Clinical trial results:
A phase 3, single-dose, multicenter, randomized, double-blind, parallel group study to assess the efficacy and safety of palonosetron 0.25 mg administered as a 30-minute IV infusion compared to palonosetron 0.25 mg administered as a 30-second IV bolus for the prevention of chemotherapy-induced nausea and vomiting in cancer patients receiving highly emetogenic chemotherapy.

Summary

EudraCT number	2015-001747-37
Trial protocol	HU LT GR
Global end of trial date	09 March 2016

Results information

Result version number	v1 (current)
This version publication date	02 December 2017
First version publication date	02 December 2017

Trial information

Trial identification

Sponsor protocol code	PALO-15-17

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02557035
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Helsinn Healthcare SA
Sponsor organisation address	Via Pian Scairolo 9, Lugano, Switzerland, 6912
Public contact	Clinical Operation, Helsinn Healthcare SA, +41 91 985 21 21, daniel.voisin@helsinn.com
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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	09 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2016
Global end of trial reached?	Yes
Global end of trial date	09 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of a single intravenous dose of palonosetron 0.25 mg administered as a 30-minute infusion with oral dexamethasone versus a single intravenous dose of palonosetron 0.25 mg administered as a 30-second bolus with oral dexamethasone, in terms of proportion of patients with complete response in the acute phase (0-24 hour after start of reference HEC)

Protection of trial subjects:

This study was in compliance with the ethical principles founded in the Declaration of Helsinki, the International Conference on Harmonisation (ICH) guidelines regarding Good Clinical Practices and the European Union Directives on Clinical Trials.

The appropriateness of the clinical trial protocol, as well as the risks and benefits to study participants, were reviewed and approved by the Institutional Review Board (IRB).

Background therapy:

Oral dexamethasone

Evidence for comparator:

Palonosetron 0.25 mg administered as a 30-second IV bolus was approved in Europe in March 2005 for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy and moderately emetogenic cancer chemotherapy. Since 0.25 mg palonosetron efficacy has been demonstrated when administered as a 30-second bolus injection, the scope of the present study is to demonstrate efficacy (non-inferiority) of palonosetron 0.25 also when administered as a 30-minute infusion.

Actual start date of recruitment	30 September 2015
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	Belarus: 15
Country: Number of subjects enrolled	Bosnia and Herzegovina: 5
Country: Number of subjects enrolled	Bulgaria: 38
Country: Number of subjects enrolled	Georgia: 42
Country: Number of subjects enrolled	Greece: 14
Country: Number of subjects enrolled	Hungary: 98
Country: Number of subjects enrolled	Lithuania: 4
Country: Number of subjects enrolled	Romania: 91
Country: Number of subjects enrolled	Russian Federation: 134
Worldwide total number of subjects	441
EEA total number of subjects	245

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)	314
From 65 to 84 years	127
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study population consisted of adult (≥18 years of age) chemotherapy-naïve male and female patients with a diagnosis of malignant solid tumor requiring a first treatment with one of the protocol pre-defined reference highly emetogenic chemotherapy (HEC) regimens.

Pre-assignment

Screening details:

All patients who have met the inclusion and exclusion criteria were randomized into one of the two treatment groups. Of the 441 subjects randomized, 440 received a study drug.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

The blinding of the study medications is guaranteed by the use of identical placebos to the respective active drugs (double-dummy technique). When palonosetron 0.25 mg will be administered as 30-minute IV infusion, a 30-second IV bolus of placebo will be administered (Group 1). Oppositely, when palonosetron 0.25 mg is administered as a 30-second IV bolus, a 30-minute infusion of placebo will be administered (Group 2). Therefore, each patient will receive both one of which contains the active IMP

Arms

Are arms mutually exclusive?	Yes
Arm title	30-min Infusion

Arm description:

Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-min IV infusion with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.

Arm type	Experimental
Investigational medicinal product name	palonosetron 0.25 mg (as 50 mL solution for IV infusion)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Palonosetron 0.25 mg administered as a 30-minute (+/- 5 min) IV infusion on Day 1. The IV infusion will start 30 minutes prior to, and will be completed, before the start of the reference HEC administration. The compound which is held in a 5 mL vial (with strength of 0.25 mg) is diluted in 50 mL sterile 5% glucose solution per vial.

Arm title	30-sec Bolus

Arm description:

Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-sec IV bolus with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.

Arm type	Active comparator
Investigational medicinal product name	Palonosetron 0.25 mg bolus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Palonosetron 0.25 mg administered as a 30-second IV bolus on Day 1. The IV bolus will be administered 30 minutes before the start of the reference HEC administration.

Number of subjects in period 1	30-min Infusion	30-sec Bolus
Started	225	216
Completed	218	206
Not completed	7	10
Consent withdrawn by subject	-	2
Death	6	7
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	30-min Infusion
Reporting group description:	
Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-min IV infusion with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.	
Reporting group title	30-sec Bolus
Reporting group description:	
Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-sec IV bolus with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.	

Reporting group values	30-min Infusion	30-sec Bolus	Total
Number of subjects	225	216	441
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)	156	157	313
From 65-84 years	69	59	128
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	59.9	58.9	
standard deviation	± 8.7	± 8.5	-
Gender categorical Units: Subjects			
Female	74	71	145
Male	151	145	296

Subject analysis sets	
Subject analysis set title	Full Analysis Set: 30-min Infusion
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) was to include all patients who had been randomized to treatment and received HEC regimen and active study drug (including partial infusion). Following the intent-to-treat principle, patients were to be assigned to the study treatment group according to the treatment to which they had been randomized.	
Subject analysis set title	Per Protocol Population: 30-min Infusion
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per-Protocol (PP) population was to include all patients from the FAS who had completed the 0-24 h study period with no major protocol violations, i.e., those affecting the primary efficacy endpoint. All	

protocol violations (e.g., wrong inclusion, poor compliance, missing diaries, forbidden concomitant medications, and mis-randomizations) were to be reviewed and discussed case by case during the BDRM and decisions were to be described in the blind data review document/minutes which were to be finalized prior to database lock.

Subject analysis set title	Full Analysis Set: 30-sec Bolus
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) was to include all patients who had been randomized to treatment and received HEC regimen and active study drug (including partial infusion). Following the intent-to-treat principle, patients were to be assigned to the study treatment group according to the treatment to which they had been randomized.

Subject analysis set title	Per Protocol Population: 30-sec Bolus
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) population was to include all patients from the FAS who had completed the 0-24 h study period with no major protocol violations, i.e., those affecting the primary efficacy endpoint. All protocol violations (e.g., wrong inclusion, poor compliance, missing diaries, forbidden concomitant medications, and mis-randomizations) were to be reviewed and discussed case by case during the BDRM and decisions were to be described in the blind data review document/minutes which were to be finalized prior to database lock.

Subject analysis set title	Safety Population: 30-min Infusion
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population was to include all patients who had received active study drug (including partial infusion). Patients were to be assigned to study treatment groups according to the actual treatment received.

Subject analysis set title	Safety Population: 30-sec Bolus
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population was to include all patients who had received active study drug (including partial infusion). Patients were to be assigned to study treatment groups according to the actual treatment received.

Reporting group values	Full Analysis Set: 30-min Infusion	Per Protocol Population: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Number of subjects	225	214	215
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	156	150	157
From 65-84 years	69	64	58
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	59.9	59.8	58.9
standard deviation	± 8.7	± 8.7	± 8.5
Gender categorical Units: Subjects			
Female	74	71	71

Male	151	143	144

Reporting group values	Per Protocol Population: 30-sec Bolus	Safety Population: 30-min Infusion	Safety Population: 30-sec Bolus
Number of subjects	211	225	215
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)	154	156	157
From 65-84 years	57	69	58
85 years and over			
Age continuous			
Units: years			
arithmetic mean	58.8	59.9	58.9
standard deviation	± 8.5	± 8.7	± 8.5
Gender categorical			
Units: Subjects			
Female	69	74	71
Male	142	151	144

End points

End points reporting groups

Reporting group title	30-min Infusion

Reporting group description:

Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-min IV infusion with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.

Reporting group title	30-sec Bolus

Reporting group description:

Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-sec IV bolus with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.

Subject analysis set title	Full Analysis Set: 30-min Infusion
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) was to include all patients who had been randomized to treatment and received HEC regimen and active study drug (including partial infusion). Following the intent-to-treat principle, patients were to be assigned to the study treatment group according to the treatment to which they had been randomized.

Subject analysis set title	Per Protocol Population: 30-min Infusion
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) population was to include all patients from the FAS who had completed the 0-24 h study period with no major protocol violations, i.e., those affecting the primary efficacy endpoint. All protocol violations (e.g., wrong inclusion, poor compliance, missing diaries, forbidden concomitant medications, and mis-randomizations) were to be reviewed and discussed case by case during the BDRM and decisions were to be described in the blind data review document/minutes which were to be finalized prior to database lock.

Subject analysis set title	Full Analysis Set: 30-sec Bolus
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) was to include all patients who had been randomized to treatment and received HEC regimen and active study drug (including partial infusion). Following the intent-to-treat principle, patients were to be assigned to the study treatment group according to the treatment to which they had been randomized.

Subject analysis set title	Per Protocol Population: 30-sec Bolus
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) population was to include all patients from the FAS who had completed the 0-24 h study period with no major protocol violations, i.e., those affecting the primary efficacy endpoint. All protocol violations (e.g., wrong inclusion, poor compliance, missing diaries, forbidden concomitant medications, and mis-randomizations) were to be reviewed and discussed case by case during the BDRM and decisions were to be described in the blind data review document/minutes which were to be finalized prior to database lock.

Subject analysis set title	Safety Population: 30-min Infusion
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population was to include all patients who had received active study drug (including partial infusion). Patients were to be assigned to study treatment groups according to the actual treatment received.

Subject analysis set title	Safety Population: 30-sec Bolus
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population was to include all patients who had received active study drug (including partial infusion). Patients were to be assigned to study treatment groups according to the actual treatment received.

Primary: Complete Response in acute phase

End point title	Complete Response in acute phase

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Primary

End point timeframe:

Acute phase (0-24 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Per Protocol Population: 30-min Infusion
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[1]	225	214
Units: Proportion				
number (confidence interval 95%)	82.7 (77.2 to 87.1)	86.5 (81.3 to 90.4)	82.7 (77.2 to 87.1)	82.7 (77.1 to 87.2)

Notes:

[1] - One patient did not receive any treatment and was excluded from all analysis sets

End point values	Full Analysis Set: 30-sec Bolus	Per Protocol Population: 30-sec Bolus		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	215	211		
Units: Proportion				
number (confidence interval 95%)	86.5 (81.3 to 90.4)	86.3 (81 to 90.3)		

Statistical analyses

Statistical analysis title	Primary statistical analysis (FAS)

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to test the null hypothesis that the risk difference between 30-min Infusion and 30-sec Bolus is less than or equal to a pre-specified non-inferiority margin of -15%.

Comparison groups	Full Analysis Set: 30-sec Bolus v Full Analysis Set: 30-min Infusion
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-3.8

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-12.2
upper limit	4.7

Notes:

[2] - A non-inferiority margin of -15% was pre-specified. The null hypothesis was to be rejected and the non-inferiority of palonosetron 0.25 mg 30-min infusion versus palonosetron 0.25 mg 30-sec infusion demonstrated, if the lower limit of the 2-sided 99% CI for the difference in proportion of patients with CR was greater than -15%.

Statistical analysis title	Primary statistical analysis (PP Population)

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to test the null hypothesis that the risk difference between 30-min Infusion and 30-sec Bolus is less than or equal to a pre-specified non-inferiority margin of -15%.

Comparison groups	Per Protocol Population: 30-min Infusion v Per Protocol Population: 30-sec Bolus
Number of subjects included in analysis	425
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-3.4
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-12
upper limit	5.2

Notes:

[3] - A non-inferiority margin of -15% was pre-specified. The null hypothesis was to be rejected and the non-inferiority of palonosetron 0.25 mg 30-min infusion versus palonosetron 0.25 mg 30-sec infusion demonstrated, if the lower limit of the 2-sided 99% CI for the difference in proportion of patients with CR was greater than -15%.

Secondary: Complete Response in Delayed phase

End point title	Complete Response in Delayed phase

End point description:

Complete response in the delayed phase which is defined as the absence of chemotherapy induced nausea or vomiting and no rescue medication from >24 to 120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Delayed phase (>24 - 120 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[4]	225	215
Units: Proportion				
number (confidence interval 95%)	75.6 (69.5 to 80.7)	76.7 (70.7 to 81.9)	75.6 (69.5 to 80.7)	76.7 (70.7 to 81.9)

Notes:

[4] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	Complete Response Delayed phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	6.3

Notes:

[5] - No formal test was planned for this endpoint

Secondary: Complete Response in Overall phase

End point title	Complete Response in Overall phase

End point description:

Complete response in the overall phase which is defined as the absence of chemotherapy induced nausea or vomiting and no rescue medication from 0 to 120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Overall phase (0 - 120 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[6]	225	215
Units: Proportion				
number (confidence interval 95%)	66.7 (60.3 to 72.5)	72.6 (66.2 to 78.1)	66.7 (60.3 to 72.5)	72.6 (66.2 to 78.1)

Notes:

[6] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	Complete Response Overall phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.1
upper limit	2.1

Notes:

[7] - No formal test was planned for this endpoint

Secondary: No emetic episode in acute phase

End point title	No emetic episode in acute phase

End point description:

No emetic episodes in the acute phase which is defined as the absence of emetic episodes in 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Acute phase (0-24 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[8]	225	215
Units: Proportion				
number (confidence interval 95%)	82.7 (77.2 to 87.1)	88.4 (83.4 to 92)	82.7 (77.2 to 87.1)	88.4 (83.4 to 92)

Notes:

[8] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	No emetic episodes: Acute phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Risk difference (RD)
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.9
upper limit	0.6

Notes:

[9] - No formal test was planned for this endpoint

Secondary: No emetic episodes delayed phase

End point title	No emetic episodes delayed phase

End point description:

No emetic episodes in the delayed phase which is defined as the absence of emetic episodes in >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Delayed phase (>24 - 120 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[10]	225	215
Units: Proportion				
number (confidence interval 95%)	78.2 (72.4 to 83.1)	78.1 (72.1 to 83.1)	78.2 (72.4 to 83.1)	78.1 (72.1 to 83.1)

Notes:

[10] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	No emetic episodes: Delayed phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	7.4

Notes:

[11] - No formal test was planned for this endpoint

Secondary: No emetic episode in overall phase

End point title	No emetic episode in overall phase

End point description:

No emetic episodes in the overallphase which is defined as the absence of emetic episodes in 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Overall phase (0-120 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[12]	225	215
Units: Proportion				
number (confidence interval 95%)	68.9 (62.6 to 74.6)	74.4 (68.2 to 79.8)	68.9 (62.6 to 74.6)	74.4 (68.2 to 79.8)

Notes:

[12] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	No emetic episodes: Overall phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus

Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	Risk difference (RD)
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	2.4

Notes:

[13] - No formal test was planned for this endpoint

Secondary: No Rescue Medication in acute phase

End point title	No Rescue Medication in acute phase

End point description:

No rescue medication in the acute phase which is defined as the absence of rescue medication in 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Acute Phase (0-24 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225[14]	215	225	215
Units: Proportion				
number (confidence interval 95%)	88.9 (84.1 to 92.4)	90.7 (86.1 to 93.9)	88.9 (84.1 to 92.4)	90.7 (86.1 to 93.9)

Notes:

[14] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	No rescue medication: Acute phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[15]
Parameter estimate	Risk difference (RD)
Point estimate	-1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	3.7

Notes:

[15] - No formal test was planned for this endpoint

Secondary: No Rescue Medication in delayed phase

End point title	No Rescue Medication in delayed phase

End point description:

No rescue medication in the delayed phase which is defined as the absence of rescue medication in 0-24 hours after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Delayed phase (>24 - 120 hours)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[16]	225	215
Units: Proportion				
number (confidence interval 95%)	81.3 (75.7 to 85.9)	81.9 (76.2 to 86.4)	81.3 (75.7 to 85.9)	81.9 (76.2 to 86.4)

Notes:

[16] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	No rescue medication: Delayed phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. No test for non-inferiority was to be performed.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	Risk difference (RD)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	6.3

Notes:

[17] - No formal test was planned for this endpoint

Secondary: No Rescue Medication in overall phase

End point title	No Rescue Medication in overall phase

End point description:

No emetic episodes in the overall phase which is defined as the absence of emetic episodes in 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

End point type	Secondary

End point timeframe:

Overall phase (0-120 hour)

End point values	30-min Infusion	30-sec Bolus	Full Analysis Set: 30-min Infusion	Full Analysis Set: 30-sec Bolus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	225	215[18]	225	215
Units: Proportion				
number (confidence interval 95%)	76.9 (71 to 81.9)	78.6 (72.6 to 83.6)	76.9 (71 to 81.9)	78.6 (72.6 to 83.6)

Notes:

[18] - One patient did not receive any treatment and was excluded from all analysis sets

Statistical analyses

Statistical analysis title	No rescue medication: Overall phase- Analysis

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to test the null hypothesis that the risk difference between 30-min Infusion and 30-sec Bolus is less than or equal to a pre-specified non-inferiority margin of -15%.

Comparison groups	Full Analysis Set: 30-min Infusion v Full Analysis Set: 30-sec Bolus
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	Risk difference (RD)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	5.4

Notes:

[19] - No formal test was planned for this endpoint

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Informed consent signature up to the follow-up visit or last patient contact which is a maximum of 37 days.

Adverse event reporting additional description:

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	30-sec Bolus

Reporting group description:

Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-sec IV bolus with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.

Reporting group title	30-min Infusion

Reporting group description:

Subjects in this arm received a single-dose of palonosetron 0.25 mg administered as a 30-min IV infusion with oral dexamethasone prior to highly emetogenic chemotherapy. 20 mg/day single-dose of dexamethasone was received on Day 1 then 8 mg bid on Days 2 to 4.

Serious adverse events	30-sec Bolus	30-min Infusion	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
number of deaths (all causes)	7	6	
number of deaths resulting from adverse events	0	1	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	30-sec Bolus	30-min Infusion	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 215 (33.49%)	80 / 225 (35.56%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bone cancer metastatic			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	2 / 215 (0.93%)	8 / 225 (3.56%)	
occurrences (all)	2	12	
Hypertensive crisis			
subjects affected / exposed	3 / 215 (1.40%)	1 / 225 (0.44%)	
occurrences (all)	3	1	
Hypotension			
subjects affected / exposed	1 / 215 (0.47%)	3 / 225 (1.33%)	
occurrences (all)	2	3	
Peripheral circulatory failure			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Phlebitis deep			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Superior vena cava syndrome			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 215 (4.65%)	4 / 225 (1.78%)	
occurrences (all)	10	4	
Chest pain			

subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Fatigue			
subjects affected / exposed	3 / 215 (1.40%)	1 / 225 (0.44%)	
occurrences (all)	3	1	
Malaise			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	2	
Hyperthermia			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Mucosal inflammation			
subjects affected / exposed	0 / 215 (0.00%)	2 / 225 (0.89%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	0 / 215 (0.00%)	3 / 225 (1.33%)	
occurrences (all)	0	3	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	1 / 215 (0.47%)	2 / 225 (0.89%)	
occurrences (all)	1	2	
Epistaxis			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Dyspnoea			

subjects affected / exposed	0 / 215 (0.00%)	3 / 225 (1.33%)	
occurrences (all)	0	3	
Hiccups			
subjects affected / exposed	3 / 215 (1.40%)	6 / 225 (2.67%)	
occurrences (all)	4	14	
Hypoxia			
subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Productive cough			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 215 (0.47%)	2 / 225 (0.89%)	
occurrences (all)	1	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 215 (1.86%)	1 / 225 (0.44%)	
occurrences (all)	4	1	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 215 (1.40%)	0 / 225 (0.00%)	
occurrences (all)	3	0	
Blood bilirubin increased			
subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Blood calcium decreased			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Blood chloride decreased			
subjects affected / exposed	1 / 215 (0.47%)	2 / 225 (0.89%)	
occurrences (all)	1	2	
Blood creatine increased			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			

subjects affected / exposed	2 / 215 (0.93%)	0 / 225 (0.00%)	
occurrences (all)	2	0	
Blood creatinine increased			
subjects affected / exposed	6 / 215 (2.79%)	2 / 225 (0.89%)	
occurrences (all)	7	2	
Blood potassium decreased			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Blood urea increased			
subjects affected / exposed	3 / 215 (1.40%)	4 / 225 (1.78%)	
occurrences (all)	3	4	
Breath sounds abnormal			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Creatinine renal clearance decreased			
subjects affected / exposed	2 / 215 (0.93%)	0 / 225 (0.00%)	
occurrences (all)	2	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 215 (1.40%)	0 / 225 (0.00%)	
occurrences (all)	3	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Monocyte count decreased			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Neutrophil count increased			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Platelet count increased			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	

Weight decreased			
subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
White blood cell count increased			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Atrial tachycardia			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Atrial flutter			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Bundle branch block right			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Sinus tachycardia			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 215 (0.00%)	3 / 225 (1.33%)	
occurrences (all)	0	3	
Nervous system disorders			

Headache			
subjects affected / exposed	4 / 215 (1.86%)	4 / 225 (1.78%)	
occurrences (all)	4	4	
Dizziness			
subjects affected / exposed	3 / 215 (1.40%)	2 / 225 (0.89%)	
occurrences (all)	3	2	
Paraesthesia			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 215 (0.93%)	2 / 225 (0.89%)	
occurrences (all)	2	3	
Granulocytopenia			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	4 / 215 (1.86%)	3 / 225 (1.33%)	
occurrences (all)	4	4	
Neutrophilia			
subjects affected / exposed	2 / 215 (0.93%)	1 / 225 (0.44%)	
occurrences (all)	2	1	
Neutropenia			
subjects affected / exposed	8 / 215 (3.72%)	7 / 225 (3.11%)	
occurrences (all)	8	9	
Pancytopenia			

subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	2 / 215 (0.93%)	4 / 225 (1.78%)	
occurrences (all)	2	7	
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	2 / 215 (0.93%)	1 / 225 (0.44%)	
occurrences (all)	2	1	
Breath odour			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Chronic gastritis			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	3 / 215 (1.40%)	5 / 225 (2.22%)	
occurrences (all)	5	5	
Diarrhoea			
subjects affected / exposed	6 / 215 (2.79%)	11 / 225 (4.89%)	
occurrences (all)	7	14	
Duodenal ulcer			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Duodenitis			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	5 / 215 (2.33%)	5 / 225 (2.22%)	
occurrences (all)	5	5	

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Retching			
subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Salivary hypersecretion			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	2 / 215 (0.93%)	1 / 225 (0.44%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	1 / 215 (0.47%)	3 / 225 (1.33%)	
occurrences (all)	1	3	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 215 (3.72%)	5 / 225 (2.22%)	
occurrences (all)	8	5	
Dermatitis			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 215 (0.47%)	2 / 225 (0.89%)	
occurrences (all)	1	2	
Chronic kidney disease			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Glycosuria			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	3 / 215 (1.40%)	2 / 225 (0.89%)	
occurrences (all)	3	2	
Pollakiuria			
subjects affected / exposed	2 / 215 (0.93%)	0 / 225 (0.00%)	
occurrences (all)	2	0	
Renal impairment			
subjects affected / exposed	3 / 215 (1.40%)	2 / 225 (0.89%)	
occurrences (all)	3	3	
Renal failure			
subjects affected / exposed	2 / 215 (0.93%)	3 / 225 (1.33%)	
occurrences (all)	2	4	
Urinary retention			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 215 (0.00%)	2 / 225 (0.89%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 215 (0.47%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 215 (0.93%)	3 / 225 (1.33%)	
occurrences (all)	2	3	
Dehydration			
subjects affected / exposed	2 / 215 (0.93%)	1 / 225 (0.44%)	
occurrences (all)	2	1	
Diabetes mellitus			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	2 / 215 (0.93%)	1 / 225 (0.44%)	
occurrences (all)	2	1	
Hyperkalaemia			
subjects affected / exposed	1 / 215 (0.47%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	1 / 215 (0.47%)	2 / 225 (0.89%)	
occurrences (all)	1	6	
Hypocalcaemia			
subjects affected / exposed	0 / 215 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	2	
Hyponatraemia			

subjects affected / exposed occurrences (all)	0 / 215 (0.00%) 0	1 / 225 (0.44%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2016	Time windows were specified in detail for study drug and additional non-investigational study drug administration (palonosetron IV bolus, palonosetron IV infusion, and dexamethasone tablets), for the reference chemotherapy administration, for the vital signs measurements at 24 h ±2 h and 120 h -6 h/+54 h and for 12-lead ECG measurement at 120 h -6 h/+54 h.

Notes:

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.

None reported.

Notes: