Clinical trial results:
Immunoglobulin for Necrotizing Soft Tissue Infections: a Randomised Controlled Trial

Summary

EudraCT number	2013-003556-20
Trial protocol	DK
Global end of trial date	28 August 2016

Results information

Result version number	v1 (current)
This version publication date	31 March 2018
First version publication date	31 March 2018

Trial information

Trial identification

Sponsor protocol code	RH4131-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02111161
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dept. of Intensive Care 4131, Copenhagen University Hospital, Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Forskningskontoret, Dept. of Intensive Care 4131, Copenhagen University Hospital, Rigshospitalet, 0045 35454131, martin.bruun.madsen.01@regionh.dk
Scientific contact	Forskningskontoret, Dept. of Intensive Care 4131, Copenhagen University Hospital, Rigshospitalet, 0045 35454131, martin.bruun.madsen.01@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	27 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2016
Global end of trial reached?	Yes
Global end of trial date	28 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the effect of intravenous, polyspecific immunoglobulin G compared with placebo on the patient reported outcome measure Physical Component Summary Score (PCS) of the Short Form-36 (SF-36) in patients with necrotizing soft tissue infections.

Protection of trial subjects:

Stanard care.

Background therapy:

Standard care.

Evidence for comparator: -

Actual start date of recruitment	07 April 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	62
From 65 to 84 years	34

85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Patients recruited at Copenhagen University Hospital, Rigshospitalet.
First patient included 7 April 2014, last patient included 1 March 2016.

Pre-assignment

Screening details:

All patients with suspected necrotizing soft tissue infection were screened. A total of 129 patients were screened.

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

Blinding implementation details:

A ICU nurse not otherwise involved in the care of the patient who both IVIG and 0.9% saline in a black, opaque plastic bag, inserted an orange-coloured infusion set into the allocated intervention (IVIG or saline) and sealed the bag with a plastic strip.

Arms

Are arms mutually exclusive?	Yes
Arm title	IVIG

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Intravenous, polyspecific immunoglobulin G
Investigational medicinal product code	
Other name	IVIG
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

IVIG (Privigen, CSL Behring, Bern, Switzerland), 25 g/day for three consecutive days.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Saline 0.9%, 250 ml for three consecutive days.

Number of subjects in period 1	IVIG	Placebo
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups	
Reporting group title	IVIG
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	IVIG	Placebo	Total
Number of subjects	50	50	100
Age categorical 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)	30	32	62
From 65-84 years	16	18	34
85 years and over	4	0	4
Age continuous Units: years			
median	59	61	
inter-quartile range (Q1-Q3)	50 to 69	50 to 71	-
Gender categorical Units: Subjects			
Female	20	18	38
Male	30	32	62

End points

End points reporting groups	
Reporting group title	IVIG
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: PCS score of SF-36v2 6 months after randomisation	
End point title	PCS score of SF-36v2 6 months after randomisation
End point description:	
End point type	Primary
End point timeframe:	
6 months after randomisation	

End point values	IVIG	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	45		
Units: No unit				
median (inter-quartile range (Q1-Q3))	36 (0 to 43)	31 (0 to 47)		

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description:	
The primary analysis of the primary outcome was a regres- sion analysis adjusted for the stratification variable (site of NSTI) in the intention-to-treat population. In	
Comparison groups	IVIG v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	10

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

In the ICU

Adverse event reporting additional description:

Only SARs and SUSARs were collected as patients were ICU patients

Assessment type	Systematic

Dictionary used

Dictionary name	Own
Dictionary version	1

Reporting groups

Reporting group title	IVIG
Reporting group description: -	
Reporting group title	Placebo
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: Data not collected.

Serious adverse events	IVIG	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 50 (16.00%)	11 / 50 (22.00%)	
number of deaths (all causes)	6	6	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Thrombosis			
subjects affected / exposed	2 / 50 (4.00%)	3 / 50 (6.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 6	0 / 6	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 50 (12.00%)	8 / 50 (16.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	IVIG	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	

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.

A number of patients recieved IVIG before randomisation.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28421246