The potential of oral Camostat in early COVID-19 disease in an ambulatory setting to reduce viral load and disease burden.

Official title of the trial:
The potential of oral Camostat in early COVID-19 disease in an ambulatory setting to reduce viral load and disease burden.

EU number: 2020-003475-18

Trial number: COV-AAT

Sponsor(s) of the trial: Ghent University Hospital

Site name: Ghent University Hospital

Main address of site: C. Heymanslaan 10, 9000 Ghent

Document Revision History

Version No.	Version Date	Revision description
1.1	13OCT2020	Initial approved version
2.0	26NOV2020	Change of PI/CI to Prof Steven Callens Trial conduct in case of hospitalization has been adjusted from patient withdrawal to further study follow-up. Patient home monitoring period was adjusted from 14 days to the period of intake of study medication (5 or 10 days) Study schedule was modified
2.1	02FEB2021	The difference between withdrawal and treatment stop with continuous follow-up was explained
3.0	04JUN2021	Information about substudies which are no longer applicable, has been removed.

Who can I contact in case of questions?

Name	Function	In case of	Contact details
Callens Steven	Principal Investigator of the site	Information, problems or concerns	09/3320171 steven.callens@ugent.be
De Scheerder Marie-Angélique Caluwé Els Vanherreweghe Sophie	The trial staff	Information, problems, concerns	09/3321349 09/3322319 09/3325414
Infectioloog van wacht	Emergency contact [not emergency department of hospital]	Emergency	0474494302
Ombudsdienst UZ Gent http://www.uzgent.be/nl/patienten/ombudsdienst/paginas/default.aspx	Patient rights ombudsman	Concerns relating to your rights as a participant in a trial	09/3325234 ombudsdienst@uzgent.be
Allianz Global Corporate & Specialty	Insurance Company of the sponsor	In case of disagreement or complaint on a damage claim	Polisnr.BEL000862 03/3041600
Katya Van Driessche	Data protection officer of the **site**	Questions relating to the confidentiality of your data	09/3320987 dpo@uzgent.be
Gegevens-beschermings-autoriteit (GBA)	Belgian Data Protection Authority	Complaints relating to the confidentiality of your data	E-mail: contact@apd-gba.be

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THE TRIAL AT A GLANCE

Dear patient,

I recently informed you that you have a **COVID-19 infection**.

That is why we invite you to take part in a clinical trial (further referred to as "the trial") that is meant to evaluate an investigational medicinal product for the treatment of this infection.
Before you agree to take part in this trial, we want to fully inform you about the trial and its implications in terms of organisation, and its possible risks and benefits, so you can decide for yourself if you want to take part. This process is known as giving "**informed consent**".
This chapter will already **give you an idea** of what will happen during this trial, but we nevertheless ask you to read all the pages, even if it will take you a lot of time. It is important that you read and understand all the information. If you don't do this, you will take part in the trial without knowing what you're signing up for. So ask all your questions to the trial staff.
In this trial, the **investigational medicinal product CAMOSTAT** will be tested. This investigational product is being used in the treatment of diseases such as pancreatitis and esophagitis and has been on the market in Japan for over many years. It is known to have very little side effects and is well tolerated. It has not yet been proven that it can cure, improve or stabilise COVID infection. That is what we want to demonstrate with this trial, **so it is uncertain at this point whether you will benefit from it**. That is precisely what we want to find out: does the investigational medicinal product work, does it not work, or not enough. In the first place we want to find out whether Camostat can reduce the viral load in people infected with COVID-19, which would reduce the chance of transmission and potentially lead to a better outcome and faster cure in those infected.
In concrete terms, this means that during the trial you will receive the standard care. If you take part in the trial, you will receive in addition the investigational medicinal product Camostat or placebo. You will take the investigational medicinal product in the form of 3 tablets, 3 times a day during 5 days in a fasting state. You will take the medication and home and we will monitor you during the course of the study.

If you agree to take part in the trial, we will carry out **prior tests** to check whether you meet all the conditions to be accepted for this trial. We will monitor your clinical symptoms during the first 14 days and will equip you with a home monitor tool so you can follow-up your temperature, oxygen saturation, heart rate and respiratory rate 3 times a day. If these values are abnormal, you will be asked to remeasure or to contact the trial staff. At D0 and D5 your blood will be checked to screen for adverse events. If necessary additional blood analysis can be proposed. At D5 we will check the presence of the virus by taking a nose/throat swab. On the last study visit (D28) we will check the presence of antibodies against COVID-19. If virus is still present at D5, we can decide to prolong the treatment with an additional 5 days. An additional control will then take place at D10.

If at screening you do not meet the inclusion criteria for the main study (positive screening test but low viral load and absence of symptoms), you can exceptionally take part in a separate substudy (chapter II page 22). Here we want to analyse whether you can still transmit the virus to your close contacts by measuring viable virus in the nose/throat swab and to look whether patients with mild infections develop antibodies and immunity against

SARSCOV2. Therefore an additional swab will be taken at D0 and a blood sampling will be done at D28.

If you want you can participate in the main study without participating in the separate substudy. However, you cannot participate only in the substudy, if you are not willing to participate in the main study.

The study will take in total (maximum) 29 days (D0->D28). I need to know how well the investigational medicinal product works for you, and how well you tolerate the treatment. You will also have to fill in questionnaires. Even after the period of administration of the investigational medicinal product has ended, you will remain in the trial and will be followed up during the consultations and by questionnaires by telephone and email, in order to find out how you are doing.

It is also very important that you know that all medicinal products have **side effects**. Therefore, it is really important that you **report any side effects or any new health problem to the trial staff**.

The sponsor of this trial, the **Ghent University Hospital**, has taken out **insurance** for this trial.

You are **not allowed to become pregnant** or to get someone pregnant during the trial and for some time after it. I will discuss with you the appropriate method of contraception.
All treatments and examinations that you will undergo or receive in the context of the trial will be **free of charge for you**. All **other** treatments or examinations that you would have undergone anyway if you did not take part in the trial, **must be paid for by your health insurance and by yourself**.

The data collected during this trial will be **treated confidentially**.

You should also know that within the framework of this trial, a number of **biological samples** (e.g. blood) will be taken. These samples will be stored for a very long period of time. Me or my staff will give you clear information about this, and you will have to decide what you do or do not want. It is important to think about it carefully.

If you are hospitalized during the trial, the study-medication will be stopped for the remainder of the study. You will not undergo any study specific procedures but we will continue to follow you for the time of study (=29days), using your patient file. If you are hospitalized in Ghent University Hospital, we ask your permission to consult your file. If you are admitted in another hospital we ask your permission to contact your GP or treating physician. Once you are discharged from the hospital, you will be invited to continue study specific intervention as described.

There is one thing that I would like to emphasise very strongly: you are not obliged in any way to take part in this trial. Even if you have already started the trial, you can stop at any time. I will fully understand your decision, and will continue to take care of you as before. The authorities and an ethics committee have evaluated this trial. It is not because they have approved this trial that you should feel obliged to take part.

To be able to take part in this trial, you must, for your own safety, **agree that I, the investigator, inform your treating physicians** of your participation in this trial**.** You are **not allowed to take part in another clinical trial at the same time** without informing the researcher or the trial staff. We may refuse that participation to other trials for justified reasons. It is also very important that **you cooperate** and follow the instructions that the trial staff and I give you regarding the trial. You will receive an "emergency card", which says that you are taking part in a clinical trial. You must carry this card with you at all times; this is necessary for your safety should you have to undergo emergency treatment in a hospital where they don't know you.
If you agree to take part, you will need to sign the informed consent form. I will also sign the form and thereby confirm that you have received the necessary information about the trial.
You will receive a signed and dated copy of the form.

CHAPTER I – DESCRIPTION OF THE TRIAL AND YOUR RIGHTS WHEN PARTICIPATING

1. Why are we doing this trial

This clinical trial (further on referred to as “trial”) will evaluate the investigational medicinal product (IMP), Camostat for the treatment of COVID-19. The purpose of this trial is to learn about the role of Camostat in the treatment of COVID-19 in ambulatory setting. We want to study whether Camostat has the potential to reduce the viral load and therefore reduce the risk of transmissibility, reduces the disease burden and the time to recovery.

Camostat is a drug that has been used for a very long time in the treatment of pancreatitis in Japan and has a good tolerability profile. It is taken as a tablet and therefore can be easily taken at home.

In vitro laboratory studies have shown the potential effect of Camostat on the entry of the SARSCOV-2 virus in the lung cells. Therefore a couple of studies are currently investigating whether this drug can be of use in fighting COVID-19.

In this pilotstudy, we will look whether we see a difference in viral load between Camostat and placebo after treating COVID-19 infected individuals during 5 days. We will measure the virus in nose/throat swabs. By doing this we want to show the effect of Camostat on viral load and by consequence on transmissibility and potentially the clinical effects (time to recovery and milder symptoms).

2. Why am I being asked to take part?

You have been diagnosed with COVID-19

You are being asked to take part in this trial because you are 18 years or older, in an early stage of COVID infection or not presenting any symptoms despite having tested positive and not requiring a hospitalisation.

For your COVID infection, no treatment is currently available in Belgium that has been approved by the authorities.

The investigator or trial staff will discuss with you the requirements to be allowed to enter the trial.

3. Do I have to take part in a trial?

Your participation in a trial is voluntary and must remain free of any coercion. This means that you have the right not to take part in the trial or to withdraw at any time without giving a reason, even if you previously agreed to take part. Your decision will not affect your relationship with the investigator or your treating physician nor will it affect the quality of your future medical care.

4. What will happen during the trial?

This trial aims to include 150 participants in Ghent.

This trial is a randomised, dubbel blinded, placebo controlled trial. Randomisation will take place 2 against one, giving you 2 times more chance of being treated with Camostat compared to placebo. You will only know which arm you are randomised in after completion of the study. Also the study physician will be blinded and will only know which treatment you received after all inclusions have been finalised.

After screening and randomisation you will immediately start your medication. The first dose will be defined as D1. You will take the medication for 5 consecutive days, 3 times a day and 3 pills per intake. The drug will be taken orally. You will take the medication in a fasting state (Minimum 60 minutes before the meal and 2 hours after the previous meal). You will be asked to fill in a medication schedule reporting on the number of pills, hour of intake and relationship to the meals. If you forget a dose you can take it up to 4 hours after the time of intake. You have to take into account a minimum of 4 hours between each dose, so consequently other doses should be shifted as well. If you cannot take the dose within 4 hours than this dose will be passed. This needs to be documented in the medication schedule. If you have questions regarding dosing, you can contact the trial staff. The medications needs to be conserved at room temperature.

On day 0 and day 5 a blood analysis will be performed (max 21ml) to check for adverse events of the medication.

You will be followed during this period through telephone, email and consultations and at the hospital. You will receive a kit to perform some analysis at home 3 times per day including temperature measurement, oxygen saturation, heart rate and respiratory rate. You will be asked to register these data into an online platform or by phone. If these values are abnormal, you will be asked to remeasure or contact the trial staff. You will be asked to fill in a questionnaire on a daily basis between D1 and D14 through email or on paper, which can be given to the study personnel at the hospital visit.

The intensive monitoring phase will be prolonged up to 14 days after inclusion (D14). This period will be extended if patients still present symptoms at D14 until D28. The final visit is planned D28. In between a visit is planned at D5 to control the virus via nose/throat swab.

If you still present symptoms at D5 or the swab remains positive, the study physician will decide to prolong your treatment for an additional 5 days. If your condition requires a hospitalization, the study will be interrupted. If the treatment is prolonged, you will continue the same medication (placebo or camostat) 5 consecutive days, 3 tablets, 3 times per day, fasting. An additional visit will be planned on D10. This visit will include an additional swab. If the swab remains positive at D10, this will be repeated at D28.

At the final visit D28, we will also check your blood for antibodies.

If you are willing to participate in the main study but do not meet the inclusion criteria for the study (positive screening test but low viral load and absence of symptoms), you can exceptionally take part in a separate substudy. Here we want to analyse whether you can still transmit the virus to your close contacts, despite the low viral load by measuring viable virus in the nose/throat swab and to look whether patients with mild infections develop antibodies and immunity against SARSCOV2. Therefore an additional swab will be taken at D0 and a blood sampling will be done at D28. 10 participants can be included.

At any given time during the study you might be asked for an additional blood sampling to follow-up inflammatory parameters related to your COVID infection. This will always

be discussed with the responsible physician and is part of standard of care. If an X ray or CT from the lungs is performed during the trial, these data will be analysed in the study. These exams will only be performed as SOC and the decision to perform them will rely on your treating physician.

If these standard of care data are available, they will be analysed in the study.

Attached you can find an overview of the exams and visits and which are study specific or standard of care.

Overall, your participation in the trial will last 29 days and involve 3 or 4 visits.

If you meet all the conditions required to be enrolled in the trial and agree to take part in the trial, you will undergo the above-mentioned tests and examinations. If you have any important side effects, the investigator might determine that it is necessary to perform additional tests which will be considered as specific to the trial.

- If you are hospitalized during the trial, the study-medication will be stopped for the remainder of the study. You will not undergo any study specific procedures but we will continue to follow you for the time of study (=29days), using your patient file. If you are hospitalized in Ghent University Hospital, we ask your permission to consult your file. If you are admitted in another hospital we ask your permission to contact your GP or treating physician. Once you are discharged from the hospital, you will be invited to continue study specific intervention as described below: Discharge before D14: daily questionnaires until D14. If symptoms are still present at D14, this will be prolonged until D28.
- Discharge after D14: if you still present symptoms, daily questionnaires will be continued until D28.
- D28 study visit will be done as described above except when a patient is still hospitalised at that time.
- If you leave the hospital after D28, you will not undergo any study specific interventions. In this case we ask you to use your medical file to collect data regarding your COVID infection as described above.

We expect that you will use Camostat/placebo as described above.

5. Will I benefit from the trial?

The information obtained during a trial may contribute to a better understanding of the use of the investigational medicinal product (referred to as “IMP”) or to the development of a new medicinal product for the treatment of yourself or future patients.

The IMP may or may not be beneficial in treating your COVID infection or relieving your symptoms. Even if it is beneficial to you, a potential return or worsening of symptoms, illness or disease is still possible.

6. What are the possible risks and discomforts of taking part?

6.1. What are the possible side effects of Camostat/placebo?

Participation in a trial involves some risk.

All medicinal products can have side effects. Some of these side effects are already known, and some are not known. Even if previous studies have shown that Camostat/placebo was/were normally well tolerated, you may still experience the following side effects:

- Hypersensitivity reactions: rash (0.4%), pruritus (0.2%), nausea (0.3%), abdominal discomfort (0.2%), bloating (0.2%), diarrhea (0.2%)
- Liver enzyme disturbances (0.2%), thrombopenia, hypokalaemia
- The placebo contains lactose which might induce gastro-intestinal complaints in patients with lactose intolerance.

Because this IMP is still under investigation, other currently unknown risks and discomforts could occur. **Therefore, it is very important that you report <u>any</u> new or worsened health problems immediately to the investigator, regardless of whether or not you think it has to do with the trial (or to Camostat/placebo), and even when it is already described in this document. If you need to use other medication, discuss this with the investigator before taking it. If, for any reason, you consult another treating physician during the trial you must inform him/her that you are taking part in a trial and present your emergency card. This could be important in determining a diagnosis and giving you the correct treatment if needed.**

If you experience adverse effects of the medication, these will be registered and in function of severity we will decide whether you can continue the treatment.

We do not know whether the drug will have an effect on your disease. During the trial you will get the same standard of care as people that are not involved in the trial. If your disease worsens, you will be admitted in the hospital. Your participation in this trial does not change this standard of care nor any treatments that might be available at that time for treating COVID-19.

6.2. What are the possible risks or discomforts of the <u>examinations</u> during the trial?

The examinations of the trial may cause the following discomforts and risks:

The **taking of blood** to check for adverse events (max 21ml at D0 and D5) and the analysis of antibodies at D28 (9ml) may cause pain, bleeding, bruising or infection localised around the injection site. Similarly, some participants may feel dizzy or even faint during the procedure. The staff who take the blood will do all they can to minimize these discomforts.

The nose/throat swab can be experienced as uncomfortable.

6.3. Can I take <u>other medicines</u> during the trial?

Do not hesitate to ask your investigator for more explanation about the use of other medicines and food supplements.

6.4. Will my participation to the trial have an impact on my daily activities?

The fact that you are infected with COVID 19 might have an important effect on your daily activities, probably due to related symptoms and isolation measurements.

We will ask you to complete questionnaires and to do home monitoring and transfer these data 3x/day. Therefore we will ask an additional effort from you besides taking the medication correctly. We will also ask you for 2 visits at the clinic.

6.5. Can my partner or I get pregnant or can I breastfeed during the trial?

This section is intended solely for participants with a potential to get pregnant or participants who may get their partners pregnant.

Female participant**:** Because the effects of Camostat on an unborn child or infant are not known, you will not be allowed to take part in this trial if

- you are pregnant,
- wish to become pregnant in the near future or
- if you are breastfeeding.

It is also not allowed to do egg/ovum donation during your participation in the trial.

If you take part in the trial, you must use one of the authorised methods of contraception, during the trial: abstinence, intra-uterin device with a fail ratio of less than 1%, sterilisation of the male partner, approved hormonal contraception. Please discuss this point with your investigator if this applies to you. Please inform the investigator in case you would decide during the trial to change your method of contraception.

You will be required to have a pregnancy test (urine) at trial start before the first dose of Camostat/placebo. A repeated pregnancy test must be done if you miss any periods or your menstrual cycle becomes irregular.

Nevertheless, if you become pregnant during the trial, you should inform immediately the investigator and your treating physician. (S)he will ask you to sign a specific informed consent (for the pregnant participant) to follow up your pregnancy and its outcome. Upon your approval we will follow-up the evolution of the pregnancy, birth and first months of your child.

Male participant:

Taking Camostat/placebo could have an effect on your sperm and could lead to an unknown risk for an unborn child.

If you take part in the trial, you must use contraception and you should not be sperm donor for the duration of the trial. Please discuss this point with the investigator if this applies to you.

You commit to inform your female partner of your participation in this trial and of the potential risk to an unborn child.

Nevertheless, if your partner becomes pregnant during the trial, you should inform immediately the investigator. If you agree, (s)he will contact your partner to ask her to

be followed up during her pregnancy and its outcome and to sign a specific informed consent (for the pregnant partner).

7. What If something goes wrong within the trial?

Even if there is no fault, the sponsor is liable for harm caused to you whether directly or indirectly related to your participation in the trial. The sponsor has taken an appropriate insurance (a so called “NO FAULT INSURANCE”) for this liability (Ref. 1). A copy of the insurance certificate can be obtained from the investigator or trial staff.

If you (or in the event of death, your rightful claimants) seek compensation for a harm to your health as a direct or indirect result of participating in the trial, you must inform your investigator or trial staff promptly.

If the investigator believes that a link between the new or worsened health problem(s) and the trial is possible, he/she will inform the trial sponsor. The sponsor will then immediately initiate the declaration procedure to its insurance company. If the company considers it necessary, it will appoint an expert to assess whether there is a link between your reported health problem(s) and the trial. The insurance does not cover the natural progression of your disease/condition or the known side effects of the treatment you would have received without taking part to the trial (*that is* your standard treatment).

Whenever you feel it is appropriate or if you or your rightful claimants disagree either with the investigator or with the expert appointed by the insurance company, you may contact the insurance company or proceedings may be brought against the insurance company. You will find the contact details on the front page of this form.

8. What if other treatment options or new information on the IMP become available during the course of the trial?

During the course of the trial, important new information might become available, possibly affecting your decision to (further) participate. For example other treatments for your COVID 19 or important new information on the IMP may become available. It is the duty of the investigator to discuss this new information with you and to give you the opportunity to re-consider your participation in the trial.

If you decide to stop taking part in the trial or if you are no longer able to participate, your investigator will see to it that you continue to receive the best possible medical care.

9. Can my participation in the trial end prematurely?

As explained in detail below, your trial participation will end prematurely when

- you decide to withdraw your consent,
- the investigator decides to end your trial participation or the stop the study treatment, or
- other entities interrupt or end the trial.

In any case, if your trial participation ends prematurely, the investigator will discuss your future medical care with you. The sponsor can continue to retain and use any data that have already been collected before the end of your participation. This is to avoid skewing / biasing results of the trial (as described in I. § 12.4., page 17).

If you experience a side effect at the moment of stopping the IMP, the investigator may contact you in the future to see if it has resolved or not after the end of the trial participation.

If you experience a new side effect after the end of your trial participation you may contact the investigator to ask for a follow-up.

9.1. You decide to withdraw your consent

You are entitled to withdraw your consent for any reason, at any time, without having to justify your decision. However, for your safety, you should inform the investigator of your decision. Although it is not mandatory, it may be useful for the investigator and for the sponsor to know the reason of your decision (for example side effects, frequency of clinical visits,…).

If you withdraw your consent, this means you decide to stop

- the treatment with the IMP, and
- all trial-related visits and examinations.

Please discuss with your investigator to evaluate the practical modalities of your withdrawal (in light of your situation), including any follow up-visits or procedures.

In any case, no new data will be sent to the sponsor.

If your biological samples (e.g. blood samples, urine samples) have already been used or analysed before the withdrawal of your consent, the sponsor still has the right to use the results from those tests.

The biological samples that have been collected (but not tested) before the withdrawal of your consent and the data obtained from it, can also still be used by the sponsor. You may ask for a destruction of those samples. If this impacts the validity of the trial, the destruction may be postponed till the end of the trial.

In case you have signed an additional consent form for the use of your samples in future research, and you choose not to withdraw this separate consent, your samples can still be used for this research.

9.2. The investigator decides to end your trial participation.

The investigator will end your trial participation because

- you become pregnant during the trial,
- it is better for your health,
- he/she determines that you are not following the instructions given to participants, or

any other reason that will be explained.

The investigator can also decide to stop the treatment (eg in case of side effects). In this case, the investigators will continue to follow-up the outcome of your study participation. In this case all planned visits and sample collections can be continued conform the protocol.

9.3. Other entities may interrupt or end the trial

The sponsor and the competent Belgian health authorities may interrupt or end the trial because

- the information gathered shows that the IMP is not effective (does not deliver a sufficient level of improvement in the health of the trial participants),
- the IMP causes more (serious) side effects than anticipated, or
- any other reason that will be duly motivated by such party.

10. Which treatment will I get after my participation in the trial?

After you stopped the treatment with the IMP, the investigator will assess your health. If necessary, he/she will prescribe you the best standard treatment available or refer you to another treating physician of your choice.

11. Will my participation in the trial involve extra costs for me?

11.1. Examinations and treatments paid by the sponsor

The sponsor has arranged to compensate the hospital or site for

- the time devoted to the trial by the investigator and the trial staff,
- the visits/consultations and all scheduled examinations specific to the trial,
- the investigational treatment (IMP and any other medication and material specifically used for the trial).

In the annex to this ICF you will find the treatments or examinations that you will have to undergo, with the specifications which ones are trial specific and which ones are part of your standard care. The treatments and examinations that are trial specific will be paid by the sponsor and will not be charged to you. The standard procedures or examinations for your condition (i.e. standard of care) will be charged to you or your mutual insurance fund (Belgian social security).

If you need more details or if you are not affiliated with a mutual insurance fund (Belgian social security), please contact the trial staff.

The visits and treatments which are a consequence of a side effect are also considered as trial specific.

11.2. Other expenses paid by the sponsor

The study will provide the medication and monitoring kits. They will not reimburse any additional costs.

12. Which data are collected about me during the trial and what will happen with them?

12.1. Which data are collected and processed during the trial?

The collected and processed personal data concern information about your health and medical condition. This includes your medical history, some of your background information (for example your age, sex, and ethnic origin) and the results of examinations required by the trial.

12.2. How will the investigator treat my personal data?

The investigator is bound by professional secrecy about the data collected.

This means that he/she will never reveal your identity, including in a scientific publication or a lecture and that he/she will encode your data (*that is* by replacing your identity by an identification code in the trial) before sending them to the sponsor.

Therefore, the investigator and the trial staff under the responsibility of the investigator, will be the only ones able to establish a link between your identity and the data transmitted during the trial, with the exceptions listed under section 12.6.

The data transmitted to the sponsor will not allow the sponsor to identify you.

12.3. What will happen to information about me collected during the trial?

Your participation in the trial means that your personal data

- are collected by the investigator, and
- are used in an encoded form by the trial sponsor.

The investigator and the sponsor can only use the encoded personal data for research purposes in connection with scientific publications within the context of the trial that you participate in, or for a broader use of the encoded data if described below.

In addition, the sponsor may provide access to the encoded data to external researchers (that are not involved in this trial). In the event an external researcher wants to use the data in a project not yet described in this document, this project will have to be approved by an Ethics Committee. If your encoded trial data are sold, you will not benefit from this.

If side effects appear during the study that could be linked to the treatment with camostat, this information will be transferred to the company which provides this medication (Ono Pharmaceutical Co, Ltd.), without transferring personal data.

12.4. How will my data be handled?

Your trial data will be processed in accordance with the General Data Protection Regulation (GDPR, Ref. 2) and the Belgian law on data protection of 30th July 2018 (Ref. 3). The sponsor is responsible for this processing.

Processing your personal data in this trial is allowed because we are conducting scientific research and

- You have given your **consent.**

12.5. Do I have access to my data collected and processed during the trial and can I rectify them ?

You are entitled to ask the investigator what data are being collected about you and how those data will be used in connection with the trial.

You have the right to withdraw your consent for the processing of personal data. However personal data collected before withdrawal will be kept to avoid skewing of results in the trial.

Your right

- to inspect and access these data
- to ask for correction if they are incorrect

is postponed for the following reasons, including to avoid skewing of results in the trials because of the blinded character of the study. This means that neither the study physician or yourself have information on which study arm you are randomised in. Access to the study data therefore might influence the interpretation of the study results. Please ask your investigator when you can have access to your personal data.

It is not possible

- to have all your data erased
- to restrict the processing of your data.
- to object to the processing of your personal data

for the following reasons, including to avoid skewing of results in the trial.

12.6. Who, other than the Investigator and his staff, has access to my personal data?

To verify the quality of the trial, it is possible that your personal **un**coded data or information in your medical records relevant for the trial, will be examined by people outside the trial staff but under the responsibility of the investigator. These persons must be subject to professional secrecy or a confidentiality agreement. The following might be considered:

- the personnel designated by the sponsor of the trial (MONITORS and AUDITORS), and people or organisations providing services for or collaborating with the sponsor. They will however never transfer your name and contact details to the sponsor.
- inspectors of competent health authorities worldwide
- an independent audit group
- people designated by the Ethics Committee

For the needs of the trial, the encoded trial data may be sent to other EU and non-EU countries and may be reviewed by

- personnel (other than the inspectors) of competent health authorities of Belgium (Federal agency for medicines and health products, FAMHP) and other EU and non-EU countries,
- the evaluating Belgian Ethics Committee(s),
- external researchers,
- the sponsor of the trial, personnel designated by the sponsor, and people or organisations providing services for or collaborating with the sponsor, and/or
- group companies of the sponsor in Belgium, and in other EU and non-EU countries.

The European regulation and the Belgian legislation on data protection have requirements for transferring data to non-EU countries. The sponsor must ensure equivalent guarantees regarding personal data protection standards before transferring the encoded data to non-EU countries. If for this purpose, there is a data protection agreement, a copy of this agreement may be obtained via the investigator. You can always contact your investigator to obtain more information about any such transfers.

To register the parameters obtained by the monitoring tool that you receive, we are using a data platform provided by the company Byteflies. Your data will be linked to the sensor Dot ID and will be coded. The company therefore is not able to link this data to your person and cannot use the obtained data for other purposes than those mentioned in the study. We will provide you with a flyer including information on the correct usage of the monitoring kit and how the data should be transferred.

We ask you to return the monitoring material in a good state.

In this study, questionnaires will be asked to be filled in by providing a valid e-mailadress. Only pseudomysed data will be used for the analysis of the data and in all reports or publication about the study.

12.7. What will happen to the results of the trial?

After trial closure, a description and the results of this clinical trial will be published in specialised medical journals. A copy of the scientific publication or a summary for laypersons can be obtained from the investigator or the trial staff.

A description of the trial will also be available on https://www.Clinicaltrials.gov. You can search these websites at any time using the trial number given on the front page of the informed consent form. The websites will include a summary of the results within 1 year after the end of the trial (Ref. 4).

These websites or publications will not include information that can identify you.

12.8. Will my data be used for other purposes than for the trial in which I take part?

The results of the trial will be used to answer the scientific questions of the trial. In addition, the sponsor would like to use your data obtained from this trial, in connection with other research and development activities (and the associated scientific publications). These activities may concern

- the way Camostat and drugs of the same group work,
- the disease/condition for which Camostat is evaluated in this trial or
- other diseases and health problems which could benefit from Camostat, or from related diagnostic tests.

Any additional research outside of the trial, must be approved by a Belgian recognized Ethics Committee.

At the end of this form you agree or disagree to the use of your trial data for other purposes by ticking the appropriate check-box in Chapter III, page 23.

12.9. How long will my data be kept?

After the end of the trial your encoded data will be retained for at least 25 years (Ref. 5) to ensure the validity of the research. This will also be the case if you stopped trial participation prematurely.

13. Which biological samples are collected from me during the trial and what will happen with them?

13.1. Which biological samples are collected from me during the trial?

Biological samples are samples of human body material (for example blood, tissue, urine, faecal stool, ….)
In this trial, the following biological sample(s) will be taken:

- nose/throat swab (max 4 in the core study D0-D5-D10 and D28)
- blood sampling (2x 21ml at D0 and D5 to screen for side effects, 1x9ml D28, additional blood sampling standard of care or tolerability 1x9ml, 3x6ml.

13.2. What will happen to the collected biological samples?

The collected biological samples will be managed and stored at the biobank Ghent University Hospital for 25 years.

These biological samples will be analysed for the objectives of the trial. Some analysis will be performed by external partners. The viral load and the antibodies will be measured in the lab of Sciensano in Brussels.

Leftover material from the samples send to external partners will be destroyed. Leftover samples from the analysis done at Ghent University and back-up samples will be stored at the Biobank HCRC.

Genetic analyses will also be performed on your samples. The purpose of these analyses is to analyse the genetic material of the virus.

These genetic analyses will deliver essential information for the trial. If you do not want these analyses to be conducted, you will not be allowed to participate in the trial.

It may happen by chance and in addition to the trial objectives, that the results of the analysis of your biological samples reveal information that may be important to your health or the health of your blood relatives. These data are called ”incidental findings” and will be treated as described in Chapter I, § 15, page 21.

13.3. How will my biological samples be handled?

The procedure to encode your biological samples is the same as that used for your personal data (see I § 12.3, page 16, Ref. 6). Samples sent to the sponsor or to organisations working in collaboration with the sponsor, will only be labelled with your trial identification code.

As part of the trial, the sponsor might transfer (a part of) your samples to a laboratory that is working with them. This laboratory may only use your samples as specified in this document. The tracking of your samples will be ensured by the sponsor unless you have accepted anonymization of your samples.

Your biological samples are deemed to be a “donation”. You will not receive any financial benefit associated with the development of new therapies derived from the use of your biological samples, and which may have commercial value.

13.4. What happens with any remainders of biological samples once the analyses described in this document have been carried out?

The sponsor shall use the biological samples within the context of the trial as described above.

Since scientific progress in this area is constant, the sponsor would like to, with your consent retain a part of the remainders of your biological samples for 25 years. The sponsor will use them for future research, outside the trial that you will participate in, to better understand the disease, its treatment and the responses to this treatment, and Camostat. The retention of the remainders of your samples goes together with the retention of the accompanying encoded personal data.

You agree or disagree to the retention of the remainders of your biological samples for future research by ticking the appropriate check-box in Chapter III, page 23.

If you agree, any future research, additional to what is described above, may only be conducted according to the legislation on the use of human tissue material (Ref. 7) and with the approval of a Belgian recognized Ethics Committee. As a general rule, you will

be asked to sign an additional informed consent form in which the additional research is specified.

13.5. Will any additional biological samples be collected and used for additional research?

In this trial, no additional biological samples will be collected.

14. Who has reviewed and approved the trial documents?

The documents of the trial have been reviewed by

- The Belgian competent health authorities (FAMHP) or if applicable by the competent national health authorities of other EU members states and
- An independent Belgian Ethics Committee

It is the task of the competent health authorities and the Ethics Committees to protect people who take part in a trial. The health authorities will ensure that the trial is conducted in accordance with the applicable legislation.

You should not under any circumstances take their approval as an incentive to take part in the trial.

15. What happens in case of incidental findings?

If by chance and in addition to the trial objectives a result is discovered during the trial that may be important to your health or the health of your blood relatives (called ”incidental findings”), the sponsor will inform the investigator. With your consent the investigator will notify you and your treating physician about your results and potential consequences. If necessary, the investigator and/or the treating physician will advise you on the next steps.

You agree or disagree to being informed of it by ticking the appropriate check-box in Chapter III, page 23.

CHAPTER II – SUBSTUDY SCREENING FAILURES

If after screening it appears that you are not eligible for the core study, you can still participate in a separate substudy.
You are eligible for this study if you meet all the criteria for the core study except that your PCR value shows too little virus.
The sponsor in this case will invite you to participate in a substudy to analyse COVID-19 infection in patient without symptoms and with a low viral load to see whether these individuals present antibodies against COVID and whether they present a risk of transmissibility.
Therefore, we would like to take an additional naso-pharyngeal (or nose-throat)swab at inclusion (D0), and a blood sample at D28. Besides these 2 interventions, there are no additional interventions planned in this substudy. You agree or disagree to being informed of it by ticking the appropriate check-box in Chapter III, page 23.

CHAPTER III – Informed consent

PARTICIPANT

PREREQUISITES FOR YOUR PARTICIPATION IN THE TRIAL

- I declare that I have been informed of and that I understand the purpose of the clinical trial, its duration, possible risks and discomforts, the precautions that I have to take and what is expected of me. My rights have been explained to me and I have understood those rights.
- I have had enough time to think about taking part in this trial and to discuss it with a trusted person (for example friends, relatives, treating physician, …).
- I have had the opportunity to ask any questions that came to mind and have obtained a satisfactory response to my questions.
- I understand that my participation in this trial is voluntarily and free from any coercion and that I am free to stop at any time my trial participation.
- I understand that data about me will be collected and that they will be treated confidentially.
- I agree to my personal data being processed as described in Chapter I, § 12, page 16.
- I agree that my email address is used to send the questionnaires related to the study.
- I understand that the sponsor has taken out an insurance in case I should suffer any damage in connection with my participation in this trial.
- I understand that when participating in this trial, I will not have any costs except those related to the standard of care treatment of my disease (as described in the annex).
- I agree to my treating physician(s) being informed of my participation in this trial.
- I agree not to take part in any other trial at the same time without first informing the investigator or the trial staff, who might not permit me to participate for a good reason.
- I understand that I need to cooperate and follow the investigator's and trial staff's instructions regarding the trial.
- I understand that participation to the trial might end for me without my consent if I need other treatment, do not follow the trial plan, have a trial-related injury, or for any other justified reason.
- I understand that genetic analysis will be conducted on my biological samples.
- I certify that all the information I have given about my medical history is correct. I understand that my failure to inform the investigator or designee about any exclusion criteria may harm myself.

USE OF THE MEASUREMENT KIT

- I understand and accept that I have received the measurement kit provided to me in good condition and will ensure its correct use and preservation for the duration of the study.
- I will return this kit to the study nurses at the last study visit (D28).
- I understand and accept that in the event of late returns, damage, improper use or loss, the Ghent University Hospital reserves the right to recover the damage.
- I understand and agree that the device should not be given to a third party under any circumstances.
- I understand and agree that in the event of damage, it is strictly forbidden to send the device to third parties for repair.

☐ **I agree**	☐ **I do not agree**

OPTIONAL CONSENTS WHICH ARE NO PREREQUISITE FOR YOUR PARTICIPATION IN THIS TRIAL.

1. As specified in Chapter I, § 12.8, page 19, the sponsor would like to be able to use your data obtained from this trial in connection with other research and development activities (and the associated scientific publications) on the condition that such research purposes have been approved by a Belgian recognized Ethics Committee.

   Do you agree with the use of your data obtained in this trial for other research purposes?

   (Tick as appropriate. If you leave this question open, we assume the answer is 'I do not agree'.)

☐ **I agree**	☐ **I do not agree**

2. As specified in Chapter I, § 13.4, page 20, the sponsor would like to retain the remainders of your biological samples for 25 years for future research outside the trial that you will participate in. The samples will be used to better understand the disease, its treatment and the responses to this treatment, and [name of IMP(s)/comparator].

   Do you agree with the retention of the remainders of your biological samples and the accompanying personal data for future research outside the trial?

   (Tick as appropriate. If you leave this question open, we assume the answer is 'I do not agree'.)

☐ **I agree**	☐ **I do not agree**

3. As described in Chapter I, § 13, page 19, and § 15, page 21, it may happen that incidental findings are discovered that may be important to your health or the health of your blood relatives.

   If this happens: do you want the investigator to inform you (directly or via your treating physician) of this result?

   (Tick as appropriate. If you leave this question open, we assume the answer is 'yes, I want to be informed'.)

☐ **No, I do not want to be informed**	☐ **Yes, I want to be informed**

4. As described in Chapter II, page 22, the sponsor would like to invite you to participate in a substudy to analyse the COVID-19 infection in patient without symptoms and with a low viral load. Your participation in this substudy is not required for the core study and includes that you consent with additional sampling. You will not take any study medication, or undergo other analysis than those described in Chapter II.

   Do you agree to participate in this substudy (screening failures substudy)?

   (Tick as appropriate. If you leave this question open, we assume the answer is 'I do not agree'.)

☐ **I agree**	☐ **I do not agree**

I consent to take part in the trial, with the above restrictions and I have received a signed and dated copy of all pages of this document.

Participant's surname and first name:

Date (DD/MMM/YYYY):

Time:

Participant's signature:

INVESTIGATOR

I, the undersigned investigator, confirm that

- the participant has been verbally provided with the necessary information about the trial, has been explained the content and has been given an original signed document.
- I have verified that the participant has understood the trial.
- I have given the participant sufficient time to agree to take part and to ask any questions.
- no pressure was applied to persuade the participant to agree to take part in the trial.
- I operate in accordance with the ethical principles set out in the latest version of the “Helsinki Declaration”, the “Good Clinical Practices” and the Belgian Law (Ref. 8).

Investigator’s, Surname and first name:

Date (DD/MMM/YYYY):

Time:

Investigator’s signature:

ANNEX: FLOWCHART OF THE STUDY

	D0	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20	D21	D22	D23	D24	D25	D26	D27	D28
Check inclusion and exclusion criteria	x																												
COVID screening test	x																												
ICF signing	x																												
Pregnancy test (if applicable)	x																												
Randomisation of study medication (Camostat versus placebo)	x																												
delivery of study medication	x					(x)																							
Intake of studymedication (3 tablets 3x/day)		x	x	x	x	x	(x)	(x)	(x)	(x)	(x)																		
Sociodemographic data	x																												
Consultation with clinical assessment and parameter check	x					x					(x)																		x
Nose-throat swab	x					x					(x)																		(x)
Lab (baseline and toxicity screening)	x					x																							
Questionnaire symptoms		x	x	x	x	x	x	x	x	x	x	x	x	x	x	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))	(((x)))
Home monitoring (temperature, oxygen saturation, heart rate, respiratory rate) 3 times a day (except on scheduled visits (2x/day).		x	x	x	x	x	(x)	(x)	(x)	(x)	(x)																		
Monitoring side effects and medication intake		x	x	x	x	x	(x)	(x)	(x)	(x)	(x)																		
Medication log check						x					(x)																		x
Questionning participants on compliance and tolerance						x					(x)																		x
Neutralising antibodies																													x
Substudy PK/PD analysis		x*	x*	x*	x*	x*																							
Substudy COVIM2.0 blood analyis	x																												x
Substudy COVIM2.0 viral culture	x					x***					x***																		x***
Substudy sweat analysis D5						x																							
Substudy screen failures viral culture	x																												
Substudy screen failures antibody measurement																													x

(x)=if medication is to be continued after D5 for an additional 5 days as defined
(((x)))= based on clinical necessity and availibility
(((x)))= if symptoms persist after D14
* to be planned between 2 medication intakes between D1 and D5
** if PCR positive at D5, repeat at D10; if PCR positive at D10, repeat at D28
*** if PCR positive

study window: 48 hours for all study related visits

GLOSSARY

DPA: The Data Protection Authority ensures that personal data are handled with care and thoroughly protected, and that your future privacy also remains guaranteed.

FAMHP: Federal agency for medicines and health products

IMP: investigational medical product

NO FAULT INSURANCE:

The sponsor is liable for any injury or any damage that the participant has suffered, and which is directly or indirectly related to the clinical trial. You do not have to prove any mistake in this respect.

MONITOR and AUDITOR

Both the monitor and auditor work for the sponsor. The monitor takes care of a continuous quality check during the course of a trial. The auditor performs a quality check after the trial. They verify if the trial is being/was conducted according to the protocol, if the reported data are liable and if the clinical trial was conducted according the applicable rules.

REFERENCES

[1] This is in accordance with Article 29 of the Belgian Law of 7 May 2004 related to experiments on humans.

[2] General Data Protection Regulation No 2016/679 of the European Parliament and of the council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC.

[3] The Belgian Law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data.

[4] In accordance with section 4.3. of the Commission Guideline: Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 - (2012/C 302/03). [From the moment the Clinical trial regulation enters into force : In accordance with article 37 of the Clinical trial regulation No 536/2014 of the European Parliament and of the council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC; sponsor have to provide summary results of clinical trials in a format understandable to laypersons.]

[5] In accordance with article 58 of the Clinical trial regulation No 536/2014 of the European Parliament and of the council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

[6] Belgian Law of 19 December 2008 on the acquisition and use of human body material with a view to medical application to humans or scientific research, and the applicable royal decrees.

[7] This is in accordance with Article 21 of the Belgian Law of 19 December 2008 on the acquisition and use of human body material with a view to medical application to humans or scientific research, and the applicable royal decrees.

[8] Belgian Law of 7 May 2004 related to experiments on humans, and the applicable royal decrees.