



Clinical trial results:

An Open-label, Randomized, Phase I/II Trial Investigating the Safety and Efficacy of IO102 in Combination with Pembrolizumab, with or without Chemotherapy, as First-line Treatment for Patients with Metastatic Non-Small Cell Lung Cancer

Summary

EudraCT number	2018-000139-28
Trial protocol	ES GB DE NL
Global end of trial date	12 April 2022

Results information

Result version number	v1 (current)
This version publication date	04 April 2024
First version publication date	04 April 2024
Summary attachment (see zip file)	iCTR synopsis (IO102-012_Interim_CTR_Synopsis_12October2022_24JAN24.pdf) CTR Addendum synopsis (IO102-012_CTR_Addendum_Synopsis_19May2023_24JAN24.pdf)

Trial information

Trial identification

Sponsor protocol code	IO102-012
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03562871
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IO Biotech ApS
Sponsor organisation address	Ole Maaløes Vej 3, Copenhagen N, Denmark, DK-2200
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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	19 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 April 2022
Global end of trial reached?	Yes
Global end of trial date	12 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective:

a) Phase I (Safety Run-in): to investigate the safety of IO102 in combination with either pembrolizumab (pembro) alone or pembro + chemotherapy (carboplatin and pemetrexed) in patients with metastatic non-small cell lung cancer (NSCLC), that were eligible for pembro treatment as first-line therapy for stage IV disease.

b) Phase II part: to assess the efficacy of IO102 in combination with either pembro alone or pembro + chemotherapy versus either pembro alone or pembro + chemotherapy as measured by objective response rate (ORR) per investigator assessment in patients with metastatic NSCLC, that were eligible for pembro treatment as first-line therapy.

Secondary objective:

To investigate the safety profile and the secondary measures of efficacy including disease control rate (DCR), time to event parameters including duration of response (DOR), progression free survival (PFS), overall survival (OS), and tumor shrinkage.

Protection of trial subjects:

As per attached synopsis

Background therapy:

Pembrolizumab (Keytruda®), with or without chemotherapy doublet (carboplatin + pemetrexed)

Evidence for comparator: -

Actual start date of recruitment	19 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Spain: 92
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	110
EEA total number of subjects	101

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)	57
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient on trial: 19 September 2018

Last patient last visit: 12 April 2022

This was a multicentre study that involved 17 participating sites: nine centres in Spain, six centres in Germany, one centre in the United Kingdom, and one centre in The Netherlands.

Pre-assignment

Screening details:

Male or female, aged ≥ 18 years, diagnosis of metastatic NSCLC (Cohort A) or non-squamous NSCLC (Cohort B) with no prior systemic treatment for their metastatic disease, had PD-L1 tumor expression $\geq 50\%$ (Cohort A) or $< 50\%$ (Cohort B), measurable disease, adequate organ function, and an ECOG performance status of 0 or 1.

Period 1

Period 1 title	Phase I and Phase II (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study. No blinding of the patients or investigators was necessary.

N.B.: Phase II patients were randomized to the experimental treatment (A1 and B1) or the control treatment (A2 and B2) on a 2:1 ratio, depending on the level of tumor PD-L1 expression.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A1 (Phase II)

Arm description:

PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A1 (IO102 + Pembrolizumab)

Arm type	Experimental
Investigational medicinal product name	IO102
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 μ g SC Q3W, administered on Day 1 of each 3-week cycle for a maximum of 35 cycles.

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

Dosage and administration details:

200mg IV Q3W, administered as a 30-minute infusion on Day 1 of each 3-week cycle for a maximum of 35 cycles.

Arm title	Arm A2 (Phase II)
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Arm description:

PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A2 (Pembrolizumab)

Arm type	Active comparator
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Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
200mg IV Q3W, administered as a 30-minute infusion on Day 1 of each 3-week cycle for a maximum of 35 cycles.	
Arm title	Arm B1 (Phase II)
Arm description:	
PD-L1 expression <50%, Phase II Cohort B treatment B1 (IO102 + Pembrolizumab + Chemotherapy)	
Arm type	Experimental
Investigational medicinal product name	IO102
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use
Dosage and administration details:	
100 µg SC Q3W, administered on Day 1 of each 3-week cycle for a maximum of 35 cycles.	
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
200mg IV Q3W, administered as a 30-minute infusion on Day 1 of each 3-week cycle for a maximum of 35 cycles.	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
500mg/m ² IV Q3W administered as 10min infusion at least one hour after administration of pembrolizumab, on Day 1 of each 3-week cycle for a maximum of 35 cycles.	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
5mg/mL/min IV Q3W administered as 15-60min infusion immediately after administration of pemetrexed, on Day 1 of each 3-week cycle for a maximum of 4 cycles.	
Arm title	Arm B2 (Phase II)
Arm description:	
PD-L1 expression <50%, Phase II Cohort B treatment B2 (Pembrolizumab + Chemotherapy)	
Arm type	Active comparator
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
200mg IV Q3W, administered as a 30-minute infusion on Day 1 of each 3-week cycle for a maximum of 35 cycles.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:
500mg/m² IV Q3W administered as 10min infusion at least one hour after administration of pembrolizumab, on Day 1 of each 3-week cycle for a maximum of 35 cycles.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:
5mg/mL/min IV Q3W administered as 15-60min infusion immediately after administration of pemetrexed, on Day 1 of each 3-week cycle for a maximum of 4 cycles.

Arm title	Arm A (Phase I)
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Arm description:
PD-L1 expression $\geq 50\%$, Phase I Cohort A (IO102 + Pembrolizumab)

Arm type	Experimental
Investigational medicinal product name	IO102
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:
100 µg SC Q3W, administered on Day 1 of each 3-week cycle for a maximum of 35 cycles.

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

Dosage and administration details:
200 mg IV Q3W, administered as a 30-minute infusion on Day 1 of each 3-week cycle for a maximum of 35 cycles.

Arm title	Arm B (Phase I)
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Arm description:
PD-L1 expression $< 50\%$, Phase I Cohort B (IO102 + Pembrolizumab + Chemotherapy)

Arm type	Active comparator
Investigational medicinal product name	IO102
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:
100 µg SC Q3W, administered on Day 1 of each 3-week cycle for a maximum of 35 cycles.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
200mg IV Q3W, administered as a 30-minute infusion on Day 1 of each 3-week cycle for a maximum of 35 cycles.	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
500mg/m ² IV Q3W administered as 10min infusion at least one hour after administration of pembrolizumab, on Day 1 of each 3-week cycle for a maximum of 35 cycles.	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
5mg/mL/min IV Q3W administered as 15-60min infusion immediately after administration of pemetrexed, on Day 1 of each 3-week cycle for a maximum of 4 cycles.	

Number of subjects in period 1	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)
Started	32	16	33
Patients who discontinued from treatment	32	16	33
Patients not attending safety follow-up	12	4	11
Patients who discontinued from trial	32	16	33
Completed	0	0	0
Not completed	32	16	33
Physician decision	1	1	-
Disease progression	23	8	22
Adverse event, non-fatal	1	5	4
Other	7	2	4
Death	-	-	3
Need for prohibited concomitant medication	-	-	-
Patient non-compliance	-	-	-
Withdrawal of study treatment by patient	-	-	-

Number of subjects in period 1	Arm B2 (Phase II)	Arm A (Phase I)	Arm B (Phase I)
Started	17	6	6
Patients who discontinued from treatment	17	6	6
Patients not attending safety follow-up	4	1	1

Patients who discontinued from trial	17	6	6
Completed	0	0	0
Not completed	17	6	6
Physician decision	-	-	-
Disease progression	10	2	5
Adverse event, non-fatal	2	3	-
Other	2	1	-
Death	-	-	1
Need for prohibited concomitant medication	1	-	-
Patient non-compliance	1	-	-
Withdrawal of study treatment by patient	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A1 (Phase II)
Reporting group description:	
PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A1 (IO102 + Pembrolizumab)	
Reporting group title	Arm A2 (Phase II)
Reporting group description:	
PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A2 (Pembrolizumab)	
Reporting group title	Arm B1 (Phase II)
Reporting group description:	
PD-L1 expression $< 50\%$, Phase II Cohort B treatment B1 (IO102 + Pembrolizumab + Chemotherapy)	
Reporting group title	Arm B2 (Phase II)
Reporting group description:	
PD-L1 expression $< 50\%$, Phase II Cohort B treatment B2 (Pembrolizumab + Chemotherapy)	
Reporting group title	Arm A (Phase I)
Reporting group description:	
PD-L1 expression $\geq 50\%$, Phase I Cohort A (IO102 + Pembrolizumab)	
Reporting group title	Arm B (Phase I)
Reporting group description:	
PD-L1 expression $< 50\%$, Phase I Cohort B (IO102 + Pembrolizumab + Chemotherapy)	

Reporting group values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)
Number of subjects	32	16	33
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	65.4	63.7	65.4
standard deviation	± 7.94	± 6.71	± 9.60
Gender categorical			
Units: Subjects			
Female	7	5	15
Male	25	11	18
PD-L1 category			
Units: Subjects			
$< 1\%$	0	0	17
1-49%	0	0	16
$\geq 50\%$	32	16	0
ECOG performance status			
Units: Subjects			
PS 0	11	8	13
PS 1	21	8	20
Race			
Units: Subjects			
White	31	16	32
Black or African American	1	0	1

Ethnicity			
Units: Subjects			
Hispanic or Latino	2	1	0
Not Hispanic or Latino	30	15	33
PD-L1 TPS			
Units: per cent			
arithmetic mean	72.3	73.8	5.5
standard deviation	± 19.92	± 16.74	± 10.43

Reporting group values	Arm B2 (Phase II)	Arm A (Phase I)	Arm B (Phase I)
Number of subjects	17	6	6
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	62.2	67.7	51.7
standard deviation	± 9.85	± 8.38	± 17.34
Gender categorical			
Units: Subjects			
Female	6	1	4
Male	11	5	2
PD-L1 category			
Units: Subjects			
<1%	6	0	3
1-49%	11	0	3
≥50%	0	6	0
ECOG performance status			
Units: Subjects			
PS 0	5	2	2
PS 1	12	4	4
Race			
Units: Subjects			
White	17	6	6
Black or African American	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	17	6	6
PD-L1 TPS			
Units: per cent			
arithmetic mean	7.5	82.5	0.7
standard deviation	± 10.67	± 18.91	± 0.82

Reporting group values	Total		
Number of subjects	110		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	38		
Male	72		
PD-L1 category Units: Subjects			
<1%	26		
1-49%	30		
≥50%	54		
ECOG performance status Units: Subjects			
PS 0	41		
PS 1	69		
Race Units: Subjects			
White	108		
Black or African American	2		
Ethnicity Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	107		
PD-L1 TPS Units: per cent arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Arm A1 (Phase II)
Reporting group description:	
PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A1 (IO102 + Pembrolizumab)	
Reporting group title	Arm A2 (Phase II)
Reporting group description:	
PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A2 (Pembrolizumab)	
Reporting group title	Arm B1 (Phase II)
Reporting group description:	
PD-L1 expression $< 50\%$, Phase II Cohort B treatment B1 (IO102 + Pembrolizumab + Chemotherapy)	
Reporting group title	Arm B2 (Phase II)
Reporting group description:	
PD-L1 expression $< 50\%$, Phase II Cohort B treatment B2 (Pembrolizumab + Chemotherapy)	
Reporting group title	Arm A (Phase I)
Reporting group description:	
PD-L1 expression $\geq 50\%$, Phase I Cohort A (IO102 + Pembrolizumab)	
Reporting group title	Arm B (Phase I)
Reporting group description:	
PD-L1 expression $< 50\%$, Phase I Cohort B (IO102 + Pembrolizumab + Chemotherapy)	
Subject analysis set title	Phase I - ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Equivalent to the safety population (patients who received any trial treatment [IO102 and/or pembrolizumab]).	
Subject analysis set title	Phase I - per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients with measurable disease per RECIST v1.1 who received at least four cycles of IO102 treatment and had at least two post-baseline planned radiographic assessments of response. The per protocol population serves as the secondary analysis population for efficacy endpoints.	
Subject analysis set title	Phase II - ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients, regardless of whether trial medication was administered or not. The ITT population serves as the primary analysis population for efficacy endpoints.	
Subject analysis set title	Phase II - per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients with measurable disease per RECIST v1.1 who received at least four cycles of IO102 treatment and had at least two post-baseline planned radiographic assessments of response. The per protocol population serves as the secondary analysis population for efficacy endpoints.	
Subject analysis set title	Phase I/II - Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Combined Phase I and Phase II Safety Population, comprises all patients who received any trial treatment (IO102 and/or pembrolizumab).	
Subject analysis set title	Phase I/II - ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Combined Phase I and Phase II ITT Population	
Subject analysis set title	Phase I/II - per protocol

Subject analysis set type	Per protocol
Subject analysis set description:	
Combined Phase I and Phase II per protocol Population	

Primary: Safety Endpoint - Summary of adverse events (AEs)

End point title	Safety Endpoint - Summary of adverse events (AEs) ^[1]
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End point description:

The primary endpoint of Phase I of the trial included the occurrence of dose limiting toxicities (DLTs) and the incidence and severity of AEs and serious adverse events (SAEs), including events of clinical interest (ECIs), Eastern Cooperative Oncology Group (ECOG) performance status, physical examination, vital signs, electrocardiogram (ECG), and changes in laboratory values (clinical chemistry and hematology). National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 was used for grading of events.

AEs are further described in the "Adverse events" section.

End point type	Primary
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End point timeframe:

AEs and ECIs were reported from the time of treatment allocation/randomization and through 30 days following cessation of trial treatment.

Abbreviation: TEAE = treatment-emergent adverse event.

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: Safety variables were summarised descriptively.

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	16
Units: Subjects				
With at least one TEAE	32	16	33	16
Related TEAE (any study treatment)	26	13	32	16
TEAE related to IO102	22	0	22	0
TEAE related to Pembrolizumab	25	13	25	15
TEAE related to Carboplatin	0	0	30	15
TEAE related to Pemetrexed	0	0	31	16
Serious TEAE	13	5	14	9
Serious related TEAE (any study treatment)	2	0	6	6
Grade 3 or 4 TEAE	17	10	24	15
TEAE leading to discontin. of any study treatment	2	2	12	4
TEAE leading to discontinuation of IO102	2	0	7	0
TEAE leading to discontinuation of Pembrolizumab	2	2	7	4
TEAE leading to discontinuation of Carboplatin	0	0	1	1
TEAE leading to discontinuation of Pemetrexed	0	0	11	2
TEAE leading to dose interruption of Pembrolizumab	12	10	22	9
Fatal TEAE	1	1	4	0
COVID-19 Infection	1	1	2	3
DLTs	0	0	0	0

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Subjects				
With at least one TEAE	6	6		
Related TEAE (any study treatment)	3	6		
TEAE related to IO102	3	5		
TEAE related to Pembrolizumab	3	6		
TEAE related to Carboplatin	0	6		
TEAE related to Pemetrexed	0	6		
Serious TEAE	3	2		
Serious related TEAE (any study treatment)	0	1		
Grade 3 or 4 TEAE	4	4		
TEAE leading to discontin. of any study treatment	3	2		
TEAE leading to discontinuation of IO102	3	1		
TEAE leading to discontinuation of Pembrolizumab	3	1		
TEAE leading to discontinuation of Carboplatin	0	0		
TEAE leading to discontinuation of Pemetrexed	0	2		
TEAE leading to dose interruption of Pembrolizumab	3	3		
Fatal TEAE	0	1		
COVID-19 Infection	0	0		
DLTs	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy endpoint: Best Overall Response (BOR) - Phase I/II, ITT Population

End point title	Efficacy endpoint: Best Overall Response (BOR) - Phase I/II, ITT Population ^[2]
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End point description:

The primary endpoint of Phase II of the trial was the ORR evaluated by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.
ORR was defined as the rate of partial response (PR) plus complete response (CR).

End point type	Primary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 urgent safety measure [USM]) for the first 12 months, and Q12W thereafter.

Notes:

[2] - 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: The study was not formally statistically powered and no statistical hypotheses were tested. Data were summarised descriptively.

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Subjects				
Complete response (CR)	1	1	0	0
Partial response (PR)	14	6	13	9
Stable disease (SD)	10	7	18	3
Progressive disease (PD)	6	0	1	2
Not evaluable (NE)	0	0	0	1
Missing (screen failure+died prior 1st assessment)	1	2	1	2

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Subjects				
Complete response (CR)	0	0		
Partial response (PR)	3	1		
Stable disease (SD)	1	4		
Progressive disease (PD)	2	1		
Not evaluable (NE)	0	0		
Missing (screen failure+died prior 1st assessment)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy endpoint: ORR - Phase II, ITT population

End point title	Efficacy endpoint: ORR - Phase II, ITT population ^{[3][4]}
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End point description:

The primary endpoint of Phase II of the trial was the ORR evaluated by RECIST 1.1. ORR was defined as the rate of PR + CR.

ORR by baseline PD-L1 expression was a secondary endpoint and the corresponding data are provided for cohorts B and B1 combined in an attached document.

End point type	Primary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

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: The study was not formally statistically powered and no statistical hypotheses were tested. Data were summarised descriptively.

[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: Only ORR data for the four Phase II arms are provided under this section.

ORR data for the two Phase I arms are provided separately.

This is so that 95% confidence interval data can be entered when available (i.e., for Phase II arms but not for Phase I arms).

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Ratio				
number (confidence interval 95%)				
ORR	0.469 (0.309 to 0.636)	0.438 (0.231 to 0.668)	0.394 (0.247 to 0.563)	0.529 (0.310 to 0.738)

Attachments (see zip file)	ORR by baseline PD-L1 expression/Attachment 1 _IO102-
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Statistical analyses

No statistical analyses for this end point

Primary: Efficacy endpoint: ORR - Phase I, ITT Population

End point title	Efficacy endpoint: ORR - Phase I, ITT Population ^[5] ^[6]
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End point description:

The ORR was evaluated by RECIST 1.1.

ORR was defined as the rate of PR + CR.

Although ORR was the primary endpoint for Phase II, it was a secondary endpoint for Phase I.

ORR by baseline PD-L1 expression was a secondary endpoint for both phases and the corresponding data are provided for cohorts B and B1 combined in an attached document.

End point type	Primary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

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: The study was not formally statistically powered and no statistical hypotheses were tested. Data were summarised descriptively.

[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: Only ORR data for the two Phase I arms are provided under this section.

ORR data for the four Phase II arms are provided separately.

This is so that 95% confidence interval data can be entered when available (i.e., for Phase II arms but not for Phase I arms).

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Ratio				
number (not applicable)				
ORR	0.500	0.167		

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: DCR - Phase II, ITT population

End point title	Efficacy endpoint: DCR - Phase II, ITT population ^[7]
End point description:	DCR was defined as the ratio of CR + PR + stable disease (SD) (for 24 weeks or more).
End point type	Secondary
End point timeframe:	Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

Notes:

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

Justification: Only DCR data for the four Phase II arms are provided under this section.

DCR data for the two Phase I arms are provided separately.

This is so that 95% confidence interval data can be entered when available (i.e., for Phase II arms but not for Phase I arms).

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Ratio				
number (confidence interval 95%)				
DCR	0.563 (0.393 to 0.718)	0.500 (0.280 to 0.720)	0.727 (0.558 to 0.849)	0.706 (0.469 to 0.867)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: DCR - Phase I, ITT population

End point title	Efficacy endpoint: DCR - Phase I, ITT population ^[8]
End point description:	DCR was defined as the ratio of CR + PR + SD (for 24 weeks or more).
End point type	Secondary
End point timeframe:	Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

Notes:

[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: Only DCR data for the two Phase I arms are provided under this section. DCR data for the four Phase II arms are provided separately. This is so that 95% confidence interval data can be entered when available (i.e., for Phase II arms but not for Phase I arms).

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Ratio				
number (not applicable)				
DCR	0.500	0.500		

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: Time to response (TTR)

End point title	Efficacy endpoint: Time to response (TTR) ^[9]
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End point description:

The TTR was defined as the time from first study treatment administration until confirmed CR or confirmed PR. This occurrence of confirmed CR or PR was defined as TTR event. For patients with no report of confirmed CR or PR, observation was censored on the date of their last disease assessment.

TTR cumulative incidence curves for Cohort A (both phases) and Cohort B (both phases) are provided in Attachment 2.

End point type	Secondary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

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: TTR results are provided in an attachment.

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Months				
arithmetic mean (standard deviation)				
Time to response (months)	3.32 (± 2.00)	5.82 (± 5.75)		

Attachments (see zip file)	TTR/Attachment 2 _IO102-012_Efficacy
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Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: DOR

End point title	Efficacy endpoint: DOR
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End point description:

The DOR was defined as the time from first observation of a confirmed CR or a confirmed PR to Progressive Disease (PD) or death. In case an assessment of PD or a death record did not exist, the DOR was censored at the time of the last tumor assessment.

DOR for cohort A (both phases) and cohort B (both phases) is provided in Attachment 3. DOR by PD-L1 score TPS <1% and TPS >1-49% for cohort B (both phases) is also included in Attachment 3.

End point type	Secondary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Subjects				
Number of patients with objective response	15	7	13	9
Number of DOR events	8	2	10	8

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Subjects				
Number of patients with objective response	3	1		
Number of DOR events	3	1		

Attachments (see zip file)	DOR/Attachment 3 _IO102-012_Efficacy
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Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: PFS

End point title	Efficacy endpoint: PFS
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End point description:

The PFS was defined as the time from first study treatment administration until the first occurrence of PD or death. Patients who had not progressed or died were censored on the date of their last disease

assessment.

PFS for cohort A (both phases) and cohort B (both phases) is provided in Attachment 4.
PFS by PD-L1 score TPS <1% and TPS >1-49% for cohort B (both phases) is also included in Attachment 4.

End point type	Secondary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Subjects				
Number of PFS events	25	11	30	15

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Subjects				
Number of PFS events	6	6		

Attachments (see zip file)	PFS/Attachment 4 _IO102-012_Efficacy
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Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: OS

End point title	Efficacy endpoint: OS
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End point description:

The OS was defined as the time from first study treatment administration until death of any cause. Patients for whom no death was captured in the clinical database were censored at the most recent date they were known to be alive.

The OS for cohort A (both phases) and cohort B (both phases) is provided in Attachment 5.
OS by PD-L1 score TPS <1% and TPS >1-49% for cohort B (both phases) is also included in Attachment 5.

End point type	Secondary
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End point timeframe:

Patients had their disease assessed Q9W (or Q12W as part of the COVID-19 USM) for the first 12 months, and Q12W thereafter.

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Subjects				
Number of OS events (deaths)	20	8	24	11

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Subjects				
Number of OS events (deaths)	4	4		

Attachments (see zip file)	OS/Attachment 5 _IO102-012_Efficacy endpoint_OS_24JAN24.
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Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy endpoint: Time to First Subsequent Treatment or Death (TFST)

End point title	Efficacy endpoint: Time to First Subsequent Treatment or Death (TFST)
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End point description:

The TFST was defined as the time from first study treatment administration until the commencement of first subsequent treatment or death, whichever occurred first. This occurrence of a first Subsequent Treatment or death was defined as TFST event. For patients with no report of first subsequent treatment or death, observation was censored on the most recent date the patients were known to be alive.

TFST for cohort A (both phases) and cohort B (both phases) is provided in Attachment 6.

End point type	Secondary
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End point timeframe:

Time from first study treatment administration until the commencement of first subsequent treatment or death.

End point values	Arm A1 (Phase II)	Arm A2 (Phase II)	Arm B1 (Phase II)	Arm B2 (Phase II)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	33	17
Units: Number of TFST events				
Number of TFST events	24	11	28	14

End point values	Arm A (Phase I)	Arm B (Phase I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Number of TFST events				
Number of TFST events	4	5		

Attachments (see zip file)	TFST/Attachment 6 _IO102-012_Efficacy
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were monitored from the time patients provided written informed consent and throughout the trial duration, until 30 days after the last dose of trial treatment.

Adverse event reporting additional description:

AEs were graded and recorded throughout the trial and during the follow-up period according to NCI CTCAE (Version 4.03).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Phase I cohort A
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Reporting group description:

PD-L1 expression $\geq 50\%$, Phase I Cohort A (IO102 + Pembrolizumab)

Reporting group title	Phase I cohort B
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Reporting group description:

PD-L1 expression $< 50\%$, Phase I Cohort B (IO102 + Pembrolizumab + Chemotherapy)

Reporting group title	Phase II cohort A treatment A1
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Reporting group description:

PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A1 (IO102 + Pembrolizumab)

Reporting group title	Phase II cohort A treatment A2
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Reporting group description:

PD-L1 expression $\geq 50\%$, Phase II Cohort A treatment A2 (Pembrolizumab)

Reporting group title	Phase II cohort B treatment B1
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Reporting group description:

PD-L1 expression $< 50\%$, Phase II Cohort B treatment B1 (IO102 + Pembrolizumab + Chemotherapy)

Reporting group title	Phase II cohort B treatment B2
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Reporting group description:

PD-L1 expression $< 50\%$, Phase II Cohort B treatment B2 (Pembrolizumab + Chemotherapy)

Reporting group title	Overall trial population
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Reporting group description:

All patients who received any trial treatment (IO102 and/or pembrolizumab), regardless of the duration of treatment.

Serious adverse events	Phase I cohort A	Phase I cohort B	Phase II cohort A treatment A1
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	2 / 6 (33.33%)	13 / 32 (40.63%)
number of deaths (all causes)	4	4	20
number of deaths resulting from adverse events	0	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
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 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
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 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (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
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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			
Femur fracture			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
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			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 tamponade			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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			
Dysarthria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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	Additional description: SAE of anaemia (phase I cohort B) was not related to IO102, not related to pembrolizumab but was definitely related to carboplatin and definitely related to pemetrexed.		
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (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
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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			
Inguinal hernia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (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
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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

Enterocolitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Anuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 kidney disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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			
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (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
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Endocarditis bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	3 / 32 (9.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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
Submandibular abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (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

Serious adverse events	Phase II cohort A treatment A2	Phase II cohort B treatment B1	Phase II cohort B treatment B2
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)	14 / 33 (42.42%)	9 / 16 (56.25%)
number of deaths (all causes)	8	24	11
number of deaths resulting from adverse events	1	4	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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
Bladder cancer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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
Hypovolaemic shock			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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			
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (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
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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			
Pulmonary embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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			
Atrial fibrillation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
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 tamponade			

subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dysarthria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Hypoxic-ischaemic encephalopathy			

subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
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	Additional description: SAE of anaemia (phase I cohort B) was not related to IO102, not related to pembrolizumab but was definitely related to carboplatin and definitely related to pemetrexed.		
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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 / 16 (0.00%)	1 / 33 (3.03%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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 haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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			
Anuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			

subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
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 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis bacterial			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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	1 / 16 (6.25%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (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 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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
Submandibular abscess			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (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

Serious adverse events	Overall trial population		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 109 (42.20%)		
number of deaths (all causes)	71		
number of deaths resulting from adverse events	7		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour associated fever			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac tamponade			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders Dysarthria	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Seizure	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Syncope	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Dizziness	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Hypoxic-ischaemic encephalopathy	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 1		
Paraesthesia	subjects affected / exposed	1 / 109 (0.92%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders				
Anaemia	Additional description: SAE of anaemia (phase I cohort B) was not related to IO102, not related to pembrolizumab but was definitely related to carboplatin and definitely related to pemetrexed.			

subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	2 / 109 (1.83%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Anuria			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			

subjects affected / exposed	5 / 109 (4.59%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Bronchitis				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	3 / 109 (2.75%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Endocarditis bacterial				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Infection				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	7 / 109 (6.42%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	1 / 109 (0.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				

subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Submandibular abscess			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dehydration			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase I cohort A	Phase I cohort B	Phase II cohort A treatment A1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	32 / 32 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	4
Intermittent claudication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Subclavian vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	2 / 6 (33.33%)	3 / 6 (50.00%)	8 / 32 (25.00%)
occurrences (all)	2	6	11
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	5 / 32 (15.63%)
occurrences (all)	1	1	5
Injection site induration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 32 (3.13%)
occurrences (all)	0	2	1

Oedema peripheral subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1	3 / 32 (9.38%) 3
Pyrexia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 6 (33.33%) 3	9 / 32 (28.13%) 10
Chest discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	6 / 32 (18.75%) 8
Feeling hot subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Injection site reaction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	2 / 32 (6.25%) 2
Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	7 / 32 (21.88%)
occurrences (all)	0	2	8
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	15 / 32 (46.88%)
occurrences (all)	1	3	17
Haemoptysis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	3 / 32 (9.38%)
occurrences (all)	2	0	3
Pleural effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	3 / 32 (9.38%)
occurrences (all)	4	0	3
Pulmonary embolism			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Catarrh			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	5 / 32 (15.63%)
occurrences (all)	0	0	5
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Wheezing subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Psychiatric disorders			
Disorientation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 2	0 / 32 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Apathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Investigations			
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	6 / 32 (18.75%) 6
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	3 / 32 (9.38%) 3
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 6 (33.33%) 3	5 / 32 (15.63%) 7

Blood potassium increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 32 (0.00%) 0
Blood urea increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 2	0 / 32 (0.00%) 0
Blood uric acid increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 6 (16.67%) 2	0 / 32 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	3 / 32 (9.38%) 3
International normalised ratio increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 32 (0.00%) 0
Blood alkaline phosphatase subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	2 / 32 (6.25%) 2
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	2 / 32 (6.25%) 2
Blood calcium increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Glomerular filtration rate			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Sputum abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
White blood cells urine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Post procedural haematuria			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Arrhythmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	3	0	0
Neurotoxicity			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Head discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Paresis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 6 (83.33%)	8 / 32 (25.00%)
occurrences (all)	0	6	8
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 6 (50.00%)	0 / 32 (0.00%)
occurrences (all)	0	6	0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	3 / 32 (9.38%)
occurrences (all)	0	2	4

Febrile neutropenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	2 / 32 (6.25%) 2
Ear and labyrinth disorders			
Deafness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Ear discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Excessive cerumen production subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Hypoacusis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Eye disorders			
Eye pruritus subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Eyelid oedema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 32 (0.00%) 0
Retinal vein occlusion subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Conjunctival cyst subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Dry eye			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Erythema of eyelid			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Eye disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	3 / 6 (50.00%)	6 / 32 (18.75%)
occurrences (all)	2	3	9
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 6 (50.00%)	9 / 32 (28.13%)
occurrences (all)	0	4	10
Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	3 / 6 (50.00%)	3 / 32 (9.38%)
occurrences (all)	1	3	3
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	2 / 32 (6.25%)
occurrences (all)	0	3	3

Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	2 / 32 (6.25%) 4
Dyspepsia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	2 / 32 (6.25%) 2
Dysphagia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Leukoplakia oral subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Oesophagitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Hepatobiliary disorders Hypertransaminasaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	3 / 32 (9.38%) 3
Steatohepatitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 32 (0.00%) 0
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 32 (3.13%) 1
Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 32 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	1 / 32 (3.13%) 1
Erythema multiforme			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	8 / 32 (25.00%)
occurrences (all)	1	0	13
Rash			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	6 / 32 (18.75%)
occurrences (all)	1	1	8
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Intertrigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Parapsoriasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Renal impairment			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Urinary tract disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Nocturia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Hypothyroidism			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	2	1	0
Adrenal insufficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	9 / 32 (28.13%)
occurrences (all)	4	2	12
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	5 / 32 (15.63%)
occurrences (all)	2	1	7
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	3 / 32 (9.38%)
occurrences (all)	2	0	5
Sjogren's syndrome			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Systemic lupus erythematosus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Polymyalgia rheumatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Escherichia infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0

Localised infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	8 / 32 (25.00%)
occurrences (all)	2	3	13
Rhinitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	3
Lymphangitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	4 / 32 (12.50%)
occurrences (all)	1	3	4
Hyperuricaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 6 (0.00%)	5 / 32 (15.63%)
occurrences (all)	3	0	7
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	2 / 32 (6.25%)
occurrences (all)	0	3	2
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Hypophosphataemia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	2 / 32 (6.25%)
occurrences (all)	0	2	3
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Malnutrition			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase II cohort A treatment A2	Phase II cohort B treatment B1	Phase II cohort B treatment B2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	32 / 33 (96.97%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Intermittent claudication			

subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Subclavian vein thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	4 / 16 (25.00%)	18 / 33 (54.55%)	10 / 16 (62.50%)
occurrences (all)	4	22	18
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	10 / 33 (30.30%)	3 / 16 (18.75%)
occurrences (all)	1	11	4
Injection site induration			
subjects affected / exposed	0 / 16 (0.00%)	4 / 33 (12.12%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)	4 / 33 (12.12%)	4 / 16 (25.00%)
occurrences (all)	0	7	6
Pyrexia			
subjects affected / exposed	3 / 16 (18.75%)	8 / 33 (24.24%)	3 / 16 (18.75%)
occurrences (all)	4	10	4
Chest discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)	4 / 33 (12.12%)	2 / 16 (12.50%)
occurrences (all)	0	4	2
Feeling hot			

subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Gait disturbance			
subjects affected / exposed	0 / 16 (0.00%)	3 / 33 (9.09%)	2 / 16 (12.50%)
occurrences (all)	0	3	2
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 16 (0.00%)	4 / 33 (12.12%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Mucosal inflammation			
subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	4 / 16 (25.00%)
occurrences (all)	1	4	6
Pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 33 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	2
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 16 (18.75%)	7 / 33 (21.21%)	3 / 16 (18.75%)
occurrences (all)	3	7	3
Dyspnoea			
subjects affected / exposed	4 / 16 (25.00%)	8 / 33 (24.24%)	4 / 16 (25.00%)
occurrences (all)	4	11	5
Haemoptysis			
subjects affected / exposed	2 / 16 (12.50%)	3 / 33 (9.09%)	1 / 16 (6.25%)
occurrences (all)	5	3	1
Pleural effusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Productive cough			

subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	2 / 16 (12.50%)
occurrences (all)	1	2	2
Pulmonary embolism			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Catarrh			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dysphonia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Hiccups			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Pneumonitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Tachypnoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Apathy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Confusional state			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 16 (12.50%)	4 / 33 (12.12%)	6 / 16 (37.50%)
occurrences (all)	2	7	9
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	5 / 33 (15.15%)	4 / 16 (25.00%)
occurrences (all)	1	8	8
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	2 / 16 (12.50%)	8 / 33 (24.24%)	3 / 16 (18.75%)
occurrences (all)	2	13	3
Blood potassium increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Blood uric acid increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	4 / 33 (12.12%)	2 / 16 (12.50%)
occurrences (all)	1	4	3

International normalised ratio increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Blood alkaline phosphatase			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 16 (6.25%)	3 / 33 (9.09%)	4 / 16 (25.00%)
occurrences (all)	1	4	4
Blood bilirubin increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Blood calcium increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Glomerular filtration rate			

subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Sputum abnormal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 16 (6.25%)	4 / 33 (12.12%)	1 / 16 (6.25%)
occurrences (all)	1	4	1
White blood cells urine			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Post procedural haematuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin wound			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cardiac disorders			

Pericardial effusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Neurotoxicity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	3 / 16 (18.75%)
occurrences (all)	2	3	3
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)	5 / 33 (15.15%)	1 / 16 (6.25%)
occurrences (all)	0	5	1
Head discomfort			

subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 16 (0.00%)	5 / 33 (15.15%)	3 / 16 (18.75%)
occurrences (all)	0	6	4
Paresis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Taste disorder			
subjects affected / exposed	0 / 16 (0.00%)	3 / 33 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 16 (12.50%)	23 / 33 (69.70%)	11 / 16 (68.75%)
occurrences (all)	3	34	16
Neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	9 / 33 (27.27%)	7 / 16 (43.75%)
occurrences (all)	1	12	10
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	8 / 33 (24.24%)	5 / 16 (31.25%)
occurrences (all)	0	11	5
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Leukopenia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	2 / 16 (12.50%)
occurrences (all)	0	3	2
Lymphopenia			
subjects affected / exposed	0 / 16 (0.00%)	4 / 33 (12.12%)	0 / 16 (0.00%)
occurrences (all)	0	9	0
Ear and labyrinth disorders			
Deafness			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Ear discomfort subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 33 (6.06%) 2	0 / 16 (0.00%) 0
Excessive cerumen production subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Hypoacusis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Eye disorders			
Eye pruritus subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Eyelid oedema subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	3 / 33 (9.09%) 3	1 / 16 (6.25%) 1
Retinal vein occlusion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Conjunctival cyst subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Dry eye subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	3 / 33 (9.09%) 3	1 / 16 (6.25%) 1
Erythema of eyelid subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Eye disorder subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Eye pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1

Lacrimation increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	4 / 33 (12.12%) 4	3 / 16 (18.75%) 4
Vision blurred subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	12 / 33 (36.36%) 14	4 / 16 (25.00%) 8
Diarrhoea subjects affected / exposed occurrences (all)	5 / 16 (31.25%) 7	7 / 33 (21.21%) 10	4 / 16 (25.00%) 7
Dry mouth subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	2 / 33 (6.06%) 2	1 / 16 (6.25%) 1
Nausea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	12 / 33 (36.36%) 14	5 / 16 (31.25%) 9
Stomatitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	3 / 33 (9.09%) 3	1 / 16 (6.25%) 1
Vomiting subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	4 / 33 (12.12%) 6	2 / 16 (12.50%) 4
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 33 (6.06%) 2	0 / 16 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 33 (3.03%) 1	1 / 16 (6.25%) 1
Dysphagia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 33 (3.03%) 2	1 / 16 (6.25%) 1
Leukoplakia oral			

subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Oesophagitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hypertransaminaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Steatohepatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Erythema multiforme			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 16 (12.50%)	6 / 33 (18.18%)	4 / 16 (25.00%)
occurrences (all)	3	7	6
Rash			
subjects affected / exposed	0 / 16 (0.00%)	6 / 33 (18.18%)	4 / 16 (25.00%)
occurrences (all)	0	7	5
Alopecia			

subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Dermatitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Hyperhidrosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Intertrigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Onycholysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Palmar erythema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Parapsoriasis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Rash macular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Rash pruritic subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	3 / 33 (9.09%) 3	0 / 16 (0.00%) 0
Skin hyperpigmentation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Renal impairment subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Urinary tract disorder subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Chronic kidney disease subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	3 / 33 (9.09%) 3	0 / 16 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	2 / 16 (12.50%) 3
Nocturia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 33 (3.03%) 1	1 / 16 (6.25%) 1
Renal failure subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 33 (0.00%) 0	1 / 16 (6.25%) 1
Endocrine disorders			

Hyperthyroidism			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	4 / 16 (25.00%)	1 / 33 (3.03%)	5 / 16 (31.25%)
occurrences (all)	4	1	5
Adrenal insufficiency			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 16 (18.75%)	13 / 33 (39.39%)	6 / 16 (37.50%)
occurrences (all)	4	15	11
Back pain			
subjects affected / exposed	1 / 16 (6.25%)	4 / 33 (12.12%)	1 / 16 (6.25%)
occurrences (all)	1	4	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	6 / 33 (18.18%)	2 / 16 (12.50%)
occurrences (all)	0	7	3
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)	3 / 33 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Sjogren's syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Bone pain			

subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Flank pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 16 (6.25%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Muscular weakness			
subjects affected / exposed	2 / 16 (12.50%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Polymyalgia rheumatica			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Escherichia infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	4 / 33 (12.12%)	1 / 16 (6.25%)
occurrences (all)	0	4	1
Respiratory tract infection			
subjects affected / exposed	2 / 16 (12.50%)	6 / 33 (18.18%)	5 / 16 (31.25%)
occurrences (all)	2	7	5

Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Conjunctivitis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Fungal infection			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Gingivitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	2 / 16 (12.50%)
occurrences (all)	0	1	3
Oral candidiasis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Paronychia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Tonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	3 / 33 (9.09%) 3	1 / 16 (6.25%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	4 / 33 (12.12%) 4	1 / 16 (6.25%) 1
Lymphangitis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3	8 / 33 (24.24%) 8	4 / 16 (25.00%) 8
Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 33 (0.00%) 0	0 / 16 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 4	8 / 33 (24.24%) 14	2 / 16 (12.50%) 3
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	3 / 33 (9.09%) 6	2 / 16 (12.50%) 2
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 33 (6.06%) 2	0 / 16 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 33 (6.06%) 2	1 / 16 (6.25%) 1
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 33 (6.06%) 2	2 / 16 (12.50%) 2
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 33 (6.06%) 6	2 / 16 (12.50%) 2
Hyperkalaemia			

subjects affected / exposed	2 / 16 (12.50%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	3	2	1
Hypocalcaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 33 (6.06%)	0 / 16 (0.00%)
occurrences (all)	0	6	0
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 33 (3.03%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Malnutrition			
subjects affected / exposed	1 / 16 (6.25%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Overall trial population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	108 / 109 (99.08%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	7		
Intermittent claudication			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Subclavian vein thrombosis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
General disorders and administration site conditions			

Administration site erythema			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	45 / 109 (41.28%)		
occurrences (all)	63		
Fatigue			
subjects affected / exposed	21 / 109 (19.27%)		
occurrences (all)	23		
Injection site induration			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	8		
Oedema peripheral			
subjects affected / exposed	13 / 109 (11.93%)		
occurrences (all)	18		
Pyrexia			
subjects affected / exposed	26 / 109 (23.85%)		
occurrences (all)	32		
Chest discomfort			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	12 / 109 (11.01%)		
occurrences (all)	14		
Feeling hot			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	2		
Gait disturbance			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	5		
Influenza like illness			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Injection site reaction			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		

Mucosal inflammation subjects affected / exposed occurrences (all)	9 / 109 (8.26%) 13		
Pain subjects affected / exposed occurrences (all)	5 / 109 (4.59%) 5		
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	21 / 109 (19.27%) 23		
Dyspnoea subjects affected / exposed occurrences (all)	34 / 109 (31.19%) 41		
Haemoptysis subjects affected / exposed occurrences (all)	10 / 109 (9.17%) 14		
Pleural effusion subjects affected / exposed occurrences (all)	4 / 109 (3.67%) 4		
Productive cough subjects affected / exposed occurrences (all)	9 / 109 (8.26%) 12		
Pulmonary embolism subjects affected / exposed occurrences (all)	3 / 109 (2.75%) 3		
Rhinorrhoea subjects affected / exposed occurrences (all)	3 / 109 (2.75%) 3		
Catarrh subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Dysphonia			

subjects affected / exposed occurrences (all)	6 / 109 (5.50%) 6		
Hiccups subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Pneumonitis subjects affected / exposed occurrences (all)	8 / 109 (7.34%) 8		
Tachypnoea subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Wheezing subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Psychiatric disorders Disorientation subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 2		
Anxiety subjects affected / exposed occurrences (all)	4 / 109 (3.67%) 4		
Apathy subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Confusional state subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Insomnia subjects affected / exposed occurrences (all)	4 / 109 (3.67%) 4		
Investigations Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Alanine aminotransferase increased			

subjects affected / exposed	19 / 109 (17.43%)		
occurrences (all)	25		
Aspartate aminotransferase increased			
subjects affected / exposed	14 / 109 (12.84%)		
occurrences (all)	21		
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	3		
Blood creatinine increased			
subjects affected / exposed	20 / 109 (18.35%)		
occurrences (all)	28		
Blood potassium increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	5		
Blood uric acid increased			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	4		
Gamma-glutamyltransferase increased			
subjects affected / exposed	11 / 109 (10.09%)		
occurrences (all)	12		
International normalised ratio increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	4		
Blood alkaline phosphatase			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			

subjects affected / exposed	10 / 109 (9.17%)		
occurrences (all)	11		
Blood bilirubin increased			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	6		
Blood calcium increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Blood cholesterol increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Blood phosphorus decreased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
C-reactive protein increased			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Glomerular filtration rate			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Glomerular filtration rate decreased			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	5		
Sputum abnormal			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Weight decreased			

subjects affected / exposed occurrences (all)	7 / 109 (6.42%) 7		
White blood cells urine subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Amylase increased subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Injury, poisoning and procedural complications			
Anaemia postoperative subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Post procedural haematuria subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Fracture subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Limb injury subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Skin wound subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Cardiac disorders			
Pericardial effusion subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Arrhythmia subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Palpitations subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Supraventricular tachycardia			

subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	3		
Neurotoxicity			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	5		
Somnolence			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	8		
Dysgeusia			
subjects affected / exposed	7 / 109 (6.42%)		
occurrences (all)	7		
Head discomfort			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	10 / 109 (9.17%)		
occurrences (all)	12		
Paresis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	3		

Taste disorder subjects affected / exposed occurrences (all)	3 / 109 (2.75%) 3		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	49 / 109 (44.95%) 67		
Neutropenia subjects affected / exposed occurrences (all)	20 / 109 (18.35%) 29		
Thrombocytopenia subjects affected / exposed occurrences (all)	18 / 109 (16.51%) 22		
Febrile neutropenia subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Leukopenia subjects affected / exposed occurrences (all)	4 / 109 (3.67%) 5		
Lymphopenia subjects affected / exposed occurrences (all)	6 / 109 (5.50%) 11		
Ear and labyrinth disorders			
Deafness subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Ear discomfort subjects affected / exposed occurrences (all)	2 / 109 (1.83%) 2		
Excessive cerumen production subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Hypoacusis subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Eye disorders			

Eye pruritus			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Eyelid oedema			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	6		
Retinal vein occlusion			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Conjunctival cyst			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	6		
Erythema of eyelid			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Eye disorder			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Lacrimation increased			
subjects affected / exposed	8 / 109 (7.34%)		
occurrences (all)	9		
Vision blurred			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	28 / 109 (25.69%)		
occurrences (all)	37		
Diarrhoea			

subjects affected / exposed	28 / 109 (25.69%)		
occurrences (all)	38		
Dry mouth			
subjects affected / exposed	8 / 109 (7.34%)		
occurrences (all)	8		
Nausea			
subjects affected / exposed	25 / 109 (22.94%)		
occurrences (all)	31		
Stomatitis			
subjects affected / exposed	7 / 109 (6.42%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	11 / 109 (10.09%)		
occurrences (all)	17		
Abdominal pain upper			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	6		
Dyspepsia			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Dysphagia			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	4		
Leukoplakia oral			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Oesophagitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Salivary hypersecretion			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		

Steatohepatitis			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Hyperbilirubinaemia			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Erythema multiforme			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	21 / 109 (19.27%)		
occurrences (all)	30		
Rash			
subjects affected / exposed	18 / 109 (16.51%)		
occurrences (all)	22		
Alopecia			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Dermatitis			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	3		
Dermatitis allergic			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Hyperhidrosis			

subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	4		
Intertrigo			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Onycholysis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Palmar erythema			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Parapsoriasis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Rash macular			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Rash pruritic			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Skin hyperpigmentation			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Renal impairment			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Urinary tract disorder			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Chronic kidney disease			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Dysuria			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	5		
Nocturia			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Renal failure			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Hypothyroidism			
subjects affected / exposed	13 / 109 (11.93%)		
occurrences (all)	13		
Adrenal insufficiency			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	35 / 109 (32.11%)		
occurrences (all)	48		
Back pain			
subjects affected / exposed	14 / 109 (12.84%)		
occurrences (all)	16		
Musculoskeletal chest pain			
subjects affected / exposed	11 / 109 (10.09%)		
occurrences (all)	13		
Musculoskeletal pain			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	8 / 109 (7.34%)		
occurrences (all)	10		
Sjogren's syndrome			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Systemic lupus erythematosus			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Arthritis			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	3		
Flank pain			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	5		

Musculoskeletal discomfort subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Myalgia subjects affected / exposed occurrences (all)	5 / 109 (4.59%) 5		
Polymyalgia rheumatica subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 2		
Infections and infestations			
Diverticulitis subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Escherichia infection subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Localised infection subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 109 (7.34%) 8		
Respiratory tract infection subjects affected / exposed occurrences (all)	24 / 109 (22.02%) 32		
Rhinitis subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1		
Bronchitis subjects affected / exposed occurrences (all)	3 / 109 (2.75%) 3		
Cellulitis subjects affected / exposed occurrences (all)	4 / 109 (3.67%) 4		
Conjunctivitis			

subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Fungal infection			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Gingivitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	2		
Lower respiratory tract infection			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	4		
Oral candidiasis			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	3		
Paronychia			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	5		
Tonsillitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	8		
Lymphangitis			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	21 / 109 (19.27%)		
occurrences (all)	27		
Hyperuricaemia			
subjects affected / exposed	2 / 109 (1.83%)		
occurrences (all)	2		
Hypoalbuminaemia			
subjects affected / exposed	21 / 109 (19.27%)		
occurrences (all)	31		
Hypokalaemia			
subjects affected / exposed	9 / 109 (8.26%)		
occurrences (all)	13		
Hypomagnesaemia			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	5		
Hypophosphataemia			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	8		
Hypercalcaemia			
subjects affected / exposed	6 / 109 (5.50%)		
occurrences (all)	6		
Hyperglycaemia			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	8		
Hyperkalaemia			
subjects affected / exposed	5 / 109 (4.59%)		
occurrences (all)	8		
Hypocalcaemia			
subjects affected / exposed	3 / 109 (2.75%)		
occurrences (all)	7		
Hyponatraemia			
subjects affected / exposed	4 / 109 (3.67%)		
occurrences (all)	4		
Malnutrition			
subjects affected / exposed	1 / 109 (0.92%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2018	<p>Global amendment 1, Protocol v2.0, dated 17-Sep-2018</p> <p>Changes in the Conduct of the Trial:</p> <ul style="list-style-type: none">- Eligibility criteria updated to clarify:<ul style="list-style-type: none">a) permissible genomic tumor aberrations in line with KEYNOTE-024 and KEYNOTE-189.b) the permissible prior anti-cancer therapy and to align with KEYNOTE-042 to ensure the patient population was comparable.c) the location and timeframes of prior radiotherapy which would exclude patients from the trial to ensure no added toxicity after curatively intended radiotherapy and to align with KEYNOTE-189 and KEYNOTE-021.d) the permissible participation in a trial of an investigational agent or device (and related timeframes) prior to inclusion in the trial.- Addition of exclusion criterion of prior allogeneic tissue/solid organ transplant in line with standard text from Merck.- Secondary endpoints in the Trial Summary section updated for consistency with protocol Section 4.- Schedule of assessments updated to clarify the use of archival tissue for screening, the requirements for biopsies, and to introduce a nadir period to ensure all lab values were known prior to biopsy.- Trial design updated to clarify:<ul style="list-style-type: none">a) the decision process by the SMC for expansion of the cohort, recruitment into Phase II and Cohort B.b) the process for sequential patient enrolment and clarify the trial pause criteria.- DLT definition updated to clarify the decision process by the SMC.- Therapeutic background updated to clarify IO102 mode of action.- Trial diagram updated to clarify AE and ECI reporting requirements and End of Trial definition.- Trial treatment section updated to clarify IO102 dose and duration of treatments.- Contraception guidance updated to include use of highly effective contraception methods and requirements for female contraception.- Blood sampling for biomarkers mandated to ensure enough material for the analysis. Clarification re. number of samples.- General administrative changes and corrections were also made.
03 April 2020	<p>Global amendment 2, Protocol v3.0, dated 03-Apr-2020</p> <p>Changes in the Conduct of the Trial:</p> <ul style="list-style-type: none">- Urgent Safety Measures were implemented in response to the COVID-19 pandemic to allow Investigators to minimize or eliminate the immediate hazard of COVID-19 by reducing the number of hospital visits associated with this clinical trial. Pembrolizumab and IO102 could be administered on a Q6W basis, rather than Q3W, and radiological tumor assessments for patients in the first 12 months of the trial could be carried out Q12W rather than Q9W to coincide with the new dosing schedule. Investigators could also discontinue pemetrexed maintenance and combination chemotherapy given to Cohort B1 and B2 patients. Furthermore, patients suspected of having COVID-19 could be given a COVID-19 polymerase chain reaction test.- IO102 preparation updated per regulatory request regarding the preparation of IO102 in a laminar flow cabinet. Timing of IO102 preparation also updated.- General administrative changes and corrections were also made throughout the protocol. <p>Changes in the Planned Analyses:</p> <ul style="list-style-type: none">- Statistical methods section was updated to clarify how the statistical analysis plan was being updated as a result of the COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported