

## Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies

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**SUMMARY** The coronavirus disease 2019 (COVID-19) virus is spreading rapidly, and scientists are endeavoring to discover drugs for its efficacious treatment in China. Chloroquine phosphate, an old drug for treatment of malaria, is shown to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicenter clinical trials conducted in China. The drug is recommended to be included in the next version of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China for treatment of COVID-19 infection in larger populations in the future.

**Keywords** COVID-19, SARS-CoV-2, 2019-nCoV, pneumonia, chloroquine

The coronavirus disease 2019 (COVID-19) virus, emerged in December 2019, has spread rapidly, with cases now confirmed in multiple countries. As of February 16, 2020, the virus has caused 70,548 infections and 1,770 deaths in mainland China and 413 infections in Japan (1). A great deal of effort has been made to find effective drugs against the virus in China (2). On February 17, 2020, the State Council of China held a news briefing indicating that chloroquine phosphate, an old drug for treatment of malaria, had demonstrated marked efficacy and acceptable safety in treating COVID-19 associated pneumonia in multicenter clinical trials conducted in China (3).

In the early *in vitro* studies, chloroquine was found to block COVID-19 infection at low-micromolar concentration, with a half-maximal effective concentration (EC<sub>50</sub>) of 1.13 μM and a half-cytotoxic concentration (CC<sub>50</sub>) greater than 100 μM (4). A number of subsequent clinical trials (ChiCTR2000029939, ChiCTR2000029935, ChiCTR2000029899, ChiCTR2000029898, ChiCTR2000029868, ChiCTR2000029837, ChiCTR2000029826, ChiCTR2000029803, ChiCTR2000029762, ChiCTR2000029761, ChiCTR2000029760, ChiCTR2000029740, ChiCTR2000029609, ChiCTR2000029559, and ChiCTR2000029542) have been quickly conducted in China to test the efficacy and safety of chloroquine or hydroxychloroquine in the treatment of COVID-19 associated pneumonia in more

than 10 hospitals in Wuhan, Jingzhou, Guangzhou, Beijing, Shanghai, Chongqing, and Ningbo (5). Thus far, results from more than 100 patients have demonstrated that chloroquine phosphate is superior to the control treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course according to the news briefing. Severe adverse reactions to chloroquine phosphate were not noted in the aforementioned patients. Given these findings, a conference was held on February 15, 2020; participants including experts from government and regulatory authorities and organizers of clinical trials reached an agreement that chloroquine phosphate has potent activity against COVID-19. The drug is recommended for inclusion in the next version of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China.

Chloroquine is used to prevent and treat malaria and is efficacious as an anti-inflammatory agent for the treatment of rheumatoid arthritis and lupus erythematosus. Studies revealed that it also has potential broad-spectrum antiviral activities by increasing endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV (6,7). The anti-viral and anti-inflammatory activities of chloroquine may account for its potent efficacy in treating patients with COVID-19 pneumonia.

Chloroquine is a cheap and safe drug that has been used for more than 70 years. In light of the urgent clinical demand, chloroquine phosphate is recommended to treat COVID-19 associated pneumonia in larger populations in the future.

## References

1. Notification of 2019-nCoV infection. National Health Commission of the People's Republic of China. <http://www.nhc.gov.cn/xcs/yqfkdt/202002/18546da875d74445bb537ab014e7a1c6.shtml> (accessed February 17, 2020). (in Chinese)
2. Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). *Biosci Trends*. 2020.
3. Audio transcript of the news briefing held by the State Council of China on February 17, 2020. The National Health Commission of the People's Republic of China. <http://www.nhc.gov.cn/xcs/yqfkdt/202002/f12a62d10c2a48c6895cedf2faea6e1f.shtml> (accessed February 18, 2020). (in Chinese)
4. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *in vitro*. *Cell Res*. 2020.
5. Chinese Clinical Trial Registry. <http://www.chictr.org.cn/searchproj.aspx?title=%E6%B0%AF%E5%96%B9&offi>  
*cialname=&subjectid=&secondaryid=&applier=&study leader=&ethicalcommitteesanction=&sponsor=&studyailment=&studyailmentcode=&studytype=0&studystage=0&studydesign=0&minstudyexecutetime=&maxstudyexecutetime=&recruitmentstatus=0&gender=0&agreetosign=&secsponsor=&regno=&regstatus=0&country=&province=&city=&institution=&institutionlevel=&measure=&intercode=&sourceofspends=&createyear=0&isuploadrf=&whetherpublic=&btngo=btn&verifycode=&page=1* (accessed February 18, 2019).
6. Savarino A, Boelaert JR, Cassone A, Majori G, Cauda R. Effects of chloroquine on viral infections: an old drug against today's diseases? *Lancet Infect Dis*. 2003; 3:722-727.
7. Yan Y, Zou Z, Sun Y, Li X, Xu KF, Wei Y, Jin N, Jiang C. Anti-malaria drug chloroquine is highly effective in treating avian influenza A H5N1 virus infection in an animal model. *Cell Res*. 2013; 23:300-302.

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