



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 with anti-CD3 scFV

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

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

| | | | |
|---|----------------------|----------------------|-----------------------|
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 2 / 13 (15.38%) 3 | 0 / 29 (0.00%) 0 |
| Genital parasthesia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 4 | 0 / 29 (0.00%) 0 |
| Pruritus genital subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 0 |
| Scrotal pain subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 0 |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 8 | 4 / 13 (30.77%) 5 | 9 / 29 (31.03%) 10 |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 2 / 13 (15.38%) 2 | 3 / 29 (10.34%) 3 |
| Pleural effusion subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Nasal congestion subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 0 / 13 (0.00%) 0 | 4 / 29 (13.79%) 4 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 1 / 13 (7.69%) 1 | 2 / 29 (6.90%) 2 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 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 occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 0 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 5 | 1 / 13 (7.69%) 1 | 6 / 29 (20.69%) 8 |
| Lipase increased subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 14 | 1 / 13 (7.69%) 2 | 7 / 29 (24.14%) 11 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 7 | 1 / 13 (7.69%) 1 | 4 / 29 (13.79%) 4 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 8 | 1 / 13 (7.69%) 1 | 5 / 29 (17.24%) 8 |
| Amylase increased subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 21 | 0 / 13 (0.00%) 0 | 3 / 29 (10.34%) 5 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 8 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Weight decreased subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 13 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Weight increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 1 / 13 (7.69%) 1 | 1 / 29 (3.45%) 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 occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 0 |
| Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 5 | 0 / 13 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Eye disorders Periorbital oedema subjects affected / exposed occurrences (all) | 10 / 43 (23.26%) 14 | 2 / 13 (15.38%) 3 | 7 / 29 (24.14%) 10 |
| Vision blurred subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 0 / 13 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Photophobia subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 4 | 0 / 13 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 16 / 43 (37.21%) 23 | 2 / 13 (15.38%) 2 | 12 / 29 (41.38%) 19 |
| Diarrhoea subjects affected / exposed occurrences (all) | 10 / 43 (23.26%) 15 | 4 / 13 (30.77%) 5 | 14 / 29 (48.28%) 19 |
| Vomiting subjects affected / exposed occurrences (all) | 14 / 43 (32.56%) 23 | 1 / 13 (7.69%) 1 | 9 / 29 (31.03%) 14 |
| Abdominal pain subjects affected / exposed occurrences (all) | 9 / 43 (20.93%) 13 | 1 / 13 (7.69%) 1 | 5 / 29 (17.24%) 6 |
| Constipation subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 7 | 3 / 13 (23.08%) 3 | 4 / 29 (13.79%) 5 |
| Dyspepsia | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Dysphagia subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 13 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 13 (0.00%) 0 | 1 / 29 (3.45%) 6 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 1 / 13 (7.69%) 1 | 1 / 29 (3.45%) 1 |
| Stomatitis subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 13 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 13 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Gastritis subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Toothache subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Colitis subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 0 / 13 (0.00%) 0 | 2 / 29 (6.90%) 5 |
| Small intestinal perforation subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 0 / 13 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 1 / 13 (7.69%) 1 | 0 / 29 (0.00%) 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 erythrodysesthesia 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 |
| Paronychia | | | |
| 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 occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 7 (14.29%) 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 occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Pruritus genital subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Scrotal pain subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 3 / 20 (15.00%) 3 | 0 / 7 (0.00%) 0 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 4 | 0 / 7 (0.00%) 0 | |
| Pleural effusion subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 7 (14.29%) 1 | |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Rhinorrhea subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 7 (14.29%) 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 alkaline phosphatase increased | | | |
| 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 occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Radiation skin injury subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 7 (0.00%) 0 | |
| Cardiac disorders | | | |
| Tachycardia subjects affected / exposed occurrences (all) | 3 / 20 (15.00%) 3 | 1 / 7 (14.29%) 1 | |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 7 / 20 (35.00%) 11 | 2 / 7 (28.57%) 3 | |
| Dizziness subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 7 (0.00%) 0 | |
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 7 (14.29%) 2 | |
| Dysarthria subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Syncope subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 7 (0.00%) 0 | |
| Blood and lymphatic system disorders | | | |

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

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