# Clinical trial results:
# A Phase 3, Open-label, Non-controlled, Multi-dose, Extension Study to Evaluate the Long-term Safety and Tolerability of IGSC, 20% in Japanese Subjects With Primary Immunodeficiency Disease (PID)

## Summary

| | |
|---|---|
| EudraCT number | 2022-003400-32 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 25 April 2024 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 November 2024 |
| First version publication date | 03 November 2024 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | TAK-664-3002 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04842643 |
| WHO universal trial number (UTN) | U1111-1265-9447 |
| Other trial identifiers | JRCT: jRCT2041210006 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 95 Hayden Avenue, Lexington, United States, MA 02421 |
| Public contact | Study Director, Takeda, TrialDisclosures@takeda.com |
| Scientific contact | Study Director, Takeda, TrialDisclosures@takeda.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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 25 April 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 April 2024 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of the study is to evaluate the long-term safety and tolerability of subcutaneous immunoglobulin (IGSC), 20% in Japanese participants with primary immunodeficiency disease (PID).

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 27 April 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Japan: 12 |
| Worldwide total number of subjects | 12 |
| EEA total number of subjects | 0 |

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) | 2 |
| Adolescents (12-17 years) | 1 |
| Adults (18-64 years) | 8 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 8 investigative sites in Japan from 27 April 2021 to 25 April 2024.

### Pre-assignment

Screening details:

Participants with PID who completed core study TAK-664-3001 (2022- 001873-29) enrolled to receive IGCS, 20 percent (%) in current extension study (TAK-664-3002 [2022-003400-32]). As per planned analysis, the data was collected, analyzed and reported for a single arm only and per dose level wise data was not collected in this study.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | IGSC, 20% |

Arm description:

Participants who completed Epoch 2 of core study TAK-664-3001 (2022-001873-29), received between 50 to 200 mg/kg of Immune globulin subcutaneous (IGSC) infusion, 20% infusion once a week (Epoch 2 regimen) and 100 to 400 mg/kg of IGSC infusion, 20% biweekly (Epoch 3 regimen) until the study drug becomes commercially available.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Immune Globulin Subcutaneous, 20% Solution (IGSC, 20%) |
| Investigational medicinal product code | |
| Other name | Immune Globulin Infusion (Human) |
| Pharmaceutical forms | Infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received IGSC 20% infusion once a week or two weeks.

| **Number of subjects in period 1** | IGSC, 20% |
|---|---|
| Started | 12 |
| Completed | 10 |
| Not completed | 2 |
| Physician decision | 1 |
| Not specified | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | IGSC, 20% |

Reporting group description:

Participants who completed Epoch 2 of core study TAK-664-3001 (2022-001873-29), received between 50 to 200 mg/kg of Immune globulin subcutaneous (IGSC) infusion, 20% infusion once a week (Epoch 2 regimen) and 100 to 400 mg/kg of IGSC infusion, 20% biweekly (Epoch 3 regimen) until the study drug becomes commercially available.

| Reporting group values | IGSC, 20% | Total | |
|---|---|---|---|
| Number of subjects | 12 | 12 | |
| Age Categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 36.0 | | |
| standard deviation | ± 21.68 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 5 | 5 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 12 | 12 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 0 | 0 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 12 | 12 | |
| Unknown or Not Reported | 0 | 0 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | IGSC, 20% |

Reporting group description:

Participants who completed Epoch 2 of core study TAK-664-3001 (2022-001873-29), received between 50 to 200 mg/kg of Immune globulin subcutaneous (IGSC) infusion, 20% infusion once a week (Epoch 2 regimen) and 100 to 400 mg/kg of IGSC infusion, 20% biweekly (Epoch 3 regimen) until the study drug becomes commercially available.

| | |
|---|---|
| Subject analysis set title | IGSC: 2-13 Years |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants aged 2-13 years and who completed Epoch 2 of core study TAK-664-3001 (2022-001873-29), received between 50 to 200 mg/kg of IGSC infusion, 20% infusion once a week (Epoch 2 regimen) and 100 to 400 mg/kg of IGSC infusion, 20% biweekly (Epoch 3 regimen) until the study drug becomes commercially available.

| | |
|---|---|
| Subject analysis set title | IGSC: >=14 Years |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants aged >=14 years and who completed Epoch 2 of core study TAK-664-3001 (2022-001873-29), received between 50 to 200 mg/kg of IGSC infusion, 20% infusion once a week (Epoch 2 regimen) and 100 to 400 mg/kg of IGSC infusion, 20% biweekly (Epoch 3 regimen) until the study drug becomes commercially available.

### Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and Non-serious TEAEs

| | |
|---|---|
| End point title | Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and Non-serious TEAEs[1] |

End point description:

TEAEs were defined as adverse events (AEs) with onset after date-time of first dose of study drug (intravenous immunoglobulin [IGIV] or IGSC), or medical conditions present prior to the start of study drug (IGIV or IGSC) but increased in severity or relationship after date-time of first dose of study drug (IGIV or IGSC). A serious TEAE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. All-Treated Set consisted of all enrolled participants who received IGSC, 20% administration at least once in this study.

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

End point timeframe:

From first dose of study drug up to 3 years in current extension study

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 descriptive data was planned to be analyzed for this endpoint.

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: participants | | | | |
| TEAEs | 12 | | | |
| Serious TEAEs | 3 | | | |
| Non-Serious TEAEs | 12 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Drug-related and Non-related TEAEs

| End point title | Number of Participants With Drug-related and Non-related TEAEs[2] |
|---|---|

End point description:

TEAEs were defined as adverse events (AEs) with onset after date-time of first dose of study drug (intravenous immunoglobulin [IGIV] or IGSC), or medical conditions present prior to the start of study drug (IGIV or IGSC) but increased in severity or relationship after date-time of first dose of study drug (IGIV or IGSC). Any TEAE that was recorded by the investigator as "probably related" or "possibly related" to study drug was considered as study drug related AE, and any AE recorded as "unlikely related" or "not related" was considered as unrelated AE. All-Treated Set consisted of all enrolled participants who received IGSC, 20% administration at least once in this study.

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

End point timeframe:

From first dose of study drug up to 3 years in current extension study

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 descriptive data was planned to be analyzed for this endpoint.

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: participants | | | | |
| Drug-related TEAEs | 9 | | | |
| Non-related TEAEs | 12 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Severe, Local and Systemic TEAEs

| End point title | Number of Participants With Severe, Local and Systemic |
|---|---|

End point description:

A severe TEAE was an AE that caused considerable interference with the participant's usual activities. Local TEAEs were defined as AEs that were included in the MedDRA Higher Level Group Term "administration site reactions" or contained the phrase "injection site" or "infusion site". Systemic TEAEs were defined as AEs that were not included in the Medical Dictionary for Regulatory Activities (MedDRA) Higher Level Group Term "administration site reactions" and did not contain the phrase "injection site" or "infusion site". All-Treated Set consisted of all enrolled participants who received IGSC, 20% administration at least once in this study.

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

End point timeframe:

From first dose of study drug up to 3 years in current extension study

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 descriptive data was planned to be analyzed for this endpoint.

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: participants | | | | |
| Severe TEAEs | 3 | | | |
| Local TEAEs | 8 | | | |
| Systemic TEAEs | 12 | | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With TEAEs Leading to Premature Discontinuation From Study and Infusion-associated TEAEs

| End point title | Number of Participants With TEAEs Leading to Premature Discontinuation From Study and Infusion-associated TEAEs[4] |
|---|---|

End point description:

Infusion associated TEAEs were defined as any TEAE that began during study drug infusion or within 72 hours of completion of study drug infusion. TEAEs leading to premature discontinuation from study and infusion-associated TEAEs were reported. All-Treated Set consisted of all enrolled participants who received IGSC, 20% administration at least once in this study.

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

End point timeframe:

From first dose of study drug up to 3 years in current extension study

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 descriptive data was planned to be analyzed for this endpoint.

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: participants | | | | |
| TEAEs Leading to Premature Discontinuation | 0 | | | |
| Infusion-associated TEAEs | 12 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Trough Levels of Total Immune Globulin G (IgG) and IgG1, IgG2, IgG3, IgG4 Antibodies Subclasses Following Weekly Administration of IGSC, 20%

| End point title | Serum Trough Levels of Total Immune Globulin G (IgG) and IgG1, IgG2, IgG3, IgG4 Antibodies Subclasses Following Weekly Administration of IGSC, 20% |
|---|---|

End point description:

Serum trough levels of total IgG and IgG1, IgG2, IgG3, IgG4 antibodies subclasses were determined by using standard assay methods. All-Treated Set consisted of all enrolled participants who received IGSC,

20% administration at least once in this study. Here” number of subjects analyzed" signified participants who were evaluable for this endpoint. Here "99999" means geometric mean and 95% confidence interval (CI) could not be calculated because the values were below lower limit of quantification (LLOQ).

| End point type | Secondary |
|---|---|

End point timeframe:

At End of treatment (i.e. 3 years) in current extension study

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: grams per liter (g/L) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IgG 1 | 6.14 (4.25 to 8.87) | | | |
| IgG 2 | 3.52 (2.35 to 5.28) | | | |
| IgG 3 | 99999 (99999 to 99999) | | | |
| IgG 4 | 0.305 (0.165 to 0.567) | | | |
| IgG Total | 11.0 (7.29 to 16.5) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Trough Levels of IgG and IgG1, IgG2, IgG3, IgG4 Antibodies Subclasses Following Biweekly Administration of IGSC, 20%

| End point title | Serum Trough Levels of IgG and IgG1, IgG2, IgG3, IgG4 Antibodies Subclasses Following Biweekly Administration of IGSC, 20% |
|---|---|

End point description:

Serum trough levels of IgG and IgG1, IgG2, IgG3, IgG4 antibodies subclasses were determined by using standard assay methods. All-Treated Set consisted of all enrolled participants who received IGSC, 20% administration at least once in this study. Here” number of subjects analyzed" signified participants who were evaluable for this endpoint. Here "99999" means geometric mean and 95% CI could not be calculated because the values were below LLOQ.

| End point type | Secondary |
|---|---|

End point timeframe:

At End of treatment (i.e. 3 years) in current extension study

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 7 | | | |
| Units: g/L | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IgG 1 | 5.36 (4.55 to 6.33) | | | |
| IgG 2 | 3.42 (3.03 to 3.86) | | | |
| IgG 3 | 99999 (99999 to 99999) | | | |
| IgG 4 | 0.250 (0.219 to 0.284) | | | |
| IgG Total | 8.98 (7.78 to 10.4) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Annual Rate of All Infections

| End point title | Annual Rate of All Infections |
|---|---|

End point description:

The annual rate of infections was calculated as the mean number of infections per participant per year. Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: infections per year | | | | |
| arithmetic mean (standard deviation) | 1.42 (± 1.119) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Annual Rate of Validated Acute Serious Bacterial Infections (ASBI)

| End point title | Annual Rate of Validated Acute Serious Bacterial Infections (ASBI) |
|---|---|

End point description:

The ASBI rate was calculated as the mean number of acute serious bacterial infections per participants per year. Annual rate of validated acute serious bacterial infections per participant was assessed. Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: infections per year | | | | |
| arithmetic mean (standard deviation) | 0.00 (± 0.000) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Days Participants not Able to Attend School or Work to Perform Normal Daily Activities due to Illness/Infection

| End point title | Number of Days Participants not Able to Attend School or Work to Perform Normal Daily Activities due to Illness/Infection |
|---|---|

End point description:

Number of days not able to attend school or work to perform normal daily activities due to illness/infection are standardized per year (365.25 days). Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: days | | | | |
| median (full range (min-max)) | 1.91 (0.0 to 31.9) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Days Participants on Antibiotics

| End point title | Number of Days Participants on Antibiotics |
|---|---|

End point description:

Number of days on antibiotics was defined as the number of days those antibiotics were taken as concomitant medications and was standardized to per year (365.25 days). Number of days participants on antibiotics were reported. Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| End point values | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: days | | | | |
| median (full range (min-max)) | 2.55 (0.0 to 57.8) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Length of Hospital Stay due to Illness or Infection

| End point title | Length of Hospital Stay due to Illness or Infection |
|---|---|

End point description:

Length of hospital stay per stay was standardized to per year (365.25 days). Number of days due to illness or infection were reported. Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001. Here" number of subjects analyzed" signified participants

who were evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: days | | | | |
| median (full range (min-max)) | 0.00 (0.0 to 3.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Hospitalizations due to Illness or Infection

| End point title | Number of Hospitalizations due to Illness or Infection |
|---|---|

End point description:

Number of hospitalizations were standardized to per year (365.25 days). Hospitalizations were measured by asking participants to report the number of nights they have stayed overnight in the hospital during the year, for something related to their own health. Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: hospitalization | | | | |
| arithmetic mean (standard deviation) | 0.21 (± 0.370) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Acute Physician Visits due to Illness/Infection

| End point title | Number of Acute Physician Visits due to Illness/Infection |
|---|---|

End point description:

Number of acute physician visits is standardized to per year (365.25 days). Number of acute (urgent or unscheduled) physician visits due to illness/infection were reported. Reported timeframe included timeframe of core study TAK-664-3001 (NCT04346108) (Max approximately 1.5 year) and of current extension study (Max approximately 3 years) as data of this outcome measure was collected from first dose of core study to end of current extension study and the data is presented for participants who entered in current study from core study as per plan. The Core Study All-Treated Set consisted of participants who received at least 1 dose of study drug (IGIV or IGSC) in TAK-664-3001.

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug in core study TAK-664-3001 up to end of current extension study TAK-664-3002 (up to approximately 4.5 years)

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: visits per year | | | | |
| arithmetic mean (standard deviation) | 2.66 (± 2.652) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Their Response for Treatment Preference Questionnaire

| End point title | Number of Participants With Their Response for Treatment Preference Questionnaire |
|---|---|

End point description:

Treatment preference questionnaire is a self-administered questionnaire developed to assess participant's preference towards the administration of new IGSC therapy. There are 4-items on questionnaire, which investigate participant's preference on clinic/hospital/home setting of receiving the immunoglobulin therapy, the participant's rating on the frequency and method of administration, and the participant's preference to continue receiving the IGSC treatment. All-Treated Set. For first question “Before participation in the trial(s), where did you receive your immunoglobulin therapy” participants were allowed to select multiple answers for options (“At the hospital”; “At home”; “Other”) for their treatment. As a result, the sum of responders in the arm “IGSC, 20%: >=14 Years” for the first question were higher than the total number of participants analyzed in the category. As pre-specified in protocol, data was planned to be reported as per age criteria (2-13 years and >=14 years).

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug up to 3 years in current extension study

| End point values | IGSC: 2-13 Years | IGSC: >=14 Years | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 | 9 | | |
| Units: participants | | | | |
| Before participation: Received therapy at home | 0 | 0 | | |
| Before participation:Received therapy at hospital | 3 | 8 | | |
| Before participation:Received therapy: Other | 0 | 4 | | |
| Where you prefer to receive therapy:At Hospital | 1 | 1 | | |
| Where you prefer to receive therapy:At Home | 0 | 6 | | |
| Where you prefer to receive therapy:NoPreference | 2 | 2 | | |
| Frequency of Administration: Like very much | 1 | 1 | | |
| Frequency of Administration: Like | 1 | 4 | | |
| Frequency of Administration: No preference | 1 | 3 | | |
| Frequency of Administration: Dislike | 0 | 1 | | |
| Frequency of Administration: Dislike very much | 0 | 0 | | |
| Number of needlesticks per month: Like very much | 1 | 1 | | |
| Number of needlesticks per month: Like | 1 | 5 | | |
| Number of needlesticks per month: No preference | 1 | 2 | | |
| Number of needlesticks per month:Dislike | 0 | 1 | | |
| Number of needlesticks per month:Dislike verymuch | 0 | 0 | | |
| Time spent for treatment per month:Like verymuch | 0 | 3 | | |
| Time spent for treatment per month: Like | 1 | 2 | | |
| Time spent for treatment per month: No preference | 1 | 1 | | |
| Time spent for treatment per month: Dislike | 1 | 3 | | |
| Timespent for treatment permonth:Dislike verymuch | 0 | 0 | | |
| The ease of administration: Like very much | 1 | 3 | | |
| The ease of administration: Like | 2 | 4 | | |
| The ease of administration: No preference | 0 | 1 | | |
| The ease of administration: Dislike | 0 | 1 | | |
| The ease of administration: Dislike very much | 0 | 0 | | |
| Ability to fit treatment: Like very much | 1 | 5 | | |
| Ability to fit treatment: Like | 2 | 1 | | |
| Ability to fit treatment: No preference | 0 | 3 | | |
| Ability to fit treatment: Dislike | 0 | 0 | | |
| Ability to fit treatment: Dislike very much | 0 | 0 | | |
| The overall convenience: Like very much | 0 | 4 | | |

| | | | | |
|---|---|---|---|---|
| The overall convenience: Like | 3 | 3 | | |
| The overall convenience: No preference | 0 | 2 | | |
| The overall convenience: Dislike | 0 | 0 | | |
| The overall convenience: Dislike very much | 0 | 1 | | |
| Total Time administration took: Like very much | 1 | 1 | | |
| Total Time administration took: Like | 1 | 5 | | |
| Total Time administration took: No preference | 1 | 1 | | |
| Total Time administration took: Dislike | 1 | 2 | | |
| Total Time administration took: Dislike very much | 0 | 0 | | |
| Complexity of administration: Like very much | 0 | 2 | | |
| Complexity of administration process: Like | 3 | 4 | | |
| Complexity of administration: No preference | 0 | 2 | | |
| Complexity of administration: Dislike | 0 | 1 | | |
| Complexity of administration: Dislike verymuch | 0 | 0 | | |
| Ability to self-administer: Like very much | 2 | 6 | | |
| Ability to self-administer: Like | 1 | 3 | | |
| Ability to self-administer: No preference | 0 | 0 | | |
| Ability to self-administer: Dislike very much | 0 | 0 | | |
| Ability to self-administer: Dislike | 0 | 0 | | |
| Choose to continue receiving IGSC: Yes | 3 | 7 | | |
| Choose to continue receiving IGSC: No | 0 | 2 | | |
| Factor influenced decision: Twoway needle needed | 0 | 1 | | |
| Factor influenced decision:Canbe selfadministered | 1 | 0 | | |
| Factor influenced decision: Easy administration | 0 | 1 | | |
| Factor influenced decision: Feel relieved | 0 | 1 | | |
| Factor influenced decision: IgG levels stabilized | 0 | 1 | | |
| Factorinfluencedecision:Timeto clean affected area | 0 | 1 | | |
| Factor influence decision:Atopicdermatitisimprove | 1 | 0 | | |
| Factor influenced decision: No answer | 1 | 0 | | |
| Factor influenced decision: No more coughing | 0 | 1 | | |
| Factor influenced decision: The values are stable | 0 | 1 | | |
| Factor influenced decision: Time is short | 0 | 1 | | |
| Factor influencedecision:Stable medicalcondition | 0 | 1 | | |
| Potential to selfadminister: Like very much | 2 | 5 | | |
| Potential to selfadminister: Like | 0 | 4 | | |
| Potential to selfadminister: No preference | 0 | 0 | | |
| Potential to selfadminister:Dislike very much | 1 | 0 | | |

| | | | | |
|---|---|---|---|---|
| Potential to selfadminister: Dislike | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Tolerability Events Related to the Infusion of Study Drug

| End point title | Number of Participants With Tolerability Events Related to the Infusion of Study Drug |
|---|---|

End point description:

An infusion was considered tolerable if the infusion rate was not reduced, or the infusion was not interrupted or stopped, due to a TEAE related to study drug infusion. A tolerability event was considered to have occurred if an infusion was not tolerable. The Safety Analysis Set (SAS) consisted of all participants who received at least 1 dose of study drug (IGIV or IGSC).

| End point type | Secondary |
|---|---|

End point timeframe:

From first dose of study drug up to 3 years in current extension study

| **End point values** | IGSC, 20% | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: participants | | | | |
| Infusion rate was reduced | 1 | | | |
| Infusion was interrupted | 4 | | | |
| Infusions was stopped | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 3 years in current extension study

Adverse event reporting additional description:

As per planned analysis, the data for this AE section was collected, analyzed and reported for a single arm only and per dose level wise data was not collected . All-Treated Set consisted of all enrolled participants who received IGSC, 20% administration at least once in this study.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | IGSC, 20% |

Reporting group description:

Participants who completed Epoch 2 of core study TAK-664-3001 (NCT04346108), received between 50 to 200 mg/kg of IGSC infusion, 20% infusion once a week (Epoch 2 regimen) and 100 to 400 mg/kg of IGSC infusion, 20% biweekly (Epoch 3 regimen) until the study drug becomes commercially available.

| **Serious adverse events** | IGSC, 20% | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Rhegmatogenous retinal detachment | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | IGSC, 20% | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 12 / 12 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Colon adenoma<br>subjects affected / exposed<br>occurrences (all)<br><br>Skin papilloma<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>1<br><br><br>2 / 12 (16.67%)<br>3 | | |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>1 | | |
| General disorders and administration site conditions<br>Influenza like illness<br>subjects affected / exposed<br>occurrences (all)<br><br>Chills<br>subjects affected / exposed<br>occurrences (all)<br><br>Administration site discolouration<br>subjects affected / exposed<br>occurrences (all)<br><br>Infusion site bruising<br>subjects affected / exposed<br>occurrences (all)<br><br>Malaise<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>2<br><br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>2 | | |

| | | | | |
|---|---|---|---|---|
| Injection site swelling | | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | | | |
| occurrences (all) | 12 | | | |
| Injection site reaction | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Injection site pain | | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | | |
| occurrences (all) | 4 | | | |
| Injection site haemorrhage | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Injection site erythema | | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | | |
| occurrences (all) | 7 | | | |
| Injection site bruising | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Infusion site swelling | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 7 | | | |
| Infusion site pruritus | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 5 | | | |
| Infusion site pain | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Infusion site erythema | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 4 | | | |
| Puncture site pain | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Vaccination site joint erythema | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |

| | | | |
|---|---|---|---|
| Vaccination site pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | <br>2 / 12 (16.67%)<br>2<br><br><br>5 / 12 (41.67%)<br>15 | | |
| Immune system disorders<br>Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)<br><br>Drug hypersensitivity<br>subjects affected / exposed<br>occurrences (all)<br><br>Allergy to arthropod bite<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1 | | |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>2 | | |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>1 | | |
| Investigations<br>Occult blood positive<br>subjects affected / exposed<br>occurrences (all)<br><br>Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Platelet count decreased | <br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1<br><br> | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Heat illness | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Lip injury | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Post-traumatic pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Procedural dizziness | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin injury | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Wound | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Vaccination complication | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | | |
| occurrences (all) | 12 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Sinus headache<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Retrograde amnesia<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Post herpetic neuralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Dizziness<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>2 | | |
| Headache<br>subjects affected / exposed<br>occurrences (all) | 6 / 12 (50.00%)<br>26 | | |
| Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Orthostatic intolerance<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Ear and labyrinth disorders<br>Vertigo positional<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Vertigo<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>2 | | |
| Sudden hearing loss<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Eye disorders<br>Asthenopia<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | |
| Blepharitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Chorioretinopathy | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Dental caries | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | |
| occurrences (all) | 6 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Aphthous ulcer | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Gingival pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |

| | | | | |
|---|---|---|---|---|
| Haemorrhoids thrombosed<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all) | 2 / 12 (16.67%)<br>2 | | | |
| Haematochezia<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all) | 2 / 12 (16.67%)<br>8 | | | |
| Toothache<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Tooth resorption<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Skin and subcutaneous tissue disorders | | | | |
| Hyperkeratosis<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Eczema asteatotic<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>2 | | | |
| Dyshidrotic eczema<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Acne<br>subjects affected / exposed<br>occurrences (all) | 2 / 12 (16.67%)<br>2 | | | |
| Drug eruption<br>subjects affected / exposed<br>occurrences (all) | 1 / 12 (8.33%)<br>1 | | | |
| Dermatitis atopic | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Cutaneous amyloidosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 2 | | |
| Prurigo | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 2 | | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Nodal osteoarthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Impetigo | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Hordeolum | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | |
| occurrences (all) | 6 | | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |

| | | | | |
|---|---|---|---|---|
| COVID-19 | | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | | | |
| occurrences (all) | 6 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Laryngitis | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | | |
| occurrences (all) | 5 | | | |
| Oral herpes | | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | | |
| occurrences (all) | 3 | | | |
| Otitis externa | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Paronychia | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Periodontitis | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Post-acute COVID-19 syndrome | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 2 | | | |
| Pulpitis dental | | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | | |
| occurrences (all) | 2 | | | |
| Rhinovirus infection | | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | | |
| occurrences (all) | 1 | | | |
| Sinusitis | | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | | | |
| occurrences (all) | 6 | | | |

| | | | |
|---|---|---|---|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 12 (16.67%)<br>9 | | |
| Metabolism and nutrition disorders<br>Diabetic ketoacidosis<br>subjects affected / exposed<br>occurrences (all)<br><br>Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 12 (8.33%)<br>1<br><br><br>1 / 12 (8.33%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 02 November 2021 | Amendment 1<br>-Changed the inclusion criteria #1 to allow participants who have completed Epoch 2 to participate in this study even if they have not completed Epoch 3 in TAK-664-3001 study.<br>- Extended the visit window from 28 days (±1 day) to 28 days (±2 days).<br>- Extend the estimated duration of this study from approximately 2 years to approximately 3 years.<br>- Added statement, For participants who discontinue Epoch 3 and enter Study TAK-664-3002, the dose regimen will be determined on a case-by-case basis.<br>- Added the few criteria for discontinuation or withdrawal of the participants. |
| 19 July 2022 | Amendment 2:<br>- Relationship of adverse event to study drug.<br>- Investigational device term was replaced with device-use in-clinical trial.<br>- A new section for description of 'Device-used-in-clinical-trial' is added.<br>- The study schema is updated.<br>- Infusions may be performed at home or at the study site, at the investigator's discretion.<br>- Added 'body weight' in the below sentence: "The dose can be modified based on participants IgG level/condition/body weight".<br>-Vital signs can be measured at participant's home.<br>-Vital signs at home will be recorded. in subject diary and will be reviewed by investigators.<br>-Participants should come to the study sites for visits when laboratory test samples are to be collected every 12 weeks. Subjects are not required to come to the study site if all procedures/assessments can be performed at home.<br>-The decision where the SC injection is administered is made during the Study TAK-664-3001, however the location of injection administration can be changed based on the Investigator's and subject's agreement<br>-Laboratory tests including assessment of IgG trough levels will be performed every 12 weeks from Visit 1<br>-Hemolysis test will be done every 24 weeks from Visit 1.<br>-Text added for physical examination, vital signs, assessment of non-drug therapies, assessment of concomitant medications, assessment of AEs, collection/review of diary, administration of study drug, and healthcare resource utilization<br>-Minor grammatical, editorial and/or administrative changes have been made. |
| 28 November 2022 | Amendment 3:<br>Interim analysis will be conducted during the study. The interim analysis data will be submitted during Japanese New Drug Application process as requested by Pharmaceuticals and Medical Devices Agency (PMDA). |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported