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

## Summary

| | |
|---|---|
| EudraCT number | 2020-003475-18 |
| Trial protocol | BE |
| Global end of trial date | 24 June 2021 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 05 May 2024 |
| First version publication date | 05 May 2024 |
| Summary attachment (see zip file) | Final Study Report (2020-003475-18_Final study report_signed.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | COV-AAT |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Ghent University Hospital |
| Sponsor organisation address | Corneel Heymanslaan 10, Ghent, Belgium, 9000 |
| Public contact | HIRUZ, Ghent University Hospital, +32 93320500, sophie.degroote@uzgent.be |
| Scientific contact | HIRUZ, Ghent University Hospital, 0477552757 93320500, sophie.degroote@uzgent.be |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 12 July 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 24 June 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 June 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The aim of the study is to assess whether Camostat, a serine protease inhibitor available in an oral formulation, has the potential to be studied as an antiviral drug in a large scale ambulatory setting to prevent transmission by decreasing viral load, to prevent symptoms after exposure (PEP) in asymptomatic individuals or to prevent disease progression in the occurrence of early symptomatology. In this pilot we will assess efficacy of the drug in terms of viral load changes at D5 compared to baseline in nasopharyngeal (or nose/throat) swabs. Cycle threshold values will be used as a surrogate for viral load.

Descriptive objectives are to assess the safety and compliance of the drug in ambulatory setting.

Protection of trial subjects:

As a precautionary measure to reduce the risk of syncope, blood sampling was performed in a semi-suppine position.

Subjects were followed-up through a home monitoring tool provided by Byteflies. The subject was asked to register heart rate, respiratory rate, temperature and oxygen saturation 3 times a day through an online platform (with back-up through email and phone). If these parameters were not within normal range as defined by cut-off criteria, the system asked either to remeasure or to contact the study-team based on the reported values. The physician checked these parameters daily, calling the patient herself if a parameter was out of normal range.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 30 November 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Belgium: 108 |
| Worldwide total number of subjects | 108 |
| EEA total number of subjects | 108 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

| | |
|---|---|
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 101 |
| From 65 to 84 years | 7 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Between November 2020 and June 2021, a total of 108 participants were enrolled in the study (first patient first vist: 6NOV2020; last patient last visit: 24JUN2021).

### Pre-assignment

Screening details:

12 subjects did not meet the in- and exclusion criteria and were excluded from randomization: 11 screen failures (Covid-19 PCR Ct >30 at screening: N=6, negative Covid-19 PCR at screening: N=1, negative Covid-19 PCR at rescreening: N=4) + 1 sampling failure at baseline. 96 participants received either camostat mesylate (N=66) or placebo (N=30).

### Period 1

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

Blinding implementation details:

The subject and all nursus/physicians that were in contact with the subject were blinded.

To minimize the risk for unblinding: 2 co-workers were delegated as unblinded personnel at the clinic. 2 others were assigned as back-up for the 2 co-workers. Unblinded personnel and their study activities were documented on the delegation log. Unblinded personnel at the clinic did not have contact with subjects. Communication between unblinded and blinded personnel concerning allocation was traceable.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Camostat Mesilate |

Arm description:

Participants should take this medication 3 times a day during 5 consecutive days. In patients with a positive PCR at day 5 (CT value with threshold below 30) and/or presence of clinical symptoms after exclusion of hospitalization criteria, the treatment will be extended up to D10 at the same dosage in both treatment arms for 5 consecutive days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Camostat Mesilate |
| Investigational medicinal product code | |
| Other name | Foipan |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Camostat Mesilate (Foipan) 100mg, 3 tablets, 3 times a day (daily dose of 900mg). After inclusion the patient will receive medication for 5 days of treatment (= 45 tablets). The patient will take the medication at home. Oral administration. Fasting state (minimum 60 minutes before the next meal and 2 hours after the previous meal). At D5, the patient will bring the empty bottle and leftover tablets to the consultation visit.
If the treatment is extended to 10 days, the patient will receive medication at D5 for 5 days of treatment (= 45 tablets). He will take the medication at home and orally in a fasting state (minimum 60 minutes before the next meal and 2 hours after the previous meal). At D10, the patient will bring the empty bottle and leftover tablets to the consultation visit.

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Participants should take this medication 3 times a day during 5 consecutive days. In patients with a positive PCR at day 5 (CT value with threshold below 30) and/or presence of clinical symptoms after exclusion of hospitalization criteria, the treatment will be extended up to D10 at the same dosage in

both treatment arms for 5 consecutive days.

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

Dosage and administration details:

After inclusion the patient will receive medication for 5 days of treatment (= 45 tablets). The patient will take the medication at home. Oral administration. Fasting state (minimum 60 minutes before the next meal and minimum 2 hours after the previous meal). At D5, the patient will bring the empty bottle and leftover tablets to the consultation visit.
If the treatment is extended to 10 days, the patient will receive medication at D5 for 5 days of treatment (= 45 tablets). He will take the medication at home and orally in a fasting state (minimum 60 minutes before the next meal and minimum 2 hours after the previous meal). At D10, the patient will bring the empty bottle and leftover tablets to the consultation visit.

| **Number of subjects in period 1[1]** | Camostat Mesilate | Placebo |
|---|---|---|
| Started | 66 | 30 |
| Completed | 61 | 29 |
| Not completed | 5 | 1 |
| Consent withdrawn by subject | 2 | - |
| Adverse event, non-fatal | 3 | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 108 enrolled participants, 12 subjects did not meet the in-and exclusion criteria for randomization. A total of 96 participants received either camostat mesylate (N=66) or placebo (N=30). Analyses were performed on the data of of 90 participants who completed treatment (N=61 camostat mesylate, N=29 placebo).

## Baseline characteristics

### Reporting groups

| Reporting group title | Camostat Mesilate |
|---|---|

Reporting group description:

Participants should take this medication 3 times a day during 5 consecutive days. In patients with a positive PCR at day 5 (CT value with threshold below 30) and/or presence of clinical symptoms after exclusion of hospitalization criteria, the treatment will be extended up to D10 at the same dosage in both treatment arms for 5 consecutive days.

| Reporting group title | Placebo |
|---|---|

Reporting group description:

Participants should take this medication 3 times a day during 5 consecutive days. In patients with a positive PCR at day 5 (CT value with threshold below 30) and/or presence of clinical symptoms after exclusion of hospitalization criteria, the treatment will be extended up to D10 at the same dosage in both treatment arms for 5 consecutive days.

| Reporting group values | Camostat Mesilate | Placebo | Total |
|---|---|---|---|
| Number of subjects | 66 | 30 | 96 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 61 | 28 | 89 |
| From 65-84 years | 5 | 2 | 7 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Median age was 40 (IQR 24-53).<br>Camostat mesylate group: mean age 38 years (IQR 25-53).<br>Placebo group: mean age 37 years (IQR 22-51). | | | |
| Units: years | | | |
| median | 37.5 | 35.00 | |
| inter-quartile range (Q1-Q3) | 24.75 to 53.00 | 21.75 to 49.50 | - |
| Gender categorical | | | |
| In total, 49 participants (54.4%) were female.<br>Camostat mesylate group: 33 (54.1%)<br>Placebo group: 16 (55.2%) | | | |
| Units: Subjects | | | |
| Female | 36 | 17 | 53 |
| Male | 30 | 13 | 43 |

### Subject analysis sets

| Subject analysis set title | Per protocol analysis |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

A total of 96 participants received either camostat mesylate (N=66) or placebo (N=30). Treatment was immediately interrupted in 4 subjects that had to be hospitalized due to clinical deterioration. Two other

subjects chose to withdraw from the study. Analyses were performed on the data of 90 participants who completed treatment (N=61 camostat mesylate, N=29 placebo).

| **Reporting group values** | Per protocol analysis | | |
|---|---|---|---|
| Number of subjects | 90 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 83 | | |
| From 65-84 years | 7 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Median age was 40 (IQR 24-53).<br>Camostat mesylate group: mean age 38 years (IQR 25-53).<br>Placebo group: mean age 37 years (IQR 22-51). | | | |
| Units: years | | | |
| median | 40 | | |
| inter-quartile range (Q1-Q3) | 24 to 53 | | |
| Gender categorical | | | |
| In total, 49 participants (54.4%) were female.<br>Camostat mesylate group: 33 (54.1%)<br>Placebo group: 16 (55.2%) | | | |
| Units: Subjects | | | |
| Female | 49 | | |
| Male | 41 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Camostat Mesilate |

Reporting group description:

Participants should take this medication 3 times a day during 5 consecutive days. In patients with a positive PCR at day 5 (CT value with threshold below 30) and/or presence of clinical symptoms after exclusion of hospitalization criteria, the treatment will be extended up to D10 at the same dosage in both treatment arms for 5 consecutive days.

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Participants should take this medication 3 times a day during 5 consecutive days. In patients with a positive PCR at day 5 (CT value with threshold below 30) and/or presence of clinical symptoms after exclusion of hospitalization criteria, the treatment will be extended up to D10 at the same dosage in both treatment arms for 5 consecutive days.

| | |
|---|---|
| Subject analysis set title | Per protocol analysis |
| Subject analysis set type | Per protocol |

Subject analysis set description:

A total of 96 participants received either camostat mesylate (N=66) or placebo (N=30). Treatment was immediately interrupted in 4 subjects that had to be hospitalized due to clinical deterioration. Two other subjects chose to withdraw from the study. Analyses were performed on the data of 90 participants who completed treatment (N=61 camostat mesylate, N=29 placebo).

### Primary: Drug efficacy in Terms of Viral Load

| | |
|---|---|
| End point title | Drug efficacy in Terms of Viral Load |

End point description:

to assess drug efficacy as change in the shedding of SARS-CoV-2 virus as measured by Ct obtained from nasopharyngeal swabs at day 1 and 5.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

from day 1 to day 5

| End point values | Camostat Mesilate | Placebo | Per protocol analysis | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 66 | 30 | 90 | |
| Units: number of cycles | 66 | 30 | 90 | |

| | |
|---|---|
| **Attachments (see zip file)** | PCR Ct at baseline and at day 5 visit/Fig2_Ct change.png |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | linear mixed-effects model |

Statistical analysis description:

Change in Ct between day 1 and day 5 was compared using a linear mixed-effects model with random intercepts for participant. Estimates for change in Ct for camostat compared to placebo and corresponding 95% confidence intervals for the linear models were reported.

| | |
|---|---|
| Comparison groups | Camostat Mesilate v Placebo v Per protocol analysis |

| | |
|---|---|
| Number of subjects included in analysis | 186 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.511 [1] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.183 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 100 |

Notes:

[1] - The estimated mean change in Ct between day 1 and day 5 between the camostat and placebo group was significantly not different.

## Secondary: (Time to) clinical improvement

| | |
|---|---|
| End point title | (Time to) clinical improvement |

End point description:

an improvement of the 5 most self-reported symptoms in at least 1 point from baseline on the 5-point Likert scale, which ever came first

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

14 days

| End point values | Camostat Mesilate | Placebo | Per protocol analysis | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 61 | 29 | 86[2] | |
| Units: total numbers (%) | 61 | 29 | 86 | |

Notes:

[2] - Out of 90 subjects, 4 did not fill out the questionnaire at baseline and consequently, the data of 8

| | |
|---|---|
| **Attachments (see zip file)** | Kaplan-Meier curve for time to clinical |

## Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Cox proportional-hazards model |

Statistical analysis description:

A Kaplan Meier curve was constructed for time to clinical improvement. Hazard ratios with 95% confidence intervals (CI) were estimated by Cox proportional-hazards model with and without adjustment for potential confounders. Patients were censored at time of last assessment or at end of trial. A two-sided α value of less than 0.05 was considered significant.

| | |
|---|---|
| Comparison groups | Camostat Mesilate v Placebo v Per protocol analysis |

| | |
|---|---|
| Number of subjects included in analysis | 176 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.511 |
| Method | see attachement |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: from day 1 to day 28 visit | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

| Reporting groups | |
|---|---|
| Reporting group title | camostat mesylate group |

Reporting group description: -

| Serious adverse events | camostat mesylate group | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 66 (4.55%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hospitalisation | | | |
| subjects affected / exposed | 3 / 66 (4.55%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | camostat mesylate group | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 66 (84.85%) | | |
| Investigations | | | |
| Neutropenia | | | |
| subjects affected / exposed | 9 / 66 (13.64%) | | |
| occurrences (all) | 9 | | |
| Leukopenia | | | |
| subjects affected / exposed | 7 / 66 (10.61%) | | |
| occurrences (all) | 7 | | |
| CRP increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 4 | | |
| lymphopenia | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | | |
| occurrences (all) | 4 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 66 (7.58%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 19 / 66 (28.79%) | | |
| occurrences (all) | 19 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 66 (10.61%) | | |
| occurrences (all) | 7 | | |
| Nausea | | | |
| subjects affected / exposed | 9 / 66 (13.64%) | | |
| occurrences (all) | 9 | | |
| Metabolism and nutrition disorders | | | |
| change in appetite | | | |
| subjects affected / exposed | 9 / 66 (13.64%) | | |
| occurrences (all) | 9 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 24 June 2021 | When recruitment dropped significantly (no inclusions for more than 2 weeks), we decided to interrupt the inclusion to perform an interim analysis according to the study protocol. The data of 90 participants, being 68.2% of the totally intended inclusion number were analysed. All included participants got a full follow-up until V28. | - |

Notes:

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

A limitation of our study is that the study visits were scheduled within a range of different days. Nevertheless, we did control for this variance in the linear mixed-effects model analysis.

Notes: