Regulation of in vitro diagnostics, therapeutics, and vaccines
WHO Update – 10 addendum
Coronavirus disease 2019 (COVID-19)
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World Health Organization

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Temporary suspension of enrollment to the hydroxychloroquine arm of the Solidarity Trial

Key Messages

1. Taking a conservative approach, WHO has temporarily suspended enrollment of patients into the hydroxychloroquine arm of the Solidarity Trial. Overall, the Solidarity Trial continues.
2. This decision has been taken in light of recent publications of evidence on the safety and efficacy of hydroxychloroquine as a treatment for patients.
3. Hydroxychloroquine is accepted as generally safe for use in patients with autoimmune diseases or malaria.

Context

More than two months ago WHO initiated the Solidarity Trial to evaluate the safety and efficacy of four drugs and drug combinations against COVID-19. Based on data from laboratory and clinical studies, Remdesivir, Lopinavir/Ritonavir, Lopinavir/Ritonavir with Interferon beta-1a, and Hydroxychloroquine or Chloroquine had been initially selected as treatment options for COVID-19. Although both chloroquine and hydroxychloroquine had both been selected as potential drugs to be tested, the Solidarity Trial was only ever pursued with hydroxychloroquine.

On Friday 22 May, the Lancet published an observational study on hydroxychloroquine and chloroquine and its effects on COVID-19 patients that have been hospitalized. The study includes observational data from nearly 100 000 patients from multiple countries. The study found that among patients randomized to receive hydroxychloroquine or chloroquine, when used alone or with a macrolide, there was a higher mortality rate and an increased frequency of irregular heartbeats.

> The Lancet article: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Response by the Executive Group of the Solidarity Trial

Over 400 hospitals in 35 countries are actively recruiting patients for the Solidarity Trial and nearly 3 500 patients have been enrolled from 17 countries. The Executive Group (EG) of the Solidarity Trial, representing 10 of the participating countries, met on Saturday 23 May and agreed to review a comprehensive analysis and critical appraisal of all evidence available globally. Until the comprehensive

review is available, the group decided to err towards a conservative approach and implement a temporary suspension of random allocation to the hydroxychloroquine arm of the trial.

On Sunday 24 May, the EG sent a letter all National Principal Investigators of the Solidarity Trial informing them of this decision. In the interim, randomization will continue to all the other arms of the Solidarity trial. Those patients previously randomised to hydroxychloroquine treatment should continue to receive hydroxychloroquine until they finish their course of treatment. All Solidarity principal investigators were asked to implement these temporary changes and inform their regulatory authority as well as ethics committee.

What happens next?

The Solidarity trial overall, including its add-on trials, is NOT SUSPENDED, and recruitment and randomization should continue with the greatest efforts. It is of utmost importance to generate data on the potential effectiveness of the included drugs.

A final decision on whether or not to continue with the HCQ arm will be made once an extensive review of the evidence is done by the Solidarity Data Safety Monitoring Board. This review, expected to be issued by mid-June, will include data from the Solidarity Trial and other ongoing trials, as well as any evidence published so far.

What about other trials that are using hydroxychloroquine and chloroquine?

In making this temporary recommendation, it should be noted that the Solidarity Executive Group does not make any judgement on whether or not there is evidence of harm, benefit or lack of benefit caused by hydroxychloroquine in relation to COVID-19 outcomes among hospitalised patients.

National Regulatory Authorities (NRAs) in countries with other ongoing trials should advise on actions, if any, to be taken by investigators. Warnings have been issued by many NRAs on the side effects of these drugs and their use has been limited in many countries to clinical trials under strict supervision in hospital settings.

The temporary suspension of hydroxychloroquine for treatment of COVID-19 patients in the Solidarity trial should not impact randomized controlled trials of prophylactic use of hydroxychloroquine.

Use of hydroxychloroquine and chloroquine in autoimmune diseases and malaria

Hydroxychloroquine and chloroquine are licensed by regulatory authorities for use in autoimmune diseases or malaria. These drugs therefore have a positive benefit-risk profile for use for these indications. The concerns from the Lancet study relate to the use of hydroxychloroquine and chloroquine to treat COVID-19.

Access to regulatory updates by WHO staff

All WHO staff have access to the Regulatory Updates at the following location:

P:\PubPersons\RPQ\COVID_Regulatory_Updates