New $>450$ to $\leq 480$ ms (n = 39)       | 6                 |  |  |  |
| QT (ms): New $>480$ to $\leq 500$ ms                | 1                 |  |  |  |
| QT (ms): New $>500$ ms                              | 0                 |  |  |  |
| PR (ms): Increase $>25\%$ and PR $>200$ ms (n = 29) | 1                 |  |  |  |
| PR (ms): New PR $>200$ ms (n = 29)                  | 6                 |  |  |  |
| QRS (ms): Increase $>25\%$ and QRS $>120$ ms        | 2                 |  |  |  |
| QRS (ms): New QRS $>120$ ms                         | 2                 |  |  |  |
| HR (bpm): Increase $>25\%$ and HR $>100$ bpm        | 0                 |  |  |  |
| HR (bpm): Decrease $>25\%$ and HR $<50$ bpm         | 0                 |  |  |  |

Notes:

[5] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Notable Changes in Hematology parameters

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Notable Changes in Hematology parameters |
|-----------------|--|

End point description:

Safety measured by the notable post-baseline changes in Hematology parameters compared to baseline as represented by Shift tables based on common toxicity criteria (CTC) grades. Each participant was counted only for the worst grade observed post-baseline. Notable change is the shift to higher grades from baseline.

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

End point timeframe:

Day 0/Infusion Day (0 and 24 hours)

|                             |                   |  |  |  |
|-----------------------------|-------------------|--|--|--|
| <b>End point values</b>     | GEP-NET           |  |  |  |
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 41 <sup>[6]</sup> |  |  |  |
| Units: Participants         | 0                 |  |  |  |

Notes:

[6] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Notable Changes in Chemistry parameters

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Notable Changes in Chemistry parameters |
|-----------------|---|

End point description:

Safety measured by the notable post-baseline changes in Chemistry parameters compared to baseline. Each participant was counted only for the worst grade observed post-baseline. Notable change is the shift to higher grades from baseline.

Key shifts were in the following parameters: creatinine and lactate dehydrogenase and creatinine clearance.

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

End point timeframe:

Day 0/Infusion Day (0 and 24 hours)

| End point values                    | GEP-NET           |  |  |  |
|-------------------------------------|-------------------|--|--|--|
| Subject group type                  | Reporting group   |  |  |  |
| Number of subjects analysed         | 41 <sup>[7]</sup> |  |  |  |
| Units: Participants                 |                   |  |  |  |
| For creatinine (increase)           | 4                 |  |  |  |
| Lactate dehydrogenase (increase)    | 3                 |  |  |  |
| For creatinine clearance (decrease) | 4                 |  |  |  |

Notes:

[7] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Notable Changes in Electrolyte parameters

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Notable Changes in Electrolyte parameters |
|-----------------|---|

End point description:

Safety measured by the notable post-baseline changes in Electrolyte parameters compared to baseline. Each participant was counted only for the worst grade observed post-baseline. Notable change is the shift to higher grades from baseline.

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

End point timeframe:

Day 0/Infusion Day (0, 2, 4, 6, 8, 12 and 24 hours)

| End point values            | GEP-NET           |  |  |  |
|-----------------------------|-------------------|--|--|--|
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 41 <sup>[8]</sup> |  |  |  |
| Units: Participants         |                   |  |  |  |
| For Potassium (increase)    | 7                 |  |  |  |
| For sodium (decrease)       | 12                |  |  |  |

Notes:

[8] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean change from baseline in blood gas parameter, pH, over 24 hours

|                 |   |
|-----------------|---|
| End point title | Mean change from baseline in blood gas parameter, pH, over 24 hours |
|-----------------|---|

End point description:

Safety measured by the mean changes in blood gas compared to baseline. Blood gas parameter: pH.

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

End point timeframe:

Day 0/Infusion Day (0, 2, 4, 6, 8, 12 and 24 hours)

| End point values                                | GEP-NET           |  |  |  |
|---|-------------------|--|--|--|
| Subject group type                              | Reporting group   |  |  |  |
| Number of subjects analysed                     | 41 <sup>[9]</sup> |  |  |  |
| Units: unitless                                 |                   |  |  |  |
| arithmetic mean (standard deviation)            |                   |  |  |  |
| Day 0/Infusion Day (Pre-dose) (hour 0) (n = 36) | 7.35 (± 0.046)    |  |  |  |
| Change from Baseline (BL) to Hour 2 (n = 36)    | -0.03 (± 0.046)   |  |  |  |
| Change from Baseline (BL) to Hour 4 (n = 36)    | -0.06 (± 0.055)   |  |  |  |
| Change from Baseline (BL) to Hour 6 (n = 36)    | -0.05 (± 0.051)   |  |  |  |
| Change from Baseline (BL) to Hour 8 (n = 35)    | -0.05 (± 0.056)   |  |  |  |
| Change from Baseline (BL) to Hour 12 (n = 33)   | -0.03 (± 0.054)   |  |  |  |
| Change from Baseline (BL) to Hour 24 (n = 35)   | -0.04 (± 0.051)   |  |  |  |

Notes:

[9] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in blood gas parameter, Lactic Acid, over 24 hours

|                 |  |
|-----------------|--|
| End point title | Mean change from baseline in blood gas parameter, Lactic Acid, over 24 hours |
|-----------------|--|

End point description:

Safety measured by the mean changes in blood gas compared to baseline. Blood gas parameter: Lactic Acid

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

End point timeframe:

Day 0/Infusion Day (0, 2, 4, 6, 8, 12 and 24 hours)

| End point values                                | GEP-NET            |  |  |  |
|---|--------------------|--|--|--|
| Subject group type                              | Reporting group    |  |  |  |
| Number of subjects analysed                     | 41 <sup>[10]</sup> |  |  |  |
| Units: mmol/L                                   |                    |  |  |  |
| arithmetic mean (standard deviation)            |                    |  |  |  |
| Day 0/Infusion Day (Pre-dose) (hour 0) (n = 35) | 1.40 (± 0.604)     |  |  |  |
| Change from Baseline (BL) to Hour 2 (n = 35)    | -0.07 (± 0.671)    |  |  |  |
| Change from Baseline (BL) to Hour 4 (n = 35)    | -0.23 (± 0.523)    |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Change from Baseline (BL) to Hour 6 (n = 35)  | -0.26 (± 0.546) |  |  |  |
| Change from Baseline (BL) to Hour 8 (n = 33)  | -0.19 (± 0.465) |  |  |  |
| Change from Baseline (BL) to Hour 12 (n = 33) | -0.21 (± 0.657) |  |  |  |
| Change from Baseline (BL) to Hour 24 (n = 34) | -0.16 (± 0.650) |  |  |  |

Notes:

[10] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in blood gas parameter, Partial Pressure Carbon Dioxide, over 24 hours

|  |  |
|--|--|
| End point title  | Mean change from baseline in blood gas parameter, Partial Pressure Carbon Dioxide, over 24 hours |
| End point description:   |  |
| Safety measured by the mean changes in blood gas compared to baseline. Blood gas parameter: Partial Pressure Carbon Dioxide. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Day 0/Infusion Day (0, 2, 4, 6, 8, 12 and 24 hours)  |  |

| End point values                                | GEP-NET            |  |  |  |
|---|--------------------|--|--|--|
| Subject group type                              | Reporting group    |  |  |  |
| Number of subjects analysed                     | 41 <sup>[11]</sup> |  |  |  |
| Units: mmHg                                     |                    |  |  |  |
| arithmetic mean (standard deviation)            |                    |  |  |  |
| Day 0/Infusion Day (Pre-done) (hour 0) (n = 36) | 50.53 (± 8.712)    |  |  |  |
| Change from Baseline (BL) to Hour 2 (n = 36)    | -1.08 (± 6.670)    |  |  |  |
| Change from Baseline (BL) to Hour 4 (n = 36)    | -2.44 (± 8.717)    |  |  |  |
| Change from Baseline (BL) to Hour 6 (n = 36)    | -4.90 (± 8.507)    |  |  |  |
| Change from Baseline (BL) to Hour 8 (n = 35)    | -4.87 (± 8.399)    |  |  |  |
| Change from Baseline (BL) to Hour 12 (n = 33)   | -5.71 (± 8.002)    |  |  |  |
| Change from Baseline (BL) to Hour 24 (n = 35)   | -2.54 (± 8.242)    |  |  |  |

Notes:

[11] - One subject was not treated.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from the administration of the study treatment up to 48 hours in addition to the infusion time, an average of 52 hours total.

Adverse event reporting additional description:

Any sign or symptom that occurs during the conduct of the trial and safety follow-up.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | All Subjects |
|-----------------------|--------------|

Reporting group description:

All subjects enrolled in the study who received one dose of arginine/lysine solution administered intravenously over a 4-hour period

| Serious adverse events                            | All Subjects   |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 41 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events                            | All Subjects     |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 11 / 41 (26.83%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Contusion   |                  |  |  |
| subjects affected / exposed                           | 1 / 41 (2.44%)   |  |  |
| occurrences (all)                                     | 1                |  |  |
| Nervous system disorders                              |                  |  |  |
| Dizziness   |                  |  |  |
| subjects affected / exposed                           | 1 / 41 (2.44%)   |  |  |
| occurrences (all)                                     | 1                |  |  |
| Headache  |                  |  |  |

|  |  |  |  |
|--|--|--|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 41 (2.44%)<br>1  |  |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 1 / 41 (2.44%)<br>1  |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Proctalgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 1 / 41 (2.44%)<br>1<br><br>2 / 41 (4.88%)<br>2<br><br>1 / 41 (2.44%)<br>1<br><br>1 / 41 (2.44%)<br>1 |  |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Respiratory acidosis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 41 (2.44%)<br>1  |  |  |
| Metabolism and nutrition disorders<br>Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)  | 5 / 41 (12.20%)<br>5   |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 18 May 2021      | Exclusion criteria #1: For Poland only, added required hyperkalemia level > 5.5mmol/L per local protocol amendment   |
| 01 December 2022 | Clarification on the sampling requirements for laboratory assessments as the Sponsor identified discrepancies in sampling used for electrolytes which were not performed as per protocol requested procedures;<br>The target enrollment number was revised from "40" to "approximately 45" to ensure at least 25 subjects have valid data to fulfill the study primary objective |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported