



## Clinical trial results:

### Intracoronary administration of melatonin for patients with acute myocardial infarction: a placebo controlled randomized study.

#### Summary

EudraCT number	2010-022400-53
Trial protocol	DK
Global end of trial date	28 June 2016

#### Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

#### Trial information

##### Trial identification

Sponsor protocol code	NLH-01
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##### Additional study identifiers

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

Notes:

##### Sponsors

Sponsor organisation name	Sjællands Universitetshospital
Sponsor organisation address	Lykkebækvej 1, Køge, Denmark,
Public contact	Ismail Gögenur, Sjællands Universitetshospital, 0045 47323012, igo@regionsjaelland.dk
Scientific contact	Ismail Gögenur, Sjællands Universitetshospital, 0045 47323012, igo@regionsjaelland.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	01 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2016
Global end of trial reached?	Yes
Global end of trial date	28 June 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

MRI to examine myocardial infarct size, area at risk and myocardial salvage index. MRI is to be performed on day 4 (+/-1).

Protection of trial subjects:

questionnaire on dizziness, konfusion, depression and headache

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	28
From 65 to 84 years	20
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Recruitment started on the 1st of juni 2013. Patients admitted with an ST-elevation myocardial infarction were screened by the cardiologist and recruited in the cardiac lab prior to the acute myocardial reperfusion at Aalborg University Hospital.

### Pre-assignment

Screening details:

A total of 526 patients were screened.

The most important screening criteria: age > 18 years, STEMI ECG-criteria, one significant coronary occlusion (>2mm) with TIMI flow 0-1, PCI within 6 hours of symptom unset, being able to provide informed consent , no prior AMI, cardiogenic shock, and atrial fibrillation.

### Period 1

Period 1 title	Overall trial (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>	Melatonin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Melatonin
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intracoronary use, Intravenous use

Dosage and administration details:

1 mg given as a bolus injection intracoronarily over 30-60 seconds

49 mg given intravenously over 6 hours

<b>Arm title</b>	Placebo
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Arm description:

Isotonic saline

Arm type	Placebo
Investigational medicinal product name	Saline, Natrium chloride
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intracoronary use, Intravenous use

Dosage and administration details:

500ml of isotonic saline

<b>Number of subjects in period 1</b>	Melatonin	Placebo
Started	24	24
Completed	24	24

## Baseline characteristics

### Reporting groups

Reporting group title	Melatonin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description:	
Isotonic saline	

Reporting group values	Melatonin	Placebo	Total
Number of subjects	24	24	48
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			
Units: years			
arithmetic mean	61.7	64	
standard deviation	± 12	± 11	-
Gender categorical			
Units: Subjects			
Female	4	6	10
Male	20	18	38

## End points

### End points reporting groups

Reporting group title	Melatonin
Reporting group description:	-
Reporting group title	Placebo
Reporting group description:	Isotonic saline

### Primary: myocardial salvage index

End point title	myocardial salvage index
End point description:	
End point type	Primary
End point timeframe:	Assessed at day 4 (+/- 1 day) from primary percutaneous coronary intervention

End point values	Melatonin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	19		
Units: %	55	62		

### Statistical analyses

Statistical analysis title	primary analysis
Comparison groups	Melatonin v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

## Adverse events

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

Timeframe for reporting adverse events:

Adverse events were assessed for each patient from inclusion in the trial until 90 days after the inclusion. Period: 01.06.2013 - 01.06.2016

Assessment type	Systematic
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### Dictionary used

Dictionary name	ICD
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Dictionary version	10
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### Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	Melatonin
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Reporting group description: -

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 of the subjects included experiences any adverse events (non-serious). We systematically screened for dizziness, headache, confusion and depression.

Serious adverse events	Placebo	Melatonin	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 24 (25.00%)	6 / 24 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	5 / 24 (20.83%)	6 / 24 (25.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction	Additional description: Reinfarction after the primary treatment		
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Melatonin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	





## **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