# A randomised, double-blind, placebo-controlled, Phase III trial to determine the efficacy and safety of inhaled SNG001 for the treatment of patients hospitalised due to moderate COVID-19

Published: 29-03-2021
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Primary Objective:To evaluate recovery in patients with moderate COVID-19 after administration of SNG001 compared to placebo.Secondary Objectives:a. To evaluate the efficacy of SNG001 compared to placebo in patients with moderate COVID-19, using a...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Viral infectious disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON51111

**Source**
ToetsingOnline

**Brief title**
SPRINTER

### Condition

- Viral infectious disorders

**Synonym**
Corona virus infection: COVID19 infection

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Parexel Nederland
**Source(s) of monetary or material Support:** Farmaceutische industrie

## Intervention

**Keyword:** moderate COVID-19, Phase III, SNG001

## Outcome measures

### Primary outcome

Primary Endpoints:

a. Time to hospital discharge, defined by the OSCI score of 2 or below, with no rebound at subsequent assessments.

b. Time to recovery, where recovery is defined as the OSCI score of 1 or below, with no

rebound at subsequent assessments.

### Secondary outcome

Key Secondary Endpoints:

a. Progression to severe disease or death, defined by the OSCI score of 5 or above within 35 days of first dose (or randomization date if the patient not dosed).

b. Progression to intubation or death, defined by the OSCI score of 6 or above within 35 days of first dose (or randomization date if the patient not dosed).

c. Death within 35 days of first dose (or randomization date if the patient not dosed).

Secondary Endpoints:

d. Recovery, where recovery is defined as the OSCI score of 1 or below, with no rebound at subsequent assessments, at Days 7, 14, 21 and 28.

e. Hospital discharge by Days 7, 14, 21 and 28.

f. Improvement across the entire OSCI by Days 7, 14, 21 and 28.

g. Changes in breathlessness, cough and sputum scale (BCSS) score during the study period, including disaggregated breathlessness and cough scores.

h. Changes in National Early Warning Score 2 (NEWS2) during the hospitalisation period.

i. Daily assessment of COVID-19 symptoms and limitation of usual activities.

j. Quality of life measured using EQ-5D-5L.

k. Long-COVID-19 symptoms.

l. Safety and tolerability - vital signs, AEs concomitant medications, and immunogenicity.

# Study description

**Background summary**

Background:
Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) is a global threat and there is a need to assess new treatments which will prevent and effectively treat severe lower respiratory tract (LRT) illness caused by the SARS-CoV-2. Interferon beta (IFN-f3) has showed antiviral activity against SARS-CoV-2 in cell-based assays (1). IFN-f3 driven anti-viral responses have been shown to be compromised/deficient in older people (2) and those with chronic airways diseases (3, 4). These, and other patient groups are at high risk of developing severe LRT illness which can be fatal (5). The IFN-f3 deficiency can be overcome through the administration of exogenous IFN-f3. This has been shown both in vitro, using cells from patients, and in clinical trials using SNG001 (an inhaled IFN-f31a formulation for nebulisation). We hypothesise that SNG001 will rectify the deficiency in the lungs in at-risk patients and prevent severe LRT illness in the context of SARS-CoV-2 infection.

The SG016 hospital pilot study was completed in May 2020. During this pilot study, 101 hospitalised adults, >=18 years of age, with confirmed or suspected SARS-CoV-2 infection were randomised to receive SNG001 or placebo. Results of the pilot study showed that the risks of developing severe COVID-19 (the disease caused by SARS-CoV-2) were markedly reduced in patients receiving SNG001 compared to placebo and additionally that patients who received SNG001 were more than twice as likely to recover from COVID-19 as those on placebo. In addition, there was a significant reduction in breathlessness in patients receiving SNG001, compared to placebo (6).
SNG001 has been well tolerated in all clinical studies to date. Around 280 patients have been treated with SNG001. Of the 280, approximately 50 had chronic obstructive pulmonary disease (COPD), 50 had confirmed COVID-19 with varying underlying diseases i.e. heart disease, lung disease, diabetes etc and the remaining 168 had asthma. The majority of the 280 patients had or were suspected to have an active respiratory viral infection (rhinovirus, influenza, coronavirus, SARS-CoV-2, etc) at the time of randomisation.

SNG001 is pH neutral, rather than acidic and does not contain excipients such as mannitol, human serum albumin (HSA) and arginine, which are present in the injectable IFN-f3 formulations and which may have their own unwanted effects if delivered to the lungs.
SNG001 has historically been delivered using the I-neb, a mesh nebuliser made by Philips Respironics. The I-neb has been tested to ensure the drug retains its activity after aerosolization. A dose escalating trial established a target lung dose which induced an antiviral response in the lungs that was present 24 hours after dose administration.
In this trial the Aerogen Ultra device will be used. The Ultra is mesh nebuliser that is widely available and is better suited to single patient usage in the hospital setting. Laboratory assessments found that both the I-neb and the Ultra had similar levels of protein content in and similar IFN-f3 activity post nebulisation.

The primary endpoint is recovery in patients with confirmed SARS-CoV-2 infection who are hospitalised due to moderate COVID-19, after administration of SNG001 compared to placebo, where moderate COVID-19 is defined as presence of clinical signs and symptoms necessitating administration of oxygen therapy by mask or nasal prongs and recovery is defined as no limitation of activities according to the Ordinal Scale of Clinical Improvement (OSCI), with no rebound at subsequent assessments. The OSCI to be used in this trial is the 18th February 2020 version as recommended by the World Health Organization (WHO) (7).

**Study objective**

Primary Objective:
To evaluate recovery in patients with moderate COVID-19 after administration of SNG001 compared to placebo.

Secondary Objectives:
a. To evaluate the efficacy of SNG001 compared to placebo in patients with moderate COVID-19, using a range of endpoints.
b. To assess the general safety and tolerability of SNG001 compared to placebo when administered to patients with moderate COVID-19.

## Study design

Study Design:
Eligible patients will be randomised in a 1:1 ratio to receive SNG001 two syringes or placebo two syringes.
Patients who had positive virus test for SARS-CoV-2 prior to hospitalisation will be randomised no later than 48 hours after hospital admission. If the virus test was performed more than 96 hours prior to hospitalisation, the test will have to be repeated in the hospital prior to randomisation. Only patients whose repeated virus test is positive will be randomised, no later than 48 hours after confirmation of SARS-CoV-2 infection.
Patients who had positive virus test for SARS-CoV-2 after hospitalisation will be randomised no later than 48 hours after confirmation of SARS-CoV-2 infection.

SNG001 or placebo will be administered via the Ultra nebuliser. Patients will receive a dose of SNG001 or placebo once a day for 14 days and will be followed up for up to 90 days after completion of study medication (or randomization date if the patient not dosed). Study data will be collected from patients daily, as per the study schedule. Efficacy will be determined though differences between the groups in the OSCI scores, and the secondary endpoints. Adverse events (AEs) and concomitant medications will be monitored throughout the study period.
A Data Safety Monitoring Committee (DSMC) will perform a review of the safety data before 100 patients complete study treatment, to ensure the safety of study patients. The DSMC will also meet as and when necessary, i.e. if a safety issue arises or when the DSMC requests a further meeting.

## Intervention

The treatments
If the patient qualifies to take part in this study, he/she will be assigned to one of 2 treatment groups. For this study, we will have 2 groups:
• Treatment group 1 will receive the study drug SNG001.
• Treatment group 2 will receive the placebo.

Patients will be required to take study medication or placebo once a day for 14 days. Patients will have to inhale the study medication through a mouthpiece that is connected to a nebuliser. Patients will need to take the study medication at about the same time every day, ensuring that there is at least 8 hours between doses.

**Study burden and risks**

Avonex is the name of one of the interferon β drugs, a type of drugs, that is given by injection to patients with multiple sclerosis. Avonex works similar to SNG001. The only difference is that SNG001 is taken by inhalation and Avonex is taken by injection. The side effects of interferon β (Avonex) when it is given as an injection may be different in type, frequency and severity compared to SNG001 that is being given via inhalation. Some of SNG001 will go through the lungs into the bloodstream, this is normal. However, compared to blood levels found after interferon β injection, the blood levels after inhalation would be much lower and not detectable in most patients, and this will reduce the chance of the side effects in this list.

This list describes the side effect profile of interferon β (Avonex) taken from the medicines European product safety label that would be relevant to inhaled SNG001.

Very common: more than 1 out of 10 subjects treated
• Flu like symptoms - muscle aches, chills or fever, sweating, lack of energy, headache and feeling sick (nausea)

Common: 1 to 10 out of 100 subjects treated
• Loss of appetite
• Feeling weak and tired
• Difficulty sleeping
• Depression
• Flushing
• Runny nose
• Diarrhoea (loose stools)
• Feeling or being sick (nausea or vomiting)
• Numbness
• Rash, injection site pain, bruising or redness of the skin
• Increased sweating, night sweats
• Pain in your muscles, joints, arms, legs or neck
• Muscle cramps, stiffness in the joints and muscles
• Changes to blood tests (white cells/haematocrit/potassium and urea nitrogen)
• Symptoms you might not notice are tiredness, repeated infection, unexplained bruising or bleeding

The risks of interferon β when given via injection are well known, but the full risks of inhaling interferon β are not yet known. No safety concerns were raised in previous studies when this drug was inhaled by asthmatics, patients with chronic obstructive pulmonary disease (either in a stable state, when they had a cold or a worsening of disease) and the most recent study in patients with COVID 19 treated with inhaled SNG001. There were no significant changes in the results of safety tests performed in these studies.

Administration of medications by nebuliser may cause local irritation such as cough, wheezing or sore throat.
As with other medications, people treated with interferon β may be at risk of developing allergic reactions or anaphylaxis. Symptoms of an allergic reaction generally include overall body itching, hives (a sort of rash), skin flushing or rash. Anaphylaxis is a more serious allergic reaction that may involve dizziness, vomiting, low blood pressure and difficulty breathing. No cases of anaphylaxis have been reported in patients treated with SNG001 in completed clinical studies.

This list describes the uncommon and rare side effect profile of interferon β (Avonex) taken from the medicines European product safety label that would be relevant to inhaled SNG001.

Uncommon: (less than 1 in 100 people affected)
• Hair loss
• Reduction in platelet count (cell in the blood)
• Changes to your monthly period (female patients only)

Rare: (less than 1 in 1000 people affected)
• Difficulty breathing
• Rare clotting disorder of the blood
• Rare kidney disorders

Potential risks of the study procedures:
Blood Samples: Blood samples will be taken from a vein in the patient's arm during the study. The taking of a blood sample may cause some discomfort and bruising and there is a potential for infection. Other risks of taking blood, although rare, include nerve damage, dizziness and fainting.

Blood pressure and heart rate: An inflatable cuff will be placed on the patient's arm and a machine will measure his/her blood pressure and heart rate, after he/she have been sitting down for 10 minutes. He/she may experience mild discomfort in his/her arm while the cuff is inflated.

# Contacts

**Public**
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**Scientific**

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Male or female, >=18 years of age at the time of consent.
2. Admitted to hospital due to the severity of their COVID-19.
3. Positive virus test for SARS-CoV-2 using a validated molecular assay or antigen assay. Patients who had positive virus test for SARS-CoV-2 prior to hospitalisation will be randomised no later than 48 hours after hospital admission. If the virus test was performed more than 96 hours prior to hospitalisation, the test will have to be repeated in the hospital prior to randomisation. Only patients whose repeated virus test is positive will be randomised, no later than 48 hours after confirmation of SARS-CoV-2 infection. Patients who had positive virus test for SARS-CoV-2 after hospitalisation will be randomised no later than 48 hours after confirmation of SARS-CoV-2 infection.
4. Require oxygen therapy via nasal prongs or mask (OSCI score of 4).
5. Provided informed consent.
6. Female patients must be >=1 year post-menopausal, surgically sterile, or using a highly effective method of contraception. Acceptable highly effective methods of contraception include;
• bilateral tubal occlusion
• intrauterine device (provided coils are copper-banded)
• levonorgestrel intrauterine system (e.g., Mirena*)
• medroxyprogesterone injections (e.g., Depo-Provera*)

• etonogestrel implants (e.g., Implanon*, Norplan*)
• normal and low dose combined oral pills
• norelgestromin/ ethinylestradiol transdermal system
• intravaginal device (e.g., ethinylestradiol and etonogestrel), desogestrel (e.g., Cerazette*)
• total sexual abstinence (defined as refraining from heterosexual intercourse)
• vasectomised sexual partner.
Women should have been stable on their chosen method of birth control for a minimum of 3 months before entering the trial and should continue with birth control for 1 month after the last dose of inhaled IFN-β1a/matching placebo. In addition to the highly effective method of contraception (except for the practice of total sexual abstinence), a condom (in UK with spermicides) should be used by the male partner for sexual intercourse from randomisation (Visit 2) and for 1 month after the last dose of inhaled IFN-β1a/matching placebo to prevent pregnancy.
7. Women not of childbearing potential are defined as women who are either permanently sterilized (hysterectomy, bilateral oophorectomy, or bilateral salpingectomy), or who are postmenopausal. Women will be considered post-menopausal if they have been amenorrhoeic for 12 months prior to the planned date of randomisation without an alternative medical cause. The following age specific requirements apply:
• Women <50 years old would be considered post-menopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatment and if follicle stimulating hormone (FSH) levels are in the postmenopausal range.
• Women >=50 years old would be considered post-menopausal if they have been amenorrhoeic for 12 months or more following cessation of all exogenous hormonal treatment.
If, in the setting of the pandemic, the use of an acceptable birth control method is not possible, the decision to enrol a woman of childbearing potential should be based on the benefit-risk for the patient, which should be discussed with the patient at the time of the informed consent.

## Exclusion criteria

1. Evidence of ongoing SARS-CoV-2 infection for more than 3 weeks, confirmed by a validated molecular assay or validated antigen assay.
2. Non-invasive ventilation or high-flow oxygen (OSCI score of 5).
3. Mechanical ventilation (continuous or intermittent CPAP or intubation) or admission to intensive care (OSCI score of >= 6).
4. Previous SARS-CoV-2 infection confirmed by a validated molecular assay or validated antigen assay.
5. Any condition, including findings in the patients* medical history or in the pre-randomisation study assessments that in the opinion of the Investigator, constitute a risk or a contraindication for the participation of the patient

into the study or that could interfere with the study objectives, conduct or evaluation.
6. Participation in previous clinical trials of SNG001.
7. Current or previous participation in another clinical trial where the patient has received a dose of an Investigational Medicinal Product (IMP) containing small molecules within 30 days or 5 half-lives (whichever is longer) prior to entry into this study or containing biologicals within 3 months prior to entry into this study.
8. Inability to use a nebuliser with a mouthpiece.
9. Inability to comply with the requirements for storage conditions of study medication in the home setting.
10. History of hypersensitivity to natural or recombinant IFN-β or to any of the excipients in the drug preparation.
11. Females who are breast-feeding, lactating, pregnant or intending to become pregnant.
12. Previous SARS-CoV-2 vaccination.

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 08-06-2021 |
| Enrollment: | 30 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |

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|---|---|
| Brand name: | SNG001 |
| Generic name: | SNG001 |

## Ethics review

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|---|---|
| Approved WMO Date: | 29-03-2021 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 29-03-2021 |
| Application type: | First submission |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 27-05-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 27-05-2021 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 12-07-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 12-07-2021 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 12-07-2021 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |

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|---|---|
| Approved WMO Date: | 12-07-2021 |
| Application type: | First submission |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 21-08-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 21-08-2021 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 26-08-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 26-08-2021 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 04-11-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 04-11-2021 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |
| Approved WMO Date: | 11-02-2022 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |

Approved WMO

| | |
|---|---|
| Date: | 11-02-2022 |
| Application type: | Amendment |
| Review commission: | METC Isala Klinieken (Zwolle) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2020-004743-83-NL |
| CCMO | NL76537.075.21 |

# Study results

Date completed: 10-02-2022

**Summary results**
Trial ended prematurely