Clinical trial results:
Open clinical trial to evaluate safety, tolerability, and efficacy of Dexdor for sedation in paediatric patients in intensive care settings. Multi-centre trial in Russia for marketing registration of Dexdor

Summary

EudraCT number	2018-003063-64
Trial protocol	Outside EU/EEA
Global end of trial date	21 May 2018

Results information

Result version number	v1 (current)
This version publication date	06 December 2018
First version publication date	06 December 2018

Trial information

Trial identification

Sponsor protocol code	3005031

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Orion Corporation, Orion Pharma
Sponsor organisation address	Orionintie 1, Espoo, Finland, 02200
Public contact	Clinical Trial Information Desk, Orion Corporation, Orion Pharma, 358 104261, clinicaltrials@orionpharma.com
Scientific contact	Clinical Trial Information Desk, Orion Corporation, Orion Pharma, 358 104261, clinicaltrials@orionpharma.com

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?	Yes
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	21 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2018
Global end of trial reached?	Yes
Global end of trial date	21 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of efficacy of Dexdor for prolonged sedation in paediatric patients;
Evaluation of safety and tolerability of Dexdor in paediatric population.

Protection of trial subjects:

Sedation level was monitored throughout the study, and rescue and pain medication was administered, when needed. Vital signs (e.g. heart rate, systolic and diastolic blood pressure, body temperature, ventilation frequency (for patients with spontaneous ventilation)) was assessed frequently after start of study treatment.
Continuous cardiac and respiratory monitoring was done throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 March 2017
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	Russian Federation: 60
Worldwide total number of subjects	60
EEA total number of subjects	0

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)	60
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Children aged 12-17 years, with clinical need for prolonged sedation were recruited in 5 study centers in Russian.

Pre-assignment

Screening details:

The investigator assessed and pre-screened patients staying in ICU. Clinical situations that need prolonged sedation were e.g. trauma, injuries or surgical corrections. Patients with clinical need for prolonged (at least 24h) sedation (target RASS = 0 to -3), and who met all the inclusion criteria and none of the exclusion criteria were included.

Period 1

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

Arms

Arm title	Dexdor infusion

Arm description:

Dexdor was administered as follows: the starting dose is 0.7 mcg/kg/h for 1 hour, then down- or up-titrating with 0.1–0.4 mcg/kg/h steps every 30 minutes depending on sedation level; additional analgesics as needed. In case of inadequate sedation at the highest dose (1.4 mcg/kg/h) another sedative medication (according to accepted standards in each hospital) were carefully added to sedation.

Arm type	Experimental
Investigational medicinal product name	Dexmedetomidine 100 microg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Starting dose 0.7 microg/kg/h for 1 hour, then down- or up-titrating with 0.1–0.4 microg/kg/h steps every 30 minutes depending on sedation level.

Number of subjects in period 1	Dexdor infusion
Started	60
Completed	59
Not completed	1
Patient was transferred to another hospital	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
Adolescents (12-17 years)	60	60	
Gender categorical Units: Subjects			
Female	31	31	
Male	29	29	

End points

End points reporting groups

Reporting group title	Dexdor infusion

Reporting group description:

Dexdor was administered as follows: the starting dose is 0.7 mcg/kg/h for 1 hour, then down- or up-titrating with 0.1–0.4 mcg/kg/h steps every 30 minutes depending on sedation level; additional analgesics as needed. In case of inadequate sedation at the highest dose (1.4 mcg/kg/h) another sedative medication (according to accepted standards in each hospital) were carefully added to sedation.

Primary: Percentage of patients requiring additional analgesics and sedatives

End point title	Percentage of patients requiring additional analgesics and sedatives[1]

End point description:

Percentage of patients requiring additional analgesics and sedatives (with calculation of cumulative dose per hour for each particular medication).
RESULT: 0.9825 % of patients didn't need additional sedatives or analgesics (90% C.I. 0.8776-0.9977).

End point type	Primary

End point timeframe:

From start of the treatment up to maximum 5 days

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: Statistical results are reported in End point description-field, due to technical reasons (only one treatment group, no comparisons).

End point values	Dexdor infusion			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: percent	1			

Statistical analyses

No statistical analyses for this end point

Primary: The time spent in target sedation range

End point title	The time spent in target sedation range[2]

End point description:

Maintaining the target sedation level endpoint was defined as the proportion of time during study treatment with a RASS score within the individually-prescribed target range without rescue medication. The total amount of time that the patient remains within their target RASS range without rescue medication were divided by the amount of time of the treatment period.
RESULT: Proportion of time within the target sedation range without rescue medication. Mean % (SD) 88.9 (9.9), N=57,
Proportion of time within the target sedation range without rescue medication: Estimate of the least squares mean, 90% C.I.: 92.2 (86.04, 95.80). N=57

End point type	Primary

End point timeframe:

From start of the treatment up to maximum 5 days

Notes:

[2] - 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: Statistical results are reported in End point description-field, due to technical reasons (only one treatment group, no comparisons).

End point values	Dexdor infusion			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: percent	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From signing an informed consent up to end of study visit on the 7th day after stopping the study treatment	
Adverse event reporting additional description:	
Safety population = patients who received at least one dose of study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Dexdor infusion
Reporting group description:	
Safety population = subjects who received at least one dose of study treatment.	

Serious adverse events	Dexdor infusion		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (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	Dexdor infusion		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 60 (45.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Hypotension			

subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Feeling jittery			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Hyperthermia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	4		
Withdrawal syndrome			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Pelvic adhesions			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	4		
Pulmonary embolism			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Respiratory failure			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			

subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	10		
Factitious disorder			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Hallucination			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Investigations			
Blood pressure decreased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Heart rate decreased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Oxygen saturation decreased			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	8		
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Bradycardia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Tachycardia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	3		
Nervous system disorders			

Amnesia subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4		
Cerebral ventricle dilatation subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 3		
Dizziness subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Intracranial pressure increased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Psychomotor hyperactivity subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Sensory disturbance subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Eye disorders Dysmetropsia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all)	20 / 60 (33.33%) 21		
Pneumatosis intestinalis subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2		
Musculoskeletal and connective tissue disorders Muscle spasms			

subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Infections and infestations Laryngitis subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1		
Metabolism and nutrition disorders Hypovolaemia subjects affected / exposed occurrences (all)	 1 / 60 (1.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2017	Down- and up-titrating steps of Dexdor infusion were changed to allow more individual dosing. Assessment of efficacy variables was clarified (baseline RASS assessment was added). List of indications for planned administration of the investigational product was updated.
02 September 2017	List of indications for planned administration of the investigational product was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported