Clinical trial results:
Pharmacokinetic study of the opioid ketobemidone in children and adolescens after intravenous administration

Summary

EudraCT number	2006-006717-32
Trial protocol	SE
Global end of trial date	03 June 2008

Results information

Result version number	v1 (current)
This version publication date	21 May 2021
First version publication date	21 May 2021
Summary attachment (see zip file)	Published article 2009 (AAS2009fulltext.pdf)

Trial information

Trial identification

Sponsor protocol code	554

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Ethics committee Karolinska Institutet Stockholm : 2007/4:1

Notes:

Sponsors

Sponsor organisation name	Stockholms Läns Landsting
Sponsor organisation address	Karolinska University Hospital, Stockholm, Sweden, 17176
Public contact	Stefan Lundeberg, Karolinska University Hospital, +46 851777189, stefan.lundeberg@sll.se
Scientific contact	Pediatric Pain treatment Service, Karolinska University Hospital, +46 851770000, stefan.lundeberg@sll.se

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	03 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2008
Global end of trial reached?	Yes
Global end of trial date	03 June 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determination of elimination half life of ketobemidone after intravenous injection in children

Protection of trial subjects:

Postoperative pain management following standard protocol at the hospital. The study drug was part of the pain treatment.

Background therapy:

Standard analgesic treatment with paracetamol, clonidine and opioids as needed.

Evidence for comparator:

Not applicable

Actual start date of recruitment	10 September 2007
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	5
Infants and toddlers (28 days-23 months)	15
Children (2-11 years)	10
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

30 children who underwent a planned surgical procedure and in need of postoperative opioid treatment.

Pre-assignment

Screening details:

31 children were screened and 30 participated and consent was given.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Ketobemidone

Arm description:

Study drug used for all enrolled patients

Arm type	Experimental
Investigational medicinal product name	Ketobemidone hydrochloride
Investigational medicinal product code	N02AB01
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.05 mg/kg for neonates and up to 3 months of age, 0.1 mg/kg over the age of 3 months.

Number of subjects in period 1	Ketobemidone
Started	30
Completed	30

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description:

Three groups: neonates up to 90 days; 1-2.5 years; 7-10 years

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	5	5	
Infants and toddlers (28 days-23 months)	15	15	
Children (2-11 years)	10	10	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Children neonates to 3 months (group A) 1 to 2.5 years (groupB) and 7-10 years (groupC)			
Units: years			
median	2.5		
full range (min-max)	0 to 11	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	17	17	
Children			
Children aged 0-11 years			
Units: Subjects			
Age	30	30	
Children			
Children divided in 3 groups			
Units: Age			
median	2.5		
full range (min-max)	0 to 11	-	

Subject analysis sets

Subject analysis set title	Ketobemidone plasma concentration
Subject analysis set type	Full analysis

Subject analysis set description:

Plasma concentration of ketobemidone were analysed. Blood sampling was perfomed at 6 occasions after bolus dose was given.

Subject analysis set title	Ketobemidone comparison group
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Age groups as described

Reporting group values	Ketobemidone plasma concentration	Ketobemidone comparison group	
Number of subjects	30	24	
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	5		
Infants and toddlers (28 days-23 months)	15		
Children (2-11 years)	10		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Children neonates to 3 months (group A) 1 to 2.5 years (groupB) and 7-10 years (groupC)			
Units: years			
median	27		
full range (min-max)	5 to 35		
Gender categorical			
Units: Subjects			
Female	15		
Male	9		
Children			
Children aged 0-11 years			
Units: Subjects			
Age	30		
Children			
Children divided in 3 groups			
Units: Age			
median	2.5		
full range (min-max)	0 to 11		

End points

End points reporting groups

Reporting group title	Ketobemidone
Reporting group description:	
Study drug used for all enrolled patients	
Subject analysis set title	Ketobemidone plasma concentration
Subject analysis set type	Full analysis
Subject analysis set description:	
Plasma concentration of ketobemidone were analysed. Blood sampling was perfomed at 6 occasions after bolus dose was given.	
Subject analysis set title	Ketobemidone comparison group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age groups as described	

Primary: Pharmacokinetic parameter

End point title	Pharmacokinetic parameter
End point description:	
Last patient enrolled	
End point type	Primary
End point timeframe:	
September 2007 to April 2008	

End point values	Ketobemidone plasma concentration	Ketobemidone comparison group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: ng/ml				
number (not applicable)	24	24		

Statistical analyses

Statistical analysis title	AUC
Statistical analysis description:	
AUC /mg/kg in relation to age groups	
Comparison groups	Ketobemidone comparison group v Ketobemidone plasma concentration
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	≤ 0.05
Method	Spearman Rank Correlation

Notes:
[1] - comparison between age groups

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From time of administration of bolus dose of ketobemidone and up to 72 hours post injection.

Assessment type	Systematic

Dictionary used

Dictionary name	CRF protocol
Dictionary version	1

Reporting groups

Reporting group title	Ketobemidone

Reporting group description:

Children administered a bolus dose of ketobemidone

Serious adverse events	Ketobemidone		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Ketobemidone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (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: Nausea was registered in 2 patients but this might have been caused by several factors as the surgical procedure, the anesthesia as well as the post operative analgesics including ketobemidone or other given opioids

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.

Nausea as a non serious side effects could be explained by many factors including the use of ketobemidone, surgical procedure and anesthesia.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/19839946