Clinical trial results:
A Phase Ib/II Open-label, Multi-center Study of the Safety and Efficacy of IMCgp100 in Combination with Durvalumab (MEDI4736) or Tremelimumab or the Combination of Durvalumab and Tremelimumab Compared to IMCgp100 Alone in Patients with Advanced Melanoma

Summary

EudraCT number	2015-002971-12
Trial protocol	GB DK IT
Global end of trial date	31 August 2023

Results information

Result version number	v1 (current)
This version publication date	17 July 2025
First version publication date	17 July 2025

Trial information

Trial identification

Sponsor protocol code	IMCgp100-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02535078
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Immunocore Limited
Sponsor organisation address	92 Park Drive, Milton Park, Abingdon, United Kingdom, OX14 4RY
Public contact	Information Desk, Immunocore Limited, 44 01235438600, info@immunocore.com
Scientific contact	Regulatory Affairs, Immunocore Limited , 1 2673324508, Regaffairsgroup@immunocore.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	19 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2023
Global end of trial reached?	Yes
Global end of trial date	31 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study was a Phase Ib/II, multi-center, open-label study of tebentafusp (IMCgp100) as a single agent, and in combination with durvalumab and/or tremelimumab, in metastatic cutaneous melanoma.

The purpose of this study was to characterize the safety, tolerability, pharmacokinetics (PK), pharmacodynamics, and to evaluate the anti-tumor activity of tebentafusp (IMCgp100) in combination with durvalumab (MEDI4736, programmed death-ligand 1 [PD-L1] inhibitor), tremelimumab (CLTA-4 inhibitor), and the combination of durvalumab with tremelimumab, compared to single-agent tebentafusp (IMCgp100) alone administered intravenously (iv) or subcutaneously (sc).

As of Amendment 9, a potential Phase II portion of the study was to be opened after identification of the recommended Phase II dose (RP2D) for Arm 5 (tebentafusp sc monotherapy). However, the Phase II portion of the study was never initiated. Arm 5 was conducted in the US only.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice (GCP) standards, the Declaration of Helsinki, and all applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	United Kingdom: 23
Country: Number of subjects enrolled	United States: 54
Worldwide total number of subjects	112
EEA total number of subjects	34

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	73
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 22 study sites in 6 countries.

Pre-assignment

Screening details:

Prescreening: HLA-A*0201 positive (eligible) / non-HLA-A*0201 subtype (not eligible; eg, *0202, *0203 etc), or HLA-A2 negative (not eligible)
All patients screened N=151
n=38 screen failure. Most common reason for screen failure was presence of untreated or symptomatic CNS metastases or CNS metastases that currently required local therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1: Tebentafusp + Durvalumab

Arm description:

IV Tebentafusp (IMCgp100) with durvalumab(MEDI4736)

Arm type	Experimental
Investigational medicinal product name	Tebentafusp
Investigational medicinal product code	
Other name	IMCgp100
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Soluble gp100-specific T cell receptor withanti-CD3 scFV

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	MEDI4736
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Anti-PD-L1 monoclonal antibody

Arm title	Arm 2: Tebentafusp + Tremelimumab

Arm description:

IV Tebentafusp (IMCgp100) with tremelimumab

Arm type	Experimental
Investigational medicinal product name	Tebentafusp
Investigational medicinal product code	
Other name	IMCgp100
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Soluble gp100-specific T cell receptor withanti-CD3 scFV

Investigational medicinal product name	Tremelimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:
Anti-CTLA-4 monoclonal antibody

Arm title	Arm 3: Tebentafusp + Durvalumab +Tremelimumab

Arm description:
IV Tebentafusp (IMCgp100) with durvalumab (MEDI4736) and tremelimumab

Arm type	Experimental
Investigational medicinal product name	Tebentafusp
Investigational medicinal product code	
Other name	IMCgp100
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:
Soluble gp100-specific T cell receptor withanti-CD3 scFV

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	MEDI4736
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Anti-PD-L1 monoclonal antibody

Investigational medicinal product name	Tremelimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:
Anti-CTLA-4 monoclonal antibody

Arm title	Arm 4a: Tebentafusp IV Monotherapy

Arm description:
Tebentafusp (IMCgp100) (single agent) IV infusion once weekly

Arm type	Experimental
Investigational medicinal product name	Tebentafusp
Investigational medicinal product code	
Other name	IMCgp100
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Soluble gp100-specific T cell receptor withanti-CD3 scFV

Arm title	Arm 4b: Tebentafusp IV Monotherapy

Arm description:
Tebentafusp (IMCgp100) (single agent) IV infusion 3 times weekly

Arm type	Experimental

Investigational medicinal product name	Tebentafusp
Investigational medicinal product code	
Other name	IMCgp100
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Soluble gp100-specific T cell receptor withanti-CD3 scFV

Number of subjects in period 1	Arm 1: Tebentafusp + Durvalumab	Arm 2: Tebentafusp + Tremelimumab	Arm 3: Tebentafusp + Durvalumab +Tremelimumab
Started	43	13	29
Completed	36	8	24
Not completed	7	5	5
Consent withdrawn by subject	3	2	1
Not specified	-	1	-
Lost to follow-up	-	1	1
Sponsor termination	4	1	3

Number of subjects in period 1	Arm 4a: Tebentafusp IV Monotherapy	Arm 4b: Tebentafusp IV Monotherapy
Started	20	7
Completed	13	6
Not completed	7	1
Consent withdrawn by subject	2	1
Not specified	1	-
Lost to follow-up	1	-
Sponsor termination	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1: Tebentafusp + Durvalumab
Reporting group description: IV Tebentafusp (IMCgp100) with durvalumab(MEDI4736)	
Reporting group title	Arm 2: Tebentafusp + Tremelimumab
Reporting group description: IV Tebentafusp (IMCgp100) with tremelimumab	
Reporting group title	Arm 3: Tebentafusp + Durvalumab +Tremelimumab
Reporting group description: IV Tebentafusp (IMCgp100) with durvalumab (MEDI4736) and tremelimumab	
Reporting group title	Arm 4a: Tebentafusp IV Monotherapy
Reporting group description: Tebentafusp (IMCgp100) (single agent) IV infusion once weekly	
Reporting group title	Arm 4b: Tebentafusp IV Monotherapy
Reporting group description: Tebentafusp (IMCgp100) (single agent) IV infusion 3 times weekly	

Reporting group values	Arm 1: Tebentafusp + Durvalumab	Arm 2: Tebentafusp + Tremelimumab	Arm 3: Tebentafusp + Durvalumab +Tremelimumab
Number of subjects	43	13	29
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	29	11	18
From 65-84 years	14	2	11
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.9	53.4	57.1
standard deviation	± 13.09	± 12.34	± 13.19
Gender categorical Units: Subjects			
Female	18	3	11
Male	25	10	18
Race Units: Subjects			
Asian	1	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islanders	0	0	0
Black or African American	0	0	0

White	40	13	29
Not Reported	2	0	0
Not allowed as per local regulatory	0	0	0
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	40	13	27
Not Reported	2	0	1
Unknown	1	0	1
Other	0	0	0

Reporting group values	Arm 4a: Tebentafusp IV Monotherapy	Arm 4b: Tebentafusp IV Monotherapy	Total
Number of subjects	20	7	112
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	4	73
From 65-84 years	9	3	39
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	58.6	53.3	
standard deviation	± 16.28	± 11.94	-
Gender categorical Units: Subjects			
Female	5	3	40
Male	15	4	72
Race Units: Subjects			
Asian	0	0	1
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islanders	0	0	0
Black or African American	0	0	0
White	20	7	109
Not Reported	0	0	2
Not allowed as per local regulatory	0	0	0
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	19	6	105
Not Reported	0	1	4

Unknown	0	0	2
Other	0	0	0

End points

End points reporting groups

Reporting group title	Arm 1: Tebentafusp + Durvalumab
Reporting group description: IV Tebentafusp (IMCgp100) with durvalumab(MEDI4736)	
Reporting group title	Arm 2: Tebentafusp + Tremelimumab
Reporting group description: IV Tebentafusp (IMCgp100) with tremelimumab	
Reporting group title	Arm 3: Tebentafusp + Durvalumab +Tremelimumab
Reporting group description: IV Tebentafusp (IMCgp100) with durvalumab (MEDI4736) and tremelimumab	
Reporting group title	Arm 4a: Tebentafusp IV Monotherapy
Reporting group description: Tebentafusp (IMCgp100) (single agent) IV infusion once weekly	
Reporting group title	Arm 4b: Tebentafusp IV Monotherapy
Reporting group description: Tebentafusp (IMCgp100) (single agent) IV infusion 3 times weekly	

Primary: Number of participants with dose-limiting toxicities (DLTs)

End point title	Number of participants with dose-limiting toxicities (DLTs)[1][2]
End point description: The number of participants with a DLT is reported. A DLT was defined as an AE or abnormal laboratory finding assessed as having had a suspected relationship to investigational product; being unrelated to disease, disease progression, intercurrent illness, or concomitant medications; and met other protocol-defined criteria.	
End point type	Primary
End point timeframe: Up to ~2 years	

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: There are no statistical analyses for descriptive data

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No subjects in Arm 4b were included in the DLT data set (i.e. there were no participants in this arm with at least one DLT)

End point values	Arm 1: Tebentafusp + Durvalumab	Arm 2: Tebentafusp + Tremelimumab	Arm 3: Tebentafusp + Durvalumab +Tremelimumab	Arm 4a: Tebentafusp IV Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	7	28	14
Units: Participants	1	1	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[3]

End point description:

ORR was defined as the percentage of participants achieving complete response (CR) or partial response (PR). ORR was assessed using RECIST version 1.1.

End point type	Primary

End point timeframe:

Up to ~2 years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary objective of Phase II was ORR of tebentafusp using RECIST version 1.1 criteria. Phase II was not initiated.

End point values	Arm 1: Tebentafusp + Durvalumab	Arm 2: Tebentafusp + Tremelimumab	Arm 3: Tebentafusp + Durvalumab +Tremelimumab	Arm 4a: Tebentafusp IV Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	13	28	20
Units: Percentage of participants				
number (confidence interval 90%)	11.6 (4.7 to 22.9)	0 (0 to 20.6)	13.8 (4.9 to 28.8)	0 (0 to 13.9)

End point values	Arm 4b: Tebentafusp IV Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage of participants				
number (confidence interval 90%)	0 (0 to 34.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 up to 90 days post-treatment	
Adverse event reporting additional description:	
All treated participants are included. The summary row for nonserious AEs shows the number of participants with any AE. Only events meeting >5% cutoff are presented.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Arm 1: Tebentafusp + Durvalumab
Reporting group description:	
IV Tebentafusp (IMCgp100) with durvalumab(MEDI4736)	
Reporting group title	Arm 2: Tebentafusp + Tremelimumab
Reporting group description:	
IV Tebentafusp (IMCgp100) with tremelimumab	
Reporting group title	Arm 3: Tebentafusp + Durvalumab + Tremelimumab
Reporting group description:	
IV Tebentafusp (IMCgp100) with durvalumab (MEDI4736) and tremelimumab	
Reporting group title	Arm 4a: Tebentafusp IV Monotherapy
Reporting group description:	
Tebentafusp (IMCgp100) (single agent) IV infusion once weekly	
Reporting group title	Arm 4b: Tebentafusp IV Monotherapy
Reporting group description:	
Tebentafusp (IMCgp100) (single agent) IV infusion 3 times weekly	

Serious adverse events	Arm 1: Tebentafusp + Durvalumab	Arm 2: Tebentafusp + Tremelimumab	Arm 3: Tebentafusp + Durvalumab + Tremelimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 43 (39.53%)	3 / 13 (23.08%)	11 / 29 (37.93%)
number of deaths (all causes)	31	8	18
number of deaths resulting from adverse events			0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lymph nodes			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			

subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic ocular melanoma			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (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
Hypertension			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 13 (15.38%)	2 / 29 (6.90%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst torsion			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Pleural effusion			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
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			
Confusional state			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (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
Mental status changes			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (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
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Dizziness			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemorrhage intracranial			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Headache			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Seizure			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Spinal cord compression			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Abdominal pain upper			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
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	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Colitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Frequent bowel movements			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
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 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
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			

Cholestasis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 43 (4.65%)	2 / 13 (15.38%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Rash macular			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (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
Rash maculo-papular			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Rash papular			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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

Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
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 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
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 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (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
Failure to thrive			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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
Hypoglycaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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

Hyponatraemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (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

Serious adverse events	Arm 4a: Tebentafusp IV Monotherapy	Arm 4b: Tebentafusp IV Monotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	4 / 7 (57.14%)	
number of deaths (all causes)	13	6	
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lymph nodes			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic ocular melanoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst torsion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Frequent bowel movements			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm 1: Tebentafusp + Durvalumab	Arm 2: Tebentafusp + Tremelimumab	Arm 3: Tebentafusp + Durvalumab + Tremelimumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 43 (100.00%)	13 / 13 (100.00%)	29 / 29 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Gastrointestinal melanoma			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Metastases to central nervous system			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 43 (11.63%)	2 / 13 (15.38%)	3 / 29 (10.34%)
occurrences (all)	7	2	5
Hypertension			
subjects affected / exposed	5 / 43 (11.63%)	1 / 13 (7.69%)	3 / 29 (10.34%)
occurrences (all)	18	1	5
Flushing			
subjects affected / exposed	4 / 43 (9.30%)	0 / 13 (0.00%)	3 / 29 (10.34%)
occurrences (all)	4	0	4
Deep vein thrombosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Lymphodema			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Embolism			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	24 / 43 (55.81%)	6 / 13 (46.15%)	15 / 29 (51.72%)
occurrences (all)	50	13	50
Fatigue			
subjects affected / exposed	24 / 43 (55.81%)	4 / 13 (30.77%)	14 / 29 (48.28%)
occurrences (all)	30	4	16
Chills			

subjects affected / exposed	11 / 43 (25.58%)	3 / 13 (23.08%)	5 / 29 (17.24%)
occurrences (all)	21	5	12
Oedema peripheral			
subjects affected / exposed	10 / 43 (23.26%)	4 / 13 (30.77%)	6 / 29 (20.69%)
occurrences (all)	12	5	8
Face odema			
subjects affected / exposed	8 / 43 (18.60%)	2 / 13 (15.38%)	2 / 29 (6.90%)
occurrences (all)	12	2	2
Influenza like illness			
subjects affected / exposed	4 / 43 (9.30%)	1 / 13 (7.69%)	3 / 29 (10.34%)
occurrences (all)	9	1	3
Peripheral swelling			
subjects affected / exposed	5 / 43 (11.63%)	3 / 13 (23.08%)	1 / 29 (3.45%)
occurrences (all)	6	4	2
Generalised oedema			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	2
Pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	2
Chest pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Multiple organ dysfunction			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	4	0	3
Reproductive system and breast disorders			

Vaginal haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	2 / 13 (15.38%)	0 / 29 (0.00%)
occurrences (all)	0	3	0
Genital parasthesia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	4	0
Pruritus genital			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Scrotal pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Vaginal discharge			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 43 (16.28%)	4 / 13 (30.77%)	9 / 29 (31.03%)
occurrences (all)	8	5	10
Dyspnoea			
subjects affected / exposed	3 / 43 (6.98%)	2 / 13 (15.38%)	3 / 29 (10.34%)
occurrences (all)	3	2	3
Pleural effusion			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	3	0	2
Nasal congestion			
subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	4 / 29 (13.79%)
occurrences (all)	2	0	4
Rhinorrhea			
subjects affected / exposed	3 / 43 (6.98%)	1 / 13 (7.69%)	2 / 29 (6.90%)
occurrences (all)	3	1	2
Dyspnoea exertional			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	3	0	2
Epistaxis			

subjects affected / exposed	4 / 43 (9.30%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	4	0	0
Hypoxia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Pneumonitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Pulmonary embolism			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Depression			
subjects affected / exposed	1 / 43 (2.33%)	2 / 13 (15.38%)	0 / 29 (0.00%)
occurrences (all)	1	2	0
Confusional state			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	2	1	1
Anxiety			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Restlessness			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

Mental status changes			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 43 (11.63%)	1 / 13 (7.69%)	6 / 29 (20.69%)
occurrences (all)	5	1	8
Lipase increased			
subjects affected / exposed	7 / 43 (16.28%)	1 / 13 (7.69%)	7 / 29 (24.14%)
occurrences (all)	14	2	11
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 43 (13.95%)	1 / 13 (7.69%)	4 / 29 (13.79%)
occurrences (all)	7	1	4
Blood alklaline phosphatase incrased			
subjects affected / exposed	6 / 43 (13.95%)	1 / 13 (7.69%)	5 / 29 (17.24%)
occurrences (all)	8	1	8
Amylase increased			
subjects affected / exposed	6 / 43 (13.95%)	0 / 13 (0.00%)	3 / 29 (10.34%)
occurrences (all)	21	0	5
Blood creatinine increased			
subjects affected / exposed	4 / 43 (9.30%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	8	0	2
Weight decreased			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	3	0	2
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	2	1	2

Sunburn			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	1	2	1
Contusion			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Radiation skin injury			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	5 / 43 (11.63%)	0 / 13 (0.00%)	4 / 29 (13.79%)
occurrences (all)	9	0	6
Sinus tachycardia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Palpitations			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 43 (13.95%)	2 / 13 (15.38%)	4 / 29 (13.79%)
occurrences (all)	6	8	5
Dizziness			
subjects affected / exposed	5 / 43 (11.63%)	2 / 13 (15.38%)	3 / 29 (10.34%)
occurrences (all)	5	3	3
Paraesthesia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	7	0	0
Dysarthria			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Syncope			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	5	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Eye disorders			
Periorbital oedema			
subjects affected / exposed	10 / 43 (23.26%)	2 / 13 (15.38%)	7 / 29 (24.14%)
occurrences (all)	14	3	10
Vision blurred			
subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Photophobia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	4	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	16 / 43 (37.21%)	2 / 13 (15.38%)	12 / 29 (41.38%)
occurrences (all)	23	2	19
Diarrhoea			
subjects affected / exposed	10 / 43 (23.26%)	4 / 13 (30.77%)	14 / 29 (48.28%)
occurrences (all)	15	5	19
Vomiting			
subjects affected / exposed	14 / 43 (32.56%)	1 / 13 (7.69%)	9 / 29 (31.03%)
occurrences (all)	23	1	14
Abdominal pain			
subjects affected / exposed	9 / 43 (20.93%)	1 / 13 (7.69%)	5 / 29 (17.24%)
occurrences (all)	13	1	6
Constipation			
subjects affected / exposed	7 / 43 (16.28%)	3 / 13 (23.08%)	4 / 29 (13.79%)
occurrences (all)	7	3	5
Dyspepsia			

subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Dysphagia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	3	0	1
Abdominal discomfort			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Abdominal pain upper			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	6
Gastrooesophogeal reflux disease			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	2	1	1
Stomatitis			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	3	0	1
Flatulence			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Toothache			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Colitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	5
Small intestinal perforation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	2	1	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	30 / 43 (69.77%)	7 / 13 (53.85%)	24 / 29 (82.76%)
occurrences (all)	68	31	76
Pruritus			
subjects affected / exposed	29 / 43 (67.44%)	8 / 13 (61.54%)	17 / 29 (58.62%)
occurrences (all)	62	31	40
Dry skin			
subjects affected / exposed	13 / 43 (30.23%)	4 / 13 (30.77%)	4 / 29 (13.79%)
occurrences (all)	15	4	4
Rash maculo-papular			
subjects affected / exposed	13 / 43 (30.23%)	3 / 13 (23.08%)	3 / 29 (10.34%)
occurrences (all)	22	6	14
Hair colour changes			
subjects affected / exposed	7 / 43 (16.28%)	0 / 13 (0.00%)	7 / 29 (24.14%)
occurrences (all)	7	0	7
Vitiligo			
subjects affected / exposed	8 / 43 (18.60%)	2 / 13 (15.38%)	5 / 29 (17.24%)
occurrences (all)	8	2	5
Erythema			
subjects affected / exposed	7 / 43 (16.28%)	0 / 13 (0.00%)	6 / 29 (20.69%)
occurrences (all)	15	0	9
Skin exfoliation			
subjects affected / exposed	9 / 43 (20.93%)	1 / 13 (7.69%)	4 / 29 (13.79%)
occurrences (all)	12	2	4
Alopecia			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Skin hyperpigmentation			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Skin hypopigmentation			
subjects affected / exposed	4 / 43 (9.30%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	4	1	0
Dermatitis acneiform			

subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	3 / 29 (10.34%)
occurrences (all)	0	1	4
Hyperhidrosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Rash macular			
subjects affected / exposed	3 / 43 (6.98%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	3	1	0
Dermatitis bullous			
subjects affected / exposed	1 / 43 (2.33%)	2 / 13 (15.38%)	0 / 29 (0.00%)
occurrences (all)	1	2	0
Photosensitivity reaction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	2 / 29 (6.90%)
occurrences (all)	0	3	2
Skin fissures			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Eczema			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Xeroderma			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrom			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	3 / 29 (10.34%)
occurrences (all)	1	1	3
Hyperthyroidism			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	4 / 29 (13.79%)
occurrences (all)	0	0	4
Adrenal insufficiency			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 43 (18.60%)	1 / 13 (7.69%)	10 / 29 (34.48%)
occurrences (all)	12	1	15
Pain in extremity			
subjects affected / exposed	9 / 43 (20.93%)	3 / 13 (23.08%)	4 / 29 (13.79%)
occurrences (all)	14	3	4
Back pain			
subjects affected / exposed	8 / 43 (18.60%)	1 / 13 (7.69%)	5 / 29 (17.24%)
occurrences (all)	10	1	8
Myalgia			
subjects affected / exposed	4 / 43 (9.30%)	1 / 13 (7.69%)	5 / 29 (17.24%)
occurrences (all)	6	1	5
Musculoskeletal chest pain			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Groin pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	3
Muscular weakness			
subjects affected / exposed	1 / 43 (2.33%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Limb discomfort			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	4 / 43 (9.30%)	2 / 13 (15.38%)	4 / 29 (13.79%)
occurrences (all)	5	2	5
Nasopharyngitis			
subjects affected / exposed	5 / 43 (11.63%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	8	0	3
Conjunctivitis			
subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	3 / 29 (10.34%)
occurrences (all)	2	0	3
Upper respiratory tract infection			
subjects affected / exposed	2 / 43 (4.65%)	1 / 13 (7.69%)	3 / 29 (10.34%)
occurrences (all)	2	1	3
Sinusitis			
subjects affected / exposed	3 / 43 (6.98%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Paronchyia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 43 (25.58%)	2 / 13 (15.38%)	5 / 29 (17.24%)
occurrences (all)	13	2	5
Hyponatraemia			

subjects affected / exposed	5 / 43 (11.63%)	1 / 13 (7.69%)	2 / 29 (6.90%)
occurrences (all)	7	1	2
Hypophosphataemia			
subjects affected / exposed	5 / 43 (11.63%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	7	0	5
Hypomagnesaemia			
subjects affected / exposed	6 / 43 (13.95%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	9	0	3
Hypoalbuminaemia			
subjects affected / exposed	4 / 43 (9.30%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	9	1	3
Hypoglycaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 13 (7.69%)	1 / 29 (3.45%)
occurrences (all)	0	1	2
Hyperglycaemia			
subjects affected / exposed	2 / 43 (4.65%)	0 / 13 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 13 (15.38%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Vitamin D deficiency			
subjects affected / exposed	0 / 43 (0.00%)	0 / 13 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Hypokalaemia			
subjects affected / exposed	4 / 43 (9.30%)	0 / 13 (0.00%)	3 / 29 (10.34%)
occurrences (all)	12	0	5

Non-serious adverse events	Arm 4a: Tebentafusp IV Monotherapy	Arm 4b: Tebentafusp IV Monotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	7 / 7 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal melanoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Metastases to central nervous system			

subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 20 (15.00%)	3 / 7 (42.86%)	
occurrences (all)	5	3	
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Flushing			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lymphodema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 20 (50.00%)	3 / 7 (42.86%)	
occurrences (all)	18	4	
Fatigue			
subjects affected / exposed	9 / 20 (45.00%)	0 / 7 (0.00%)	
occurrences (all)	10	0	
Chills			
subjects affected / exposed	4 / 20 (20.00%)	2 / 7 (28.57%)	
occurrences (all)	7	2	
Oedema peripheral			

subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Face odema			
subjects affected / exposed	5 / 20 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	6	0	
Influenza like illness			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Peripheral swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Generalised oedema			
subjects affected / exposed	3 / 20 (15.00%)	1 / 7 (14.29%)	
occurrences (all)	4	2	
Pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Multiple organ dysfunction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Genital parasthesia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pruritus genital			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Scrotal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vaginal discharge			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 20 (15.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Dyspnoea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Pleural effusion			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Nasal congestion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rhinorrhea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dyspnoea exertional			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypoxia			

subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pneumonitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pulmonary embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Confusional state			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Restlessness			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Mental status changes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Lipase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Blood alklaline phosphatase incrased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Amylase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Weight increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Sunburn			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Contusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Radiation skin injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Sinus tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 20 (35.00%)	2 / 7 (28.57%)	
occurrences (all)	11	3	
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	2	
Dysarthria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			

Lymphopenia			
subjects affected / exposed	4 / 20 (20.00%)	2 / 7 (28.57%)	
occurrences (all)	9	3	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Vision blurred			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Photophobia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 20 (45.00%)	1 / 7 (14.29%)	
occurrences (all)	16	1	
Diarrhoea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	6 / 20 (30.00%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Abdominal pain			
subjects affected / exposed	7 / 20 (35.00%)	0 / 7 (0.00%)	
occurrences (all)	11	0	
Constipation			
subjects affected / exposed	4 / 20 (20.00%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Dyspepsia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dysphagia			

subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Abdominal discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Gastrooesophogeal reflux disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Gastritis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Small intestinal perforation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	16 / 20 (80.00%)	6 / 7 (85.71%)	
occurrences (all)	58	17	
Pruritus			
subjects affected / exposed	14 / 20 (70.00%)	4 / 7 (57.14%)	
occurrences (all)	30	5	
Dry skin			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hair colour changes			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Vitiligo			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Skin exfoliation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin hyperpigmentation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin hypopigmentation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			

subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Rash macular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dermatitis bullous			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin fissures			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Xeroderma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hyperkeratosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Palmar-plantar erythrodysaesthesia syndrom			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hyperthyroidism			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Adrenal insufficiency			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Back pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Groin pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Nasopharyngitis			

subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Conjunctivitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Herpes simplex			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Paronchyia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 20 (15.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Hyponatraemia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 7 (14.29%)	
occurrences (all)	6	1	
Hypophosphataemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	
occurrences (all)	1	3	

Hypomagnesaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypoglycaemia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	
occurrences (all)	2	3	
Hyperglycaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2015	AM1: The primary purpose of the amendment was to modify the dosing regimen and DLT criteria.
31 March 2016	AM2: The primary purpose of the amendment was to modify the intra-patient dosing regimen.
03 March 2017	AM3: The primary purpose was to modify enrollment criteria.
29 June 2017	AM4: The primary purpose was to update nomenclature of dose levels and of the recommended Phase 2 dose (RP2D).
26 October 2017	AM5: The primary purpose was to clarify recommended toxicity management and dose modification guidance.
18 June 2018	AM6: The primary purpose was to further update recommended toxicity management and dose modification.
22 January 2019	AM7: The primary purpose was to optimize IMCgp100 monotherapy.
29 January 2019	AM8: The primary purpose was to update toxicity management guidelines for Grade 3 and 4 non-immune mediated reactions.
24 December 2021	AM9: The primary purpose was to modify dose escalation of SC IMGgp100 (US only).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported