



## Clinical trial results:

**An open-label, Phase II, platform trial evaluating safety and efficacy of multiple ezabenlimab anti-PD-1 based combination regimens in PD-(L)1 naïve and PD-(L)1 pretreated patient populations with advanced and/or metastatic solid tumours who have had at least one line of systemic therapy**

### Summary

EudraCT number	2018-002344-81
Trial protocol	GB
Global end of trial date	03 December 2024

### Results information

Result version number	v1 (current)
This version publication date	19 December 2025
First version publication date	19 December 2025

### Trial information

#### Trial identification

Sponsor protocol code	1381-0009
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03697304
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintrriage.rdg@boehringer-ingelheim.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	17 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2024
Global end of trial reached?	Yes
Global end of trial date	03 December 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this research trial was to evaluate patient clinical response to ezabenlimab (BI 754091) in combination with combination partners presented in individual Modules.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. If a subject continued to take trial medication, close monitoring was adhered to and all adverse events recorded. Rules were implemented in all trials whereby doses would be reduced if required. Thereafter, if further events were reported, the subject would be withdrawn from the trial. Symptomatic treatment of tumor associated symptoms were allowed throughout.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	United Kingdom: 64
Country: Number of subjects enrolled	United States: 236
Worldwide total number of subjects	323
EEA total number of subjects	0

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)	163
From 65 to 84 years	151
85 years and over	9

## Subject disposition

### Recruitment

Recruitment details:

Platform trial evaluating the safety and efficacy of different ezabenlimab (BI 754091) treatment regimens on patients with different types of advanced/metastatic tumors: module C evaluated ezabenlimab in combination with BI 836880, and module A evaluated ezabenlimab in combination with BI 754111.

### Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

### Period 1

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

Blinding implementation details:

This trial was conducted open-label in both treatment modules.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Module C, Cohort 1: GEC patients

Arm description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma (GEC) with at least one prior systemic treatment, who failed standard therapy, for whom no further effective options existed, and with no prior PD-1 or PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, in the form of i.v. infusion, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	Ezabenlimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Concentrate for solution for infusion, Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

<b>Arm title</b>	Module C, Cohort 2: 2ary resistance patients
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Arm description:

Patients with any advanced or metastatic solid tumor (excluding non-squamous lung cancer, non-small-cell lung cancer, and melanoma) who had received prior anti-PD-1- or anti-PD-L1-based treatment and progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 4 months) and minimum treatment duration of 2 months on the previous anti-PD-1- or anti-PD-L1-based treatment without progressive disease, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880 on Day 1, intravenously, on Day1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	Ezabenlimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Concentrate for solution for infusion, Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

<b>Arm title</b>	Module C, Cohort 3: 1ary resistance patients
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Arm description:

Patients with select advanced or metastatic solid tumors with prior anti-PD-1- or anti-PD-L1-based treatment without achieving benefit ( stable disease duration of less than 4 months or progressive disease in less than 4 months while on treatment), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	Ezabenlimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Solution for infusion, Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

<b>Arm title</b>	Module C, Cohort 4: CRC patients
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Arm description:

Patients with locally advanced, unresectable or metastatic second-line or greater, microsatellite-stable colorectal cancer (CRC) without prior anti-PD-1- or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	Ezabenlimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Concentrate for solution for infusion, Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.	
<b>Arm title</b>	Module C, Cohort 5: EC patients

**Arm description:**

Patients with advanced endometrial carcinoma (EC), excluding microsatellite instability-high or mismatch repair deficient types, who progressed following one line of chemotherapy, were not eligible for curative surgery or radiation, and had not been previously treated with anti-PD-1- or anti-PD-L1-based therapies, were administered 240 mg of ezabenzimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

**Dosage and administration details:**

720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	Ezabenzimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Concentrate for solution for infusion, Solution for infusion
Routes of administration	Intravenous use

**Dosage and administration details:**

240 mg of ezabenzimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

<b>Arm title</b>	Module A, Cohort 1: GEC patients
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**Arm description:**

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma, who received prior anti-PD-1 or anti-PD-L1-based treatment, were administered 240 mg of ezabenzimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	BI 754111
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

**Dosage and administration details:**

600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	Ezabenzimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

**Dosage and administration details:**

240 mg of ezabenzimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

<b>Arm title</b>	Module A, Cohort 2: 2ary resistance patients
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**Arm description:**

Patients with any advanced or metastatic solid tumors who had been previously treated with anti-PD-1

or anti-PD-L1-based therapies, and who progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 6 months) and minimum treatment duration of 2 months without experiencing disease progression, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	BI 754111
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	Ezabenlimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

<b>Arm title</b>	Module A, Cohort 3: 1ary resistance patients
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Arm description:

Patients with select advanced or metastatic solid tumor types, who have been previously treated with previous anti-PD-1 or anti-PD-L1-based therapies without achieving benefit (stable disease for less than 6 months or progressive disease in less than 6 months), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Arm type	Experimental
Investigational medicinal product name	Ezabenlimab
Investigational medicinal product code	
Other name	BI 754091
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles.

Investigational medicinal product name	BI 754111
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Number of subjects in period 1 <sup>[1]</sup>	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients
Started	28	30	28
Completed	0	0	0
Not completed	28	30	28
Adverse event, serious fatal	1	2	4

Physician decision	-	2	-
Consent withdrawal	1	2	-
Adverse event, non-fatal	4	4	2
Progressive disease	21	20	22
Other than listed	1	-	-

<b>Number of subjects in period 1<sup>[1]</sup></b>	Module C, Cohort 4: CRC patients	Module C, Cohort 5: EC patients	Module A, Cohort 1: GEC patients
Started	30	18	2
Completed	0	0	0
Not completed	30	18	2
Adverse event, serious fatal	-	1	-
Physician decision	-	-	-
Consent withdrawal	4	4	-
Adverse event, non-fatal	4	4	1
Progressive disease	22	8	1
Other than listed	-	1	-

<b>Number of subjects in period 1<sup>[1]</sup></b>	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients
Started	33	42
Completed	0	0
Not completed	33	42
Adverse event, serious fatal	1	-
Physician decision	1	1
Consent withdrawal	1	1
Adverse event, non-fatal	5	3
Progressive disease	25	37
Other than listed	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: From the 323 patients screened, 211 started treatment.

## Baseline characteristics

### Reporting groups

Reporting group title	Module C, Cohort 1: GEC patients
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#### Reporting group description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma (GEC) with at least one prior systemic treatment, who failed standard therapy, for whom no further effective options existed, and with no prior PD-1 or PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, in the form of i.v. infusion, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 2: 2ary resistance patients
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#### Reporting group description:

Patients with any advanced or metastatic solid tumor (excluding non-squamous lung cancer, non-small-cell lung cancer, and melanoma) who had received prior anti-PD-1- or anti-PD-L1-based treatment and progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 4 months) and minimum treatment duration of 2 months on the previous anti-PD-1- or anti-PD-L1-based treatment without progressive disease, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880 on Day 1, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 3: 1ary resistance patients
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#### Reporting group description:

Patients with select advanced or metastatic solid tumors with prior anti-PD-1- or anti-PD-L1-based treatment without achieving benefit (stable disease duration of less than 4 months or progressive disease in less than 4 months while on treatment), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 4: CRC patients
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#### Reporting group description:

Patients with locally advanced, unresectable or metastatic second-line or greater, microsatellite-stable colorectal cancer (CRC) without prior anti-PD-1- or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 5: EC patients
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#### Reporting group description:

Patients with advanced endometrial carcinoma (EC), excluding microsatellite instability-high or mismatch repair deficient types, who progressed following one line of chemotherapy, were not eligible for curative surgery or radiation, and had not been previously treated with anti-PD-1- or anti-PD-L1-based therapies, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 1: GEC patients
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#### Reporting group description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma, who received prior anti-PD-1 or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 2: 2ary resistance patients
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#### Reporting group description:

Patients with any advanced or metastatic solid tumors who had been previously treated with anti-PD-1 or anti-PD-L1-based therapies, and who progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 6 months) and minimum treatment duration of 2 months without experiencing disease progression, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 3: 1ary resistance patients
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#### Reporting group description:

Patients with select advanced or metastatic solid tumor types, who have been previously treated with previous anti-PD-1 or anti-PD-L1-based therapies without achieving benefit (stable disease for less than 6 months or progressive disease in less than 6 months), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients
Number of subjects	28	30	28
Age categorical			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	23	14	19
From 65-84 years	5	15	8
85 years and over	0	1	1
Age Continuous			
Treated set: all patients treated with at least one dose of trial medications.			
Units: years			
arithmetic mean	56.5	63.2	60.6
standard deviation	± 10.7	± 13.3	± 10.9
Sex: Female, Male			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Participants			
Female	8	10	7
Male	20	20	21
Race/Ethnicity, Customized			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	2
Black or African American	0	0	1
Other	20	12	5
White	7	16	20
Ethnicity (NIH/OMB)			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
Hispanic or Latino	0	2	1
Not Hispanic or Latino	8	16	22
Unknown or Not Reported	20	12	5

Reporting group values	Module C, Cohort 4: CRC patients	Module C, Cohort 5: EC patients	Module A, Cohort 1: GEC patients
Number of subjects	30	18	2
Age categorical			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
In utero	0	0	0

Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	4	1
From 65-84 years	9	14	1
85 years and over	1	0	0
Age Continuous			
Treated set: all patients treated with at least one dose of trial medications.			
Units: years			
arithmetic mean	57.7	67.8	61.0
standard deviation	± 13.5	± 11.3	± 14.1
Sex: Female, Male			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Participants			
Female	13	18	1
Male	17	0	1
Race/Ethnicity, Customized			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	2	2	0
Black or African American	1	2	0
Other	1	1	0
White	25	13	2
Ethnicity (NIH/OMB)			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
Hispanic or Latino	3	0	0
Not Hispanic or Latino	27	17	2
Unknown or Not Reported	0	1	0

Reporting group values	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	Total
Number of subjects	33	42	211
Age categorical			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	18	109
From 65-84 years	22	23	97
85 years and over	1	1	5

Age Continuous			
Treated set: all patients treated with at least one dose of trial medications.			
Units: years			
arithmetic mean	68.6	64.9	
standard deviation	± 7.2	± 10.4	-
Sex: Female, Male			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Participants			
Female	14	22	93
Male	19	20	118
Race/Ethnicity, Customized			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
American Indian or Alaska Native	1	0	2
Asian	0	1	10
Black or African American	4	2	10
Other	0	3	42
White	28	36	147
Ethnicity (NIH/OMB)			
Treated set: all patients treated with at least one dose of trial medications.			
Units: Subjects			
Hispanic or Latino	0	4	10
Not Hispanic or Latino	33	37	162
Unknown or Not Reported	0	1	39

## End points

### End points reporting groups

Reporting group title	Module C, Cohort 1: GEC patients
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#### Reporting group description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma (GEC) with at least one prior systemic treatment, who failed standard therapy, for whom no further effective options existed, and with no prior PD-1 or PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, in the form of i.v. infusion, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 2: 2ary resistance patients
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#### Reporting group description:

Patients with any advanced or metastatic solid tumor (excluding non-squamous lung cancer, non-small-cell lung cancer, and melanoma) who had received prior anti-PD-1- or anti-PD-L1-based treatment and progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 4 months) and minimum treatment duration of 2 months on the previous anti-PD-1- or anti-PD-L1-based treatment without progressive disease, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880 on Day 1, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 3: 1ary resistance patients
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#### Reporting group description:

Patients with select advanced or metastatic solid tumors with prior anti-PD-1- or anti-PD-L1-based treatment without achieving benefit (stable disease duration of less than 4 months or progressive disease in less than 4 months while on treatment), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 4: CRC patients
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#### Reporting group description:

Patients with locally advanced, unresectable or metastatic second-line or greater, microsatellite-stable colorectal cancer (CRC) without prior anti-PD-1- or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 5: EC patients
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#### Reporting group description:

Patients with advanced endometrial carcinoma (EC), excluding microsatellite instability-high or mismatch repair deficient types, who progressed following one line of chemotherapy, were not eligible for curative surgery or radiation, and had not been previously treated with anti-PD-1- or anti-PD-L1-based therapies, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 1: GEC patients
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#### Reporting group description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma, who received prior anti-PD-1 or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 2: 2ary resistance patients
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#### Reporting group description:

Patients with any advanced or metastatic solid tumors who had been previously treated with anti-PD-1 or anti-PD-L1-based therapies, and who progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 6 months) and minimum treatment duration of 2 months without experiencing disease progression, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 3: 1ary resistance patients
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#### Reporting group description:

Patients with select advanced or metastatic solid tumor types, who have been previously treated with previous anti-PD-1 or anti-PD-L1-based therapies without achieving benefit (stable disease for less than 6 months or progressive disease in less than 6 months), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

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**Primary: [Module C] Objective response (OR)**

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End point title	[Module C] Objective response (OR) <sup>[1][2]</sup>
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End point description:

Confirmed objective response (OR), defined as the percentage of participants with best overall response of complete response (CR) or partial response (PR), assessed by the investigator according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). Complete response (CR) was defined as the disappearance of all target lesions and partial response (PR) was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference.

Treated set of the module C: all patients treated with at least one dose of trial medications.

End point type	Primary
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End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 188.3 weeks.

Notes:

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

Justification: No further statistical analysis was defined for the primary endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module C.

End point values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients	Module C, Cohort 4: CRC patients
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	28	30
Units: Percentage of participants				
number (confidence interval 95%)	14.3 (4.0 to 32.7)	23.3 (9.9 to 42.3)	0.0 (0.0 to 12.3)	3.3 (0.1 to 17.2)

End point values	Module C, Cohort 5: EC patients			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Percentage of participants				
number (confidence interval 95%)	44.4 (21.5 to 69.2)			

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: [Module C] Objective response (OR) - Bayesian hierarchical model**

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End point title	[Module C] Objective response (OR) - Bayesian hierarchical model <sup>[3][4]</sup>
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**End point description:**

Confirmed objective response (OR), defined as the objective response rate (ORR) of participants with best overall response of complete response (CR) or partial response (PR), assessed by the investigator according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). Complete response (CR) was defined as the disappearance of all target lesions and partial response (PR) was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference. The estimated objective response rate is presented by the posterior medians of the Bayesian hierarchical model and by the correspondent credible intervals. The median is actually the posterior median and the confidence interval is actually the credible interval.

Treated set of the module C: all patients treated with at least one dose of trial medications.

End point type	Primary
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**End point timeframe:**

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 188.3 weeks.

**Notes:**

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

Justification: No further statistical analysis was defined for the primary endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module C.

End point values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients	Module C, Cohort 4: CRC patients
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	28	30
Units: Estimated ORR				
median (confidence interval 97.5%)	11.95 (3.72 to 25.31)	20.21 (9.61 to 36.1)	2.75 (0.17 to 10.15)	5.26 (0.83 to 14.87)

End point values	Module C, Cohort 5: EC patients			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Estimated ORR				
median (confidence interval 97.5%)	36.13 (17.15 to 59.63)			

**Statistical analyses**

No statistical analyses for this end point

**Primary: [Module A] Objective response (OR)**

End point title	[Module A] Objective response (OR) <sup>[5][6]</sup>
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**End point description:**

Confirmed objective response (OR), defined as the percentage of participants with best overall response of complete response (CR) or partial response (PR), assessed by the investigator according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). Complete response (CR) was defined as the disappearance of all target lesions and partial response (PR) was defined as decrease of at least

30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference.

Treated set of the module A: all patients treated with at least one dose of trial medications.

End point type	Primary
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End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 152.4 weeks.

Notes:

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

Justification: No further statistical analysis was defined for the primary endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module A.

End point values	Module A, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	33	42	
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 84.2)	6.1 (0.7 to 20.2)	9.5 (2.7 to 22.6)	

## Statistical analyses

No statistical analyses for this end point

## Primary: [Module A] Objective response (OR) - Bayesian hierarchical model

End point title	[Module A] Objective response (OR) - Bayesian hierarchical model <sup>[7][8]</sup>
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End point description:

Confirmed objective response (OR), defined as the objective response rate (ORR) of participants with best overall response of complete response (CR) or partial response (PR), assessed by the investigator according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). Complete response (CR) was defined as the disappearance of all target lesions and partial response (PR) was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference. The estimated objective response rate is presented by the posterior medians of the Bayesian hierarchical model and by the correspondent credible intervals. The median is actually the posterior median and the confidence interval is actually the credible interval.

Treated set of the module A: all patients treated with at least one dose of trial medications.

End point type	Primary
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End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 152.4 weeks.

Notes:

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

Justification: No further statistical analysis was defined for the primary endpoint.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module A.

End point values	Module A, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	33	42	
Units: Estimated ORR				
median (confidence interval 97.5%)	9.69 (0.88 to 35.04)	8.23 (2.12 to 18.91)	6.67 (2.3 to 16.02)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: [Module C] Duration of response (DoR)

End point title	[Module C] Duration of response (DoR) <sup>[9]</sup>
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End point description:

Duration of response (DoR) was defined as the time from first documented complete response (CR) or partial response (PR) (RECIST v1.1) among patients with objective response (OR), according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). Complete response (CR) was defined as the disappearance of all target lesions and partial response (PR) was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference. DoR parameters were calculated based on Kaplan-Meier estimation.

Treated set of the module C: all patients treated with at least one dose of trial medications. Only patients that had an OR were included in the analysis.

End point type	Secondary
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End point timeframe:

From first documented CR or PR (RECIST v1.1) until the earlier of disease progression or death. Up to 174.6 weeks.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was analyzed on Module C.

End point values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients	Module C, Cohort 4: CRC patients
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	2	2
Units: Weeks				
median (full range (min-max))	105.95 (12.3 to 174.6)	30.90 (6.4 to 81.3)	8.50 (8.4 to 8.6)	25.00 (12.1 to 37.9)

End point values	Module C, Cohort 5: EC patients			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Weeks				
median (full range (min-max))	47.30 (6.1 to 143.1)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: [Module C] Disease control (DC)

End point title	[Module C] Disease control (DC) <sup>[10]</sup>
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End point description:

Disease Control (DC) defined as the percentage of patients with best overall response of complete response (CR), partial response (PR), or stable disease (SD), assessed by the investigator according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). CR was defined as the disappearance of all target lesions, PR was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study, and PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study.

Treated set of the module C: all patients treated with at least one dose of trial medications.

End point type	Secondary
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End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 188.3 weeks.

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module C.

End point values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients	Module C, Cohort 4: CRC patients
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	28	30
Units: Percentage of participants				
number (confidence interval 95%)	57.1 (37.2 to 75.5)	73.3 (54.1 to 87.7)	42.9 (24.5 to 62.8)	56.7 (37.4 to 74.5)

End point values	Module C, Cohort 5: EC patients			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Percentage of participants				
number (confidence interval 95%)	77.8 (52.4 to 93.6)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: [Module C] Disease control (DC) - bayesian hierarchical model (BHM)

End point title	[Module C] Disease control (DC) - bayesian hierarchical model (BHM) <sup>[11]</sup>
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End point description:

Defined as the disease control rate (DCR) of participants with best overall response of CR, PR, or stable disease (SD), assessed by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions, PR as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference, SD as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study, and PD as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. The estimated DCR is presented by the posterior medians of the BHM and by the correspondent credible intervals. The median is actually the posterior median and the confidence interval is actually the credible interval.

Treated set of the module C: all patients treated with at least one dose of trial medications.

End point type	Secondary
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End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 188.3 weeks.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module C.

End point values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients	Module C, Cohort 4: CRC patients
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	28	30
Units: Estimated DCR				
median (confidence interval 97.5%)	64.7 (45.4 to 77.8)	70.4 (56.7 to 83.8)	44.7 (29.1 to 59.8)	57.5 (42.1 to 71.5)

End point values	Module C, Cohort 5: EC patients			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Estimated DCR				
median (confidence interval 97.5%)	82.2 (66.7 to 96.1)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: [Module C] Progression-free survival (PFS)

End point title	[Module C] Progression-free survival (PFS) <sup>[12]</sup>
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End point description:

Progression-free survival (PFS) was defined as the time from first treatment administration until progressive disease (PD), according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1), or death from any cause, whichever occurred earlier. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. PFS parameters were calculated based on Kaplan-Meier estimation.

Treated set of the module C: all patients treated with at least one dose of trial medications.

End point type	Secondary
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End point timeframe:

From first drug administration until PD or death, whichever occurred earlier. Up to approximately 186.1 weeks.

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module C.

End point values	Module C, Cohort 1: GEC patients	Module C, Cohort 2: 2ary resistance patients	Module C, Cohort 3: 1ary resistance patients	Module C, Cohort 4: CRC patients
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	28	30
Units: Weeks				
median (confidence interval 95%)	13.4 (6.1 to 33.7)	29.1 (13.0 to 48.7)	6.1 (5.7 to 12.1)	12.6 (6.1 to 23.6)

End point values	Module C, Cohort 5: EC patients			
Subject group type	Reporting group			
Number of subjects analysed	18 <sup>[13]</sup>			
Units: Weeks				
median (confidence interval 95%)	75.0 (24.9 to 99999)			

Notes:

[13] - 99999 = not calculable due

## Statistical analyses

No statistical analyses for this end point

## Secondary: [Module A] Disease control (DC)

End point title [Module A] Disease control (DC)<sup>[14]</sup>

End point description:

Disease Control (DC) defined as the percentage of patients with best overall response of complete response (CR), partial response (PR), or stable disease (SD), assessed by the investigator according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). CR was defined as the disappearance of all target lesions, PR was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study, and PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study.

Treated set of the module A: all patients treated with at least one dose of trial medications.

End point type Secondary

End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 152.4 weeks.

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module A.

End point values	Module A, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	33	42	
Units: Percentage of participants				
number (confidence interval 95%)	0 (0.0 to 84.2)	42.4 (25.5 to 60.8)	45.2 (29.8 to 61.3)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: [Module A] Duration of response (DoR)

End point title [Module A] Duration of response (DoR)<sup>[15]</sup>

End point description:

Duration of response (DoR) was defined as the time from first documented complete response (CR) or partial response (PR) (RECIST v1.1) among patients with objective response (OR), according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1). Complete response (CR) was defined as the disappearance of all target lesions and partial response (PR) was defined as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference. DoR parameters were calculated based on Kaplan-Meier estimation.

Treated set of the module A: all patients treated with at least one dose of trial medications. Only patients that had an OR were included in the analysis.

End point type Secondary

End point timeframe:

From first documented CR or PR (RECIST v1.1) until the earlier of disease progression or death. Up to 63.6 weeks.

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module A.

End point values	Module A, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[16]</sup>	3	8	
Units: Weeks				
median (full range (min-max))	( to )	12.30 (5.7 to 31.4)	28.30 (0.1 to 63.6)	

Notes:

[16] - No patient had OR in this cohort.

## Statistical analyses

No statistical analyses for this end point

## Secondary: [Module A] Disease control (DC) - bayesian hierarchical model

End point title	[Module A] Disease control (DC) - bayesian hierarchical
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End point description:

Defined as the disease control rate (DCR) of participants with best overall response of CR, PR, or stable disease (SD), assessed by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions, PR as decrease of at least 30% in the sum of the diameter of target lesions taking the baseline sum diameters as reference, SD as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study, and PD as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. The estimated DCR is presented by the posterior medians of the BHM and by the correspondent credible intervals. The median is actually the posterior median and the confidence interval is actually the credible interval.

Treated set of the module A: all patients treated with at least one dose of trial medications.

End point type	Secondary
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End point timeframe:

From first drug administration until the earliest of disease progression, death or last evaluable tumor assessment before start of subsequent anti-cancer therapy. Up to approximately 152.4 weeks.

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module A.

End point values	Module A, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	33	42	
Units: Estimated DCR				
median (confidence interval 97.5%)	10.83 (1.7 to 28.79)	42.83 (28.86 to 57.14)	44.18 (31.57 to 57.68)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: [Module A] Progression-free survival (PFS)

End point title	[Module A] Progression-free survival (PFS) <sup>[18]</sup>
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End point description:

Progression-free survival (PFS) was defined as the time from first treatment administration until progressive disease (PD), according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (v1.1), or death from any cause, whichever occurred earlier. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. PFS parameters were calculated based on Kaplan-Meier estimation. Progression free survival was collected, according to the clinical trial protocol until July 2021.

Treated set of the module A: all patients treated with at least one dose of trial medications.

End point type	Secondary
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End point timeframe:

From first drug administration until PD, death, or cut-off date of July 2021, whichever occurred earlier. Up to approximately 104.7 weeks.

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed on Module A.

End point values	Module A, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2 <sup>[19]</sup>	33	42	
Units: Weeks				
median (confidence interval 95%)	5.9 (5.7 to 99999)	6.7 (5.9 to 11.9)	8.9 (5.7 to 16.9)	

Notes:

[19] - 99999 = not calculable due low number of events

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event reporting and all-cause mortality: From first until last drug administration plus residual effect period (30 days). Up to approximately 192.6 weeks for module C and approximately 156.7 weeks for module A.

Adverse event reporting additional description:

Treated set: all patients treated with at least one dose of trial medications.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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### Reporting groups

Reporting group title	Module A, Cohort 1: GEC patients
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Reporting group description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma, who received prior anti-PD-1 or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 1: GEC patients
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Reporting group description:

Patients with locally advanced, unresectable or metastatic gastric adenocarcinoma or gastro-oesophageal adenocarcinoma (GEC) with at least one prior systemic treatment, who failed standard therapy, for whom no further effective options existed, and with no prior PD-1 or PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, in the form of i.v. infusion, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 2: 2ary resistance patients
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Reporting group description:

Patients with any advanced or metastatic solid tumors who had been previously treated with anti-PD-1 or anti-PD-L1-based therapies, and who progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 6 months) and minimum treatment duration of 2 months without experiencing disease progression, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 2: 2ary resistance patients
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Reporting group description:

Patients with any advanced or metastatic solid tumor (excluding non-squamous lung cancer, non-small-cell lung cancer, and melanoma) who had received prior anti-PD-1- or anti-PD-L1-based treatment and progressed after achieving benefit (at least stable disease with a minimum duration of benefit of 4 months) and minimum treatment duration of 2 months on the previous anti-PD-1- or anti-PD-L1-based treatment without progressive disease, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along 720 mg of BI 836880 on Day 1, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module A, Cohort 3: 1ary resistance patients
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Reporting group description:

Patients with select advanced or metastatic solid tumor types, who have been previously treated with previous anti-PD-1 or anti-PD-L1-based therapies without achieving benefit (stable disease for less than 6 months or progressive disease in less than 6 months), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 600 mg of BI 754111, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 3: 1ary resistance patients
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Reporting group description:

Patients with select advanced or metastatic solid tumors with prior anti-PD-1- or anti-PD-L1-based treatment without achieving benefit ( stable disease duration of less than 4 months or progressive disease in less than 4 months while on treatment), were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.

Reporting group title	Module C, Cohort 4: CRC patients
Reporting group description:	
Patients with locally advanced, unresectable or metastatic second-line or greater, microsatellite-stable colorectal cancer (CRC) without prior anti-PD-1- or anti-PD-L1-based treatment, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.	
Reporting group title	Module C, Cohort 5: EC patients
Reporting group description:	
Patients with advanced endometrial carcinoma (EC), excluding microsatellite instability-high or mismatch repair deficient types, who progressed following one line of chemotherapy, were not eligible for curative surgery or radiation, and had not been previously treated with anti-PD-1- or anti-PD-L1-based therapies, were administered 240 mg of ezabenlimab (BI 754091), intravenously, on Day 1 of 21-day cycles, along with 720 mg of BI 836880, intravenously, on Day 1 of 21-day cycles.	

<b>Serious adverse events</b>	Module A, Cohort 1: GEC patients	Module C, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	11 / 28 (39.29%)	13 / 33 (39.39%)
number of deaths (all causes)	0	24	29
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUMOUR ASSOCIATED FEVER			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 THROMBOSIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			

subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
HYPERTENSION			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
DEATH			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 RELATED THROMBOSIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
FATIGUE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
MALAISE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
LOCALISED OEDEMA			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
IMPLANT SITE PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 / 2 (0.00%)	2 / 28 (7.14%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
PROSTATITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPIRATION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
DYSPNOEA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
ORGANISING PNEUMONIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
PLEURAL EFFUSION			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
Psychiatric disorders			
DELIRIUM			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
TROPONIN I INCREASED			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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			
HIP FRACTURE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
FALL			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
PROCEDURAL PNEUMOTHORAX			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

HUMERUS FRACTURE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 ARREST			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
MYOCARDITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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

SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
ENCEPHALOPATHY			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
SYNCOPE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BANDAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
NEUTROPENIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
DIARRHOEA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
ILEUS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 ENTEROCOLITIS			

subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
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 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
OESOPHAGEAL OBSTRUCTION			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (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
OESOPHAGEAL PERFORATION			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 HAEMORRHAGE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILE DUCT STONE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC FAILURE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
HYPERTRANSAMINASAEMIA			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 INJURY			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 CHOLESTATIC			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
HAEMATURIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE-MEDIATED NEPHRITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
HYDRONEPHROSIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
NEPHRITIS			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
URINARY RETENTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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			
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
ENCEPHALITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

INFECTED FISTULA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
PHARYNGITIS BACTERIAL			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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 ASPIRATION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
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 INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEVICE INFECTION			

subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
HYPOKALAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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
LACTIC ACIDOSIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
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	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (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

<b>Serious adverse events</b>	Module C, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	Module C, Cohort 3: 1ary resistance patients
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 30 (60.00%)	12 / 42 (28.57%)	12 / 28 (42.86%)
number of deaths (all causes)	20	32	22
number of deaths resulting from adverse events	2	1	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps) BASAL CELL CARCINOMA			

subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 ASSOCIATED FEVER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
TUMOUR THROMBOSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 30 (0.00%)	3 / 42 (7.14%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 0	1 / 3	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
HYPERTENSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 RELATED THROMBOSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
FATIGUE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
FACE OEDEMA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
MALAISE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
LOCALISED OEDEMA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
IMPLANT SITE PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
PYREXIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA			

subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
Reproductive system and breast disorders			
PROSTATITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
ASPIRATION			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORGANISING PNEUMONIA			

subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
<b>PLEURAL EFFUSION</b>			
subjects affected / exposed	2 / 30 (6.67%)	1 / 42 (2.38%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	3 / 6	2 / 2	3 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>PNEUMOTHORAX</b>			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
<b>PULMONARY EMBOLISM</b>			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
<b>RESPIRATORY FAILURE</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
<b>Psychiatric disorders</b>			
<b>DELIRIUM</b>			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
<b>Investigations</b>			
<b>BLOOD CREATININE INCREASED</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>TROPONIN I INCREASED</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>Injury, poisoning and procedural</b>			

complications			
HIP FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
FALL			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
PROCEDURAL PNEUMOTHORAX			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
HUMERUS FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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			
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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

ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
MYOCARDITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
SOMNOLENCE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
ENCEPHALOPATHY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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

TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
SYNCOPE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
BANDAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 THROMBOCYTOPENIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
NEUTROPENIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DIARRHOEA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 ENTEROCOLITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
NAUSEA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
OESOPHAGEAL OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
OESOPHAGEAL PERFORATION			

subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>PANCREATITIS</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>RECTAL HAEMORRHAGE</b>			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
<b>SMALL INTESTINAL OBSTRUCTION</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>UPPER GASTROINTESTINAL HAEMORRHAGE</b>			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
<b>VOMITING</b>			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
<b>Hepatobiliary disorders</b>			
<b>BILE DUCT STENOSIS</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>BILE DUCT STONE</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>BILIARY OBSTRUCTION</b>			

subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
HYPERTRANSAMINASAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
LIVER INJURY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
JAUNDICE CHOLESTATIC			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATURIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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 NEPHRITIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDRONEPHROSIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
NEPHRITIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (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
URINARY RETENTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
BACK PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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			
COVID-19			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
ENCEPHALITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
INFECTED FISTULA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
MENINGITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
PHARYNGITIS BACTERIAL			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3

PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 6
PNEUMONIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
SKIN INFECTION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (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
HYPOKALAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
LACTIC ACIDOSIS			

subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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
<b>HYPONATRAEMIA</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (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

<b>Serious adverse events</b>	Module C, Cohort 4: CRC patients	Module C, Cohort 5: EC patients	
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	13 / 30 (43.33%)	11 / 18 (61.11%)	
number of deaths (all causes)	17	4	
number of deaths resulting from adverse events	1	1	
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
<b>BASAL CELL CARCINOMA</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>MYELODYSPLASTIC SYNDROME</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>TUMOUR ASSOCIATED FEVER</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>TUMOUR THROMBOSIS</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vascular disorders</b>			
<b>DEEP VEIN THROMBOSIS</b>			

subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSION			
subjects affected / exposed	2 / 30 (6.67%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	6 / 6	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
DEATH			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
DEVICE RELATED THROMBOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FACE OEDEMA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALAISE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOCALISED OEDEMA			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMPLANT SITE PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OEDEMA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
PROSTATITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPIRATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORGANISING PNEUMONIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
DELIRIUM			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TROPONIN I INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
HIP FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL PNEUMOTHORAX			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

HUMERUS FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SOMNOLENCE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALOPATHY			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BANDAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	3 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE-MEDIATED ENTEROCOLITIS			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL PERFORATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILE DUCT STONE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILIARY OBSTRUCTION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC FAILURE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTRANSAMINASAEMIA			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIVER INJURY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAUNDICE CHOLESTATIC			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATURIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE-MEDIATED NEPHRITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYDRONEPHROSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHRITIS			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

INFECTED FISTULA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHARYNGITIS BACTERIAL			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
SKIN INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCALCAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LACTIC ACIDOSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Module A, Cohort 1: GEC patients	Module C, Cohort 1: GEC patients	Module A, Cohort 2: 2ary resistance patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	27 / 28 (96.43%)	33 / 33 (100.00%)
Vascular disorders			
HYPOTENSION			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	6 / 33 (18.18%)
occurrences (all)	0	0	9
HOT FLUSH			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 2 (0.00%)	3 / 28 (10.71%)	1 / 33 (3.03%)
occurrences (all)	0	21	2
LYMPHOEDEMA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	1 / 33 (3.03%)
occurrences (all)	0	6	1
ADMINISTRATION SITE REACTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	4 / 33 (12.12%)
occurrences (all)	0	6	4
EARLY SATIETY			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
FACE OEDEMA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	1 / 2 (50.00%)	7 / 28 (25.00%)	12 / 33 (36.36%)
occurrences (all)	1	36	20
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	2
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	3 / 33 (9.09%)
occurrences (all)	0	9	4
PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
PYREXIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	4 / 33 (12.12%)
occurrences (all)	0	0	6
SENSATION OF FOREIGN BODY			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	0	3	4
COUGH			
subjects affected / exposed	1 / 2 (50.00%)	1 / 28 (3.57%)	4 / 33 (12.12%)
occurrences (all)	1	3	4
DYSPNOEA			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	6 / 33 (18.18%)
occurrences (all)	0	6	6
DYSPHONIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
NASAL CONGESTION			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
LARYNGEAL PAIN			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
LOWER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
HAEMOTHORAX			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
PLEURAL EFFUSION			
subjects affected / exposed	1 / 2 (50.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences (all)	1	3	1
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
ANXIETY			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
CONFUSIONAL STATE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
DEPRESSION			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	2 / 33 (6.06%) 2
Product issues DEVICE DISLOCATION subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
Investigations BLOOD CREATININE INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	2 / 33 (6.06%) 3
BLOOD BILIRUBIN INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	0 / 33 (0.00%) 0
BLOOD ALKALINE PHOSPHATASE INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
ASPARTATE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	1 / 33 (3.03%) 1
ALANINE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	2 / 33 (6.06%) 3
RED BLOOD CELL COUNT INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
PLATELET COUNT DECREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
BLOOD UREA INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
VITAMIN D DECREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0

WEIGHT DECREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	5 / 28 (17.86%) 15	7 / 33 (21.21%) 11
WEIGHT INCREASED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
Injury, poisoning and procedural complications			
CORNEAL ABRASION subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
ROAD TRAFFIC ACCIDENT subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
MUSCLE STRAIN subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
INFUSION RELATED REACTION subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	4 / 28 (14.29%) 12	3 / 33 (9.09%) 5
SPINAL COMPRESSION FRACTURE subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	2 / 33 (6.06%) 2
FALL subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	1 / 33 (3.03%) 1
WOUND subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
Cardiac disorders			
ATRIAL FIBRILLATION subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
TACHYCARDIA subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	2 / 33 (6.06%) 2
ATRIAL TACHYCARDIA			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
Nervous system disorders			
APHASIA			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
DYSGEUSIA			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
DIZZINESS			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	6 / 33 (18.18%) 6
HEADACHE			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 28 (7.14%) 9	6 / 33 (18.18%) 7
MEMORY IMPAIRMENT			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	1 / 33 (3.03%) 2
NEUROPATHY PERIPHERAL			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
PARALYSIS RECURRENT LARYNGEAL NERVE			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	1 / 33 (3.03%) 1
SYNCOPE			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	4 / 28 (14.29%) 15	5 / 33 (15.15%) 7
THROMBOCYTOPENIA			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	1 / 33 (3.03%) 1
Ear and labyrinth disorders EAR DISCOMFORT subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
EAR PAIN subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	0 / 33 (0.00%) 0
HYPOACUSIS subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
Eye disorders PERIORBITAL OEDEMA subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
CONJUNCTIVOCHALASIS subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	0 / 33 (0.00%) 0
VISION BLURRED subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 28 (0.00%) 0	3 / 33 (9.09%) 3
Gastrointestinal disorders ABDOMINAL PAIN subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	8 / 28 (28.57%) 27	3 / 33 (9.09%) 4
ABDOMINAL DISTENSION subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 28 (3.57%) 3	2 / 33 (6.06%) 2
ABDOMINAL PAIN UPPER subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 28 (7.14%) 6	1 / 33 (3.03%) 1
CONSTIPATION subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 28 (7.14%) 9	6 / 33 (18.18%) 6
COLITIS			

subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	0 / 33 (0.00%)
occurrences (all)	0	6	0
ASCITES			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	1 / 33 (3.03%)
occurrences (all)	0	9	1
EPIGASTRIC DISCOMFORT			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
FLATULENCE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
DYSPHAGIA			
subjects affected / exposed	0 / 2 (0.00%)	3 / 28 (10.71%)	0 / 33 (0.00%)
occurrences (all)	0	9	0
DYSPEPSIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences (all)	0	6	1
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
DIARRHOEA			
subjects affected / exposed	1 / 2 (50.00%)	9 / 28 (32.14%)	7 / 33 (21.21%)
occurrences (all)	1	48	11
ORAL PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
ORAL DISCOMFORT			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	2 / 2 (100.00%)	5 / 28 (17.86%)	12 / 33 (36.36%)
occurrences (all)	3	21	19
GINGIVAL PAIN			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences (all)	0	3	0

GINGIVAL BLEEDING	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
	occurrences (all)	0	0	0
PANCREATITIS ACUTE	subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
	occurrences (all)	1	0	0
VOMITING	subjects affected / exposed	1 / 2 (50.00%)	4 / 28 (14.29%)	5 / 33 (15.15%)
	occurrences (all)	2	24	10
TOOTHACHE	subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
	occurrences (all)	0	3	0
STOMATITIS	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
	occurrences (all)	0	0	1
Hepatobiliary disorders				
CHOLECYSTITIS	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
	occurrences (all)	0	0	0
HYPERTRANSAMINASAEMIA	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
	occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders				
DRY SKIN	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	2 / 33 (6.06%)
	occurrences (all)	0	0	2
HAND DERMATITIS	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
	occurrences (all)	0	0	0
PRURITUS	subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	1 / 33 (3.03%)
	occurrences (all)	0	6	1
RASH	subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
	occurrences (all)	0	0	1
RASH PRURITIC				

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
RASH PAPULAR			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	3 / 33 (9.09%)
occurrences (all)	0	6	5
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	0	3	2
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
DYSURIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
POLLAKIURIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
PROTEINURIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
NOCTURIA			
subjects affected / exposed	1 / 2 (50.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
URINARY INCONTINENCE			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
HYPERTHYROIDISM			

subjects affected / exposed	0 / 2 (0.00%)	2 / 28 (7.14%)	3 / 33 (9.09%)
occurrences (all)	0	6	3
HYPOTHYROIDISM			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	0	3	2
Musculoskeletal and connective tissue disorders			
FLANK PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	4 / 33 (12.12%)
occurrences (all)	0	0	6
BACK PAIN			
subjects affected / exposed	0 / 2 (0.00%)	5 / 28 (17.86%)	3 / 33 (9.09%)
occurrences (all)	0	15	3
ARTHRALGIA			
subjects affected / exposed	0 / 2 (0.00%)	5 / 28 (17.86%)	8 / 33 (24.24%)
occurrences (all)	0	27	11
GROIN PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	4 / 33 (12.12%)
occurrences (all)	0	0	4
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	0	3	3
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
MYALGIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	0	3	4
NECK PAIN			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
PAIN IN EXTREMITY			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	4 / 33 (12.12%)
occurrences (all)	0	0	7
PAIN IN JAW			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
CYSTITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	3 / 28 (10.71%)	0 / 33 (0.00%)
occurrences (all)	0	9	0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
GROIN ABSCESS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
GASTROINTESTINAL VIRAL INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
FUNGAL INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
FOLLICULITIS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	3 / 33 (9.09%)
occurrences (all)	0	3	4
RHINITIS			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
PNEUMONIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	4 / 33 (12.12%)
occurrences (all)	0	6	4
ORAL HERPES			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
SKIN INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	3 / 28 (10.71%)	1 / 33 (3.03%)
occurrences (all)	0	12	1
TOOTH ABSCESS			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 2 (0.00%)	3 / 28 (10.71%)	6 / 33 (18.18%)
occurrences (all)	0	9	9
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 2 (50.00%)	1 / 28 (3.57%)	7 / 33 (21.21%)
occurrences (all)	1	3	12
DECREASED APPETITE			
subjects affected / exposed	0 / 2 (0.00%)	3 / 28 (10.71%)	8 / 33 (24.24%)
occurrences (all)	0	9	8
HYPERCALCAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
HYPERLIPIDAEMIA			

subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
HYPERKALAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
HYPOKALAEMIA			
subjects affected / exposed	1 / 2 (50.00%)	1 / 28 (3.57%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
HYPERURICAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 2 (0.00%)	0 / 28 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3

Non-serious adverse events	Module C, Cohort 2: 2ary resistance patients	Module A, Cohort 3: 1ary resistance patients	Module C, Cohort 3: 1ary resistance patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 30 (90.00%)	41 / 42 (97.62%)	26 / 28 (92.86%)
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	9
HOT FLUSH			

subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	3	0	3
HYPERTENSION			
subjects affected / exposed	9 / 30 (30.00%)	1 / 42 (2.38%)	6 / 28 (21.43%)
occurrences (all)	39	1	18
LYMPHOEDEMA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
ADMINISTRATION SITE REACTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	2 / 30 (6.67%)	2 / 42 (4.76%)	2 / 28 (7.14%)
occurrences (all)	6	2	6
EARLY SATIETY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
FACE OEDEMA			
subjects affected / exposed	3 / 30 (10.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	9	0	3
FATIGUE			
subjects affected / exposed	8 / 30 (26.67%)	19 / 42 (45.24%)	8 / 28 (28.57%)
occurrences (all)	36	26	24
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	6	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	2 / 30 (6.67%)	2 / 42 (4.76%)	1 / 28 (3.57%)
occurrences (all)	6	2	3
OEDEMA PERIPHERAL			

subjects affected / exposed occurrences (all)	6 / 30 (20.00%) 27	4 / 42 (9.52%) 4	4 / 28 (14.29%) 12
PAIN			
subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	2 / 42 (4.76%) 2	0 / 28 (0.00%) 0
PYREXIA			
subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 6	5 / 42 (11.90%) 6	1 / 28 (3.57%) 6
SENSATION OF FOREIGN BODY			
subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA EXERTIONAL			
subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	2 / 42 (4.76%) 2	0 / 28 (0.00%) 0
COUGH			
subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 12	10 / 42 (23.81%) 11	0 / 28 (0.00%) 0
DYSPNOEA			
subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 9	4 / 42 (9.52%) 4	5 / 28 (17.86%) 15
DYSPHONIA			
subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 3	1 / 42 (2.38%) 1	1 / 28 (3.57%) 3
NASAL CONGESTION			
subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 42 (2.38%) 1	0 / 28 (0.00%) 0
LARYNGEAL PAIN			
subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
LOWER RESPIRATORY TRACT CONGESTION			

subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	2 / 42 (4.76%)	3 / 28 (10.71%)
occurrences (all)	3	2	15
HAEMOTHORAX			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
PLEURAL EFFUSION			
subjects affected / exposed	3 / 30 (10.00%)	2 / 42 (4.76%)	1 / 28 (3.57%)
occurrences (all)	15	2	3
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
SINUS CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	3	1	0
ANXIETY			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	2 / 28 (7.14%)
occurrences (all)	3	1	6
CONFUSIONAL STATE			
subjects affected / exposed	0 / 30 (0.00%)	3 / 42 (7.14%)	1 / 28 (3.57%)
occurrences (all)	0	3	3
DEPRESSION			
subjects affected / exposed	2 / 30 (6.67%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	9	1	0
Product issues			
DEVICE DISLOCATION			

subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	4 / 30 (13.33%)	2 / 42 (4.76%)	3 / 28 (10.71%)
occurrences (all)	15	3	12
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	7	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	2 / 28 (7.14%)
occurrences (all)	0	2	6
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	2 / 28 (7.14%)
occurrences (all)	9	1	9
RED BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	6	0	0
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
VITAMIN D DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	2 / 30 (6.67%)	7 / 42 (16.67%)	4 / 28 (14.29%)
occurrences (all)	6	7	15
WEIGHT INCREASED			

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 6	1 / 42 (2.38%) 1	1 / 28 (3.57%) 6
Injury, poisoning and procedural complications			
CORNEAL ABRASION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences (all)	3	1	6
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	3 / 30 (10.00%)	3 / 42 (7.14%)	1 / 28 (3.57%)
occurrences (all)	9	3	3
WOUND			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
ATRIAL TACHYCARDIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

APHASIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences (all)	3	1	3
DIZZINESS			
subjects affected / exposed	2 / 30 (6.67%)	4 / 42 (9.52%)	0 / 28 (0.00%)
occurrences (all)	6	4	0
HEADACHE			
subjects affected / exposed	4 / 30 (13.33%)	3 / 42 (7.14%)	2 / 28 (7.14%)
occurrences (all)	12	3	6
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
PARALYSIS RECURRENT LARYNGEAL NERVE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
SYNCOPE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 30 (6.67%)	6 / 42 (14.29%)	1 / 28 (3.57%)
occurrences (all)	6	13	3
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

EAR DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
EAR PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	6
HYPOACUSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
PERIORBITAL OEDEMA			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	6	0	3
CONJUNCTIVOCHALASIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	2 / 30 (6.67%)	4 / 42 (9.52%)	2 / 28 (7.14%)
occurrences (all)	9	4	6
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 30 (10.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	9	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 30 (3.33%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences (all)	3	1	3
CONSTIPATION			
subjects affected / exposed	3 / 30 (10.00%)	10 / 42 (23.81%)	2 / 28 (7.14%)
occurrences (all)	9	11	6
COLITIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
ASCITES			

subjects affected / exposed	2 / 30 (6.67%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences (all)	12	1	6
EPIGASTRIC DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 30 (0.00%)	3 / 42 (7.14%)	3 / 28 (10.71%)
occurrences (all)	0	3	9
DYSPEPSIA			
subjects affected / exposed	2 / 30 (6.67%)	2 / 42 (4.76%)	1 / 28 (3.57%)
occurrences (all)	9	2	3
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	3
DIARRHOEA			
subjects affected / exposed	6 / 30 (20.00%)	4 / 42 (9.52%)	5 / 28 (17.86%)
occurrences (all)	18	5	21
ORAL PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences (all)	0	1	3
ORAL DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	7 / 30 (23.33%)	9 / 42 (21.43%)	3 / 28 (10.71%)
occurrences (all)	36	15	9
GINGIVAL PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

PANCREATITIS ACUTE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	6 / 30 (20.00%)	5 / 42 (11.90%)	2 / 28 (7.14%)
occurrences (all)	24	6	6
TOOTHACHE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 42 (4.76%)	1 / 28 (3.57%)
occurrences (all)	0	2	3
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
HYPERTRANSAMINASAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
HAND DERMATITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	1 / 30 (3.33%)	3 / 42 (7.14%)	2 / 28 (7.14%)
occurrences (all)	3	3	6
RASH			
subjects affected / exposed	2 / 30 (6.67%)	1 / 42 (2.38%)	2 / 28 (7.14%)
occurrences (all)	6	1	6
RASH PRURITIC			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
RASH PAPULAR			

subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
RASH MACULO-PAPULAR subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 3	3 / 42 (7.14%) 3	0 / 28 (0.00%) 0
RASH ERYTHEMATOUS subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
Renal and urinary disorders			
HAEMATURIA subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 42 (2.38%) 1	0 / 28 (0.00%) 0
DYSURIA subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 3	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
NEPHROLITHIASIS subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	1 / 28 (3.57%) 3
POLLAKIURIA subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
PROTEINURIA subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 3	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
NOCTURIA subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
URINARY INCONTINENCE subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 42 (2.38%) 1	0 / 28 (0.00%) 0
Endocrine disorders			
HYPERTHYROIDISM subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	0 / 28 (0.00%) 0
HYPOTHYROIDISM			

subjects affected / exposed	4 / 30 (13.33%)	7 / 42 (16.67%)	3 / 28 (10.71%)
occurrences (all)	12	7	9
Musculoskeletal and connective tissue disorders			
FLANK PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
BACK PAIN			
subjects affected / exposed	1 / 30 (3.33%)	6 / 42 (14.29%)	1 / 28 (3.57%)
occurrences (all)	3	7	3
ARTHRALGIA			
subjects affected / exposed	5 / 30 (16.67%)	5 / 42 (11.90%)	5 / 28 (17.86%)
occurrences (all)	18	6	24
GROIN PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	2 / 30 (6.67%)	2 / 42 (4.76%)	0 / 28 (0.00%)
occurrences (all)	6	3	0
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 30 (3.33%)	2 / 42 (4.76%)	0 / 28 (0.00%)
occurrences (all)	3	2	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	2 / 30 (6.67%)	1 / 42 (2.38%)	1 / 28 (3.57%)
occurrences (all)	9	2	3
MYALGIA			
subjects affected / exposed	0 / 30 (0.00%)	3 / 42 (7.14%)	1 / 28 (3.57%)
occurrences (all)	0	3	3
NECK PAIN			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	4 / 28 (14.29%)
occurrences (all)	6	0	12
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 30 (0.00%)	3 / 42 (7.14%)	1 / 28 (3.57%)
occurrences (all)	0	5	3
PAIN IN JAW			

subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 42 (0.00%) 0	1 / 28 (3.57%) 6
Infections and infestations			
CYSTITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	3	0	3
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
GROIN ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
GASTROINTESTINAL VIRAL INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
FUNGAL INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
FOLLICULITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	9
RHINITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
PNEUMONIA			

subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	2 / 28 (7.14%)
occurrences (all)	0	1	6
ORAL HERPES			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
SKIN INFECTION			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	9	0	3
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	3
TOOTH ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	3
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 30 (3.33%)	5 / 42 (11.90%)	1 / 28 (3.57%)
occurrences (all)	6	5	3
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 30 (10.00%)	5 / 42 (11.90%)	3 / 28 (10.71%)
occurrences (all)	15	5	9
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	2 / 30 (6.67%)	5 / 42 (11.90%)	2 / 28 (7.14%)
occurrences (all)	12	9	6
DECREASED APPETITE			
subjects affected / exposed	5 / 30 (16.67%)	9 / 42 (21.43%)	1 / 28 (3.57%)
occurrences (all)	15	10	3
HYPERCALCAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	4 / 42 (9.52%)	0 / 28 (0.00%)
occurrences (all)	3	4	0
HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	3
HYPERKALAEMIA			

subjects affected / exposed	2 / 30 (6.67%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	9	2	0
HYPOMAGNESAEMIA			
subjects affected / exposed	3 / 30 (10.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	9	0	0
HYPOKALAEMIA			
subjects affected / exposed	2 / 30 (6.67%)	0 / 42 (0.00%)	2 / 28 (7.14%)
occurrences (all)	18	0	6
HYPOCALCAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 42 (2.38%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
HYPONATRAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 42 (0.00%)	0 / 28 (0.00%)
occurrences (all)	6	0	0

<b>Non-serious adverse events</b>	Module C, Cohort 4: CRC patients	Module C, Cohort 5: EC patients	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 30 (96.67%)	18 / 18 (100.00%)	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
HOT FLUSH			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	6	
HYPERTENSION			

subjects affected / exposed	8 / 30 (26.67%)	7 / 18 (38.89%)	
occurrences (all)	45	33	
LYMPHOEDEMA			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	6	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
ADMINISTRATION SITE REACTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
CHILLS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
EARLY SATIETY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
FACE OEDEMA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
FATIGUE			
subjects affected / exposed	11 / 30 (36.67%)	8 / 18 (44.44%)	
occurrences (all)	51	24	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
OEDEMA PERIPHERAL			
subjects affected / exposed	12 / 30 (40.00%)	6 / 18 (33.33%)	
occurrences (all)	54	18	
PAIN			

subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
PYREXIA			
subjects affected / exposed	1 / 30 (3.33%)	3 / 18 (16.67%)	
occurrences (all)	3	9	
SENSATION OF FOREIGN BODY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
DYSпноEA EXERTIONAL			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
COUGH			
subjects affected / exposed	6 / 30 (20.00%)	5 / 18 (27.78%)	
occurrences (all)	33	15	
DYSпноEA			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	6	0	
DYSPHONIA			
subjects affected / exposed	3 / 30 (10.00%)	0 / 18 (0.00%)	
occurrences (all)	15	0	
NASAL CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	12	
LARYNGEAL PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
LOWER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
OROPHARYNGEAL PAIN			

subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	6	
HAEMOTHORAX			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
PLEURAL EFFUSION			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	9	0	
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 30 (3.33%)	2 / 18 (11.11%)	
occurrences (all)	3	6	
RHINORRHOEA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	12	
SINUS CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	3	
ANXIETY			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	6	
CONFUSIONAL STATE			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	12	0	
DEPRESSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Product issues			
DEVICE DISLOCATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Investigations			

BLOOD CREATININE INCREASED			
subjects affected / exposed	6 / 30 (20.00%)	1 / 18 (5.56%)	
occurrences (all)	24	3	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	6	0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	5 / 30 (16.67%)	0 / 18 (0.00%)	
occurrences (all)	24	0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 30 (13.33%)	1 / 18 (5.56%)	
occurrences (all)	15	6	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 30 (6.67%)	3 / 18 (16.67%)	
occurrences (all)	9	12	
RED BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
PLATELET COUNT DECREASED			
subjects affected / exposed	4 / 30 (13.33%)	1 / 18 (5.56%)	
occurrences (all)	39	3	
BLOOD UREA INCREASED			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	6	0	
VITAMIN D DECREASED			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	6	0	
WEIGHT DECREASED			
subjects affected / exposed	13 / 30 (43.33%)	3 / 18 (16.67%)	
occurrences (all)	45	12	
WEIGHT INCREASED			
subjects affected / exposed	1 / 30 (3.33%)	2 / 18 (11.11%)	
occurrences (all)	3	9	
Injury, poisoning and procedural complications			

CORNEAL ABRASION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
MUSCLE STRAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
INFUSION RELATED REACTION			
subjects affected / exposed	3 / 30 (10.00%)	2 / 18 (11.11%)	
occurrences (all)	9	12	
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
FALL			
subjects affected / exposed	3 / 30 (10.00%)	0 / 18 (0.00%)	
occurrences (all)	9	0	
WOUND			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
TACHYCARDIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
ATRIAL TACHYCARDIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	6	
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
DYSGEUSIA			

subjects affected / exposed	3 / 30 (10.00%)	1 / 18 (5.56%)	
occurrences (all)	12	3	
DIZZINESS			
subjects affected / exposed	1 / 30 (3.33%)	3 / 18 (16.67%)	
occurrences (all)	3	12	
HEADACHE			
subjects affected / exposed	2 / 30 (6.67%)	4 / 18 (22.22%)	
occurrences (all)	6	12	
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
PARALYSIS RECURRENT LARYNGEAL NERVE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
SYNCOPE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	6	3	
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			
EAR DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
EAR PAIN			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
<b>HYPOACUSIS</b>			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
<b>Eye disorders</b>			
<b>PERIORBITAL OEDEMA</b>			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	9	
<b>CONJUNCTIVOCHALASIS</b>			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
<b>VISION BLURRED</b>			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
<b>Gastrointestinal disorders</b>			
<b>ABDOMINAL PAIN</b>			
subjects affected / exposed	4 / 30 (13.33%)	3 / 18 (16.67%)	
occurrences (all)	15	9	
<b>ABDOMINAL DISTENSION</b>			
subjects affected / exposed	3 / 30 (10.00%)	2 / 18 (11.11%)	
occurrences (all)	9	6	
<b>ABDOMINAL PAIN UPPER</b>			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
<b>CONSTIPATION</b>			
subjects affected / exposed	3 / 30 (10.00%)	4 / 18 (22.22%)	
occurrences (all)	9	12	
<b>COLITIS</b>			
subjects affected / exposed	0 / 30 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	9	
<b>ASCITES</b>			
subjects affected / exposed	2 / 30 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	12	0	
<b>EPIGASTRIC DISCOMFORT</b>			

subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0
FLATULENCE		
subjects affected / exposed	1 / 30 (3.33%)	0 / 18 (0.00%)
occurrences (all)	3	0
DYSPHAGIA		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
DYSPEPSIA		
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	9
GASTROOESOPHAGEAL REFLUX DISEASE		
subjects affected / exposed	3 / 30 (10.00%)	2 / 18 (11.11%)
occurrences (all)	9	6
DIARRHOEA		
subjects affected / exposed	5 / 30 (16.67%)	8 / 18 (44.44%)
occurrences (all)	27	45
ORAL PAIN		
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)
occurrences (all)	3	3
ORAL DISCOMFORT		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
NAUSEA		
subjects affected / exposed	11 / 30 (36.67%)	7 / 18 (38.89%)
occurrences (all)	42	36
GINGIVAL PAIN		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
GINGIVAL BLEEDING		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
PANCREATITIS ACUTE		
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0

VOMITING			
subjects affected / exposed	10 / 30 (33.33%)	7 / 18 (38.89%)	
occurrences (all)	36	42	
TOOTHACHE			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	3	
STOMATITIS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	15	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
HYPERTRANSAMINASAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	3	
HAND DERMATITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
PRURITUS			
subjects affected / exposed	5 / 30 (16.67%)	2 / 18 (11.11%)	
occurrences (all)	15	6	
RASH			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	6	3	
RASH PRURITIC			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
RASH PAPULAR			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
RASH MACULO-PAPULAR			

subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	3	
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	3 / 30 (10.00%)	0 / 18 (0.00%)	
occurrences (all)	12	0	
DYSURIA			
subjects affected / exposed	3 / 30 (10.00%)	0 / 18 (0.00%)	
occurrences (all)	9	0	
NEPHROLITHIASIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
POLLAKIURIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	6	3	
PROTEINURIA			
subjects affected / exposed	5 / 30 (16.67%)	1 / 18 (5.56%)	
occurrences (all)	18	3	
NOCTURIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
URINARY INCONTINENCE			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	6	
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	1 / 30 (3.33%)	2 / 18 (11.11%)	
occurrences (all)	3	6	
HYPOTHYROIDISM			
subjects affected / exposed	6 / 30 (20.00%)	5 / 18 (27.78%)	
occurrences (all)	21	15	
Musculoskeletal and connective tissue disorders			

FLANK PAIN			
subjects affected / exposed	1 / 30 (3.33%)	2 / 18 (11.11%)	
occurrences (all)	3	6	
BACK PAIN			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	6	
ARTHRALGIA			
subjects affected / exposed	2 / 30 (6.67%)	2 / 18 (11.11%)	
occurrences (all)	9	6	
GROIN PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
MUSCLE SPASMS			
subjects affected / exposed	2 / 30 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	6	6	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	6	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
MYALGIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	3	
NECK PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 30 (3.33%)	4 / 18 (22.22%)	
occurrences (all)	3	18	
PAIN IN JAW			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Infections and infestations			
CYSTITIS			

subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
COVID-19		
subjects affected / exposed	2 / 30 (6.67%)	4 / 18 (22.22%)
occurrences (all)	9	12
CLOSTRIDIUM DIFFICILE COLITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
INFLUENZA		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
GROIN ABSCESS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	15
GASTROINTESTINAL VIRAL INFECTION		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
FUNGAL INFECTION		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
FOLLICULITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
SINUSITIS		
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)
occurrences (all)	3	3
RHINITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	3
PNEUMONIA		
subjects affected / exposed	1 / 30 (3.33%)	2 / 18 (11.11%)
occurrences (all)	3	6
ORAL HERPES		
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	9

SKIN INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
TOOTH ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	6	
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 30 (13.33%)	5 / 18 (27.78%)	
occurrences (all)	12	15	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	2 / 30 (6.67%)	3 / 18 (16.67%)	
occurrences (all)	6	9	
DECREASED APPETITE			
subjects affected / exposed	5 / 30 (16.67%)	5 / 18 (27.78%)	
occurrences (all)	18	15	
HYPERCALCAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
HYPERKALAEMIA			
subjects affected / exposed	2 / 30 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	6	6	
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 18 (5.56%)	
occurrences (all)	3	3	
HYPOKALAEMIA			

subjects affected / exposed	5 / 30 (16.67%)	0 / 18 (0.00%)	
occurrences (all)	15	0	
HYPOCALCAEMIA			
subjects affected / exposed	2 / 30 (6.67%)	3 / 18 (16.67%)	
occurrences (all)	12	12	
HYPOALBUMINAEMIA			
subjects affected / exposed	3 / 30 (10.00%)	0 / 18 (0.00%)	
occurrences (all)	9	0	
HYPERURICAEMIA			
subjects affected / exposed	4 / 30 (13.33%)	2 / 18 (11.11%)	
occurrences (all)	18	6	
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
HYPONATRAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	30	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2019	Module A protocol amendment 1: description of the risk of infusion-related reactions with the combination of ezabenlimab and BI 754111 based on the most recent safety information; amendment of inclusion criteria to clarify that prior use of PD-1 investigational agents was not exclusionary; addition of Pre-treatment medication to the study prior to administration of the study treatment in order to reduce the risk of infusion related reactions; removal of the 5 year limit on holding trial samples to allow for more flexibility; clarification for collection of the Cycle 3 day1 tumor tissue biopsy; clarification that AEs would be reported through the entire residual effect period; addition of an interim futility analysis; update of bayesian hierarchical modelling parameters based on updated projected ORR; addition of an additional blood collection on Cycle 3 Day 1 to better track ADA levels.
07 May 2019	Master protocol amendment 1: addition of inclusion criteria in the synopsis; clarification of the main inclusion and exclusion criteria in the synopsis; addition of text to provide details on how to crossover to another module after progression on their previous treatment module; removal of the word multiple to clarify that there would be a limited number of modules; addition of safety and efficacy information to update the benefit-risk section of the protocol; clarification of the standard of care for advanced cancer patients; addition of text to provide safety guidance when a patient moves from one module to another; addition of text to provide guidance for male patients with partners of childbearing potential; clarification of exclusion criterion 2; modification of exclusion criteria to address UK regulatory concern; clarification of exclusion criteria 10; addition of further detail about transition timelines and patient assignment between modules after progression on a previous treatment module; update to correct the number of highly effective methods of birth control that should be used by a patient; update of language about drug-induced liver injury per Boehringer Ingelheim revised template text to clarify that all liver elevations meeting potential Hy's Law criteria require expedited reporting as an adverse event of special interest (AESI) on the serious adverse event (SAE) form; addition of pre-treatment medication to the study prior to administration of the study treatment to reduce the risk of infusion related reactions;
07 May 2019	Master protocol amendment 1 (continuation): addition of what to do in the event of a Grade 3 or higher infusion related reaction; addition of a decision tree to illustrate when the Potential DILI Checklist is initiated and when it can be considered complete; addition of a guidance for the pregnant partner of a male trial participant; clarification that pharmacodynamic (PD) reporting exemptions do not apply to hepatic injury reporting; clarification that liver injury was to be reported as an AESI; collection of additional baseline data such as Baseline PD-L1 expression level, microsatellite instability (MSI), and tumor mutation burden (TMB); Update of planned analyses section on how each module would contribute to the overall development plan of each combination; addition of details on what to do in the event of an infusion related reaction.
14 July 2021	Module A protocol amendment 2: appointment of a new Coordinating Investigator to the study; clarification that ECGs were not required until the end of trial (EOT) visit unless the Investigator deemed them necessary; addition that the sponsor determined that sufficient PFS and OS data had been collected; and amendment of the follow-up visits since very few patients remained on study drug; amendment that biomarker samples would no longer be collected and analyzed.

14 July 2021	Module C protocol amendment 1: Change in Coordinating Investigator; addition of a statement to the flow chart footnotes to indicate that the date of an assessment was to be considered Day 1 of the window; modification of inclusion criterion 2 to remove the requirement for $\geq 1$ line of prior systemic anticancer treatment in the metastatic setting; modification of inclusion criterion 3 to clarify target lesions; modification of inclusion criterion 4 to no longer allow patients with no archival tumour tissue sample and who were not biopsiable to participate in the study after discussion with the Medical Monitor; modification of exclusion criterion 2 to clarify exclusion guidelines for toxicity related to prior treatment; modification of exclusion criterion 4 and the flow chart to provide additional guidelines around blood pressure and pulse measurements; modification of exclusion criterion 6 to remove the restriction of vitamin K antagonists and other anticoagulants and to allow low-molecular-weight heparin and aspirin at doses for prevention/prophylaxis; modification of the trial design to indicate that Module values take precedence over the Master CTP.; clarification of Cohort to exclude all melanoma; clarification that, for cohort 5, hormonal monotherapy does not count as a line of therapy; addition of a window for infusion time, removal of shortening of infusion time to 30 minutes; addition of a statement, for management of an infusion-related reaction, that steroids were to be limited to prednisone 10 mg daily or equivalent;
14 July 2021	Module C protocol amendment 1 (continuation): addition of a statement to indicate that pre-treatment medications should be administered at sufficient time before initiation of infusion to allow the agents to exert their effects; addition of a drug re-administration criterion for Cycle 1; addition of a guidance for re-dosing to indicate that if the reduced dose was tolerable and deemed in the best interest of the patient, the Investigator should re-escalate; allowance of treatment with one of the 2 investigational agents if an adverse event (AE) could be clearly attributed to one of the 2 drugs; prohibition of concomitant medications known to prolong the QT interval; addition of pre-treatment to reduce the risk of infusion-related reactions; addition of the updated guidance for the EOT visit; clarification of the timing of pharmacokinetic (PK) collections from the start of ezabenlimab infusion; clarification that, before Cycle 1, blood pressure guidelines follow inclusion/exclusion criterion.
14 July 2021	Master protocol amendment 2: Change in Coordinating Investigator; modification of inclusion criterion 5 to clarify that patients with an Eastern Cooperative Oncology Group (ECOG) performance score of 0 or 1 could enrol; modification of inclusion criterion 6 to no longer allow patients without archival tumour tissue sample and who could not be biopsied to participate in the study; modification of exclusion criterion 3 to indicate that major surgery could be assessed by the Investigator or Medical Monitor; modification of exclusion criterion 5 to indicate that patients could be enrolled onto the study following a 7-day washout period after the end of systemic treatment for active infection; modification of exclusion criterion 12 to indicate that known, untreated, asymptomatic central nervous system metastases were to be considered an exclusion criterion.
28 March 2022	Module C protocol amendment 2: Change in The Trial Clinical Monitor; addition of treatment duration limitation was added due to program discontinuation; clarification that progression-free survival (PFS) and overall survival (OS) were no longer collected; removal of biopsies, blood samples for PK, levels of BI 836880 and ezabenlimab, biomarkers, and other assessments; modification of tumor assessments to be performed according to institutional practices and SOC; decision to terminate the trial was made; decision that no interim analyses would be performed.
12 June 2023	Master protocol amendment 3: Update of the role title from Trial Clinical Monitor to Clinical Trial Leader; BI 754091 was changed to its INN ezabenlimab; Correction of the terminology of the algorithm for patient assignment for consistency with rest of the document; Update of the role title from Team Member Medicine to Clinical Program Lead.
13 June 2023	Module C protocol amendment 3: Change in the Clinical Trial Leader; update of the role title from Trial Clinical Monitor to Clinical Trial Leader; addition of details on ezabenlimab Chemistry, Manufacturing, and Controls Tables 1 and 2 were added.

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Notes:

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported