



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
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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 IGSC, 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%
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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%
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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			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	36.0		
standard deviation	± 21.68	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	5	5	
Race (NIH/OMB)			
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)			
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]
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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
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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
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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
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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]
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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
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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%
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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%
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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 Validated Acute Serious Bacterial Infections (ASBI)

End point title	Annual Rate of Validated Acute Serious Bacterial Infections (ASBI)
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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
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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 (\pm 0.000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Rate of All Infections

End point title	Annual Rate of All Infections
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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
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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: 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
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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
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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
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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
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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: Number of Hospitalizations due to Illness or Infection

End point title	Number of Hospitalizations due to Illness or Infection
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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
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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 (\pm 0.370)			

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
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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
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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 Acute Physician Visits due to Illness/Infection

End point title	Number of Acute Physician Visits due to Illness/Infection
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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
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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
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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
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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		
Factorinfluenceddecision: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 influenceddecision: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		
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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
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	IGSC, 20%
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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			
subjects affected / exposed	12 / 12 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin papilloma			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Administration site discolouration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Infusion site bruising			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		

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

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

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 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Retrograde amnesia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Post herpetic neuralgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Dizziness subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
Headache subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 26		
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Orthostatic intolerance subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Ear and labyrinth disorders Vertigo positional subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Vertigo subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
Sudden hearing loss subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Eye disorders Asthenopia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 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 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Haemorrhoids subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Haematochezia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Stomatitis subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 8		
Toothache subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Tooth resorption subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Skin and subcutaneous tissue disorders			
Hyperkeratosis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Eczema asteatotic subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
Dyshidrotic eczema subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Acne subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Drug eruption subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 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 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 9		
Metabolism and nutrition disorders			
Diabetic ketoacidosis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Hyperlipidaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2021	Amendment 1 <ul style="list-style-type: none">-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.- Extended the visit window from 28 days (± 1 day) to 28 days (± 2 days).- Extend the estimated duration of this study from approximately 2 years to approximately 3 years.- 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.- Added the few criteria for discontinuation or withdrawal of the participants.
19 July 2022	Amendment 2: <ul style="list-style-type: none">- Relationship of adverse event to study drug.- Investigational device term was replaced with device-use in-clinical trial.- A new section for description of 'Device-used-in-clinical-trial' is added.- The study schema is updated.- Infusions may be performed at home or at the study site, at the investigator's discretion.- Added 'body weight' in the below sentence: "The dose can be modified based on participants IgG level/condition/body weight".-Vital signs can be measured at participant's home.-Vital signs at home will be recorded. in subject diary and will be reviewed by investigators.-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.-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-Laboratory tests including assessment of IgG trough levels will be performed every 12 weeks from Visit 1-Hemolysis test will be done every 24 weeks from Visit 1.-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-Minor grammatical, editorial and/or administrative changes have been made.
28 November 2022	Amendment 3: 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