World Health Organization

WHO R&D Blueprint

COVID-1

Informal consultation on the potential role of chloroquine in the clinical management of COVID 19 infection

WHO reference number

Geneva, Switzerland, 13th March 2020

R&DBlueprint

Powering research
to prevent epidemics

Table of Contents

Appropriate WHO Confidentiality Undertakings were signed and submitted to WHO by all participating experts

INTRODUCTION

Currently, there are no therapeutic agents licensed and available for the treatment of COVID 19. On the 27th of January, WHO convened a meeting of experts to examine the available evidence and prioritize promising therapeutic agents for further evaluation in the ongoing outbreak. 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, 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. At the time of convening this meeting, about 500 clinical trials were ongoing in China, with at least 13 evaluating chloroquine's efficacy.

This expert consultation convened clinical care partners and experts in the field of randomized controlled trials (RCTs), preclinical studies, and chloroquine pharmacology for evaluating newly available evidence.

OBJECTIVES OF THE CONSULTATION

The objectives of this consultation were:

1. To review and critically appraise the existing evidence regarding chloroquine and hydroxychloroquine;

2. To decide on the further evaluation of chloroquine- based on currently available evidence – in humans infected with SARS-CoV-2 to reduce mortality and disease progression.

This Consultation represents an initial step towards the evaluation of chloroquine against the SARS-CoV-2. There are ongoing efforts to identify additional candidate therapeutics and to expand the body of evidence available on each of the candidates.

Agenda items

- Introduction and roll-call.
- Update on current evidence on chloroquine.
- Conclusions and next steps.

Participants

Chair: Marco Cavaleri

Name	Position	Institutional Affiliation
Marco Cavaleri	Head of Anti-infectives and Vaccines	European Medicines Agency, Netherlands
Eric Pelfrene	Office of Anti-infectives and Vaccines	European Medicines Agency, Netherlands
Sina Bavari	Independent Consultant	
Karl Erlandson	Interdisciplinary Scientist	Biomedical Advanced Research and Development Authority,

Name	Position	Institutional Affiliation
		US Department of Health and Human Services
Yaseen Arabi	Chairman, Intensive Care Department	King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
John Marshall	Co-Director, Critical Illness and Injury Research Centre, St Michael Hospital, Canada	Co-Director, Critical Illness Research, St Michaels Hospital
Ross Upshur	Director, Primary Care Research Unit, Sunnybrook and Women's College Health Sciences Centre, Canada Research Chair in Primary Care Research	University of Toronto, Canada
John Beigel	Associate Director for Clinical Research	NIH, USA
Thomas Fleming	Professor of Biostatistics	University of Washington
John Farley	Director, Office of Infectious Diseases	FDA, USA
Philip Krause	Deputy Director CBER/OVRR	FDA, USA
Regine Lehnert	Doctor	Federal Institute for Drugs and Medical Devices, Germany
Monalisa Chatterji	Senior Program Officer, Discovery & Translational Science	Bill & Melinda Gates Foundation, USA
Michael Kaufmann	Manager- Advisory	PriceWaterhouse Cooper,USA

Name	Position	Institutional Affiliation
David Vaughn	Senior Program Officer	Bill & Melinda Gates Foundation, USA
Ken Duncan	Discovery & Translational Sciences team Lead	Bill & Melinda Gates Foundation, USA
Nicholas White	Professor of Tropical Medicine	Mahidol University, Thailand
Robert Walker	Chief Medical Officer and Director, Division of Clinical Development	Biomedical Advanced Research and Development Authority, US Department of Health and Human Services
Julia Tree	Microbiological Services	Public Health England
Scott Miller	Deputy Director, medical interventions	Bill & Melinda Gates Foundation, USA
Frederick Hayden	Professor Emeritus, Medicine: Infectious Diseases and International Health	University of Virginia
Jacqueline Kirchner	Senior Program Officer	Bill & Melinda Gates Foundation, USA
Elizabeth Higgs	Global health science advisor for the Division of Clinical Research (DCR)	NIH. USA
Helen Rees	Professor, Wits Reproductive Health and HIV Institute	University of Witwatersrand, South Africa
Matthew Frieman	Associate Professor, Microbiology and Immunology	University of Maryland School of Medicine

Other invited experts but only those listed in the table above participated: Hilary Marston (US NIH), Philip Coyne (US PHS), Sina Bavari (Independent consultant), Marco Cavaleri (EMA), Jeremy Farrar (Wellcome Trust, UK), Markus Mueller (University of Wien), Bin Du (Peking), Yi Guan (Hong Kong); Wannian Liang (MOH China), Bruno Lina (France), Claire Madelaine William Dowling (CEPI, USA)

WHO Secretariat: Alejandro Costa, Janet Diaz, Ana Maria Henao-Restrepo, Marie-Pierre Preziosi, Vasee Moorthy, Ximena Riveros Balta, Kolawole Salami, Emer Cooke, Deusdedit Mubangizi, Matthias Mario Stahl, and Pierre Gsell.

OVERVIEW OF THE DELIBERATIONS

Overall considerations

- Chloroquine has shown in vitro activity against some viruses, including chikungunya, dengue, and influenzas, but in vivo studies in animal models and randomized controlled trials (RCTs) in humans have been largely disappointing. Chloroquine pre-treatment (prophylaxis) was associated with an enhancement of viral replication and disease with chikungunya in NHPs due to delays in immune responses. Chloroquine treatment of chikungunya infection in humans did not affect viremia or clinical parameters during the acute stage of the disease. However, it reduced levels of C-reactive Protein (CRP) and specific cytokines.