



Clinical trial results:

Perioperative ketorolac in high risk breast cancer patients with and without inflammation. A prospective randomized placebo-controlled trial.

Summary

EudraCT number	2012-003774-76
Trial protocol	BE
Global end of trial date	01 September 2015

Results information

Result version number	v1 (current)
This version publication date	07 January 2021
First version publication date	07 January 2021

Trial information

Trial identification

Sponsor protocol code	1.0
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01806259
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cliniques universitaires Saint-Luc
Sponsor organisation address	Avenue Hippocrate, 10, Brussels, Belgium, 1200
Public contact	Dpt of Anesthesiology, Cliniques universitaires Saint-Luc, forgetpatrice@yahoo.fr
Scientific contact	Dpt of Anesthesiology, Cliniques universitaires Saint-Luc, forgetpatrice@yahoo.fr

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 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test if the use of Ketorolac at the moment of the operative incision reduces the number of recurrence in patients with breast cancer.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH), Good Clinical Practice (GCP) regulations/guidelines, United States Food and Drug Administration (FDA) regulations/guidelines, and country-specific national and local laws.

Background therapy:

Ketorolac: one dose of Ketorolac 30 mg intravenously before surgery.

Evidence for comparator:

Placebo: one dose of Ketorolac of NaCL 0.9% 3ml intravenously before surgery.

Actual start date of recruitment	01 February 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 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)	136

From 65 to 84 years	65
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Between February 2013 and July 2015, 203 patients from 4 sites in Belgium.

Pre-assignment

Screening details:

After written informed consent, breast cancer patients scheduled for curative surgery were randomized to receive a dose of Ketorolac or placebo prior to the surgical incision upon induction of anesthesia.

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

Blinding implementation details:

Randomization and blinding performed by the pharmacist in charge of preparing the product under study in each center.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Ketorolac 30 mg
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Arm description:

Patients received one dose of 30 mg of Ketorolac slowly intravenously before the incision.

Arm type	Experimental
Investigational medicinal product name	Ketorolac
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

One dose of 30 mg intravenous.

Arm title	Placebo
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Arm description:

Patients received one dose of NaCL 0.9% 3 ml slowly intravenously before the incision.

Arm type	Placebo
Investigational medicinal product name	Sodium Chloride
Investigational medicinal product code	
Other name	Isotonic saline solution, Normal saline solution, Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

One dose of NaCL 0.9% 3 ml slowly intravenously.

Number of subjects in period 1	Ketorolac 30 mg	Placebo
Started	96	107
Completed	96	107

Baseline characteristics

Reporting groups

Reporting group title	Ketorolac 30 mg
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Reporting group description:

Patients received one dose of 30 mg of Ketorolac slowly intravenously before the incision.

Reporting group title	Placebo
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Reporting group description:

Patients received one dose of NaCL 0.9% 3 ml slowly intravenously before the incision.

Reporting group values	Ketorolac 30 mg	Placebo	Total
Number of subjects	96	107	203
Age categorical			
Units: Subjects			
Adults (18-64 years)	65	71	136
From 65-84 years	30	35	65
85 years and over	1	1	2
Age continuous			
Units: years			
arithmetic mean	56.1	55.4	
standard deviation	± 14	± 13.9	-
Gender categorical			
Units: Subjects			
Female	95	107	202
Male	1	0	1

End points

End points reporting groups

Reporting group title	Ketorolac 30 mg
Reporting group description: Patients received one dose of 30 mg of Ketorolac slowly intravenously before the incision.	
Reporting group title	Placebo
Reporting group description: Patients received one dose of NaCL 0.9% 3 ml slowly intravenously before the incision.	

Primary: Recurrence-free Survival

End point title	Recurrence-free Survival
End point description:	
End point type	Primary
End point timeframe: 5 years	

End point values	Ketorolac 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	107		
Units: Number	80	96		

Statistical analyses

Statistical analysis title	Disease-free survival (DFS)
Comparison groups	Ketorolac 30 mg v Placebo
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.517
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.31

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

30 days.

Adverse event reporting additional description:

Any type of adverse event possibly linked to the IMP.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE Grade
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Dictionary version	4.03
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Reporting groups

Reporting group title	Ketorolac 30 mg
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Reporting group description:

Patients received one dose of 30 mg of Ketorolac slowly intravenously before the incision.

Reporting group title	Placebo
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Reporting group description:

Patients received one dose of NaCl 0.9% 3 ml slowly intravenously before the incision.

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: There were no side effects identified in the study.

Serious adverse events were due to the participants' initial illness.

Serious adverse events	Ketorolac 30 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 96 (8.33%)	7 / 107 (6.54%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Hematoma			
subjects affected / exposed	1 / 96 (1.04%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Other not specified			
subjects affected / exposed	7 / 96 (7.29%)	7 / 107 (6.54%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ketorolac 30 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 96 (0.00%)	0 / 107 (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

None reported