Should camostat mesilate be used in the treatment of COVID-19?

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This rapid review summarizes the available evidence on the efficacy and safety of camostat mesilate in treating patients with COVID-19. This may change as new evidence emerges.

KEY FINDINGS

There is currently insufficient evidence on the use of camostat mesilate in the treatment of COVID-19 patients.

- **Camostat mesilate is approved and used in Japan for the treatment of acute symptoms of chronic pancreatitis and postoperative reflux esophagitis**
- **SARS-CoV-2 uses the serine protease TMPRSS2 for spike protein priming. Camostat mesilate blocks TMPRSS2 and has been shown to inhibit infection with SARS-CoV-2 in vitro.**
- **There is currently insufficient evidence to support the use of camostat mesialte for COVID-19 patients**
- **Currently, there are five (5) ongoing trials on the use of camostat mesilate for the treatment of COVID-19 patients**
- **To date, there is no mention of camostat mesilate in the WHO Interim Guidance, US CDC Clinical Interim Guidelines, and Chinese Clinical Guidance for COVID-19 management**

RESULTS

Characteristics of Included Studies

Currently there are no completed studies or clinical trials on the use of camostat mesilate for the treatment of COVID-19. However, five (5) relevant trials registered in *Clinicaltrials.gov* were found. Three (3) trials are currently in the recruitment phase. (8–12)

Recommendations from Other Guidelines

- To date, no formal recommendations were given for camostat mesilate in the WHO, CDC, Infectious Diseases Society of America, and Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment.(13–16)

CONCLUSION

- At present, there is insufficient evidence to support the use of camostat mesialte for COVID-19 patients

Declaration of Conflict of Interest

No conflict of interest

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Appendix 1. Characteristics of clinical trials

No.	Clinical Trial ID / Title	Status	Start and estimated primary completion date	Study design	Country	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	The Impact of Camostat Mesilate on COVID-19 Infection: An Investigator-initiated Randomized, Placebo-controlled, Phase IIa Trial (CamoCO-19)	Recruiting	4 April to 31 December 2020	Randomized controlled trial	Denmark	**Cohort 1 (Hospitalized patients)** Documented COVID-19 infection as evidenced by positive PCR (or comparable clinical assay) for SARS-CoV-2 Less than 48 hours since time of hospital admission OR if hospital-acquired COVID-19 is suspected, less than 48 hrs since onset of symptoms Adolescents and adults age >=18 years Subject or legally authorized representative able to give informed consent Admitted to hospital **Cohort 2 (Outpatients)** Documented COVID-19 infection as evidenced by positive PCR (or comparable clinical assay) for SARS-CoV-2 One or more of the following symptoms of COVID-19 infection: fever, cough, expectoration, shortness of breath, myalgia, fatigue, or head ache No more than 5 days since the beginning of symptom onset Adolescents and adults age >=18 years Subject (or legally authorized representative, for Cohort 1 only) able to give informed consent	Camostat mesilate 100mg/pill 2 pills 3 times daily for 5 days	Placebo 2 pills 3 times daily for 5 days	<u>Primary outcome measure:</u> *Cohort 1:* Days to clinical improvement from study enrolment [Time Frame: 30 days] Clinical improvement defined as live hospital discharge OR a 2-point improvement (from time of enrolment) in disease severity rating on the 7-point ordinal scale *Cohort 2:* Days to clinical improvement from study enrolment [Time Frame: 30 days] Days to clinical improvement from study enrolment defined no fever for at least 48 hrs AND improvement in other symptoms (e.g. cough, expectoration, myalgia, fatigue, or head ache) <u>Secondary outcome measures:</u> Safety evaluation, as measured by AEs, Adverse Reactions (ARs), SAEs, Serious ARs (SARs) [Time Frame: 30 days] Cohort 1: Clinical status as assessed by

						Do not require immediate hospitalization (newly diagnosed COVID-19 patients who are discharged within 24 hrs of hospital admission are eligible for enrollment) Must be willing to fill out a daily symptom diary Must be available for a daily phone call Must be willing to take their own temperature at least once a day			the 7-point ordinal scale at day 7, 14 and 30 [Time Frame: 30 days] The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen; 6) Not hospitalized, limitation on activities; 7) Not hospitalized, no limitations on activities. Cohort 1: Day 30 mortality [Time Frame: 30 days] Mortality Cohort 1: Change in NEW(2) score from baseline to day 30 [Time Frame: 30 days] NEWS2 Cohort 1: Admission to ICU [Time Frame: 30 days] ICU Cohort 1: Use of invasive mechanical ventilation or ECMO [Time Frame: 30 days]

									invasive mechanical ventilation or ECMO Cohort 1: Duration of supplemental oxygen (days) [Time Frame: 30 days] Nasal or high-flow oxygen Cohort 1+2: Days to self-reported recovery (e.g. limitations in daily life activities) during telephone interviews conducted at day 30 [Time Frame: 30 days] Subjective clinical improvement Cohort 2: Number participant-reported secondary infection of housemates [Time Frame: 30 days] No of new COVID-19 infections in the household Cohort 2: Time to hospital admission related to COVID-19 infection [Time Frame: 30 days] Hospital admission
2	Evaluation of the Efficacy and Safety of Camostat Mesilate + Hydroxychloroquine Combination Therapy in Hospitalized Patients With Moderate COVID-19 Infection	Not yet recruiting	01 June 2020 to 01 June 2021	Randomized controlled trial	Germany	Participants ≥18 years of age with SARS-CoV-2 infection confirmed by PCR before randomization Hospitalized and requiring medical care for COVID-19, (status 3 or 4 of 7-point ordinal clinical status scale) SpO2 ≥93% on room air Evidence of pulmonary infiltrate on chest X ray/and or CT scan	Camostat (400 mg tid) + hydroxychloroquine (400 mg bid day1, 200 mg bid d2-d7)	Placebo (tid) + hydroxychloroquine (400 mg bid day1, 200 mg bid d2-d7)	<u>Primary outcome measure:</u> Not hospitalized [Time Frame: day 14 from baseline] <u>Secondary outcome measures:</u> Time to improvement of 2 categories from admission on a 7-point ordinal scale Proportion of participants in each group with normalization of fever Proportion of participants in each group with oxygen

									saturation > 94% on room air for >24h Time to fever normalization (if febrile at baseline) Time to first negative SARS-CoV-2 PCR in NP swap (if pos. at baseline) Time to first negative SARS-CoV-2 PCR in lower respiratory tract specimens (sputum, bronchoalveolar lavage, tracheal aspirate) (if positive at baseline) Duration of oxygen therapy Proportion of participants in each group with need for mechanical ventilation Duration of hospitalization All-cause mortality
3	The Effect of Camostat Mesylate on COVID-19 Infection in Ambulatory Patients: An Investigator-Initiated Randomized, Placebo-Controlled, Phase IIa Trial	Not yet recruiting	30 April 2020 to 31 May 2021	Randomized controlled trial	US	Adults 18 years and older Diagnosed with COVID-19 within past 2 days and not exhibiting manifestations requiring hospitalization For females of reproductive potential: use of highly effective contraception For males of reproductive potential: use of condoms or other methods to ensure effective contraception with partner	Camostat mesylate 200mg taken orally, 3 times daily, for 7 days	Placebo taken orally, 3 times daily, for 7 days	<u>Primary outcome measure:</u> Change in SARS-COV-2 viral load [Time Frame: 2 days] <u>Secondary outcome measures:</u> Change in SARS-COV-2 viral load [Time Frame: 7 days] Change in positive COVID-19 status [Time Frame: 7 days] Change in COVID-19 symptom severity [Time Frame: 7 days] Change in COVID-19 symptom severity [Time Frame: 14 days] Change in COVID-19 symptom frequency [Time Frame: 7 days]

									Change in COVID-19 symptom frequency [Time Frame: 14 days] Change in body temperature [Time Frame: 7 days] Change in body temperature [Time Frame: 14 days]
4	An Open-Label Study to Compare the Efficacy, Safety, and Tolerability of Hydroxychloroquine Combined With Azithromycin Compared to Hydroxychloroquine Combined With Camostat Mesylate and to "no Treatment" in Hospitalized Patients Suffering From a Mild or Moderate SARS CoV 2 Virus (COSTA)	Recruiting	11 April 2020 to 11 October 2020	Randomized controlled trial	Israel	18 years and above COVID-19 confirmed by a real-time RT-PCR tests 7 days prior to clinical trial enrollment Mild disease (no pneumonia) with at least one of the following risk factors: Age > 55, prior lung or kidney disease, DM with HbA1c > 7.6%, hypertension, CVD, immunosupressed, organ transplantation, HIV with a CD4 cell count of less than 250 cells/mm3, heavy smoking, BMI > 30. Moderate disease - pneumonia, Tachypnea > 24 BPM, tachycardia > 125 BPM, O2 saturation 93% or less	Hydroxychloroquine 400 mg BID on day 1 and then 200 mg BID on days 2-5 + Camostat mesilate 200 mg TID for 10 days	Hydroxychloroquine 400 mg BID on day 1 and then 200 mg BID on days 2-5 + Azithromycin 500 mg QD on day 1 and 250 mg QD on days 2-5	<u>Primary outcome measures:</u> Clinical state as reflected by NEWS scoring [Time Frame: 7 days] Positive PCR [Time Frame: 7 days] <u>Secondary outcome measures:</u> Prevention of ICU [Time Frame: 14 days] Prevention of assisted ventilation [Time Frame: 14 days] Prevention of ECMO [Time Frame: 14 days] Death [Time Frame: 14 days] Positive PCR [Time Frame: 14 days]
5	Randomized, Multi-arm Phase II Trial of Novel Agents for Treatment of High-risk COVID-19 Positive Patients	Recruiting	01 May 2020 to May 2021	Randomized controlled trial	US	Age ≥18 years Laboratory-confirmed SARS-CoV-2 infection within the past 7 days or the presence of symptoms or physical examination signs providing high probability of COVID-19 disease Patients must have adequate organ and marrow function measured within the last 6 months Subjects must have at least one of the following high-risk features for clinical deterioration: Hypertension	Camostat mesilate 2 tab TID after a meal (600 mg total daily dose) Days 1-14	Hydroxychloroquine 3 tabs (600 mg total daily dose) Days 1-14 Hydroxychloroquine and Azithromycin Hydroxychloroquine 3 tabs (600 mg total daily dose) Days 1-14 Azithromycin Day 1: 2 tabs (500 mg total daily dose) Days 2-5: 1 tab (250 mg total daily dose)	<u>Primary outcome measure:</u> Clinical deterioration [Time frame: 14 days] Proportion of patients experiencing clinical deterioration. Clinical deterioration is defined as a less than a 2-point change from the initial COVID 7-Point Ordinal Outcomes Scale within 14 days from the study start. This scale ranges from 1-7. Lower scores indicate

						Diabetes Mellitus Moderate to severe Chronic Obstructive Pulmonary Disease, Emphysema or Asthma Immunocompromised Age > 50 BMI > 40 Living in a nursing home or long-term facility Underlying serious heart condition		Hydroxychloroquine and Ivermectin Hydroxychloroquine 3 tabs (600 mg total daily dose) Days 1-14 Ivermectin: Days 1-2: Weight < 75kg: 4 tabs (12 mg total daily dose) Days 1-2: Weight > 75kg: 5 tabs (15 mg total daily dose)	worse outcomes (death); higher scores indicate fewer symptoms and better outcomes. <u>Secondary outcome measures:</u> Change in Viral Load [Time Frame: 40 days] Rate of Organ Failure [Time Frame: 28 days] Progression to ICU Care or Ventilation [Time Frame: 28 days] Change in Clinical Status [Time Frame: 14 days] Mortality [Time Frame: 14 day] Rate of severe adverse events [Time Frame: 14 days] Oxygen-free days [Time Frame: 28 days] Venitlator-free days [Time Frame: 28 days] Vasopressor-free days [Time Frame: 28 days] ICU-free days [Time Frame: 28 days] Hospital-free days [Time Frame: 28 days] Patients meeting Hy's Law criteria [Time Frame: 28 days] Liver Function [Time Frame: 28 days] Heart Function [Time Frame: 28 days]