Clinical trial results:
Pilot study: Targeting the inflammatory response after breast cancer surgery with lidocaïne and dexamethasone

Summary

EudraCT number	2012-002222-70
Trial protocol	NL
Global end of trial date	08 November 2016

Results information

Result version number	v1 (current)
This version publication date	14 January 2021
First version publication date	14 January 2021
Summary attachment (see zip file)	Published article (jpr-252377-acute-cytokine-response-during-breast-cancer-surgery-potent.pd.pdf)

Trial information

Trial identification

Sponsor protocol code	Lidobreast

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboud University Medical Center
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525GA
Public contact	Head of Department Anesthesiology, Radboud University Medical Center, K.Vissers@anes.umcn.nl
Scientific contact	Head of Department Anesthesiology, Radboud University Medical Center, K.Vissers@anes.umcn.nl

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 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 November 2016
Global end of trial reached?	Yes
Global end of trial date	08 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is the impact of administering intravenous lidocaïne and dexamethasone on cytokine levels.

Protection of trial subjects:

We aimed to reduce the study burden as much as possible by performing study-measurements coupled to normal care.
Pain scores at baseline and 4 hours postoperative = normal care.
Blood sample for determining cytokine levels at baseline: from the iv canula which was placed before surgery. At 4 hours postoperative: 1 extra vena punction was done, or from the iv canula (if this was possible)
Monitoring of studymedication, which was given during surgery and on the post operative ward. Normal respiratory, haemodynamic and neurologic monitoring was done, which could catch the side effects of lidocaine.

Internal monitoring was performed at the start, during and end of each pilot study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 June 2013
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	Netherlands: 55
Worldwide total number of subjects	55
EEA total number of subjects	55

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	40
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The investigations and data collection for the first study were carried out between November 2014 and March 2015, for the second study between October and December 2015, and for the third study between June and October 2016.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	55
Number of subjects completed	55

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, Data analyst, Carer, Assessor

Arms

Arm title	Overall study

Arm description:

Overall study is pilot 1, 2 and 3 together, all patients recieved lidocaïne or placebo
In pilot 1, patients received no dexamethason
In pilot 3 patients received dexamethason 4 mg
In pilot 3 patients recieved dexamethason 8 mg
During all 3 studies the same protocol was followed

In total, 55 subjects were enrolled and randomized to receive the study medication (20 subjects in study 1, 17 subjects in study 2, and 18 subjects in study 3). Seven patients were excluded for analysis for the following reasons: the pharmacy was unable to provide study medication for 2 patients (study 1, n = 1; study 3, n =1); the protocol was violated in 3 patients of study 1; the surgical procedure was changed in 1 patient in study 2, and 1 patient withdrew consent in study 3

Arm type	Active comparator
Investigational medicinal product name	Lidocaine Hydrochloride 1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During induction of anesthesia patients will receive 1.5mg/kg intravenous lidocaine. After induction of anesthesia patients will receive 2mg/kg/hr intravenous lidocaine until 1 hour after the operation has ended

Number of subjects in period 1	Overall study
Started	55
Completed	48
Not completed	7
Consent withdrawn by subject	1
change of surgery	1
pharmacy was unable to deliver study medication	2
Protocol deviation	3

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	55	55	
Age categorical 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)	40	40	
From 65-84 years	15	15	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	55	55	
Male	0	0	

Subject analysis sets

Subject analysis set title	Effect of dexamethasone and lidocaine on cytokine levels
Subject analysis set type	Full analysis

Subject analysis set description:

The primary outcome measure were the influence of lidocaine and dexamethasone on the difference between plasma levels of cytokines IL-6, IL-10, IL-1β, IL-1Ra, ratio IL-β to IL-1Ra, and the ratio IL-6 to IL-10 at 4 hours postoperative (T2) versus baseline (T0).

Reporting group values	Effect of dexamethasone and lidocaine on cytokine levels		
Number of subjects	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)	35		
From 65-84 years	13		

85 years and over	0		

Gender categorical Units: Subjects			
Female Male	48		

End points

End points reporting groups

Reporting group title	Overall study

Reporting group description:

Overall study is pilot 1, 2 and 3 together, all patients recieved lidocaïne or placebo
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Primary: Influence of lidocaine and dexamethasone on postoperative cytokine levels

End point title	Influence of lidocaine and dexamethasone on postoperative cytokine levels[1]

End point description:

End point type	Primary

End point timeframe:

Between baseline and 4 hours postoperative

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: When filling the form, it constantly gives warnings, probably I do something wrong, but cannot find what it is.

Multiple linear regression analysis was used to evaluate the null hypothesis that lidocaine or dexamethasone had no effect on ΔIL-6, ΔIL-10, ΔIL-1β, ΔIL-1Ra, ΔIL-6/IL-10 and ΔIL-1β/IL-1Ra. Descriptive analysis preceded formal statistical analysis. Based on a striking pattern in the dataset, we introduced 'post hoc' the duration of surgery as an independent variable.

End point values	Effect of dexamethasone and lidocaine on cytokine levels			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: pg/mL				
arithmetic mean (standard deviation)	2.28 (± 1.58)			

Attachments (see zip file)	Effect on cytokines of lidoc/dex/Table 2_Revised_.docx raw cytokine levels/Supplementary Tables_S2_revised.docx

Statistical analyses

No statistical analyses for this end point

Secondary: The difference within study groups of pain scores and analgesic use

End point title	The difference within study groups of pain scores and analgesic use

End point description:

End point type	Secondary

End point timeframe:

directly after surgery and at 4 hours postoperative

End point values	Effect of dexamethasone and lidocaine on cytokine levels			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: numeric rating scale	48			

Attachments (see zip file)	lidocaine, dexamethason cytokines/Table 2_Revised_.docx

Statistical analyses

No statistical analyses for this end point

Secondary: the difference within study groups of the 30-day complication rate

End point title	the difference within study groups of the 30-day complication rate

End point description:

End point type	Secondary

End point timeframe:

Within 30 days after surgery

End point values	Overall study	Effect of dexamethasone and lidocaine on cytokine levels		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	48	48		
Units: Clavien Dindo Classification	48	48		

Statistical analyses

No statistical analyses for this end point

Secondary: the correlation of cytokine ratios with pain scores and postoperative complications were evaluated

End point title	the correlation of cytokine ratios with pain scores and postoperative complications were evaluated

End point description:

End point type	Secondary

End point timeframe:

baseline (painscore and cytokines), 4 hours after surgery (pain scores and cytokines), and 30days after surgery (complications according to Clavien Dindo Classification)

End point values	Overall study			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: cytokine ratios, pain scores and CDC	48			

Attachments (see zip file)	Correlation pain score and cytokines/Supplementary Table cytokine levels, pain scores, and complications/Table

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse were reported until discharge of the patient from the hospital

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	4

Reporting groups

Reporting group title	nausea

Reporting group description:

postoperative nausea

Serious adverse events	nausea		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	nausea		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		

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: Non-serious adverse event is the same ad adverse events
4 patients had postoperative nausea

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2015	Amendment for pilot 2: addition of dexamethason 4 mg to all patients
02 March 2016	Pilot 3: addition of dexamethason 8 mg to all patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported