Clinical trial results:
ONO-7847 Japanese Clinical Study in Pediatric Patients: Multicenter, Open-label, Uncontrolled Study for the Prevention of CINV

Summary

EudraCT number	2018-000663-80
Trial protocol	Outside EU/EEA
Global end of trial date	25 November 2013

Results information

Result version number	v1 (current)
This version publication date	15 July 2018
First version publication date	15 July 2018

Trial information

Trial identification

Sponsor protocol code	ONO-7847-03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ONO Pharmaceutical Co., Ltd.
Sponsor organisation address	8-2, Kyutaromachi 1-chome, Chuo-ku, Osaka, Japan, 541-8564
Public contact	Clinical Development Planning, ONO Pharmaceutical Co., Ltd., 06 6263-3902,
Scientific contact	Clinical Development Planning, ONO Pharmaceutical Co., Ltd., 06 6263-3902,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2013
Global end of trial reached?	Yes
Global end of trial date	25 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to confirm the safety, efficacy, and pharmacokinetics (PK) of ONO-7847 (fosaprepitant dimeglumine) when used for the prevention of chemotherapy-induced nausea and vomiting (CINV) in Japanese pediatric participants with malignant tumors who were scheduled to receive chemotherapy including any cisplatin, cyclophosphamide, or carboplatin.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

The following additional measure defined for this individual study was in place for the protection of study participants: Investigator-prescribed rescue therapy medication was allowed for the treatment of emergent nausea and vomiting.

Background therapy:

Acceptable rescue therapy medications for severe nausea (inability to ingest food or water) included: 5-Hydroxytryptamine (5-HT3) receptor antagonists (granisetron, ondansetron, azasetron); Phenothiazines (chlorpromazine, prochlorperazine, perphenazine); Butyrophenones (haloperidol, droperidol); Benzamides (sulpiride, tiapride, sultopride); Dopamine receptor antagonists (metoclopramide, itopride, domperidone); Corticosteroids (dexamethasone, methylprednisolone); Benzodiazepines (diazepam, nitrazepam, triazolam) and/or Antihistamines (hydroxyzine, dimenhydrinate, diphenhydramine).

Evidence for comparator: -

Actual start date of recruitment	17 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 27
Worldwide total number of subjects	27
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	5
Children (2-11 years)	10
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Japanese pediatric participants, aged 6 months to 18 years, with malignant tumors who were scheduled to receive emetogenic chemotherapy were recruited for this study.

Pre-assignment

Screening details:

Participants were divided into the following four age brackets: 6 months to <2 years; 2 years to <6 years; 6 years to <12 years and 12 years to 18 years.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	ONO-7847: 6 mos to <2 yrs

Arm description:

Participants aged 6 mos to <2 yrs received a single administration of ONO-7847 3 mg/kg via intravenous (IV) infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Arm type	Experimental
Investigational medicinal product name	ONO-7847
Investigational medicinal product code	
Other name	fosaprepitant dimegulmine
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg to 150 mg, depending on age of participant

Investigational medicinal product name	Granisetron
Investigational medicinal product code	
Other name	KYTRIL®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 ug/kg

Investigational medicinal product name	Dexamethasone phosphate
Investigational medicinal product code	
Other name	DECADRON®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.1 mg/kg to 4 mg, depending on age of participant

Arm title	ONO-7847: 2 yrs to <6 yrs

Arm description:

Participants aged 2 yrs to <6 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Arm type	Experimental

Investigational medicinal product name	ONO-7847
Investigational medicinal product code	
Other name	fosaprepitant dimegulmine
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg to 150 mg, depending on age of participant

Investigational medicinal product name	Dexamethasone phosphate
Investigational medicinal product code	
Other name	DECADRON®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.1 mg/kg to 4 mg, depending on age of participant

Investigational medicinal product name	Granisetron
Investigational medicinal product code	
Other name	KYTRIL®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 ug/kg

Arm title	ONO-7847: 6 yrs to <12 yrs

Arm description:

Participants aged 6 yrs to <12 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Arm type	Experimental
Investigational medicinal product name	ONO-7847
Investigational medicinal product code	
Other name	fosaprepitant dimegulmine
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg to 150 mg, depending on age of participant

Investigational medicinal product name	Dexamethasone phosphate
Investigational medicinal product code	
Other name	DECADRON®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.1 mg/kg to 4 mg, depending on age of participant

Investigational medicinal product name	Granisetron
Investigational medicinal product code	
Other name	KYTRIL®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 ug/kg

Arm title	ONO-7847: 12 yrs to 18 yrs

Arm description:

Participants aged 12 yrs to 18 yrs received a single administration of ONO-7847 150 mg via IV infusion on Day 1 PLUS dexamethasone 4 mg via IV infusion on Days 1-2 and 8 mg on Day 3 PLUS granisetron

40 ug/kg via IV infusion on Days 1-5.

Arm type	Experimental
Investigational medicinal product name	ONO-7847
Investigational medicinal product code	
Other name	fosaprepitant dimegulmine
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg to 150 mg, depending on age of participant

Investigational medicinal product name	Granisetron
Investigational medicinal product code	
Other name	KYTRIL®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 ug/kg

Investigational medicinal product name	Dexamethasone phosphate
Investigational medicinal product code	
Other name	DECADRON®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.1 mg/kg to 4 mg, depending on age of participant

Number of subjects in period 1	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs
Started	5	5	5
Completed	5	5	5

Number of subjects in period 1	ONO-7847: 12 yrs to 18 yrs
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	ONO-7847: 6 mos to <2 yrs
Reporting group description:	
Participants aged 6 mos to <2 yrs received a single administration of ONO-7847 3 mg/kg via intravenous (IV) infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	
Reporting group title	ONO-7847: 2 yrs to <6 yrs
Reporting group description:	
Participants aged 2 yrs to <6 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	
Reporting group title	ONO-7847: 6 yrs to <12 yrs
Reporting group description:	
Participants aged 6 yrs to <12 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	
Reporting group title	ONO-7847: 12 yrs to 18 yrs
Reporting group description:	
Participants aged 12 yrs to 18 yrs received a single administration of ONO-7847 150 mg via IV infusion on Day 1 PLUS dexamethasone 4 mg via IV infusion on Days 1-2 and 8 mg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	

Reporting group values	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs
Number of subjects	5	5	5
Age Categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	5	0	0
Children (2-11 years)	0	5	5
Adolescents (12-17 years)	0	0	0
Age Continuous Units: years			
arithmetic mean	0.96	3.60	9.00
standard deviation	± 0.09	± 1.14	± 1.87
Gender Categorical Units: Subjects			
Female	2	2	3
Male	3	3	2

Reporting group values	ONO-7847: 12 yrs to 18 yrs	Total	
Number of subjects	12	27	
Age Categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	0	5	
Children (2-11 years)	0	10	
Adolescents (12-17 years)	12	12	

Age Continuous Units: years			
arithmetic mean	15.42		
standard deviation	± 1.51	-	
Gender Categorical Units: Subjects			
Female	2	9	
Male	10	18	

End points

End points reporting groups

Reporting group title	ONO-7847: 6 mos to <2 yrs
Reporting group description:	
Participants aged 6 mos to <2 yrs received a single administration of ONO-7847 3 mg/kg via intravenous (IV) infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	
Reporting group title	ONO-7847: 2 yrs to <6 yrs
Reporting group description:	
Participants aged 2 yrs to <6 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	
Reporting group title	ONO-7847: 6 yrs to <12 yrs
Reporting group description:	
Participants aged 6 yrs to <12 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	
Reporting group title	ONO-7847: 12 yrs to 18 yrs
Reporting group description:	
Participants aged 12 yrs to 18 yrs received a single administration of ONO-7847 150 mg via IV infusion on Day 1 PLUS dexamethasone 4 mg via IV infusion on Days 1-2 and 8 mg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.	

Primary: Percentage of Participants With A Complete Response (No Vomiting and No Use of Rescue Therapy)

End point title	Percentage of Participants With A Complete Response (No Vomiting and No Use of Rescue Therapy)[1]
End point description:	
A Complete Response (CR) was defined as no vomiting and no use of rescue therapy. The percentage of participants who experienced a CR is presented by treatment phase (Overall Phase: 0-120 hr, Acute Phase: 0-24 hr and Delayed Phase: 24-120 hr), where "0 hours" was defined as the start of the initial moderately or highly emetogenic chemotherapy on Day 1. The analysis population consisted of all participants who met key enrollment criteria, received ≥1 dose of both granisetron and dexamethasone, received any cisplatin, cyclophosphamide, or carboplatin, received ≥1 dose of ONO-7847 and had ≥1 post-treatment efficacy observation.	
End point type	Primary
End point timeframe:	
Up to 120 hours after start of emetogenic chemotherapy (Up to 5 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for or conducted on this primary end point.

End point values	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs	ONO-7847: 12 yrs to 18 yrs
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	12
Units: Percentage of Participants				
number (confidence interval 95%)				
Overall Phase (0-120 hr)	80.0 (28.4 to 99.5)	40.0 (5.3 to 85.3)	40.0 (5.3 to 85.3)	25.0 (5.5 to 57.2)
Acute Phase (0-24 hr)	80.0 (28.4 to 99.5)	80.0 (28.4 to 99.5)	100.0 (47.8 to 100.0)	75.0 (42.8 to 94.5)

Delayed Phase (24-120 hr)	100.0 (47.8 to 100.0)	40.0 (5.3 to 85.3)	40.0 (5.3 to 85.3)	25.0 (5.5 to 57.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experienced an Adverse Drug Reaction (ADR)

End point title	Percentage of Participants Who Experienced an Adverse Drug Reaction (ADR)[2]

End point description:

Adverse events (AEs) for which a causal relationship could not be ruled out (i.e., those with a causal relationship of Definitely, Probably or Possibly related to study treatment) were to be handled as "adverse drug reactions" (ADRs). The percentage of participants who experienced an ADR is presented. The analysis population consisted of all allocated participants who received 1 dose of study treatment.

End point type	Primary

End point timeframe:

Up to 14 days postdose (Up to 15 days)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for or conducted on this primary end point.

End point values	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs	ONO-7847: 12 yrs to 18 yrs
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	12
Units: Percentage of Participants				
number (not applicable)	20.0	20.0	20.0	8.3

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Treatment Due to an ADR

End point title	Percentage of Participants Who Discontinued Study Treatment Due to an ADR[3]

End point description:

AEs for which a causal relationship could not be ruled out (i.e., those with a causal relationship of Definitely, Probably or Possibly related to study treatment) were to be handled as ADRs. The percentage of participants who discontinued study treatment due to an ADR is presented. The analysis population consisted of all allocated participants who received 1 dose of study treatment.

End point type	Primary

End point timeframe:

Day 1

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for or conducted on this primary end point.

End point values	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs	ONO-7847: 12 yrs to 18 yrs
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	12
Units: Percentage of Participants				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days postdose (Up to 15 days)

Adverse event reporting additional description:

The analysis population consisted of all allocated participants who received 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0J

Reporting groups

Reporting group title	ONO-7847: 6 mos to <2 yrs

Reporting group description:

Participants aged 6 mos to <2 yrs received a single administration of ONO-7847 3 mg/kg via intravenous (IV) infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Reporting group title	ONO-7847: 2 yrs to <6 yrs

Reporting group description:

Participants aged 2 yrs to <6 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Reporting group title	ONO-7847: 6 yrs to <12 yrs

Reporting group description:

Participants aged 6 yrs to <12 yrs received a single administration of ONO-7847 3 mg/kg via IV infusion on Day 1 PLUS dexamethasone 0.1 mg/kg via IV infusion on Days 1-2 and 0.2 mg/kg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Reporting group title	ONO-7847: 12 yrs to 18 yrs

Reporting group description:

Participants aged 12 yrs to 18 yrs received a single administration of ONO-7847 150 mg via IV infusion on Day 1 PLUS dexamethasone 4 mg via IV infusion on Days 1-2 and 8 mg on Day 3 PLUS granisetron 40 ug/kg via IV infusion on Days 1-5.

Serious adverse events	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ONO-7847: 12 yrs to 18 yrs		

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ONO-7847: 6 mos to <2 yrs	ONO-7847: 2 yrs to <6 yrs	ONO-7847: 6 yrs to <12 yrs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	2 / 5 (40.00%)	2 / 5 (40.00%)	5 / 5 (100.00%)
occurrences (all)	2	2	5

Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Catheter site pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Hiccups			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 5 (0.00%)	3 / 5 (60.00%)	1 / 5 (20.00%)
occurrences (all)	0	3	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 5 (40.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood chloride decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood potassium decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood sodium decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Glucose urine present			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haematocrit decreased			

subjects affected / exposed	3 / 5 (60.00%)	4 / 5 (80.00%)	1 / 5 (20.00%)
occurrences (all)	3	4	1
Heart rate increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	5 / 5 (100.00%)
occurrences (all)	6	5	5
Neutrophil count decreased			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	5 / 5 (100.00%)
occurrences (all)	5	5	5
Platelet count decreased			
subjects affected / exposed	2 / 5 (40.00%)	4 / 5 (80.00%)	4 / 5 (80.00%)
occurrences (all)	2	4	4
Red blood cell count decreased			
subjects affected / exposed	3 / 5 (60.00%)	4 / 5 (80.00%)	1 / 5 (20.00%)
occurrences (all)	3	4	1
Weight decreased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	2 / 5 (40.00%)
occurrences (all)	1	1	2
Weight increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	5 / 5 (100.00%)
occurrences (all)	5	5	5
Urine ketone body present			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 5 (60.00%)
occurrences (all)	0	0	3
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 5 (80.00%)	5 / 5 (100.00%)	4 / 5 (80.00%)
occurrences (all)	4	5	4
Febrile neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 5 (40.00%)	2 / 5 (40.00%)
occurrences (all)	1	2	2
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Anal fissure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Aphthous stomatitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 5 (20.00%)	2 / 5 (40.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lip ulceration			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Proctalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	4 / 5 (80.00%)
occurrences (all)	0	0	4
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	2 / 5 (40.00%)	2 / 5 (40.00%)
occurrences (all)	1	4	3
Gastrointestinal hypomotility			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nail discolouration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oliguria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Urethral pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urinary tract pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myositis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Pain in jaw			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasopahryngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Wound infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	2 / 5 (40.00%)	1 / 5 (20.00%)	3 / 5 (60.00%)
occurrences (all)	2	1	3

Non-serious adverse events	ONO-7847: 12 yrs to 18 yrs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Embolism			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

Catheter site erythema subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Catheter site pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Puncture site pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Immune system disorders Hypogammaglobulinaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Epistaxis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hiccups subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Blood bilirubin increased			

subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	2			
Blood chloride decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Blood cholesterol increased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Blood creatine phosphokinase increased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Blood potassium decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Blood sodium decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Glucose urine present				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Haematocrit decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Heart rate increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				

subjects affected / exposed	11 / 12 (91.67%)		
occurrences (all)	13		
Neutrophil count decreased			
subjects affected / exposed	10 / 12 (83.33%)		
occurrences (all)	10		
Platelet count decreased			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	6		
Red blood cell count decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	10 / 12 (83.33%)		
occurrences (all)	11		
Urine ketone body present			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Hypoaesthesia			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	5		
Febrile neutropenia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Anal fissure			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Aphthous stomatitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Diarrhoea			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Lip dry subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Lip ulceration subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 5		
Proctalgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Stomatitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Vomiting subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 5		
Gastrointestinal hypomotility subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Erythema subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		

Nail discolouration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pain of skin			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oliguria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urethral pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urinary tract pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Myositis			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Nasopahryngitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Paronychia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Periodontitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Wound infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Clostridium difficile infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Hyponatraemia subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4		
Decreased appetite subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported