



Clinical trial results:

Simvastatin add-on to Escitalopram in patients with comorbid obesity and major depression: A multicenter, randomized, double-blind, placebo-controlled trial

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-002947-27 |
| Trial protocol | DE |
| Global end of trial date | 06 June 2024 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 23 August 2025 |
| First version publication date | 23 August 2025 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | SIMCODE |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04301271 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Charité - Universitätsmedizin Berlin |
| Sponsor organisation address | Chariteplatz 1, Berlin, Germany, 10117 |
| Public contact | Klinik für Psychiatrie und Psychotherapie Prof. Dr. Christian Otte, Charité – Universitätsmedizin Berlin, +49 30450 517531, simcode-studie@charite.de |
| Scientific contact | Klinik für Psychiatrie und Psychotherapie Prof. Dr. Christian Otte, Charité – Universitätsmedizin Berlin, +49 30450 517531, simcode-studie@charite.de |

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 | 24 July 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 06 June 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 June 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To examine whether add-on 40 mg/d Simvastatin to standard antidepressant medication (Escitalopram 20 mg/d) improves depression to a greater extent than adjunct placebo in patients with major depression and comorbid obesity

Protection of trial subjects:

The conduct of this study met all legal and regulatory current requirements (current ICH-GCP-guidelines) and in accordance with ethical principles of the Declaration of Helsinki.

Background therapy:

Major depressive disorder (MDD) and obesity are both linked to a higher risk of cardiovascular disease and stroke, further increasing their public health and economic impact. Importantly, MDD and obesity frequently co-occur and the presence of one condition increases the risk for developing the other. Statins (3-hydroxy-3-methylglutaryl Co-A reductase inhibitors) are among the most prescribed medications worldwide with well-established safety and efficacy. Recent guidelines recommend use of statins in primary prevention of cardiovascular disease, which has been linked to both MDD and obesity. However, no randomized controlled study so far has tested the antidepressive potential of statins in patients with MDD and comorbid obesity. Importantly, this is a difficult-to-treat population that often exhibits a chronic course of MDD and treatment resistance.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 02 March 2020 |
| 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 | Germany: 160 |
| Worldwide total number of subjects | 160 |
| EEA total number of subjects | 160 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 160 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 9 study center in Germany between 05/09/2020 and 05/06/2024.
Recruitment start / start of study: (first patient first visit) Q1 2020 – postponed due to COVID-19 pandemic to Q3 2020

Pre-assignment

Screening details:

211 have been screened according the inclusion and exclusion criteria and 161 patients with comorbid obesity (body mass index ≥ 30) and major depression have been randomized.¹ Excluded after randomization because of consent withdrawn.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Treatment (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

Arms

| | |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | No |
| Arm title | Simvastatin + Escitalopram |

Arm description:

Simvastatin is a lipid-lowering agent that is derived synthetically from a fermentation product of *Aspergillus terreus*. After oral ingestion, Simvastatin, which is an inactive lactone, is hydrolyzed to the corresponding β -hydroxyacid form. This is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol.
Simvastatin belongs to the statin class of medications, which are used to lower the risk of cardiovascular disease and manage abnormal lipid levels by inhibiting the endogenous production of cholesterol in the liver.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Simvastatin |
| Investigational medicinal product code | C10AA01 |
| Other name | CAS 79902-63-9, SimvaHexal, MAN 52531.04.00 |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Fixed dose 40 mg/d without adjustment, orally once daily at bedtime over 12 weeks. It was be provided as add-on medication to standard antidepressant treatment [Escitalopram (fixed dose 10 mg/d week 1 - 2 and 20 mg/d week 3 - 12)].

| | |
|--|--|
| Investigational medicinal product name | Escitalopram |
| Investigational medicinal product code | N06AB10 |
| Other name | CAS 219861-08-2, CIPRALEX, MAN 55880.03.00 (08.April 2003) |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

placebo will be provided as add-on medication to standard antidepressant treatment with Escitalopram. Fixed dose of Escitalopram 10 mg/d in first two weeks, then increase to 20 mg/d oral film-coated tablets.

| | |
|------------------|------------------------|
| Arm title | Placebo + Escitalopram |
|------------------|------------------------|

Arm description:

Escitalopram is a selective inhibitor of serotonin (5-HT) re-uptake with high affinity for the primary binding site. It also binds to an allosteric site on the serotonin transporter, with a 1000 fold lower affinity. Escitalopram has no or low affinity for a number of receptors including 5-HT1A, 5-HT2, DA D1 and D2 receptors, α 1-, α 2-, β -adrenoceptors, histamine H1, muscarine cholinergic, benzodiazepine, and opioid receptors.

| | |
|--|-----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Escitalopram |
| Investigational medicinal product code | N06AB10 |
| Other name | CAS 219861-08-2 |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Fixed dose of Escitalopram 10 mg/d in first two weeks, then increase to 20 mg/d oral film-coated tablets.

Tablet core: Microcrystalline cellulose, Colloidal anhydrous silica, Talc, Croscarmellose sodium, Magnesium stearate.

Film coating: Hypromellose 6cP (E464), Titanium dioxide (E171), Macrogol 3000

| | |
|--|----------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Based on the randomization codes, the pharmacy centrally provided for each center sequentially numbered, tamper-proof containers, which are equal in weight and similar in appearance containing IMP or placebo.

Tablet core: Microcrystalline cellulose, Colloidal anhydrous silica, Talc, Croscarmellose sodium, Magnesium stearate.

Film coating: Hypromellose 6cP (E464), Titanium dioxide (E171), Macrogol 3000

| Number of subjects in period 1 | Simvastatin + Escitalopram | Placebo + Escitalopram |
|--------------------------------|----------------------------|------------------------|
| Started | 81 | 79 |
| Completed | 81 | 79 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | Simvastatin + Escitalopram |
|-----------------------|----------------------------|

Reporting group description:

Simvastatin is a lipid-lowering agent that is derived synthetically from a fermentation product of *Aspergillus terreus*. After oral ingestion, Simvastatin, which is an inactive lactone, is hydrolyzed to the corresponding β -hydroxyacid form. This is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol.

Simvastatin belongs to the statin class of medications, which are used to lower the risk of cardiovascular disease and manage abnormal lipid levels by inhibiting the endogenous production of cholesterol in the liver.

| | |
|-----------------------|------------------------|
| Reporting group title | Placebo + Escitalopram |
|-----------------------|------------------------|

Reporting group description:

Escitalopram is a selective inhibitor of serotonin (5-HT) re-uptake with high affinity for the primary binding site. It also binds to an allosteric site on the serotonin transporter, with a 1000 fold lower affinity. Escitalopram has no or low affinity for a number of receptors including 5-HT_{1A}, 5-HT₂, DA D₁ and D₂ receptors, α ₁-, α ₂-, β -adrenoceptors, histamine H₁, muscarine cholinergic, benzodiazepine, and opioid receptors.

| Reporting group values | Simvastatin + Escitalopram | Placebo + Escitalopram | Total |
|---|----------------------------|------------------------|-------|
| Number of subjects | 81 | 79 | 160 |
| 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 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 81 | 79 | 160 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 39 | 39 | |
| full range (min-max) | 20 to 64 | 19 to 63 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 63 | 63 | 126 |
| Male | 18 | 16 | 34 |
| Chronic depression | | | |
| Chronic depression was defined as duration of current depressive episode for 104 weeks or longer. | | | |
| Units: Subjects | | | |
| no | 64 | 56 | 120 |
| yes | 12 | 15 | 27 |
| no records | 5 | 8 | 13 |
| Hypertension | | | |
| Units: Subjects | | | |

| | | | |
|---|--------------|--------------|-----|
| no | 24 | 19 | 43 |
| yes | 57 | 60 | 117 |
| LDL >100mg/dL | | | |
| Units: Subjects | | | |
| no | 17 | 18 | 35 |
| yes | 62 | 60 | 122 |
| no records | 2 | 1 | 3 |
| Body Mass Index | | | |
| Body mass index is calculated as weight in kilograms divided by height in meters squared. | | | |
| Units: score | | | |
| median | 38.7 | 37.6 | |
| inter-quartile range (Q1-Q3) | 33.5 to 43.1 | 34.7 to 41.4 | - |
| MADRS | | | |
| MADRS = Montgomery-Åsberg DepressionvRating Scale | | | |
| Units: score | | | |
| arithmetic mean | 25.8 | 25.2 | |
| standard deviation | ± 4.8 | ± 5.2 | - |
| Duration of current episode | | | |
| Units: week | | | |
| median | 27 | 40 | |
| inter-quartile range (Q1-Q3) | 16 to 53 | 20 to 82 | - |

End points

End points reporting groups

| | |
|---|----------------------------|
| Reporting group title | Simvastatin + Escitalopram |
| Reporting group description: Simvastatin is a lipid-lowering agent that is derived synthetically from a fermentation product of <i>Aspergillus terreus</i> . After oral ingestion, Simvastatin, which is an inactive lactone, is hydrolyzed to the corresponding β -hydroxyacid form. This is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol. Simvastatin belongs to the statin class of medications, which are used to lower the risk of cardiovascular disease and manage abnormal lipid levels by inhibiting the endogenous production of cholesterol in the liver. | |
| Reporting group title | Placebo + Escitalopram |
| Reporting group description: Escitalopram is a selective inhibitor of serotonin (5-HT) re-uptake with high affinity for the primary binding site. It also binds to an allosteric site on the serotonin transporter, with a 1000 fold lower affinity. Escitalopram has no or low affinity for a number of receptors including 5-HT _{1A} , 5-HT ₂ , DA D ₁ and D ₂ receptors, α ₁ -, α ₂ -, β -adrenoceptors, histamine H ₁ , muscarine cholinergic, benzodiazepine, and opioid receptors. | |

Primary: Change score in MADRS

| | |
|--|-----------------------|
| End point title | Change score in MADRS |
| End point description: MADRS (Montgomery-Asberg-Depression Rating Scale) The MADRS is a rating scale to measure depression severity. Each MADRS item is rated on a 0 to 6 scale. Total score range from 0-60, where higher MADRS scores indicate higher levels of depressive symptoms. | |
| End point type | Primary |
| End point timeframe: 12 weeks | |

| End point values | Simvastatin + Escitalopram | Placebo + Escitalopram | | |
|--------------------------------------|----------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 79 | | |
| Units: score | | | | |
| arithmetic mean (standard deviation) | 12 (\pm 8) | 12 (\pm 9) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Sensitivity analyses MADRS |
| Comparison groups | Simvastatin + Escitalopram v Placebo + Escitalopram |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 160 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.71 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.08 |
| upper limit | 3.02 |
| Variability estimate | Standard deviation |

Secondary: change LDL

| | |
|------------------------|------------|
| End point title | change LDL |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Simvastatin + Escitalopram | Placebo + Escitalopram | | |
|--------------------------------------|----------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 79 | | |
| Units: mg/dl | | | | |
| arithmetic mean (standard deviation) | 87 (± 35) | 120 (± 31) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | exploratory analysis |
| Comparison groups | Simvastatin + Escitalopram v Placebo + Escitalopram |
| Number of subjects included in analysis | 160 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.14 |

| | |
|----------------------|--------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.39 |
| Variability estimate | Standard deviation |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall study

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------------|
| Reporting group title | Placebo + Escitalopram |
|-----------------------|------------------------|

Reporting group description: -

| | |
|-----------------------|----------------------------|
| Reporting group title | Simvastatin + Escitalopram |
|-----------------------|----------------------------|

Reporting group description: -

| Serious adverse events | Placebo + Escitalopram | Simvastatin + Escitalopram | |
|---|-----------------------------------|----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 1 / 81 (1.23%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Surgical and medical procedures | | | |
| Surgical and medical procedures - Other, specify | Additional description: Curretage | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 81 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy, puerperium and perinatal conditions - Other, specify | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 81 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy loss | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 81 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 81 (1.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Placebo + Escitalopram | Simvastatin + Escitalopram | |
|---|------------------------|----------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 43 / 79 (54.43%) | 62 / 81 (76.54%) | |
| General disorders and administration site conditions | | | |
| polydipsia | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 1 / 81 (1.23%) | |
| occurrences (all) | 2 | 1 | |
| Flu like symptoms | | | |
| subjects affected / exposed | 9 / 79 (11.39%) | 7 / 81 (8.64%) | |
| occurrences (all) | 9 | 8 | |
| Fatigue/ Malaise | | | |
| subjects affected / exposed | 10 / 79 (12.66%) | 10 / 81 (12.35%) | |
| occurrences (all) | 10 | 11 | |
| Reproductive system and breast disorders | | | |
| sexual dysfunction | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 7 / 81 (8.64%) | |
| occurrences (all) | 2 | 7 | |
| Irregular menstruation | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 2 / 81 (2.47%) | |
| occurrences (all) | 1 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 0 / 81 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Psychiatric disorders | | | |
| Libido decreased | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 2 / 81 (2.47%) | |
| occurrences (all) | 2 | 3 | |
| Insomnia | | | |

| | | | |
|--|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 6 / 79 (7.59%) 6 | 4 / 81 (4.94%) 4 | |
| Restlessness subjects affected / exposed occurrences (all) | 7 / 79 (8.86%) 8 | 6 / 81 (7.41%) 7 | |
| Investigations CPK increased subjects affected / exposed occurrences (all) | 7 / 79 (8.86%) 7 | 5 / 81 (6.17%) 5 | |
| ALT /GPT increased subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 | 2 / 81 (2.47%) 2 | |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 3 / 81 (3.70%) 3 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 20 / 79 (25.32%) 20 | 23 / 81 (28.40%) 23 | |
| Migraine subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 2 / 81 (2.47%) 2 | |
| Restless legs syndrome subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 2 | 0 / 81 (0.00%) 0 | |
| Tremor subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 | 2 / 81 (2.47%) 2 | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 6 / 79 (7.59%) 6 | 10 / 81 (12.35%) 10 | |
| Eye disorders Blurred vision subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 2 | 1 / 81 (1.23%) 1 | |

| | | | |
|---|------------------|------------------|--|
| Gastrointestinal disorders | | | |
| diarrhea | | | |
| subjects affected / exposed | 9 / 79 (11.39%) | 7 / 81 (8.64%) | |
| occurrences (all) | 10 | 8 | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | 5 / 81 (6.17%) | |
| occurrences (all) | 3 | 5 | |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 0 / 81 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 3 / 81 (3.70%) | |
| occurrences (all) | 1 | 3 | |
| Nausea | | | |
| subjects affected / exposed | 12 / 79 (15.19%) | 17 / 81 (20.99%) | |
| occurrences (all) | 12 | 17 | |
| Constipation | | | |
| subjects affected / exposed | 5 / 79 (6.33%) | 1 / 81 (1.23%) | |
| occurrences (all) | 5 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 7 / 79 (8.86%) | 3 / 81 (3.70%) | |
| occurrences (all) | 8 | 3 | |
| Urticaria | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | 1 / 81 (1.23%) | |
| occurrences (all) | 3 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| muscle ache/neck pain | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | 2 / 81 (2.47%) | |
| occurrences (all) | 4 | 2 | |
| back pain/ lumbago | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 3 / 81 (3.70%) | |
| occurrences (all) | 2 | 3 | |
| Infections and infestations | | | |
| COVID-19 | | | |

| | | | |
|-----------------------------------|---|----------------|--|
| subjects affected / exposed | 3 / 79 (3.80%) | 1 / 81 (1.23%) | |
| occurrences (all) | 3 | 1 | |
| Upper respiratory tract infection | Additional description: Tonsillitis/Sinusitis | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 1 / 81 (1.23%) | |
| occurrences (all) | 2 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 15 June 2021 | update protocol Version 1.3. dated 26/05/2021 and PICF dated 11/05/2021; Change in inclusion criteria, change in cancellation criteria |
| 06 December 2021 | update Protokol Version 1.4 ,dated 24/09/2021 and PICF , dated 24/09/2021; Changes according to SmPC - SimvaHEXAL Information from May 2020 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported