Clinical trial results:
A multicenter, randomized, double-blind, parallel group study to evaluate the efficacy and safety of two different doses of palonosetron compared to ondansetron in the prevention of CINV in pediatric patients undergoing single and repeated cycles of MEC or HEC

Summary

EudraCT number	2010-022872-30
Trial protocol	GB HU AT BG EE DE FR CZ
Global end of trial date	26 October 2012

Results information

Result version number	v1 (current)
This version publication date	17 April 2016
First version publication date	17 April 2016

Trial information

Trial identification

Sponsor protocol code	PALO-10-20

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01442376
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Helsinn Healthcare SA
Sponsor organisation address	Via Pian Scairolo 9 , Lugano/Pazzallo, Switzerland, 6912
Public contact	Spinelli Tulla, Helsinn Healthcare SA, +41 91 985 21 21, tulla.spinelli@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	24 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objectives of the trial:
- The primary objective is to evaluate the efficacy of two different doses of IV palonosetron in the prevention of chemotherapy induced nausea and vomiting in moderately emetogenic (MEC) or highly emetogenic (HEC) patients through 120 hours after start of chemotherapy in single and repeated chemotherapy cycles.

Protection of trial subjects:

For all patients, written informed consent signed by the parent(s)/legal guardian(s) was obtained prior to enrollment. For patients of appropriate age and intellectual maturity, the signed assent form was obtained in compliance with local laws and regulations.

Background therapy:

NA

Evidence for comparator:

Ondansetron (Zofran®), another 5-HT3 receptor antagonist, was chosen as the active comparator in this study because it is one of the most frequently prescribed antiemetic agents and is approved for intravenous (IV) and oral use in adults and children for CINV in many countries.

Actual start date of recruitment	12 September 2011
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	Chile: 29
Country: Number of subjects enrolled	Peru: 19
Country: Number of subjects enrolled	Romania: 58
Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Serbia: 27
Country: Number of subjects enrolled	Ukraine: 27
Country: Number of subjects enrolled	United States: 27
Country: Number of subjects enrolled	Poland: 65
Country: Number of subjects enrolled	Austria: 20
Country: Number of subjects enrolled	Bulgaria: 20
Country: Number of subjects enrolled	Czech Republic: 63
Country: Number of subjects enrolled	Estonia: 8
Country: Number of subjects enrolled	France: 7

Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 65
Worldwide total number of subjects	493
EEA total number of subjects	310

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)	45
Children (2-11 years)	298
Adolescents (12-17 years)	150
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The target population was pediatric patients aged from full-term neonates to <17 years scheduled to receive at least one moderately or highly emetogenic chemotherapeutic agent for histologically or cytologically confirmed malignant disease. For patients aged ≥10 years ECOG PS ≤2 was requested.

Pre-assignment

Screening details:

Out of total 502 randomized patients, 8 patients (2 palonosetron 10 mcg/kg, 4 palonosetron 20 mcg/kg and 2 ondansetron) did not receive the study drug and 1 patient (palonosetron 10 mcg/kg) received study drug but did not receive highly or moderate emetogenic chemotherapy (HEC or MEC), was excluded from the FAS, but included in Safety Population.

Period 1

Period 1 title	Overall Period (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 10 mcg/kg

Arm description:

Palonosetron and placebo to Ondansetron
Intervention:
Drug: Palonosetron
Palonosetron: Single dose Palonosetron IV 10 mcg/kg up to a maximum total dose of 0.75 mg
Placebo to Ondansetron

Arm type	Experimental
Investigational medicinal product name	Palonosetron
Investigational medicinal product code	NA
Other name	Aloxi
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose Palonosetron IV 10 mcg/kg up to a maximum total dose of 0.75 mg.

Investigational medicinal product name	Placebo to Ondansetron
Investigational medicinal product code	NA
Other name	NA
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose matching placebo IV.

Arm title	Palonosetron 20 mcg/kg

Arm description:

Palonosetron and Placebo to Ondansetron
Intervention:
Drug: Palonosetron
Palonosetron: Single dose Palonosetron IV 20 mcg/kg up to a maximum total dose of 1.5 mg
Placebo to Ondansetron

Arm type	Experimental

Investigational medicinal product name	Palonosetron
Investigational medicinal product code	NA
Other name	Aloxi
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose Palonosetron IV 20 mcg/kg up to a maximum total dose of 1.5 mg.

Investigational medicinal product name	Placebo to Ondansetron
Investigational medicinal product code	NA
Other name	NA
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose matching placebo IV.

Arm title	Ondansetron

Arm description:

Ondansetron and placebo to Palonosetron
Drug:
Comparator: Ondansetron
Ondansetron: Single three (every 4 hours) Ondansetron IV doses 0.15 mg/kg up to a maximum total dose of 32 mg
Placebo to Palonosetron

Arm type	Active comparator
Investigational medicinal product name	Ondansetron
Investigational medicinal product code	NA
Other name	Zofran
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single three (every 4 hours) Ondansetron IV doses 0.15 mg/kg up to a maximum total dose of 32 mg.

Investigational medicinal product name	Placebo to Palonosetron
Investigational medicinal product code	NA
Other name	NA
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose matching placebo IV.

Number of subjects in period 1	Palonosetron 10 mcg/kg	Palonosetron 20 mcg/kg	Ondansetron
Started	166	165	162
Completed	166	160	159
Not completed	0	5	3
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	2	1
Not eligible for subsequent cycles	-	2	-
Death	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Palonosetron 10 mcg/kg
Reporting group description:	
Palonosetron and placebo to Ondansetron Intervention: Drug: Palonosetron Palonosetron: Single dose Palonosetron IV 10 mcg/kg up to a maximum total dose of 0.75 mg Placebo to Ondansetron	
Reporting group title	Palonosetron 20 mcg/kg
Reporting group description:	
Palonosetron and Placebo to Ondansetron Intervention: Drug: Palonosetron Palonosetron: Single dose Palonosetron IV 20 mcg/kg up to a maximum total dose of 1.5 mg Placebo to Ondansetron	
Reporting group title	Ondansetron
Reporting group description:	
Ondansetron and placebo to Palonosetron Drug: Comparator: Ondansetron Ondansetron: Single three (every 4 hours) Ondansetron IV doses 0.15 mg/kg up to a maximum total dose of 32 mg Placebo to Palonosetron	

Reporting group values	Palonosetron 10 mcg/kg	Palonosetron 20 mcg/kg	Ondansetron
Number of subjects	166	165	162
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			
arithmetic mean	8.07	8.39	8.18
standard deviation	± 4.81	± 4.91	± 5.17
Gender categorical Units: Subjects			
Female	78	89	64
Male	88	76	98
Age, customised Units: Subjects			
<2 years	15	15	15
2 to <6 years	54	54	54

6 to <12 years	46	46	44
12 to <17 years	51	50	49
Ethnicity Units: Subjects			
Hispanic or Latino	26	26	12
Not Hispanic or Latino	140	139	150
Race Units: Subjects			
Asian	2	0	0
Black or African American	2	0	0
White	156	154	159
More than one race	5	11	3
Unknown or Not Reported	1	0	0
Emetogenicity of chemotherapy in Cycle 1 Units: Subjects			
MEC	112	116	111
HEC	54	49	51

Reporting group values	Total		
Number of subjects	493		
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			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	231		
Male	262		
Age, customised Units: Subjects			
<2 years	45		
2 to <6 years	162		
6 to <12 years	136		
12 to <17 years	150		
Ethnicity Units: Subjects			
Hispanic or Latino	64		
Not Hispanic or Latino	429		

Race Units: Subjects			
Asian	2		
Black or African American	2		
White	469		
More than one race	19		
Unknown or Not Reported	1		
Emetogenicity of chemotherapy in Cycle 1 Units: Subjects			
MEC	339		
HEC	154		

End points

End points reporting groups

Reporting group title	Palonosetron 10 mcg/kg
Reporting group description:	
Palonosetron and placebo to Ondansetron Intervention: Drug: Palonosetron Palonosetron: Single dose Palonosetron IV 10 mcg/kg up to a maximum total dose of 0.75 mg Placebo to Ondansetron	

Reporting group title	Palonosetron 20 mcg/kg
Reporting group description:	
Palonosetron and Placebo to Ondansetron Intervention: Drug: Palonosetron Palonosetron: Single dose Palonosetron IV 20 mcg/kg up to a maximum total dose of 1.5 mg Placebo to Ondansetron	

Reporting group title	Ondansetron
Reporting group description:	
Ondansetron and placebo to Palonosetron Drug: Comparator: Ondansetron Ondansetron: Single three (every 4 hours) Ondansetron IV doses 0.15 mg/kg up to a maximum total dose of 32 mg Placebo to Palonosetron	

Primary: Proportion of Patients With Complete Response 0 to 24 Hours (Acute Phase) in Cycle 1

End point title	Proportion of Patients With Complete Response 0 to 24 Hours (Acute Phase) in Cycle 1
End point description:	
Complete Response (CR) was defined as no vomiting, no retching, and no use of antiemetic rescue medication from 0 to 24 hours (acute phase) after T0 (start of administration of the most emetogenic chemotherapy) during first cycle. Time 0 (T0) is defined as the time when the patient starts the first cycle of chemotherapy. Full Analysis Set (FAS) population which included all randomized patients receiving the active study drug and HEC or MEC. Following the intent-to-treat principle, patients were assigned to the study treatment group according to the randomized treatment.	
End point type	Primary
End point timeframe:	
0 to 24 hours after T0	

End point values	Palonosetron 10 mcg/kg	Palonosetron 20 mcg/kg	Ondansetron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	165	162	
Units: percentage of patients				
number (confidence interval 95%)	54.2 (46.3 to 61.9)	59.4 (51.5 to 66.9)	58.6 (50.6 to 66.2)	

Statistical analyses

Statistical analysis title	Palonosetron 20 mcg/kg vs. Ondansetron

Statistical analysis description:

The stratum adjusted Mantel-Haenszel method was used to compute the confidence interval (CI) of the difference in proportion. If the lower bound of the 97.5% CI of either the difference (CR0-24h palonosetron 20 mcg/kg - CR0-24h ondansetron) or the difference (CR0-24h palonosetron 10 mcg/kg - CR0-24h ondansetron) was strictly superior to the non-inferiority margin (δ=-0.15) then the null hypothesis (H0) was rejected. A power of 80% was used for sample size computation.

Comparison groups	Palonosetron 20 mcg/kg v Ondansetron
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Risk difference (RD)
Point estimate	0.36
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-11.7
upper limit	12.4

Notes:

[1] - Non-inferiority margin of 15% at an alpha level of 2.5% in a 1-sided test (equivalent to 5.0% 2-sided test) to reject the null hypothesis that the study drug was inferior to the active control drug by more than the non-inferiority margin.

Statistical analysis title	Palonosetron 10 mcg/kg vs. Ondansetron

Statistical analysis description:

The stratum adjusted Mantel-Haenszel method was used to compute the confidence interval (CI) of the difference in proportion. If the lower bound of the 97.5% CI of either the difference (CR0-24h palonosetron 20 mcg/kg - CR0-24h ondansetron) or the difference (CR0-24h palonosetron 10 mcg/kg - CR0-24h ondansetron) was strictly superior to the non-inferiority margin (δ=-0.15) then the null hypothesis (H0) was rejected. A power of 80% was used for sample size computation.

Comparison groups	Ondansetron v Palonosetron 10 mcg/kg
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Risk difference (RD)
Point estimate	-4.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-16.4
upper limit	7.6

Notes:

[2] - Non-inferiority margin of 15% at an alpha level of 2.5% in a 1-sided test (equivalent to 5.0% 2-sided test) to reject the null hypothesis that the study drug was inferior to the active control drug by more than the non-inferiority margin.

Secondary: Proportion of Patients With Complete Response >24 to 120 Hours (Delayed Phase) in Cycle 1

End point title	Proportion of Patients With Complete Response >24 to 120 Hours (Delayed Phase) in Cycle 1

End point description:

Complete Response (CR) was defined as no vomiting, no retching, and no use of antiemetic rescue medication from >24 to 120 hours (delayed phase) after T0 (start of administration of the most emetogenic chemotherapy) during first cycle. Full Analysis Set (FAS) population.

End point type	Secondary

End point timeframe:

>24 to 120 hours (delayed phase) after T0

End point values	Palonosetron 10 mcg/kg	Palonosetron 20 mcg/kg	Ondansetron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	165	162	
Units: percentage of patients				
number (confidence interval 95%)	28.9 (22.3 to 36.5)	38.8 (31.4 to 46.7)	28.4 (21.7 to 36.1)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 30 days post treatment

Adverse event reporting additional description:

Safety population (SAF), which allocated patients to treatment groups based on the treatment actually received. Patients received study treatment on Study Day 1 of each cycle for up to 4 cycles. The number of patients included in the SAF at each cycle was the following: 494 (cycle 1), 260 (cycle 2), 146 (cycle 3) and 69 (cycle 4).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Palonosetron 10 mcg/kg

Reporting group description:

Palonosetron and placebo to Ondansetron
Intervention:
Drug: Palonosetron
Palonosetron: Single dose Palonosetron IV 10 mcg/kg up to a maximum total dose of 0.75 mg
Placebo to Ondansetron

Reporting group title	Palonosetron 20 mcg/kg

Reporting group description:

Palonosetron and placebo to Ondansetron
Intervention:
Drug: Palonosetron
Palonosetron: Single dose Palonosetron IV 20 mcg/kg up to a maximum total dose of 1.5 mg
Placebo to Ondansetron

Reporting group title	Ondansetron

Reporting group description:

Ondansetron and Placebo to Palonosetron
Drug:
Comparator: Ondansetron
Ondansetron: Single three (every 4 hours) Ondansetron IV doses 0.15 mg/kg up to a maximum total dose of 32 mg
Placebo to Palonosetron

Serious adverse events	Palonosetron 10 mcg/kg	Palonosetron 20 mcg/kg	Ondansetron
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 167 (40.72%)	62 / 163 (38.04%)	70 / 164 (42.68%)
number of deaths (all causes)	0	3	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 167 (3.59%)	3 / 163 (1.84%)	7 / 164 (4.27%)
occurrences causally related to treatment / all	0 / 7	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	3 / 167 (1.80%)	1 / 163 (0.61%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device complication			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 167 (1.20%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tachypnoea			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Apathy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
White blood cell count decreased			
subjects affected / exposed	6 / 167 (3.59%)	6 / 163 (3.68%)	4 / 164 (2.44%)
occurrences causally related to treatment / all	0 / 9	0 / 8	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	2 / 167 (1.20%)	3 / 163 (1.84%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocyte count decreased			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Radiation skin injury			

subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Aplasia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 167 (0.60%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hydrocephalus			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute disseminated encephalomyelitis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Grand mal convulsion			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurotoxicity			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			

subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	27 / 167 (16.17%)	30 / 163 (18.40%)	23 / 164 (14.02%)
occurrences causally related to treatment / all	0 / 31	0 / 38	0 / 35
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	17 / 167 (10.18%)	14 / 163 (8.59%)	15 / 164 (9.15%)
occurrences causally related to treatment / all	0 / 21	0 / 17	0 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	12 / 167 (7.19%)	10 / 163 (6.13%)	11 / 164 (6.71%)
occurrences causally related to treatment / all	0 / 14	0 / 13	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	14 / 167 (8.38%)	8 / 163 (4.91%)	9 / 164 (5.49%)
occurrences causally related to treatment / all	0 / 17	0 / 11	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	10 / 167 (5.99%)	4 / 163 (2.45%)	9 / 164 (5.49%)
occurrences causally related to treatment / all	0 / 12	0 / 7	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	6 / 167 (3.59%)	2 / 163 (1.23%)	6 / 164 (3.66%)
occurrences causally related to treatment / all	0 / 9	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile bone marrow aplasia			

subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agranulocytosis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 167 (2.40%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 167 (0.00%)	2 / 163 (1.23%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	1 / 167 (0.60%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Caecitis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal mucosal disorder			

subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 167 (0.60%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis bullous			

subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin erosion			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tubular disorder			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	4 / 167 (2.40%)	1 / 163 (0.61%)	3 / 164 (1.83%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 167 (1.20%)	1 / 163 (0.61%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candidiasis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device related infection			
subjects affected / exposed	2 / 167 (1.20%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 167 (0.00%)	2 / 163 (1.23%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			

subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			

subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal skin infection			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			

subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 167 (0.60%)	3 / 163 (1.84%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	1 / 167 (0.60%)	0 / 163 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 167 (0.00%)	1 / 163 (0.61%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 163 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Palonosetron 10 mcg/kg	Palonosetron 20 mcg/kg	Ondansetron
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 167 (75.45%)	112 / 163 (68.71%)	125 / 164 (76.22%)
Investigations			
Platelet count decreased			
subjects affected / exposed	10 / 167 (5.99%)	9 / 163 (5.52%)	10 / 164 (6.10%)
occurrences (all)	13	12	19
White blood cell count decreased			
subjects affected / exposed	12 / 167 (7.19%)	15 / 163 (9.20%)	15 / 164 (9.15%)
occurrences (all)	14	18	24
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 167 (10.18%)	9 / 163 (5.52%)	16 / 164 (9.76%)
occurrences (all)	24	10	28
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	65 / 167 (38.92%)	60 / 163 (36.81%)	61 / 164 (37.20%)
occurrences (all)	107	89	105
Febrile neutropenia			
subjects affected / exposed	11 / 167 (6.59%)	4 / 163 (2.45%)	4 / 164 (2.44%)
occurrences (all)	13	4	7
Leukopenia			
subjects affected / exposed	37 / 167 (22.16%)	27 / 163 (16.56%)	43 / 164 (26.22%)
occurrences (all)	74	59	104
Neutropenia			
subjects affected / exposed	35 / 167 (20.96%)	31 / 163 (19.02%)	22 / 164 (13.41%)
occurrences (all)	60	51	40
Thrombocytopenia			
subjects affected / exposed	35 / 167 (20.96%)	33 / 163 (20.25%)	37 / 164 (22.56%)
occurrences (all)	69	61	90
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	32 / 167 (19.16%)	19 / 163 (11.66%)	21 / 164 (12.80%)
occurrences (all)	40	35	38

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	15 / 167 (8.98%)	13 / 163 (7.98%)	18 / 164 (10.98%)
occurrences (all)	20	16	24
Constipation			
subjects affected / exposed	8 / 167 (4.79%)	10 / 163 (6.13%)	8 / 164 (4.88%)
occurrences (all)	9	12	9
Diarrhoea			
subjects affected / exposed	13 / 167 (7.78%)	6 / 163 (3.68%)	14 / 164 (8.54%)
occurrences (all)	14	7	15
Nausea			
subjects affected / exposed	8 / 167 (4.79%)	6 / 163 (3.68%)	13 / 164 (7.93%)
occurrences (all)	10	8	19
Stomatitis			
subjects affected / exposed	11 / 167 (6.59%)	12 / 163 (7.36%)	12 / 164 (7.32%)
occurrences (all)	15	14	16
Vomiting			
subjects affected / exposed	13 / 167 (7.78%)	17 / 163 (10.43%)	22 / 164 (13.41%)
occurrences (all)	21	39	31
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 167 (4.79%)	4 / 163 (2.45%)	9 / 164 (5.49%)
occurrences (all)	8	4	10
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	6 / 167 (3.59%)	3 / 163 (1.84%)	9 / 164 (5.49%)
occurrences (all)	8	3	9

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.

None reported

Notes: