Clinical trial results:
Pharmacological treatment of insomnia in palliative care
A randomized, double-blind, placebo controlled, parallel-group, multicenter trial investigating the short time effectiveness of zopiclone on self-reported sleep quality in patients with advanced cancer who use opioids and who report insomnia

Summary

EudraCT number	2015-005306-11
Trial protocol	NO
Global end of trial date	01 May 2021

Results information

Result version number	v1 (current)
This version publication date	15 October 2022
First version publication date	15 October 2022

Trial information

Trial identification

Sponsor protocol code	SleepRCT_270215

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02807922
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	St. Olavs Hospital, Trondheim University Hospital
Sponsor organisation address	Postboks 3250 Torgarden, Trondheim, Norway, 7006
Public contact	Pål Klepstad, St. Olavs Hospital, Trondheim University Hospital, +47 72575709, pal.klepstad@ntnu.no
Scientific contact	Pål Klepstad, St. Olavs Hospital, Trondheim University Hospital, +47 72575709, pal.klepstad@ntnu.no

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 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 May 2021
Global end of trial reached?	Yes
Global end of trial date	01 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to study the short time effectiveness of zopiclone on patient reported sleep quality in patients with advanced cancer who use opioids and who report insomnia.

Protection of trial subjects:

The trial was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with Good Clinical Practice. The protocol was considered as a low-risk study. The patients were instructed to contact the investigator immediately should they manifest any signs or symptoms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2016
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	Norway: 41
Worldwide total number of subjects	41
EEA total number of subjects	41

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)	0
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment	
Recruitment details: -	
Pre-assignment	
Screening details: -	
Pre-assignment period milestones	
Number of subjects started	41
Number of subjects completed	41

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, Monitor, Data analyst
Arms	
Are arms mutually exclusive?	Yes
Arm title	Zopiclone
Arm description: Zopiclone "Actavis"	
Arm type	Active comparator
Investigational medicinal product name	Actavis
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 3.75 mg, 5 mg, 7.5	
Arm title	Placebo
Arm description: Placebo	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 3.75 mg, 5 mg, and 7.5 mg	

Number of subjects in period 1	Zopiclone	Placebo
Started	20	21
Completed	18	21
Not completed	2	0
Consent withdrawn by subject	1	-
Due to radiotherapy at another hospital	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Zopiclone
Reporting group description:	
Zopiclone "Actavis"	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Reporting group values	Zopiclone	Placebo	Total
Number of subjects	20	21	41
Age categorical			
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	20	21	41
85 years and over	0	0	0
Age continuous			
Units: years			
median	61	68	
standard deviation	± 55.6	± 57.1	-
Gender categorical			
Units: Subjects			
Female	8	9	17
Male	12	12	24

Subject analysis sets	
Subject analysis set title	Primary endpoint
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients analysed	

Reporting group values	Primary endpoint		
Number of subjects	39		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	39		
85 years and over	0		
Age continuous			
Units: years			
median			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female	17		
Male	22		

End points

End points reporting groups

Reporting group title	Zopiclone
Reporting group description: Zopiclone "Actavis"	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	Primary endpoint
Subject analysis set type	Full analysis
Subject analysis set description: Patients analysed	

Primary: Sleep quality

End point title	Sleep quality
End point description:	
End point type	Primary
End point timeframe: Sleep quality at night 6 with treatment	

End point values	Zopiclone	Placebo	Primary endpoint	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	21	39	
Units: 0-10				
arithmetic mean (confidence interval 95%)	2.9 (2.3 to 3.8)	4.5 (3.6 to 5.4)	2.9 (2.3 to 3.8)	

Statistical analyses

Statistical analysis title	Independent student’s t-test
Statistical analysis description: In the comparison of sleep quality between the two groups after night 6 of using the study drug, independent student’s t-test was used for continues variables	
Comparison groups	Placebo v Zopiclone
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: The treatment is 6 subsequent nights with zopiclone or placebo	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4
Reporting groups	
Reporting group title	Zopiclone
Reporting group description: Zopiclone "Actavis"	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	Zopiclone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 21 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Zopiclone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	0 / 21 (0.00%)	
Nervous system disorders			
Dizziness	Additional description: temporary dizziness		
subjects affected / exposed	1 / 18 (5.56%)	0 / 21 (0.00%)	
occurrences (all)	1	0	

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.

The main limitation is the number of patients enrolled. Because of slow recruitment the trial was stopped before the pre-defined target of patients was reached. However, the risk for a potential type two error was mitigated by the statistically signi

Notes: