



## Clinical trial results:

**An open label, dose escalation followed by dose expansion, safety and tolerability trial of CAN04, a fully humanized monoclonal antibody against IL1RAP, in subjects with solid malignant tumors**

### Summary

EudraCT number	2017-001111-36
Trial protocol	BE NO DK NL DE AT SE EE ES LT LV
Global end of trial date	14 March 2024

### Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025
Summary attachment (see zip file)	CAN04CLIN001 Summary Attachment (CAN04CLIN001 EudraCT Summary Attachment.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	CAN04CLIN001
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03267316
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Cantargia AB
Sponsor organisation address	Scheelevagen 27, Lund, Sweden, 22363
Public contact	Regulatory Affairs , Cantargia AB, +46 (0)46 2756260, regulatory@cantargia.com
Scientific contact	Regulatory Affairs , Cantargia AB, +46 (0)46 2756260, regulatory@cantargia.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 March 2024
Global end of trial reached?	Yes
Global end of trial date	14 March 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Part I

- To define the Maximum Tolerated Dose (MTD) or Recommended Phase 2 dose (RP2D) of CAN04, given weekly (Q1W) in subjects with relapsed or refractory non small cell lung cancer (NSCLC), pancreatic ductal adenocarcinoma (PDAC), triple negative breast cancer (TNBC) or colorectal cancer (CRC).

Part II

- To determine the safety and tolerability of CAN04 in subjects with squamous or non-squamous NSCLC or PDAC tumors, when given as monotherapy or in combination with standard of care (SoC) chemotherapy regimen and to identify the RP2D of CAN04 in combination with SoC chemotherapy.

Protection of trial subjects:

Priming dose of CAN04 in combination with pre-medication with corticosteroids, paracetamol and antihistamines was introduced during Part I and used to reduce the risk of infusion related reactions. The priming dose was for PDEXx and NCP arms replaced with a ramping infusion of CAN04 for patients being able to start treatment with CAN04 and chemotherapy on the same day.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 August 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	36 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 22
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 40
Country: Number of subjects enrolled	Denmark: 28
Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Latvia: 14
Country: Number of subjects enrolled	Lithuania: 30

Worldwide total number of subjects	167
EEA total number of subjects	167

Notes:

<b>Subjects enrolled per age group</b>	
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)	96
From 65 to 84 years	69
85 years and over	2

## Subject disposition

### Recruitment

Recruitment details:

Overall recruitment period for the study was between 26-Aug-2017 to 12-Apr-2023 and subjects were recruited among 26 centres in Belgium, the Netherlands, Denmark, Norway, Austria, Sweden, Germany, Spain, Estonia, Latvia, Lithuania.

### Pre-assignment

Screening details:

Subjects should have a measurable disease in accordance with irRC (enrolled prior to protocol version 7) or iRECIST (enrolled from protocol version 7) by CT or MR scan. If received any previous treatment with chemo-, biologic/targeted- or radiation therapy a wash-out period of 4 weeks applied (6 weeks for treatments known having delayed toxicity).

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Part I - Dose escalation

Arm description:

Phase 1 dose-escalation arm (3+3 design) to assess the safety of CAN04 monotherapy administered at 1, 1.5, 3, 6, and 10 mg/kg in patients with unresectable NSCLC, PDAC, CRC, or TNBC that were refractory to standard therapy or for whom no standard therapy existed. The primary aim was to assess safety and to define the MTD or RP2D of CAN04 administered once weekly.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

CAN04 monotherapy was administered at 1, 1.5, 3, 6, or 10 mg/kg depending on cohort once weekly. For cohort 2 and 3 a priming dose of 1.0 mg/kg was used and from cohort 4 and onwards a priming dose of 0.5 mg/kg was used. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). A prolonged infusion time (120 minutes) was applied for the priming dose only from second part of cohort 4 onwards. From cohort 2 onwards premedication with corticosteroids, antihistamine and paracetamol was given before first administration.

<b>Arm title</b>	Part II Monotherapy Arm A
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Arm description:

Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly in patients with unresectable squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

CAN04 monotherapy was administered at 10 mg/kg once weekly. A priming dose of 0.5 mg/kg was given at first administration. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). A prolonged infusion time (120 minutes) was applied for the priming dose only. Premedication with corticosteroids, antihistamine and paracetamol was given before first administration.

<b>Arm title</b>	Part II Monotherapy Arm B
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**Arm description:**

Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly for first 6 weeks followed by biweekly administration in patients with unresectable squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

CAN04 monotherapy was administered at 10 mg/kg once weekly for first 6 weeks followed by biweekly administration. A priming dose of 0.5 mg/kg was given at first administration. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). A prolonged infusion time (120 minutes) was applied for the priming dose only. Premedication with corticosteroids, antihistamine and paracetamol was given before first administration.

<b>Arm title</b>	Part II Monotherapy Arm E
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**Arm description:**

Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 15 mg/kg once weekly for first 6 weeks followed by biweekly administration in patients with unresectable, locally advanced or metastatic squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

CAN04 monotherapy was administered at 15 mg/kg once weekly for first 6 weeks followed by biweekly administration. A priming dose of 0.5 mg/kg was given at first administration. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). A prolonged infusion time (120 minutes) was applied for the priming dose only. Premedication with corticosteroids, antihistamine and paracetamol was given before first administration.

<b>Arm title</b>	Part II Combination therapy Arm C
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**Arm description:**

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and cisplatin in patients with stage III or IV squamous or non-squamous non-small cell lung cancer (NSCLC) who were candidates for 1st line of standard chemotherapy regimen with cisplatin/gemcitabine or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with cisplatin/gemcitabine. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase but a provisional MTD was reached on 5 mg/kg and dose reduced to 1 mg/kg and re-escalated to 2.5 mg/kg.

Arm type	Experimental
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Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

CAN04 was administered at assigned dose (5, 1 or 2.5 mg/kg) once weekly for first 6 weeks followed by biweekly administration. A priming dose of 0.5 mg/kg was given at first administration. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). A prolonged infusion time (120 minutes) was applied for the priming dose only. Before first administration of CAN04 premedication with corticosteroids, antihistamine and paracetamol was given.

CAN04 alone or with gemcitabine as maintenance therapy was allowed once the 4-6 cycles in combination with cisplatin was completed.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	L01BC05
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use, Intravenous drip use

**Dosage and administration details:**

Gemcitabine was administered at 1250 mg/m<sup>2</sup> on Days 1 and 8 in cycles of 21 days in combination with cisplatin for 4-6 cycles. CAN04 alone or with gemcitabine as maintenance therapy was subsequently allowed. Treatment with gemcitabine started with second administration of CAN04.

Administration of gemcitabine followed the recommendations for premedication and administration outlined for the indication and in combination with cisplatin in the SmPC of the marketed product and in alignment with local clinical practice.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	L01XA01
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

Cisplatin was administered at 75 to 100 mg/m<sup>2</sup> on Day 1 in cycles of 21 days in combination with gemcitabine for 4 - 6 cycles. Treatment with cisplatin started with second administration of CAN04.

Administration of cisplatin followed the recommendations for premedication and administration outlined for the indication and in combination with gemcitabine in the SmPC of the marketed product and in alignment with local clinical practice.

<b>Arm title</b>	Part II Combination therapy Arm NCP
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**Arm description:**

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with carboplatin and pemetrexed in patients with stage III or IV non-squamous non-small cell lung cancer (NSCLC) who were candidates for 1st line of standard chemotherapy regimen with carboplatin/pemetrexed or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with carboplatin/pemetrexed.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

CAN04 was administered at 2.5 mg/kg on Day 1 and on Day 8 in cycles of 21 days. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). Assigned full dose was administered at first administration as a 4 hour ramping infusion. Before first administration of CAN04 premedication with corticosteroids, antihistamine and paracetamol was given.

CAN04 alone or with pemetrexed as maintenance therapy was subsequently allowed after 4-6 cycles of carboplatin was completed.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	L01XA02
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

Carboplatin was administered at AUC 5 mg/ml/min on Day 1 in cycles of 21 days for 4-6 cycles.

Administration of carboplatin followed the recommendations for premedication and administration outlined for the indication in the SmPC of the marketed product and in alignment with local clinical practice.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	L01BA04
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

Pemetrexed was administered at 500 mg/m<sup>2</sup> on Day 1 in cycles of 21 days in combination with carboplatin for 4-6 cycles. CAN04 alone or with pemetrexed as maintenance therapy was subsequently allowed.

Administration of pemetrexed followed the recommendations for premedication and administration outlined for the indication in the SmPC of the marketed product and in alignment with local clinical practice.

<b>Arm title</b>	Part II Combination therapy Arm D
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Arm description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase. After 7.5 mg/kg was found to be above MTD the expansion phase was done with 5 mg/kg.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use, Intravenous drip use

Dosage and administration details:

CAN04 was administered at assigned dose (5, or 7.5 mg/kg) once weekly for first 6 weeks followed by biweekly administration. A priming dose of 0.5 mg/kg was given at first administration. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). A prolonged infusion time (120 minutes) was applied for the priming dose only. Before first administration of CAN04 premedication with corticosteroids, antihistamine and paracetamol was given.

CAN04 alone or with gemcitabine or nab-paclitaxel as maintenance therapy was allowed once the investigator discontinued gemcitabine or nab-paclitaxel due to toxicity.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	L01BC05
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

Gemcitabine was administered at 1000 mg/m<sup>2</sup> on Days 1, 8 and 15 in cycles of 28 days. CAN04 alone

or with nab-paclitaxel as maintenance therapy was subsequently allowed if investigator discontinued gemcitabine due to toxicity. Treatment with gemcitabine started with second administration of CAN04.

Administration of gemcitabine followed the recommendations for premedication and administration outlined for the indication and in combination with nab-paclitaxel in the SmPC of the marketed product and in alignment with local clinical practice.

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	L01CD01
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

Nab-paclitaxel was administered at 125 mg/m<sup>2</sup> on Days 1, 8 and 15 in cycles of 28 days. CAN04 alone or with gemcitabine as maintenance therapy was subsequently allowed if investigator discontinued nab-paclitaxel due to toxicity. Treatment with nab-paclitaxel started with second administration of CAN04.

Administration of nab-paclitaxel followed the recommendations for premedication and administration outlined for the indication and in combination with gemcitabine in the SmPC of the marketed product and in alignment with local clinical practice.

<b>Arm title</b>	Part II Combination therapy Arm PDEX1
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Arm description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 1 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX1 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

CAN04 was administered at 1.0 mg/kg on Day 1 and Day 15 in cycles of 28. During Cycle 1 CAN04 was administered also on Day 8. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). Assigned full dose was administered at first administration as a 4 hour ramping infusion. Before first administration of CAN04 premedication with corticosteroids, antihistamine and paracetamol was given.

CAN04 alone or with gemcitabine or nab-paclitaxel as maintenance therapy was allowed once the investigator discontinued gemcitabine or nab-paclitaxel due to toxicity.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	L01BC05
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous drip use , Intravenous use

Dosage and administration details:

Gemcitabine was administered at 1000 mg/m<sup>2</sup> on Days 1, 8 and 15 in cycles of 28 days. CAN04 alone or with nab-paclitaxel as maintenance therapy was subsequently allowed if investigator discontinued gemcitabine due to toxicity.

Administration of gemcitabine followed the recommendations for premedication and administration outlined for the indication and in combination with nab-paclitaxel in the SmPC of the marketed product and in alignment with local clinical practice.

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	L01CD01
Other name	



Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

Nab-paclitaxel was administered at 125 mg/m<sup>2</sup> on Days 1, 8 and 15 in cycles of 28 days. CAN04 alone or with gemcitabine as maintenance therapy was subsequently allowed if investigator discontinued nab-paclitaxel due to toxicity.

Administration of nab-paclitaxel followed the recommendations for premedication and administration outlined for the indication and in combination with gemcitabine in the SmPC of the marketed product and in alignment with local clinical practice.

<b>Arm title</b>	Part II Combination therapy Arm PDEX2.5
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**Arm description:**

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 2.5 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX2.5 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Arm type	Experimental
Investigational medicinal product name	CAN04
Investigational medicinal product code	
Other name	Nadunolimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

CAN04 was administered at 2.5 mg/kg on Day 1 and Day 15 in cycles of 28. During Cycle 1 CAN04 was administered also on Day 8. CAN04 is a concentrate for infusion diluted to the appropriate concentration in normal saline and was administered via intravenous infusion over a 60-minute period (an infusion period of 55-70 minutes was allowed). Assigned full dose was administered at first administration as a 4 hour ramping infusion. Before first administration of CAN04 premedication with corticosteroids, antihistamine and paracetamol was given.

CAN04 alone or with gemcitabine or nab-paclitaxel as maintenance therapy was allowed once the investigator discontinued gemcitabine or nab-paclitaxel due to toxicity.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	L01BC05
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

Gemcitabine was administered at 1000 mg/m<sup>2</sup> on Days 1, 8 and 15 in cycles of 28 days. CAN04 alone or with nab-paclitaxel as maintenance therapy was subsequently allowed if investigator discontinued gemcitabine due to toxicity.

Administration of gemcitabine followed the recommendations for premedication and administration outlined for the indication and in combination with nab-paclitaxel in the SmPC of the marketed product and in alignment with local clinical practice.

Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	L01CD01
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous drip use , Intravenous use

**Dosage and administration details:**

Nab-paclitaxel was administered at 125 mg/m<sup>2</sup> on Days 1, 8 and 15 in cycles of 28 days. CAN04 alone or with gemcitabine as maintenance therapy was subsequently allowed if investigator discontinued nab-paclitaxel due to toxicity.

Administration of nab-paclitaxel followed the recommendations for premedication and administration outlined for the indication and in combination with gemcitabine in the SmPC of the marketed product

and in alignment with local clinical practice.

<b>Number of subjects in period 1</b>	Part I - Dose escalation	Part II Monotherapy Arm A	Part II Monotherapy Arm B
Started	22	10	10
Completed	17	7	10
Not completed	5	3	0
Adverse event, serious fatal	-	-	-
Physician decision	3	-	-
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	2	2	-
Death	-	1	-
Termination of the study	-	-	-
General health deterioration	-	-	-

<b>Number of subjects in period 1</b>	Part II Monotherapy Arm E	Part II Combination therapy Arm C	Part II Combination therapy Arm NCP
Started	6	33	10
Completed	4	25	5
Not completed	2	8	5
Adverse event, serious fatal	1	-	-
Physician decision	-	-	-
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	1	1	-
Death	-	3	2
Termination of the study	-	2	2
General health deterioration	-	-	1

<b>Number of subjects in period 1</b>	Part II Combination therapy Arm D	Part II Combination therapy Arm PDEX1	Part II Combination therapy Arm PDEX2.5
Started	36	20	20
Completed	25	16	10
Not completed	11	4	10
Adverse event, serious fatal	2	-	-
Physician decision	-	-	1
Consent withdrawn by subject	3	1	2
Adverse event, non-fatal	4	1	4

Death	2	2	2
Termination of the study	-	-	1
General health deterioration	-	-	-

## Baseline characteristics

### Reporting groups

Reporting group title	Part I - Dose escalation
Reporting group description: Phase 1 dose-escalation arm (3+3 design) to assess the safety of CAN04 monotherapy administered at 1, 1.5, 3, 6, and 10 mg/kg in patients with unresectable NSCLC, PDAC, CRC, or TNBC that were refractory to standard therapy or for whom no standard therapy existed. The primary aim was to assess safety and to define the MTD or RP2D of CAN04 administered once weekly.	
Reporting group title	Part II Monotherapy Arm A
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly in patients with unresectable squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.	
Reporting group title	Part II Monotherapy Arm B
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly for first 6 weeks followed by biweekly administration in patients with unresectable squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.	
Reporting group title	Part II Monotherapy Arm E
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 15 mg/kg once weekly for first 6 weeks followed by biweekly administration in patients with unresectable, locally advanced or metastatic squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.	
Reporting group title	Part II Combination therapy Arm C
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and cisplatin in patients with stage III or IV squamous or non-squamous non-small cell lung cancer (NSCLC) who were candidates for 1st line of standard chemotherapy regimen with cisplatin/gemcitabine or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with cisplatin/gemcitabine. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase but a provisional MTD was reached on 5 mg/kg and dose reduced to 1 mg/kg and re-escalated to 2.5 mg/kg.	
Reporting group title	Part II Combination therapy Arm NCP
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with carboplatin and pemetrexed in patients with stage III or IV non-squamous non-small cell lung cancer (NSCLC) who were candidates for 1st line of standard chemotherapy regimen with carboplatin/pemetrexed or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with carboplatin/pemetrexed.	
Reporting group title	Part II Combination therapy Arm D
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase. After 7.5 mg/kg was found to be above MTD the expansion phase was done with 5 mg/kg.	
Reporting group title	Part II Combination therapy Arm PDEX1
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 1 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen	

with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX1 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Reporting group title	Part II Combination therapy Arm PDEX2.5
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 2.5 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX2.5 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Reporting group values	Part I - Dose escalation	Part II Monotherapy Arm A	Part II Monotherapy Arm B
Number of subjects	22	10	10
Age categorical Units: Subjects			
Adults (18-64 years)	15	5	6
From 65-84 years	7	5	4
85 years and over	0	0	0
Age continuous Units: years			
median	63.0	61.0	63.5
full range (min-max)	39 to 81	49 to 72	40 to 73
Gender categorical Units: Subjects			
Female	8	2	2
Male	14	8	8
Child-bearing Potential Units: Subjects			
No	7	2	2
Yes	1	0	0
Not applicable	14	8	8
Ethnicity Units: Subjects			
Not Hispanic or Latino	14	2	5
Not reported	8	8	5
Race Units: Subjects			
White	14	2	5
Asian	0	0	0
Not reported	8	8	5
Primary Disease Units: Subjects			
NSCLC - subtype not defined	4	2	4
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	6	8	6
CRC	12	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location			

at Study Entry			
Units: Subjects			
Yes	9	6	9
No	13	4	1
Number of prior lines of treatment for metastatic disease			
Units: Subjects			
No prior lines		0	0
1 prior line		4	3
2 prior lines		2	3
3 prior lines		3	2
4 prior lines		1	0
5 prior lines		0	2
Not recorded	22	0	0
ECOG status			
Units: Subjects			
ECOG = 0	15	3	5
ECOG = 1	7	7	5
Height			
Units: cm			
median	174.5	177.6	179.0
full range (min-max)	155 to 191	165 to 198	172 to 185
Weight			
Units: kg			
median	79.1	72.3	75.7
full range (min-max)	53 to 124	45 to 126	62 to 107
Body Mass Index			
Units: kg/m2			
median	25.6	23.3	24.5
full range (min-max)	18 to 44	16 to 34	21 to 32

<b>Reporting group values</b>	Part II Monotherapy Arm E	Part II Combination therapy Arm C	Part II Combination therapy Arm NCP
Number of subjects	6	33	10
Age categorical			
Units: Subjects			
Adults (18-64 years)	5	17	3
From 65-84 years	1	16	7
85 years and over	0	0	0
Age continuous			
Units: years			
median	62.0	64.0	66.5
full range (min-max)	58 to 73	39 to 77	55 to 76
Gender categorical			
Units: Subjects			
Female	3	11	5
Male	3	22	5
Child-bearing Potential			
Units: Subjects			
No	3	10	5
Yes	0	1	0
Not applicable	3	22	5

Ethnicity			
Units: Subjects			
Not Hispanic or Latino	4	32	10
Not reported	2	1	0
Race			
Units: Subjects			
White	4	32	10
Asian	0	0	0
Not reported	2	1	0
Primary Disease			
Units: Subjects			
NSCLC - subtype not defined	3	1	0
NSCLC - squamous	0	14	0
NSCLC - non-squamous	0	18	10
PDAC	3	0	0
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry			
Units: Subjects			
Yes	5	32	9
No	1	1	1
Number of prior lines of treatment for metastatic disease			
Units: Subjects			
No prior lines	0	17	7
1 prior line	1	16	3
2 prior lines	2	0	0
3 prior lines	2	0	0
4 prior lines	0	0	0
5 prior lines	1	0	0
Not recorded	0	0	0
ECOG status			
Units: Subjects			
ECOG = 0	3	14	2
ECOG = 1	3	19	8
Height			
Units: cm			
median	171.8	172.0	169.5
full range (min-max)	162 to 188	152 to 189	151 to 175
Weight			
Units: kg			
median	77.7	68.0	69.5
full range (min-max)	74 to 99	53 to 108	54 to 88
Body Mass Index			
Units: kg/m2			
median	27.1	25.6	26.8
full range (min-max)	22 to 34	18 to 34	20 to 29
<b>Reporting group values</b>	Part II Combination therapy Arm D	Part II Combination therapy Arm PDEX1	Part II Combination therapy Arm PDEX2.5
Number of subjects	36	20	20

Age categorical Units: Subjects			
Adults (18-64 years)	22	12	11
From 65-84 years	13	8	8
85 years and over	1	0	1
Age continuous Units: years			
median	62.0	63.0	61.5
full range (min-max)	46 to 87	43 to 78	43 to 89
Gender categorical Units: Subjects			
Female	17	7	8
Male	19	13	12
Child-bearing Potential Units: Subjects			
No	16	6	8
Yes	1	1	0
Not applicable	19	13	12
Ethnicity Units: Subjects			
Not Hispanic or Latino	30	19	20
Not reported	6	1	0
Race Units: Subjects			
White	30	18	20
Asian	0	1	0
Not reported	6	1	0
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	0	0
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	36	20	20
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	33	19	18
No	3	1	2
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	33	18	18
1 prior line	1	2	2
2 prior lines	1	0	0
3 prior lines	1	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			



ECOG = 0	23	7	4
ECOG = 1	13	13	16

Height Units: cm median full range (min-max)	170.0 158 to 205	172.5 150 to 194	173.5 147 to 184
Weight Units: kg median full range (min-max)	73.7 48 to 107	66 50 to 95	73.7 42 to 96
Body Mass Index Units: kg/m2 median full range (min-max)	24.4 17 to 36	23.1 18 to 31	25.3 17 to 33

<b>Reporting group values</b>	Total		
Number of subjects	167		
Age categorical Units: Subjects			
Adults (18-64 years)	96		
From 65-84 years	69		
85 years and over	2		
Age continuous Units: years median full range (min-max)	-		
Gender categorical Units: Subjects			
Female	63		
Male	104		
Child-bearing Potential Units: Subjects			
No	59		
Yes	4		
Not applicable	104		
Ethnicity Units: Subjects			
Not Hispanic or Latino	136		
Not reported	31		
Race Units: Subjects			
White	135		
Asian	1		
Not reported	31		
Primary Disease Units: Subjects			
NSCLC - subtype not defined	14		
NSCLC - squamous	14		
NSCLC - non-squamous	28		
PDAC	99		

CRC	12		
TNBC	0		
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	140		
No	27		
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	93		
1 prior line	32		
2 prior lines	8		
3 prior lines	8		
4 prior lines	1		
5 prior lines	3		
Not recorded	22		
ECOG status Units: Subjects			
ECOG = 0	76		
ECOG = 1	91		
Height Units: cm median full range (min-max)	-		
Weight Units: kg median full range (min-max)	-		
Body Mass Index Units: kg/m <sup>2</sup> median full range (min-max)	-		

### Subject analysis sets

Subject analysis set title	Part I - Dose escalation 1 mg/kg
Subject analysis set type	Safety analysis
Subject analysis set description: Cohort 1 (1 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.	
Subject analysis set title	Part I - Dose escalation 1.5 mg/kg
Subject analysis set type	Safety analysis
Subject analysis set description: Cohort 2 (1.5 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.	
Subject analysis set title	Part I - Dose escalation 3 mg/kg
Subject analysis set type	Safety analysis
Subject analysis set description: Cohort 3 (3 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least dose (even partial) of CAN04.	
Subject analysis set title	Part I - Dose escalation 6 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Cohort 4 (6 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 10 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Cohort 5 (10 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm C 5 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects allocated to the 5 mg/kg cohort of Arm C. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm C 1 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects allocated to the 1 mg/kg cohort of Arm C. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm C 2.5 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects allocated to the 2.5 mg/kg cohort of Arm C. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm D 5 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects allocated to the 5 mg/kg cohort of Arm D. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm D 7.5 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects allocated to the 7.5 mg/kg cohort of Arm D. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part I - Dose escalation), i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 1 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 1.5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 3 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

For monotherapy cohorts/arms mITT is the same as reporting groups and any safety analysis sets. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 6 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 10 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy Arm A mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part II Monotherapy Arm A) , i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy Arm B mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part II Monotherapy Arm B) , i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy Arm E mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part II Monotherapy Arm E) , i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes subjects from mITT subject analysis sets Part II Monotherapy Arm A mITT, Part II Monotherapy Arm B mITT and Part II Monotherapy Arm E mITT. Subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Combination therapy Arm C mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm C, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm C 5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm C allocated to the 5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm C 1 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm C allocated to the 1 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm C 2.5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm C allocated to the 2.5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm NCP mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm NCP, who have received at least one dose (even

partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm D mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm D, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm D 5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm D allocated to the 5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm D 7.5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm C allocated to the 7.5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm PDEX1 mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm PDEX1, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part II Combination therapy Arm PDEX2.5 mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects enrolled in Part II Combination therapy Arm PDEX2.5, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.

Subject analysis set title	Part I - Dose escalation 1 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part I - Dose escalation 1.5 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part I - Dose escalation 3 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part I - Dose escalation 6 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part I - Dose escalation 10 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Monotherapy Arm A - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one

evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Monotherapy Arm B - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Monotherapy Arm E - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm C 1 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm C 2.5 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm D 5 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm PDEX1 - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part II Combination therapy Arm PDEX2.5 - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

Subject analysis set title	Part I: Dose escalation - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.

<b>Reporting group values</b>	Part I - Dose escalation 1 mg/kg	Part I - Dose escalation 1.5 mg/kg	Part I - Dose escalation 3 mg/kg
Number of subjects	3	3	3
Age categorical Units: Subjects			
Adults (18-64 years)	2	1	1
From 65-84 years	1	2	2
85 years and over	0	0	0
Age continuous Units: years			
median	62.0	68.0	71.0
full range (min-max)	61 to 71	48 to 74	62 to 77
Gender categorical Units: Subjects			
Female	1	1	2
Male	2	2	1
Child-bearing Potential Units: Subjects			
No	1	1	2
Yes	0	0	0
Not applicable	2	2	1
Ethnicity Units: Subjects			
Not Hispanic or Latino	3	2	1
Not reported	0	1	2
Race Units: Subjects			
White	3	2	1
Asian	0	0	0
Not reported	0	1	2
Primary Disease Units: Subjects			
NSCLC - subtype not defined	1	1	1
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	0	0	1
CRC	2	2	1
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	1	1	1
No	2	2	2
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	0
1 prior line	0	0	0
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0

Not recorded	3	3	3
ECOG status			
Units: Subjects			
ECOG = 0	2	2	1
ECOG = 1	1	1	2
Height			
Units: cm			
median	175.0	175.0	161.0
full range (min-max)	160 to 180	155 to 176	155 to 178
Weight			
Units: kg			
median	69.6	71.0	87.6
full range (min-max)	66 to 91	61 to 79	68 to 98
Body Mass Index			
Units: kg/m2			
median	25.6	25.6	31.0
full range (min-max)	23 to 28	23 to 26	28 to 34

<b>Reporting group values</b>	Part I - Dose escalation 6 mg/kg	Part I - Dose escalation 10 mg/kg	Part II Combination therapy Arm C 5 mg/kg
Number of subjects	7	6	13
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	5	4
From 65-84 years	1	1	9
85 years and over	0	0	0
Age continuous			
Units: years			
median	62.0	63.0	66.0
full range (min-max)	39 to 81	48 to 66	61 to 77
Gender categorical			
Units: Subjects			
Female	1	3	5
Male	6	3	8
Child-bearing Potential			
Units: Subjects			
No	1	2	5
Yes	0	1	0
Not applicable	6	3	8
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	3	5	12
Not reported	4	1	1
Race			
Units: Subjects			
White	3	5	12
Asian	0	0	0
Not reported	4	1	1
Primary Disease			
Units: Subjects			
NSCLC - subtype not defined	0	1	1



NSCLC - squamous	0	0	5
NSCLC - non-squamous	0	0	7
PDAC	3	2	0
CRC	4	3	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	3	3	13
No	4	3	0
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	7
1 prior line	0	0	6
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	7	6	0
ECOG status Units: Subjects			
ECOG = 0	5	5	4
ECOG = 1	2	1	9
Height Units: cm median full range (min-max)	181.0 165 to 188	168.0 155 to 191	169.0 152 to 179
Weight Units: kg median full range (min-max)	84.5 53 to 103	80.7 53 to 124	69.0 57 to 90
Body Mass Index Units: kg/m2 median full range (min-max)	24.9 18 to 32	26.3 20 to 44	25.8 19 to 32
<b>Reporting group values</b>	Part II Combination therapy Arm C 1 mg/kg	Part II Combination therapy Arm C 2.5 mg/kg	Part II Combination therapy Arm D 5 mg/kg
Number of subjects	17	3	28
Age categorical Units: Subjects			
Adults (18-64 years)	11	2	17
From 65-84 years	6	1	10
85 years and over	0	0	0
Age continuous Units: years median full range (min-max)	64.0 39 to 77	63.0 61 to 75	62.5 52 to 87
Gender categorical Units: Subjects			
Female	5	1	12

Male	12	2	16
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Child-bearing Potential Units: Subjects			
No	4	1	12
Yes	1	0	0
Not applicable	12	2	16
Ethnicity Units: Subjects			
Not Hispanic or Latino	17	3	24
Not reported	0	0	4
Race Units: Subjects			
White	17	3	24
Asian	0	0	0
Not reported	0	0	4
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	0	0
NSCLC - squamous	7	2	0
NSCLC - non-squamous	10	1	0
PDAC	0	0	28
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	16	3	25
No	1	0	3
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	10	0	25
1 prior line	7	3	1
2 prior lines	0	0	1
3 prior lines	0	0	1
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			
ECOG = 0	9	1	18
ECOG = 1	8	2	10
Height Units: cm			
median	176.0	164.0	170.0
full range (min-max)	153 to 189	161 to 176	161 to 205
Weight Units: kg			
median	70.0	64.9	73.7
full range (min-max)	53 to 108	60 to 66	48 to 107

Body Mass Index			
Units: kg/m2			
median	24.4	22.3	24.7
full range (min-max)	18 to 34	21 to 26	17 to 30

<b>Reporting group values</b>	Part II Combination therapy Arm D 7.5 mg/kg	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT
Number of subjects	8	22	3
Age categorical			
Units: Subjects			
Adults (18-64 years)	5	15	2
From 65-84 years	3	7	1
85 years and over	0	0	0
Age continuous			
Units: years			
median	60.0	63.0	62.0
full range (min-max)	46 to 79	39 to 81	61 to 71
Gender categorical			
Units: Subjects			
Female	5	8	1
Male	3	14	2
Child-bearing Potential			
Units: Subjects			
No	4	7	1
Yes	1	1	0
Not applicable	3	14	2
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	6	14	3
Not reported	2	8	0
Race			
Units: Subjects			
White	6	14	3
Asian	0	0	0
Not reported	2	8	0
Primary Disease			
Units: Subjects			
NSCLC - subtype not defined	0	4	1
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	8	6	0
CRC	0	12	2
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry			
Units: Subjects			
Yes	8	9	1
No	0	13	2
Number of prior lines of treatment for metastatic disease			
Units: Subjects			
No prior lines	8	0	0

1 prior line	0	0	0
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	22	3
ECOG status			
Units: Subjects			
ECOG = 0	5	15	2
ECOG = 1	3	7	1
Height			
Units: cm			
median	165.0	174.5	175.0
full range (min-max)	158 to 194	155 to 191	160 to 180
Weight			
Units: kg			
median	74.1	79.1	69.6
full range (min-max)	51 to 95	53 to 124	66 to 91
Body Mass Index			
Units: kg/m2			
median	23.9	25.6	25.6
full range (min-max)	19 to 36	18 to 44	23 to 28

<b>Reporting group values</b>	Part I - Dose escalation 1.5 mg/kg mITT	Part I - Dose escalation 3 mg/kg mITT	Part I - Dose escalation 6 mg/kg mITT
Number of subjects	3	3	7
Age categorical			
Units: Subjects			
Adults (18-64 years)	1	1	6
From 65-84 years	2	2	1
85 years and over	0	0	0
Age continuous			
Units: years			
median	68.0	71.0	62.0
full range (min-max)	48 to 74	62 to 77	39 to 81
Gender categorical			
Units: Subjects			
Female	1	2	1
Male	2	1	6
Child-bearing Potential			
Units: Subjects			
No	1	2	1
Yes	0	0	0
Not applicable	2	1	6
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	2	1	3
Not reported	1	2	4
Race			
Units: Subjects			
White	2	1	3

Asian	0	0	0
Not reported	1	2	4
Primary Disease Units: Subjects			
NSCLC - subtype not defined	1	1	0
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	0	1	3
CRC	2	1	4
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	1	1	3
No	2	2	4
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	0
1 prior line	0	0	0
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	3	3	7
ECOG status Units: Subjects			
ECOG = 0	2	1	5
ECOG = 1	1	2	2
Height Units: cm			
median	175.0	161.0	181.0
full range (min-max)	155 to 176	155 to 178	165 to 188
Weight Units: kg			
median	71.0	87.6	84.5
full range (min-max)	61 to 79	68 to 98	53 to 103
Body Mass Index Units: kg/m2			
median	25.6	31.0	24.9
full range (min-max)	23 to 26	28 to 34	18 to 32

<b>Reporting group values</b>	Part I - Dose escalation 10 mg/kg mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT
Number of subjects	6	10	10
Age categorical Units: Subjects			
Adults (18-64 years)	5	5	6
From 65-84 years	1	5	4
85 years and over	0	0	0

Age continuous Units: years median full range (min-max)	63.0 48 to 66	61.0 49 to 72	63.5 40 to 73
Gender categorical Units: Subjects			
Female	3	2	2
Male	3	8	8
Child-bearing Potential Units: Subjects			
No	2	2	2
Yes	1	0	0
Not applicable	3	8	8
Ethnicity Units: Subjects			
Not Hispanic or Latino	5	2	5
Not reported	1	8	5
Race Units: Subjects			
White	5	2	5
Asian	0	0	0
Not reported	1	8	5
Primary Disease Units: Subjects			
NSCLC - subtype not defined	1	2	4
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	2	8	6
CRC	3	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	3	6	9
No	3	4	1
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	0
1 prior line	0	4	3
2 prior lines	0	2	3
3 prior lines	0	3	2
4 prior lines	0	1	0
5 prior lines	0	0	2
Not recorded	6	0	0
ECOG status Units: Subjects			
ECOG = 0	5	3	5
ECOG = 1	1	7	5

Height Units: cm median full range (min-max)	168.0 155 to 191	177.6 165 to 198	179.0 172 to 185
Weight Units: kg median full range (min-max)	80.7 53 to 124	72.3 45 to 126	75.7 62 to 107
Body Mass Index Units: kg/m2 median full range (min-max)	26.3 20 to 44	23.3 16 to 34	24.5 21 to 32

<b>Reporting group values</b>	Part II Monotherapy Arm E mITT	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT
Number of subjects	6	26	30
Age categorical Units: Subjects			
Adults (18-64 years)	5	16	17
From 65-84 years	1	10	13
85 years and over	0	0	0
Age continuous Units: years median full range (min-max)	62.0 58 to 73	63.5 40 to 73	64.0 39 to 77
Gender categorical Units: Subjects			
Female	3	7	10
Male	3	19	20
Child-bearing Potential Units: Subjects			
No	3	7	9
Yes	0	0	1
Not applicable	3	19	20
Ethnicity Units: Subjects			
Not Hispanic or Latino	4	11	30
Not reported	2	15	0
Race Units: Subjects			
White	4	11	30
Asian	0	0	0
Not reported	2	15	0
Primary Disease Units: Subjects			
NSCLC - subtype not defined	3	9	1
NSCLC - squamous	0	0	13
NSCLC - non-squamous	0	0	16
PDAC	3	17	0
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location			

at Study Entry			
Units: Subjects			
Yes	5	20	29
No	1	6	1
Number of prior lines of treatment for metastatic disease			
Units: Subjects			
No prior lines	0	0	15
1 prior line	1	8	15
2 prior lines	2	7	0
3 prior lines	2	7	0
4 prior lines	0	1	0
5 prior lines	1	3	0
Not recorded	0	0	0
ECOG status			
Units: Subjects			
ECOG = 0	3	11	14
ECOG = 1	3	15	16
Height			
Units: cm			
median	171.8	177.5	172.0
full range (min-max)	162 to 188	162 to 198	152 to 189
Weight			
Units: kg			
median	77.7	77.1	68.0
full range (min-max)	74 to 99	45 to 126	53 to 108
Body Mass Index			
Units: kg/m2			
median	27.1	25.2	24.4
full range (min-max)	22 to 34	16 to 34	18 to 34

<b>Reporting group values</b>	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT
Number of subjects	11	16	3
Age categorical			
Units: Subjects			
Adults (18-64 years)	4	11	5
From 65-84 years	7	5	1
85 years and over	0	0	0
Age continuous			
Units: years			
median	66.0	62.0	63.0
full range (min-max)	61 to 77	39 to 77	61 to 75
Gender categorical			
Units: Subjects			
Female	4	5	1
Male	7	11	2
Child-bearing Potential			
Units: Subjects			
No	4	4	1
Yes	0	1	0
Not applicable	7	11	2



Ethnicity Units: Subjects			
Not Hispanic or Latino	11	16	3
Not reported	0	0	0
Race Units: Subjects			
White	11	16	3
Asian	0	0	0
Not reported	0	0	0
Primary Disease Units: Subjects			
NSCLC - subtype not defined	1	0	0
NSCLC - squamous	5	6	2
NSCLC - non-squamous	5	10	1
PDAC	0	0	0
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	11	15	3
No	0	1	0
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	6	9	0
1 prior line	5	7	3
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			
ECOG = 0	4	9	1
ECOG = 1	7	7	2
Height Units: cm			
median	169.0	174.0	164.0
full range (min-max)	152 to 179	153 to 189	161 to 176
Weight Units: kg			
median	69.0	69.0	64.9
full range (min-max)	57 to 90	53 to 108	60 to 66
Body Mass Index Units: kg/m2			
median	27.4	23.4	22.3
full range (min-max)	19 to 32	18 to 34	21 to 26
<b>Reporting group values</b>	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm D 5 mg/kg mITT
Number of subjects	10	33	25

Age categorical Units: Subjects			
Adults (18-64 years)	3	20	15
From 65-84 years	7	12	9
85 years and over	0	1	1
Age continuous Units: years			
median	66.5	62.0	63.0
full range (min-max)	55 to 76	46 to 87	52 to 87
Gender categorical Units: Subjects			
Female	5	15	10
Male	5	18	15
Child-bearing Potential Units: Subjects			
No	5	14	10
Yes	0	1	0
Not applicable	5	18	15
Ethnicity Units: Subjects			
Not Hispanic or Latino	10	27	21
Not reported	0	6	4
Race Units: Subjects			
White	10	27	21
Asian	0	0	0
Not reported	0	6	4
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	0	0
NSCLC - squamous	0	0	0
NSCLC - non-squamous	10	0	0
PDAC	0	33	25
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	9	30	22
No	1	3	3
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	7	30	22
1 prior line	3	1	1
2 prior lines	0	1	1
3 prior lines	0	1	1
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			

ECOG = 0	2	22	17
ECOG = 1	8	11	8

Height Units: cm median full range (min-max)	169.5 151 to 175	170.0 158 to 205	170.0 161 to 205
Weight Units: kg median full range (min-max)	69.5 54 to 88	73.8 48 to 107	73.8 48 to 107
Body Mass Index Units: kg/m2 median full range (min-max)	26.8 20 to 29	24.3 17 to 36	24.4 17 to 30

<b>Reporting group values</b>	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Number of subjects	8	20	20
Age categorical Units: Subjects			
Adults (18-64 years)	5	12	11
From 65-84 years	3	8	8
85 years and over	0	0	1
Age continuous Units: years median full range (min-max)	60.0 46 to 79	63.0 43 to 78	61.5 43 to 89
Gender categorical Units: Subjects			
Female	5	7	8
Male	3	13	12
Child-bearing Potential Units: Subjects			
No	4	6	8
Yes	1	1	0
Not applicable	3	13	12
Ethnicity Units: Subjects			
Not Hispanic or Latino	6	19	20
Not reported	2	1	0
Race Units: Subjects			
White	6	18	20
Asian	0	1	0
Not reported	2	1	0
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	0	0
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0

PDAC	8	20	20
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	8	19	18
No	0	1	2
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	8	18	18
1 prior line	0	2	2
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			
ECOG = 0	5	7	4
ECOG = 1	3	13	16
Height Units: cm median full range (min-max)	165.5 158 to 194	172.5 150 to 194	173.5 147 to 184
Weight Units: kg median full range (min-max)	74.1 51 to 95	66.0 50 to 95	73.7 42 to 96
Body Mass Index Units: kg/m2 median full range (min-max)	23.9 19 to 36	23.1 18 to 31	25.3 17 to 33

<b>Reporting group values</b>	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population
Number of subjects	3	3	3
Age categorical Units: Subjects			
Adults (18-64 years)	2	1	1
From 65-84 years	1	2	2
85 years and over	0	0	0
Age continuous Units: years median full range (min-max)	62.0 61 to 71	68.0 48 to 74	71.0 62 to 77
Gender categorical Units: Subjects			
Female	1	1	2
Male	2	2	1

Child-bearing Potential Units: Subjects			
No	1	1	2
Yes	0	0	0
Not applicable	2	2	1
Ethnicity Units: Subjects			
Not Hispanic or Latino	3	2	1
Not reported	0	1	2
Race Units: Subjects			
White	3	2	1
Asian	0	0	0
Not reported	0	1	2
Primary Disease Units: Subjects			
NSCLC - subtype not defined	1	1	1
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	0	0	1
CRC	2	2	1
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	1	1	1
No	2	2	2
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	0
1 prior line	0	0	0
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	3	3	3
ECOG status Units: Subjects			
ECOG = 0	2	2	1
ECOG = 1	1	1	2
Height Units: cm			
median	175.0	175.0	161.0
full range (min-max)	160 to 180	155 to 176	155 to 178
Weight Units: kg			
median	69.6	71.0	87.6
full range (min-max)	66 to 91	61 to 79	68 to 98
Body Mass Index Units: kg/m2			
median	25.6	25.6	31.0

full range (min-max)	23 to 28	23 to 26	28 to 34
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Reporting group values	Part I - Dose escalation 6 mg/kg - PK population	Part I - Dose escalation 10 mg/kg - PK population	Part II Monotherapy Arm A - PK population
Number of subjects	7	6	10
Age categorical Units: Subjects			
Adults (18-64 years)	6	5	5
From 65-84 years	1	1	5
85 years and over	0	0	0
Age continuous Units: years			
median	62.0	63.0	61.0
full range (min-max)	39 to 81	48 to 66	49 to 72
Gender categorical Units: Subjects			
Female	1	3	2
Male	6	3	8
Child-bearing Potential Units: Subjects			
No	1	2	2
Yes	0	1	0
Not applicable	6	3	8
Ethnicity Units: Subjects			
Not Hispanic or Latino	3	5	2
Not reported	4	1	8
Race Units: Subjects			
White	3	5	2
Asian	0	0	0
Not reported	4	1	8
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	1	2
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	3	2	8
CRC	4	3	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	3	3	6
No	4	3	4
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	0

1 prior line	0	0	4
2 prior lines	0	0	2
3 prior lines	0	0	3
4 prior lines	0	0	1
5 prior lines	0	0	0
Not recorded	7	6	0
ECOG status			
Units: Subjects			
ECOG = 0	5	5	3
ECOG = 1	2	1	7
Height			
Units: cm			
median	181.0	168.0	177.6
full range (min-max)	165 to 188	155 to 191	165 to 198
Weight			
Units: kg			
median	84.5	80.7	72.3
full range (min-max)	53 to 103	53 to 124	45 to 126
Body Mass Index			
Units: kg/m2			
median	24.9	26.3	23.3
full range (min-max)	18 to 32	20 to 44	16 to 34

<b>Reporting group values</b>	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Number of subjects	10	6	12
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	5	4
From 65-84 years	4	1	8
85 years and over	0	0	0
Age continuous			
Units: years			
median	63.5	62.0	66.0
full range (min-max)	40 to 73	58 to 73	61 to 77
Gender categorical			
Units: Subjects			
Female	2	3	4
Male	8	3	8
Child-bearing Potential			
Units: Subjects			
No	2	3	4
Yes	0	0	0
Not applicable	8	3	8
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	5	4	12
Not reported	5	2	0
Race			
Units: Subjects			

White	5	4	12
Asian	0	0	0
Not reported	5	2	0
Primary Disease Units: Subjects			
NSCLC - subtype not defined	4	3	1
NSCLC - squamous	0	0	5
NSCLC - non-squamous	0	0	6
PDAC	6	3	0
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	9	5	12
No	1	1	0
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0	0	7
1 prior line	3	1	5
2 prior lines	3	2	0
3 prior lines	2	2	0
4 prior lines	0	0	0
5 prior lines	2	1	0
Not recorded	0	0	0
ECOG status Units: Subjects			
ECOG = 0	5	3	4
ECOG = 1	5	3	8
Height Units: cm			
median	179.0	171.8	169.5
full range (min-max)	172 to 185	162 to 188	152 to 179
Weight Units: kg			
median	75.7	77.7	74.0
full range (min-max)	62 to 107	74 to 99	57 to 90
Body Mass Index Units: kg/m2			
median	24.5	27.1	26.6
full range (min-max)	21 to 32	22 to 34	19 to 32

<b>Reporting group values</b>	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population
Number of subjects	15	3	26
Age categorical Units: Subjects			
Adults (18-64 years)	10	2	16
From 65-84 years	5	1	9
85 years and over	0	0	1



Age continuous Units: years median full range (min-max)	64.0 39 to 77	63.0 61 to 75	62.5 52 to 87
Gender categorical Units: Subjects			
Female	4	1	11
Male	11	2	15
Child-bearing Potential Units: Subjects			
No	3	1	11
Yes	1	0	0
Not applicable	11	2	15
Ethnicity Units: Subjects			
Not Hispanic or Latino	15	3	22
Not reported	0	0	4
Race Units: Subjects			
White	15	3	22
Asian	0	0	0
Not reported	0	0	4
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	0	0
NSCLC - squamous	6	2	0
NSCLC - non-squamous	9	1	0
PDAC	0	0	26
CRC	0	0	0
TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	14	3	23
No	1	0	3
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	9	0	23
1 prior line	6	3	1
2 prior lines	0	0	1
3 prior lines	0	0	1
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			
ECOG = 0	9	1	17
ECOG = 1	6	2	9

Height Units: cm median full range (min-max)	180.0 153 to 189	164.0 161 to 176	170.0 161 to 205
Weight Units: kg median full range (min-max)	75.0 53 to 108	64.9 60 to 66	73.7 48 to 107
Body Mass Index Units: kg/m2 median full range (min-max)	25.7 18 to 34	22.3 21 to 26	24.7 17 to 30

<b>Reporting group values</b>	Part II Combination therapy Arm D 7.5 mg/kg - PK population	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population
Number of subjects	8	18	19
Age categorical Units: Subjects			
Adults (18-64 years)	5	11	11
From 65-84 years	3	7	7
85 years and over	0	0	1
Age continuous Units: years median full range (min-max)	60.0 46 to 79	63.0 48 to 78	60.0 43 to 89
Gender categorical Units: Subjects			
Female	5	6	7
Male	3	12	12
Child-bearing Potential Units: Subjects			
No	4	6	7
Yes	1	0	0
Not applicable	3	12	12
Ethnicity Units: Subjects			
Not Hispanic or Latino	6	17	19
Not reported	2	1	0
Race Units: Subjects			
White	6	16	19
Asian	0	1	0
Not reported	2	1	0
Primary Disease Units: Subjects			
NSCLC - subtype not defined	0	0	0
NSCLC - squamous	0	0	0
NSCLC - non-squamous	0	0	0
PDAC	8	18	19
CRC	0	0	0

TNBC	0	0	0
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	8	17	17
No	0	1	2
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	8	16	17
1 prior line	0	2	2
2 prior lines	0	0	0
3 prior lines	0	0	0
4 prior lines	0	0	0
5 prior lines	0	0	0
Not recorded	0	0	0
ECOG status Units: Subjects			
ECOG = 0	5	6	4
ECOG = 1	3	12	15
Height Units: cm median full range (min-max)	165.5 158 to 194	173.5 150 to 194	175.0 147 to 184
Weight Units: kg median full range (min-max)	74.1 51 to 95	67.3 50 to 95	75.0 51 to 96
Body Mass Index Units: kg/m2 median full range (min-max)	23.9 19 to 36	22.8 18 to 31	25.9 19 to 33

<b>Reporting group values</b>	Part I: Dose escalation - PK population		
Number of subjects	22		
Age categorical Units: Subjects			
Adults (18-64 years)	15		
From 65-84 years	7		
85 years and over	0		
Age continuous Units: years median full range (min-max)	63.0 39 to 81		
Gender categorical Units: Subjects			
Female	8		
Male	14		
Child-bearing Potential Units: Subjects			
No	7		

Yes	1		
Not applicable	14		
Ethnicity Units: Subjects			
Not Hispanic or Latino	14		
Not reported	8		
Race Units: Subjects			
White	14		
Asian	0		
Not reported	8		
Primary Disease Units: Subjects			
NSCLC - subtype not defined	4		
NSCLC - squamous	0		
NSCLC - non-squamous	0		
PDAC	6		
CRC	12		
TNBC	0		
Tumour Still Present at Primary Location at Study Entry Units: Subjects			
Yes	9		
No	13		
Number of prior lines of treatment for metastatic disease Units: Subjects			
No prior lines	0		
1 prior line	0		
2 prior lines	0		
3 prior lines	0		
4 prior lines	0		
5 prior lines	0		
Not recorded	22		
ECOG status Units: Subjects			
ECOG = 0	15		
ECOG = 1	7		
Height Units: cm			
median	174.5		
full range (min-max)	155 to 191		
Weight Units: kg			
median	79.1		
full range (min-max)	53 to 124		
Body Mass Index Units: kg/m2			
median	25.6		
full range (min-max)	18 to 44		

## End points

### End points reporting groups

Reporting group title	Part I - Dose escalation
Reporting group description: Phase 1 dose-escalation arm (3+3 design) to assess the safety of CAN04 monotherapy administered at 1, 1.5, 3, 6, and 10 mg/kg in patients with unresectable NSCLC, PDAC, CRC, or TNBC that were refractory to standard therapy or for whom no standard therapy existed. The primary aim was to assess safety and to define the MTD or RP2D of CAN04 administered once weekly.	
Reporting group title	Part II Monotherapy Arm A
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly in patients with unresectable squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.	
Reporting group title	Part II Monotherapy Arm B
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly for first 6 weeks followed by biweekly administration in patients with unresectable squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.	
Reporting group title	Part II Monotherapy Arm E
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 15 mg/kg once weekly for first 6 weeks followed by biweekly administration in patients with unresectable, locally advanced or metastatic squamous or non-squamous NSCLC or PDAC that were refractory to standard therapy or for whom no standard therapy existed.	
Reporting group title	Part II Combination therapy Arm C
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and cisplatin in patients with stage III or IV squamous or non-squamous non-small cell lung cancer (NSCLC) who were candidates for 1st line of standard chemotherapy regimen with cisplatin/gemcitabine or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with cisplatin/gemcitabine. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase but a provisional MTD was reached on 5 mg/kg and dose reduced to 1 mg/kg and re-escalated to 2.5 mg/kg.	
Reporting group title	Part II Combination therapy Arm NCP
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with carboplatin and pemetrexed in patients with stage III or IV non-squamous non-small cell lung cancer (NSCLC) who were candidates for 1st line of standard chemotherapy regimen with carboplatin/pemetrexed or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with carboplatin/pemetrexed.	
Reporting group title	Part II Combination therapy Arm D
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase. After 7.5 mg/kg was found to be above MTD the expansion phase was done with 5 mg/kg.	
Reporting group title	Part II Combination therapy Arm PDEX1
Reporting group description: Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 1 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen	

with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX1 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Reporting group title	Part II Combination therapy Arm PDEX2.5
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 2.5 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who were candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX2.5 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Subject analysis set title	Part I - Dose escalation 1 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Cohort 1 (1 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 1.5 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Cohort 2 (1.5 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 3 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Cohort 3 (3 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 6 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Cohort 4 (6 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 10 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Cohort 5 (10 mg/kg) of Part I dose escalation (monotherapy). Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm C 5 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Subjects allocated to the 5 mg/kg cohort of Arm C. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm C 1 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Subjects allocated to the 1 mg/kg cohort of Arm C. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm C 2.5 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Subjects allocated to the 2.5 mg/kg cohort of Arm C. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm D 5 mg/kg
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Subjects allocated to the 5 mg/kg cohort of Arm D. Subjects have received at least one dose (even

partial) of CAN04.

Subject analysis set title	Part II Combination therapy Arm D 7.5 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects allocated to the 7.5 mg/kg cohort of Arm D. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part I - Dose escalation), i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 1 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 1.5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 3 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

For monotherapy cohorts/arms mITT is the same as reporting groups and any safety analysis sets. Subjects have received at least one dose (even partial) of CAN04.

Subject analysis set title	Part I - Dose escalation 6 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part I - Dose escalation 10 mg/kg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding safety subject analysis set, i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy Arm A mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part II Monotherapy Arm A) , i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy Arm B mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part II Monotherapy Arm B) , i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy Arm E mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This mITT subject analysis set includes same subjects as included in the corresponding reporting group (Part II Monotherapy Arm E) , i.e., subjects have received at least one dose (even partial) of CAN04 (monotherapy).

Subject analysis set title	Part II Monotherapy mITT
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Subject analysis set type	Modified intention-to-treat
Subject analysis set description: This mITT subject analysis set includes subjects from mITT subject analysis sets Part II Monotherapy Arm A mITT, Part II Monotherapy Arm B mITT and Part II Monotherapy Arm E mITT. Subjects have received at least one dose (even partial) of CAN04 (monotherapy).	
Subject analysis set title	Part II Combination therapy Arm C mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm C, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm C 5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm C allocated to the 5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm C 1 mg/kg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm C allocated to the 1 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm C 2.5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm C allocated to the 2.5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm NCP mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm NCP, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm D mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm D, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm D 5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm D allocated to the 5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm D 7.5 mg/kg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm C allocated to the 7.5 mg/kg cohort, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm PDEX1 mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm PDEX1, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part II Combination therapy Arm PDEX2.5 mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects enrolled in Part II Combination therapy Arm PDEX2.5, who have received at least one dose (even partial) of CAN04 and applicable combination treatment was initiated.	
Subject analysis set title	Part I - Dose escalation 1 mg/kg - PK population



Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part I - Dose escalation 1.5 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part I - Dose escalation 3 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part I - Dose escalation 6 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part I - Dose escalation 10 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Monotherapy Arm A - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Monotherapy Arm B - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Monotherapy Arm E - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm C 1 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm C 2.5 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm D 5 mg/kg - PK population

Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm PDEX1 - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part II Combination therapy Arm PDEX2.5 - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	
Subject analysis set title	Part I: Dose escalation - PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The PK population includes all subjects who have received CAN04 and have provided at least one evaluable pre-dose and post-dose PK blood sample.	

### Primary: Incidence of Grade ≥3 adverse events related to CAN04 administration

End point title	Incidence of Grade ≥3 adverse events related to CAN04 administration <sup>[1]</sup>
End point description: Incidence of Grade 3 and higher Adverse Events related to CAN04 administration and according to the National Cancer Institute - Common Terminology Criteria for Adverse Events (CTCAE, version 4.03).	
End point type	Primary
End point timeframe: Adverse events were collected from ICF signature until 28 days after last administration of study drug.	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive statistics is presented. Since no comparator arm is included in the study no statistical comparisons have been performed.	

End point values	Part I - Dose escalation	Part II Monotherapy Arm A	Part II Monotherapy Arm B	Part II Monotherapy Arm E
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	10	10	6
Units: percent				
number (confidence interval 95%)	9 (1 to 29)	10 (0 to 45)	0 (0 to 31)	17 (0 to 64)

End point values	Part II Combination therapy Arm C	Part II Combination therapy Arm NCP	Part II Combination therapy Arm D	Part II Combination therapy Arm PDEX1
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	10	36	20
Units: percent				
number (confidence interval 95%)	58 (39 to 75)	90 (55 to 100)	61 (43 to 77)	55 (32 to 77)

End point values	Part II Combination therapy Arm PDEX2.5	Part I - Dose escalation 1 mg/kg	Part I - Dose escalation 1.5 mg/kg	Part I - Dose escalation 3 mg/kg
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	3	3	3
Units: percent				
number (confidence interval 95%)	80 (56 to 94)	0 (0 to 71)	0 (0 to 71)	33 (1 to 91)

End point values	Part I - Dose escalation 6 mg/kg	Part I - Dose escalation 10 mg/kg	Part II Combination therapy Arm C 5 mg/kg	Part II Combination therapy Arm C 1 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	6	13	17
Units: percent				
number (confidence interval 95%)	14 (0 to 58)	0 (0 to 46)	85 (55 to 98)	41 (18 to 67)

End point values	Part II Combination therapy Arm C 2.5 mg/kg	Part II Combination therapy Arm D 5 mg/kg	Part II Combination therapy Arm D 7.5 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	28	8	
Units: percent				
number (confidence interval 95%)	33 (1 to 91)	57 (37 to 76)	75 (35 to 97)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Concentration at the end of infusion - Single dose

End point title	Pharmacokinetics: Concentration at the end of infusion - Single dose
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End point description:

Pharmacokinetics: Concentration at the end of infusion (C<sub>inf</sub> end) - Single dose (Dose 1)

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg

given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
End point timeframe:	
Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.	

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[2]</sup>	3	2	6
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	14487 ( $\pm$ 71)	19801 ( $\pm$ 37)	5681 ( $\pm$ 30)

Notes:

[2] - Not evaluable due to concentration below lower limit of quantification.

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	8922 ( $\pm$ 12)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Maximum concentration - Single dose

End point title	Pharmacokinetics: Maximum concentration - Single dose
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End point description:

Maximum concentration (C<sub>max</sub>) - Single dose (Dose 1)

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
End point timeframe:	
Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.	

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	7
Units: ng/mL				
geometric mean (geometric coefficient of variation)	17581 (± 17)	20227 (± 61)	26244 (± 23)	6927 (± 21)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	10028 (± 15)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Time taken to reach maximum concentration - Single dose

End point title	Pharmacokinetics: Time taken to reach maximum concentration - Single dose
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End point description:

Time taken to reach maximum concentration (t max) - Single dose (Dose 1).

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
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End point timeframe:

Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	7
Units: h				
median (full range (min-max))	5.3 (2.6 to 8.0)	3.1 (2.0 to 3.1)	3.1 (2.1 to 4.1)	2.1 (1.3 to 8.0)

<b>End point values</b>	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: h				
median (full range (min-max))	4.3 (1.0 to 9.0)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Terminal half-life - Single dose

End point title	Pharmacokinetics: Terminal half-life - Single dose
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End point description:

Pharmacokinetics: Terminal half-life ( $t_{1/2}$ ) - Single dose (Dose 1).

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
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End point timeframe:

Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing,.

<b>End point values</b>	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	7
Units: h				
geometric mean (geometric coefficient of variation)	57.9 ( $\pm$ 56)	43.8 ( $\pm$ 11)	81.0 ( $\pm$ 3)	31.4 ( $\pm$ 47)

<b>End point values</b>	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			

Units: h				
geometric mean (geometric coefficient of variation)	36.5 (± 33)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Clearance - Single dose

End point title	Pharmacokinetics: Clearance - Single dose
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End point description:

Pharmacokinetics: Clearance (CL) - Single dose.

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
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End point timeframe:

Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	2
Units: mL/h				
geometric mean (geometric coefficient of variation)	53.1 (± 51)	51.2 (± 25)	28.5 (± 25)	75.6 (± 18)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: mL/h				
geometric mean (geometric coefficient of variation)	61.3 (± 29)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Apparent volume of distribution during the terminal phase - Single dose

End point title	Pharmacokinetics: Apparent volume of distribution during the terminal phase - Single dose
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End point description:

Pharmacokinetics: Apparent volume of distribution during the terminal phase (V<sub>z</sub>) - Single dose

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
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End point timeframe:

Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	2
Units: L				
geometric mean (geometric coefficient of variation)	4.44 (± 4)	3.23 (± 30)	3.33 (± 23)	5.79 (± 7)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: L				
geometric mean (geometric coefficient of variation)	3.82 (± 24)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Area under the curve from time 0 to infinity - Single dose

End point title	Pharmacokinetics: Area under the curve from time 0 to infinity - Single dose
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End point description:

Pharmacokinetics: Area under the curve from time 0 to infinity (AUC<sub>0-∞</sub>) - Single dose

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
End point timeframe:	
Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.	

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	2
Units: (µg·h/mL)				
geometric mean (geometric coefficient of variation)	1392 (± 88)	1374 (± 23)	2701 (± 45)	638 (± 8)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: (µg·h/mL)				
geometric mean (geometric coefficient of variation)	807 (± 12)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Area under the curve from time 0 to time 24h - Single dose

End point title	Pharmacokinetics: Area under the curve from time 0 to time 24h - Single dose
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End point description:

Pharmacokinetics: Area under the curve from time 0 to time 24h (AUC<sub>0-24</sub>) - Single dose (Dose 1)

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
End point timeframe:	
Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.	

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	7
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	283 (± 34)	350 (± 37)	475 (± 34)	122 (± 25)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	188 (± 12)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Area under the curve from time 0 to time 168 h - Single dose

End point title	Pharmacokinetics: Area under the curve from time 0 to time 168 h - Single dose
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End point description:

Pharmacokinetics: Area under the curve from time 0 to time 168 h (AUC<sub>0-168</sub>) - Single dose (Dose 1)

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
End point timeframe:	
Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.	

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	7
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	1178 (± 64)	1294 (± 22)	2074 (± 44)	305 (± 61)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	586 (± 44)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Mean residence time - Single dose

End point title	Pharmacokinetics: Mean residence time - Single dose
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End point description:

Pharmacokinetics: Mean residence time (MRT) - Single dose (Dose 1)

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
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End point timeframe:

Subjects were sampled repeatedly at Pre (0) and end of infusion, 2, 4, 8, 24 and 168 h post start of dosing.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	2	2
Units: h				
arithmetic mean (standard deviation)	73.3 (± 51.3)	41.6 (± 6.3)	102.0 (± 2.2)	57.4 (± 20.4)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: h				
arithmetic mean (standard deviation)	41.0 (± 7.3)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Concentration at the end of infusion - Repeated dose

End point title	Pharmacokinetics: Concentration at the end of infusion - Repeated dose
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End point description:

Pharmacokinetics: Concentration at the end of infusion (C<sub>inf</sub> end) - Repeated dose

Part I:

Infusion time was initially 1 hour. For cohorts 2 (1.5 mg/kg) and 3 (3.0 mg/kg), the dose level for the first administration was maintained at 1.0 mg/kg as a priming dose and only subsequent doses were given at escalated doses. From cohort 4 onwards, the initial priming dose was reduced to 0.5 mg/kg given over 2 hours. Doses were given with 7-day (168 hour) intervals.

End point type	Secondary
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End point timeframe:

Part I: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 3.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: ng/mL				
geometric mean (geometric coefficient of variation)	28124 (± 8)	29223 (± 55)	97890 (± 35)	127281 (± 20)

<b>End point values</b>	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	289947 ( $\pm$ 21)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Maximum concentration - Repeated dose

End point title	Pharmacokinetics: Maximum concentration - Repeated dose
End point description: Pharmacokinetics: Maximum concentration (C <sub>max</sub> ) - Repeated dose.	
End point type	Secondary
End point timeframe: Part I: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 3. Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 6.	

<b>End point values</b>	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: ng/mL				
geometric mean (geometric coefficient of variation)	28560 ( $\pm$ 7)	34429 ( $\pm$ 33)	110813 ( $\pm$ 25)	133944 ( $\pm$ 20)

<b>End point values</b>	Part I - Dose escalation 10 mg/kg - PK population	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	5	7	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)	275333 ( $\pm$ 31)	382798 ( $\pm$ 47)	420840 ( $\pm$ 21)	637385 ( $\pm$ 20)

End point values	Part II Combination therapy Arm C 5 mg/kg - PK population	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	9	2	21
Units: ng/mL				
geometric mean (geometric coefficient of variation)	133286 (± 29)	22450 (± 68)	49614 (± 75)	105182 (± 44)

End point values	Part II Combination therapy Arm D 7.5 mg/kg - PK population	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	11	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	213576 (± 31)	16300 (± 69)	42809 (± 45)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Time taken to reach maximum concentration - Repeated dose

End point title	Pharmacokinetics: Time taken to reach maximum concentration - Repeated dose
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End point description:

Pharmacokinetics: Time taken to reach maximum concentration (t<sub>max</sub>) - Repeated dose

End point type	Secondary
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End point timeframe:

Part I: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 3.

Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 6.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: h				
median (full range (min-max))	2.0 (1.6 to 2.1)	2.0 (1.0 to 2.0)	2.0 (2.0 to 3.0)	2.0 (0.9 to 2.0)

End point values	Part I - Dose escalation 10 mg/kg - PK population	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	7	4
Units: h				
median (full range (min-max))	1.8 (1.0 to 24.4)	3.0 (2.0 to 4.1)	2.0 (2.0 to 8.0)	2.3 (2.0 to 4.0)

End point values	Part II Combination therapy Arm C 5 mg/kg - PK population	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	9	2	21
Units: h				
median (full range (min-max))	2.0 (2.0 to 8.0)	4.0 (2.0 to 8.0)	2.0 (2.0 to 2.1)	2.1 (2.0 to 8.0)

End point values	Part II Combination therapy Arm D 7.5 mg/kg - PK population	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	11	11	
Units: h				
median (full range (min-max))	2.1 (2.0 to 8.0)	1.0 (0.8 to 1.2)	1.1 (0.9 to 1.1)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Terminal half-life - Repeated dose

End point title	Pharmacokinetics: Terminal half-life - Repeated dose
End point description:	Pharmacokinetics: Terminal half-life ( $t_{1/2}$ ) - Repeated dose
End point type	Secondary
End point timeframe:	Part I: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 3. Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 6.

<b>End point values</b>	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	3	4
Units: h				
geometric mean (geometric coefficient of variation)	47.3 (± 7)	75.7 (± 4)	54.2 (± 23)	135.4 (± 65)

<b>End point values</b>	Part I - Dose escalation 10 mg/kg - PK population	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	6	7	4
Units: h				
geometric mean (geometric coefficient of variation)	82.6 (± 21)	214.1 (± 149)	265.8 (± 43)	246.3 (± 132)

<b>End point values</b>	Part II Combination therapy Arm C 5 mg/kg - PK population	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	9	2	21
Units: h				
geometric mean (geometric coefficient of variation)	225.4 (± 26)	105.5 (± 109)	111.6 (± 56)	201.1 (± 42)

<b>End point values</b>	Part II Combination therapy Arm D 7.5 mg/kg - PK population	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	4	8	
Units: h				
geometric mean (geometric coefficient of variation)	252.7 (± 20)	118.3 (± 46)	189.0 (± 25)	



## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Clearance - Repeated dose

End point title Pharmacokinetics: Clearance - Repeated dose

End point description:

Pharmacokinetics: Clearance (CL) - Repeated dose

End point type Secondary

End point timeframe:

Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 2.

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	10	6	10
Units: mL/h				
geometric mean (geometric coefficient of variation)	25.2 (± 42)	26.5 (± 27)	22.4 (± 46)	26.5 (± 21)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	22	7
Units: mL/h				
geometric mean (geometric coefficient of variation)	32.3 (± 47)	35.5 (± 14)	27.8 (± 34)	19.0 (± 39)

End point values	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	14		
Units: mL/h				
geometric mean (geometric coefficient of variation)	38.0 (± 22)	32.3 (± 19)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Apparent volume of distribution during the terminal phase - Repeated dose

End point title	Pharmacokinetics: Apparent volume of distribution during the terminal phase - Repeated dose
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End point description:

Pharmacokinetics: Apparent volume of distribution during the terminal phase (V<sub>z</sub>) - Repeated dose

End point type	Secondary
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End point timeframe:

Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 2.

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	10	6	10
Units: L				
geometric mean (geometric coefficient of variation)	4.7 (± 23)	4.7 (± 18)	4.2 (± 36)	4.3 (± 21)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	22	7
Units: L				
geometric mean (geometric coefficient of variation)	4.0 (± 28)	3.9 (± 11)	4.3 (± 24)	4.2 (± 18)

End point values	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	14		
Units: L				
geometric mean (geometric coefficient of variation)	3.2 (± 23)	3.9 (± 13)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Area under the curve from time 0 to infinity - Repeated dose

End point title	Pharmacokinetics: Area under the curve from time 0 to infinity - Repeated dose
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End point description:

Pharmacokinetics: Area under the curve from time 0 to infinity (AUC<sub>0-∞</sub>) - Repeated dose

End point type	Secondary
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End point timeframe:

Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 2.

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	10	6	10
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	30279 (± 54)	29434 (± 34)	53430 (± 48)	13601 (± 25)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	22	7
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	2708 (± 82)	4476 (± 9)	13493 (± 41)	28187 (± 52)

End point values	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population		
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Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	14		
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	1754 (± 30)	5463 (± 26)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Area under the curve from time 0 to time t - Repeated dose

End point title	Pharmacokinetics: Area under the curve from time 0 to time t - Repeated dose
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End point description:

Pharmacokinetics: Area under the curve from time 0 to time t (AUC<sub>0-t</sub>) - Repeated dose

End point type	Secondary
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End point timeframe:

Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 6 except for PDEX1 and PDEX2.5 after dose 4.

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	7	4	10
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	33245 (± 130)	67402 (± 95)	89810 (± 103)	27274 (± 40)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	21	6
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	1367 (± 570)	3041 (± 111)	17274 (± 61)	38778 (± 41)

End point values	Part II Combination therapy Arm	Part II Combination therapy Arm		
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	PDEX1 - PK population	PDEX2.5 - PK population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	9		
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	2108 (± 55)	8972 (± 38)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Area under the curve from time 0 to time 24h - Repeated dose

End point title	Pharmacokinetics: Area under the curve from time 0 to time 24h - Repeated dose
End point description:	Pharmacokinetics: Area under the curve from time 0 to time 24h (AUC0-24) - Repeated dose
End point type	Secondary
End point timeframe:	Part I: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 3.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	3	5
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	576 (± 5)	673 (± 18)	2303 (± 26)	3030 (± 14)

End point values	Part I - Dose escalation 10 mg/kg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	5845 (± 34)			

## Statistical analyses

**Secondary: Pharmacokinetics: Area under the curve from time 0 to time 168 h - Repeated dose**

End point title	Pharmacokinetics: Area under the curve from time 0 to time 168 h - Repeated dose
End point description:	Pharmacokinetics: Area under the curve from time 0 to time 168 h (AUC <sub>0-168</sub> ) - Repeated dose
End point type	Secondary
End point timeframe:	Part I: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 2. Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 6.

End point values	Part I - Dose escalation 1 mg/kg - PK population	Part I - Dose escalation 1.5 mg/kg - PK population	Part I - Dose escalation 3 mg/kg - PK population	Part I - Dose escalation 6 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	2263 (± 24)	2441 (± 28)	8947 (± 27)	9795 (± 28)

End point values	Part I - Dose escalation 10 mg/kg - PK population	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	7	4
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	21370 (± 21)	42871 (± 80)	48969 (± 26)	72244 (± 24)

End point values	Part II Combination therapy Arm C 5 mg/kg - PK population	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	9	2	21
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	15693 (± 38)	2117 (± 123)	5058 (± 45)	11396 (± 51)

End point values	Part II	Part II	Part II	
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	Combination therapy Arm D 7.5 mg/kg - PK population	Combination therapy Arm PDEX1 - PK population	Combination therapy Arm PDEX2.5 - PK population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	4	8	
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	24927 (± 38)	1561 (± 52)	5671 (± 35)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Mean residence time - Repeated dose

End point title	Pharmacokinetics: Mean residence time - Repeated dose
End point description:	
Pharmacokinetics: Mean residence time (MRT) - Repeated dose	
End point type	Secondary
End point timeframe:	
Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 2.	

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	10	6	10
Units: h				
arithmetic mean (standard deviation)	186 (± 47)	177 (± 36)	187 (± 45)	150 (± 24)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	22	7
Units: h				
arithmetic mean (standard deviation)	112 (± 54)	90 (± 8)	147 (± 43)	224 (± 103)

End point values	Part II Combination therapy Arm	Part II Combination therapy Arm		
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	PDEX1 - PK population	PDEX2.5 - PK population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	14		
Units: h				
arithmetic mean (standard deviation)	60 ( $\pm$ 31)	101 ( $\pm$ 18)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Area under the curve from time 0 to tau (AUC0- $\tau$ ) - Single dose

End point title	Pharmacokinetics: Area under the curve from time 0 to tau (AUC0- $\tau$ ) - Single dose
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End point description:

Pharmacokinetics: Area under the curve from time 0 to tau (AUC0- $\tau$ ) - Single dose

Arms A, B, E, C (5 mg/kg; 1 mg/kg; 2.5 mg/kg), and D (5 mg/kg; 7.5 mg/kg): Assessment was done at dose 2 due to initial priming dose.

Arms PDEX 1 and PDEX 2.5: Assessment was done at dose 1.

End point type	Secondary
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End point timeframe:

Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after first full dose.

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	10	6	11
Units: $\mu\text{g}\cdot\text{h/mL}$				
geometric mean (geometric coefficient of variation)	18021 ( $\pm$ 38)	17557 ( $\pm$ 26)	31805 ( $\pm$ 46)	7459 ( $\pm$ 67)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	3	24	8
Units: $\mu\text{g}\cdot\text{h/mL}$				
geometric mean (geometric coefficient of variation)	1636 ( $\pm$ 85)	3585 ( $\pm$ 6)	7694 ( $\pm$ 75)	12551 ( $\pm$ 69)



End point values	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	17		
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	1124 (± 116)	3198 (± 68)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Area under the curve from time 0 to tau - Repeated dose

End point title	Pharmacokinetics: Area under the curve from time 0 to tau - Repeated dose
End point description:	Pharmacokinetics: Area under the curve from time 0 to tau (AUC <sub>0-τ</sub> ) - Repeated dose
End point type	Secondary
End point timeframe:	Part II: Subjects were sampled repeatedly at 1, 2 and 24 h after dose 6.

End point values	Part II Monotherapy Arm A - PK population	Part II Monotherapy Arm B - PK population	Part II Monotherapy Arm E - PK population	Part II Combination therapy Arm C 5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	7	4	10
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	33245 (± 130)	67402 (± 95)	89810 (± 103)	27274 (± 40)

End point values	Part II Combination therapy Arm C 1 mg/kg - PK population	Part II Combination therapy Arm C 2.5 mg/kg - PK population	Part II Combination therapy Arm D 5 mg/kg - PK population	Part II Combination therapy Arm D 7.5 mg/kg - PK population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	21	6
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	1367 (± 570)	3041 (± 111)	17274 (± 61)	38778 (± 41)

End point values	Part II Combination therapy Arm PDEX1 - PK population	Part II Combination therapy Arm PDEX2.5 - PK population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	9		
Units: µg·h/mL				
geometric mean (geometric coefficient of variation)	2108 (± 55)	8972 (± 38)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Changes in serum concentration of sIL1RAP

End point title	Pharmacokinetics: Changes in serum concentration of sIL1RAP
End point description:	Pharmacokinetics: Changes in sIL1RAP from pre-dose visit 1 to pre-dose visit 3.
End point type	Secondary
End point timeframe:	Part I: Samples was collected predose visit 1 and predose visit 3

End point values	Part I: Dose escalation - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: ng/mL				
arithmetic mean (standard deviation)	277 (± 100)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: immune related Overall Response Rate (irORR) by irRC

End point title	Efficacy: immune related Overall Response Rate (irORR) by irRC
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End point description:

The immune related Overall Response Rate (irORR) is defined as the proportion of responders, i.e., subjects who achieve a immune related Best Overall Response (irBOR) of immune related Complete Response (irCR) or immune related Partial Response (irPR) assessed by immune related Response Criteria (irRC). A confirmatory scan was required. Not evaluable subjects are considered non-responders.

End point type	Secondary
End point timeframe:	
At screening followed by 8-week intervals after first CAN04 dose while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.	

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT	Part I - Dose escalation 1.5 mg/kg mITT	Part I - Dose escalation 3 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	3	3	3
Units: %				
number (confidence interval 95%)	0 (0 to 15)	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)

End point values	Part I - Dose escalation 6 mg/kg mITT	Part I - Dose escalation 10 mg/kg mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	6	10	10
Units: %				
number (confidence interval 95%)	0 (0 to 41)	0 (0 to 46)	0 (0 to 31)	0 (0 to 31)

End point values	Part II Monotherapy Arm E mITT	Part II Monotherapy mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	26		
Units: %				
number (confidence interval 95%)	0 (0 to 46)	0 (0 to 13)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: immune Overall Response Rate (iORR) by iRECIST

End point title	Efficacy: immune Overall Response Rate (iORR) by iRECIST
End point description:	
The immune Overall Response Rate (iORR) is defined as the proportion of responders, i.e., subjects who achieve a confirmed immune Best Overall Response (iBOR) of immune Complete Response (iCR) or immune Partial Response (iPR) assessed by immune Response Evaluation Criteria in Solid Tumours (iRECIST). A confirmatory scan was required. Not evaluable subjects are considered non-responders.	
End point type	Secondary

End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	16	3
Units: %				
number (confidence interval 95%)	53 (34 to 72)	55 (23 to 83)	50 (25 to 75)	67 (9 to 99)

End point values	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	33	25	8
Units: %				
number (confidence interval 95%)	60 (26 to 88)	24 (11 to 42)	20 (7 to 41)	38 (9 to 76)

End point values	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: %				
number (confidence interval 95%)	45 (23 to 69)	30 (12 to 54)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Overall Response Rate (ORR) by RECIST 1.1

End point title	Efficacy: Overall Response Rate (ORR) by RECIST 1.1
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End point description:

The Overall Response Rate (ORR) is defined as the proportion of confirmed responders, i.e., subjects who achieve a Best Overall Response (BOR) of Complete Response (CR) or Partial Response (PR) assessed by Response Evaluation Criteria in Solid Tumours (RECIST version 1.1). A confirmatory scan was required. Not evaluable subjects are considered non-responders.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT	Part I - Dose escalation 1.5 mg/kg mITT	Part I - Dose escalation 3 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	3	3	3
Units: %				
number (confidence interval 95%)	0 (0 to 15)	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)

End point values	Part I - Dose escalation 6 mg/kg mITT	Part I - Dose escalation 10 mg/kg mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	6	10	10
Units: %				
number (confidence interval 95%)	0 (0 to 41)	0 (0 to 46)	0 (0 to 31)	0 (0 to 31)

End point values	Part II Monotherapy Arm E mITT	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	26	30	11
Units: %				
number (confidence interval 95%)	0 (0 to 46)	0 (0 to 13)	53 (34 to 72)	55 (23 to 83)

End point values	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	3	10	33
Units: %				
number (confidence interval 95%)	50 (25 to 75)	67 (9 to 99)	60 (26 to 88)	24 (11 to 42)

End point values	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	8	20	20

Units: %				
number (confidence interval 95%)	20 (7 to 41)	38 (9 to 76)	45 (23 to 69)	30 (12 to 54)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: immune related Duration of Response (irDoR) by irRC

End point title	Efficacy: immune related Duration of Response (irDoR) by irRC
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End point description:

Duration of response (irDOR) is defined as the time from first confirmed response (irCR or irPR) to disease progression assessed by immune related Response Criteria (irRC) or death from any cause or censoring.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week interval after first CAN04 dose while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT	Part I - Dose escalation 1.5 mg/kg mITT	Part I - Dose escalation 3 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[3]</sup>	0 <sup>[4]</sup>	0 <sup>[5]</sup>	0 <sup>[6]</sup>
Units: months				
median (confidence interval 95%)	( to )	( to )	( to )	( to )

Notes:

[3] - irDoR could not be estimated due to no responders.

[4] - irDoR could not be estimated due to no responders.

[5] - irDoR could not be estimated due to no responders.

[6] - irDoR could not be estimated due to no responders.

End point values	Part I - Dose escalation 6 mg/kg mITT	Part I - Dose escalation 10 mg/kg mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[7]</sup>	0 <sup>[8]</sup>	0 <sup>[9]</sup>	0 <sup>[10]</sup>
Units: months				
median (confidence interval 95%)	( to )	( to )	( to )	( to )

Notes:

[7] - irDoR could not be estimated due to no responders.

[8] - irDoR could not be estimated due to no responders.

[9] - irDoR could not be estimated due to no responders.

[10] - irDoR could not be estimated due to no responders.

End point values	Part II Monotherapy Arm E mITT	Part II Monotherapy mITT		
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Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 <sup>[11]</sup>	0 <sup>[12]</sup>		
Units: months				
median (confidence interval 95%)	( to )	( to )		

Notes:

[11] - irDoR could not be estimated due to no responders.

[12] - irDoR could not be estimated due to no responders.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: immune Duration of Response (iDoR) by iRECIST

End point title	Efficacy: immune Duration of Response (iDoR) by iRECIST
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End point description:

Duration of immune Response (iDOR) is defined as the time from first time the criteria for confirmed response (iCR or iPR) are met to disease progression assessed by immune Response Evaluation Criteria in Solid Tumours (iRECIST) or death from any cause or censoring.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm PDEX1 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	8	8	9
Units: months				
median (confidence interval 95%)	5.8 (3.7 to 11.2)	4.6 (3.6 to 7.5)	6.1 (3.7 to 13.8)	5.6 (3.6 to 11.8)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Duration of Response (DoR) by RECIST 1.1

End point title	Efficacy: Duration of Response (DoR) by RECIST 1.1
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End point description:

Duration of response (DOR) is defined as the time from first confirmed response (CR or PR) to disease progression assessed by Response Evaluation Criteria in Solid Tumours (RECIST version 1.1) or death from any cause or censoring.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT	Part I - Dose escalation 1.5 mg/kg mITT	Part I - Dose escalation 3 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[13]</sup>	0 <sup>[14]</sup>	0 <sup>[15]</sup>	0 <sup>[16]</sup>
Units: months				
median (confidence interval 95%)	( to )	( to )	( to )	( to )

Notes:

[13] - DoR could not be estimated due to no responders.

[14] - DoR could not be estimated due to no responders.

[15] - DoR could not be estimated due to no responders.

[16] - DoR could not be estimated due to no responders.

End point values	Part I - Dose escalation 6 mg/kg mITT	Part I - Dose escalation 10 mg/kg mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[17]</sup>	0 <sup>[18]</sup>	0 <sup>[19]</sup>	0 <sup>[20]</sup>
Units: months				
median (confidence interval 95%)	( to )	( to )	( to )	( to )

Notes:

[17] - DoR could not be estimated due to no responders.

[18] - DoR could not be estimated due to no responders.

[19] - DoR could not be estimated due to no responders.

[20] - DoR could not be estimated due to no responders.

End point values	Part II Monotherapy Arm E mITT	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 1 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[21]</sup>	0 <sup>[22]</sup>	16	8
Units: months				
median (confidence interval 95%)	( to )	( to )	5.8 (3.7 to 11.2)	4.6 (3.6 to 7.5)

Notes:

[21] - DoR could not be estimated due to no responders.

[22] - DoR could not be estimated due to no responders.

End point values	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm PDEX1 mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	9		
Units: months				
median (confidence interval 95%)	6.1 (3.7 to 13.8)	5.6 (3.6 to 11.8)		



## Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: immune related Progression-Free Survival (irPFS) at 6 months by irRC

End point title	Efficacy: immune related Progression-Free Survival (irPFS) at 6 months by irRC
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End point description:

Probability for subjects for immune related Progression Free Survival (irPFS) assessed by immune related Response Criteria (irRC) at 6 month after first CAN04 dose.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	3		
Units: %				
number (confidence interval 95%)	6 (0 to 23)	33 (1 to 77)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: immune Progression-Free Survival (iPFS) at 6 months by iRECIST

End point title	Efficacy: immune Progression-Free Survival (iPFS) at 6 months by iRECIST
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End point description:

Probability for subjects for immune Progression Free Survival (iPFS) assessed by immune Response Evaluation Criteria in Solid Tumours (iRECIST) at 6 month after first CAN04 dose.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	16	3
Units: %				
number (confidence interval 95%)	57 (37 to 73)	82 (45 to 95)	36 (13 to 59)	67 (5 to 95)

End point values	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	33	25	8
Units: %				
number (confidence interval 95%)	70 (33 to 89)	42 (25 to 59)	48 (27 to 66)	25 (4 to 56)

End point values	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: %				
number (confidence interval 95%)	61 (35 to 79)	63 (35 to 81)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Progression-Free Survival (PFS) at 6 months by RECIST 1.1

End point title	Efficacy: Progression-Free Survival (PFS) at 6 months by RECIST 1.1
End point description:	Probability for subjects for Progression Free Survival (PFS) assessed by Response Evaluation Criteria in Solid Tumours (RECIST version 1.1) at 6 month after first CAN04 dose.
End point type	Secondary
End point timeframe:	At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	3	30	11
Units: %				
number (confidence interval 95%)	5 (0 to 20)	33 (1 to 77)	57 (37 to 73)	82 (45 to 95)

End point values	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	3	10	33
Units: %				
number (confidence interval 95%)	36 (13 to 59)	67 (5 to 95)	60 (25 to 83)	33 (17 to 49)

End point values	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	8	20	20
Units: %				
number (confidence interval 95%)	35 (17 to 54)	25 (4 to 56)	61 (35 to 79)	56 (30 to 76)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: immune Progression-Free Survival (iPFS) at 12 months by iRECIST

End point title	Efficacy: immune Progression-Free Survival (iPFS) at 12 months by iRECIST
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End point description:

Probability for subjects for immune Progression Free Survival (iPFS) assessed by immune Response Evaluation Criteria in Solid Tumours (iRECIST) at 12 months after first CAN04 dose.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	16	3
Units: %				
number (confidence interval 95%)	16 (5 to 32)	22 (4 to 50)	7 (1 to 28)	33 (1 to 77)

End point values	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	33	25	20
Units: %				
number (confidence interval 95%)	25 (4 to 55)	16 (6 to 31)	22 (8 to 40)	17 (4 to 37)

End point values	Part II Combination therapy Arm PDEX2.5 mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: %				
number (confidence interval 95%)	19 (4 to 43)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Progression-Free Survival (PFS) at 12 months by RECIST 1.1

End point title	Efficacy: Progression-Free Survival (PFS) at 12 months by RECIST 1.1
End point description: Probability for subjects for Progression Free Survival (PFS) assessed by Response Evaluation Criteria in Solid Tumours (RECIST version 1.1) at 12 months after first CAN04 dose.	
End point type	Secondary
End point timeframe: At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.	

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	16	3
Units: %				
number (confidence interval 95%)	16 (5 to 32)	22 (4 to 50)	7 (1 to 28)	33 (1 to 77)

End point values	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	33	25	20
Units: %				
number (confidence interval 95%)	25 (4 to 55)	13 (4 to 27)	18 (6 to 35)	17 (4 to 37)

End point values	Part II Combination therapy Arm PDEX2.5 mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: %				
number (confidence interval 95%)	19 (5 to 40)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: immune related Progression-Free Survival (irPFS) by irRC

End point title	Efficacy: immune related Progression-Free Survival (irPFS) by irRC
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End point description:

immune related Progression Free Survival (irPFS) from first CAN04 dose until confirmed disease progression by immune related Response Criteria (irRC), start of new line of systemic anti-cancer therapy or death.

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part I - Dose escalation mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT	Part II Monotherapy mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	10	10	26
Units: months				
median (confidence interval 95%)	1.9 (1.8 to 3.2)	1.7 (0.2 to 2.4)	1.9 (0.8 to 2.8)	1.8 (1.4 to 2.2)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: immune Progression-Free Survival (iPFS) by iRECIST

End point title	Efficacy: immune Progression-Free Survival (iPFS) by iRECIST
End point description: immune Progression Free Survival (iPFS) from first CAN04 dose until confirmed disease progression by immune Response Evaluation Criteria in Solid Tumours (iRECIST), start of new line of systemic anticancer therapy or death.	
End point type	Secondary
End point timeframe: At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.	

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	16	33
Units: months				
median (confidence interval 95%)	7.0 (5.5 to 8.8)	8.8 (5.6 to 13.0)	5.5 (2.7 to 7.4)	5.6 (2.0 to 7.4)

End point values	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	8	20	20
Units: months				
median (confidence interval 95%)	5.6 (2.8 to 9.3)	3.7 (0.6 to 8.5)	7.2 (3.7 to 9.2)	7.4 (5.1 to 11.2)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: Progression-Free Survival (PFS) by RECIST 1.1

End point title	Efficacy: Progression-Free Survival (PFS) by RECIST 1.1
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End point description:

Progression Free Survival (PFS) from first CAN04 dose until confirmed disease progression by Response Evaluation Criteria in Solid Tumours (RECIST version 1.1)

End point type	Secondary
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End point timeframe:

At screening followed by 8-week intervals after first CAN04 dose (Arm NCP: 6-week intervals for 36 weeks, thereafter every 9 weeks) while on trial treatment until confirmed disease progression, start of new line of systemic anti-cancer therapy or death.

End point values	Part I - Dose escalation mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT	Part II Monotherapy mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	10	10	26
Units: months				
median (confidence interval 95%)	1.9 (1.8 to 1.9)	1.7 (0.2 to 1.9)	1.8 (0.8 to 2.2)	1.8 (1.2 to 1.9)

End point values	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	16	33
Units: months				
median (confidence interval 95%)	7.0 (5.5 to 8.8)	8.8 (5.6 to 13.0)	5.5 (2.7 to 7.4)	3.7 (1.9 to 5.8)

End point values	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	8	20	20
Units: months				

median (confidence interval 95%)	3.7 (1.9 to 7.1)	3.7 (0.6 to 8.5)	7.2 (2.7 to 9.2)	7.3 (4.9 to 9.3)
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## Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: Overall Survival (OS) at 12 months

End point title	Efficacy: Overall Survival (OS) at 12 months
End point description:	Probability for subjects to be alive 12 months after first CAN04 dose.
End point type	Secondary
End point timeframe:	Follow-up for Overall Survival was performed 12, 24 and 36 months after End of Treatment visit.

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 1 mg/kg mITT	Part I - Dose escalation 3 mg/kg mITT	Part I - Dose escalation 10 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	3	3	6
Units: %				
number (confidence interval 95%)	23 (8 to 41)	67 (5 to 95)	67 (5 to 95)	17 (1 to 52)

End point values	Part II Monotherapy Arm B mITT	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	26	30	11
Units: %				
number (confidence interval 95%)	30 (7 to 58)	12 (3 to 27)	57 (37 to 73)	55 (23 to 78)

End point values	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	3	10	33
Units: %				
number (confidence interval 95%)	57 (28 to 78)	67 (5 to 95)	48 (16 to 75)	56 (38 to 71)



<b>End point values</b>	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	8	20	20
Units: %				
number (confidence interval 95%)	54 (33 to 71)	63 (23 to 86)	63 (38 to 81)	56 (31 to 75)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Overall Survival (OS) at 24 months

End point title	Efficacy: Overall Survival (OS) at 24 months
End point description:	
Probability for subjects to be alive 24 months after first CAN04 dose.	
End point type	Secondary
End point timeframe:	
Follow-up for Overall Survival was performed 12, 24 and 36 months after End of Treatment visit.	

<b>End point values</b>	Part II Monotherapy Arm B mITT	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	26	30	11
Units: %				
number (confidence interval 95%)	10 (1 to 36)	4 (0 to 16)	29 (14 to 46)	36 (11 to 63)

<b>End point values</b>	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	3	10	33
Units: %				
number (confidence interval 95%)	21 (5 to 45)	33 (1 to 77)	24 (2 to 62)	30 (15 to 46)

End point values	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	8	20	20
Units: %				
number (confidence interval 95%)	32 (14 to 51)	25 (4 to 56)	32 (13 to 52)	22 (7 to 43)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Overall Survival (OS) at 36 months

End point title	Efficacy: Overall Survival (OS) at 36 months
End point description: Probability for subjects to be alive 36 months after first CAN04 dose.	
End point type	Secondary
End point timeframe: Follow-up for Overall Survival was performed 12, 24 and 36 months after End of Treatment visit.	

End point values	Part II Monotherapy Arm B mITT	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	26	30	11
Units: %				
number (confidence interval 95%)	10 (1 to 36)	4 (0 to 16)	16 (5 to 32)	18 (3 to 44)

End point values	Part II Combination therapy Arm C 1 mg/kg mITT	Part II Combination therapy Arm C 2.5 mg/kg mITT	Part II Combination therapy Arm NCP mITT	Part II Combination therapy Arm D mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	3	10	33
Units: %				
number (confidence interval 95%)	14 (2 to 37)	33 (1 to 77)	24 (2 to 62)	9 (2 to 23)

End point values	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT	Part II Combination therapy Arm PDEX2.5 mITT	
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	20	20	
Units: %				
number (confidence interval 95%)	12 (2 to 30)	13 (2 to 33)	15 (3 to 36)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: Overall Survival (OS)

End point title	Efficacy: Overall Survival (OS)
End point description:	Overall Survival (OS) from first CAN04 dose until death of any cause.
End point type	Secondary
End point timeframe:	Follow-up for Overall Survival was performed 12, 24 and 36 months after End of Treatment visit.

End point values	Part I - Dose escalation mITT	Part I - Dose escalation 6 mg/kg mITT	Part II Monotherapy Arm A mITT	Part II Monotherapy Arm B mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	7	10	10
Units: months				
median (confidence interval 95%)	6.3 (3.7 to 9.2)	5.1 (1.1 to 9.2)	2.7 (0.2 to 4.9)	5.1 (1.0 to 12.2)

End point values	Part II Monotherapy mITT	Part II Combination therapy Arm C mITT	Part II Combination therapy Arm C 5 mg/kg mITT	Part II Combination therapy Arm C 1 mg/kg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	30	11	16
Units: months				
median (confidence interval 95%)	3.8 (2.3 to 5.3)	13.9 (11.1 to 19.4)	13.7 (9.1 to 30.4)	14.9 (6.0 to 22.0)

End point values	Part II Combination therapy Arm D mITT	Part II Combination therapy Arm D 5 mg/kg mITT	Part II Combination therapy Arm D 7.5 mg/kg mITT	Part II Combination therapy Arm PDEX1 mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	25	8	20
Units: months				

median (confidence interval 95%)	12.6 (8.0 to 19.2)	12.6 (6.5 to 24.6)	13.0 (0.7 to 25.7)	12.9 (9.9 to 25.7)
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<b>End point values</b>	Part II Combination therapy Arm PDEX2.5 mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: months				
median (confidence interval 95%)	14.2 (6.9 to 15.6)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from ICF signature until 28 days after end of treatment with CAN04.

Adverse event reporting additional description:

All adverse events reported spontaneously by the subject or observed by the investigator was recorded although reported adverse events below refers to treatment emergent adverse events.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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### Reporting groups

Reporting group title	Part I - Dose escalation
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Reporting group description:

Phase 1 dose-escalation arm (3+3 design) to assess the safety of CAN04 monotherapy administered at 1 (n=3), 1.5 (n=3), 3 (n=3), 6 (n=7), and 10 (n=6) mg/kg in patients with unresectable NSCLC, PDAC, CRC, or TNBC that was refractory to standard therapy or for whom no standard therapy existed. The primary aim was to assess safety and to define the MTD or RP2D of CAN04 administered once weekly.

Reporting group title	Part II Monotherapy Arm A
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly in patients with unresectable squamous or non-squamous NSCLC or PDAC that was refractory to standard therapy or for whom no standard therapy existed.

Reporting group title	Part II Monotherapy Arm B
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 10 mg/kg (RP2D) once weekly for first 6 weeks followed by biweekly administration in patients with unresectable squamous or non-squamous NSCLC or PDAC that was refractory to standard therapy or for whom no standard therapy existed.

Reporting group title	Part II Monotherapy Arm E
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and early signs of efficacy of CAN04 monotherapy administered at 15 mg/kg once weekly for first 6 weeks followed by biweekly administration in patients with unresectable, locally advanced or metastatic squamous or non-squamous NSCLC or PDAC that was refractory to standard therapy or for whom no standard therapy existed.

Reporting group title	Part II Combination therapy Arm C
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and cisplatin in patients with unresectable, locally advanced or metastatic squamous or non-squamous NSCLC who was candidates for 1st line of standard chemotherapy regimen with cisplatin/gemcitabine or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with cisplatin/gemcitabine. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase but a provisional MTD was reached on 5 mg/kg (n=13) and dose reduced to 1 mg/kg (n=17) and re-escalated to 2.5 mg/kg (n=3).

Reporting group title	Part II Combination therapy Arm NCP
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Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with carboplatin and pemetrexed in patients with stage III or IV non-squamous NSCLC who was candidates for 1st line of standard chemotherapy regimen with carboplatin/pemetrexed or who relapsed after 1st line with pembrolizumab monotherapy and was candidates for 2nd line of standard chemotherapy regimen with carboplatin/pemetrexed.

Reporting group title	Part II Combination therapy Arm D
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#### Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who was candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel. The arm was initially designed with a limited dose escalation phase as a 3+3 design and 3 dose levels: 5, 7.5, and 10 mg/kg (the monotherapy RP2D). After the identification of MTD/RP2D, it was planned to continue the arm with a dose expansion phase, and after 7.5 mg/kg (n=8) was found to be above MTD expansion phase was done with 5 mg/kg (n=28).

Reporting group title	Part II Combination therapy Arm PDEX1
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#### Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 1 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who was candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX1 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

Reporting group title	Part II Combination therapy Arm PDEX2.5
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#### Reporting group description:

Part II dose expansion arm to assess safety and tolerability, and preliminary signs of efficacy of CAN04 at 2.5 mg/kg in combination with gemcitabine and nab-paclitaxel in patients with stage III or IV pancreatic ductal adenocarcinoma who was candidates for 1st line of standard chemotherapy regimen with gemcitabine/nab-paclitaxel.

The starting dose selected in Arm PDEX2.5 was chosen to explore doses below the MTD (5.0 mg/kg) after the completion of Part II Combination therapy Arm D.

<b>Serious adverse events</b>	Part I - Dose escalation	Part II Monotherapy Arm A	Part II Monotherapy Arm B
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 22 (40.91%)	7 / 10 (70.00%)	4 / 10 (40.00%)
number of deaths (all causes)	22	10	9
number of deaths resulting from adverse events	2	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Embolic			

subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Venous thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Elective surgery			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Hospitalisation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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

Chest pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Death			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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			
Bronchial obstruction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0



Pleural effusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Pneumothorax			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 embolism			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 oedema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
C-reactive protein increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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			
Infusion related reaction			
subjects affected / exposed	4 / 22 (18.18%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Arrhythmia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Nervous system disorders</b>			
Aphasia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Dysarthria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Presyncope			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Radicular pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (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
Spinal cord compression			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Blood and lymphatic system disorders</b>			
Anaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Disseminated intravascular			

coagulation			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (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
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Leukopenia	Additional description: 'White blood cell count decreased' is reported as 'Leukopenia'		
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia	Additional description: 'Neutrophil count decreased' is reported as 'Neutropenia'		
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Pancytopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Thrombocytopenia	Additional description: 'Platelet Count Decreased' is reported as 'Thrombocytopenia'		
subjects affected / exposed	1 / 22 (4.55%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (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

Ascites			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (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 haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Intestinal stenosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Melaena			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			

subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Subileus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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			
Bile duct stenosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (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
Cholestasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Hepatitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Hepatotoxicity			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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			
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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			
Catheter site infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (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
Cholangitis infective			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 infectious			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Escherichia sepsis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (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
Klebsiella infection			



subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis bacterial			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Septic shock			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 enterococcal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Urosepsis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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 device infection			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (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
Wound infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Hypokalaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part II Monotherapy Arm E	Part II Combination therapy Arm C	Part II Combination therapy Arm NCP
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	22 / 33 (66.67%)	2 / 10 (20.00%)
number of deaths (all causes)	6	25	6
number of deaths resulting from adverse events	1	3	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Subclavian vein thrombosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (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
Venous thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Elective surgery			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (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
Hospitalisation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 6 (16.67%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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			
Bronchial obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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			
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Arrhythmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Myocardial infarction			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Radicular pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Spinal cord compression			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 / 6 (0.00%)	3 / 33 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia	Additional description: 'White blood cell count decreased' is reported as 'Leukopenia'		
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia	Additional description: 'Neutrophil count decreased' is reported as 'Neutropenia'		
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Thrombocytopenia	Additional description: 'Platelet Count Decreased' is reported as 'Thrombocytopenia'		
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			



Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (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 / 33 (0.00%)	0 / 10 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 / 33 (0.00%)	0 / 10 (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
Intestinal stenosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Melaena			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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	1 / 6 (16.67%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Subileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 / 33 (0.00%)	0 / 10 (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			
Bile duct stenosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Cholestasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Hepatitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Hepatotoxicity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Chronic kidney disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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			
Catheter site infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis infective			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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%)	1 / 33 (3.03%)	0 / 10 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Enterocolitis infectious			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 / 33 (0.00%)	0 / 10 (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 / 33 (0.00%)	0 / 10 (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
Klebsiella infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Lymphadenitis bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 33 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Septic shock			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Urosepsis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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 device infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (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
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (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
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part II Combination therapy Arm D	Part II Combination therapy Arm PDEX1	Part II Combination therapy Arm PDEX2.5
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 36 (66.67%)	9 / 20 (45.00%)	11 / 20 (55.00%)
number of deaths (all causes)	28	16	15
number of deaths resulting from adverse events	2	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Elective surgery			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hospitalisation			

subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0



Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Product issues			
Device dislocation			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	5 / 36 (13.89%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radicular pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Disseminated intravascular coagulation</b>			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Haemolytic uraemic syndrome</b>			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Febrile neutropenia</b>			
subjects affected / exposed	5 / 36 (13.89%)	2 / 20 (10.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	5 / 5	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Leukopenia</b>			
Additional description: 'White blood cell count decreased' is reported as 'Leukopenia'			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Neutropenia</b>			
Additional description: 'Neutrophil count decreased' is reported as 'Neutropenia'			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Pancytopenia</b>			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Thrombocytopenia</b>			
Additional description: 'Platelet Count Decreased' is reported as 'Thrombocytopenia'			

subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal stenosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			

subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			

subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Musculoskeletal and connective tissue disorders</b>			
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
Catheter site infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis infective			
subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0



Infection				
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Influenza				
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Klebsiella infection				
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Lymphadenitis bacterial				
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pleural infection				
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pneumonia				
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Sepsis				
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Septic shock				
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Urinary tract infection enterococcal				

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	<b>Part I - Dose escalation</b>	<b>Part II Monotherapy Arm A</b>	<b>Part II Monotherapy Arm B</b>
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)	10 / 10 (100.00%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cancer pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemangioma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Metastases to central nervous system			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	2 / 22 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypertension			

subjects affected / exposed	2 / 22 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral artery occlusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Subclavian vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Superficial vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Thrombophlebitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			

subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	2 / 22 (9.09%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Chills			
subjects affected / exposed	2 / 22 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Device related thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Drug intolerance			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	7 / 22 (31.82%)	6 / 10 (60.00%)	6 / 10 (60.00%)
occurrences (all)	12	6	6
Feeling hot			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			

subjects affected / exposed	3 / 22 (13.64%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Localised oedema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Medical device site pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nodule			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 22 (9.09%)	4 / 10 (40.00%)	2 / 10 (20.00%)
occurrences (all)	4	6	2
Secretion discharge			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Swelling face			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Thirst subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Xerosis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Dysphonia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 10 (10.00%) 1	1 / 10 (10.00%) 1
Dyspnoea subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	4 / 10 (40.00%) 4	4 / 10 (40.00%) 4
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Hiccups subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nasal mucosal disorder			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0



Hallucination subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Listless subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nervousness subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Product issues Device occlusion subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Bilirubin conjugated increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Blood creatinine increased			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	3 / 22 (13.64%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Weight increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

Arthropod bite			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Incision site haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Inflammation of wound			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	6 / 22 (27.27%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	7	4	1
Rib fracture			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin wound			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tachycardia			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nervous system disorders			
Amnesia			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Anosmia			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Aphasia			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Ataxia			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Balance disorder			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Disturbance in attention			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Dizziness			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 10 (20.00%) 3	2 / 10 (20.00%) 2
Dysgeusia			
subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 10 (10.00%) 1	1 / 10 (10.00%) 1
Headache			
subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Intracranial pressure increased			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Neuralgia			
subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0

Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Paraesthesia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Paresis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Piriformis syndrome subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Polyneuropathy subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Taste disorder subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Blood and lymphatic system disorders Anaemia			

subjects affected / exposed	2 / 22 (9.09%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Febrile neutropenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Leukopenia	Additional description: 'White blood cell count decreased' is reported as 'Leukopenia'.		
subjects affected / exposed	1 / 22 (4.55%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutropenia	Additional description: 'Neutrophil count decreased' is reported as 'Neutropenia'.		
subjects affected / exposed	2 / 22 (9.09%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Neutrophilia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia	Additional description: 'Platelet Count Decreased' is reported as 'Thrombocytopenia'.		
subjects affected / exposed	2 / 22 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Thrombocytosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 22 (4.55%)	4 / 10 (40.00%)	2 / 10 (20.00%)
occurrences (all)	1	5	2
Abdominal pain upper			
subjects affected / exposed	4 / 22 (18.18%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	5	2	1
Anal haemorrhage			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	0 / 22 (0.00%)	2 / 10 (20.00%)	2 / 10 (20.00%)
occurrences (all)	0	2	2
Constipation			
subjects affected / exposed	6 / 22 (27.27%)	5 / 10 (50.00%)	4 / 10 (40.00%)
occurrences (all)	7	5	4
Diarrhoea			
subjects affected / exposed	6 / 22 (27.27%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	8	1	1
Dry mouth			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Duodenal ulcer			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	2 / 22 (9.09%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	2	2	1
Dysphagia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Eructation			



subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastric dilatation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Loose tooth			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucous stools			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	5 / 22 (22.73%)	5 / 10 (50.00%)	4 / 10 (40.00%)
occurrences (all)	8	5	4
Oral mucosal blistering			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral pain			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Steatorrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Terminal ileitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tongue coated			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	5 / 22 (22.73%)	4 / 10 (40.00%)	4 / 10 (40.00%)
occurrences (all)	7	5	4
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Biliary obstruction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cholecystitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Cholestasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hepatic cytolysis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hepatic pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hepatotoxicity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Portal vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 22 (4.55%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Eczema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Erythema			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nail discolouration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail ridging			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	4 / 22 (18.18%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	4	2	1
Pruritus allergic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Skin exfoliation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Umbilical haematoma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Incontinence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paraneoplastic glomerulonephritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal failure			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 10 (10.00%) 1	2 / 10 (20.00%) 2
Back pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 10 (20.00%) 2	1 / 10 (10.00%) 1
Bone pain subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 10 (10.00%) 1	1 / 10 (10.00%) 2
Joint swelling subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Limb discomfort subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Muscle spasm subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Muscular weakness subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Musculoskeletal chest pain			

subjects affected / exposed	2 / 22 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Covid-19			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cholangitis infective			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Erysipelas			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Fungal foot infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis Escherichia coli			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1



Paronychia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	3	1	1
Prostatic abscess			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Root canal infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Spontaneous bacterial peritonitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	5 / 22 (22.73%)	4 / 10 (40.00%)	5 / 10 (50.00%)
occurrences (all)	7	4	5
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Food intolerance			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Hypomagnesaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Iron deficiency			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part II Monotherapy Arm E	Part II Combination therapy Arm C	Part II Combination therapy Arm NCP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	30 / 33 (90.91%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Haemangioma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metastases to central nervous system			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Capillary leak syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	3 / 33 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral artery occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Subclavian vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Superficial vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Thrombophlebitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Varicose vein subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	6 / 33 (18.18%) 8	1 / 10 (10.00%) 1
Catheter site pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	4 / 33 (12.12%) 5	2 / 10 (20.00%) 2
Chills subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 33 (3.03%) 1	0 / 10 (0.00%) 0
Device related thrombosis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 33 (3.03%) 1	0 / 10 (0.00%) 0
Disease progression subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Drug intolerance subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Face oedema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	2 / 10 (20.00%) 2
Fatigue subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 5	8 / 33 (24.24%) 8	1 / 10 (10.00%) 1
Feeling hot			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Localised oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Medical device site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Nodule			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	5 / 33 (15.15%)	2 / 10 (20.00%)
occurrences (all)	1	7	2
Pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	3 / 33 (9.09%)	0 / 10 (0.00%)
occurrences (all)	3	3	0
Secretion discharge			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Thirst			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Xerosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	1 / 6 (16.67%)	5 / 33 (15.15%)	1 / 10 (10.00%)
occurrences (all)	1	6	1
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			

subjects affected / exposed	1 / 6 (16.67%)	3 / 33 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Dyspnoea exertional			
subjects affected / exposed	1 / 6 (16.67%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal mucosal disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Pulmonary embolism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			



Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	0 / 10 (0.00%)
occurrences (all)	0	4	0
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Listless			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervousness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	3 / 10 (30.00%)
occurrences (all)	0	7	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	3 / 33 (9.09%)	3 / 10 (30.00%)
occurrences (all)	1	3	7
Bilirubin conjugated increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 33 (6.06%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Blood uric acid increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	6 / 33 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	7	0
Cardiac murmur			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
International normalised ratio increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	0 / 10 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 33 (3.03%) 1	1 / 10 (10.00%) 1
Weight increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	5 / 33 (15.15%) 5	0 / 10 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Incision site haemorrhage subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	1 / 10 (10.00%) 1
Inflammation of wound subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Infusion related reaction subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	5 / 33 (15.15%) 5	2 / 10 (20.00%) 2
Rib fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Skin wound subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Wound			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	0 / 10 (0.00%) 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	0 / 10 (0.00%)
occurrences (all)	0	5	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	3 / 33 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	5	0
Intracranial pressure increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Paresis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Piriformis syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	1 / 10 (10.00%)
occurrences (all)	0	6	1
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Somnolence			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	19 / 33 (57.58%)	10 / 10 (100.00%)
occurrences (all)	0	28	17
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Leukopenia	Additional description: 'White blood cell count decreased' is reported as 'Leukopenia'.		
subjects affected / exposed	0 / 6 (0.00%)	3 / 33 (9.09%)	4 / 10 (40.00%)
occurrences (all)	0	4	10
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Neutropenia	Additional description: 'Neutrophil count decreased' is reported as 'Neutropenia'.		
subjects affected / exposed	0 / 6 (0.00%)	24 / 33 (72.73%)	9 / 10 (90.00%)
occurrences (all)	0	68	32
Neutrophilia			

subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	4	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia	Additional description: 'Platelet Count Decreased' is reported as 'Thrombocytopenia'.		
subjects affected / exposed	0 / 6 (0.00%)	24 / 33 (72.73%)	4 / 10 (40.00%)
occurrences (all)	0	64	14
Thrombocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye swelling			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	1	4	0
Anal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	5 / 33 (15.15%)	0 / 10 (0.00%)
occurrences (all)	2	9	0
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	9 / 33 (27.27%)	1 / 10 (10.00%)
occurrences (all)	2	18	1



Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Duodenal ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	2	3	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eructation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastric dilatation			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Loose tooth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucous stools			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	9 / 33 (27.27%)	1 / 10 (10.00%)
occurrences (all)	5	15	1
Oral mucosal blistering			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Steatorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Terminal ileitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tongue coated			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Vomiting subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 4	5 / 33 (15.15%) 7	0 / 10 (0.00%) 0
Hepatobiliary disorders			
Bile duct stenosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Biliary obstruction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Cholecystitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Cholestasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Hepatic cytolysis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 33 (3.03%) 1	0 / 10 (0.00%) 0
Hepatic pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Hepatotoxicity subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 33 (3.03%) 1	0 / 10 (0.00%) 0
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Portal vein thrombosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	6 / 33 (18.18%) 8	1 / 10 (10.00%) 1
Blister			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	3 / 33 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Nail discolouration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail ridging			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	4 / 33 (12.12%)	1 / 10 (10.00%)
occurrences (all)	0	6	1
Pruritus allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 6 (16.67%)	4 / 33 (12.12%)	1 / 10 (10.00%)
occurrences (all)	1	6	1
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Umbilical haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Chronic kidney disease			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Incontinence			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Paraneoplastic glomerulonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 33 (12.12%)	2 / 10 (20.00%)
occurrences (all)	1	4	2
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	8 / 33 (24.24%)	1 / 10 (10.00%)
occurrences (all)	0	10	1
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			

subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasm			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	6 / 33 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	6	0
Spinal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Covid-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	3
Cholangitis infective			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Erysipelas			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal foot infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis Escherichia coli			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0



Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 33 (9.09%)	2 / 10 (20.00%)
occurrences (all)	0	3	3
Prostatic abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Root canal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Spontaneous bacterial peritonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Tooth infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	3 / 33 (9.09%) 3	0 / 10 (0.00%) 0
Metabolism and nutrition disorders			
Cachexia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Decreased appetite subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	6 / 33 (18.18%) 8	0 / 10 (0.00%) 0
Diabetes mellitus inadequate control subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Dyslipidaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	1 / 10 (10.00%) 1
Food intolerance subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	4 / 33 (12.12%) 10	0 / 10 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 33 (0.00%) 0	0 / 10 (0.00%) 0
Hypocalcaemia			

subjects affected / exposed	0 / 6 (0.00%)	2 / 33 (6.06%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	6 / 33 (18.18%)	2 / 10 (20.00%)
occurrences (all)	0	7	2
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	12 / 33 (36.36%)	1 / 10 (10.00%)
occurrences (all)	0	21	2
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 33 (3.03%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 33 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part II Combination therapy Arm D	Part II Combination therapy Arm PDEX1	Part II Combination therapy Arm PDEX2.5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 36 (97.22%)	19 / 20 (95.00%)	20 / 20 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Haemangioma			

subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metastases to central nervous system			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	1 / 36 (2.78%)	2 / 20 (10.00%)	1 / 20 (5.00%)
occurrences (all)	1	3	2
Deep vein thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Flushing			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	5 / 36 (13.89%)	3 / 20 (15.00%)	2 / 20 (10.00%)
occurrences (all)	6	3	4
Hypotension			
subjects affected / exposed	3 / 36 (8.33%)	3 / 20 (15.00%)	1 / 20 (5.00%)
occurrences (all)	3	3	1
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Peripheral artery occlusion			

subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Phlebitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Subclavian vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Superficial vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Varicose vein			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 36 (11.11%)	4 / 20 (20.00%)	2 / 20 (10.00%)
occurrences (all)	4	7	2
Catheter site pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	3 / 20 (15.00%)
occurrences (all)	3	1	4
Chills			
subjects affected / exposed	7 / 36 (19.44%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	11	1	0
Device related thrombosis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Drug intolerance			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	21 / 36 (58.33%)	9 / 20 (45.00%)	11 / 20 (55.00%)
occurrences (all)	38	13	16
Feeling hot			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
General physical health deterioration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Inflammation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	2	1	2
Localised oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 36 (0.00%)	2 / 20 (10.00%)	2 / 20 (10.00%)
occurrences (all)	0	2	2
Medical device site pain			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Nodule			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	17 / 36 (47.22%)	10 / 20 (50.00%)	8 / 20 (40.00%)
occurrences (all)	25	15	15
Pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	2
Peripheral swelling			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	13 / 36 (36.11%)	6 / 20 (30.00%)	7 / 20 (35.00%)
occurrences (all)	32	6	12
Secretion discharge			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast			

disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	5 / 36 (13.89%)	5 / 20 (25.00%)	4 / 20 (20.00%)
occurrences (all)	6	9	6
Dysphonia			
subjects affected / exposed	0 / 36 (0.00%)	3 / 20 (15.00%)	1 / 20 (5.00%)
occurrences (all)	0	3	1
Dyspnoea			
subjects affected / exposed	8 / 36 (22.22%)	6 / 20 (30.00%)	6 / 20 (30.00%)
occurrences (all)	10	7	8
Dyspnoea exertional			
subjects affected / exposed	3 / 36 (8.33%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Epistaxis			
subjects affected / exposed	6 / 36 (16.67%)	5 / 20 (25.00%)	4 / 20 (20.00%)
occurrences (all)	9	6	6
Hiccups			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	3
Nasal mucosal disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	2 / 36 (5.56%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	2	2	0
Pleural effusion			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Pneumonitis			



subjects affected / exposed	3 / 36 (8.33%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	4	1	1
Productive cough			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Pulmonary embolism			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Throat irritation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 36 (8.33%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Confusional state			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Depressed mood			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Depression			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Hallucination			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 20 (10.00%)	1 / 20 (5.00%)
occurrences (all)	2	5	1
Listless			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Nervousness subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Product issues Device occlusion subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 11	6 / 20 (30.00%) 10	5 / 20 (25.00%) 5
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 11	4 / 20 (20.00%) 7	4 / 20 (20.00%) 5
Bilirubin conjugated increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	3 / 20 (15.00%) 6	6 / 20 (30.00%) 8
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 20 (5.00%) 1	1 / 20 (5.00%) 1
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 5	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0

C-reactive protein increased subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	2 / 20 (10.00%) 2	1 / 20 (5.00%) 1
Cardiac murmur subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	4 / 20 (20.00%) 6	8 / 20 (40.00%) 8
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	4 / 20 (20.00%) 4	1 / 20 (5.00%) 1
Weight decreased subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 3	3 / 20 (15.00%) 3	2 / 20 (10.00%) 4
Weight increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	1 / 20 (5.00%) 1
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 8	1 / 20 (5.00%) 2	0 / 20 (0.00%) 0
Incision site haemorrhage subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Inflammation of wound			

subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	13 / 36 (36.11%)	3 / 20 (15.00%)	3 / 20 (15.00%)
occurrences (all)	23	4	3
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	2	2	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Anosmia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Aphasia			

subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Disturbance in attention			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 36 (8.33%)	4 / 20 (20.00%)	2 / 20 (10.00%)
occurrences (all)	3	5	2
Dysgeusia			
subjects affected / exposed	6 / 36 (16.67%)	5 / 20 (25.00%)	3 / 20 (15.00%)
occurrences (all)	7	6	3
Headache			
subjects affected / exposed	7 / 36 (19.44%)	4 / 20 (20.00%)	3 / 20 (15.00%)
occurrences (all)	11	7	5
Intracranial pressure increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Neuropathy peripheral			
subjects affected / exposed	2 / 36 (5.56%)	6 / 20 (30.00%)	3 / 20 (15.00%)
occurrences (all)	2	6	3
Paraesthesia			
subjects affected / exposed	3 / 36 (8.33%)	3 / 20 (15.00%)	0 / 20 (0.00%)
occurrences (all)	3	3	0
Paresis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			

subjects affected / exposed	7 / 36 (19.44%)	7 / 20 (35.00%)	3 / 20 (15.00%)
occurrences (all)	8	7	3
Piriformis syndrome			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	1 / 36 (2.78%)	2 / 20 (10.00%)	3 / 20 (15.00%)
occurrences (all)	1	3	3
Sciatica			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Somnolence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	4
Syncope			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 36 (41.67%)	13 / 20 (65.00%)	11 / 20 (55.00%)
occurrences (all)	30	22	21
Febrile neutropenia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Leukocytosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	2
Leukopenia	Additional description: 'White blood cell count decreased' is reported as 'Leukopenia'.		

subjects affected / exposed	13 / 36 (36.11%)	6 / 20 (30.00%)	3 / 20 (15.00%)
occurrences (all)	58	7	4
Lymphadenopathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 20 (10.00%)	2 / 20 (10.00%)
occurrences (all)	4	2	2
Neutropenia	Additional description: 'Neutrophil count decreased' is reported as 'Neutropenia'.		
subjects affected / exposed	28 / 36 (77.78%)	14 / 20 (70.00%)	16 / 20 (80.00%)
occurrences (all)	84	41	31
Neutrophilia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Thrombocytopenia	Additional description: 'Platelet Count Decreased' is reported as 'Thrombocytopenia'.		
subjects affected / exposed	14 / 36 (38.89%)	8 / 20 (40.00%)	8 / 20 (40.00%)
occurrences (all)	33	14	21
Thrombocytosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Hypoacusis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Cataract			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Dry eye			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Eye inflammation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 36 (0.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Lacrimation increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Visual acuity reduced			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Abdominal pain			
subjects affected / exposed	13 / 36 (36.11%)	5 / 20 (25.00%)	4 / 20 (20.00%)
occurrences (all)	16	8	7
Abdominal pain upper			



subjects affected / exposed	7 / 36 (19.44%)	6 / 20 (30.00%)	2 / 20 (10.00%)
occurrences (all)	7	6	2
Anal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Constipation			
subjects affected / exposed	14 / 36 (38.89%)	7 / 20 (35.00%)	3 / 20 (15.00%)
occurrences (all)	19	8	4
Diarrhoea			
subjects affected / exposed	15 / 36 (41.67%)	10 / 20 (50.00%)	9 / 20 (45.00%)
occurrences (all)	24	14	17
Dry mouth			
subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	2	2	2
Duodenal ulcer			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	6 / 36 (16.67%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	8	1	0
Dysphagia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Flatulence			
subjects affected / exposed	2 / 36 (5.56%)	3 / 20 (15.00%)	2 / 20 (10.00%)
occurrences (all)	2	3	4
Gastric dilatation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal sounds abnormal			

subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 36 (0.00%)	2 / 20 (10.00%)	2 / 20 (10.00%)
occurrences (all)	0	3	3
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Ileus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Loose tooth			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Mucous stools			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	24 / 36 (66.67%)	12 / 20 (60.00%)	9 / 20 (45.00%)
occurrences (all)	65	18	17
Oral mucosal blistering			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Oral pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Steatorrhoea			

subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	7 / 36 (19.44%)	5 / 20 (25.00%)	4 / 20 (20.00%)
occurrences (all)	10	11	4
Terminal ileitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tongue coated			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	13 / 36 (36.11%)	8 / 20 (40.00%)	6 / 20 (30.00%)
occurrences (all)	21	16	17
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Biliary obstruction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Cholecystitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Cholestasis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Hepatic cytolysis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatic pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Hepatotoxicity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Portal vein thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	17 / 36 (47.22%)	10 / 20 (50.00%)	4 / 20 (20.00%)
occurrences (all)	18	11	5
Blister			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Dry skin			
subjects affected / exposed	1 / 36 (2.78%)	2 / 20 (10.00%)	2 / 20 (10.00%)
occurrences (all)	1	2	2
Eczema			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	1 / 36 (2.78%)	2 / 20 (10.00%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Hyperhidrosis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	2	1	2
Nail discolouration			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Nail disorder			

subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Nail ridging			
subjects affected / exposed	0 / 36 (0.00%)	3 / 20 (15.00%)	1 / 20 (5.00%)
occurrences (all)	0	3	2
Night sweats			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Onycholysis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	7 / 36 (19.44%)	5 / 20 (25.00%)	1 / 20 (5.00%)
occurrences (all)	8	8	2
Pruritus allergic			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	10 / 36 (27.78%)	2 / 20 (10.00%)	3 / 20 (15.00%)
occurrences (all)	16	3	6
Rash maculo-papular			
subjects affected / exposed	6 / 36 (16.67%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	6	2	1
Skin exfoliation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Umbilical haematoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Chronic kidney disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Incontinence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paraneoplastic glomerulonephritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 36 (11.11%)	5 / 20 (25.00%)	3 / 20 (15.00%)
occurrences (all)	4	7	3

Back pain			
subjects affected / exposed	8 / 36 (22.22%)	3 / 20 (15.00%)	3 / 20 (15.00%)
occurrences (all)	11	6	5
Bone pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Bursitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Limb discomfort			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Muscle spasm			
subjects affected / exposed	1 / 36 (2.78%)	3 / 20 (15.00%)	0 / 20 (0.00%)
occurrences (all)	1	6	0
Muscular weakness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	4 / 36 (11.11%)	3 / 20 (15.00%)	1 / 20 (5.00%)
occurrences (all)	5	6	1
Neck pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Pain in extremity subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	3 / 20 (15.00%) 5	1 / 20 (5.00%) 1
Spinal pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Tendonitis subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Infections and infestations			
Bacterial infection subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Covid-19 subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1
Cholangitis infective subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Erysipelas subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 3	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Fungal foot infection subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0
Fungal infection subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0
Gastroenteritis			



subjects affected / exposed	2 / 36 (5.56%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Gastroenteritis Escherichia coli			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Haemophilus infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Infection			
subjects affected / exposed	4 / 36 (11.11%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	4	1	2
Nasopharyngitis			
subjects affected / exposed	3 / 36 (8.33%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	6	0	2
Onychomycosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	4 / 36 (11.11%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	7	0	1
Paronychia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Prostatic abscess			

subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Root canal infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Spontaneous bacterial peritonitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Tooth infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	13 / 36 (36.11%)	10 / 20 (50.00%)	7 / 20 (35.00%)
occurrences (all)	30	15	12
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Dyslipidaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Food intolerance			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	4
Hypoalbuminaemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Hypocalcaemia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Hypoglycaemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypokalaemia			
subjects affected / exposed	8 / 36 (22.22%)	2 / 20 (10.00%)	3 / 20 (15.00%)
occurrences (all)	11	2	3
Hypomagnesaemia			
subjects affected / exposed	3 / 36 (8.33%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	9	1	0
Hyponatraemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Iron deficiency			
subjects affected / exposed	0 / 36 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Metabolic acidosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2017	The protocol was amended according to the decisions of the Dose Escalation Committee (DEC) evaluating the first dose cohort with implementation of pre-medication (corticosteroids, antihistamines and paracetamol) at 1st dosing, extended blood sampling to be able to evaluate any infusion related reactions).
29 March 2018	The protocol was amended to include: 1) Update of Dose Limiting Toxicity (DLT) criteria list: The DEC will judge if infusion related reactions that appear <24 hours after the first administration of CAN04 are to be considered as a DLT. The DEC has the mandate to decide whether these specific events are to be graded as DLTs or not. 2) Update in procedures for first CAN04 dose: Initial dose of up to 1.0 mg/kg will be given. The dose and infusion rate for this first administration to be decided by the DEC. 3) Addition of treatment options of infusion related reactions.
12 July 2018	The protocol was amended to include the final design for Part II, focused on NSCLC and PDAC patients receiving either CAN04 monotherapy or CAN04 in combination with standard of care. Main changes included: 1) Adjustment of the protocol according to the decisions of the Dose Escalation Committee on the initial priming dose to reduce risk for infusion related reactions. 2) Update to include further details of Part II of the study (Arm A, B, C and D). 3) Combination treatment and definition of Arm C (NSCLC) and Arm D (PDAC). 4) Inclusion of quality of life assessment specific for NSCLC. 5) PK and biomarker assessment schedule adjustment.
21 December 2018	The protocol was amended to include changes requested by various Competent Authorities and Ethic Committees.
04 January 2019	The protocol was amended to remove the note that in Germany only ultrasound-guided procedures to collect new biopsies was allowed.
29 July 2019	The protocol was amended to include: 1) Addition of Arm E (up to 12 subjects) to evaluate CAN04 at 15 mg/kg monotherapy and if pre-medication with corticosteroids at priming dose could be reduced without interfering with anticipated incidence and severity of infusion-related reactions. 2) Adjustment of duration of CT/MRI follow-up. 3) Update in dosing procedures for first CAN04 dosing for Part II (0.5 mg/kg over 120 min). 4) Addition of inclusion criterion for Arms C and D (Subjects who underwent (neo)adjuvant treatments was eligible if the (neo)adjuvant treatment ended at least 6 months prior to inclusion). 5) Adjustment of treatment delay instructions. 6) Addition of ADA and PK sampling at FU visit (28 days after last dose of CAN04).

10 March 2020	<p>The protocol was amended as follows:</p> <ol style="list-style-type: none"> <li>1) Decision to use 5mg/kg CAN04 as pharmacologically active dose (PAD) and discontinuation of Arm E.</li> <li>2) Updates in the dosage, dose expansion, and dose modification criteria sections in line with the choice of PAD dose.</li> <li>3) Inclusion of rationale for the choice of PAD dose.</li> <li>4) Updates the Treatment Limiting Toxicity (TLT) and AE/SAE sections in line with the choice of PAD dose.</li> <li>5) Change in efficacy endpoint evaluation (from iRC to iRECIST).</li> <li>6) Updates in the inclusion/exclusion criteria for clarity, to avoid protocol deviations.</li> <li>7) Update to state that assessment of CA 19-9 in PDAC (Arm D) is mandatory.</li> <li>8) Updates in statistical considerations to align with the choice of 5.0 mg/kg CAN04 as PAD and discontinuation of Arm E.</li> <li>9) Inclusion of country-specific changes from V6.1, V6.2, and V6.3 of the protocol.</li> </ol>
05 November 2020	<p>The protocol was amended to include:</p> <ol style="list-style-type: none"> <li>1) Arm C modifications: a) Reduction of assigned dose of CAN04 from 5.0 mg/kg to 1mg/kg. Rationale for the change was safety measures to reduce risk for neutropenia and febrile neutropenia; b) Included the possibility to escalate the CAN04 dose to 2.5 mg/kg if the safety and efficacy observed in subjects newly dosed with 1.0 mg/kg support it; c) Modification of inclusion and exclusion criteria to allow for subjects progressed on all standard of care previous targeted therapies.</li> <li>2) Addition of 2 new parallel safety expansion cohorts of 20 subjects each with subjects with unresectable locally advanced or metastatic PDAC to be treated with gemcitabine/nab-paclitaxel and 2 lower doses of CAN04: Arm PDEX2.5 with 2.5 mg/kg and Arm PDEX1 with 1.0 mg/kg. a) These new arms test a novel administration schedule for CAN04: (i) removal of the priming dose of 0.5 mg/kg; (ii) schedule modification, with CAN04 being administered on Day 1 and 15 in cycles of 28 days, with exception for Cycle 1 where, in addition, CAN04 also was administered on Day 8; b) Paired tumour biopsies was not required in these new expansion cohorts.</li> </ol>
13 August 2021	<p>The protocol was amended to include:</p> <ol style="list-style-type: none"> <li>1) Addition of a new experimental arm (Arm NCP) to evaluate a new platinum combination with carboplatin and pemetrexed together with CAN04 in subjects with stage III or stage IV non-squamous NSCLC who was candidates for 1st line of standard chemotherapy regimen with carboplatin/pemetrexed or who relapsed after 1st line with pembrolizumab monotherapy. a) The Arm NCP aimed to include in total up to 40 patients and aimed to start with a run-in-phase to identify a safe and potentially efficacious dose to be used in the following expansion phase to evaluate the initial antitumour effect. b) CAN04 to be administered on Day 1 in combination with standard carboplatin and pemetrexed and on Day 8 (CAN04 alone) in cycles of 21 days. Safety Review Committee to decide to de-escalate to 1.0 mg/kg if 2.5 mg/kg was above Maximum Tolerated Dose (MTD). It was also possible to escalate to 5.0 mg/kg if 2.5 mg/kg was not the MTD, based on safety, efficacy and PK data.</li> <li>2) Addition of exclusion criterion excluding patients with biliary stent placement or cholangitis less than 30 days before the calculated first administration of CAN04 and antibiotic therapy less than 14 days prior to study treatment.</li> <li>3) Inclusion of country-specific changes from V8.1 of the protocol.</li> <li>4) Implementation of decisions from Safety Review Committee meeting to implement primary prophylaxis with G-CSF in Arm C and to escalate CAN04 dose in Arm C from 1 to 2.5 mg/kg in remaining patients to be enrolled.</li> </ol>

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
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12 April 2023	Early cessation of recruitment in NCP arm. All study arms were recruited and completed according to protocol with the exception of Arm NCP. The decision to prematurely end enrolment into the NCP arm (aimed to enroll 40 subjects but terminated after 10 subjects) was made due to strategic reasons and was not related to any safety or efficacy considerations.	-
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Notes:

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early cessation of recruitment in NCP arm due to strategic reasons leading to a small number of subjects analyzed for this specific arm.

Notes:

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## Online references

<http://www.ncbi.nlm.nih.gov/pubmed/40680438>

<http://www.ncbi.nlm.nih.gov/pubmed/34903842>

<http://www.ncbi.nlm.nih.gov/pubmed/39385434>