Clinical trial results:
Modulation of lung injury complicating lung resection

Summary

EudraCT number	2006-004442-16
Trial protocol	GB
Global end of trial date	01 July 2009

Results information

Result version number	v1 (current)
This version publication date	19 February 2020
First version publication date	19 February 2020

Trial information

Trial identification

Sponsor protocol code	cro524

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00655928
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensingston Campus, London, United Kingdom, SW7 2AZ
Public contact	Mark J Griffiths, Imperial College London, +44 020 7351 8523, m.griffiths@imperial.ac.uk
Scientific contact	Mark J Griffiths, Imperial College London, +44 020 7351 8523, m.griffiths@imperial.ac.uk

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 July 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2009
Global end of trial reached?	Yes
Global end of trial date	01 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate whether it is possible to reduce the amount of lung injury/inflammation caused by one-lung ventilation during lung surgery by giving an antioxidant, acetylcysteine, prior to surgery.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2007
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	United Kingdom: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	40
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adults undergoing elective lung resection for cancer at the Royal Brompton Hospital, London, UK were eligible. Recruitment was between Aug 2008 and July 2009.

Pre-assignment

Screening details:

90 participants were assessed for eligibility, excluded 38 participants and randomised 52.

Period 1

Period 1 title	Randomization
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Randomization period

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	N-acetylcysteine (NAC)

Arm description:

Randomization period

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Placebo	N-acetylcysteine (NAC)
Started	26	26
Completed	24	23
Not completed	2	3
Consent withdrawn by subject	1	1
Physician decision	1	2

Period 2

Period 2 title	Treatment
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind

Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	N-acetylcysteine (NAC)

Arm description:

Eligible adults were randomized to receive preoperative infusion of N-acetylcysteine (240 mg/kg over 12 h)

Arm type	Experimental
Investigational medicinal product name	N-acetylcysteine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Preoperative infusion of N-acetylcysteine, 240 mg/kg in 1000 mL 0.9% saline over 12 h.

Arm title	Placebo

Arm description:

Eligible adults were randomized to receive preoperative infusion of placebo.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Preoperative infusion of 1000 mL 0.9% saline over 12 h.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The group of participants who actually received the allocated treatment.

Number of subjects in period 2[2]	N-acetylcysteine (NAC)	Placebo
Started	23	24
Completed	23	24

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The group of participants who actually received the allocated treatment.

Baseline characteristics

Reporting groups	
Reporting group title	N-acetylcysteine (NAC)
Reporting group description:	
Eligible adults were randomized to receive preoperative infusion of N-acetylcysteine (240 mg/kg over 12 h)	
Reporting group title	Placebo
Reporting group description:	
Eligible adults were randomized to receive preoperative infusion of placebo.	

Reporting group values	N-acetylcysteine (NAC)	Placebo	Total
Number of subjects	23	24	47
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			
geometric mean	68	63.8	
standard deviation	± 10.1	± 11.5	-
Gender categorical			
Units: Subjects			
Female	8	9	17
Male	15	15	30
Spirometry, FEV1			
Units: litres			
arithmetic mean	2.23	2.56	
standard deviation	± 0.97	± 0.81	-
Duration of one-lung ventilation			
Measure Description: One lung ventilation is a process that refers to mechanical separation of the two lungs to allow ventilation of only one lung, while the other lung is compressed by the surgeon or allowed to passively deflate.			
Units: minutes			
geometric mean	134	137	
standard deviation	± 42	± 59	-

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Randomization period	
Reporting group title	N-acetylcysteine (NAC)
Reporting group description: Randomization period	
Reporting group title	N-acetylcysteine (NAC)
Reporting group description: Eligible adults were randomized to receive preoperative infusion of N-acetylcysteine (240 mg/kg over 12 h)	
Reporting group title	Placebo
Reporting group description: Eligible adults were randomized to receive preoperative infusion of placebo.	

Primary: Post-operative Plasma IL-6	
End point title	Post-operative Plasma IL-6
End point description: Plasma IL-6 was measured in duplicate using ELISA	
End point type	Primary
End point timeframe: Post operative, 24 hours	

End point values	N-acetylcysteine (NAC)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: pg/ml				
geometric mean (inter-quartile range (Q1-Q3))	126 (80 to 180)	111 (72 to 162)		

Statistical analyses

Statistical analysis title	IL 6
Comparison groups	N-acetylcysteine (NAC) v Placebo

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 months	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	N-acetylcysteine (NAC)
Reporting group description:	
Eligible adults were randomized to receive preoperative infusion of N-acetylcysteine (240 mg/kg over 12 h)	
Reporting group title	Placebo
Reporting group description:	
Eligible adults were randomized to receive preoperative infusion of placebo.	

Serious adverse events	N-acetylcysteine (NAC)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 23 (60.87%)	12 / 24 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Acut lung injury			
subjects affected / exposed	1 / 23 (4.35%)	2 / 24 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Postoperative complication			
subjects affected / exposed	13 / 23 (56.52%)	10 / 24 (41.67%)	
occurrences causally related to treatment / all	0 / 13	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	N-acetylcysteine (NAC)	Placebo	
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 23 (34.78%)	5 / 24 (20.83%)	
Infections and infestations			
Respiratory infection			
subjects affected / exposed	6 / 23 (26.09%)	3 / 24 (12.50%)	
occurrences (all)	6	3	
Wound infection			
subjects affected / exposed	2 / 23 (8.70%)	0 / 24 (0.00%)	
occurrences (all)	2	0	
Pleural fluid infection			
subjects affected / exposed	2 / 23 (8.70%)	2 / 24 (8.33%)	
occurrences (all)	2	2	
Intravascular cannula infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	
occurrences (all)	1	0	

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26503312