For patients

Informed Consent Document for

CAME COVID study

“CAM (Clarithromycin) Effectivity for COVID-19 pneumonia which does not require oxygen administration. A multicenter, randomized-controlled, open-label, three-armed parallel group comparison, exploratory trial.”

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Department: ________________________________
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1. Introduction

This informed consent document aims to explain to you a clinical study “CAM (Clarithromycin) Effectivity for coronavirus disease 2019 (COVID-19) pneumonia which does not require oxygen administration. A multicenter, randomized-controlled, open-label, three-armed parallel group comparison, exploratory trial” (CAME COVID study), which is conducted in the name of the department (name of medical institution).

Clarithromycin is not approved for the treatment of mild COVID-19 that does not require oxygen administration. This clinical trial aims to explore whether clarithromycin is as efficacious for mild COVID-19 as expected.

After hearing a full explanation of this study and understanding the content of the study, you will be given the opportunity to decide whether or not you will participate in this study of your own free will.

If you choose to participate in this study, please sign the informed consent form and give it to one of your attending physicians. If you decide not to participate in this study, you will not suffer any disadvantages in subsequent treatments.

- Withdrawal from participation in this study.

You can withdraw your consent to participate in this study at any time, even after you agree to participate in this study. In case of withdrawal of consent, give the signed consent withdrawal form to one of your attending physicians, or inform them verbally that
you wish to withdraw your consent.

Even if you withdraw your consent to participate in this study, you will not suffer any disadvantages in subsequent treatments. If you withdraw your consent to participate in this study, the information and samples obtained will be discarded.
2. What is a clinical trial?

The current diagnosis and treatment for diseases are established through long-term progress and development. Further progression and development of medical science are important to develop safer and more efficacious treatments. Many experiments and studies are required to develop ways of diagnosing and treating diseases, including investigations using healthy volunteers or patients. Such medical investigations on human subjects are called “clinical trials.”

To conduct clinical trials, human rights and patient safety need to be considered. This study was conducted according to the Clinical Trials Act (rules for preserving human rights and the safety of participating patients). This study was approved by the certified review board below, which has obtained a certification from the Ministry of Health, Labour and Welfare in Japan after a strict examination. This study was approved by the administrator of the medical institution. A summary of the plan of this study was submitted to the Ministry of Health, Labour and Welfare in Japan and registered in the clinical study database (jRCT) established by the Ministry of Health, Labour and Welfare in Japan.

The standard operation procedures, list of committee members, and records of the examination (title of clinical studies, examination results) of the certified review board are publicly available on the website of the Clinical Research Center, Nagasaki University Hospital (http://www.mh.nagasaki-u.ac.jp/research/index.html).
Name of certified review board:

The Clinical Research Review Board in Nagasaki University

Certification number:

CRB7180001

Address:

1-7-1, Sakamoto, Nagasaki, Nagasaki

Tel:

095-819-7229

3. About your disease

COVID-19 causes symptoms such as fever, cough, shortness of breath, and dyspnea if pneumonia occurs. The severity of COVID-19 differs depending on one’s age and underlying health conditions. Elderly and people with chronic diseases (such as severe heart diseases or diabetes mellitus) are more likely to have severe symptoms that can lead to death. Patients with COVID-19 that do not require oxygen administration often spontaneously recover after some time. However, patients with severe COVID-19 may need mechanical ventilation to administer oxygen as part of their treatment plan. Unfortunately, no treatment strategy has been established for COVID-19 pneumonia.
4. Background, purpose, and significance of this study

<Background>

The COVID-19 pandemic is currently a major concern worldwide. In Japan, 932,361 positive cases have been confirmed using a polymerase chain reaction (PCR) test, and 15,190 deaths have been reported by the Ministry of Health, Labour, and Welfare in Japan as of August 1, 2021. The proportion of COVID-19 patients leading to death tends to be lower in Japan than in Western countries. Nevertheless, in Japan, approximately 5% of patients with COVID-19 have required hospitalization, 1.4% have had severe symptoms requiring intensive care, and 1.6% have died. Although dexamethasone was reported to be effective in patients with moderate-to-severe COVID-19, no treatment strategy to prevent exacerbation has been established for patients with mild COVID-19 that do not require oxygen administration.

In this study, we focused on clarithromycin, an antiviral agent that is expected to prevent exacerbations of COVID-19. Clarithromycin has been widely used for general infectious diseases and has been reported to improve symptoms such as coughing, sputum, inflammation, and exacerbation in patients with influenza.

<Purpose>
This study aims to investigate the safety and efficacy of clarithromycin in patients with mild COVID-19 who do not require oxygen administration.

5. Study agent in this study

If you are assigned to the groups in which the study agent is administered, you will be asked to take the following medical agent that has been commercially available and widely used for treating general infectious diseases. For the treatment of general infectious diseases, 400 mg daily is usually administered. For the treatment of pulmonary atypical mycobacteriosis, 800 mg daily is usually administered. The same doses will be administered in this study.

The cost of this study agent is funded by the study and will be provided to you by one of your attending physicians.

<Summary of the study agent in this study>

General name: Clarithromycin

Brand name: Clarith tablets 200

Active constituent: Clarithromycin 200 mg/tablet

Manufacture: Taisho Pharmaceutical Co., Ltd.

Dose and usage: See “Study intervention (treatments)” (page 6).

Administration period: every day for seven days.
6. Methods of this study

(1) Patients who can participate in this study

Patients who meet the following criteria can participate in this study:

1) Patients who were positive for SARS-CoV-2 using either a PCR test or LAMP method within three days before informed consent was obtained.

2) Patients with pneumonia seen on routine chest radiography or chest CT.

3) Japanese patients aged 20 years or older.

4) Patients who give their written consent form to participate in the study.

Patients who met any of the following criteria cannot participate in this study:

1) Patients who have had symptoms for eight days or longer.

2) Patients treated with macrolide antimicrobial agents.

3) Patients treated with steroids (except inhalants) or immunosuppressive agents.

4) Patients diagnosed with influenza.

5) Patients whose SpO₂ is less than or equal to 93% (at room).

6) Patients with hepatic dysfunction. (AST/ALT more than five times the facility standard value or Child-Pugh B/C).

7) Patients with renal dysfunction. (Cre more than twice the facility standard value and eGFR of <30 ml/min)

8) Patients whose peripheral blood neutrophils are less than 1,000/uL.
9) Patients with a history of hypersensitivity to macrolide antimicrobial agents.

10) Patients who are pregnant or breastfeeding.

11) Patients vaccinated against COVID-19.

12) Patients with other conditions that the investigator thinks are inappropriate for them to participate in the study.

The attending physicians will judge whether or not you can participate in this study based on your treatment history, current disease condition, current use of other medical agents, and/or screening test results.

Even if you want to participate in this study, the attending physician may deem that you cannot participate due to the screening test results.

(2) Study intervention (treatments)

The treatment or use of medicinal agents for study purposes is called an “intervention”

This study has three intervention groups. If you agree to participate, you will receive one of the three interventions. Neither you nor the attending physician can select the intervention. See “Randomization and blinding” below for more information on how the different interventions are allocated.
Group A: receive 800 mg clarithromycin daily

If you are assigned to this group, you will receive 400 mg of clarithromycin twice daily (after breakfast and dinner).

Group B: receive 400 mg clarithromycin daily

If you are assigned to this group, you will receive 200 mg of clarithromycin twice daily (after breakfast and dinner).

Group C: receive standard treatment group without clarithromycin

If you are assigned to this group, you will not receive clarithromycin. Instead, you will receive standard care for COVID-19.

The components of this standard care will be explained to you by an attending physician.

<Randomization and blinding>

Participants will be randomly divided into three groups in an approximate ratio of 1:1:1. This grouping method is called “random assignment.” Random assignment is performed using a specific web system on a computer. Neither you nor the attending physician can select the intervention. This means that you may not receive the intervention (treatment).
<Flow of this study>

The flow of this study is shown in the Figure below.
1. Obtaining consent

You will be asked to participate in this study if you meet the criteria described on page 5. If you agree to participate in this study, please sign the informed consent form.

2. Registration/Random assignment

If you consent to participate in this study, an attending physician will register you onto a specific website for random assignment. Following this, you will be informed which intervention (treatment) you will receive by an attending physician.

3. At the registration or observation point, day one (baseline)
The tests conducted at the registration or observation point on day one (baseline) are as follows:

- Vital signs, PCR tests, general blood tests, special blood tests, chest radiography, computerized tomography, special nasal drip tests, safety information (adverse events*).

*Adverse events are designated as untoward medical events, including worsening of a pre-existing underlying disease.

4 Start of intervention (treatment)/supply of diary

As described on page 6, you will be asked to start receiving the study intervention (treatment) based on your assigned group.

In addition, a diary is supplied to you. Please record the following information every day during the participation period of this study (until observation point day 14).

- Meal intake.

- On a four-point scale, subjective symptoms (cough, shortness of breath, fatigue, headaches, loss of smell, loss of taste, and general unwellness). Since this is important information in this study, please record all symptoms.

- Use of medical agents.
⑤ Observation point day four

The tests conducted on days three to five during hospitalization are as follows:

- Vital signs, PCR tests, general blood tests, special blood tests, chest radiography, computerized tomography, special nasal drip tests, and safety information (adverse events).

⑥ Observation point day eight

The tests conducted on days seven to nine during hospitalization are as follows:

- Vital signs, PCR tests, general blood tests, special blood tests, chest radiography, computerized tomography, special nasal drip tests, and safety information (adverse events).

⑦ Observation point day 14

The ambulatory tests conducted on days 14 to 17 are as follows.

- Vital signs, PCR tests, general blood tests, special blood tests, chest radiography, computerized tomography, special nasal drip tests, and safety information (adverse events).

⑧ Sample preservation (serum)
For future study, serum (7 mL × four times) will be obtained and preserved at Nagasaki University Hospital, Department of Respiratory Medicine, for ten years after the end of this study.

(3) Schedule

The tests and investigations in this study will be conducted based on the following schedule.

<table>
<thead>
<tr>
<th>Observation items</th>
<th>Registration</th>
<th>day 1</th>
<th>day 2</th>
<th>day 3</th>
<th>day 4 (± 1 day)</th>
<th>day 5</th>
<th>day 6</th>
<th>day 7</th>
<th>day 8 (± 1 day)</th>
<th>day 14 (± 3 days)</th>
<th>discontinuation</th>
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<tbody>
<tr>
<td>1. Eligibility</td>
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<td>2. Subjects’ characteristics</td>
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<td>3. Severity of COVID-19</td>
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<td>4. Vital signs</td>
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<td>5. Quantity of oxygen administration</td>
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<td>6. PCR test for SARS-CoV-2</td>
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<td>7. Hematology tests</td>
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<td>8. General blood biochemical tests</td>
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<td>9. Blood coagulation tests</td>
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<td>10. Chest radiography and computed tomography</td>
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<td>11. Nasal drip tests</td>
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<td>12. Special blood tests</td>
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<td>13. Medication adherence of study agent</td>
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<td>14. Medications of other pharmaceutical agents</td>
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<td>15. Meal intake</td>
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<td>16. Subjective symptoms</td>
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<td>17. Adverse events</td>
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<td>18. Preservation of blood serum</td>
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- Mandatory item, △ Optional item

* Data should be obtained before administration of the study agent in groups A or B.
** Data obtained within 72 h before consent can be used in all groups.

*** Length of hospital stay can be changed based on the subjects' disease condition.

(4) Observation items

All tests and investigations will be conducted according to the schedule described above.

1. Eligibility

   Sex, date of birth (age), inclusion and exclusion criteria, and date that consent is obtained.

2. Background characteristics

   Height, weight, BMI, date of COVID-19 onset, date of SARS-CoV-2 detection, date of hospitalization, anamnesis, and comorbidities.

3. Severity of COVID-19

   i) Severity classification according to the COVID-19 Infectious Disease Treatment Guidelines by the Ministry of Health, Labour and Welfare in Japan.
ii) Pneumonia severity index.

iii) A-DROP is defined in the guidelines for the management of community-acquired pneumonia in adults released from the Japanese Respiratory Society.

4. Vital signs

Body temperature, blood pressure, pulse SpO$_2$, frequency of breath

*SpO$_2$ is recorded daily during hospitalization.

5. Quantity of oxygen administration

Daily quantity of oxygen administration during hospitalization.

6. PCR test for SARS-CoV-2

The nasal mucosa is sampled by nasopharynx swabbing. The viral load of SARS-CoV-2 will be tested by PCR to amplify the viral gene.

7. Hematology testing

Red blood cells, hemoglobin, hematocrit, white blood cells, neutrophils, lymphocytes, eosinophils, monocytes, basophils, and platelets.
8. General blood biochemical tests

- Total bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-guanosine triphosphate, total cholesterol, total protein, albumin, blood urea nitrogen, creatinine, estimated glomerular filtration rate based on creatinine, lactate dehydrogenase, creatine phosphokinase, brain natriuretic peptide, troponin T, C-reactive protein, procalcitonin, ferritin, Na, pH, HbA1c, and glucose.

9. Blood coagulation tests

- Prothrombin time, activated partial thromboplastin time, and d-dimer.

10. Chest radiography and computerized tomography

- Condition of pneumonia.

11. Nasal drip tests

- Interleukin (IL)-1beta, IL-6, IL-8, IL-10, IL-17, tumor necrosis factor-alpha, interferon-gamma, beta-defensin, granulocyte-macrophage colony-stimulating factor, and immunoglobulin A.
12. Special blood tests

Cytokines, chemokines, IL-33, immunoglobulin M, immunoglobulin G, and immunoglobulin A.

13. Medication adherence of study agent

You are asked to record whether you take clarithromycin every day in a diary.

14. Other pharmaceutical agents/medications

Use of pharmaceutical agents other than clarithromycin.

15. Meal intake

You are asked to record your meal intake every day in the diary provided.

16. Subjective symptoms

You are asked to record your subjective symptoms (cough, shortness of breath, fatigue, headaches, loss of smell, loss of taste, and general unwellness) on a four-point scale every day in a diary.

17. Adverse events

During the observation period of each participant, information on adverse events
(any untoward medical events, including the worsening of a pre-existing underlying disease) will be collected.

(5) Prohibited drugs

The following drugs are prohibited during participation in this study:

- Macrolide antimicrobial agents
- Immunosuppressive agents
- Anticancer agents

If severe risk is expected by prohibiting the drugs above, the attending physician will take appropriate measures, such as discontinuation of the study intervention.

(6) Restricted drugs and treatments

No drug or treatment is restricted in this study.

However, please tell your attending physician if you need to start taking a new drug or treatment.

(7) Participation period

If you agree to participate in this study, the participation period will be 14 days (+ three days).

If you withdraw your consent, your participation will end at the time of withdrawal.
(8) Discontinuation of study in each participant

If any of the following occurs, your participation in this study may be discontinued, even after you agree to participate in this study:

1) When you voluntarily want to discontinue the study or withdraw consent to participate in this study.

2) If the attending physician identifies a significant issue after the registration that may affect the study.

3) When the continuation of the study agent is judged not to be appropriate due to worsening of the primary disease or complications.

4) When continuation of the study is judged to be difficult due to the occurrence of any adverse events.

5) If pregnancy is found.

6) When investigators judge that discontinuation of the study is appropriate due to other reasons.

<Measurements after discontinuation>

If your participation in this study is discontinued, data obtained until discontinuation will be used. In addition, even if your participation in the study is discontinued, follow-up observations will be frequently conducted to ensure your safety.
(9) Treatment after the participation period

If further treatment for COVID-19 is required after discharge from the hospital or after the observation period of this study, standard treatment will be provided to you.

(10) Provision of test results

You can review your test results obtained in this study if you ask your attending physician.

7. Other treatments

Many types of drugs other than the study agent in this study are available for COVID-19, and various treatment methods have been tested for COVID-19. However, no treatment strategy has yet been established for COVID-19.

If you do not participate in this study, the standard treatment for COVID-19 will be provided to you. Ask the attending physician for details on this standard treatment.

8. Study execution period

(1) Study execution period.

From the date of publication of this study on jRCT to July 31, 2022.
(2) Patient enrollment period:

From the date of publication of this study on jRCT to February 28, 2022.

9. Number of participants

We plan to enroll 60 patients in this study.

10. Expected benefits, burden, and side effects

(1) Expected benefits

If you participate in this study, nasal drip tests and special blood tests will be performed. The fees for these tests will be funded by the study. Thus, participating in this study could reduce your financial burden.

In addition, since the attending physicians review your condition more carefully than usual, you may receive more thorough treatment than if you do not participate in this study.

Furthermore, since the results of this study may contribute to the future treatment of patients with COVID-19, your participation in this study may benefit society as a whole.

(2) Expected burden
If you participate in this study, you need to be hospitalized for about eight days as a
general health insurance treatment. In addition, several tests are required to be
conducted as part of this study (PCR, nasal drip, and special blood tests). PCR tests will
be conducted at registration or observation point day one (baseline), observation point
day four, and observation point day eight (three times). Nasal drip tests will be conducted
at registration or observation point day one (baseline), observation point day four,
observation point day eight, and observation point day 14 (four times). For the special
blood tests, an additional 7 mL/time of blood will be collected in addition to general blood
collection at registration or observation point day one (baseline), observation point day
four, observation point day eight, and observation point day 14 (four times). If you feel
unwell during the tests, the tests will be immediately discontinued, and appropriate
measures will be taken. Furthermore, for the preservation of serum for future studies, an
additional 7 mL/time of blood will be collected at registration or observation point day
one (baseline), observation point day four, observation point day eight, and observation
point day 14 (four times).

Since random assignment is conducted, you may not receive the treatment you would
prefer.

In addition, clarithromycin administration may cause side effects, as described below.
You also need to record your meal intake and subjective symptoms in a diary every day
during your participation period.
(3) Expected side effects

<Known severe side effects of clarithromycin>

(from the package insert of Clarith tablets 200; version September 2, 2020)

Shock, anaphylaxis (frequency unknown), QT prolongation, ventricular tachycardia (including torsades de pointes), ventricular fibrillation (frequency unknown), fulminant hepatitis, hepatic dysfunction, jaundice, hepatic failure (frequency unknown), thrombocytopenia, pancytopenia, hemolytic anemia, leukopenia, agranulocytosis (frequency unknown), toxic epidermal necrolysis (TEN) (frequency unknown), TEN, Stevens-Johnson syndrome group, erythema multiforme (frequency unknown), PIE syndrome group, interstitial pneumonia (frequency unknown), pseudomembranous colitis, hemorrhagic colitis (frequency unknown), rhabdomyolysis (frequency unknown), seizure (frequency unknown), IgA vasculitis (frequency unknown), and drug-induced hypersensitivity syndrome group (frequency unknown).

Other side effects that are not described above may also occur. If you notice anything unusual, please inform your attending physician.

If any information that may affect your decision to continue participating in this study becomes apparent during the participation period, we will immediately inform you. In such
cases, you may be asked to sign a further informed consent form.

11. Compensation against health hazards

This study has been scientifically planned based on previous studies and will be carefully conducted. If any health hazards, such as side effects, occur during or after the study, an attending physician will provide appropriate treatment. If you notice anything unusual, please inform your attending physician.

This study is covered by “clinical research insurance” in case of emergency. Suppose you suffer health problems because of participating in this research, and it is determined that there is a causal relationship with this research (or that a causal relationship cannot be denied). In that case, the clinical research insurance will provide monetary compensation to you or your family for death, permanent disability, or medical expenses and benefits necessary to treat the health problems. In addition, the principal investigator and subcontracting physicians will be covered by the physician’s liability insurance in case of any negligence issues. However, health damage caused by intentional or gross negligence may not be covered, or compensation may be limited.
12. Your financial burden and remuneration

<Your financial burden>

You need to receive treatment while hospitalized for about eight days as general health insurance treatment. The days of hospitalization may change based on the disease condition. The fees for the tests required and the study agent (clarithromycin) are funded by this study.

<Remuneration>

For participating in the study (tests and diary recording), you will receive 5,000 yen after observation point day eight (at discharge) and observation point day 14 (ambulatory tests) (a total of 10,000 yen) on a QUO card.

13. Information about this study

If you want to know more information about this study (study plan or other relevant information), this can be provided to you except for the personal information of other participants or the information that may affect the study execution. Please ask your attending physician if you require further information.

A summary of the study plan is also publicly available at jRCT
(https://jrcr.niph.go.jp/). Personal information will continue to be protected, even when the results of this study are published.

14. Protection of personal information

To protect personal information, a number (so called “central registration number”) will be assigned to each participant. This central registration number is used for all information or samples in this study (anonymization). A table will be used to identify you and your central registration number. This table will be stored only at this medical institution and will not be supplied to other medical institutions.

To ensure that this study is conducted properly, monitoring/auditing staff or staff from the Ministry of Health, Labour, and Welfare may survey your medical records directly. Such monitoring and auditing is conducted in accordance with the Personal Information Protection Act, and private information (name, address, and telephone number) is protected. By signing the informed consent form of this study, you consent to your records being audited in the future.

The results of this study may be published at scientific meetings, in articles, or in documents that need to be submitted to the Ministry of Health, Labour and Welfare. However, identifiable information will not be provided outside of this medical institution.
15. Provision and storage of information and samples

(1) Provision of information and samples

This is a multicenter study.

The information obtained in this study will be stored at a third-party data center (Soiken Inc.). Your information will be collected using a central registration number, as is described in ‘14. Protection of personal information’.

The samples obtained in this study (nasal drip, blood, PCR test samples) will be sent to the test department at Nagasaki University Hospital to measure the levels of inflammatory cytokines. Samples or images of chest radiography and computerized tomography will be collected using the central registration number, as is described in ‘14. Protection of personal information’.

Your personal information will not be disclosed to anyone outside of this medical institution.

(2) Storage of information and samples

Your samples obtained in this study (nasal drip, blood, PCR test samples) will be sent to the test department at Nagasaki University Hospital to measure the levels of inflammatory cytokines. Samples will then be stored at the Department of Respiratory Medicine, Nagasaki University Hospital, for ten years.
Appropriate measures will be taken to avoid personal information being disclosed to others outside our medical institution when discarding the samples.

All information is stored during the study and five years after the end of this study. After the end of the storage period, all information, including your data, will be anonymized and destroyed physically or electromagnetically.

16. **Secondary use of samples obtained in this study**

Since blood samples obtained from you in this study may be important for future medical studies, your blood sample (serum) will be stored for ten years after the end of this study. If the samples are secondarily used for future studies, protocols for the studies will be developed and then reviewed by an appropriate institutional review board.

After the end of the storage period, Nagasaki University Hospital will discard the samples according to the rules of our institution.

17. **Discontinuation of the whole study**

Even after participating in this study, the study itself could be discontinued in the following cases:

1) Critical information about the quality, safety, and efficacy of the study agent is
obtained.

2) The recruiting of study subjects is difficult, and the planned number of study subjects to be enrolled is challenging to achieve.

3) If the study results can be expected before the achievement of the planned number of study subjects, based on the purpose or contents of this study.

4) The purpose of this study was achieved before the achievement of the planned number of study subjects or before the end of the study execution period.

5) When a protocol modification is required but unable to be executed.

18. Things you need to comply with during the study

To ensure your safety and the collection of accurate information, please comply with
the following during the study:

- Take the study agent in accordance with the dose and usage instructions of the attending physician.
- Record your medication, meal intake, and your subjective symptoms in your diary every day.
- If you are taking any medical agents prescribed by another department or institution or over-the-counter drugs bought at a pharmacy, please inform your attending physician.
- When you want to discontinue the study or withdraw your consent to participate in this study, at any time, even before or after the start of the study intervention (treatment), inform the attending physician as soon as possible.
- Visit the medical institution and take the required tests and examinations on the date and time instructed by your attending physician.
- If you receive a consultation from another department or institution, please inform your attending physician. In addition, please inform your attending physician before any such consultations, if possible.
- **If you notice anything unusual (including bone fracture or accident), inform one of the attending physicians as soon as possible.**
19. Conflicts of interest and source of study funding

(1) Conflict of interest

Conflict of interest refers to a situation in which a third-party may be concerned that research is not being conducted fairly and appropriately, such as falsification of research data or preferential treatment of a specific company, due to financial interests with an outside party.

The principal investigator of this study, the responsible investigator and sub-investigators in each medical institution for conducting the study, and other persons related to this study have reported any such conflicts of interest. The management standards of the conflict of interest and management plan of the conflicts of interest identified have been submitted, inspected, and approved by the Clinical Research Review Board of Nagasaki University.

(2) Funder of this study

This study was financially supported by Taisho Pharmaceutical Co., Ltd. (3-24-1, Takada, Toshima-ku, Tokyo). Taisho Pharmaceutical Co., Ltd. was not involved in this study, including its planning, execution, data management, statistical analysis, evaluation, or write-up.
20. Intellectual property rights

The results of this study may result in intellectual property rights such as patent rights. However, the principal investigator will own any such intellectual property rights, not the participants.

21. Study organizations

«Principal investigator»

Prof. Hiroshi Mukae

Department of Respiratory Medicine, Nagasaki University Hospital

Address: 1-7-1, Sakamoto, Nagasaki, Nagasaki

Tel: 095-819-7271

«Collaborating medical institutions and responsible investigators»

<table>
<thead>
<tr>
<th>Medical institution</th>
<th>Responsible investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagasaki University Hospital</td>
<td>Hiroshi Mukae</td>
</tr>
<tr>
<td>1-7-1, Sakamoto, Nagasaki, Nagasaki</td>
<td></td>
</tr>
<tr>
<td>095-819-7271</td>
<td></td>
</tr>
<tr>
<td>Nagasaki Harbor Medical Center</td>
<td>Toyomitsu Sawai</td>
</tr>
<tr>
<td>Hospital</td>
<td>Address</td>
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<tr>
<td>Sasebo City General Hospital</td>
<td>9-3, Hirase-machi, Sasebo, Nagasaki</td>
</tr>
<tr>
<td>Japan Community Health care Organization Isahaya General Hospital</td>
<td>24-1, Eisyo-Higashi-machi, Isahaya, Nagasaki</td>
</tr>
<tr>
<td>Japanese Red Cross Nagasaki Genbaku Hospital</td>
<td>3-15, Shigesato-cho, Nagasaki, Nagasaki</td>
</tr>
<tr>
<td>Hospital of the University of Occupational and Environmental Health, Japan</td>
<td>1-1, Iseigaoka, Yahata-Nishi-ku, Kitakyushu, Fukuoka</td>
</tr>
<tr>
<td>Wakamatsu Hospital of the University of Occupational and Environmental Health, Japan</td>
<td>1-17-1, Hama-cho, Wakamatsu-ku, Kitakyusyu, Fukuoka</td>
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<tr>
<td>093-761-0090</td>
<td>Kitakyusyu City Yahata Hospital</td>
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<tr>
<td></td>
<td>2-6-2, Ogura, Yahata-Higashi-ku, Kitakyusyu, Fukuoka</td>
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<td>093-662-6565</td>
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<td>Fukuoka University Chikushi Hospital</td>
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<td></td>
<td>1-1-1, Zokumyouin, Chikuno, Fukuoka</td>
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<td>092-921-1011</td>
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<td></td>
<td>Saiseikai Nagasaki Hospital</td>
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<tr>
<td></td>
<td>2-5-1, Katafuchi, Nagasaki</td>
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<tr>
<td></td>
<td>095-826-9236</td>
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</tbody>
</table>

**22. Contact details**

If you would like more information or have any concerns, do not hesitate to contact the following:

Person in charge: ____________________________

Department: ____________________________
Address: ________________________________

Tel: ________________________________

23. Consultation regarding your opinions and complaints

__________ established a consultation service for patients and their families (excluding medical treatments and contents of the clinical study).

Consultation service: ________________________________

Address: ________________________________

Tel: ________________________________
Informed Consent Form

CAME COVID study

“CAM (Clarithromycin) Effectivity for COVID-19 pneumonia which does not require oxygen administration. A multicenter, randomized-controlled, open-label, three-armed parallel group comparison, exploratory trial.”

<Contents to be explained>

1. Introduction
2. What is a clinical trial?
3. About your disease
4. Background, purpose, and significance of this study
5. Study agent in this study
6. Methods of this study
7. Other treatments
8. Study execution period
9. Number of participants
10. Expected benefits, burden, and side effects
11. Compensation against health hazards
12. Your financial burden and remuneration
13. Information about this study
14. Protection of personal information
15. Provision and storage of information and samples
16. Secondary use of samples obtained in this study
17. Discontinuation of the whole study
18. Things you need to comply with during the study
19. Conflicts of interest and source of study funding
20. Intellectual property rights
21. Study organizations
22. Contact details
23. Consultation regarding your opinions and complaints

● I have explained the study to the patient.

Date of explanation: ___________________________
Signature of explainer: ________________

● I received a full explanation of the study, have understood its aim, what is expected, and agree to participate in this study of my own free will.

I received the informed consent documents and a copy of this informed consent form.

Date of consent: ______________________

Your signature: ______________________
Consent Withdrawal Form

________________________

________________________

CAME COVID study

“CAM (Clarithromycin) Effectivity for COVID-19 pneumonia which does not require oxygen administration. A multicenter, randomized-controlled, open-label, three-armed parallel group comparison, exploratory trial.”

● Although I received a full explanation of the study and initially agreed to participate, I would now like to withdraw my consent.

Date of withdrawal: ________________________

Your signature: ________________________
I confirm that the patient signed the above form to withdraw their consent.

Date of confirmation: ______________________

Signature of physician: ______________________