Clinical trial results:
A Phase 3, Multicenter, Randomized, Open-Label, Active-Controlled Study Of Trastuzumab Deruxtecan (DS-8201A), An Anti-HER2-Antibody Drug Conjugate, Versus Treatment Of Investigator's Choice For HER2-Positive, Unresectable And/Or Metastatic Breast Cancer Subjects Previously Treated With T-DM1 (DESTINY-Breast02)

Summary

EudraCT number	2018-000221-31
Trial protocol	GB BE CZ FR GR DE IT ES
Global end of trial date	22 December 2025

Results information

Result version number	v2 (current)
This version publication date	23 October 2026
First version publication date	30 September 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	DS8201-A-U301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03523585
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC CTI: 184017

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo, Inc.
Sponsor organisation address	211 Mount Airy Rd., Basking Ridge, United States, 07920
Public contact	Contact for Clinical Trial Information, Daiichi Sankyo, Inc., +1 908 9926400, CTRinfo_us@daiichisankyo.com
Scientific contact	Contact for Clinical Trial Information, Daiichi Sankyo, Inc., +1 908 9926400, CTRinfo_us@daiichisankyo.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	04 March 2026
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 December 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to compare the progression-free survival (PFS) benefit of trastuzumab deruxtecan to investigator's choice for HER2-positive, unresectable and/or metastatic breast cancer subjects previously treated with T-DM1.

Protection of trial subjects:

The study protocol, patient information and consent form, the IB, any patient written instructions to be given to the patient, available safety information, patient recruitment procedures (eg, advertisements), information about payments and compensation available to the patients, and documentation evidencing the investigator's qualifications should be submitted to the EC or IRB for ethical review and approval according to local regulations, prior to the study start.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 September 2018
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	Australia: 21
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 59
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Spain: 44
Country: Number of subjects enrolled	France: 57
Country: Number of subjects enrolled	United Kingdom: 35
Country: Number of subjects enrolled	Greece: 14
Country: Number of subjects enrolled	Israel: 18
Country: Number of subjects enrolled	Italy: 53
Country: Number of subjects enrolled	Japan: 70
Country: Number of subjects enrolled	Korea, Republic of: 94
Country: Number of subjects enrolled	Türkiye: 52
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	608
EEA total number of subjects	195

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)	485
From 65 to 84 years	119
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

A total of 608 participants were enrolled at study sites in 15 countries. The final safety results are being reported based on a data cut-off date of 23 December 2025.

Pre-assignment

Screening details:

Participants in TPC group were randomized to 1 of the following 2 regimens: trastuzumab/capecitabine or lapatinib/capecitabine. As prespecified in the protocol, patients were assessed and reported separately per comparator arm for the disposition, baseline characteristics, and safety tables. For efficacy, all TPC patients are reported combined.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Trastuzumab Deruxtecan (T-DXd)

Arm description:

Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received T-DXd as a sterile intravenous (IV) solution at a dose of 5.4 mg/kg every 3 weeks (Q3W).

Arm type	Experimental
Investigational medicinal product name	Trastuzumab deruxtecan
Investigational medicinal product code	
Other name	DS-8201a, T-DXd
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5.4 mg/kg every 3 weeks (Q3W)

Arm title	Trastuzumab+Capecitabine

Arm description:

Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Trastuzumab/Capecitabine.

Arm type	Experimental
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In combination with trastuzumab:
1250 mg/m^2 administered orally (PO) twice daily approximately 12 hours apart (equivalent to 2500 mg/m^2 total daily dose) on Days 1 to 14 of a 21-day (± 2 days) schedule

In combination with lapatinib:
1000 mg/m^2 PO twice daily approximately 12 hours apart

(equivalent to 2000 mg/m^2 total daily dose) on Days 1 to 14 of a 21-day (± 2 days) schedule

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Investigator's choice Standard of Care when combined with capecitabine

Arm title	Lapatinib+Capecitabine

Arm description:

Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Lapatinib/Capecitabine.

Arm type	Experimental
Investigational medicinal product name	Lapatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In combination with capecitabine:
1250 mg PO daily on Days 1 to 21 of a 21-day (± 2 days) schedule

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In combination with trastuzumab:
1250 mg/m^2 administered orally (PO) twice daily approximately 12 hours apart (equivalent to 2500 mg/m^2 total daily dose) on Days 1 to 14 of a 21-day (± 2 days) schedule

In combination with lapatinib:
1000 mg/m^2 PO twice daily approximately 12 hours apart
(equivalent to 2000 mg/m^2 total daily dose) on Days 1 to 14 of a 21-day (± 2 days) schedule

Number of subjects in period 1	Trastuzumab Deruxtecan (T-DXd)	Trastuzumab+Capecitabine	Lapatinib+Capecitabine
Started	406	91	111
Randomized	406	91	111
Randomized but Not Treated	2	4	3
Completed	0	0	0
Not completed	406	91	111
Adverse event, serious fatal	5	5	1
Consent withdrawn by subject	38	11	6
Physician decision	3	1	-
Adverse event, non-fatal	89	-	9
Progressive Disease	204	64	80

Other, not specified	35	-	-
Study terminated by sponsor	1	-	-
Randomized But Not Treated	2	4	3
Lost to follow-up	2	-	-
Clinical Progression	26	6	11
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Trastuzumab Deruxtecan (T-DXd)
Reporting group description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received T-DXd as a sterile intravenous (IV) solution at a dose of 5.4 mg/kg every 3 weeks (Q3W).	
Reporting group title	Trastuzumab+Capecitabine
Reporting group description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Trastuzumab/Capecitabine.	
Reporting group title	Lapatinib+Capecitabine
Reporting group description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Lapatinib/Capecitabine.	

Reporting group values	Trastuzumab Deruxtecan (T-DXd)	Trastuzumab+Capecitabine	Lapatinib+Capecitabine
Number of subjects	406	91	111
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	54.6	55.7	54.6
standard deviation	± 11.99	± 11.4	± 11.06
Gender categorical Units: Subjects			
Female	403	89	111
Male	3	2	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	122	20	36
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	10	2	5
White	257	66	61
More than one race	0	0	0
Unknown or Not Reported	15	3	8
Age categorical Units: Subjects			
18-64 years	321	73	91
65-84 years	82	17	20
85 years and over	3	1	0

Reporting group values	Total		
Number of subjects	608		

Age Categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	603		
Male	5		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2		
Asian	178		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	17		
White	384		
More than one race	0		
Unknown or Not Reported	26		
Age categorical Units: Subjects			
18-64 years	485		
65-84 years	119		
85 years and over	4		

End points

End points reporting groups

Reporting group title	Trastuzumab Deruxtecan (T-DXd)
Reporting group description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received T-DXd as a sterile intravenous (IV) solution at a dose of 5.4 mg/kg every 3 weeks (Q3W).	
Reporting group title	Trastuzumab+Capecitabine
Reporting group description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Trastuzumab/Capecitabine.	
Reporting group title	Lapatinib+Capecitabine
Reporting group description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Lapatinib/Capecitabine.	
Subject analysis set title	Treatment of Investigator's/Physician's Choice (TPC)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Trastuzumab/Capecitabine or Lapatinib/Capecitabine.	

Primary: Progression-Free Survival (PFS) Based on Blinded Independent Central Review (BICR) in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine

End point title	Progression-Free Survival (PFS) Based on Blinded Independent Central Review (BICR) in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine[1]
End point description:	
Progression-free survival (PFS) by BICR was defined as the time from the date of randomization to the earlier of the dates of the first objective documentation of disease progression (as per RECIST v1.1) or death due to any cause.	
End point type	Primary
End point timeframe:	
Baseline up to 46 months postdose	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are reported for the T-DXd vs TPC arm.

End point values	Trastuzumab Deruxtecan (T-DXd)	Treatment of Investigator's/ Physician's Choice (TPC)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	406	202		
Units: months				
median (confidence interval 95%)	17.8 (14.3 to 20.8)	6.9 (5.5 to 8.4)		

Statistical analyses

Statistical analysis title	T-DXd vs TPC

Statistical analysis description:

T-DXd vs TPC

Comparison groups	Trastuzumab Deruxtecan (T-DXd) v Treatment of Investigator's/Physician's Choice (TPC)
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.000001 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.3589
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.284
upper limit	0.4535

Notes:

[2] - Stratified Log-rank p-value

[3] - Stratified Log-rank p-value

Secondary: Overall Survival (OS) in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine

End point title	Overall Survival (OS) in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine[4]

End point description:

Overall survival (OS) was defined as the time from the date of randomization to the date of death due to any cause. If there is no death reported for a subject before the data cutoff for OS analysis, OS will be censored at the last contact date at which the subject is known to be alive.

End point type	Secondary

End point timeframe:

Baseline up to 46 months postdose

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are reported for the T-DXd vs TPC arm.

End point values	Trastuzumab Deruxtecan (T-DXd)	Treatment of Investigator's/ Physician's Choice (TPC)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	406	202		
Units: months				

median (confidence interval 95%)	39.2 (32.7 to 99999)	26.5 (21.0 to 99999)		

Statistical analyses

Statistical analysis title	T-DXd vs TPC

Statistical analysis description:

T-DXd vs TPC

Comparison groups	Trastuzumab Deruxtecan (T-DXd) v Treatment of Investigator's/Physician's Choice (TPC)
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0021 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.6575
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5023
upper limit	0.8605

Notes:

[5] - Stratified Log-rank p-value

[6] - Stratified Log-rank p-value

Secondary: Percentage of Participants with Objective Response Rate (ORR) in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine

End point title	Percentage of Participants with Objective Response Rate (ORR) in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine[7]

End point description:

The Objective Response Rate (ORR) was defined as the percentage of participants who achieved a best overall response of confirmed Complete Response (CR) or Partial Response (PR), assessed by BICR and investigator assessment based on RECIST version 1.1. CR was defined as a disappearance of all target lesions and PR was defined as at least a 30% decrease in the sum of diameters of target lesions. Confirmed ORR based on BICR and Investigator Assessment is reported.

End point type	Secondary

End point timeframe:

Baseline up to 46 months postdose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are reported for the T-DXd vs TPC arm.

End point values	Trastuzumab Deruxtecan (T-DXd)	Treatment of Investigator's/ Physician's Choice (TPC)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	406	202		
Units: Percentage of Participants				
number (confidence interval 95%)				
BICR	69.7 (65.0 to 74.1)	29.2 (23.0 to 36.0)		
Investigator Assessment	74.1 (69.6 to 78.3)	26.7 (20.8 to 33.4)		

Statistical analyses

Statistical analysis title	T-DXd vs TPC

Statistical analysis description:

Statistical Analysis for Investigator Assessment

Comparison groups	Trastuzumab Deruxtecan (T-DXd) v Treatment of Investigator's/Physician's Choice (TPC)
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.0001 [9]
Method	Cochran-Mantel-Haenszel

Notes:

[8] - Cochran-Mantel-Haenszel test adjusted for stratification factors: hormone receptor status, prior treatment with pertuzumab, and history of visceral disease, as defined by the IXRS.
[9] - Cochran-Mantel-Haenszel test adjusted for stratification factors: hormone receptor status, prior treatment with pertuzumab, and history of visceral disease, as defined by the IXRS.

Statistical analysis title	T-DXd vs TPC

Statistical analysis description:

Statistical analysis for BICR Assessment

Comparison groups	Trastuzumab Deruxtecan (T-DXd) v Treatment of Investigator's/Physician's Choice (TPC)
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	< 0.0001 [11]
Method	Cochran-Mantel-Haenszel

Notes:

[10] - Cochran-Mantel-Haenszel test adjusted for stratification factors: hormone receptor status, prior treatment with pertuzumab, and history of visceral disease, as defined by the IXRS.
[11] - Cochran-Mantel-Haenszel test adjusted for stratification factors: hormone receptor status, prior treatment with pertuzumab, and history of visceral disease, as defined by the IXRS.

Secondary: Duration of Response (DoR) Based on BICR in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine

End point title	Duration of Response (DoR) Based on BICR in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine[12]

End point description:

Duration of Response (DoR) was defined as the time from the date of the first documentation of objective response (complete response [CR] or partial response [PR]) to the date of the first objective documentation of progressive disease (PD) or death due to any cause. DoR in participants with confirmed CR/PR based on BICR and investigator assessment is reported.

End point type	Secondary

End point timeframe:

Baseline up to 46 months postdose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are reported for the T-DXd vs TPC arm.

End point values	Trastuzumab Deruxtecan (T-DXd)	Treatment of Investigator's/ Physician's Choice (TPC)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	283	59		
Units: months				
median (confidence interval 95%)	19.6 (15.9 to 99999)	8.3 (5.8 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) Based on Investigator Assessment in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine

End point title	Progression-Free Survival (PFS) Based on Investigator Assessment in Participants with HER2-positive, Unresectable and/or Metastatic Breast Cancer Participants Previously Treated with Trastuzumab Emtansine[13]

End point description:

Progression-free survival (PFS) by investigator assessment was defined as the time from the date of randomization to the earlier of the dates of the first objective documentation of disease progression (as per RECIST v1.1) or death due to any cause.

End point type	Secondary

End point timeframe:

Up to 46 months

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are reported for the T-DXd vs TPC arm.

End point values	Trastuzumab Deruxtecan (T-DXd)	Treatment of Investigator's/ Physician's Choice (TPC)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	406	202		
Units: months				

median (confidence interval 95%)	16.7 (14.3 to 19.6)	5.5 (4.4 to 7.0)		

Statistical analyses

Statistical analysis title	T-DXd vs TPC
Statistical analysis description: T-DXd vs TPC	
Comparison groups	Trastuzumab Deruxtecan (T-DXd) v Treatment of Investigator's/Physician's Choice (TPC)
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.000001 [15]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.2828
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.227
upper limit	0.3524

Notes:

[14] - Stratified Log-rank p-value.

[15] - Stratified Log-rank p-value.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) were collected from the date of signing the informed consent form up to 47 days after last dose of the study drug, up 46 months.

Adverse event reporting additional description:

A TEAE is an AE that occurs, having been absent before the first dose of drug, or has worsened in severity or seriousness after the initiating the drug until 47 days after last dose. AEs were assessed in the Safety Analysis Set at data cut-off date of 23 December 2025. Mortality was analyzed in the Full Analysis Set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.1

Reporting groups

Reporting group title	Trastuzumab Deruxtecan (T-DXd)

Reporting group description:

Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received T-DXd as a sterile intravenous (IV) solution at a dose of 5.4 mg/kg every 3 weeks (Q3W).

Reporting group title	Lapatinib+Capecitabine

Reporting group description:

Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Lapatinib/Capecitabine.

Reporting group title	Trastuzumab+Capecitabine

Reporting group description:

Participants with HER2 positive, unresectable and/or metastatic breast cancer participants previously treated with standard of care HER2 therapies, including ado-trastuzumab emtansine (T-DM1), who received investigator's choice treatment, Trastuzumab/Capecitabine.

Serious adverse events	Trastuzumab Deruxtecan (T-DXd)	Lapatinib+Capecitabine	Trastuzumab+Capecitabine
Total subjects affected by serious adverse events			
subjects affected / exposed	117 / 404 (28.96%)	27 / 108 (25.00%)	19 / 87 (21.84%)
number of deaths (all causes)	143	46	40
number of deaths resulting from adverse events	15	6	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Metastases To Meninges			
alternative dictionary used:			

MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metastases To Ovary			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Transitional Cell Cancer of the Renal Pelvis and Ureter			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Cancer Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
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 disorders			
Deep Vein Thrombosis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	1 / 108 (0.93%)	0 / 87 (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
Brachiocephalic Vein Thrombosis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Lymphoedema			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Orthostatic Hypotension			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Embolism			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Urgency			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Hypotension			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Peripheral Ischaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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

Vena Cava Thrombosis			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 404 (0.74%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 404 (0.74%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease Progression			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 404 (0.74%)	3 / 108 (2.78%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 3	0 / 3	0 / 1
General Physical Health Deterioration			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Non-Cardiac Chest Pain			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 404 (0.25%)	1 / 108 (0.93%)	0 / 87 (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
Gait disturbance			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Oedema Peripheral			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pain			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Reproductive system and breast disorders			
Breast Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial Lung Disease			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	5 / 404 (1.24%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	9 / 404 (2.23%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	9 / 9	0 / 1	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Haemoptysis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pleural Effusion			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	3 / 108 (2.78%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Laryngeal Haemorrhage			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Lung Disorder			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pneumothorax			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	1 / 108 (0.93%)	0 / 87 (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

Pulmonary Embolism alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	1 / 108 (0.93%)	0 / 87 (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
Pulmonary Oedema alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pulmonary Fibrosis alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pulmonary Haemorrhage alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hypoxia alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Malignant Pleural Effusion alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pulmonary Tumour Thrombotic Microangiopathy alternative dictionary used: MedDRA 28.1			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Mental Status Changes			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Suicide Attempt			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Investigations			
Hepatic Enzyme Increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Pancreatic Enzymes Increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Radiation Necrosis			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (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
Hip Fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Head Injury			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Lumbar Vertebral Fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Overdose			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Subdural Haematoma			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Wrist Fracture			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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

Accidental Overdose			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral Injury			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Lower Limb Fracture			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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 28.1			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Stress Cardiomyopathy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Cardiac Tamponade			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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 Myocardial Infarction			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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 Arrest			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Cardiac Failure			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Myocardial Ischaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Pericardial Effusion			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Nervous system disorders			
Brain Oedema			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Depressed Level Of Consciousness			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Dizziness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Epilepsy			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Generalised Tonic-Clonic Seizure			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Headache			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hemiplegia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Monoplegia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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

Syncope alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Vasogenic Cerebral Oedema alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Seizure alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Ischaemia alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage Intracranial alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Dysarthria alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Blood and lymphatic system disorders			
Anaemia alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	4 / 404 (0.99%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Haemolysis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pancytopenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Thrombocytopenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Scleritis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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 disorders			
Nausea			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	5 / 404 (1.24%)	0 / 108 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	6 / 404 (1.49%)	0 / 108 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	4 / 6	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	3 / 87 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Diarrhoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	3 / 404 (0.74%)	1 / 108 (0.93%)	3 / 87 (3.45%)
occurrences causally related to treatment / all	2 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Duodenal Ulcer			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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

Faecaloma alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Gastritis alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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 Haemorrhage alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Haemorrhoidal Haemorrhage alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Varices Haemorrhage alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large Intestinal Obstruction alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Stomatitis alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Constipation			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Antral Vascular Ectasia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Haematemesis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Duodenal Ulcer Haemorrhage			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hepatobiliary disorders			
Cholangitis			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Cholecystitis			
alternative dictionary used: MedDRA 28.1			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hyperbilirubinaemia			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Skin and subcutaneous tissue disorders			
Skin Hyperpigmentation			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Renal and urinary disorders			
Acute Kidney Injury			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis Haemorrhagic			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune Thyroiditis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (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
Muscular Weakness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Neck Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Osteonecrosis Of Jaw			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pain In Extremity			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Back Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Covid-19			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	12 / 404 (2.97%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	8 / 404 (1.98%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	2 / 8	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Device Related Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (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
Covid-19 Pneumonia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (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
Influenza			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (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
Pneumocystis Jirovecii Pneumonia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (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
Urinary Tract Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Appendicitis alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	1 / 108 (0.93%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post Procedural Infection alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hepatitis B alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Mastitis alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Pyelonephritis alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Wound Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Sepsis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Abdominal Sepsis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Respiratory Tract Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingivitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neutropenic Sepsis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	0 / 108 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis Bacterial			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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 Tract Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	0 / 404 (0.00%)	1 / 108 (0.93%)	0 / 87 (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
Pseudomembranous Colitis			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Metabolism and nutrition disorders			
Dehydration			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	4 / 404 (0.99%)	1 / 108 (0.93%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased Appetite			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hypercalcaemia			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hypokalaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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
Hyponatraemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	0 / 108 (0.00%)	0 / 87 (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

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

Non-serious adverse events	Trastuzumab Deruxtecan (T-DXd)	Lapatinib+Capecitabine	Trastuzumab+Capecitabine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	398 / 404 (98.51%)	102 / 108 (94.44%)	79 / 87 (90.80%)
Investigations			
Weight Decreased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	77 / 404 (19.06%)	6 / 108 (5.56%)	2 / 87 (2.30%)
occurrences (all)	81	6	2
Neutrophil Count Decreased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	83 / 404 (20.54%)	7 / 108 (6.48%)	7 / 87 (8.05%)
occurrences (all)	283	17	8
Alanine Aminotransferase Increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	63 / 404 (15.59%)	15 / 108 (13.89%)	6 / 87 (6.90%)
occurrences (all)	103	16	6
White Blood Cell Count Decreased			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	61 / 404 (15.10%)	4 / 108 (3.70%)	5 / 87 (5.75%)
occurrences (all)	178	10	10
Platelet Count Decreased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	54 / 404 (13.37%)	7 / 108 (6.48%)	5 / 87 (5.75%)
occurrences (all)	116	7	7
Aspartate Aminotransferase Increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	70 / 404 (17.33%)	19 / 108 (17.59%)	5 / 87 (5.75%)
occurrences (all)	120	21	8
Blood Bilirubin Increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	22 / 404 (5.45%)	17 / 108 (15.74%)	5 / 87 (5.75%)
occurrences (all)	30	29	6
Blood Alkaline Phosphatase Increased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	27 / 404 (6.68%)	4 / 108 (3.70%)	4 / 87 (4.60%)
occurrences (all)	33	4	4
Lymphocyte Count Decreased			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	32 / 404 (7.92%)	2 / 108 (1.85%)	2 / 87 (2.30%)
occurrences (all)	73	2	3
Gamma-Glutamyltransferase Increased			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	21 / 404 (5.20%)	1 / 108 (0.93%)	1 / 87 (1.15%)
occurrences (all)	24	1	1
Weight Increased			
alternative dictionary used: MedDRA 28.1			
subjects affected / exposed	22 / 404 (5.45%)	1 / 108 (0.93%)	4 / 87 (4.60%)
occurrences (all)	23	1	5
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	85 / 404 (21.04%)	5 / 108 (4.63%)	7 / 87 (8.05%)
occurrences (all)	146	5	8
Dysgeusia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	34 / 404 (8.42%)	1 / 108 (0.93%)	3 / 87 (3.45%)
occurrences (all)	41	1	3
Dizziness			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	36 / 404 (8.91%)	9 / 108 (8.33%)	5 / 87 (5.75%)
occurrences (all)	45	11	5
Neuropathy Peripheral			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	12 / 404 (2.97%)	4 / 108 (3.70%)	6 / 87 (6.90%)
occurrences (all)	16	4	6
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	71 / 404 (17.57%)	6 / 108 (5.56%)	4 / 87 (4.60%)
occurrences (all)	193	10	4
Anaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	120 / 404 (29.70%)	14 / 108 (12.96%)	13 / 87 (14.94%)
occurrences (all)	260	15	15
Thrombocytopenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	45 / 404 (11.14%)	7 / 108 (6.48%)	4 / 87 (4.60%)
occurrences (all)	83	15	7
Leukopenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	26 / 404 (6.44%)	2 / 108 (1.85%)	2 / 87 (2.30%)
occurrences (all)	56	2	2
Lymphopenia			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	26 / 404 (6.44%)	1 / 108 (0.93%)	1 / 87 (1.15%)
occurrences (all)	58	1	1
General disorders and administration site conditions			
Fatigue			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	149 / 404 (36.88%)	32 / 108 (29.63%)	20 / 87 (22.99%)
occurrences (all)	255	42	23
Asthenia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	101 / 404 (25.00%)	13 / 108 (12.04%)	6 / 87 (6.90%)
occurrences (all)	209	13	9
Pyrexia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	58 / 404 (14.36%)	8 / 108 (7.41%)	5 / 87 (5.75%)
occurrences (all)	84	9	5
Oedema Peripheral			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	32 / 404 (7.92%)	5 / 108 (4.63%)	4 / 87 (4.60%)
occurrences (all)	44	5	4
Mucosal Inflammation			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	17 / 404 (4.21%)	9 / 108 (8.33%)	6 / 87 (6.90%)
occurrences (all)	24	10	7
Eye disorders			
Dry Eye			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	24 / 404 (5.94%)	6 / 108 (5.56%)	4 / 87 (4.60%)
occurrences (all)	26	6	4
Gastrointestinal disorders			
Nausea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	293 / 404 (72.52%)	44 / 108 (40.74%)	29 / 87 (33.33%)
occurrences (all)	929	54	34
Vomiting			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	154 / 404 (38.12%)	14 / 108 (12.96%)	9 / 87 (10.34%)
occurrences (all)	345	22	12
Abdominal Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	50 / 404 (12.38%)	11 / 108 (10.19%)	7 / 87 (8.05%)
occurrences (all)	68	14	9
Dyspepsia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	50 / 404 (12.38%)	12 / 108 (11.11%)	6 / 87 (6.90%)
occurrences (all)	64	12	6
Diarrhoea			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	118 / 404 (29.21%)	69 / 108 (63.89%)	33 / 87 (37.93%)
occurrences (all)	258	158	44
Constipation			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	147 / 404 (36.39%)	9 / 108 (8.33%)	12 / 87 (13.79%)
occurrences (all)	213	12	13
Abdominal Pain Upper			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	43 / 404 (10.64%)	11 / 108 (10.19%)	7 / 87 (8.05%)
occurrences (all)	144	14	7
Stomatitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	49 / 404 (12.13%)	25 / 108 (23.15%)	11 / 87 (12.64%)
occurrences (all)	72	28	14
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	60 / 404 (14.85%)	13 / 108 (12.04%)	7 / 87 (8.05%)
occurrences (all)	77	14	8
Dyspnoea			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	34 / 404 (8.42%)	10 / 108 (9.26%)	3 / 87 (3.45%)
occurrences (all)	41	13	3
Epistaxis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	34 / 404 (8.42%)	7 / 108 (6.48%)	5 / 87 (5.75%)
occurrences (all)	40	8	5
Pneumonitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	26 / 404 (6.44%)	0 / 108 (0.00%)	0 / 87 (0.00%)
occurrences (all)	26	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	150 / 404 (37.13%)	4 / 108 (3.70%)	4 / 87 (4.60%)
occurrences (all)	169	4	4
Rash			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	34 / 404 (8.42%)	19 / 108 (17.59%)	3 / 87 (3.45%)
occurrences (all)	47	21	4
Dry Skin			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	11 / 404 (2.72%)	6 / 108 (5.56%)	3 / 87 (3.45%)
occurrences (all)	11	6	3
Pruritus			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	22 / 404 (5.45%)	6 / 108 (5.56%)	2 / 87 (2.30%)
occurrences (all)	27	6	2
Rash Maculo-Papular			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	6 / 404 (1.49%)	6 / 108 (5.56%)	2 / 87 (2.30%)
occurrences (all)	7	6	3
Palmar-Plantar Erythrodysaesthesia Syndrome			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	7 / 404 (1.73%)	52 / 108 (48.15%)	48 / 87 (55.17%)
occurrences (all)	9	66	66
Dermatitis Acneiform			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	2 / 404 (0.50%)	10 / 108 (9.26%)	0 / 87 (0.00%)
occurrences (all)	2	15	0
Skin Toxicity			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	1 / 404 (0.25%)	6 / 108 (5.56%)	1 / 87 (1.15%)
occurrences (all)	1	8	1
Psychiatric disorders			
Insomnia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	28 / 404 (6.93%)	5 / 108 (4.63%)	6 / 87 (6.90%)
occurrences (all)	31	5	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	49 / 404 (12.13%)	7 / 108 (6.48%)	7 / 87 (8.05%)
occurrences (all)	68	7	7
Back Pain			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	42 / 404 (10.40%)	5 / 108 (4.63%)	1 / 87 (1.15%)
occurrences (all)	49	5	1
Pain In Extremity			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	27 / 404 (6.68%)	4 / 108 (3.70%)	4 / 87 (4.60%)
occurrences (all)	33	4	5
Myalgia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	25 / 404 (6.19%)	4 / 108 (3.70%)	4 / 87 (4.60%)
occurrences (all)	44	4	4
Muscle Spasms			
alternative dictionary used: MedDRA 25.0			

subjects affected / exposed	14 / 404 (3.47%)	7 / 108 (6.48%)	4 / 87 (4.60%)
occurrences (all)	24	7	4
Infections and infestations			
Urinary Tract Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	36 / 404 (8.91%)	3 / 108 (2.78%)	3 / 87 (3.45%)
occurrences (all)	63	3	3
Covid-19			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	55 / 404 (13.61%)	3 / 108 (2.78%)	1 / 87 (1.15%)
occurrences (all)	67	3	1
Nasopharyngitis			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	25 / 404 (6.19%)	2 / 108 (1.85%)	3 / 87 (3.45%)
occurrences (all)	35	2	3
Paronychia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	10 / 404 (2.48%)	12 / 108 (11.11%)	3 / 87 (3.45%)
occurrences (all)	14	21	4
Upper Respiratory Tract Infection			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	26 / 404 (6.44%)	3 / 108 (2.78%)	3 / 87 (3.45%)
occurrences (all)	38	3	3
Metabolism and nutrition disorders			
Decreased Appetite			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	126 / 404 (31.19%)	20 / 108 (18.52%)	15 / 87 (17.24%)
occurrences (all)	176	25	16
Hypokalaemia			
alternative dictionary used: MedDRA 25.0			
subjects affected / exposed	33 / 404 (8.17%)	6 / 108 (5.56%)	7 / 87 (8.05%)
occurrences (all)	45	6	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2018	This amendment updated the starting dose of DS-8201a, revised eligibility criteria, clarified the process if treatment is delayed, updated criteria for dose modifications, revised definitions, and further clarified details for key study assessments.
08 March 2019	This amendment updated the eligibility criteria, clarified study objectives/endpoints, and further clarified details for key study assessments.
26 April 2019	This amendment clarified details regarding ILD biomarkers, monitoring plan, dose modification, and follow-up plans.
23 April 2020	This amendment was primarily driven by the addition of an interim analysis.
05 August 2020	This amendment was primarily driven by the addition of biomarker analyses to evaluate the impact of the global pandemic caused by COVID-19 at the patient-level and study-level. The exploratory endpoints were also revised to include evaluation of progression-free survival on the next line of therapy (PFS2), and withdrawal of consent language was clarified.
17 March 2022	The main purpose of this amendment is to introduce alternative timing for the primary analysis.
24 April 2023	Key changes include updates to frequency of tumor assessments, removal of anti-drug antibody (ADA) and biomarker sample collection for on-treatment patients, and updates to the adverse event management guidelines.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported