Clinical trial results:
Phase 3b, Randomized, Open-label, Active-controlled Trial Evaluating the Efficacy and Safety of Oral Vadadustat Once Daily (QD) and Three Times Weekly (TIW) for the Maintenance Treatment of Anemia in Hemodialysis Subjects Converting from Erythropoiesis-Stimulating Agents (ESAs)

Summary

EudraCT number	2019-004851-36
Trial protocol	HU PL CZ IT
Global end of trial date	22 June 2022

Results information

Result version number	v1 (current)
This version publication date	19 September 2024
First version publication date	19 September 2024

Trial information

Trial identification

Sponsor protocol code	404-201-00012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04313153
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Akebia Therapeutics
Sponsor organisation address	245 First St #1400, Cambridge, Massachusetts, United States, 02142
Public contact	Clinical Trial Information Desk, Akebia Therapeutics, Inc., Akebia Therapeutics 245 First St #1400, Cambridge Massachusetts 02142 United States, +1 6178446128, trials@akebia.com
Scientific contact	Clinical Trial Information Desk, Akebia Therapeutics, Inc., Akebia Therapeutics 245 First St #1400, Cambridge Massachusetts 02142 United States, +1 6178446128, trials@akebia.com

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	22 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy and safety of vadadustat compared to darbepoetin alfa for the maintenance treatment of anemia in hemodialysis participants after conversion from current erythropoiesis-stimulating agent (ESA) therapy.

Protection of trial subjects:

At the first visit, prior to initiation of any study-related procedures, the parent(s) or legal guardian(s) of the participants gave their written consent to participate in the study after having been informed about the nature and purpose of the study, participation / termination conditions, and risks and benefits. Before the informed consent document was signed, the investigator, or a person designated by the investigator, provided the participant or the participant's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial were answered to the satisfaction of the subject or the participant's legally acceptable representative.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 May 2020
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	Czechia: 26
Country: Number of subjects enrolled	Hungary: 33
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 229
Worldwide total number of subjects	319
EEA total number of subjects	90

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)	193
From 65 to 84 years	126
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a randomized, open-label, active-controlled study of vadadustat versus darbepoetin alfa for the maintenance treatment of anemia in hemodialysis participants, after conversion from erythropoiesis-stimulating agent (ESA therapy).

Pre-assignment

Screening details:

A total of 319 participants were enrolled in the study. Participants were randomized 1:1:1 to vadadustat once daily (QD), vadadustat three times weekly (TIW), or darbepoetin alfa, stratified with respect to geographic region and mean weekly darbepoetin alfa dose (or ESA equivalent) calculated over a period of 8 weeks prior to Screening Visit 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vadadustat QD

Arm description:

Participants were randomized to receive vadadustat QD orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (less than or equal to [<=] 0.45 micrograms per kilograms per week [mcg/kg/week]), participants received an initial vadadustat daily dose of 300 milligrams (mg) daily. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat daily dose of 450 mg daily. Vadadustat was titrated to achieve and maintain target hemoglobin (Hb) levels. The dose range for titration was 150 to 900 mg vadadustat QD.

Arm type	Experimental
Investigational medicinal product name	Vadadustat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One 150 mg or 450 mg vadadustat tablet was to be taken each day.

Arm title	Vadadustat TIW

Arm description:

Participants were randomized to receive vadadustat TIW orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (<= 0.45 mcg/kg/week), participants received an initial vadadustat dose of 600 mg TIW. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat dose of 750 mg TIW. Vadadustat was titrated to achieve and maintain target Hb levels. The dose range for titration was 150 to 1200 mg vadadustat TIW.

Arm type	Experimental
Investigational medicinal product name	Vadadustat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One 150 mg or 450 mg vadadustat tablet was to be taken three times weekly.

Arm title	Darbepoetin alfa

Arm description:

Participants were randomized to receive darbepoetin alfa as a solution in single-dose prefilled syringes via intravenous (IV) injection through dialysis vascular access. For participants who had received darbepoetin alfa during screening, the initial dosing regimen was approximately the same weekly dose that they were receiving prior to randomization. For participants who had received darbepoetin alfa for the first time, the initial dosing regimen was determined by the United States Package Insert (USPI) or European Union Summary of product characteristics (EU SmPC), per the medical judgment of the investigator.

Arm type	Experimental
Investigational medicinal product name	Darbepoetin alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intravenous use

Dosage and administration details:

One single-dose prefilled syringes was given by IV injection through dialysis vascular access.

Number of subjects in period 1	Vadadustat QD	Vadadustat TIW	Darbepoetin alfa
Started	105	106	108
Completed	54	50	67
Not completed	51	56	41
Adverse Event (Includes Death)	14	19	10
Consent withdrawn by subject	7	6	2
Physician decision	4	2	1
Change In Dialysis Modality	-	1	2
Unspecified	5	3	2
Change Of In-Center Hemodialysis From TIW	1	-	-
Lost to follow-up	1	-	2
Met Criteria For Trial Medication Stopping Rules	16	20	19
Receipt Of Any Transplantation	-	2	3
Lack of efficacy	3	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Vadadustat QD
Reporting group description:	
Participants were randomized to receive vadadustat QD orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (less than or equal to [<=] 0.45 micrograms per kilograms per week [mcg/kg/week]), participants received an initial vadadustat daily dose of 300 milligrams (mg) daily. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat daily dose of 450 mg daily. Vadadustat was titrated to achieve and maintain target hemoglobin (Hb) levels. The dose range for titration was 150 to 900 mg vadadustat QD.	
Reporting group title	Vadadustat TIW
Reporting group description:	
Participants were randomized to receive vadadustat TIW orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (<= 0.45 mcg/kg/week), participants received an initial vadadustat dose of 600 mg TIW. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat dose of 750 mg TIW. Vadadustat was titrated to achieve and maintain target Hb levels. The dose range for titration was 150 to 1200 mg vadadustat TIW.	
Reporting group title	Darbepoetin alfa
Reporting group description:	
Participants were randomized to receive darbepoetin alfa as a solution in single-dose prefilled syringes via intravenous (IV) injection through dialysis vascular access. For participants who had received darbepoetin alfa during screening, the initial dosing regimen was approximately the same weekly dose that they were receiving prior to randomization. For participants who had received darbepoetin alfa for the first time, the initial dosing regimen was determined by the United States Package Insert (USPI) or European Union Summary of product characteristics (EU SmPC), per the medical judgment of the investigator.	

Reporting group values	Vadadustat QD	Vadadustat TIW	Darbepoetin alfa
Number of subjects	105	106	108
Age categorical Units:			
<65 years	59	65	69
≥65 years	46	41	39
Age continuous Units: years			
arithmetic mean	60.9	61.2	60.8
standard deviation	± 13.4	± 12.5	± 12.8
Gender categorical Units: Subjects			
Female	47	46	43
Male	58	60	65
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	1	2	0
Asian	4	1	3
Black Or African American	31	30	33
Native Hawaiian or Other Pacific Islander	0	2	1
White	68	67	71
Not Reported	1	3	0
Reported as Other	0	1	0

Reporting group values	Total		
Number of subjects	319		
Age categorical Units:			
<65 years	193		
≥65 years	126		
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	136		
Male	183		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	3		
Asian	8		
Black Or African American	94		
Native Hawaiian or Other Pacific Islander	3		
White	206		
Not Reported	4		
Reported as Other	1		

End points

End points reporting groups

Reporting group title	Vadadustat QD

Reporting group description:

Participants were randomized to receive vadadustat QD orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (less than or equal to [<=] 0.45 micrograms per kilograms per week [mcg/kg/week]), participants received an initial vadadustat daily dose of 300 milligrams (mg) daily. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat daily dose of 450 mg daily. Vadadustat was titrated to achieve and maintain target hemoglobin (Hb) levels. The dose range for titration was 150 to 900 mg vadadustat QD.

Reporting group title	Vadadustat TIW

Reporting group description:

Participants were randomized to receive vadadustat TIW orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (<= 0.45 mcg/kg/week), participants received an initial vadadustat dose of 600 mg TIW. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat dose of 750 mg TIW. Vadadustat was titrated to achieve and maintain target Hb levels. The dose range for titration was 150 to 1200 mg vadadustat TIW.

Reporting group title	Darbepoetin alfa

Reporting group description:

Participants were randomized to receive darbepoetin alfa as a solution in single-dose prefilled syringes via intravenous (IV) injection through dialysis vascular access. For participants who had received darbepoetin alfa during screening, the initial dosing regimen was approximately the same weekly dose that they were receiving prior to randomization. For participants who had received darbepoetin alfa for the first time, the initial dosing regimen was determined by the United States Package Insert (USPI) or European Union Summary of product characteristics (EU SmPC), per the medical judgment of the investigator.

Primary: Change from Baseline in Hb to the average over the Primary evaluation period (PEP) (Weeks 20 to 26)

End point title	Change from Baseline in Hb to the average over the Primary evaluation period (PEP) (Weeks 20 to 26)[1]

End point description:

The Baseline Hb was defined as the average of the last 2 central laboratory Hb values taken on or prior to the first dose date. The average for the PEP was calculated as the average of all Hb measurements from the central laboratory within the three visit windows during Weeks 20 through 26, regardless of intercurrent events. Analysis was conducted using an analysis of covariance (ANCOVA) model with multiple imputation for missing data with randomization stratification factors and Baseline Hb as covariates. Change from Baseline was calculated as PEP value minus the Baseline value. Randomized population was defined as all participants randomized.

End point type	Primary

End point timeframe:

Baseline; Weeks 20 to 26

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: Per protocol, statistical analysis was not planned for this endpoint

End point values	Vadadustat QD	Vadadustat TIW	Darbepoetin alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	106	108	
Units: Grams per deciliter (g/dL)				
least squares mean (standard error)	0.07 (± 0.12)	-0.19 (± 0.12)	0.34 (± 0.12)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hb to the average over the Secondary evaluation period (SEP) (Weeks 46 to 52)

End point title	Change from Baseline in Hb to the average over the Secondary evaluation period (SEP) (Weeks 46 to 52)

End point description:

The Baseline Hb was defined as the average of the last 2 central laboratory Hb values taken on or prior to the first dose date. The average for the SEP was calculated as the average of all Hb measurements from the central laboratory within the three visit windows during Weeks 46 through 52, regardless of intercurrent events. Analysis was conducted using an ANCOVA model with multiple imputation for missing data with randomization stratification factors and Baseline Hb as covariates. Change from Baseline was calculated as SEP value minus the Baseline value.
Randomized population.

End point type	Secondary

End point timeframe:

Baseline; Weeks 46 to 52

End point values	Vadadustat QD	Vadadustat TIW	Darbepoetin alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	106	108	
Units: g/dL				
least squares mean (standard error)	0.04 (± 0.15)	0.03 (± 0.15)	0.44 (± 0.15)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug (Day 1) up to Week 56 (from first dose of study drug to last dose + 4 weeks of follow-up)

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) are defined as those adverse events (AEs) that began or worsened after treatment initiation and are reported for the Safety Population which consisted of all participants in the randomized population who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Vadadustat QD

Reporting group description:

Participants were randomized to receive vadadustat QD orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (less than or equal to [<=] 0.45 micrograms per kilograms per week [mcg/kg/week]), participants received an initial vadadustat daily dose of 300 milligrams (mg) daily. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat daily dose of 450 mg daily. Vadadustat was titrated to achieve and maintain target hemoglobin (Hb) levels. The dose range for titration was 150 to 900 mg vadadustat QD.

Reporting group title	Darbepoetin alfa

Reporting group description:

Participants were randomized to receive darbepoetin alfa as a solution in single-dose prefilled syringes via intravenous (IV) injection through dialysis vascular access. For participants who had received darbepoetin alfa during screening, the initial dosing regimen was approximately the same weekly dose that they were receiving prior to randomization. For participants who had received darbepoetin alfa for the first time, the initial dosing regimen was determined by the United States Package Insert (USPI) or European Union Summary of product characteristics (EU SmPC), per the medical judgment of the investigator.

Reporting group title	Vadadustat TIW

Reporting group description:

Participants were randomized to receive vadadustat TIW orally. Vadadustat starting daily dose was determined by pre-Baseline mean weekly darbepoetin alfa dose (or ESA equivalent). In the low darbepoetin alfa dose group (<= 0.45 mcg/kg/week), participants received an initial vadadustat dose of 600 mg TIW. In the high darbepoetin alfa dose group (> 0.45 and <= 1.5 mcg/kg/week), participants received an initial vadadustat dose of 750 mg TIW. Vadadustat was titrated to achieve and maintain target Hb levels. The dose range for titration was 150 to 1200 mg vadadustat TIW.

Serious adverse events	Vadadustat QD	Darbepoetin alfa	Vadadustat TIW
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 105 (44.76%)	47 / 108 (43.52%)	47 / 104 (45.19%)
number of deaths (all causes)	12	7	9
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of appendix			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Prostate cancer			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Liposarcoma			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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 adenocarcinoma			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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			
Hypertensive crisis			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypertensive emergency			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	0 / 104 (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
Jugular vein thrombosis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Steal syndrome			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Orthostatic hypotension			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Arteriovenous fistula operation			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
General disorders and administration site conditions			
Asthenia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Non-cardiac chest pain			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	3 / 105 (2.86%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Contrast media allergy			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Kidney transplant rejection			

alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	2 / 108 (1.85%)	0 / 104 (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
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Uterine haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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, thoracic and mediastinal disorders			
Acute pulmonary oedema			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	0 / 108 (0.00%)	0 / 104 (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
Chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Acute respiratory failure			

alternative dictionary used: MedDRA 25			
subjects affected / exposed	3 / 105 (2.86%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Respiratory failure			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anticoagulation drug level above therapeutic			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Alanine aminotransferase increased			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Transaminases increased			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Liver function test increased			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Hepatic enzyme increased			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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			
Ankle fracture			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula site complication			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	0 / 108 (0.00%)	0 / 104 (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
Arteriovenous fistula site haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Arteriovenous fistula thrombosis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	3 / 108 (2.78%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous graft thrombosis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Humerus fracture			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Wrist fracture			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access site haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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

Traumatic haemothorax			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Traumatic haematoma			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Post procedural haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Rib fracture			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Spinal compression fracture			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Congenital, familial and genetic disorders			
Haemorrhagic arteriovenous malformation			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Cardiac disorders			

Angina pectoris alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	1 / 104 (0.96%)
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 left ventricular failure alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	0 / 108 (0.00%)	6 / 104 (5.77%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Atrioventricular block complete alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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 arrest alternative dictionary used: MedDRA 25			

subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Cardiac failure			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	1 / 108 (0.93%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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 failure congestive			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	1 / 108 (0.93%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Coronary artery disease			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	3 / 104 (2.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure acute			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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			
Ataxia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Bell's palsy			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Embolic stroke			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Syncope			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Seizure			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Presyncope			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Myelopathy			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Ischaemic stroke			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	0 / 104 (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
Haemorrhagic stroke			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Generalised tonic-clonic seizure			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Encephalopathy			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Toxic encephalopathy			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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			
Anaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	3 / 105 (2.86%)	5 / 108 (4.63%)	5 / 104 (4.81%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Vitreous haemorrhage			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	3 / 104 (2.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Duodenal ulcer haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Gastritis haemorrhagic			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Chronic gastritis			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Impaired gastric emptying			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic duct obstruction			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Pancreatitis acute			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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 gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	2 / 108 (1.85%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
Cholecystitis acute			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Diabetic foot			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Intertrigo			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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 and urinary disorders			
Renal cyst haemorrhage			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			

alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Azotaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Endocrine disorders			
Hyperparathyroidism secondary			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Parathyroid hyperplasia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Intervertebral disc protrusion			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Fracture pain			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Cervical spinal stenosis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	0 / 104 (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
Back pain			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis bacterial			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Asymptomatic COVID-19			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	4 / 108 (3.70%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Device related sepsis			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida pneumonia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Cellulitis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	2 / 108 (1.85%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cryptococcal fungaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Device related bacteraemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	7 / 105 (6.67%)	4 / 108 (3.70%)	8 / 104 (7.69%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 3	0 / 2	0 / 3
Diabetic foot infection			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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

Diverticulitis alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	2 / 108 (1.85%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal haemorrhagic alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Endocarditis alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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 staphylococcal alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	2 / 108 (1.85%)	0 / 104 (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
Muscle abscess alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising soft tissue infection			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
Osteomyelitis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	2 / 108 (1.85%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	2 / 108 (1.85%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	1 / 108 (0.93%)	3 / 104 (2.88%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia aspiration			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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

Pneumonia staphylococcal alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Renal abscess alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	3 / 108 (2.78%)	3 / 104 (2.88%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic shock alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Staphylococcal osteomyelitis alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
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 sepsis alternative dictionary used: MedDRA 25			

subjects affected / exposed	0 / 105 (0.00%)	1 / 108 (0.93%)	0 / 104 (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
SARS-CoV-2 sepsis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Vascular graft infection			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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
Metabolism and nutrition disorders			
Hypocalcaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	0 / 105 (0.00%)	0 / 108 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	4 / 108 (3.70%)	4 / 104 (3.85%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	3 / 108 (2.78%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	0 / 104 (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
Failure to thrive			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypoglycaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	1 / 108 (0.93%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	1 / 105 (0.95%)	0 / 108 (0.00%)	0 / 104 (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

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

Non-serious adverse events	Vadadustat QD	Darbepoetin alfa	Vadadustat TIW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 105 (43.81%)	46 / 108 (42.59%)	49 / 104 (47.12%)
Injury, poisoning and procedural complications			
Fall			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	10 / 105 (9.52%)	5 / 108 (4.63%)	6 / 104 (5.77%)
occurrences (all)	12	7	7
Vascular disorders			
Hypertension			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	6 / 105 (5.71%)	10 / 108 (9.26%)	11 / 104 (10.58%)
occurrences (all)	7	10	14

Blood and lymphatic system disorders			
Anaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	5 / 105 (4.76%)	7 / 108 (6.48%)	7 / 104 (6.73%)
occurrences (all)	5	9	7
General disorders and administration site conditions			
Oedema peripheral			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	6 / 105 (5.71%)	3 / 108 (2.78%)	0 / 104 (0.00%)
occurrences (all)	6	3	0
Gastrointestinal disorders			
Vomiting			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	10 / 105 (9.52%)	6 / 108 (5.56%)	4 / 104 (3.85%)
occurrences (all)	13	6	4
Nausea			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	12 / 105 (11.43%)	6 / 108 (5.56%)	6 / 104 (5.77%)
occurrences (all)	14	6	7
Diarrhoea			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	14 / 105 (13.33%)	6 / 108 (5.56%)	15 / 104 (14.42%)
occurrences (all)	15	8	19
Abdominal pain			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	4 / 105 (3.81%)	8 / 108 (7.41%)	4 / 104 (3.85%)
occurrences (all)	4	8	4
Musculoskeletal and connective tissue disorders			
Back pain			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	2 / 105 (1.90%)	2 / 108 (1.85%)	6 / 104 (5.77%)
occurrences (all)	2	2	6
Infections and infestations			
COVID-19			
alternative dictionary used: MedDRA 25			

subjects affected / exposed	12 / 105 (11.43%)	10 / 108 (9.26%)	11 / 104 (10.58%)
occurrences (all)	12	10	12
Metabolism and nutrition disorders			
Hypoglycaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	6 / 105 (5.71%)	3 / 108 (2.78%)	1 / 104 (0.96%)
occurrences (all)	7	3	1
Hyperkalaemia			
alternative dictionary used: MedDRA 25			
subjects affected / exposed	4 / 105 (3.81%)	9 / 108 (8.33%)	5 / 104 (4.81%)
occurrences (all)	6	13	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2021	The amendment alters the trial design and/or increases the potential risk to the participant, the currently approved written ICF will require similar modification. In such cases, after approval/favorable opinion of the new ICF by the IRB/IEC, repeat written informed consent will be obtained from participants enrolled in the trial before expecting continued participation and before the amendment-specified changes in the trial are implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Per the protocol, all results data are summarized by the arm to which participants were randomized; no separate analysis was performed to report results for initial vadadustat dose received in either of the vadadustat QD or vadadustat TIW arms.

Notes: