



Clinical trial results: STEROID TREATMENT AS ANTI-INFLAMMATORY AND NEUROPROTECTIVE AGENT FOLLOWING OUT-OF-HOSPITAL CARDIAC ARREST. A RANDOMIZED TRIAL.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2020-000855-11 |
| Trial protocol | DK |
| Global end of trial date | 28 February 2023 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 10 February 2024 |
| First version publication date | 10 February 2024 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | HJE-STEROHCA-001 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-----------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04624776 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | The STEROHCA Trial: Acronym |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Rigshospitalet |
| Sponsor organisation address | Blegdamsvej 9, Copenhagen OE, Denmark, 2100 |
| Public contact | Department of Cardiology, Copenhagen University Hospital, Rigshospitalet, 45 35450572, christian.hassager@regionh.dk |
| Scientific contact | Department of Cardiology, Copenhagen University Hospital, Rigshospitalet, 45 35450572, christian.hassager@regionh.dk |

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 | 28 February 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 July 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 February 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Patients suffering from out-of-hospital cardiac arrest (OHCA) who remain in a comatose state post-resuscitation face elevated risk of mortality due to the post-cardiac arrest syndrome (PCAS). PCAS features systemic inflammation, which is associated to poor outcomes in OHCA. Hence, attenuating inflammation could potentially be beneficial following OHCA. The primary objective of this trial was to determine the efficacy of the anti-inflammatory glucocorticoid "methylprednisolone" compared with placebo. The co-primary endpoints were serial measurements of interleukin-6 and neuron-specific-enolase as markers of systemic inflammation and brain injury at admission and 24, 48 and 72 hours after admission in patients admitted after resuscitated OHCA. The secondary endpoints included other biomarkers for inflammation and brain injury, markers of organ injury, safety, and survival. The primary results have been published: <https://doi.org/10.1007/s00134-023-07247-w>

Protection of trial subjects:

All patients included in the trial were treated according to international post-resuscitation guidelines, and trial participation did not restrict additional treatment. Concurrent enrollment in other trials was permissible. Patients were screened for contraindications to the intervention before enrollment, and the trial was monitored and evaluated for safety throughout the study period. The intervention, methylprednisolone, has known immunosuppressive effects and can induce hyperglycemia, but as part of standard of care, all patients received prophylactic antibiotics to potentially reduce the incidence of infections and continuous intravenous insulin for hyperglycaemia during the initial intensive care unit stay.

Background therapy:

After resuscitated out-of-hospital cardiac arrest, patients underwent standard care following International post-resuscitation guidelines. This included targeted temperature management at 36°C for comatose patients, sedation primarily utilizing propofol and fentanyl, and the administration of vasopressors and inotropes as necessary. Furthermore, all comatose patients received prophylactic antibiotic treatment with intravenous piperacillin/tazobactam or cefuroxime in the event of a β -lactam allergy. Continuous intravenous insulin was also administered to address hyperglycemia.

Evidence for comparator:

No significant effect was expected by the comparator (Placebo: isotonic saline 0.9%)

| | |
|---|---------------------------------------|
| Actual start date of recruitment | 10 October 2020 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy, Scientific research |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Denmark: 137 |
| Worldwide total number of subjects | 137 |
| EEA total number of subjects | 137 |

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) | 58 |
| From 65 to 84 years | 74 |
| 85 years and over | 5 |

Subject disposition

Recruitment

Recruitment details:

The recruitment period was completed in 21 months (expected period was 18 months as defined in the protocol)

Pre-assignment

Screening details:

In the study period, 207 out of 1976 patients in the study region were eligible for inclusion, with 158 patients being randomized (80 methylprednisolone, 78 placebo). Of these, 137 patients encompassed the modified intention-to-treat (21 patients excluded; methylprednisolone 12, placebo 9), which this report is based on.

Period 1

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

Blinding implementation details:

After opening a medicine box, the including prehospital physician and accompanying medical assistant became unblinded. Subsequently, the prehospital staff played no further role in the patient's treatment or the study post-admission. Treatment allocation remained blinded for the patient, all hospital personnel, as well as all study investigators and staff.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description: -

| | |
|--|-----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Saline |
| Investigational medicinal product code | |
| Other name | Isotonic saline, NaCl 0.9% |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intraosseous use, Intravenous use |

Dosage and administration details:

Placebo consisted of administration of 4 mL of isotonic saline (NaCl 0.9%)

| | |
|------------------|--------------------|
| Arm title | Methylprednisolone |
|------------------|--------------------|

Arm description: -

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Solu-medrol |
| Investigational medicinal product code | 6132 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intraosseous use, Intravenous use |

Dosage and administration details:

A dosis of 250 mg methylprednisolone suspended in isotonic saline to a total volume of 4 mL prior to infusion. Administration was done over a period of minimum 5 minutes.

| Number of subjects in period 1 | Placebo | Methylprednisolone |
|---------------------------------------|---------|--------------------|
| Started | 69 | 68 |
| Completed | 69 | 68 |

Baseline characteristics

Reporting groups

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

| Reporting group values | Placebo | Methylprednisolone | Total |
|--|----------|--------------------|-------|
| Number of subjects | 69 | 68 | 137 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Age at time of OHCA | | | |
| Units: years | | | |
| median | 66 | 67 | |
| inter-quartile range (Q1-Q3) | 56 to 75 | 57 to 74 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 12 | 25 |
| Male | 56 | 56 | 112 |

End points

End points reporting groups

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

Primary: Interleukin 6, IL-6

| | |
|---|---------------------|
| End point title | Interleukin 6, IL-6 |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Measured at admission, 24, 48, and 72 hours | |

| End point values | Placebo | Methylprednisolone | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: pg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Admission | 15.0 (10.4 to 21.7) | 15.0 (10.4 to 21.6) | | |
| 24 hours | 29.8 (18.9 to 46.8) | 2.1 (1.3 to 3.2) | | |
| 48 hours | 10.1 (6.7 to 15.1) | 5.7 (3.8 to 8.4) | | |
| 72 hours | 3.4 (2.2 to 5.4) | 4.3 (2.7 to 6.6) | | |

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | Interleukin 6, mixed model analysis |
| Statistical analysis description: | |
| Interleukin 6 levels from admission to 72 hours after admission | |
| Comparison groups | Placebo v Methylprednisolone |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | ≤ 0.0001 ^[2] |
| Method | Mixed models analysis |

Notes:

[1] - Linear mixed model without baseline adjustment

[2] - P value for the treatment-by-time interaction listed above. Time specific comparisons of methylprednisolone vs placebo at admission: $p=0.9$, 24 hours: $p<0.0001$, 48 hours: $p=0.05$, and 72 hours: $p=0.5$.

Primary: Neuron-specific enolase, NSE

| | |
|-----------------|------------------------------|
| End point title | Neuron-specific enolase, NSE |
|-----------------|------------------------------|

End point description:

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

End point timeframe:

Measured at admission, 24, 48, and 72 hours

| End point values | Placebo | Methylprednisolone | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: ug/L | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Admission | 17.2 (14.8 to 20.0) | 19.6 (16.9 to 22.7) | | |
| 24 hours | 17.2 (14.3 to 20.7) | 19.1 (15.9 to 22.9) | | |
| 48 hours | 14.8 (11.2 to 19.4) | 18.8 (14.4 to 24.6) | | |
| 72 hours | 14.7 (11.1 to 19.5) | 15.7 (11.9 to 20.9) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Neuron-specific enolase, mixed model analysis |
|----------------------------|---|

Statistical analysis description:

Neuron-specific enolase levels from admission to 72 hours after admission

| | |
|-------------------|------------------------------|
| Comparison groups | Methylprednisolone v Placebo |
|-------------------|------------------------------|

| | |
|---|-----|
| Number of subjects included in analysis | 137 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|----------------------|
| Analysis type | other ^[3] |
|---------------|----------------------|

| | |
|---------|-----------------------|
| P-value | = 0.22 ^[4] |
|---------|-----------------------|

| | |
|--------|-----------------------|
| Method | Mixed models analysis |
|--------|-----------------------|

Notes:

[3] - Linear mixed model without baseline adjustment

[4] - P value for the treatment-by-time interaction listed above. Time specific comparisons of methylprednisolone vs placebo at admission: $p=0.24$, 24 hours: $p=0.42$, 48 hours: $p=0.21$, and 72 hours: $p=0.75$.

Secondary: Survival after 180 days

| | |
|-----------------|-------------------------|
| End point title | Survival after 180 days |
|-----------------|-------------------------|

End point description:

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

End point timeframe:

Survival 180 days after cardiac arrest

| End point values | Placebo | Methylprednisolone | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: No. | | | | |
| number (not applicable) | | | | |
| Alive at 180 days | 44 | 51 | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Survival after 180 days |
| Comparison groups | Placebo v Methylprednisolone |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.17 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.35 |
| upper limit | 1.2 |

Secondary: Cerebral Performance Category (CPC) after 180 days

| | |
|-----------------|--|
| End point title | Cerebral Performance Category (CPC) after 180 days |
|-----------------|--|

End point description:

A score of ≥ 3 indicating a poor neurologic outcome, including death

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

End point timeframe:

CPC evaluated 180 days after cardiac arrest

| End point values | Placebo | Methylprednisolone | | |
|-------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: Score | | | | |
| number (not applicable) | | | | |
| 180 days after cardiac arrest | 26 | 19 | | |

Statistical analyses

| Statistical analysis title | CPC score 180 days after OHCA |
|---|-------------------------------|
| Statistical analysis description: | |
| Comparing poor neurologic outcome (score ≥ 3) in the two treatment arms | |
| Comparison groups | Placebo v Methylprednisolone |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.28 |
| Method | Fisher exact |

Secondary: Modified Rankin Scale (mRS) after 180 days

| End point title | Modified Rankin Scale (mRS) after 180 days |
|---|--|
| End point description: | |
| A score of ≥ 4 indicating a poor neurologic outcome, including death | |
| End point type | Secondary |
| End point timeframe: | |
| mRS evaluated 180 days after cardiac arrest | |

| End point values | Placebo | Methylprednisolone | | |
|-------------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: Score | | | | |
| number (not applicable) | | | | |
| 180 days after cardiac arrest | 17 | 26 | | |

Statistical analyses

| Statistical analysis title | mRS score 180 days after OHCA |
|---|-------------------------------|
| Statistical analysis description: | |
| Comparing poor neurologic outcome (score ≥ 4) in the two treatment arms | |
| Comparison groups | Placebo v Methylprednisolone |

| | |
|---|---------------|
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.14 |
| Method | Fisher exact |

Secondary: C-reactive protein, CRP

| | |
|---|-------------------------|
| End point title | C-reactive protein, CRP |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Measured at admission, 24, 48, and 72 hours | |

| End point values | Placebo | Methylprednisolone | | |
|--|--------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: mg/L | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Admission | 3.15 (2.18 to 4.13) | 2.13 (1.49 to 2.78) | | |
| 24 hours | 72.40 (55.91 to 88.89) | 24.90 (19.31 to 30.49) | | |
| 48 hours | 122.82 (90.08 to 155.56) | 35.58 (26.28 to 44.89) | | |
| 72 hours | 96.46 (69.61 to 123.30) | 45.35 (32.88 to 57.81) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | CRP, mixed model analysis |
| Statistical analysis description: | |
| CRP levels from admission to 72 hours after admission | |
| Comparison groups | Placebo v Methylprednisolone |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | < 0.0001 ^[6] |
| Method | Mixed models analysis |

Notes:

[5] - Linear mixed model without baseline adjustment

[6] - P value for the treatment-by-time interaction listed above. Time specific comparisons of methylprednisolone vs placebo at admission: p=0.08, 24 hours: p <0.0001, 48 hours: p<0.0001, and

72 hours: $p < 0.001$.

Secondary: Neurofilament light chain, NfL

| | |
|-----------------|--------------------------------|
| End point title | Neurofilament light chain, NfL |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

Measured at admission, 24, 48, and 72 hours

| End point values | Placebo | Methylprednisolone | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 68 | | |
| Units: pg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Admission | 68.3 (54.3 to 82.2) | 68.0 (53.9 to 82.2) | | |
| 24 hours | 184.1 (98.0 to 270.2) | 190.4 (103.2 to 277.5) | | |
| 48 hours | 230.5 (110.3 to 350.7) | 248.8 (121.9 to 375.8) | | |
| 72 hours | 243.2 (120.0 to 366.3) | 263.2 (132.8 to 393.6) | | |

Statistical analyses

| | |
|----------------------------|---------------------------|
| Statistical analysis title | NfL, mixed model analysis |
|----------------------------|---------------------------|

Statistical analysis description:

NfL levels from admission to 72 hours after admission

| | |
|-------------------|------------------------------|
| Comparison groups | Placebo v Methylprednisolone |
|-------------------|------------------------------|

| | |
|---|-----|
| Number of subjects included in analysis | 137 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|----------------------|
| Analysis type | other ^[7] |
|---------------|----------------------|

| | |
|---------|-----------------------|
| P-value | = 0.96 ^[8] |
|---------|-----------------------|

| | |
|--------|-----------------------|
| Method | Mixed models analysis |
|--------|-----------------------|

Notes:

[7] - Linear mixed model without baseline adjustment

[8] - P value for the treatment-by-time interaction listed above. Time specific comparisons of methylprednisolone vs placebo at admission: $p=0.9$, 24 hours: $p=0.9$, 48 hours: $p=0.8$, and 72 hours: $p=0.8$.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From time of randomization till 180 days after cardiac arrest

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

Dictionary used

| | |
|-----------------|----------------|
| Dictionary name | Study protocol |
|-----------------|----------------|

| | |
|--------------------|-----|
| Dictionary version | 3.1 |
|--------------------|-----|

Reporting groups

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

Reporting group description: -

| | |
|-----------------------|--------------------|
| Reporting group title | Methylprednisolone |
|-----------------------|--------------------|

Reporting group description: -

| Serious adverse events | Placebo | Methylprednisolone | |
|--|---|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 37 / 69 (53.62%) | 35 / 68 (51.47%) | |
| number of deaths (all causes) | 25 | 17 | |
| number of deaths resulting from adverse events | | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 10 / 69 (14.49%) | 7 / 68 (10.29%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 13 / 69 (18.84%) | 12 / 68 (17.65%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Bleeding | Additional description: Defined as the occurrence of bleeding, either diagnosed in-hospital or requiring in-hospital treatment. | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 68 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Dialysis | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 68 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 5 / 68 (7.35%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Metabolic disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 68 (1.47%) | |
| 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: 1 %

| Non-serious adverse events | Placebo | Methylprednisolone | |
|---|------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 69 (47.83%) | 49 / 68 (72.06%) | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 7 / 69 (10.14%) | 7 / 68 (10.29%) | |
| occurrences (all) | 8 | 9 | |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Bleeding | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 2 / 68 (2.94%) | |
| occurrences (all) | 3 | 2 | |

| | | | |
|--|------------------------|------------------------|--|
| Electrolyte imbalance subjects affected / exposed occurrences (all) | 15 / 69 (21.74%) 17 | 25 / 68 (36.76%) 30 | |
| Infections and infestations Infection subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 5 | 2 / 68 (2.94%) 3 | |
| Metabolism and nutrition disorders Metabolic disorder subjects affected / exposed occurrences (all) | 8 / 69 (11.59%) 8 | 27 / 68 (39.71%) 30 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36414975>

<http://www.ncbi.nlm.nih.gov/pubmed/37943300>