Clinical trial results:
CLINICAL PHASE 3 STUDY TO MONITOR THE SAFETY, TOLERABILITY, AND EFFICACY OF SUBCUTANEOUS HUMAN IMMUNOGLOBULIN (CUTAQUIG®) ADMINISTERED AT MODIFIED DOSING REGIMENS IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISEASES

Summary

EudraCT number	2019-002999-13
Trial protocol	Outside EU/EEA
Global end of trial date	03 January 2022

Results information

Result version number	v1 (current)
This version publication date	20 July 2023
First version publication date	20 July 2023

Trial information

Trial identification

Sponsor protocol code	SCGAM-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03939533
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma
Sponsor organisation address	Oberlaaer Straße 235, Vienna, Austria,
Public contact	Clinical Trials Information, CRMG, 43 610 321 220, ctgov@clinicalresearchmgt.com
Scientific contact	Clinical Trials Information, CRMG, 1 4136865213, ctgov@clinicalresearchmgt.com
Sponsor organisation name	Octapharma
Sponsor organisation address	Oberlaaer St 235, 1100, Vienna, Austria,
Public contact	Patrick Murphy, CRMG, 1 4136865213, p.murphy@crmg-usa.com
Scientific contact	Elisabeth Sussitz, Octapharma, 43 1610320,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2022
Global end of trial reached?	Yes
Global end of trial date	03 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The co-primary objectives of this study are to assess CUTAQUIG administered using the following infusion parameters:
• Compare total IgG trough levels from weekly infusions to every other week infusions
• Safety and tolerability when administered at increased infusion volumes at each infusion site
• Safety and tolerability when administered at increased infusion flow rates at each infusion site
• Safety and tolerability when administered on an every other week dosing regimen

Protection of trial subjects:

IRB Reviewed and approved

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 October 2019
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	United States: 64
Worldwide total number of subjects	64
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)	3
Adolescents (12-17 years)	2
Adults (18-64 years)	45
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with a history of primary immunodeficiency (PI) disease that were currently on a stable does of SCIG treatment were enrolled at 16 research sites across the US between October 2019 and January 2022

Pre-assignment

Screening details:

Subjects with a history of primary immunodeficiency (PI) disease that were currently on a stable does of SCIG treatment were enrolled at 16 research sites across the US between October 2019 and January 2022

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 : Increased Volume Cohort

Arm description:

Increased volume at each infusion site - patients will receive CUTAQUIG weekly and increase infusion volumes every 4 weeks

Arm type	Experimental
Investigational medicinal product name	CUTAQUIG Human normal immunoglobulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks

Arm title	Increased Infusion Rate Cohort - Cohort 2

Arm description:

Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks

Arm type	Experimental
Investigational medicinal product name	CUTAQUIG Human normal immunoglobulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks

Arm title	Every Other Week Dosing Cohort - Cohort 3

Arm description:

Every other week dosing - patients will receive CUTAQUIG every other week at the equivalent of twice their body-weight dependent [mg/kg] weekly dose

Arm type	Experimental

Investigational medicinal product name	CUTAQUIG Human normal immunoglobulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks

Number of subjects in period 1	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3
Started	15	15	34
Completed	12	13	30
Not completed	3	2	4
Terminated due to patient decision	3	2	4

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 : Increased Volume Cohort
Reporting group description:	
Increased volume at each infusion site - patients will receive CUTAQUIG weekly and increase infusion volumes every 4 weeks	
Reporting group title	Increased Infusion Rate Cohort - Cohort 2
Reporting group description:	
Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks	
Reporting group title	Every Other Week Dosing Cohort - Cohort 3
Reporting group description:	
Every other week dosing - patients will receive CUTAQUIG every other week at the equivalent of twice their body-weight dependent [mg/kg] weekly dose	

Reporting group values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3
Number of subjects	15	15	34
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	1	2
Adolescents (12-17 years)	0	1	1
Adults (18-64 years)	10	9	26
From 65-84 years	5	4	5
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51.20	47.88	50.81
standard deviation	± 17.27	± 20.53	± 18.54
Gender categorical Units: Subjects			
Female	10	11	27
Male	5	4	7
Type of PI Disease Units: Subjects			
CVID	14	13	30
XLA	0	1	0
OTHER	1	1	4

Reporting group values	Total		
Number of subjects	64		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	3		
Adolescents (12-17 years)	2		
Adults (18-64 years)	45		
From 65-84 years	14		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	48		
Male	16		
Type of PI Disease Units: Subjects			
CVID	57		
XLA	1		
OTHER	6		

End points

End points reporting groups

Reporting group title	Cohort 1 : Increased Volume Cohort
Reporting group description:	
Increased volume at each infusion site - patients will receive CUTAQUIG weekly and increase infusion volumes every 4 weeks	
Reporting group title	Increased Infusion Rate Cohort - Cohort 2
Reporting group description:	
Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks	
Reporting group title	Every Other Week Dosing Cohort - Cohort 3
Reporting group description:	
Every other week dosing - patients will receive CUTAQUIG every other week at the equivalent of twice their body-weight dependent [mg/kg] weekly dose	

Primary: IgG Trough Levels

End point title	IgG Trough Levels
End point description:	
Mean change from baseline in individual total IgG trough levels in cohort 3 from weekly infusions to end of study every other week infusions, and for cohort 1 and cohort 2 (weekly infusions) change from baseline to end of study	
End point type	Primary
End point timeframe:	
24 Weeks	

End point values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	34	
Units: g/L				
log mean (standard deviation)	0.144 (± 0.7303)	0.065 (± 1.1046)	-0.593 (± 1.0791)	

Statistical analyses

Statistical analysis title	Primary Endpoint Analysis Cohort 3
Statistical analysis description:	
For subjects in Cohort 3, the mean total IgG trough levels were maintained with every other week dosing (mean [SD] = 9.927 [2.0146] g/L) compared to weekly dosing (mean [SD] = 10.364 [1.96322] g/L) for the FAS. A decrease of <1g/L total IgG trough levels is not considered to be clinically meaningful, confirmed by the statistically significant difference (p = 0.0017, 97.5% CI = -0.799, Infinity) supporting the primary endpoint that the decrease is not >1g/L.	
Comparison groups	Every Other Week Dosing Cohort - Cohort 3 v Cohort 1 : Increased Volume Cohort

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0017
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-0.0799
Variability estimate	Standard deviation
Dispersion value	1.424

Notes:

[1] - Pre-specified threshold

Secondary: Serious Bacterial Infection Rates

End point title	Serious Bacterial Infection Rates

End point description:

Number of subjects who reported SBIs during the study

End point type	Secondary

End point timeframe:

Duration of Study

End point values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	34	
Units: Participants				
Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of Infections

End point title	Rates of Infections

End point description:

Infection Rates per Person Year in the treatment period of 24 weeks

End point type	Secondary

End point timeframe:

Treatment Period of 24 Weeks

End point values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	34	
Units: Infections per person-year				
arithmetic mean (standard deviation)				
Infections per person-year	3.16 (± 4.082)	2.22 (± 2.555)	1.66 (± 1.918)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Resolution of Infections

End point title	Time to Resolution of Infections

End point description:

The amount of days it took for infectious disease occurrence and resolution for subjects during the treatment period of 24 weeks

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	34	
Units: Days				
median (full range (min-max))				
Days	23.5 (1 to 160)	20.0 (11 to 85)	16.0 (6 to 65)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antiobiotic Usage

End point title	Antiobiotic Usage

End point description:

Amount of subjects treated with antibiotics during the study

End point type	Secondary

End point timeframe:

Duration of Study

End point values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	34	
Units: Participants				
Participants	10	8	21	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Antibiotic Treatment Episodes Annualized

End point title	Number of Antibiotic Treatment Episodes Annualized

End point description:

Total number of treatment episodes annualized calculated as the sum of all unique episodes of antibiotics of all subjects from first dose day of cutaquig to last study visit/number of person years exposure

End point type	Secondary

End point timeframe:

Duration of Study

End point values	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	34	
Units: Treatment Episodes				
number (not applicable)				
Treatment Episodes	4.53	1.96	2.38	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Duration of Study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Cohort 1 : Increased Volume Cohort
Reporting group description:	
Increased volume at each infusion site - patients will receive CUTAQUIG weekly and increase infusion volumes every 4 weeks	
Reporting group title	Increased Infusion Rate Cohort - Cohort 2
Reporting group description:	
Increased infusion rate - patients will receive CUTAQUIG weekly and increase infusion rates every 4 weeks	
Reporting group title	Every Other Week Dosing Cohort - Cohort 3
Reporting group description:	
Every other week dosing - patients will receive CUTAQUIG every other week at the equivalent of twice their body-weight dependent [mg/kg] weekly dose	

Serious adverse events	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	1 / 34 (2.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1 : Increased Volume Cohort	Increased Infusion Rate Cohort - Cohort 2	Every Other Week Dosing Cohort - Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)	12 / 15 (80.00%)	30 / 34 (88.24%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	7 / 34 (20.59%)
occurrences (all)	0	4	16
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	2	7	1
Infusion site erythema			
subjects affected / exposed	4 / 15 (26.67%)	8 / 15 (53.33%)	8 / 34 (23.53%)
occurrences (all)	7	54	12
Infusion site pain			
subjects affected / exposed	2 / 15 (13.33%)	4 / 15 (26.67%)	3 / 34 (8.82%)
occurrences (all)	2	10	7
Infusion site pruritus			
subjects affected / exposed	4 / 15 (26.67%)	5 / 15 (33.33%)	6 / 34 (17.65%)
occurrences (all)	15	19	10
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	2 / 34 (5.88%)
occurrences (all)	1	4	3
Ear and labyrinth disorders			
Ear infection			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Gastrointestinal disorders			

Diarrhea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	3 / 34 (8.82%)
occurrences (all)	1	0	4
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	2 / 34 (5.88%)
occurrences (all)	0	9	5
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	2 / 34 (5.88%)
occurrences (all)	2	3	2
Sinusitis			
subjects affected / exposed	4 / 15 (26.67%)	5 / 15 (33.33%)	6 / 34 (17.65%)
occurrences (all)	4	8	9
Urinary tract infection			
subjects affected / exposed	3 / 15 (20.00%)	1 / 15 (6.67%)	1 / 34 (2.94%)
occurrences (all)	3	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported