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CE - LETTER TO THE EDITOR

Camostat mesilate therapy for COVID-19

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Dear Editor,

Novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global threat. Antivirals and vaccines need to be developed to control the disease. This not only entails a considerable expense, it would also take some time for a newly developed drug to be tested for safety and, in the meantime, several more deaths would be inevitable. Under these exigent conditions, the administration of the already developed safe drugs should be the smartest shortcut.

TMPRSS2 is a serine protease that primes the spike protein of highly pathogenic human coronaviruses, such as severe acute respiratory syndrome-related coronavirus (SARS-CoV) and Middle East respiratory syndrome-related coronavirus (MERS-CoV), and facilitates its entry into the host cell. Camostat mesilate (CM), an inhibitor of TMPRSS2, blocked the spread and pathogenesis of SARS-CoV in a pathogenic mouse model and would be expected to show similar effect in MERS-CoV [1, 2]. Hoffmann et al. determined that the SARS-CoV-2 requires TMPRSS2 [3]. Furthermore, using a sample of SARS-CoV-2 virus isolated from a patient, they found that CM blocks the entry of the virus into the lung cells.

CM was developed in Japan as a protease inhibitor in the 1980s and because most of the studies on this compound have been published in Japanese, very little information is available outside of Japan. In Japan, CM therapy for acute symptoms of chronic pancreatitis is covered by health insurance since 1985, and it has also been used to treat postoperative reflux esophagitis since 1994; the oral doses used in these cases are 600 and 300 mg/day, respectively. In a multi-centre, double-blind study on 189 subjects, 3% of the subjects in the group administered 900 mg CM daily for 8 weeks showed side effects (oedema and urticaria); however, there were no side effects over the 8 weeks period in the groups that received a daily CM dose less than 600 mg [4]. In the recent years in Japan, the number of people taking CM for 1 year is estimated to be about 100,000, where only one case of acute eosinophilic pneumonia by CM was reported in 2016 [5]. This case was of a 75-year-old man, where pulmonary infiltration with peripheral blood eosinophilia appeared after taking CM for 10 days. The cause is presumed to be an allergic reaction. His temperature decreased and blood eosinophilia and pulmonary involvements were improved 2 weeks later with the cessation of the drug. However, bilateral ground-glass opacities were temporarily detected on chest CT. Since this CT finding is similar to COVID-19 pneumonia, one must be aware of elevated peripheral blood eosinophilia when using CM for COVID-19 treatment.

In an experiment on a mouse model, CM was effective in protecting the mice against death, following a lethal SARS-CoV infection, with a survival rate of 60% [2]. In this study, the weights of mice were not described, but the average weight was estimated to be approximately 20 g considering the fact that 6 to 8-week-old female BALB/c mice were used. Assuming the weights of a mouse and an adult human to be 20 g and 60 kg, respectively, the equivalent CM dose for humans would be approximately 2.14 mg/kg. CM has a plasma half-life of 100 min and is almost completely eliminated in 4–5 h. Thus, taking 600 mg (200 mg, three times) of CM daily is expected to reduce the SARS-CoV-2 infection. The biggest advantage of using CM for the treatment of COVID-19 is its low cost (one 100 mg tablet is priced as low as USD 0.10–0.40). This pragmatic treatment has the potential to save the lives of many people, including those belonging to the low-income groups. However, to date, there are no clinical data on the use of the drug in blocking or at least reducing viral spread and pathogenesis of CoVs; therefore, human clinical trials are expected.

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Compliance with ethical standards

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Statement of human and animal rights This article does not contain any study with human and animals performed by any of the authors.

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