



Clinical trial results:

The effects of different vasopressors on the innate immune response during experimental human endotoxemia, a pilot proof-of-principle study

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-002706-36 |
| Trial protocol | NL |
| Global end of trial date | 21 March 2016 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 08 May 2021 |
| First version publication date | 08 May 2021 |
| Summary attachment (see zip file) | Effect of vasopressors on the macro- and microcirculation during systemic inflammation in humans in vivo (shk.0000000000001357.pdf) Norepinephrine Dysregulates the Immune Response and Compromises Host Defense during Sepsis (rccm.202002-0339oc (1).pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | VASOPRESSOR-LPS |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | CMO: 2015-2079 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Radboud University Nijmegen Medical Centre |
| Sponsor organisation address | Geert Grooteplein 10, Nijmegen, Netherlands, 6500 HB |
| Public contact | Research IC, office of Roel Stolk, Radboudumc, roeland.stolk@radboudumc.nl |
| Scientific contact | Research IC, office of Roel Stolk, Radboudumc, roeland.stolk@radboudumc.nl |

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

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to investigate whether noradrenaline exerts immunomodulatory effects in humans in vivo during experimental human endotoxemia. (administration of lipopolysaccharide [LPS] in healthy volunteers).

Protection of trial subjects:

All subjects provided written informed consent.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 01 January 2016 |
| 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 | Netherlands: 40 |
| Worldwide total number of subjects | 40 |
| 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) | 40 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

40 healthy male volunteers were included.

Pre-assignment

Screening details:

All subjects were screened by physical examination, electrocardiography and routine laboratory exams.

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 40 |
| Number of subjects completed | 40 |

Period 1

| | |
|------------------------------|---|
| Period 1 title | Infusion of study medication (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

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

Arm description: -

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Noradrenaline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

five-hour infusion of 0.05 µg/kg/min norepinephrine

| | |
|--|---|
| Investigational medicinal product name | lipopolysaccharide (E. coliderived LPS) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

intravenous bolus injection with 2 ng/kg lipopolysaccharide

| | |
|------------------|---------------|
| Arm title | Phenylephrine |
|------------------|---------------|

Arm description: -

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fenylefrine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

five hour infusion of 0.5 µg/kg/min phenylephrine

| | |
|---|---|
| Investigational medicinal product name | lipopolysaccharide (E. coliderived LPS) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous bolus use |
| Dosage and administration details: intravenous bolus injection with 2 ng/kg lipopolysaccharide | |
| Arm title | Vasopressin |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Agripresin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: five hour infusion of 0.04 IU/min vasopressin | |
| Investigational medicinal product name | lipopolysaccharide (E. coliderived LPS) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous bolus use |
| Dosage and administration details: intravenous bolus injection with 2 ng/kg lipopolysaccharide | |
| Arm title | Placebo |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | NaCl |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: five hour infusion of placebo (NaCl 0.9%) | |
| Investigational medicinal product name | lipopolysaccharide (E. coliderived LPS) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous bolus use |
| Dosage and administration details: intravenous bolus injection with 2 ng/kg lipopolysaccharide | |

| Number of subjects in period 1 | Norepinephrine | Phenylephrine | Vasopressin |
|---------------------------------------|----------------|---------------|-------------|
| Started | 10 | 10 | 10 |
| Completed | 10 | 10 | 10 |

| Number of subjects in period 1 | Placebo |
|---------------------------------------|---------|
| Started | 10 |
| Completed | 10 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|----------------|
| Reporting group title | Norepinephrine |
| Reporting group description: - | |
| Reporting group title | Phenylephrine |
| Reporting group description: - | |
| Reporting group title | Vasopressin |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | Norepinephrine | Phenylephrine | Vasopressin |
|---------------------------------------|----------------|---------------|-------------|
| Number of subjects | 10 | 10 | 10 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 10 | 10 | 10 |
| Gender categorical Units: Subjects | | | |
| Male | 10 | 10 | 10 |

| Reporting group values | Placebo | Total | |
|---------------------------------------|---------|-------|--|
| Number of subjects | 10 | 40 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 10 | 40 | |
| Gender categorical Units: Subjects | | | |
| Male | 10 | 40 | |

End points

End points reporting groups

| | |
|--------------------------------|----------------|
| Reporting group title | Norepinephrine |
| Reporting group description: - | |
| Reporting group title | Phenylephrine |
| Reporting group description: - | |
| Reporting group title | Vasopressin |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

Primary: Mean arterial pressure

| | |
|---|------------------------|
| End point title | Mean arterial pressure |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Before and after LPS administration (t=-90, -30, 0, 90, 210, 270 min) | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: mmHg | | | | |
| arithmetic mean (standard error) | | | | |
| t=-90 | 92 (± 8) | 92 (± 10) | 94 (± 8) | 95 (± 8) |
| t=-30 | 105 (± 6) | 102 (± 9) | 95 (± 4) | 96 (± 6) |
| t=90 | 101 (± 8) | 95 (± 12) | 98 (± 10) | 94 (± 7) |
| t=270 | 82 (± 5) | 77 (± 5) | 81 (± 7) | 84 (± 7) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: Heart rate

| | |
|-----------------|------------|
| End point title | Heart rate |
|-----------------|------------|

| |
|------------------------|
| End point description: |
|------------------------|

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

| |
|----------------------|
| End point timeframe: |
|----------------------|

| |
|---|
| Before and after LPS administration (t=-90, -30, 0, 90, 210, 270 min) |
|---|

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: bpm | | | | |
| arithmetic mean (standard error) | | | | |
| t=-90 | 61 (± 8) | 64 (± 8) | 67 (± 8) | 62 (± 10) |
| t=-30 | 57 (± 12) | 56 (± 8) | 65 (± 10) | 61 (± 11) |
| t=90 | 70 (± 9) | 72 (± 13) | 77 (± 8) | 78 (± 12) |
| t=270 | 87 (± 10) | 86 (± 6) | 94 (± 11) | 82 (± 9) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: Cardiac output (PCA)

| | |
|-----------------|----------------------|
| End point title | Cardiac output (PCA) |
|-----------------|----------------------|

| |
|------------------------|
| End point description: |
|------------------------|

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

| |
|----------------------|
| End point timeframe: |
|----------------------|

| |
|---|
| Before and after LPS administration (t=-90, -30, 0, 90, 210, 270 min) |
|---|

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: Flow (unit) | | | | |
| arithmetic mean (standard error) | | | | |
| t=-90 | 6.95 (± 2.80) | 7.58 (± 4.33) | 6.57 (± 3.30) | 8.11 (± 3.22) |
| t=-30 | 5.75 (± 2.38) | 6.97 (± 2.32) | 5.54 (± 1.88) | 7.89 (± 2.66) |
| t=90 | 6.09 (± 2.79) | 10.01 (± 5.01) | 5.25 (± 2.97) | 9.80 (± 2.89) |
| t=270 | 12.38 (± 3.35) | 15.55 (± 3.19) | 11.79 (± 3.18) | 13.24 (± 6.23) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two- way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |

Primary: Systemic vascular resistance (PCA)

| | |
|---|------------------------------------|
| End point title | Systemic vascular resistance (PCA) |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Before and after LPS administration (t=-90, -30, 0, 90, 210, 270 min) | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: Resistance (unit) | | | | |
| arithmetic mean (standard error) | | | | |
| t=-90 | 15.57 (± 6.94) | 14.76 (± 5.95) | 17.59 (± 7.88) | 13.98 (± 6.99) |
| t=-30 | 21.38 (± 10.2) | 15.73 (± 3.96) | 18.70 (± 5.7) | 13.45 (± 4.38) |
| t=90 | 19.50 (± 7.99) | 11.84 (± 5.61) | 23.03 (± 10.96) | 10.71 (± 4.75) |
| t=270 | 7.09 (± 2.09) | 5.12 (± 1.12) | 7.62 (± 3.41) | 7.72 (± 4.03) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: TNF-a AUC

| | |
|------------------------|-----------|
| End point title | TNF-a AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Study period | |

| | | | | |
|--------------------------------------|----------------------|----------------------|----------------------|----------------------|
| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 37526 (\pm 16717) | 41009 (\pm 15641) | 54772 (\pm 33812) | 38151 (\pm 19731) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: IL-6 AUC

| | |
|---------------------------|----------|
| End point title | IL-6 AUC |
| End point description: | |
| IL-6 Area Under the Curve | |
| End point type | Primary |

End point timeframe:

Study period

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|--------------------------------------|-----------------|-----------------|------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 76582 (± 34609) | 63212 (± 24427) | 132229 (± 73580) | 89017 (± 32579) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: IL-8 AUC

| | |
|------------------------|----------|
| End point title | IL-8 AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Study period | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 47912 (± 15395) | 49282 (± 12597) | 61667 (± 20259) | 57342 (± 22089) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: IL-10 AUC

| | |
|------------------------|-----------|
| End point title | IL-10 AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Study period | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|--------------------------------------|----------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 19970 (\pm 16423) | 19068 (\pm 9330) | 14479 (\pm 8151) | 11566 (\pm 4530) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: MCP-1 AUC

| | |
|------------------------|-----------|
| End point title | MCP-1 AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Study period | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|--------------------------------------|------------------------|-----------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 310530 (\pm 126410) | 314506 (\pm 55854) | 437264 (\pm 155595) | 433810 (\pm 149740) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: IP10 AUC

| | |
|------------------------|----------|
| End point title | IP10 AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Study period | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|--------------------------------------|-------------------------|--------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 2072000 (\pm 873679) | 2731000 (\pm 1072000) | 3397000 (\pm 1707000) | 4640000 (\pm 3920000) |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |

| | |
|---|---------------|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: G-CSF AUC

| | |
|------------------------|-----------|
| End point title | G-CSF AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Study period | |

| End point values | Norepinephrine | Phenylephrine | Vasopressin | Placebo |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 10 | 10 |
| Units: AUC | | | | |
| arithmetic mean (standard deviation) | 23828 (± 14986) | 28077 (± 15249) | 47197 (± 27734) | 33041 (± 26548) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Two way analysis of variance |
| Comparison groups | Norepinephrine v Phenylephrine v Vasopressin v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout complete study period

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 4.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Norepinephrine |
|-----------------------|----------------|

Reporting group description: -

| | |
|-----------------------|---------------|
| Reporting group title | Phenylephrine |
|-----------------------|---------------|

Reporting group description: -

| | |
|-----------------------|-------------|
| Reporting group title | Vasopressin |
|-----------------------|-------------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | Norepinephrine | Phenylephrine | Vasopressin |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | Placebo | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Norepinephrine | Phenylephrine | Vasopressin |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | 10 / 10 (100.00%) | 10 / 10 (100.00%) |
| General disorders and administration site conditions | | | |

| | | | |
|---|-------------------------|-------------------------|-------------------------|
| Flu-like symptoms subjects affected / exposed occurrences (all) | 10 / 10 (100.00%) 10 | 10 / 10 (100.00%) 10 | 10 / 10 (100.00%) 10 |
|---|-------------------------|-------------------------|-------------------------|

| | | | |
|---|-------------------|--|--|
| Non-serious adverse events | Placebo | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | | |
| General disorders and administration site conditions | | | |
| Flu-like symptoms | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | | |
| occurrences (all) | 10 | | |

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

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

| |
|--|
| 1) Low dosages of norepinephrine and phenylephrine were administered to healthy subjects |
|--|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32520577>