



# Covid-19: trials of four potential treatments to generate “robust data” of what works

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The World Health Organization (WHO) is to coordinate an international study of treatments for covid-19 that will focus on four potential treatment strategies.

Tedros Ghebreyesus, WHO director general, said on 18 March that the SOLIDARITY trial was a response to fears that “multiple small trials with different methodologies may not give us the clear, strong evidence we need about which treatments help to save lives.”<sup>1</sup>

The trial “is designed to generate the robust data we need, to show which treatments are the most effective,” he said. It will also be designed to put minimal burden on over-stretched hospitals.

The study will focus on four treatment options<sup>2</sup>: the novel antiviral drug remdesivir, developed by Gilead in response to Ebola; lopinavir and ritonavir, antiretroviral drugs used against HIV; lopinavir and ritonavir in combination with the immune system regulator interferon  $\beta$ ; the antimalarial drug chloroquine, which has reportedly been effective in China. The drugs and combinations will be tested against standard care, which is supportive treatment with supplementary oxygen and respiratory support as required.

On 13 March a consultation document for WHO’s Research and Development advisory group for covid-19 research reported: “The expert panel recommended the direct-acting antiviral agent remdesivir and the protease inhibitor lopinavir/ritonavir for evaluation in randomized clinical trials.”

“At the time [27 January], there was insufficient evidence to support chloroquine’s further investigation. However, chloroquine has received significant attention in countries as a potentially useful prophylactic and curative agent, prompting the need to examine emerging evidence to inform a decision on its potential role.”<sup>3</sup>

Countries reported to be taking part in SOLIDARITY are Argentina, Bahrain, Canada, France, Iran, Norway, South Africa, Spain, Switzerland, and Thailand. WHO said that the trial would

be simple to enter, with supporting information and registration documents expected to be published this week.

European hospitals are also being invited to take part in a similar trial, Discovery, coordinated by the French research institution INSERM.<sup>4</sup> The trial organisers plan to include 3200 patients from Belgium, France, Germany, Luxembourg, the Netherlands, Spain, Sweden, and the UK. It will begin with five French hospitals and then invite up to 20 other European institutions to join the trial and will study the same drugs and drug combinations as the WHO trial. It will be randomised but open label and will assess outcomes at 15 days.

Lead researcher Florence Ader, from the Infectious and Tropical Diseases Department of the Croix-Rousse Hospital of Lyon University Hospital and researcher at the CIRI International Research Centre in Infectiology, said: “The great strength of this trial is its adaptive nature. This means that ineffective experimental treatments can very quickly be dropped and replaced by other molecules that emerge from research efforts. We will therefore be able to make changes in real time, in line with the most recent scientific data, in order to find the best treatment for our patients.”

- 1 World Health Organization. WHO Director-General’s opening remarks at the media briefing on COVID-19. 18 March 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-18-march-2020>
- 2 World Health Organization. Thailand joins the WHO “Solidarity Trial”: global testing of effective treatments of COVID-19 across 8 countries – an aggressive effort to save lives from the pandemic (press release), 20 March 2020. <https://www.who.int/thailand/news/detail/20-03-2020-thailand-joins-the-who-solidarity-trial-global-testing-of-effective-treatments-of-covid-19-across-8-countries-an-aggressive-effort-to-save-lives-from-the-pandemic>
- 3 World Health Organization. R&D Blueprint COVID-19 Informal consultation on the potential role of chloroquine in the clinical management of COVID 19 infection. 13 March 2020. <https://www.who.int/blueprint/priority-diseases/key-action/RD-Blueprint-expert-group-on-CQ-call-Mar-13-2020.pdf?ua=1>
- 4 INSERM. Launch of a European clinical trial against covid-19. 22 March 2020. <https://presse.inserm.fr/en/launch-of-a-european-clinical-trial-against-covid-19/38737/>

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