



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 occurrences (all) | 3 / 60 (5.00%) 3 | | |
| General disorders and administration site conditions Feeling jittery subjects affected / exposed occurrences (all) Hyperthermia subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Withdrawal syndrome subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 3 / 60 (5.00%) 4 1 / 60 (1.67%) 1 | | |
| Reproductive system and breast disorders Pelvic adhesions subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Bronchospasm subjects affected / exposed occurrences (all) Pulmonary embolism subjects affected / exposed occurrences (all) Respiratory failure subjects affected / exposed occurrences (all) Sleep apnoea syndrome subjects affected / exposed occurrences (all) | 2 / 60 (3.33%) 4 1 / 60 (1.67%) 1 2 / 60 (3.33%) 2 1 / 60 (1.67%) 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 | 4 / 60 (6.67%) | | |
| occurrences (all) | 4 | | |
| Cerebral ventricle dilatation | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 3 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Sensory disturbance | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Dysmetropsia | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Dry mouth | | | |
| subjects affected / exposed | 20 / 60 (33.33%) | | |
| occurrences (all) | 21 | | |
| Pneumatosis intestinalis | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 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