



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 dose 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 dose 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: Antibiotic Usage

| | |
|--|------------------|
| End point title | Antibiotic 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