Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Reply to "Novaferon, treatment in COVID-19 patients"

Dear Editor,

We read with great interest the letter by Janapala et al. (2020) about our study of Novaferon as a potential antiviral drug in a randomized trial conducted in February, 2020 (Zheng et al., 2020a). The main points raised by these authors are addressed below.

Aerosolized interferon-α (IFNα) treatment of respiratory viral infections has been generally practiced and recommended for COVID-19 treatment in China. The recommended dose of IFNα is 5×10^6 IU twice daily by inhalation, which equals a daily dose of 100 μg IFNα (1×10^7 IU daily, relative activity 1×10^8 IU/mg). As a mutant of IFNα with enhanced antiviral potency, Novaferon by aerosolized administration was thus considered a potential treatment for COVID-19. In addition, up to 40 μg Novaferon by daily injection has been applied in cancer patients and was well tolerated in a phase I trial (available at the official website of Chinese National Medicinal Products Admiration). The inhaled dose of 20 μg Novaferon twice daily (40 μg daily) for treatment of COVID-19 was determined accordingly.

Our trial in early February paralleled the lopinavir/ritonavir trial by Cao et al. (2020) in late January. At that time, nobody was able to predict the effect of lopinavir/ritonavir on COVID-19. Lopinavir/ritonavir remained a recommended standard-of-care antiviral drug for COVID-19 in China from January until the results of the RECOVERY trial of lopinavir/ritonavir were released (RECOVERY Collaborative Group, 2020). It was rational to propose lopinavir/ritonavir as the control in our trial.

Because of lack of experience, early medical interventions for COVID-19 needed to be adjustable by physicians. It was inadequate to fix the Novaferon treatment course at 7 days. Although the small sample size prevented us from stratifying the participants with regard to the actual duration of Novaferon treatment, all enrolled participants were strictly randomized into the three observation arms. The rates of viral clearance on day 6 of treatment and the time to viral clearance basically excluded the systemic impact of the slightly different treatment courses on the individual participants, and minimized bias due to the 7–10 days of Novaferon treatment. We agree with Janapala et al. that as 95% of participants in our study had moderate COVID-19, caution should be taken in extending the results to patients with severe COVID-19.

As the median time to viral clearance in the Novaferon group and the lopinavir/ritonavir group was 4 days compared with 7 days in the Novaferon plus lopinavir/ritonavir group, we stated that both Novaferon groups with or without the combination of lopinavir/ritonavir exhibited a similar extent of viral clearance enhancement in comparison with the lopinavir/ritonavir group. The dynamic changes of viral loads in COVID-19 were related to the time of symptom onset and the disease severity (Zheng et al., 2020b). It would be valuable to stratify patients on the basis of the time from symptom onset to the time of treatment in larger COVID-19 studies.

Currently, several toxicity grading scales are applied in clinical studies. The World Health Organization toxicity grading scale referred in our article is given in World Health Organization (1979).

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Conflicts of interest

None declare.

Ethical approval

The study was anonymous, and the protocol was approved by the Ethics Committee of the First Hospital of Changsha, according to the Declaration of Helsinki, 2013. Written informed consent was obtained from all participants.

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