



## Clinical trial results:

**Effects of supplemental oxygen on systemic and cerebral hemodynamics in experimental hypovolemia: A randomized, phase IV, crossover study to study the effect of supplemental oxygen vs. room air on cerebral and systemic hemodynamics in healthy volunteers > 18 years during experimental hypovolemia in the lower body negative pressure model of hypovolemia.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-003238-35 |
| Trial protocol           | NO             |
| Global end of trial date | 14 June 2022   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 13 July 2023 |
| First version publication date | 13 July 2023 |

### Trial information

#### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 4_141221 |
|-----------------------|----------|

#### Additional study identifiers

|                                    |  |
|------------------------------------|--|
| ISRCTN number                      | -  |
| ClinicalTrials.gov id (NCT number) | NCT05150418  |
| WHO universal trial number (UTN)   | -  |
| Other trial identifiers            | Regional Committees for Medical Research Ethics - : 285164 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Oslo University Hospital   |
| Sponsor organisation address | Kirkeveien 166, Oslo, Norway, 0450   |
| Public contact               | Department of Anesthesiology, Oslo University Hospital, 47 22119690, lars.oivind.hoiseth@hotmail.com       |
| Scientific contact           | Department of Anesthesiology, Oslo University Hospital, 90749409 22119690, lars.oivind.hoiseth@hotmail.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                       | 15 April 2023 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 14 June 2022  |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 14 June 2022  |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

Supplemental oxygen is frequently administered in acutely and critically ill patients, specifically, it is often administered in trauma patients to avoid arterial hypoxemia and tissue hypoxia. There is also an increasing focus on potentially deleterious effects of hyperoxia. Further, the hemodynamic response to hyperoxia in hypovolemia is poorly understood.

The present study aims to investigate the effects of supplemental oxygen on systemic and cerebral hemodynamics in simulated hypovolemia in healthy volunteers.

Protection of trial subjects:

The trial was carried out in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 01 September 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 | Norway: 15 |
| Worldwide total number of subjects   | 15         |
| EEA total number of subjects         | 15         |

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)                      | 15 |
| From 65 to 84 years                       | 0  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Fifteen healthy volunteers were included in this single-centre study performed at Oslo University Hospital, Aker. First visit of first subject was December 2021, and last visit of last subject was June 2022.

### Pre-assignment

Screening details:

Sixteen subjects were screened for participation. Fifteen subjects entered and completed all visits.

### Period 1

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

Blinding implementation details:

The trial was blinded with a crossover design. Two treatments were administered; medical air and 100% oxygen. Subjects, investigators present during the visits were blinded. Analysis of primary outcome was performed before unblinding.

### Arms

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

Arm description:

Inhalation of medical air, 21% oxygen, 79% nitrogen.

|  |   |
|--|---|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | Medisinsk luft (Air Liquide (medicin.dkAir Liquide Gas AB)) |
| Investigational medicinal product code | V03A N05  |
| Other name                             |   |
| Pharmaceutical forms                   | Medicinal gas, liquefied                                    |
| Routes of administration               | Inhalation use  |

Dosage and administration details:

Inhalation om mask with rebreather, 15 litres/minute.

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

Arm description:

Inhalation 100% oxygen.

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | Oxygen, Conoxia           |
| Investigational medicinal product code | V03A N01                  |
| Other name                             |                           |
| Pharmaceutical forms                   | Medicinal gas, compressed |
| Routes of administration               | Inhalation use            |

Dosage and administration details:

Inhalation om mask with rebreather, 15 litres/minute.

| <b>Number of subjects in period 1</b> | Medical air | Oxygen |
|---------------------------------------|-------------|--------|
| Started                               | 15          | 15     |
| Completed                             | 15          | 15     |

## Baseline characteristics

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | Baseline |
|-----------------------|----------|

Reporting group description: -

| Reporting group values                                | Baseline | Total |  |
|---|----------|-------|--|
| Number of subjects                                    | 15       | 15    |  |
| Age categorical                                       |          |       |  |
| Units: Subjects                                       |          |       |  |
| In utero  | 0        | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0        | 0     |  |
| Newborns (0-27 days)                                  | 0        | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0        | 0     |  |
| Children (2-11 years)                                 | 0        | 0     |  |
| Adolescents (12-17 years)                             | 0        | 0     |  |
| Adults (18-64 years)                                  | 15       | 15    |  |
| From 65-84 years                                      | 0        | 0     |  |
| 85 years and over                                     | 0        | 0     |  |
| Gender categorical                                    |          |       |  |
| Units: Subjects                                       |          |       |  |
| Female  | 7        | 7     |  |
| Male  | 8        | 8     |  |

## End points

### End points reporting groups

|  |             |
|--|-------------|
| Reporting group title  | Medical air |
| Reporting group description:<br>Inhalation of medical air, 21% oxygen, 79% nitrogen. |             |
| Reporting group title  | Oxygen      |
| Reporting group description:<br>Inhalation 100% oxygen.                              |             |

### Primary: Cardiac output

|  |                |
|--|----------------|
| End point title  | Cardiac output |
| End point description:<br>Effect of treatment on cardiac output during lower body negative pressure. |                |
| End point type   | Primary        |
| End point timeframe:<br>During experimental intervention, approximately 30 min.                      |                |

| End point values                          | Medical air            | Oxygen                   |  |  |
|---|------------------------|--------------------------|--|--|
| Subject group type                        | Reporting group        | Reporting group          |  |  |
| Number of subjects analysed               | 15                     | 15                       |  |  |
| Units: litres/minute                      |                        |                          |  |  |
| arithmetic mean (confidence interval 95%) | -0.22 (-0.26 to -0.19) | 0.031 (-0.0152 to 0.077) |  |  |

### Statistical analyses

|  |                         |
|--|-------------------------|
| Statistical analysis title   | Oxygen vs. medical air. |
| Statistical analysis description:<br>Effect of oxygen compared to medical air on change in cardiac output during lower body negative pressure. |                         |
| Comparison groups  | Medical air v Oxygen    |
| Number of subjects included in analysis  | 30                      |
| Analysis specification   | Pre-specified           |
| Analysis type  | superiority             |
| P-value  | = 0.188 <sup>[1]</sup>  |
| Method   | Regression, Linear      |
| Parameter estimate   | Mean difference (net)   |
| Point estimate   | 0.031                   |

| Confidence interval |         |
|---------------------|---------|
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.015  |
| upper limit         | 0.077   |

Notes:

[1] - There was no statistically significant effect of oxygen compared to air on the changes in cardiac output during LBNP (0.031 L/min/LBNP level, 95% CI: - 0.015 to 0.077, P = 0.188).



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All AEs and SAEs were collected from the start of intervention until end of the last visit at the time points specified in the Protocol/ SoA.

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 5.0 |
|--------------------|-----|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Medical air |
|-----------------------|-------------|

Reporting group description:

Inhalation of medical air, 21% oxygen, 79% nitrogen.

|                       |        |
|-----------------------|--------|
| Reporting group title | Oxygen |
|-----------------------|--------|

Reporting group description:

Inhalation 100% oxygen.

| Serious adverse events                            | Medical air    | Oxygen         |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 15 (0.00%) | 0 / 15 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Medical air   | Oxygen         |  |
|---|---|----------------|--|
| Total subjects affected by non-serious adverse events |   |                |  |
| subjects affected / exposed                           | 3 / 15 (20.00%)   | 0 / 15 (0.00%) |  |
| Infections and infestations                           |   |                |  |
| COVID-19  |   |                |  |
| subjects affected / exposed                           | 2 / 15 (13.33%)   | 0 / 15 (0.00%) |  |
| occurrences (all)                                     | 2   | 0              |  |
| Pharyngitis   | Additional description: "Sore throat". No treatment needed (common cold). |                |  |
| subjects affected / exposed                           | 1 / 15 (6.67%)  | 0 / 15 (0.00%) |  |
| occurrences (all)                                     | 1   | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported