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 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). Camostat mesylate group: mean age 38 years (IQR 25-53). 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. Camostat mesylate group: 33 (54.1%) 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 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). Camostat mesylate group: mean age 38 years (IQR 25-53). 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. Camostat mesylate group: 33 (54.1%) 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: