Clinical trial results:
A Phase 2, Multicenter, Open-Label, 2-Cohort Study of Trastuzumab Deruxtecan (DS-8201a), an Anti-HER2 Antibody Drug Conjugate (ADC), for HER2-Over-Expressing or -Mutated, Unresectable and/or Metastatic Non Small Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2017-004781-94
Trial protocol	NL ES
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	06 June 2022
First version publication date	06 June 2022

Trial information

Trial identification

Sponsor protocol code	DS8201-A-U204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03505710
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo Inc.
Sponsor organisation address	211 Mt. Airy Rd., Baking Ridge, United States, 07920
Public contact	Global Clinical Director, Daiichi Sankyo Inc., 908 992-6400, CTRinfo@dsi.com
Scientific contact	Global Clinical Director, Daiichi Sankyo Inc., 908 992-6400, CTRinfo@dsi.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	Interim
Date of interim/final analysis	03 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the objective response rate (ORR) of trastuzumab deruxtecan in HER2-over-expressing and/or –HER2 mutated advanced NSCLC subjects.

Protection of trial subjects:

The study protocol, amendments, the informed consent form(s) (ICF[s]), and information sheets were approved by the appropriate and applicable Independent Ethics Committees (IECs) or Institutional Review Boards (IRBs). The study was conducted in compliance with the protocol, the ethical principles that have their origin in the Declaration of Helsinki, the International Council for Harmonisation (ICH) consolidated Guideline E6 for Good Clinical Practice (GCP) (CPMP/ICH/135/95), and applicable regulatory requirement(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 67
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	Netherlands: 31
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Spain: 27
Worldwide total number of subjects	181
EEA total number of subjects	76

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)	109
From 65 to 84 years	70
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Total of 181 participants were enrolled & treated at centers in Japan, US, France, Netherlands, & Spain. Primary results reported is from baseline to data cut-off date of 03 May 2021. The results presented are based on primary analysis up to 36 months. Data collection is still on-going and additional results will be provided after study completion.

Pre-assignment

Screening details:

Duration of follow-up (months) was defined as ((last visit date − enrollment date + 1)/365.25) × 12. Last visit date was the date of last clinical visit for ongoing participants, date of death for participants who died, or the last known contact date in survival follow-up for other participants who discontinued study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: HER2 Overexpressing

Arm description:

Participants with HER2-overexpressing(immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

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

Dosage and administration details:

Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Arm title	Cohort 1a: HER2 Overexpressing

Arm description:

Participants with HER2-overexpressing (immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 5.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

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

Dosage and administration details:

Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Arm title	Cohort 2: HER2 Mutated

Arm description:

Participants with HER2-mutated, unresectable and/or metastatic NSCLC who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

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

Dosage and administration details:

Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Number of subjects in period 1	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated
Started	49	41	91
Completed	2	14	15
Not completed	47	27	76
Physician decision	1	-	2
Adverse Event	12	5	27
Other Reasons	1	1	1
Death	4	3	6
Progressive Disease	22	9	34
Withdrawal by Subject	1	3	3
Clinical Progression	6	6	3

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: HER2 Overexpressing

Reporting group description:

Participants with HER2-overexpressing(immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group title	Cohort 1a: HER2 Overexpressing

Reporting group description:

Participants with HER2-overexpressing (immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 5.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group title	Cohort 2: HER2 Mutated

Reporting group description:

Participants with HER2-mutated, unresectable and/or metastatic NSCLC who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated
Number of subjects	49	41	91
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)			

Asian	13	4	31
Black or African American	4	2	1
White	31	31	40
Unknown or Not Reported	1	3	19

Reporting group values	Total		
Number of subjects	181		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	109		
From 65-84 years	70		
85 years and over	2		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	98		
Male	83		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	48		
Black or African American	7		
White	102		
Unknown or Not Reported	23		

End points

End points reporting groups

Reporting group title	Cohort 1: HER2 Overexpressing

Reporting group description:

Participants with HER2-overexpressing(immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group title	Cohort 1a: HER2 Overexpressing

Reporting group description:

Participants with HER2-overexpressing (immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 5.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group title	Cohort 2: HER2 Mutated

Reporting group description:

Participants with HER2-mutated, unresectable and/or metastatic NSCLC who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Primary: Percentage of Participants With Objective Response Rate (ORR) Based on Independent Central Review Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point title	Percentage of Participants With Objective Response Rate (ORR) Based on Independent Central Review Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)[1]

End point description:

The Objective Response Rate (ORR) was the defined as the percentage of participants who achieved a best overall response of confirmed Complete Response (CR) or Partial Response (PR), assessed by independent central review (ICR) committee 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 ICR is reported. Objective response rate was assessed in the Full Analysis Set at data cut-off date of 03 May 2021.

End point type	Primary

End point timeframe:

Up to 36 months (data cut-off)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for end point.

End point values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	41	91	
Units: Percentage of Participants				
number (confidence interval 95%)	26.5 (15.0 to 41.1)	29.3 (16.1 to 45.5)	54.9 (44.2 to 65.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response Rate (ORR) Based on Investigator Assessment Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point title	Percentage of Participants With Objective Response Rate (ORR) Based on Investigator Assessment Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)

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 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 investigator assessment is reported. Objective response rate was assessed in the Full Analysis Set at data cut-off date of 03 May 2021.

End point type	Secondary

End point timeframe:

Up to 36 months (data cut-off)

End point values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	41	91	
Units: Percentage of Participants				
number (confidence interval 95%)	28.6 (16.6 to 43.3)	31.7 (18.1 to 48.1)	61.5 (50.8 to 71.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or - Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point title	Duration of Response (DoR) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -

	Mutated Non-Small-Cell Lung Cancer (NSCLC)

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 independent central review and investigator assessment is reported. Duration of Response (DoR) was assessed in the Full Analysis Set of participants with confirmed CR/PR at data cut-off date of 03 May 2021.

End point type	Secondary

End point timeframe:

Up to 36 months (data cut-off)

End point values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[2]	12[3]	50[4]	
Units: months				
median (confidence interval 95%)				
Independent Central Review (ICR)	5.8 (4.3 to 99.9)	4.7 (4.0 to 99.9)	9.3 (5.7 to 14.7)	
Investigator Assessment (IA)	5.8 (4.7 to 99.9)	7.0 (4.2 to 99.9)	11.7 (7.2 to 16.9)	

Notes:

[2] - ICR=13 participants, IA=11 participants, 99.9 = NA due to insufficient number of events

[3] - ICR=12 participants, IA=3 participants, 99.9 = NA due to insufficient number of events

[4] - ICR=50 participants, IA=30 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or - Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point title	Progression-Free Survival (PFS) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or - Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point description:

Progression-free survival (PFS) was defined as the time from the date of enrollment 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. Progressive disease was defined as at least a 20% increase in the sum of diameters of target lesions. PFS based on independent central review and investigator assessment is reported. Progression-free survival (PFS) was assessed in the Full Analysis Set at data cut-off date of 03 May 2021.

End point type	Secondary

End point timeframe:

Up to 36 months (data cut-off)

End point values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	41[5]	91	
Units: months				
median (confidence interval 95%)				
Independent Central Review (ICR)	5.7 (2.8 to 7.2)	6.7 (4.5 to 99.9)	8.2 (6.0 to 11.9)	
Investigator Assessment (IA)	5.7 (3.8 to 7.2)	7.2 (4.1 to 8.4)	9.3 (7.1 to 14.0)	

Notes:

[5] - 99.9 = NA due to insufficient number of events

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non- Small-Cell Lung Cancer (NSCLC)

End point title	Overall Survival (OS) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point description:

Overall survival (OS) was defined as the time from the date of first dose of study drug to the date of death due to any cause. Overall survival (OS) was assessed in the Full Analysis Set at data cut-off date of 03 May 2021.

End point type	Secondary

End point timeframe:

Up to 36 months (data cut-off)

End point values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	41[6]	91	
Units: months				
median (confidence interval 95%)	12.4 (7.8 to 17.2)	99.9 (6.7 to 99.9)	17.8 (13.8 to 22.1)	

Notes:

[6] - 99.9=NA due to insufficient number of events

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Disease Control Rate (DCR) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point title	Percentage of Participants With Disease Control Rate (DCR) Following Treatment With DS8201a in Participants With HER2-Over-Expressing or -Mutated Non-Small-Cell Lung Cancer (NSCLC)

End point description:	
Disease Control Rate (DCR) was defined as the percentage of participants who achieved a best overall response of CR, PR, or stable disease (SD) during study treatment. Confirmation of CR/PR was required. DCR based on independent central review and investigator assessment is reported. Disease control rate was assessed in the Full Analysis Set at data cut-off date of 03 May 2021.	
End point type	Secondary
End point timeframe:	
Up to 36 months (data cut-off)	

End point values	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	41	91	
Units: Percentage of Participants				
number (confidence interval 95%)				
Independent Central Review (ICR)	68.9 (53.4 to 81.8)	77.5 (61.6 to 89.2)	93.0 (85.4 to 97.4)	
Investigator Assessment (IA)	75.5 (61.1 to 86.7)	78.0 (62.4 to 89.4)	94.5 (87.6 to 98.2)	

Statistical analyses

No statistical analyses for this end point

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 36 months.

Adverse event reporting additional description:

A Treatment-emergent adverse event (TEAE) is defined as an AE that occurs, having been absent before the first dose of study drug, or has worsened in severity or seriousness after the initiating the study drug until 47 days after last dose of the study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Cohort 1: HER2 Overexpressing

Reporting group description:

Participants with HER2-overexpressing(immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group title	Cohort 1a: HER2 Overexpressing

Reporting group description:

Participants with HER2-overexpressing (immunohistochemistry [IHC] 3+ or IHC 2+), unresectable and/or metastatic NSCLC adenocarcinoma who received 5.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Reporting group title	Cohort 2: HER2 Mutated

Reporting group description:

Participants with HER2-mutated, unresectable and/or metastatic NSCLC who received 6.4 mg/kg trastuzumab deruxtecan (DS-8201a).

Trastuzumab deruxtecan: Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Serious adverse events	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 49 (55.10%)	14 / 41 (34.15%)	39 / 91 (42.86%)
number of deaths (all causes)	35	11	47
number of deaths resulting from adverse events	10	5	13
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm Malignant			

subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	0 / 91 (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
Hypotension			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	0 / 91 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Disease Progression			
subjects affected / exposed	6 / 49 (12.24%)	3 / 41 (7.32%)	7 / 91 (7.69%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 6	0 / 3	0 / 7
Fatigue			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Oedema Peripheral			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	4 / 49 (8.16%)	1 / 41 (2.44%)	7 / 91 (7.69%)
occurrences causally related to treatment / all	4 / 4	1 / 1	8 / 8
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Interstitial lung disease			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	3 / 91 (3.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Pulmonary Oedema			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspnoea			
subjects affected / exposed	4 / 49 (8.16%)	1 / 41 (2.44%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoxia			
subjects affected / exposed	0 / 49 (0.00%)	2 / 41 (4.88%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary Oedema			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Haemoptysis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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			
Confusional State			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental Status Changes			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Troponin I Increased			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Troponin Increased			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram T Wave Abnormal			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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			
Fall			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation Necrosis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Transfusion Reaction			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial Effusion			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Nervous system disorders			
Respiratory Failure			

subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	3 / 91 (3.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Central Nervous System Necrosis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Encephalopathy			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1

subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Stenosis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Motility Disorder			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Ileus			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			

subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Intestinal Perforation			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intra-Abdominal Haematoma			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Nausea			
subjects affected / exposed	2 / 49 (4.08%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Obstruction			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
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			

subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	3 / 91 (3.30%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Infections and infestations			
Abdominal Sepsis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			

subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
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			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Empyema			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Enterocolitis Infectious			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Oesophageal Infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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
Pneumocystis Jirovecii Pneumonia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	4 / 49 (8.16%)	1 / 41 (2.44%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Staphylococcal			

subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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 Tract Infection			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	0 / 91 (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
Sepsis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 41 (2.44%)	0 / 91 (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
Septic Shock			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
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 Bacteraemia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	0 / 91 (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	Cohort 1: HER2 Overexpressing	Cohort 1a: HER2 Overexpressing	Cohort 2: HER2 Mutated
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 49 (93.88%)	41 / 41 (100.00%)	91 / 91 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5
Hypotension			

subjects affected / exposed	4 / 49 (8.16%)	0 / 41 (0.00%)	0 / 91 (0.00%)
occurrences (all)	4	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 49 (32.65%)	20 / 41 (48.78%)	30 / 91 (32.97%)
occurrences (all)	24	23	37
Asthenia			
subjects affected / exposed	6 / 49 (12.24%)	6 / 41 (14.63%)	16 / 91 (17.58%)
occurrences (all)	6	6	22
Malaise			
subjects affected / exposed	9 / 49 (18.37%)	3 / 41 (7.32%)	12 / 91 (13.19%)
occurrences (all)	10	3	16
Pyrexia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	16 / 91 (17.58%)
occurrences (all)	1	1	19
Oedema Peripheral			
subjects affected / exposed	2 / 49 (4.08%)	4 / 41 (9.76%)	11 / 91 (12.09%)
occurrences (all)	2	4	13
Non-Cardiac Chest Pain			
subjects affected / exposed	3 / 49 (6.12%)	4 / 41 (9.76%)	3 / 91 (3.30%)
occurrences (all)	3	4	3
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	9 / 49 (18.37%)	8 / 41 (19.51%)	17 / 91 (18.68%)
occurrences (all)	9	8	18
Cough			
subjects affected / exposed	6 / 49 (12.24%)	11 / 41 (26.83%)	14 / 91 (15.38%)
occurrences (all)	7	12	14
Pneumonitis			
subjects affected / exposed	4 / 49 (8.16%)	1 / 41 (2.44%)	12 / 91 (13.19%)
occurrences (all)	5	1	12
Epistaxis			
subjects affected / exposed	4 / 49 (8.16%)	3 / 41 (7.32%)	8 / 91 (8.79%)
occurrences (all)	4	3	8
Hiccups			

subjects affected / exposed	4 / 49 (8.16%)	2 / 41 (4.88%)	4 / 91 (4.40%)
occurrences (all)	4	4	5
Productive Cough			
subjects affected / exposed	0 / 49 (0.00%)	2 / 41 (4.88%)	5 / 91 (5.49%)
occurrences (all)	0	2	7
Rhinorrhoea			
subjects affected / exposed	3 / 49 (6.12%)	1 / 41 (2.44%)	1 / 91 (1.10%)
occurrences (all)	3	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 49 (4.08%)	0 / 41 (0.00%)	12 / 91 (13.19%)
occurrences (all)	2	0	12
Anxiety			
subjects affected / exposed	1 / 49 (2.04%)	3 / 41 (7.32%)	8 / 91 (8.79%)
occurrences (all)	1	4	8
Depression			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5
Investigations			
Neutrophil Count Decreased			
subjects affected / exposed	11 / 49 (22.45%)	2 / 41 (4.88%)	27 / 91 (29.67%)
occurrences (all)	18	3	62
White Blood Cell Count Decreased			
subjects affected / exposed	6 / 49 (12.24%)	1 / 41 (2.44%)	17 / 91 (18.68%)
occurrences (all)	14	1	50
Lymphocyte Count Decreased			
subjects affected / exposed	5 / 49 (10.20%)	1 / 41 (2.44%)	13 / 91 (14.29%)
occurrences (all)	11	1	30
Weight Decreased			
subjects affected / exposed	12 / 49 (24.49%)	6 / 41 (14.63%)	21 / 91 (23.08%)
occurrences (all)	12	6	24
Alanine Aminotransferase Increased			
subjects affected / exposed	5 / 49 (10.20%)	3 / 41 (7.32%)	14 / 91 (15.38%)
occurrences (all)	5	3	23
Aspartate Aminotransferase Increased			

subjects affected / exposed	6 / 49 (12.24%)	2 / 41 (4.88%)	17 / 91 (18.68%)
occurrences (all)	7	2	20
Platelet Count Decreased			
subjects affected / exposed	7 / 49 (14.29%)	2 / 41 (4.88%)	11 / 91 (12.09%)
occurrences (all)	7	2	19
Blood Creatinine Increased			
subjects affected / exposed	5 / 49 (10.20%)	3 / 41 (7.32%)	4 / 91 (4.40%)
occurrences (all)	6	3	4
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	3 / 49 (6.12%)	1 / 41 (2.44%)	5 / 91 (5.49%)
occurrences (all)	3	1	5
Electrocardiogram Qt Prolonged			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	6 / 91 (6.59%)
occurrences (all)	0	0	7
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 49 (20.41%)	3 / 41 (7.32%)	8 / 91 (8.79%)
occurrences (all)	11	4	9
Headache			
subjects affected / exposed	3 / 49 (6.12%)	2 / 41 (4.88%)	15 / 91 (16.48%)
occurrences (all)	3	2	16
Dysgeusia			
subjects affected / exposed	4 / 49 (8.16%)	3 / 41 (7.32%)	12 / 91 (13.19%)
occurrences (all)	4	3	12
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	5 / 91 (5.49%)
occurrences (all)	1	0	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 49 (28.57%)	10 / 41 (24.39%)	32 / 91 (35.16%)
occurrences (all)	17	11	45
Neutropenia			
subjects affected / exposed	3 / 49 (6.12%)	2 / 41 (4.88%)	6 / 91 (6.59%)
occurrences (all)	3	2	9
Eye disorders			

Dry Eye			
subjects affected / exposed	0 / 49 (0.00%)	2 / 41 (4.88%)	7 / 91 (7.69%)
occurrences (all)	0	2	7
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	28 / 49 (57.14%)	30 / 41 (73.17%)	68 / 91 (74.73%)
occurrences (all)	37	68	120
Diarrhoea			
subjects affected / exposed	13 / 49 (26.53%)	13 / 41 (31.71%)	37 / 91 (40.66%)
occurrences (all)	17	21	66
Vomiting			
subjects affected / exposed	13 / 49 (26.53%)	12 / 41 (29.27%)	41 / 91 (45.05%)
occurrences (all)	16	15	65
Constipation			
subjects affected / exposed	15 / 49 (30.61%)	10 / 41 (24.39%)	34 / 91 (37.36%)
occurrences (all)	16	10	38
Abdominal pain			
subjects affected / exposed	2 / 49 (4.08%)	5 / 41 (12.20%)	8 / 91 (8.79%)
occurrences (all)	3	5	8
Stomatitis			
subjects affected / exposed	6 / 49 (12.24%)	1 / 41 (2.44%)	6 / 91 (6.59%)
occurrences (all)	6	2	7
Gastrooesophageal Reflux Disease			
subjects affected / exposed	2 / 49 (4.08%)	1 / 41 (2.44%)	8 / 91 (8.79%)
occurrences (all)	2	1	8
Dyspepsia			
subjects affected / exposed	0 / 49 (0.00%)	2 / 41 (4.88%)	6 / 91 (6.59%)
occurrences (all)	0	2	6
Dysphagia			
subjects affected / exposed	3 / 49 (6.12%)	0 / 41 (0.00%)	5 / 91 (5.49%)
occurrences (all)	3	0	5
Abdominal Pain Upper			
subjects affected / exposed	3 / 49 (6.12%)	0 / 41 (0.00%)	4 / 91 (4.40%)
occurrences (all)	3	0	4
Haemorrhoids			

subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	7 / 91 (7.69%)
occurrences (all)	0	0	7
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 49 (20.41%)	5 / 41 (12.20%)	42 / 91 (46.15%)
occurrences (all)	10	6	42
Dry skin			
subjects affected / exposed	1 / 49 (2.04%)	0 / 41 (0.00%)	11 / 91 (12.09%)
occurrences (all)	1	0	11
Pruritus			
subjects affected / exposed	1 / 49 (2.04%)	1 / 41 (2.44%)	6 / 91 (6.59%)
occurrences (all)	1	1	6
Rash Maculo-Papular			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	6 / 91 (6.59%)
occurrences (all)	0	0	7
Eczema			
subjects affected / exposed	0 / 49 (0.00%)	0 / 41 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	2 / 49 (4.08%)	5 / 41 (12.20%)	15 / 91 (16.48%)
occurrences (all)	2	5	15
Arthralgia			
subjects affected / exposed	3 / 49 (6.12%)	0 / 41 (0.00%)	12 / 91 (13.19%)
occurrences (all)	4	0	13
Myalgia			
subjects affected / exposed	3 / 49 (6.12%)	0 / 41 (0.00%)	6 / 91 (6.59%)
occurrences (all)	3	0	6
Muscular Weakness			
subjects affected / exposed	0 / 49 (0.00%)	2 / 41 (4.88%)	5 / 91 (5.49%)
occurrences (all)	0	3	5
Muscle Spasms			

Limitations and caveats

None reported