AFAO COVID-19 Research Brief 01

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AUSTRALIAN FEDERATION OF AIDS ORGANISATIONS
Leading the community response to HIV

The AFAO COVID-19 research briefs provide updates on the latest COVID-19 research news, including vaccines, treatments and testing technologies. The research briefs are intended to inform people working in the HIV sector of developments and challenges in the COVID-19 research space and provide links to further information.

Vaccines

Unsurprisingly there is significant research underway to develop a COVID-19 vaccine. According to the World Health Organisation (WHO) there are currently sixty vaccine candidates, of these fifty-eight are at the preclinical evaluation stage. Preclinical research is undertaken in the laboratory prior to any human trials commencing. Results from preclinical research are used to determine whether it is justified to proceed to clinical studies in humans.

There are currently two vaccine candidates in phase one clinical trials. Phase one studies are mainly concerned with safety and involve initial testing of a vaccine in a small number of healthy adults, in order to test the properties of the vaccine and its tolerability for humans at different dose levels.

A phase one vaccine trial commenced in China, on 16 March 2020, its scientific title is *A Single-center, Open-label Dose-escalating Phase I Clinical Trial to Evaluate Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) in Healthy Adults Aged 18-60 Years Old*. The vaccine trial is sponsored by CanSino Biological Inc. and the Beijing Institute of Biotechnology. The trial will enrol one hundred and eight participants and test three different dose levels across three groups of thirty-six for safety and tolerability.

Another phase one vaccine is being sponsored by the National Institute of Allery and Infectious Diseases (NIAID) in the USA the scientific title of the trial is *Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults.* The Vaccine was manufactured by a company called Moderna. The trial commenced on 3 March 2020 and will enrol forty-five people into three different dose groups. Participants will receive two doses of the vaccine at day one and day twenty-nine.

Treatments and care interventions in an emergency

Numerous studies have already begun to publish data on potential treatments and interventions for COVID-19. The urgency of the pandemic requires the science to move rapidly and, for this reason, researchers are being encouraged to rapidly share findings including before peer review. The early sharing of data in a health emergency is extremely important but it does mean findings need to be treated with caution.

Further, the urgent need to find effective treatments for COVID-19 also means that results from very small and non-randomised trials are in some cases guiding the off-label use of already licenced drugs. As stated by WHO in a recent news brief 'in a health emergency where no proven treatment exists it can be ethically appropriate to offer an experimental intervention on an emergency basis outside of clinical trials'(1) (see summary below for an example of an off-label treatment). In this situation the public health challenge is to fast track access to medication to those who can most benefit from it. In the context of COVID-19 this would potentially be people over sixty-five years of age and people with existing respiratory, lung and kidney conditions.

The Australian government has waived the therapeutic good registration requirements for supply of several drugs to allow them to be investigated as potential treatments for COVID-19. The waiver applies to Hydroxychloroquine and Chloroquine, drugs which are currently used as anti-malaria drugs and to treat autoimmune diseases (see summary below) and three anti-viral drugs Remdesivir, Lopinavir and Ritonavir.

Summary of a recently published news story from the Lancet

Owens, B. (2018). Excitement around Hydroxychloroquine for treating COVID-19 causes challenges for rheumatology. The Lancet Rheumatology, published online April 1, doi.org/10.1016/S2665-9913(20)30089-8

The *Lancet Rheumatology* published a news story on 1 April 2020 about the antimalarial drug Chloroquine and its safer derivative Hydroxychloroquine. The article briefly outlines some of the evidence for these drugs as potential treatment for COVID-19 and highlights some unintended consequences of the publicity surrounding the drug. This includes people self-medicating to prevent COVID-19 and resultant drug shortages for people who routinely use these medications to control the symptoms of arthritis or systemic lupus erythematosus.

Key messages

There has been a great deal of public and media attention given to Chloroquine and Hydroxychloroquine not least due to US President Donald Trump describing it as a 'game changer'. The article notes that while there have been reports from China that Chloroquine inhibits SARS-CoV-2 in vitro and that it showed 'apparent efficacy' treating COVID-19 in people and results from a small non-randomised trial in France showing some promise for Hydroxychloroquine as a potential treatment, the clinical evidence is 'thin'. Despite limited clinical data, the US Food and Drug Administration (FDA) has authorised off-label use of Hydroxychloroquine on compassionate grounds for the treatment of COVID-19.

While the Hydroxychloroquine has shown some promise, the article notes that virologists and infectious diseases experts consider the excitement to be 'premature' given the very minimal data to support its use. Further, there have been some unintended negative consequences, of the attention given to these drugs including the poisoning of people who have self-medicated with them to prevent or treat COVID-19. Another reported unintended consequence of the new interest in Hydroxychloroquine has been shortages for people who rely on it to treat their autoimmune disease.

The hype may have got ahead of the clinical data, but the article reports that there is support for further research, and an infectious diseases physician at the University of Minnesota, David Boulware, is leading a trial to investigate whether Hydroxychloroquine could be 'efficacious as a post-exposure prophylactic to prevent the development of the disease, and prevent progression of the disease to avoid admission to hospital'. The University of Minnesota trial is likely to report initial results within the next four weeks.

Postscript

Since the publication of the *Lancet Rheumatology* article another small French study has reported on the use of hydroxychloroquine for the treatment of COVID-19. The study looked prospectively at the clinical outcomes of 11 patients hospitalised with severe COVID-19 disease who received hydroxychloroquine in combination with azithromycin. Azithromycin is an antibiotic used for the treatment of bacterial infections including pneumonia. The study found no evidence of a strong antiviral activity or clinical benefit for the patients treated with the combination of hydroxychloroquine and azithromycin. The investigator team conclude that only ongoing randomised clinical trials will offer 'a definitive answer regarding the alleged efficacy of this combination'(2).

Links to the latest Science

https://www.tga.gov.au/behind-news/coronavirus-covid-19-information-medicines-and-medical-devices

https://www.science.org.au/curious/people-medicine/covid-19-facts

References

1. https://www.who.int/news-room/commentaries/detail/off-label-use-of-medicines-for-covid-19

2. Molina, J., Delaugerre, C., Le Goff, J., Mela-Lima, B., Ponscarme, D., Goldwirt, L., de Castro, N. (2020). No evidence of rapid antiviral clearance or clinical benefit with the combination of Hydroxychloroquine and Azithromycin in patients with severe COVID-19 infection. *Médecine et Maladies Infectieuses doi.org/10.1016/j.medmal.2020.03.006*