

LETTER TO THE EDITOR

Comments on Zhang et al: Clinical trial analysis of 2019-nCoV therapy registered in China

Dear Editor,

We have read the article by Zhang et al¹ published in the recent issue of the Journal of Medical Virology. Zhang et al have made a cross-sectional survey of currently registered clinical trials concerning 2019-novel coronavirus (2019-nCoV), including the published literature. As such, they have given a preliminary assessment on the prospects of therapy for 2019-nCoV. Although we commend the significance of this study and appreciate the authors for their important work, we are concerned about the optimistic conclusions of the study. Several issues and mistakes should be paid attention to.

(a) In this study, the authors mentioned several times that the ability of carrying out clinical trials in China has improved, but there is no reliable basis for this conclusion. By searching the registration platform and literature database, the authors individually describe the status of clinical studies during the 2019-nCoV and severe acute respiratory syndrome (SARS) outbreak, and finally conclude that the awareness and ability to carry out clinical trials in China has improved during the 2019-nCoV outbreak. The authors only performed descriptive statistics on the obtained studies and did not strictly appraise the quality of these studies, including methodological quality (sample size, randomization, allocation concealment, blindness etc.)² and reporting quality (complete, clear, and transparent reporting).³ Therefore, the findings and analysis of this study were insufficient to conclude an improvement in clinical trials. In fact, a large proportion of these ongoing clinical trials are deficient in study design and/or selection of the clinical question. For example, Chen et al⁴ recently conducted a survey of 2019-nCoV registered trials and found that the sample sizes of most clinical trials were too small to obtain the expected results.

(b) This study is likely to have some limitations in searching for registered clinical trials and published literature. Only a single search term was used for each search and these terms were inconsistent across different databases. As an emerging disease, the name of the 2019-nCoV pneumonia is multitudinous, including 2019-nCoV, coronavirus disease-19 (COVID-19), and SARS-CoV-2.⁵ We suspect the possibility of extensive omission if only one search term is employed.

(c) The authors' interpretations of the findings were not rigorous and lack objectivity. For example, in the third section, the authors showed strong interests in, and expectations for, the results of the trials using tocilizumab and carrizumab as test drugs, but did not give an objective explanation to their significance. Candidate drugs should be selected on the theoretical basis and the results of previous studies (including *in vivo*, *in*

vitro, and toxicity tests), and selecting a star drug is not always effective clinically. The reasons we assume the authors are interested in these two drugs may be related to their background in oncology. In another example, authors state in the fifth section that, "we support that improvement of clinical symptoms and prognosis of disease should be used as the most important indicators to evaluate the short-term efficacy of experimental drugs." Researchers should instead select objective outcomes to measure effectiveness and safety in clinical trials, and the primary outcomes should be specifically designed according to the different populations (such as mild to moderate and severe patients). The authors supported using "improvement of clinical symptoms and prognosis of disease" as the most important outcomes due to the urgency of the outbreak. However, the critical discussions leading to this opinion were lacking in the article, an example of which is the impact of the self-limiting nature of the disease on these outcomes.

(d) There is a minor mistake in the bibliographic citation. The first clinical evidence of tumor patients was published in "Lancet Oncology,"⁶ rather than the "New England Journal."

Regardless, we appreciate Zhang et al for their timely sharing of ongoing clinical studies in China and hope our comments can contribute to a more accurate interpretation of these clinical studies. The Chinese researchers have offered valuable experience for carrying out clinical trials against the COVID-19 pandemic, and we are bound to see an explosion in high-quality research concerning COVID-19.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTION

YY and HC took initiative to write the manuscript. YY wrote first draft of the manuscript. QLS and HC contributed to writing the manuscript. All authors contributed to the critical review of the manuscript. All authors have read and approved the final version of this manuscript.

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