Clinical trial results:
A Multi-indication, Single-treatment Arm, Open-label Phase 2 Study of Regorafenib and Nivolumab in Combination in Patients with Recurrent or Metastatic Solid Tumors

Summary

EudraCT number	2020-003359-13
Trial protocol	GB FR BE IT
Global end of trial date	29 March 2024

Results information

Result version number	v1 (current)
This version publication date	05 April 2025
First version publication date	05 April 2025

Trial information

Trial identification

Sponsor protocol code	BAY73-4506/21136

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04704154
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.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	07 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy of the regorafenib and nivolumab combination by cohort

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects (or their legally authorized representative according to local legislation). Participating subjects (or their legally authorized representative according to local legislation) signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	France: 46
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Japan: 29
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	175
EEA total number of subjects	90

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	95
From 65 to 84 years	80
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 34 study centers in 8 countries/regions (6 centers in France, 5 centers in Italy, 2 centers in South Korea, 3 centers in Taiwan, 4 centers in the United Kingdom, 5 centers in Japan, 6 centers in the US and 3 centers in Belgium) from 03 February 2021 (first patient first visit) to 29 March 2024 (last patient last visit)

Pre-assignment

Screening details:

175 participants were enrolled and received study treatment. Participants were enrolled in 6 cohorts: HNSCC IO naïve (N=30), HNSCC IO treated (N=20), ESCC (N=30), PDAC (N=20), BTC (N=45), and GBM/AA (N=30)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	HNSCC (IO naive)

Arm description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) without Immune-oncology (IO), received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	Stivarga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

Arm title	HNSCC (IO treated)

Arm description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) and with Immune-oncology (IO) treated, received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Arm type	Experimental

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	Stivarga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

Arm title	ESCC

Arm description:

Participants with confirmed recurrent or metastatic Esophageal Squamous Cell Carcinoma (ESCC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	Stivarga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

Arm title	PDAC

Arm description:

Participants with confirmed recurrent or metastatic Pancreatic Duct Adenocarcinoma (PADC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Arm type	Experimental
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	Stivarga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30

mg tablets).

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

Arm title	Biliary Tract Cancer (BTC)

Arm description:

Participants with confirmed recurrent or metastatic BTC received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Arm type	Experimental
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	Stivarga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

Arm title	GBM/AA

Arm description:

Participants with Glioblastoma Multiforme (GBM) or Anaplastic Astrocytoma (AA) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	Stivarga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

Number of subjects in period 1	HNSCC (IO naive)	HNSCC (IO treated)	ESCC
Started	30	20	30
Completed	0	0	0
Not completed	30	20	30
Adverse event, serious fatal	3	-	-
Participant Decision	1	1	-
Completed max 24 infusions of Nivolumab	2	-	1
Physician decision	1	-	1
Adverse event, non-fatal	3	2	4
Progressive Disease	19	17	20
Continued in rollover study for regorafenib	1	-	4

Number of subjects in period 1	PDAC	Biliary Tract Cancer (BTC)	GBM/AA
Started	20	45	30
Completed	0	0	0
Not completed	20	45	30
Adverse event, serious fatal	-	3	-
Participant Decision	-	-	-
Completed max 24 infusions of Nivolumab	-	1	-
Physician decision	-	2	-
Adverse event, non-fatal	2	3	-
Progressive Disease	18	36	30
Continued in rollover study for regorafenib	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	HNSCC (IO naive)
Reporting group description:	
Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) without Immune-oncology (IO), received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.	
Reporting group title	HNSCC (IO treated)
Reporting group description:	
Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) and with Immune-oncology (IO) treated, received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.	
Reporting group title	ESCC
Reporting group description:	
Participants with confirmed recurrent or metastatic Esophageal Squamous Cell Carcinoma (ESCC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.	
Reporting group title	PDAC
Reporting group description:	
Participants with confirmed recurrent or metastatic Pancreatic Duct Adenocarcinoma (PADC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.	
Reporting group title	Biliary Tract Cancer (BTC)
Reporting group description:	
Participants with confirmed recurrent or metastatic BTC received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.	
Reporting group title	GBM/AA
Reporting group description:	
Participants with Glioblastoma Multiforme (GBM) or Anaplastic Astrocytoma (AA) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.	

Reporting group values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC
Number of subjects	30	20	30
Age Categorical Units: Subjects			
Adults (18-64 years)	16	10	17
From 65-84 years	14	10	13
Age Continuous Units: years			
median	63.0	64.5	62.0
full range (min-max)	26 to 76	44 to 81	49 to 76
Gender Categorical Units: Subjects			
Female	5	6	3
Male	25	14	27

Race Units: Subjects			
Asian	15	11	21
Black or African American	0	0	0
White	6	6	7
Not Reported	9	3	2

Reporting group values	PDAC	Biliary Tract Cancer (BTC)	GBM/AA
Number of subjects	20	45	30
Age Categorical Units: Subjects			
Adults (18-64 years)	13	17	22
From 65-84 years	7	28	8
Age Continuous Units: years			
median	57.0	67.0	59.5
full range (min-max)	42 to 74	32 to 81	21 to 75
Gender Categorical Units: Subjects			
Female	11	20	10
Male	9	25	20
Race Units: Subjects			
Asian	5	11	2
Black or African American	0	1	0
White	13	27	26
Not Reported	2	6	2

Reporting group values	Total		
Number of subjects	175		
Age Categorical Units: Subjects			
Adults (18-64 years)	95		
From 65-84 years	80		
Age Continuous Units: years			
median			
full range (min-max)	-		
Gender Categorical Units: Subjects			
Female	55		
Male	120		
Race Units: Subjects			
Asian	65		
Black or African American	1		
White	85		
Not Reported	24		

Subject analysis sets	
Subject analysis set title	FAS (full analysis set)
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who have received any dose of study intervention

Subject analysis set title	SAF (safety analysis set)
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants who have received any dose of study intervention. As the safety analysis set equals the full analysis, all safety related analysis were performed on the full analysis set.

Reporting group values	FAS (full analysis set)	SAF (safety analysis set)	
Number of subjects	175	175	
Age Categorical Units: Subjects			
Adults (18-64 years)	95	95	
From 65-84 years	80	80	
Age Continuous Units: years median full range (min-max)			
Gender Categorical Units: Subjects			
Female	55	55	
Male	120	120	
Race Units: Subjects			
Asian	65	65	
Black or African American	1	1	
White	85	85	
Not Reported	24	24	

End points reporting groups

Reporting group title	HNSCC (IO naive)

Reporting group description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) without Immune-oncology (IO), received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Reporting group title	HNSCC (IO treated)

Reporting group description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) and with Immune-oncology (IO) treated, received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Reporting group title	ESCC

Reporting group description:

Participants with confirmed recurrent or metastatic Esophageal Squamous Cell Carcinoma (ESCC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Reporting group title	PDAC

Reporting group description:

Participants with confirmed recurrent or metastatic Pancreatic Duct Adenocarcinoma (PADC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Reporting group title	Biliary Tract Cancer (BTC)

Reporting group description:

Participants with confirmed recurrent or metastatic BTC received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Reporting group title	GBM/AA

Reporting group description:

Participants with Glioblastoma Multiforme (GBM) or Anaplastic Astrocytoma (AA) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

Subject analysis set title	FAS (full analysis set)
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who have received any dose of study intervention

Subject analysis set title	SAF (safety analysis set)
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants who have received any dose of study intervention. As the safety analysis set equals the full analysis, all safety related analysis were performed on the full analysis set.

Primary: Overall response rate (ORR)

End point title	Overall response rate (ORR)[1]

End point description:

Tumor response was evaluated as ORR per RECIST 1.1 by local assessments for all tumor types, except for GBM/AA, where ORR per RANO by local assessment was used. ORR was defined as the proportion of participants with best overall response of complete response (CR) or partial response (PR). Participants for whom best overall tumor response was not CR or PR, as well as participants without any post-baseline tumor assessment were considered non-responders. Descriptive statistics were done, no

inferential statistical analyses were performed

End point type	Primary

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Subjects				
Overall Response Rate (ORR)	6	1	15	0

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Subjects				
Overall Response Rate (ORR)	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

Defined as the time (in days) from the first documented objective response of PR or CR, whichever is noted earlier, to disease progression or death (if death occurs before progression is documented). DOR will be defined for responders only, i.e. participants with a CR or PR.

99999: Value cannot be estimated due to censored data, insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[2]	1[3]	15[4]	0[5]
Units: Days				
median (confidence interval 80%)				
DOR Median [80% CI]	99999 (654 to 99999)	99999 (99999 to 99999)	420 (112 to 617)	(to)

Notes:

[2] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[3] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[4] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[5] - Subgroup of participants with best overall response of CR or PR who received the study treatment

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[6]	1[7]		
Units: Days				
median (confidence interval 80%)				
DOR Median [80% CI]	432 (112 to 99999)	140 (-99999 to 99999)		

Notes:

[6] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[7] - Subgroup of participants with best overall response of CR or PR who received the study treatment

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR)

End point title	Disease control rate (DCR)

End point description:

CR = Complete response; PR = Partial response; SD = Stable disease

End point type	Secondary

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Subjects				
Disease Control Rate (DCR) CR, PR or SD	16	13	22	7

End point values	Biliary Tract Cancer (BTC)	GBM/AA		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Subjects				
Disease Control Rate (DCR) CR, PR or SD	24	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

PFS was defined as the time (in days) from the start of study intervention to the date of first objectively documented progressive disease (PD) or death from any cause (if no progression was documented).

End point type	Secondary

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Days				
median (confidence interval 80%)				
Progression Free Survival (PFS) Median [80% CI]	79 (50 to 227)	105 (52 to 115)	259 (110 to 472)	53 (48 to 111)

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Days				
median (confidence interval 80%)				
Progression Free Survival (PFS) Median [80% CI]	98 (55 to 112)	55 (52 to 84)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6 months PFS

End point title	6 months PFS

End point description:

6 Months PFS rate

End point type	Secondary

End point timeframe:

Up to last participant follow 6 months (approximately 22 months)

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Proportion of participants				
number (confidence interval 80%)				
Progression-free survival rate at month 6	0.455 (0.337 to 0.573)	0.263 (0.134 to 0.393)	0.533 (0.417 to 0.650)	0.050 (0.000 to 0.112)

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Proportion of participants				
number (confidence interval 80%)				
Progression-free survival rate at month 6	0.148 (0.077 to 0.218)	0.167 (0.079 to 0.254)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS was defined as the time (in days) from the start of study intervention to the date of death due to any cause.

End point type	Secondary

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Days				
median (confidence interval 80%)				
Overall Survival Median [80% CI]	358 (198 to 418)	355 (126 to 614)	627 (431 to 865)	259 (134 to 311)

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Days				
median (confidence interval 80%)				
Overall Survival Median [80% CI]	246 (176 to 386)	245 (127 to 377)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events

End point title	Number of participants with adverse events

End point description:

AEs were considered to be treatment-emergent (TEAEs) if they started or worsened after the start of first study drug administration until 30 days after regorafenib treatment discontinuation or 100 days after the last dose of nivolumab, whatever occurred later.

End point type	Secondary

End point timeframe:

Up to the last participant has been followed for approximately 10 months, summed up to approximately 26 months

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Subjects				
Any AE	30	20	30	20
Worst grade: Grade 1	1	0	2	0
Worst grade: Grade 2	4	1	6	2
Worst grade: Grade 3	16	16	18	11
Worst grade: Grade 4	6	2	2	2
Worst grade: Grade 5 (death)	3	1	2	5

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Subjects				
Any AE	45	30		
Worst grade: Grade 1	1	0		
Worst grade: Grade 2	9	8		
Worst grade: Grade 3	23	11		
Worst grade: Grade 4	1	2		
Worst grade: Grade 5 (death)	11	9		

Statistical analyses

No statistical analyses for this end point

Secondary: 1 year OS

End point title	1 year OS

End point description:

End point type	Secondary

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 month

End point values	HNSCC (IO naive)	HNSCC (IO treated)	ESCC	PDAC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Proportion of patients				
number (confidence interval 80%)				
Overall survival rate at month 12	0.415 (0.298 to 0.532)	0.444 (0.294 to 0.595)	0.764 (0.664 to 0.864)	0.281 (0.145 to 0.418)

End point values	Biliary Tract Cancer (BTC)	GBM/AA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	30		
Units: Proportion of patients				
number (confidence interval 80%)				
Overall survival rate at month 12	0.422 (0.323 to 0.521)	0.337 (0.223 to 0.451)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the start of first study drug administration until 30 days after regorafenib treatment discontinuation or 100 days after the last dose of nivolumab, whatever occurred later.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	HNSCC (IO naive)

Reporting group description:

Participants with confirmed recurrent or metastatic HNSCC and IO naive, received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

Reporting group title	GBM/AA

Reporting group description:

Participants with GBM or AA received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

Reporting group title	PDAC

Reporting group description:

Participants with confirmed recurrent or metastatic PADC received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

Reporting group title	Biliary Tract Cancer (BTC)

Reporting group description:

Participants with confirmed recurrent or metastatic BTC received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

Reporting group title	HNSCC (IO treated)

Reporting group description:

Participants with confirmed recurrent or metastatic HNSCC and with IO treated, received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

Reporting group title	ESCC

Reporting group description:

Participants with confirmed recurrent or metastatic ESCC received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

Serious adverse events	HNSCC (IO naive)	GBM/AA	PDAC
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 30 (73.33%)	13 / 30 (43.33%)	13 / 20 (65.00%)
number of deaths (all causes)	22	27	17
number of deaths resulting from adverse events	3	9	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tumour haemorrhage			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pharyngeal cancer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Bile duct stent insertion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	2 / 30 (6.67%)	9 / 30 (30.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	2 / 2	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 9	0 / 1
Performance status decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Face oedema			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal stenosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Obstructive airways disorder			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Product issues			
Device occlusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device deposit issue			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Weight decreased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Skull fracture			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			

subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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 failure			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Atrial fibrillation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Coma			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (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
Hemiparesis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (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
Hemiplegia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (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
Neuralgia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (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
Vasogenic cerebral oedema			

subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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			
Colitis ischaemic			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Colitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (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
Intestinal obstruction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Pneumoperitoneum			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Diverticular perforation			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral cavity fistula			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cholecystitis acute			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune-mediated hepatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Hypopituitarism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Crystal arthropathy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Osteitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 30 (13.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Rectal abscess			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Biliary tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site infection			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (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
Diabetes mellitus			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Decreased appetite			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (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
Malnutrition			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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
Hypokalaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (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

Serious adverse events	Biliary Tract Cancer (BTC)	HNSCC (IO treated)	ESCC
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 45 (62.22%)	15 / 20 (75.00%)	19 / 30 (63.33%)
number of deaths (all causes)	36	17	20
number of deaths resulting from adverse events	11	1	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal cancer			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Bile duct stent insertion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
General physical health deterioration			
subjects affected / exposed	7 / 45 (15.56%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 7	0 / 1	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Face oedema			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 45 (4.44%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Laryngeal stenosis			

subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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 distress			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Device deposit issue			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Liver function test increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Skull fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Coma			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Ileus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Dysphagia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			

subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Pneumoperitoneum			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Vomiting			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Oral cavity fistula			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Cholangitis			
subjects affected / exposed	5 / 45 (11.11%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			

subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Jaundice			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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			
Ureterolithiasis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	2 / 45 (4.44%)	0 / 20 (0.00%)	0 / 30 (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
Musculoskeletal and connective tissue disorders			
Crystal arthropathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteitis			

subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Arthralgia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 45 (2.22%)	4 / 20 (20.00%)	4 / 30 (13.33%)
occurrences causally related to treatment / all	0 / 1	0 / 7	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Pyelonephritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Septic shock			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Upper respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (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
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
Medical device site infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	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	HNSCC (IO naive)	GBM/AA	PDAC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)	29 / 30 (96.67%)	20 / 20 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritumoural oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Tumour pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Hypertension			
subjects affected / exposed	5 / 30 (16.67%)	8 / 30 (26.67%)	6 / 20 (30.00%)
occurrences (all)	7	16	13
Haematoma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Thrombophlebitis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Jugular vein thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 30 (13.33%)	5 / 30 (16.67%)	8 / 20 (40.00%)
occurrences (all)	5	10	18
Asthenia			
subjects affected / exposed	10 / 30 (33.33%)	10 / 30 (33.33%)	4 / 20 (20.00%)
occurrences (all)	17	14	6
Chest discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Generalised oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			

subjects affected / exposed	4 / 30 (13.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	9	0	1
Oedema peripheral			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	2 / 20 (10.00%)
occurrences (all)	2	1	2
Pain			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	2	2	0
Pyrexia			
subjects affected / exposed	6 / 30 (20.00%)	5 / 30 (16.67%)	7 / 20 (35.00%)
occurrences (all)	6	6	14
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Alveolitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	3 / 20 (15.00%)
occurrences (all)	0	4	3
Cough			
subjects affected / exposed	1 / 30 (3.33%)	3 / 30 (10.00%)	2 / 20 (10.00%)
occurrences (all)	1	4	3

Dyspnoea			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	7	0	1
Dyspnoea exertional			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Haemoptysis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Pneumonitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Pneumothorax			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Rales			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	2 / 20 (10.00%)
occurrences (all)	0	2	2
Psychiatric disorders			
Insomnia			

subjects affected / exposed	1 / 30 (3.33%)	3 / 30 (10.00%)	3 / 20 (15.00%)
occurrences (all)	1	3	3
Depression			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Confusional state			
subjects affected / exposed	1 / 30 (3.33%)	4 / 30 (13.33%)	0 / 20 (0.00%)
occurrences (all)	1	4	0
Anxiety			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	7 / 30 (23.33%)	3 / 30 (10.00%)	2 / 20 (10.00%)
occurrences (all)	14	12	5
Amylase increased			
subjects affected / exposed	0 / 30 (0.00%)	4 / 30 (13.33%)	0 / 20 (0.00%)
occurrences (all)	0	5	0
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 30 (16.67%)	4 / 30 (13.33%)	1 / 20 (5.00%)
occurrences (all)	10	12	2
Blood bilirubin increased			
subjects affected / exposed	1 / 30 (3.33%)	6 / 30 (20.00%)	0 / 20 (0.00%)
occurrences (all)	2	11	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	6	1	0
Heart rate increased			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
International normalised ratio increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Lipase increased			
subjects affected / exposed	1 / 30 (3.33%)	6 / 30 (20.00%)	0 / 20 (0.00%)
occurrences (all)	1	13	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	1	12	0
Neutrophil count decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Neutrophil count increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	2 / 30 (6.67%)	3 / 30 (10.00%)	0 / 20 (0.00%)
occurrences (all)	2	4	0
Weight decreased			
subjects affected / exposed	6 / 30 (20.00%)	1 / 30 (3.33%)	2 / 20 (10.00%)
occurrences (all)	11	2	3
White blood cell count decreased			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	4	1
White blood cell count increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Platelet count increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
General physical condition abnormal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Subcutaneous haematoma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wound secretion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Stoma site pain			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pericarditis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1

Nervous system disorders			
Hyperaesthesia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Hemianopia homonymous			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 30 (3.33%)	6 / 30 (20.00%)	2 / 20 (10.00%)
occurrences (all)	2	13	2
Epilepsy			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	4	0
Dysgeusia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	4	0
Apraxia			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Aphasia			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Hypoaesthesia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	4	0
Neuropathy peripheral			

subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Balance disorder			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Brain oedema			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Speech disorder			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	1 / 20 (5.00%)
occurrences (all)	1	3	1
Seizure			
subjects affected / exposed	0 / 30 (0.00%)	5 / 30 (16.67%)	1 / 20 (5.00%)
occurrences (all)	0	5	1
Presyncope			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 30 (33.33%)	2 / 30 (6.67%)	6 / 20 (30.00%)
occurrences (all)	24	3	16
Eosinophilia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Leukocytosis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Neutrophilia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	1	2	1

Thrombocytopenia			
subjects affected / exposed	1 / 30 (3.33%)	5 / 30 (16.67%)	3 / 20 (15.00%)
occurrences (all)	4	9	6
Lymphopenia			
subjects affected / exposed	2 / 30 (6.67%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	3	2	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Aptyalism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	4 / 30 (13.33%)	7 / 20 (35.00%)
occurrences (all)	0	4	13
Abdominal pain upper			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	2 / 20 (10.00%)
occurrences (all)	1	1	3
Aphthous ulcer			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Ascites			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	6
Cheilitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	7 / 30 (23.33%)	11 / 30 (36.67%)	7 / 20 (35.00%)
occurrences (all)	8	15	9
Diarrhoea			
subjects affected / exposed	7 / 30 (23.33%)	6 / 30 (20.00%)	3 / 20 (15.00%)
occurrences (all)	10	11	5
Dry mouth			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Dysphagia			
subjects affected / exposed	4 / 30 (13.33%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	4	2	0
Oral discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Glossitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Large intestine perforation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	3 / 30 (10.00%)	4 / 30 (13.33%)	7 / 20 (35.00%)
occurrences (all)	3	4	10
Odynophagia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Eructation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oral pain			

subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	4	0	0
Pancreatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Periodontal disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	5 / 30 (16.67%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	16	1	4
Toothache			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	5 / 20 (25.00%)
occurrences (all)	2	0	8
Subileus			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oral cavity fistula			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	4	0	0
Anal inflammation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Cholestasis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Hepatic function abnormal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Hyperbilirubinaemia			
subjects affected / exposed	1 / 30 (3.33%)	5 / 30 (16.67%)	1 / 20 (5.00%)
occurrences (all)	1	9	3
Jaundice			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Hepatic cytolysis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Bile duct stenosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Drug-induced liver injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Decubitus ulcer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	3 / 30 (10.00%)	0 / 30 (0.00%)	2 / 20 (10.00%)
occurrences (all)	3	0	2
Erythema			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	8 / 30 (26.67%)	8 / 30 (26.67%)	5 / 20 (25.00%)
occurrences (all)	11	18	16
Skin toxicity			

subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Palmoplantar keratoderma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	2
Psoriasis			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Purpura			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	6 / 30 (20.00%)	5 / 30 (16.67%)	8 / 20 (40.00%)
occurrences (all)	7	8	14
Rash maculo-papular			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Skin exfoliation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Scar pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	2 / 30 (6.67%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	5	4	0

Hydronephrosis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Haematuria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Glycosuria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	5 / 30 (16.67%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	6	1	1
Hypopituitarism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Hypothyroidism			
subjects affected / exposed	3 / 30 (10.00%)	3 / 30 (10.00%)	3 / 20 (15.00%)
occurrences (all)	6	3	3
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	2 / 20 (10.00%)
occurrences (all)	0	1	3
Neck pain			
subjects affected / exposed	3 / 30 (10.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			

subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	4	0
Muscle spasms			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	4
Back pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Arthritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	1 / 30 (3.33%)	3 / 30 (10.00%)	1 / 20 (5.00%)
occurrences (all)	1	3	1
Amyotrophy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Muscle atrophy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sarcopenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Bronchitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vascular device infection			
subjects affected / exposed	3 / 30 (10.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0

Paronychia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	8	0	0
Pneumonia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Skin infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Oral fungal infection			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Acinetobacter bacteraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	3 / 20 (15.00%)
occurrences (all)	1	0	6
Electrolyte imbalance			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Hyperglycaemia			

subjects affected / exposed	0 / 30 (0.00%)	6 / 30 (20.00%)	3 / 20 (15.00%)
occurrences (all)	0	10	3
Hyperkalaemia			
subjects affected / exposed	2 / 30 (6.67%)	2 / 30 (6.67%)	0 / 20 (0.00%)
occurrences (all)	2	2	0
Hypoalbuminaemia			
subjects affected / exposed	5 / 30 (16.67%)	1 / 30 (3.33%)	5 / 20 (25.00%)
occurrences (all)	6	1	8
Hypocalcaemia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	8 / 30 (26.67%)	6 / 30 (20.00%)	7 / 20 (35.00%)
occurrences (all)	8	10	10
Hyponatraemia			
subjects affected / exposed	3 / 30 (10.00%)	2 / 30 (6.67%)	1 / 20 (5.00%)
occurrences (all)	3	3	1
Hypophosphataemia			
subjects affected / exposed	3 / 30 (10.00%)	1 / 30 (3.33%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Refeeding syndrome			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Cell death			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	4 / 30 (13.33%)	1 / 30 (3.33%)	1 / 20 (5.00%)
occurrences (all)	9	3	1
Type 2 diabetes mellitus			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Steroid diabetes			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Biliary Tract Cancer (BTC)	HNSCC (IO treated)	ESCC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 45 (100.00%)	20 / 20 (100.00%)	30 / 30 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritumoural oedema			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cancer pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Tumour pain			
subjects affected / exposed	2 / 45 (4.44%)	3 / 20 (15.00%)	1 / 30 (3.33%)
occurrences (all)	2	10	1
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 45 (4.44%)	2 / 20 (10.00%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Hypertension			
subjects affected / exposed	11 / 45 (24.44%)	7 / 20 (35.00%)	4 / 30 (13.33%)
occurrences (all)	25	12	7
Haematoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Jugular vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 45 (42.22%)	7 / 20 (35.00%)	9 / 30 (30.00%)
occurrences (all)	43	16	19
Asthenia			
subjects affected / exposed	12 / 45 (26.67%)	2 / 20 (10.00%)	7 / 30 (23.33%)
occurrences (all)	36	6	24
Chest discomfort			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Chest pain			
subjects affected / exposed	2 / 45 (4.44%)	0 / 20 (0.00%)	4 / 30 (13.33%)
occurrences (all)	2	0	5
Chills			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	4
Generalised oedema			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Impaired healing			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Mucosal inflammation			

subjects affected / exposed	5 / 45 (11.11%)	1 / 20 (5.00%)	4 / 30 (13.33%)
occurrences (all)	8	2	14
Oedema peripheral			
subjects affected / exposed	4 / 45 (8.89%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	6	1	2
Pain			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	4	1	0
Pyrexia			
subjects affected / exposed	17 / 45 (37.78%)	6 / 20 (30.00%)	12 / 30 (40.00%)
occurrences (all)	43	10	20
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pelvic pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Alveolitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	9 / 45 (20.00%)	2 / 20 (10.00%)	5 / 30 (16.67%)
occurrences (all)	9	2	6
Cough			
subjects affected / exposed	4 / 45 (8.89%)	2 / 20 (10.00%)	4 / 30 (13.33%)
occurrences (all)	4	2	5

Dyspnoea			
subjects affected / exposed	4 / 45 (8.89%)	2 / 20 (10.00%)	5 / 30 (16.67%)
occurrences (all)	6	2	7
Dyspnoea exertional			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences (all)	1	1	3
Epistaxis			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	3	0	0
Haemoptysis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Pleural effusion			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Pneumonitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	5 / 30 (16.67%)
occurrences (all)	0	0	10
Pneumothorax			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Rales			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Wheezing			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Psychiatric disorders			
Insomnia			

subjects affected / exposed	7 / 45 (15.56%)	4 / 20 (20.00%)	2 / 30 (6.67%)
occurrences (all)	8	4	2
Depression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 45 (4.44%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	4	1	1
Alanine aminotransferase increased			
subjects affected / exposed	4 / 45 (8.89%)	2 / 20 (10.00%)	4 / 30 (13.33%)
occurrences (all)	7	8	10
Amylase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	3 / 30 (10.00%)
occurrences (all)	0	0	4
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 45 (11.11%)	2 / 20 (10.00%)	3 / 30 (10.00%)
occurrences (all)	9	6	6
Blood bilirubin increased			
subjects affected / exposed	6 / 45 (13.33%)	2 / 20 (10.00%)	1 / 30 (3.33%)
occurrences (all)	10	2	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 45 (0.00%)	2 / 20 (10.00%)	0 / 30 (0.00%)
occurrences (all)	0	3	0
Heart rate increased			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	2 / 45 (4.44%)	1 / 20 (5.00%)	3 / 30 (10.00%)
occurrences (all)	4	1	6
Lymphocyte count decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	3	0	1
Neutrophil count increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	3 / 45 (6.67%)	2 / 20 (10.00%)	3 / 30 (10.00%)
occurrences (all)	5	2	5
Weight decreased			
subjects affected / exposed	5 / 45 (11.11%)	3 / 20 (15.00%)	6 / 30 (20.00%)
occurrences (all)	6	3	7
White blood cell count decreased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
General physical condition abnormal			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	2	0

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Subcutaneous haematoma			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Wound dehiscence			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Wound secretion			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Stoma site pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	3	0	2
Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	3 / 20 (15.00%)	2 / 30 (6.67%)
occurrences (all)	0	3	2
Pericarditis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	3	0	1

Nervous system disorders			
Hyperaesthesia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hemiparesis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hemianopia homonymous			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 45 (6.67%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Epilepsy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	5	0	2
Dizziness			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Apraxia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Memory impairment			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			

subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Balance disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 45 (0.00%)	3 / 20 (15.00%)	0 / 30 (0.00%)
occurrences (all)	0	3	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 45 (15.56%)	3 / 20 (15.00%)	5 / 30 (16.67%)
occurrences (all)	8	7	12
Eosinophilia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Thrombocytopenia			
subjects affected / exposed	9 / 45 (20.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	11	0	1
Lymphopenia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Aptyalism			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	2 / 45 (4.44%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences (all)	2	1	2
Abdominal pain			
subjects affected / exposed	11 / 45 (24.44%)	1 / 20 (5.00%)	4 / 30 (13.33%)
occurrences (all)	16	2	5
Abdominal pain upper			
subjects affected / exposed	8 / 45 (17.78%)	1 / 20 (5.00%)	5 / 30 (16.67%)
occurrences (all)	12	1	5
Aphthous ulcer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Constipation			

subjects affected / exposed	15 / 45 (33.33%)	8 / 20 (40.00%)	7 / 30 (23.33%)
occurrences (all)	20	10	10
Diarrhoea			
subjects affected / exposed	17 / 45 (37.78%)	3 / 20 (15.00%)	11 / 30 (36.67%)
occurrences (all)	31	6	25
Dry mouth			
subjects affected / exposed	3 / 45 (6.67%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences (all)	5	1	2
Dysphagia			
subjects affected / exposed	3 / 45 (6.67%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	5	1	0
Oral discomfort			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	4 / 30 (13.33%)
occurrences (all)	2	0	4
Glossitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Large intestine perforation			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Mouth haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	14 / 45 (31.11%)	2 / 20 (10.00%)	5 / 30 (16.67%)
occurrences (all)	19	2	6
Odynophagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Eructation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oral pain			

subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Pancreatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	7
Periodontal disease			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	3 / 45 (6.67%)	3 / 20 (15.00%)	3 / 30 (10.00%)
occurrences (all)	4	7	8
Toothache			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	8 / 45 (17.78%)	1 / 20 (5.00%)	3 / 30 (10.00%)
occurrences (all)	9	1	3
Subileus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oral cavity fistula			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	8	0	0
Cholestasis			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	3	0	1
Hepatic function abnormal			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	4

Hyperbilirubinaemia			
subjects affected / exposed	4 / 45 (8.89%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	9	0	0
Jaundice			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Hepatic cytolysis			
subjects affected / exposed	2 / 45 (4.44%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	2
Bile duct stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Drug-induced liver injury			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	5	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 45 (4.44%)	3 / 20 (15.00%)	1 / 30 (3.33%)
occurrences (all)	2	3	1
Decubitus ulcer			
subjects affected / exposed	2 / 45 (4.44%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Dry skin			
subjects affected / exposed	6 / 45 (13.33%)	1 / 20 (5.00%)	3 / 30 (10.00%)
occurrences (all)	6	1	3
Erythema			
subjects affected / exposed	2 / 45 (4.44%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	15 / 45 (33.33%)	9 / 20 (45.00%)	22 / 30 (73.33%)
occurrences (all)	37	28	45
Skin toxicity			

subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Palmoplantar keratoderma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	5 / 45 (11.11%)	2 / 20 (10.00%)	3 / 30 (10.00%)
occurrences (all)	5	3	4
Psoriasis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	10 / 45 (22.22%)	2 / 20 (10.00%)	14 / 30 (46.67%)
occurrences (all)	22	2	23
Rash maculo-papular			
subjects affected / exposed	5 / 45 (11.11%)	3 / 20 (15.00%)	0 / 30 (0.00%)
occurrences (all)	8	3	0
Skin exfoliation			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Scar pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	6	0	1
Urinary retention			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 45 (0.00%)	4 / 20 (20.00%)	1 / 30 (3.33%)
occurrences (all)	0	4	2

Hydronephrosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Glycosuria			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	6 / 45 (13.33%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences (all)	6	1	2
Hypopituitarism			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	6	0	0
Hypothyroidism			
subjects affected / exposed	5 / 45 (11.11%)	5 / 20 (25.00%)	8 / 30 (26.67%)
occurrences (all)	7	6	10
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	6	0	2
Neck pain			
subjects affected / exposed	0 / 45 (0.00%)	4 / 20 (20.00%)	1 / 30 (3.33%)
occurrences (all)	0	4	1
Myalgia			
subjects affected / exposed	5 / 45 (11.11%)	1 / 20 (5.00%)	4 / 30 (13.33%)
occurrences (all)	8	1	4
Musculoskeletal pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	7 / 45 (15.56%)	2 / 20 (10.00%)	1 / 30 (3.33%)
occurrences (all)	10	2	2
Back pain			
subjects affected / exposed	10 / 45 (22.22%)	0 / 20 (0.00%)	3 / 30 (10.00%)
occurrences (all)	12	0	4
Arthritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	5	0	0
Arthralgia			
subjects affected / exposed	6 / 45 (13.33%)	1 / 20 (5.00%)	5 / 30 (16.67%)
occurrences (all)	8	1	6
Amyotrophy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Sarcopenia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	2 / 45 (4.44%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Conjunctivitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Vascular device infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Paronychia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	0	1	2
Pneumonia			
subjects affected / exposed	2 / 45 (4.44%)	2 / 20 (10.00%)	4 / 30 (13.33%)
occurrences (all)	3	2	8
Skin infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	3 / 45 (6.67%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	4	1	2
Oral fungal infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Acinetobacter bacteraemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	4 / 45 (8.89%)	0 / 20 (0.00%)	3 / 30 (10.00%)
occurrences (all)	4	0	4
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Electrolyte imbalance			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	4
Hyperglycaemia			

subjects affected / exposed	1 / 45 (2.22%)	0 / 20 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	2
Hyperkalaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	5 / 45 (11.11%)	0 / 20 (0.00%)	4 / 30 (13.33%)
occurrences (all)	10	0	9
Hypocalcaemia			
subjects affected / exposed	4 / 45 (8.89%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	4	2	2
Hypoglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	14 / 45 (31.11%)	9 / 20 (45.00%)	11 / 30 (36.67%)
occurrences (all)	25	16	26
Hyponatraemia			
subjects affected / exposed	4 / 45 (8.89%)	0 / 20 (0.00%)	3 / 30 (10.00%)
occurrences (all)	8	0	6
Hypophosphataemia			
subjects affected / exposed	5 / 45 (11.11%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	5	1	1
Refeeding syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Cell death			
subjects affected / exposed	3 / 45 (6.67%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	5	0	0
Malnutrition			
subjects affected / exposed	1 / 45 (2.22%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Hypokalaemia			
subjects affected / exposed	5 / 45 (11.11%)	1 / 20 (5.00%)	4 / 30 (13.33%)
occurrences (all)	6	1	4
Type 2 diabetes mellitus			

subjects affected / exposed	0 / 45 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Steroid diabetes			
subjects affected / exposed	0 / 45 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2021	Global amendment 01 introduced the following changes: The Schedule of Activities were updated to more clearly define the timing of the CT/MRIs and the collection of AEs during follow-up. Additional wording on trial stop was added. Additional inclusion criteria for Stage 2 participants were added to clarify previous therapies allowed. Updated guidance regarding male contraception based on the updated nivolumab Investigator's Brochure. Dose modification tables for regorafenib were updated. Nivolumab toxicity management guidelines updated to reflect incorporation of CTCAE v.5.0, as well as changes consistent with updated nivolumab immune-mediated AE management algorithms. Recommended dose modification for nivolumab updated according to the newest management algorithms for studies, under CTCAE v5.0. AE management algorithms were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported