



Clinical trial results:

Phase 1/2 Study of Bempegaldesleukin in Combination With Nivolumab in Children, Adolescents, and Young Adults With Recurrent or Refractory Malignancies (PIVOT IO 020)

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2020-000854-85 |
| Trial protocol | FR ES DE IT Outside EU/EEA |
| Global end of trial date | 22 June 2022 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 06 January 2023 |
| First version publication date | 06 January 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | CA045-020 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04730349 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussee de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-002492-PIP01-18 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 August 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 June 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of bempegaldesleukin (bempeg; NKTR-214) in combination with nivolumab (nivo) in pediatric participants with malignant neoplasms that were refractory, or relapsed, or in participants for whom curative treatments are lacking.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 03 June 2021 |
| 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 | Australia: 3 |
| Country: Number of subjects enrolled | France: 6 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | United States: 3 |
| Worldwide total number of subjects | 15 |
| EEA total number of subjects | 9 |

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) | 7 |
| Adolescents (12-17 years) | 8 |

| | |
|----------------------|---|
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

15 participants were treated in Part A. Study did not progress to Part B; therefore, no participants enrolled in Part B.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) |

Arm description:

Bempegaldesleukin 0.006 mg/kg + Nivolumab 4.5 mg/kg administered intravenously every 3 weeks

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bempegaldesleukin (NKTR-214) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Bempegaldesleukin 0.006 mg/kg administered intravenously every 3 weeks

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

Dosage and administration details:

Nivolumab 4.5 mg/kg administered intravenously every 3 weeks

| | |
|------------------|---|
| Arm title | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) |
|------------------|---|

Arm description:

Bempegaldesleukin 0.006 mg/kg + Nivolumab 360 mg administered intravenously every 3 weeks

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Nivolumab 360 mg administered intravenously every 3 weeks

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Bempegaldesleukin (NKTR-214) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |

| | |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

Bempegaldesleukin 0.006 mg/kg administered intravenously every 3 weeks

| Number of subjects in period 1 | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) |
|---------------------------------------|--|--|
| Started | 8 | 7 |
| Completed | 1 | 2 |
| Not completed | 7 | 5 |
| Disease progression | 6 | 4 |
| Participant withdrew consent | 1 | - |
| Study drug toxicity | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) |
| Reporting group description: Bempegaldesleukin 0.006 mg/kg + Nivolumab 4.5 mg/kg administered intravenously every 3 weeks | |
| Reporting group title | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) |
| Reporting group description: Bempegaldesleukin 0.006 mg/kg + Nivolumab 360 mg administered intravenously every 3 weeks | |

| Reporting group values | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) | Total |
|---|--|--|-------|
| Number of subjects | 8 | 7 | 15 |
| 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) | 7 | 0 | 7 |
| Adolescents (12-17 years) | 1 | 7 | 8 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 7.5 | 14.9 | - |
| standard deviation | ± 3.9 | ± 1.5 | |
| Sex: Female, Male Units: Participants | | | |
| Female | 4 | 2 | 6 |
| Male | 4 | 5 | 9 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 1 |
| Not Hispanic or Latino | 4 | 6 | 10 |
| Unknown or Not Reported | 3 | 1 | 4 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 6 | 5 | 11 |
| Black or African American | 1 | 0 | 1 |
| Other | 1 | 2 | 3 |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) |
| Reporting group description: Bempegaldesleukin 0.006 mg/kg + Nivolumab 4.5 mg/kg administered intravenously every 3 weeks | |
| Reporting group title | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) |
| Reporting group description: Bempegaldesleukin 0.006 mg/kg + Nivolumab 360 mg administered intravenously every 3 weeks | |

Primary: Number of Participants with Dose-Limiting Toxicities (DLTs) - Part A

| | |
|--|---|
| End point title | Number of Participants with Dose-Limiting Toxicities (DLTs) - Part A ^[1] |
| End point description: Number of participants with dose-limiting toxicities (DLTs). DLTs were collected and evaluated for Part A within the DLT evaluation period, which started on Cycle 1 Day 1 (first dose) and ended at Day 42 (42 days after first dose of the study therapy). | |
| End point type | Primary |
| End point timeframe: From first dose to 42 days after first dose | |

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: Only summary statistics planned for this endpoint.

| End point values | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AEs) - Part A

| | |
|---|--|
| End point title | Number of Participants with Adverse Events (AEs) - Part A ^[2] |
| End point description: Number of participants with adverse events (AEs). An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment. | |

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| From first dose to 30 days after last dose (up to approximately 6 months) | |
| Notes: | |
| [2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. | |
| Justification: Only summary statistics planned for this endpoint. | |

| | | | | |
|-----------------------------|--|---|--|--|
| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | 8 | 7 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events (SAEs) - Part A

| | |
|--|---|
| End point title | Number of Participants with Serious Adverse Events (SAEs) - Part A ^[3] |
| End point description: | |
| Number of participants with serious adverse events (SAEs). SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event. | |
| End point type | Primary |
| End point timeframe: | |
| From first dose to 30 days after last dose (up to approximately 6 months) | |
| 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: Only summary statistics planned for this endpoint. | |

| | | | | |
|-----------------------------|--|---|--|--|
| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | 6 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Drug-Related Adverse Events - Part A

| | |
|-----------------|---|
| End point title | Number of Participants with Drug-Related Adverse Events - Part A ^[4] |
|-----------------|---|

End point description:

Number of participants with drug-related adverse events. An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[4] - 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: Only summary statistics planned for this endpoint.

| | | | | |
|-----------------------------|--|---|--|--|
| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | 6 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events Leading to Discontinuation - Part A

| | |
|-----------------|---|
| End point title | Number of Participants with Adverse Events Leading to Discontinuation - Part A ^[5] |
|-----------------|---|

End point description:

Number of participants with adverse events leading to discontinuation. An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

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

Justification: Only summary statistics planned for this endpoint.

| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | 2 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Died - Part A

| | |
|------------------------|--|
| End point title | Number of Participants Who Died - Part A ^[6] |
| End point description: | Number of participants who died. |
| End point type | Primary |
| End point timeframe: | From first dose to 30 days after last dose (up to approximately 6 months) |
| Notes: | [6] - 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: Only summary statistics planned for this endpoint. |

| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 7 | | |
| Units: Participants | 2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (C_{max}) - Part A

| | |
|------------------------|---|
| End point title | Maximum Observed Plasma Concentration (C _{max}) - Part A ^[7] |
| End point description: | Pharmacokinetics (PK) of bempegaldesleukin and nivolumab derived from serum concentration versus time data. |
| End point type | Primary |
| End point timeframe: | From first dose to 30 days after last dose (up to approximately 6 months) |

Notes:

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

Justification: Only summary statistics planned for this endpoint.

| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
|---|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[8] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

[9] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

Statistical analyses

No statistical analyses for this end point

Primary: Primary: Trough Observed Concentration (Ctrough) - Part A

| | |
|-----------------|---|
| End point title | Primary: Trough Observed Concentration (Ctrough) - Part A ^[10] |
|-----------------|---|

End point description:

Pharmacokinetics (PK) of bempegaldesleukin and nivolumab derived from serum concentration versus time data.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[10] - 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: Only summary statistics planned for this endpoint.

| End point values | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesle ukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
|---|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[11] | 0 ^[12] | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[11] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

[12] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration (AUC) - Part A

| | |
|---|--|
| End point title | Area Under the Plasma Concentration (AUC) - Part A ^[13] |
| End point description: Pharmacokinetics (PK) of bempegaldesleukin and nivolumab derived from serum concentration versus time data. | |
| End point type | Primary |
| End point timeframe: From first dose to 30 days after last dose (up to approximately 6 months) | |

Notes:

[13] - 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: Only summary statistics planned for this endpoint.

| | | | | |
|---|--|---|--|--|
| End point values | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | | |
| Units: hour*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[14] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

[15] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants assessed for all-cause mortality from first dose to study completion (up to approximately 13 months). SAEs and NSAEs were assessed from first dose to 150 days after last dose of study therapy (up to approximately 11 months).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) |
|-----------------------|--|

Reporting group description: -

| Serious adverse events | Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) | Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 7 (71.43%) | 8 / 8 (100.00%) | |
| number of deaths (all causes) | 2 | 7 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 6 / 8 (75.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 6 | |
| Injury, poisoning and procedural complications | | | |
| Skin wound | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Brain oedema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|----------------|----------------|--|
| Seizure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| 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 | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 8 (25.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal and urinary disorders | | | |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (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 | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 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 | Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg) | Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg) | |
|---|---|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 7 (100.00%) | 8 / 8 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Chills | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 4 / 8 (50.00%) | |
| occurrences (all) | 8 | 4 | |
| Generalised oedema | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 8 (12.50%) | |
| occurrences (all) | 1 | 1 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 2 / 8 (25.00%) | |
| occurrences (all) | 6 | 3 | |
| Pain | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 8 (12.50%) | |
| occurrences (all) | 2 | 1 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Reproductive system and breast disorders | | | |
| Scrotal oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 8 (12.50%) | |
| occurrences (all) | 1 | 1 | |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Lung disorder | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 8 (12.50%) | |
| occurrences (all) | 2 | 1 | |
| Pulmonary embolism | | | |

| | | | |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Psychiatric disorders | | | |
| Behaviour disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 2 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Aspartate aminotransferase increased | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 8 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 1 / 8 (12.50%) | |
| occurrences (all) | 8 | 1 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 8 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 8 (12.50%) | |
| occurrences (all) | 2 | 1 | |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Dizziness | | | |

| | | | |
|---|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 1 / 8 (12.50%) 1 | |
| Ataxia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 8 (12.50%) 1 | |
| Presyncope subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Neuralgia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 8 (12.50%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 3 | 3 / 8 (37.50%) 3 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 3 / 7 (42.86%) 7 | 1 / 8 (12.50%) 1 | |
| Eosinophilia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 8 (12.50%) 1 | |
| Febrile neutropenia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 8 (12.50%) 1 | |
| Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Eye disorders Eye pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Photophobia | | | |

| | | | |
|--|--------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 8 (12.50%) 1 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 8 (12.50%) | |
| occurrences (all) | 1 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 8 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Tooth discolouration | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 8 (25.00%) | |
| occurrences (all) | 5 | 2 | |
| Skin and subcutaneous tissue disorders | | | |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Rash | | | |

| | | | |
|---|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 3 / 8 (37.50%) 4 | |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 8 (12.50%) 1 | |
| Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 8 (12.50%) 1 | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 8 (12.50%) 1 | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Bone pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 8 (0.00%) 0 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 8 (12.50%) 1 | |
| Infections and infestations | | | |

| | | | |
|------------------------------------|----------------|----------------|--|
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vaginal infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 1 / 8 (12.50%) | |
| occurrences (all) | 3 | 1 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 8 (12.50%) | |
| occurrences (all) | 0 | 1 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hypophosphataemia | | | |

| | | | |
|-----------------------------|----------------|---------------|--|
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 8 (0.00%) | |
| occurrences (all) | 5 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 28 November 2021 | Updated the minimum days from "100" to "150" days following discontinuation of drug for collection of all serious adverse events (SAEs) and Non-Serious Adverse Events (NSAEs). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was terminated on 22-Jun-2022. This results disclosure report provides analyses from CA045-020 Part A safety analyses only. Part B of the study (expansion phase) did not enroll any participants.

Notes: