



Clinical trial results:

Randomised Phase II study of biweekly versus fractionated triweekly combination Taxotere-Cisplatin-5FU in advanced gastric and gastro-esophageal junction cancer

Summary

EudraCT number	2008-000551-10
Trial protocol	BE
Global end of trial date	07 November 2016

Results information

Result version number	v1 (current)
This version publication date	11 September 2021
First version publication date	11 September 2021
Summary attachment (see zip file)	Final Report (DoGE_Final_study_report_signed.pdf)

Trial information

Trial identification

Sponsor protocol code	DoGE01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut Jules Bordet
Sponsor organisation address	rue Héger Bordet 1, Bruxelles, Belgium, 1000
Public contact	Dr. Alain Hendlisz, Institut Jules Bordet, 32 2 541 31 96, alain.hendlisz@bordet.be
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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	19 December 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	07 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate feasibility (i.e. absence of limiting toxicity –febrile neutropenia- and absence of progression) of a biweekly and a fractionated triweekly regimen of Taxotere-Cisplatin-5-FU in advanced gastric and oesogastric junction cancer.

Protection of trial subjects:

The responsible investigator will ensure that this study is conducted in agreement with either the Declaration of Helsinki (Tokyo, Venice and Hong Kong amendments), or the laws and regulations of the country, whichever provides the greatest protection of the patient.

The protocol has been written, and the study will be conducted according to the guidelines for Good Clinical Practice issued by the European Union

The name of the patient will not be asked for or recorded. A sequential trial identification number will be allocated to each patient at registration and this number will be used to identify them and will be used on all case report forms. In order to avoid errors patient initials (maximum 4), date of birth and local hospital will also be recorded on the case report forms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2008
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	Belgium: 106
Worldwide total number of subjects	106
EEA total number of subjects	106

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)	67
From 65 to 84 years	38
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Between October 2008 and October 2013, 106 patients were recruited in 15 Belgian centers. Both treatment arms were balanced for age, sex, performance status, tumor location, and differentiation. Among the 106 patients included, 103 effectively received the treatment assigned (52 in arm 1 and 51 in arm 2).

Pre-assignment

Screening details:

The study included a screening/baseline period and a on treatment period.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1

Arm description:

Fractionated Triweekly Regimen: One cycle is defined as a 3 weeks-period on treatment. All three drugs are administered day 1-day 8 every 3 weeks

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

40 mg/m² dose on day 1 and day 8. Premedication with 8mg dexamethasone IV before Docetaxel, then followed by 8 mg orally/day day1-day 3.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

following Docetaxel at 35 mg/m² dose Day 1 and Day 8. Before cisplatin, 20 mg furosemide will be administered.

Investigational medicinal product name	5-FluoroUracil (5FU)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

will be administered last. Folinic Acid will be administered in 1 hour infusion at the dose of 400 mg/m² (or 200 mg/m² levogyre form). 5FU will be administered by protracted IV infusion of 1800 mg/m² over 24 hours.

Arm title	Arm 2
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Arm description:

Biweekly regimen: The regimen will be administered every 2 weeks. A cycle is defined as a 2 weeks-period on treatment

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

50 mg/m² dose. Premedication with 8mg dexamethasone IV before Docetaxel, then followed by 8 mg orally/day day1-day 3.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

following Docetaxel at a 50 mg/m² dose. A bolus of 20 mg furosemide will be administered along with a one hour perfusion of 1 liter saline perfusion (NaCl 09 %) before and after cisplatin.

Investigational medicinal product name	Folinic Acid and 5-FluoroUracil (5FU)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

400 mg/m² Folinic Acid IV in 1 hour (or 200mg/m² Levogyre form) followed by 48 hours perfusion of 2.0 g/m² 5FU

Number of subjects in period 1	Arm 1	Arm 2
Started	53	53
Completed	52	51
Not completed	1	2
Consent withdrawn by subject	1	-
concurrent illness	-	2

Baseline characteristics

Reporting groups

Reporting group title	Arm 1
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Reporting group description:

Fractionated Triweekly Regimen: One cycle is defined as a 3 weeks-period on treatment. All three drugs are administered day 1-day 8 every 3 weeks

Reporting group title	Arm 2
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Reporting group description:

Biweekly regimen: The regimen will be administered every 2 weeks. A cycle is defined as a 2 weeks-period on treatment

Reporting group values	Arm 1	Arm 2	Total
Number of subjects	53	53	106
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)	37	30	67
From 65-84 years	15	23	38
85 years and over	1	0	1
Age continuous			
Units: years			
arithmetic mean	60	63	
standard deviation	± 10	± 10	-
Gender categorical			
Units: Subjects			
Female	16	14	30
Male	37	39	76

End points

End points reporting groups

Reporting group title	Arm 1
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Reporting group description:

Fractionated Triweekly Regimen: One cycle is defined as a 3 weeks-period on treatment. All three drugs are administered day 1-day 8 every 3 weeks

Reporting group title	Arm 2
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Reporting group description:

Biweekly regimen: The regimen will be administered every 2 weeks. A cycle is defined as a 2 weeks-period on treatment

Subject analysis set title	Treatment received
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Among the 106 patients included, 103 received the assigned treatment (52 in arm 1 and 51 in arm 2): one patient withdrew consent 5 days after inclusion, one developed an intestinal obstruction, and one died of progressive disease on the 13th day after inclusion without receiving any treatment.

Primary: Rate of non-progressive disease at 6 weeks

End point title	Rate of non-progressive disease at 6 weeks ^[1]
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End point description:

End point type	Primary
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End point timeframe:

After 6 weeks of treatment: after 2 cycles of treatment in arm 1, after 3 cycles of treatment in arm 2

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 formal comparison between the two arms were performed, cfr. protocol.

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: percentage				
median (confidence interval 95%)	83 (71 to 91)	79 (67 to 88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of at least one episode of febrile neutropenia

End point title	Occurrence of at least one episode of febrile neutropenia
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End point description:

103 of the 106 patients received treatment: 52 in arm 1 and 51 in arm 2.

End point type	Secondary
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End point timeframe:

within the first 6 weeks of treatment:

within the first two cycles in arm 1,
within the first three cycles in arm 2

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Episode	5	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Responses

End point title	Best Responses
End point description: Forty-five patients in each arm had at least 6 weeks of treatment (2 cycles in arm 1 and 3 cycles in arm 2)	
End point type	Secondary
End point timeframe: after at least 6 weeks of treatment	

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: Patient				
Complete Response	2	2		
Partial Response	20	18		
Stable Disease	16	16		
Progression	6	4		
Non evaluable	1	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to significant event (TTSE)

End point title	Time to significant event (TTSE)
End point description:	
End point type	Secondary

End point timeframe:

Time to significant event (TTSE) was defined as the time to toxicity greater than grade II, progression, or death, whatever occurred first.

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: months				
median (confidence interval 95%)	0.51 (0.39 to 1.51)	0.75 (0.46 to 1.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival
End point description:	
End point type	Secondary
End point timeframe:	
since randomization	

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: months				
median (confidence interval 95%)	8.2 (6.0 to 14.5)	11.9 (7.4 to 15.9)		

Attachments (see zip file)	OS since randomization - in months.JPG
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Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival rate at 6 months

End point title	Overall survival rate at 6 months
End point description:	
End point type	Secondary

End point timeframe:
at 6 months since randomization

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: percentage				
arithmetic mean (standard deviation)	63 (± 7)	70.5 (± 6.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival
End point description:	
End point type	Secondary
End point timeframe: since randomization	

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: months				
median (confidence interval 95%)	5.1 (3.2 to 6.5)	5.2 (3.0 to 6.9)		

Attachments (see zip file)	image_2021-08-06_095142.png
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the first administration of study treatments until 30 days after the last dose of study treatments

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Arm 1
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Reporting group description: -

Reporting group title	Arm 2
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Reporting group description: -

Serious adverse events	Arm 1	Arm 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 52 (67.31%)	27 / 51 (52.94%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			

subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cytoreductive surgery			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrectomy			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermic chemotherapy			
	Additional description: intraperitoneal		
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour excision			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	7 / 52 (13.46%)	4 / 51 (7.84%)	
occurrences causally related to treatment / all	4 / 7	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 52 (1.92%)	4 / 51 (7.84%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			

subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	6 / 52 (11.54%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	6 / 6	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 52 (1.92%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	9 / 52 (17.31%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	9 / 9	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			

subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	4 / 52 (7.69%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	3 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			

subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	10 / 52 (19.23%)	4 / 51 (7.84%)	
occurrences causally related to treatment / all	9 / 11	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection	Additional description: Lung infection		
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sepsis			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 52 (9.62%)	5 / 51 (9.80%)	
occurrences causally related to treatment / all	5 / 6	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cell death			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 52 (1.92%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm 1	Arm 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 52 (100.00%)	51 / 51 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Embolism			
subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences (all)	2	1	
Flushing			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Hypertension			

subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	2 / 52 (3.85%)	5 / 51 (9.80%)	
occurrences (all)	2	8	
Vena cava thrombosis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 52 (1.92%)	2 / 51 (3.92%)	
occurrences (all)	1	2	
Chest pain			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Fatigue			
subjects affected / exposed	37 / 52 (71.15%)	39 / 51 (76.47%)	
occurrences (all)	54	57	
General physical health deterioration			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	
occurrences (all)	2	3	
Influenza like illness			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Mucosal inflammation			
subjects affected / exposed	6 / 52 (11.54%)	8 / 51 (15.69%)	
occurrences (all)	7	10	
Oedema			

subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	6 / 52 (11.54%)	5 / 51 (9.80%)	
occurrences (all)	7	5	
Pain			
subjects affected / exposed	1 / 52 (1.92%)	3 / 51 (5.88%)	
occurrences (all)	1	3	
Pyrexia			
subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Visceral oedema			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Reproductive system and breast disorders			
Lung disorder			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Rectocele			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Vaginal prolapse			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 52 (13.46%)	2 / 51 (3.92%)	
occurrences (all)	7	2	
Dyspnoea			
subjects affected / exposed	3 / 52 (5.77%)	8 / 51 (15.69%)	
occurrences (all)	4	9	
Epistaxis			

subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4	1 / 51 (1.96%) 2	
Hiccups			
subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 3	0 / 51 (0.00%) 0	
Nasal dryness			
subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 51 (1.96%) 1	
Oropharyngeal pain			
subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 51 (0.00%) 0	
Pulmonary embolism			
subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 51 (0.00%) 0	
Productive cough			
subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 51 (1.96%) 1	
Rhinorrhoea			
subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 2	2 / 51 (3.92%) 3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 3	0 / 51 (0.00%) 0	
Insomnia			
subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	2 / 51 (3.92%) 2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 3	1 / 51 (1.96%) 1	
Amylase increased			
subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 51 (1.96%) 1	
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences (all)	2	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences (all)	3	3	
Blood creatinine increased			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Creatinine renal clearance increased			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	2	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Lipase increased			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	12 / 52 (23.08%)	17 / 51 (33.33%)	
occurrences (all)	15	20	
White blood cell count decreased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Nasal injury			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Rib fracture			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Skin injury			

subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 51 (0.00%) 0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Atrial fibrillation			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	3 / 52 (5.77%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	8 / 52 (15.38%)	8 / 51 (15.69%)	
occurrences (all)	13	9	
Dizziness			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Head discomfort			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	4	1	
Paraesthesia			
subjects affected / exposed	3 / 52 (5.77%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Peripheral motor neuropathy			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	
occurrences (all)	2	2	
Peripheral sensory neuropathy			

subjects affected / exposed	11 / 52 (21.15%)	16 / 51 (31.37%)	
occurrences (all)	16	17	
Radial nerve palsy			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Restless legs syndrome			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	2 / 52 (3.85%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Tremor			
subjects affected / exposed	2 / 52 (3.85%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 52 (53.85%)	31 / 51 (60.78%)	
occurrences (all)	39	40	
Febrile neutropenia			
subjects affected / exposed	3 / 52 (5.77%)	4 / 51 (7.84%)	
occurrences (all)	3	4	
Leukopenia			
subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences (all)	2	4	
Lymphopenia			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Neutropenia			
subjects affected / exposed	21 / 52 (40.38%)	35 / 51 (68.63%)	
occurrences (all)	47	87	
Thrombocytopenia			
subjects affected / exposed	15 / 52 (28.85%)	10 / 51 (19.61%)	
occurrences (all)	24	19	

Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0 1 / 52 (1.92%) 1	1 / 51 (1.96%) 2 2 / 51 (3.92%) 2	
Eye disorders Blepharitis subjects affected / exposed occurrences (all) Blindness subjects affected / exposed occurrences (all) Cataract subjects affected / exposed occurrences (all) Diplopia subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all) Lacrimation increased subjects affected / exposed occurrences (all) Vision blurred subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0 1 / 52 (1.92%) 1 0 / 52 (0.00%) 0 1 / 52 (0.00%) 1 1 / 52 (1.92%) 1 2 / 52 (3.85%) 2 1 / 52 (1.92%) 1	1 / 51 (1.96%) 1 0 / 51 (0.00%) 0 1 / 51 (1.96%) 1 0 / 51 (0.00%) 0 1 / 51 (1.96%) 1 1 / 51 (1.96%) 1 1 / 51 (1.96%) 1	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Aphthous ulcer	5 / 52 (9.62%) 9 1 / 52 (1.92%) 1	8 / 51 (15.69%) 11 1 / 51 (1.96%) 1	

subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	1
Anal ulcer		
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences (all)	1	0
Ascites		
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences (all)	1	2
Constipation		
subjects affected / exposed	7 / 52 (13.46%)	12 / 51 (23.53%)
occurrences (all)	8	12
Diarrhoea		
subjects affected / exposed	33 / 52 (63.46%)	24 / 51 (47.06%)
occurrences (all)	63	38
Dyspepsia		
subjects affected / exposed	1 / 52 (1.92%)	3 / 51 (5.88%)
occurrences (all)	2	4
Dry mouth		
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences (all)	1	0
Dysphagia		
subjects affected / exposed	3 / 52 (5.77%)	9 / 51 (17.65%)
occurrences (all)	4	12
Flatulence		
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences (all)	2	9
Eructation		
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	1
Gastric ulcer		
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences (all)	1	0
Gastrointestinal pain		
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)
occurrences (all)	1	0
Melaena		

subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	31 / 52 (59.62%)	28 / 51 (54.90%)	
occurrences (all)	52	65	
Odynophagia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Oesophageal pain			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Oesophagitis			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Pneumoperitoneum			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Salivary hypersecretion			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	9 / 52 (17.31%)	17 / 51 (33.33%)	
occurrences (all)	12	24	
Vomiting			
subjects affected / exposed	24 / 52 (46.15%)	21 / 51 (41.18%)	
occurrences (all)	39	39	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	4 / 52 (7.69%)	4 / 51 (7.84%)	
occurrences (all)	4	4	
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	14 / 52 (26.92%)	25 / 51 (49.02%)	
occurrences (all)	14	25	
Dermatitis acneiform			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	
occurrences (all)	3	2	
Erythema			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Rash erythematous			
subjects affected / exposed	2 / 52 (3.85%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Nail toxicity			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Skin reaction			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Bladder discomfort			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	2	
Renal impairment			
subjects affected / exposed	5 / 52 (9.62%)	5 / 51 (9.80%)	
occurrences (all)	6	5	

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	5	1	
Bone pain			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	3 / 52 (5.77%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Muscular weakness			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences (all)	3	2	
Musculoskeletal stiffness			
subjects affected / exposed	2 / 52 (3.85%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Neck pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Pain in extremity			

subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	2 / 51 (3.92%) 2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 52 (7.69%)	3 / 51 (5.88%)	
occurrences (all)	5	3	
Conjunctivitis			
subjects affected / exposed	1 / 52 (1.92%)	4 / 51 (7.84%)	
occurrences (all)	1	4	
Fungal oesophagitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Herpes zoster			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Lip infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal fungal infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			
subjects affected / exposed	2 / 52 (3.85%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Pharyngitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	3 / 52 (5.77%)	0 / 51 (0.00%)	
occurrences (all)	3	0	

Respiratory tract infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Sepsis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Tonsillitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	33 / 52 (63.46%)	21 / 51 (41.18%)	
occurrences (all)	43	32	
Dehydration			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Hypermagnesaemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	2	
Hypoalbuminaemia			

subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Hypocalcaemia			
subjects affected / exposed	4 / 52 (7.69%)	2 / 51 (3.92%)	
occurrences (all)	6	2	
Hypokalaemia			
subjects affected / exposed	7 / 52 (13.46%)	3 / 51 (5.88%)	
occurrences (all)	10	3	
Hypomagnesaemia			
subjects affected / exposed	8 / 52 (15.38%)	5 / 51 (9.80%)	
occurrences (all)	11	8	
Hyponatraemia			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	
occurrences (all)	4	2	
Hypophosphataemia			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	5	1	
Metabolic disorder			
subjects affected / exposed	7 / 52 (13.46%)	10 / 51 (19.61%)	
occurrences (all)	8	13	
Vitamin D deficiency			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	

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