



## Clinical trial results: Early Goal-Directed Nutrition in ICU Patients – EAT-ICU Trial Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2011-002547-94  |
| Trial protocol           | DK              |
| Global end of trial date | 15 October 2016 |

### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 29 May 2018  |
| First version publication date    | 29 May 2018  |
| Summary attachment (see zip file) | EAT-ICU publication (ICM.EAT_ICU.pdf)<br>EAT-ICU appendix (ICM.EAT_ICU_Appendix.pdf) |

### Trial information

#### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 2011-420 |
|-----------------------|----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01372176 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Dept. Of Intensive Care 4131, Rigshospitalet   |
| Sponsor organisation address | Blegdamsvej 9, Copenhagen OE, Denmark, 2100  |
| Public contact               | ICU Research Group, Dept. Of Intensive Care 4131, Rigshospitalet, +45 35458333, anders.perner@regionh.dk |
| Scientific contact           | ICU Research Group, Dept. Of Intensive Care 4131, Rigshospitalet, +45 35458333, anders.perner@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                       | 31 May 2017     |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 15 October 2016 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 15 October 2016 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

This randomised trial will investigate the effect of an optimised nutrition therapy during intensive care, on short term clinical outcome and mitochondrial function in addition to long-term physical function and quality of life. We hypothesise, that early nutritional therapy, directed towards patient-specific goals for energy and protein requirements, will improve both short- and long-term outcomes.

Protection of trial subjects:

Compliance with ethical standards

Background therapy: -

Evidence for comparator: -

|   |                               |
|---|-------------------------------|
| Actual start date of recruitment                          | 03 June 2013                  |
| Long term follow-up planned                               | Yes                           |
| Long term follow-up rationale                             | Efficacy, Scientific research |
| Long term follow-up duration                              | 6 Months                      |
| Independent data monitoring committee (IDMC) involvement? | No                            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Denmark: 203 |
| Worldwide total number of subjects   | 203          |
| EEA total number of subjects         | 203          |

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)                      | 97 |
| From 65 to 84 years                       | 97 |

|                   |   |
|-------------------|---|
| 85 years and over | 9 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

EAT-ICU was a single-centre, randomised, stratified, parallel-group, clinical trial with blinded outcome assessment, conducted at the Department of Intensive Care, Copenhagen University Hospital, Rigshospitalet, Denmark between June 2013 and October 2016 (last patient randomised in April 2016, followed by 6 months followup).

### Pre-assignment

Screening details:

We consecutively screened patients 18 years of age or older within 24 h of any ICU admission for inclusion if they were (1) acutely admitted to the ICU; (2) had an expected length of stay in the ICU of more than 3 days; (3) were mechanically ventilated via a cuffed endotracheal or tracheotomy tube; (4) had a central venous catheter and (5) we

### Period 1

|                              |                                   |
|------------------------------|-----------------------------------|
| Period 1 title               | Screening period (overall period) |
| Is this the baseline period? | Yes                               |
| Allocation method            | Randomised - controlled           |
| Blinding used                | Single blind                      |
| Roles blinded                | Assessor <sup>[1]</sup>           |

Blinding implementation details:

The allocated nutrition strategy was not masked to research or clinical staff during the trial period. Investigators assessing quality of life at 6 months (the primary outcome) and rates of nosocomial infections (a secondary outcome) as well as the statistician performing the primary analysis of the primary outcome were all blinded to the intervention.

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Intervention (EGDN) |

Arm description:

See attached manuscript for description and products used in both arms.

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

Dosage and administration details:

See attached info.

|  |                       |
|--|-----------------------|
| Investigational medicinal product name | Mixamin Glucos        |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

See attached.

|  |                                    |
|--|------------------------------------|
| Investigational medicinal product name   | Glucose 50%                        |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for solution for infusion |
| Routes of administration   | Intravenous use                    |
| Dosage and administration details:<br>See attached.  |                                    |
| Investigational medicinal product name   | Vamin                              |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for infusion              |
| Routes of administration   | Intravenous use                    |
| Dosage and administration details:<br>Please see attached protocol for details.              |                                    |
| Investigational medicinal product name   | SMOFlipid                          |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for infusion              |
| Routes of administration   | Intravenous use                    |
| Dosage and administration details:<br>See attached.  |                                    |
| <b>Arm title</b>   | Control (standard care)            |
| Arm description:<br>Please see publication attached for information on conduct and products. |                                    |
| Arm type   | Active comparator                  |
| Investigational medicinal product name   | SMOFkabiven                        |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for infusion              |
| Routes of administration   | Intravenous use                    |
| Dosage and administration details:<br>See attached info.                                     |                                    |
| Investigational medicinal product name   | Mixamin Glucos                     |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for infusion              |
| Routes of administration   | Intravenous use                    |
| Dosage and administration details:<br>See attached.  |                                    |
| Investigational medicinal product name   | Glucose 50%                        |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for solution for infusion |
| Routes of administration   | Intravenous use                    |
| Dosage and administration details:<br>See attached.  |                                    |
| Investigational medicinal product name   | Vamin                              |
| Investigational medicinal product code   |                                    |
| Other name   |                                    |
| Pharmaceutical forms   | Solution for infusion              |
| Routes of administration   | Intravenous use                    |

Dosage and administration details:

Please see attached protocol.

|  |                       |
|--|-----------------------|
| Investigational medicinal product name | SMOFlipid             |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

See attached.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: I don't know why this error occurs.

| <b>Number of subjects in period 1</b> | Intervention (EGDN) | Control (standard care) |
|---------------------------------------|---------------------|-------------------------|
| Started                               | 102                 | 101                     |
| Completed                             | 100                 | 99                      |
| Not completed                         | 2                   | 2                       |
| Adverse event, serious fatal          | 1                   | 2                       |
| Consent withdrawn by subject          | 1                   | -                       |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Screening period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values                             | Screening period | Total |  |
|--|------------------|-------|--|
| Number of subjects                                 | 203              | 203   |  |
| Age categorical                                    |                  |       |  |
| Median age in years                                |                  |       |  |
| Units: Subjects                                    |                  |       |  |
| In utero   | 0                | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                | 0     |  |
| Newborns (0-27 days)                               | 0                | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                | 0     |  |
| Children (2-11 years)                              | 0                | 0     |  |
| Adolescents (12-17 years)                          | 0                | 0     |  |
| Adults (18-64 years)                               | 97               | 97    |  |
| From 65-84 years                                   | 97               | 97    |  |
| 85 years and over                                  | 9                | 9     |  |
| Age in years (median)                              | 0                | 0     |  |
| Gender categorical                                 |                  |       |  |
| Male %   |                  |       |  |
| Units: Subjects                                    |                  |       |  |
| Female   | 79               | 79    |  |
| Male   | 124              | 124   |  |

## End points

### End points reporting groups

|  |                         |
|--|-------------------------|
| Reporting group title  | Intervention (EGDN)     |
| Reporting group description:<br>See attached manuscript for description and products used in both arms.  |                         |
| Reporting group title  | Control (standard care) |
| Reporting group description:<br>Please see publication attached for information on conduct and products. |                         |

### Primary: Primary endpoint

|   |                  |
|---|------------------|
| End point title                                       | Primary endpoint |
| End point description:<br>PCS-score of SF-36.         |                  |
| End point type  | Primary          |
| End point timeframe:<br>6 months after randomisation. |                  |

| End point values                     | Intervention<br>(EGDN) | Control<br>(standard care) |  |  |
|--------------------------------------|------------------------|----------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group            |  |  |
| Number of subjects analysed          | 100                    | 99                         |  |  |
| Units: 22.9                          |                        |                            |  |  |
| arithmetic mean (standard deviation) |                        |                            |  |  |
| PCS-score                            | 22.9 (± 21.8)          | 23.0 (± 22.3)              |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title  | Primary outcome measure                       |
| Statistical analysis description:<br>For<br>the primary analysis of the primary outcome, the statistician<br>did multiple imputation, based on chained equations<br>as implemented in the R package 'mice', to account<br>for the missing PCS scores of the 23 non-responders at<br>6-month follow-up |   |
| Comparison groups   | Intervention (EGDN) v Control (standard care) |
| Number of subjects included in analysis   | 199   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | equivalence                                   |
| P-value   | < 0.05  |
| Method  | Regression, Linear                            |





## Adverse events

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

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Timeframe for reporting adverse events:

Full intervention period.

Adverse event reporting additional description:

SAR

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

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### Dictionary used

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|                 |    |
|-----------------|----|
| Dictionary name | NA |
|-----------------|----|

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|                    |   |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

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Frequency threshold for reporting non-serious adverse events: 4 %

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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: None were recorded as this study was performed in ICU patients.

## 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

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

|   |
|---|
| Please see attached information for more details. |
|---|

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28936712>

<http://www.ncbi.nlm.nih.gov/pubmed/27585532>