Clinical trial results:
Will intrathecal analgesia contribute to a faster recovery compared with epidural analgesia after open surgery for gynecological cancer. An open controlled randomized study.

Summary

EudraCT number	2013-001873-25
Trial protocol	SE
Global end of trial date	17 March 2016

Results information

Result version number	v1 (current)
This version publication date	27 April 2024
First version publication date	27 April 2024

Trial information

Trial identification

Sponsor protocol code	vers20130714

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02026687
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Region Östergötland
Sponsor organisation address	University Hospital, Linköping, Sweden, 581 83
Public contact	Lena Nilsson, Region Östergötland, +46 0101031838, lena.nilsson@regionostergotland.se
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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	17 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- to decide if one in a fast track program by the use of intrathecal analgesia and standardized criteria for discharge will have a faster physical recovery, so a larger proportion of patients can be discharged on the third day after surgery, than if epidural analgesia has been used per- and postoperatively.
- to decide if the use of perioperative intrathecal analgesia contributes to a faster recovery of health related quality of health, less postoperative symptom and influence on vital signs compared with postoperative epidural analgesia

Protection of trial subjects:

According to ethical committées approval and Sedish Regulations. Authorised monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	60
From 65 to 84 years	20

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From March 2014 to January 2016, all women who were admitted to the Department of Obstetrics and Gynaecology, University Hospital, Linköping, Sweden due to a proven or assumed gynaeco- logical abdominal malignancy were eligible for the study.

Pre-assignment

Screening details:

• Women 18 – 70 years.
• Gynecological cancer (suspected or verified) planned for explorative laparatomy through a middle-line with a curative purpose.
• WHO performance status < 2.
• ASA 1-2.
• Understand and can express themselves in Swedish.
• After verbal and written information accept participation iand signed informed consent.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Intra thecal morphine (ITM)

Arm description:

intrathecal combination of a single-dose isobar bupivacaine 15mg, morphine 0.2mg and clonidine 75µg before surgery

Arm type	Experimental
Investigational medicinal product name	Catapresan
Investigational medicinal product code	PR2
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradural use

Dosage and administration details:

clonidine 75µg injected intrathecally in a combination of a single-dose isobar bupivacaine 15mg and morphine 0.2mg through a spinal needle

Investigational medicinal product name	Marcain spinal 5 mg/ml
Investigational medicinal product code	PR6
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intrathecal use

Dosage and administration details:

an intrathecal combination of a single-dose isobar bupivacaine 15mg, morphine 0.2mg and clonidine 75µg, through a spinal needle

Investigational medicinal product name	Morfin Special 0,4 mg/ml
Investigational medicinal product code	PR7
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intratracheal use

Dosage and administration details:

An intrathecal combination of a single-dose isobar bupivacaine 15mg, morphine 0.2mg and clonidine 75µg, through a spinal needle

Arm title	Epidural analgesia (EDA)

Arm description:

The EDA group had the standard EDA regime used in the hospital. The EDA was performed by a low thoracic puncture. The epidural infusion was started after induction of the general anaesthesia but before surgery by a bolus dose of fentanyl 50–100 µg and a bolus from a mixture of bupivacaine 2.4 mg/mL, adrenalin 2.4 µg/mL and fentanyl 1.8 µg/mL. The same mixture was used as a continuous infusion, typically 4–8mL/hour, throughout surgery.

Arm type	Active comparator
Investigational medicinal product name	Carbocain adrenalin 20mg/ml + 5 mikrogram/ml
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Epidural use

Dosage and administration details:

Used as a continuous infusion, typically 4–8mL/hour, throughout surgery.

Investigational medicinal product name	Fentanyl B Braun 50 mikrogram/ml
Investigational medicinal product code	PR3
Other name	
Pharmaceutical forms	Injection
Routes of administration	Epidural use

Dosage and administration details:

The epidural infusion was started after induction of the general anaesthesia but before surgery by a bolus dose of fentanyl 50–100 µg

Number of subjects in period 1	Intra thecal morphine (ITM)	Epidural analgesia (EDA)
Started	40	40
Completed	40	40

Baseline characteristics

Reporting groups	
Reporting group title	Intra thecal morphine (ITM)
Reporting group description:	
intrathecal combination of a single-dose isobar bupivacaine 15mg, morphine 0.2mg and clonidine 75µg before surgery	
Reporting group title	Epidural analgesia (EDA)
Reporting group description:	
The EDA group had the standard EDA regime used in the hospital. The EDA was performed by a low thoracic puncture. The epidural infusion was started after induction of the general anaesthesia but before surgery by a bolus dose of fentanyl 50–100 µg and a bolus from a mixture of bupivacaine 2.4 mg/mL, adrenalin 2.4 µg/mL and fentanyl 1.8 µg/mL. The same mixture was used as a continuous infusion, typically 4–8mL/hour, throughout surgery.	

Reporting group values	Intra thecal morphine (ITM)	Epidural analgesia (EDA)	Total
Number of subjects	40	40	80
Age categorical			
Age			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
less than 50 years	6	7	13
50-60 years	20	16	36
over 60 years	14	17	31
Gender categorical			
Units: Subjects			
Female	40	40	80
Male	0	0	0

End points

End points reporting groups

Reporting group title	Intra thecal morphine (ITM)
Reporting group description:	
intrathecal combination of a single-dose isobar bupivacaine 15mg, morphine 0.2mg and clonidine 75µg before surgery	
Reporting group title	Epidural analgesia (EDA)
Reporting group description:	
The EDA group had the standard EDA regime used in the hospital. The EDA was performed by a low thoracic puncture. The epidural infusion was started after induction of the general anaesthesia but before surgery by a bolus dose of fentanyl 50–100 µg and a bolus from a mixture of bupivacaine 2.4 mg/mL, adrenalin 2.4 µg/mL and fentanyl 1.8 µg/mL. The same mixture was used as a continuous infusion, typically 4–8mL/hour, throughout surgery.	

Primary: Hospital stay

End point title	Hospital stay
End point description:	
Lenght of hospital stay	
End point type	Primary
End point timeframe:	
Days	

End point values	Intra thecal morphine (ITM)	Epidural analgesia (EDA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: Days				
median (inter-quartile range (Q1-Q3))	3.3 (3.1 to 4.8)	4.3 (3.4 to 5.4)		

Statistical analyses

Statistical analysis title	Mann-Whitney U test
Comparison groups	Intra thecal morphine (ITM) v Epidural analgesia (EDA)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Quality of life

End point title	Quality of life

End point description:

End point type	Primary

End point timeframe:

Baseline (preoperatively) and 42 days after surgery

End point values	Intra thecal morphine (ITM)	Epidural analgesia (EDA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: Arbitrary Units				
median (inter-quartile range (Q1-Q3))	38 (35 to 42)	39 (34 to 44)		

Statistical analyses

Statistical analysis title	Mann_whitney U-test
Comparison groups	Intra thecal morphine (ITM) v Epidural analgesia (EDA)
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From day of surgery until 6 weeks postoperatively	
Assessment type	Systematic

Dictionary used	
Dictionary name	CRF
Dictionary version	2013-12-23

Reporting groups	
Reporting group title	Intra thecal morphine (ITM)
Reporting group description: -	
Reporting group title	Epidural analgesia (EDA)
Reporting group description: -	

Serious adverse events	Intra thecal morphine (ITM)	Epidural analgesia (EDA)	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 40 (12.50%)	4 / 40 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events		0	
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 40 (5.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intra-abdominal infection			
subjects affected / exposed	3 / 40 (7.50%)	3 / 40 (7.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Intra thecal morphine (ITM)	Epidural analgesia (EDA)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 40 (7.50%)	6 / 40 (15.00%)	
Infections and infestations			

superficial wound infection subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3	6 / 40 (15.00%) 6	

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/30837253