



## Clinical trial results:

### Crystalloid versus colloid for goal directed haemodynamic optimisation in major abdominal cancer surgery.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-002217-36 |
| Trial protocol           | DK             |
| Global end of trial date | 30 June 2015   |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 22 September 2021   |
| First version publication date    | 22 September 2021   |
| Summary attachment (see zip file) | Original article<br>(Goal_directed_therapy_with_bolus_albumin_5_is_not.9.pdf) |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 20130021 |
|-----------------------|----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Odense University Hospital  |
| Sponsor organisation address | Sdr. Boulevard, Odense, Denmark, 5000   |
| Public contact               | Dept. Anaesthesiology V, Odense University Hospital, 0045 65413758, anders.gadegaard.jensen@rsyd.dk |
| Scientific contact           | Dept. Anaesthesiology V, Odense University Hospital, 0045 60630890, j.staehr@rn.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:

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## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 06 June 2019 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 29 June 2015 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 30 June 2015 |
| Was the trial ended prematurely?                     | No           |

Notes:

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## General information about the trial

Main objective of the trial:

To investigate differences in intraoperative global and local oxygen delivery in goal directed haemodynamic optimisation with crystalloids versus colloids.

Protection of trial subjects:

This single centre, double blind, randomised controlled trial was approved by The Regional Committees on Health Research Ethics for Southern Denmark (Ref: S-20130021) on 3 March 2014, and was registered at <https://eudract.ema.europa.eu/>, Identifier: 2013-002217-36. It was conducted at Odense University Hospital, Denmark. The study started 1 May 2014. The trial was conducted in accordance with the Helsinki declaration and guideline for good clinical practice, and monitored by an external agency.

Background therapy:

Anaesthesia and intra-operative monitoring

A standard fasting regime was followed. Standard monitoring included pulse oximetry, three lead electrocardiography, invasive arterial and central blood pressure measurement, and spirometry with inspiratory and expiratory oxygen, carbon dioxide and volatile agent analysis. In addition, bispectral index score (BIS, monitoring of anaesthesia depth, BISx Power Link, Philips Medical Systems, Eindhoven, The Netherlands) and central temperature were continuously monitored.

General anaesthesia was induced with fentanyl (1 to 3 mg kg<sup>-1</sup>) and propofol (1 to 3mg kg<sup>-1</sup>), and neuromuscular blockade with cisatracurium (0.15mg kg<sup>-1</sup>).

Anaesthesia was maintained with sevoflurane in oxygen enriched air. A thoracic epidural catheter (level Th 6 to 7) was inserted and an infusion of epidural bupivacaine (5mgml<sup>-1</sup>) 3 to 6mlh<sup>-1</sup> was continued during surgery.

Mechanical ventilation was performed with tidal volumes (V<sub>t</sub>) 6 to 8 ml kg<sup>-1</sup> ideal body weight and positive endexpiratory pressure (PEEP) PEEP 5 to 8mmHg. In thoraco-abdominal oesophageal surgery, the abdominal dissection was performed first, then, following a change to propofol-remifentanyl anaesthesia, a double lumen endotracheal tube was inserted. The patient was positioned in the left lateral decubitus jack-knife position and one-lung ventilation of the left lung was established.

All patients were extubated and transferred for postoperative care and observation in an ICU for at least 24 h following the start of surgery until the next morning. The decision to discharge from hospital was at the discretion of the surgeon in charge of the patient.

Systemic and mesenteric flow monitoring

The LiDCOplus (LiDCO Ltd, Cambridge, UK) monitor was attached and calibrated after induction of anaesthesia.

This device uses a transpulmonary lithium indicator dilution technique. Patient-specific calibration from three independently measured COs was obtained. Establishment an

Evidence for comparator:

Studies, comparing colloids with crystalloids in the peri-operative setting have yet to demonstrate a convincing and guideline changing effect.

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 April 2014 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 60 |
| Worldwide total number of subjects   | 60          |
| EEA total number of subjects         | 60          |

Notes:

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### 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)                      | 20 |
| From 65 to 84 years                       | 40 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients were screened for eligibility at the pre-operative anaesthetic consultation and were included on the day of surgery after informed consent.

### Pre-assignment

Screening details:

Patients were screened for eligibility at the pre-operative anaesthetic consultation and were included on the day of surgery after informed consent.

A total of 186 patients were screened for eligibility.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Intraoperative (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 |

### Arms

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

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

Arm description: -

|  |   |
|--|---|
| Arm type                               | Experimental                                      |
| Investigational medicinal product name | Human Albumin 5%                                  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate and solvent for solution for infusion |
| Routes of administration               | Intravenous use                                   |

Dosage and administration details:

250 ml bolus i.v. PRN.

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

Arm description: -

|  |   |
|--|---|
| Arm type                               | Placebo                                 |
| Investigational medicinal product name | NaCl 0.9%                               |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate for dispersion for infusion |
| Routes of administration               | Intravenous use                         |

Dosage and administration details:

250 mL iv PRN

| <b>Number of subjects in period 1</b> | Intervention | Control |
|---------------------------------------|--------------|---------|
| Started                               | 30           | 30      |
| Completed                             | 30           | 30      |

## Baseline characteristics

### Reporting groups

|                                |              |
|--------------------------------|--------------|
| Reporting group title          | Intervention |
| Reporting group description: - |              |
| Reporting group title          | Control      |
| Reporting group description: - |              |

| Reporting group values                             | Intervention | Control | Total |
|--|--------------|---------|-------|
| Number of subjects                                 | 30           | 30      | 60    |
| Age categorical                                    |              |         |       |
| Age (years): HA 68 [62 to 71]. NaCL 65 [59 to 72]  |              |         |       |
| Units: Subjects                                    |              |         |       |
| In utero   | 0            | 0       | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0            | 0       | 0     |
| Newborns (0-27 days)                               | 0            | 0       | 0     |
| Infants and toddlers (28 days-23 months)           | 0            | 0       | 0     |
| Children (2-11 years)                              | 0            | 0       | 0     |
| Adolescents (12-17 years)                          | 0            | 0       | 0     |
| Adults (18-64 years)                               | 10           | 10      | 20    |
| From 65-84 years                                   | 20           | 20      | 40    |
| 85 years and over                                  | 0            | 0       | 0     |
| Gender categorical                                 |              |         |       |
| Units: Subjects                                    |              |         |       |
| Female   | 7            | 11      | 18    |
| Male   | 23           | 19      | 42    |

## End points

### End points reporting groups

|                                |              |
|--------------------------------|--------------|
| Reporting group title          | Intervention |
| Reporting group description: - |              |
| Reporting group title          | Control      |
| Reporting group description: - |              |

### Primary: mDO2i

|                        |                      |
|------------------------|----------------------|
| End point title        | mDO2i <sup>[1]</sup> |
| End point description: |                      |

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Intraoperative       |         |

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: Please see published article (PMID Please see peer reviewed publication (attached, PMID 31972601).

| End point values                      | Intervention       | Control            |  |  |
|---------------------------------------|--------------------|--------------------|--|--|
| Subject group type                    | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed           | 30                 | 30                 |  |  |
| Units: ml/min/m2                      |                    |                    |  |  |
| median (inter-quartile range (Q1-Q3)) | 17.0 (7.6 to 27.5) | 12.1 (5.8 to 28.7) |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

30 days

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

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### Dictionary used

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

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|                    |    |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

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Frequency threshold for reporting non-serious adverse events: 0.05 %

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Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: We had no adverse events.



## 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