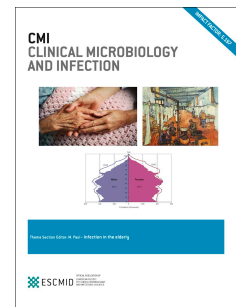


Journal Pre-proof

Re: 'Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients' by Fiolet et al

Dr Alexis Lacout, Dr Pierre Yves Marcy, Pr Christian Perronne



PII: S1198-743X(20)30579-6

DOI: <https://doi.org/10.1016/j.cmi.2020.09.027>

Reference: CMI 2247

To appear in: *Clinical Microbiology and Infection*

Received Date: 30 August 2020

Revised Date: 6 September 2020

Accepted Date: 15 September 2020

Please cite this article as: Lacout A, Marcy PY, Perronne C, Re: 'Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients' by Fiolet et al, *Clinical Microbiology and Infection*, <https://doi.org/10.1016/j.cmi.2020.09.027>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 European Society of Clinical Microbiology and Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

Re: 'Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients' by Fiolet et al

Dr Alexis LACOUT

Corresponding author

lacout.alexis@wanadoo.fr

TEL (33) 4 71 48 00 50 FAX (33) 4 71 48 53 48

Centre de diagnostic

ELSAN, Centre médico –chirurgical

83 avenue Charles de Gaulle

15000 AURILLAC FRANCE

Dr Pierre Yves MARCY

Radiodiagnostics and Interventional Radiology Department ELSAN

Polyclinique Les Fleurs

Quartier Quiez

83190 OLLIOULES, FRANCE

brozpy@gmail.com

Pr Christian PERRONNE

Infectious Diseases Unit, University Hospital Raymond Poincaré, APHP

Versailles Saint Quentin University

GARCHES, France

c.perronne@aphp.fr

Conflict of interest : none.

Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients: a systematic review and meta-analysis : genuine analysis or cherry- picking ?

To the Editor,

We read with interest the paper by Fiolet et al, entitled “Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients: a systematic review and meta-analysis” recently published in the Clinical Microbiology and Infection journal 2020 (1).

Further to this article we performed an extensive literature review, which depicted many other studies dealing with the same topic, that were published in good quality peer-reviewed journals. But regrettably, they were not considered by the authors despite (as they have stated) having performed an extensive research of the papers, as mentioned in their material and methods section (1).

The essence of a systematic review is to take into account all the data in order to make a rigorous open and fair -minded synthesis on the topic. At least three meaningful studies that meet the inclusion / exclusion criteria and were in favor of the efficacy of hydroxychloroquine and azithromycin on COVID- 19 patients have been discarded (2-4). This approach is more akin to cherry- picking than to a true systematic review without a priori considerations.

Furthermore, the authors in their article acknowledge that only one study included non-hospitalized out- patients. Fiolet et al stated : "Despite our inclusion criteria that did not specify the stage of the disease, all the studies were conducted with hospitalized patients except the RCT by Skipper et al. RCT" (1). In Skipper's study, although the difference was not statistically significant due to a small number of patients included (5), there were twice as many hospitalized patients in the placebo group (4 hospitalizations out of 231 patients with hydroxychloroquine versus 10 hospitalizations out of 234 patients with placebo). Last but not least, only 34 % of

those patients received appropriate PCR SARS-CoV-2 testing, which adds to confusion.

Heart rhythm disorders might be prevented in the hospital environment by monitoring with ECG and serum potassium measurement. The “Recovery” study did not meet the inclusion criteria as non-PCR-tested patients have been included (6). In addition, the doses of hydroxychloroquine given to COVID-19 patients in this study (2400mg on the first day, followed by nine days at 800mg/day) were high and thus potentially toxic.

We are looking for appropriate clinical trials or a thorough systematic review and meta-analysis to close the French and worldwide debate on whether treating patients with hydroxychloroquine / azithromycin at the early phase of COVID 19 infection improves their outcome.

Keywords

Hydroxychloroquine, azithromycine, COVID-19, coronavirus, meta-analysis

Conflict of interest disclosure

The authors (AL, PYM, CP) have nothing to disclose.

Authors' contributions

AL : Conceptualization, Writing original draft

PYM : Writing, review and editing

CP : Supervision

Funding :

No external funding was received,

Bibliography

1. Fiolet T, Guihur A, Rebeaud M, Mulot M, Peiffer-Smadja N, Mahamat-Saleh Y, Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients: a systematic review and meta-analysis, *Clinical Microbiology and Infection*, <https://doi.org/10.1016/j.cmi.2020.08.022>.
2. Davido B, Boussaid G, Vaugier I, et al. Impact of medical care including anti-infective agents use on the prognosis of COVID-19 hospitalized patients over time [published online ahead of print, 2020 Aug 2]. *Int J Antimicrob Agents*. 2020;106129. doi:10.1016/j.ijantimicag.2020.106129
3. Castelnovo AD, Costanzo S, Antinori A, et al. Use of hydroxychloroquine in hospitalised COVID-19 patients is associated with reduced mortality: Findings from the observational multicentre Italian CORIST study [published online ahead of print, 2020 Aug 25]. *Eur J Intern Med*. 2020;S0953-6205(20)30335-6. doi:10.1016/j.ejim.2020.08.019
4. Catteau L, Dauby N, Montourcy M, et al. Low-dose Hydroxychloroquine Therapy and Mortality in Hospitalized Patients with COVID-19: A Nationwide Observational Study of 8075 Participants [published online ahead of print, 2020 Aug 24]. *Int J Antimicrob Agents*. 2020;106144. doi:10.1016/j.ijantimicag.2020.106144

5. Skipper CP, Pastick KA, Engen NW, et al. Hydroxychloroquine in Nonhospitalized Adults With Early COVID-19: A Randomized Trial [published online ahead of print, 2020 Jul 16]. *Ann Intern Med*. 2020;M20-4207. doi:10.7326/M20-4207

6. Horby P, Mafham M, Linsell L, Bell JL, Staplin N, Emberson JR, et al. Effect of Hydroxychloroquine in Hospitalized Patients with COVID-19: Preliminary results from a multi-centre, randomized, controlled trial. *MedRxiv* 2020:2020.07.15.20151852. <https://doi.org/10.1101/2020.07.15.20151852>.