Clinical trial results:
Effects of postoperative palonosetron in ambulatory patients identified with high risk for postdischarge nausea and vomiting (PDNV) – a randomized controlled trial with comparison to placebo.

Summary

EudraCT number	2015-003956-32
Trial protocol	SE
Global end of trial date	10 April 2020

Results information

Result version number	v1 (current)
This version publication date	15 June 2023
First version publication date	15 June 2023
Summary attachment (see zip file)	Delayed results (Report of delayed results.pdf)

Trial information

Trial identification

Sponsor protocol code	POSTPAL

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Umeå University
Sponsor organisation address	x, Umeå, Sweden,
Public contact	Jakob Wallden, Umeå University, jakob.wallden@umu.se
Scientific contact	Jakob Wallden, Umeå University, +46 703644392, jakob.wallden@umu.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	15 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2020
Global end of trial reached?	Yes
Global end of trial date	10 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate if palonosetron (compared to placebo) could reduce the incidence of postdischarge nausea and vomiting (PDNV) in patients with high risk for PDNV in ambulatory surgery. In the high-risk group incidences of 40-50% are reported and a reduction in PDNV of 50% during the first 48 hours is clinically relevant.

Protection of trial subjects:

The study was conducted in compliance with the declarations of Helsinki and ICH guidelines, as well as regulations and laws in Sweden. The study was approved by the Ethical review board in Sweden and patients gave informed and written consent to participate.

Background therapy:

Standard postoperative care including multimodal analgesia.

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	Sweden: 524
Worldwide total number of subjects	524
EEA total number of subjects	524

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)	412
From 65 to 84 years	112

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at two study sites in Sweden, Sundsvall Hospital, Sundvall and Sunderby Hospital, Luleå.
Inclusion period was 2017/03/13 to 2020/04/10

Pre-assignment

Screening details:

Patients were first screened for inclusion BEFORE the surgical procedure/anesthesia. Patients needed to be included before surgery/anaesthesia as information and consent not can be provided in an immediate postoperative setting. Final inclusion in the interventional randomized part of the study depended on the PDNV-score post.

Pre-assignment period milestones

Number of subjects started	524
Number of subjects completed	170

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No resources to randomize (if PDNV3-5): 8
Reason: Number of subjects	Wrong PDNV-classification: 2
Reason: Number of subjects	Low risk for PDNV: 344

Period 1

Period 1 title	Randomisation of patients with high risk (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Palonosetron

Arm description:

Singel dose of Palonosetron 75µg intravenous before discharge to home

Arm type	Experimental
Investigational medicinal product name	Palonosetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Palonosetron 75µg intravenous

Arm title	Placebo

Arm description:

Placebo Sodium Cloride 9mg/mL, 1,5 mL

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Injection

Dosage and administration details:

1.5 ML SodiumCloride 9mg/mL

Number of subjects in period 1[1]	Palonosetron	Placebo
Started	84	86
Completed	66	70
Not completed	18	16
Lost to follow-up	18	16

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The inclusion in the RCT-part was a two-step procedure. Preopertively, a broad range of patients were included and gave consent to be included in the RCT, if the PNDV score was >3 at the evaluation before discharge. Of 559 patients included, 170 was randomized.

Baseline characteristics

Reporting groups	
Reporting group title	Palonosetron
Reporting group description:	
Singel dose of Palonosetron 75µg intravenous before discharge to home	
Reporting group title	Placebo
Reporting group description:	
Placebo Sodium Cloride 9mg/mL, 1,5 mL	

Reporting group values	Palonosetron	Placebo	Total
Number of subjects	84	86	170
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			0
85 years and over			0
Age continuous Units: years			
median	42.0	39.8	
full range (min-max)	18.3 to 79.1	18.5 to 82.1	-
Gender categorical Units: Subjects			
Female	74	76	150
Male	10	10	20
Smokers			
Smokers			
Units: Subjects			
Yes	11	6	17
No	73	80	153
ASA			
ASA physical status classification			
Units: Subjects			
Class 1	48	44	92
Class 2 or 3	36	42	78
History of motion sickness Units: Subjects			
Yes	43	46	89
No	41	40	81
Type of procedure Units: Subjects			

General Surgery	44	39	83
Orthopaedics	16	17	33
Urology	2	2	4
Gynaecology	15	18	33
ENT	6	10	16
Ophtalmic	1	0	1
History of PONV Units: Subjects			
Yes	40	48	88
No	44	38	82
Maintenance of anaesthesia Units: Subjects			
Volatile	52	55	107
Intravenous	32	30	62
Missing	0	1	1
Number of antiemetic prophylaxis Units: Subjects			
One	13	13	26
Two	53	48	101
Three	18	25	43
Nausea in PACU Units: Subjects			
yes	33	39	72
no	51	47	98
Rescue opioids at PACU Units: Subjects			
Yes	65	57	122
No	19	29	48
PDNV-score before discharge Units: Subjects			
PDNV 3	55	65	120
PDNV 4	25	17	42
PDNV 5	4	4	8
Trial site Units: Subjects			
Sundsvall	77	80	157
Sunderbyn	7	6	13
BMI			
Body Mass Index			
Units: kg m-1			
median	25.9	26.6	
full range (min-max)	19.5 to 42.8	15.6 to 41.2	-
Duration procedure			
Surgical duration "knife to last suture"			
Units: minutes			
median	58	48	
full range (min-max)	7 to 161	4 to 201	-

Subject analysis sets	
Subject analysis set title	Analysed Palonosetron
Subject analysis set type	Full analysis
Subject analysis set description: Subjects included in analysis randomized to Palonosetron	
Subject analysis set title	Analysed Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Analysed patients in the placebo group	

Reporting group values	Analysed Palonosetron	Analysed Placebo	
Number of subjects	66	70	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	42.1	45.3	
full range (min-max)	18.5 to 82.1	18.3 to 79.1	
Gender categorical Units: Subjects			
Female	59	64	
Male	7	6	
Smokers			
Smokers			
Units: Subjects			
Yes	7	5	
No	59	65	
ASA			
ASA physical status classification			
Units: Subjects			
Class 1	39	35	
Class 2 or 3	27	35	
History of motion sickness Units: Subjects			
Yes	35	38	
No	31	32	
Type of procedure Units: Subjects			
General Surgery	36	30	
Orthopaedics	13	15	

Urology	1	2	
Gynaecology	11	15	
ENT	4	8	
Ophtalmic	1	0	
History of PONV Units: Subjects			
Yes	35	38	
No	31	32	
Maintenance of anaesthesia Units: Subjects			
Volatile	26	26	
Intravenous	40	43	
Missing	0	1	
Number of antiemetic prophylaxis Units: Subjects			
One	9	9	
Two	43	41	
Three	14	20	
Nausea in PACU Units: Subjects			
yes	24	29	
no	44	41	
Rescue opioids at PACU Units: Subjects			
Yes	50	49	
No	16	21	
PDNV-score before discharge Units: Subjects			
PDNV 3	46	54	
PDNV 4	18	13	
PDNV 5	2	3	
Trial site Units: Subjects			
Sundsvall	60	65	
Sunderbyn	6	5	
BMI			
Body Mass Index			
Units: kg m-1			
median	25.6	26.5	
full range (min-max)	19.5 to 42.8	15.6 to 41.2	
Duration procedure			
Surgical duration "knife to last suture"			
Units: minutes			
median	50	49	
full range (min-max)	7 to 161	4 to 201	

End points

End points reporting groups

Reporting group title	Palonosetron
Reporting group description:	
Singel dose of Palonosetron 75µg intravenous before discharge to home	
Reporting group title	Placebo
Reporting group description:	
Placebo Sodium Cloride 9mg/mL, 1,5 mL	
Subject analysis set title	Analysed Palonosetron
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects included in analysis randomized to Palonosetron	
Subject analysis set title	Analysed Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Analysed patients in the placebo group	

Primary: Complete response

End point title	Complete response
End point description:	
Number of patients with no events of nausea, no events of vomit and not taking any rescue antiemetics	
End point type	Primary
End point timeframe:	
Discharge from ambulatory surgery until the second postoperative day (POD2)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
Yes	32	25		

Statistical analyses

Statistical analysis title	Complete response
Statistical analysis description:	
Primary analysis	
Comparison groups	Analysed Palonosetron v Analysed Placebo

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.131
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	3.37

Secondary: PDNV POD0

End point title	PDNV POD0
End point description:	
Patients reporting nausea or vomit	
End point type	Secondary
End point timeframe:	
On the day of procedure, after discharge	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
Yes	31	39		

Statistical analyses

Statistical analysis title	PNDV POD0
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.181
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	1.38

Secondary: PDNV POD1

End point title	PDNV POD1
End point description: Patients reporting nausea or vomit	
End point type	Secondary
End point timeframe: On postoperative day 1 (POD1)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
Yes	12	24		

Statistical analyses

Statistical analysis title	PDNV POD1
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.033
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.94

Secondary: PDNV POD2

End point title	PDNV POD2
End point description: Patients reporting nausea or vomit	
End point type	Secondary
End point timeframe: On postoperative day 2 (POD2)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
Yes	6	19		

Statistical analyses

Statistical analysis title	PDNV POD2
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.007
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.94

Secondary: PDNV POD3

End point title	PDNV POD3
End point description: Patients reporting nausea or vomit	
End point type	Secondary
End point timeframe: On postoperative day 3 (POD3)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Numer of patients				
Yes	10	9		

Statistical analyses

Statistical analysis title	PDNV POD3
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1.21
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	3.2

Secondary: PDNV POD1-POD2
End point title: PDNV POD1-POD2
End point description: Patients reporting nausea or vomit
End point type: Secondary
End point timeframe: On the first and second postoperative days

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
Yes	12	27		

Statistical analyses

Statistical analysis title	PDNV POD1-2
Comparison groups	Analysed Palonosetron v Analysed Placebo

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.009
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.78

Secondary: Rescue Antiemetics POD0

End point title	Rescue Antiemetics POD0
End point description:	
Patients taken rescue antiemetics	
End point type	Secondary
End point timeframe:	
Day of surgery, after discharge	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
Yes	17	21		

Statistical analyses

Statistical analysis title	Rescue POD0
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.582
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.72

Secondary: Rescue Antiemetics POD1

End point title	Rescue Antiemetics POD1
End point description: Patients taken rescue antiemetics	
End point type	Secondary
End point timeframe: Postoperative day 1 (POD1)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
yes	7	15		

Statistical analyses

Statistical analysis title	Rescue POD1
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.087
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.15

Secondary: Rescue Antiemetics POD2

End point title	Rescue Antiemetics POD2
End point description:	
End point type	Secondary
End point timeframe: On the second postoperative day (POD2)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
yes	2	10		

Statistical analyses

Statistical analysis title	Rescue POD2
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.021
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.89

Secondary: Rescue antiemetics POD3

End point title	Rescue antiemetics POD3

End point description:

End point type	Secondary

End point timeframe:

On the third postoperative day (POD3)

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Member of patients				
yes	2	5		

Statistical analyses

Statistical analysis title	REscue POD3
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.278
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	2.17

Secondary: Rescue antiemetics POD1-POD2

End point title	Rescue antiemetics POD1-POD2
End point description:	
End point type	Secondary
End point timeframe:	
On postoperative day 1 and 2 (POD1-POD2)	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
yes	8	17		

Statistical analyses

Statistical analysis title	Rescue POD1-2
Comparison groups	Analysed Placebo v Analysed Palonosetron

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.067
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.08

Other pre-specified: Headache	
End point title	Headache
End point description: Patients reporting headache	
End point type	Other pre-specified
End point timeframe: From discharge to postoperative day 3	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
yes	25	24		

Statistical analyses

Statistical analysis title	Headache
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.66
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	5.36

Other pre-specified: Visual disturbances POD0-POD3

End point title	Visual disturbances POD0-POD3
End point description: Patients reporting visual disturbances	
End point type	Other pre-specified
End point timeframe: Discharge to postoperative day 3	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
yes	14	8		

Statistical analyses

Statistical analysis title	Visual dist
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.12
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	5.36

Other pre-specified: Sleeping difficulties POD0-POD1

End point title	Sleeping difficulties POD0-POD1
End point description: Patients reporting sleeping difficulties	
End point type	Other pre-specified
End point timeframe: From discharge until postoperative day 3	

End point values	Analysed Palonosetron	Analysed Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	70		
Units: Number of patients				
yes	32	31		

Statistical analyses

Statistical analysis title	Sleepingdiff
Comparison groups	Analysed Palonosetron v Analysed Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.62
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.33

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Until postoperative day 30	
Assessment type	Systematic
Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	SWE 221130
Reporting groups	
Reporting group title	Palonosetron
Reporting group description: The groups that received the intervention in the trial	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Palonosetron	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 84 (0.00%)	0 / 86 (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	Palonosetron	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 84 (3.57%)	3 / 86 (3.49%)	
Surgical and medical procedures			
Postoperative bleeding			
subjects affected / exposed	1 / 84 (1.19%)	0 / 86 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Bradycardia	Additional description: transient bradycardia (lowest heart rate 38 beats/min) immediately after administration of the study drug in a subject with a baseline heart rate of 50 beats min/m		
subjects affected / exposed	0 / 84 (0.00%)	1 / 86 (1.16%)	
occurrences (all)	0	1	
Immune system disorders			

Allergic reaction	Additional description: Allergic reaction that required a visit to the emergency department on POD1		
subjects affected / exposed	0 / 84 (0.00%)	1 / 86 (1.16%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
hiccoughs	Additional description: on POD6		
subjects affected / exposed	1 / 84 (1.19%)	0 / 86 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Postoperative retention of urine			
subjects affected / exposed	1 / 84 (1.19%)	1 / 86 (1.16%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Backache	Additional description: Back pain on POD5		
subjects affected / exposed	1 / 84 (1.19%)	0 / 86 (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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37246062