

# ABSTRACT

## Background

In a recent survey, most physicians worldwide considered that hydroxychloroquine (HCQ) and azithromycin (AZ) are the two most effective drugs among available molecules against COVID-19. Nevertheless, to date, one preliminary clinical trial only has demonstrated its efficacy on the viral load. Additionally, a clinical study including 80 patients was published, and *in vitro* efficiency of this association was demonstrated.

## Methods

The study was performed at IHU *Méditerranée Infection*, Marseille, France. A cohort of 1061 COVID-19 patients, treated for at least 3 days with the HCQ-AZ combination and a follow-up of at least 9 days was investigated. Endpoints were death, worsening and viral shedding persistence.

## Findings

From March 3<sup>rd</sup> to April 9<sup>th</sup>, 2020, 59,655 specimens from 38,617 patients were tested for COVID-19 by PCR. Of the 3,165 positive patients placed in the care of our institute, 1061 previously unpublished patients met our inclusion criteria. Their mean age was 43.6 years old and 492 were male (46.4%). No cardiac toxicity was observed. A good clinical outcome and virological cure was obtained in 973 patients within 10 days (91.7%). Prolonged viral carriage at completion of treatment was observed in 47 patients (4.4%) and was associated to a higher viral load at diagnosis ( $p < 10^{-2}$ ) but viral culture was negative at day 10 and all but one were PCR-cleared at day 15. A poor outcome was observed for 46 patients (4.3%); 10 were transferred to intensive care units, 5 patients died (0.47%) (74-95 years old) and 31 required 10 days of hospitalization or more. Among this group, 25 patients are now cured and 16 are still hospitalized (98% of patients cured so far). Poor clinical outcome was significantly associated to older age (OR 1.11), initial higher severity (OR 10.05) and low

hydroxychloroquine serum concentration. In addition, both poor clinical and virological outcomes were associated to the use of selective beta-blocking agents and angiotensin II receptor blockers ( $P < 0.05$ ). Mortality was significantly lower in patients who had received  $\geq 3$  days of HCQ-AZ than in patients treated with other regimens both at IHU and in all Marseille public hospitals ( $p < 10^{-2}$ ).

### **Interpretation**

The HCQ-AZ combination, when started immediately after diagnosis, is a safe and efficient treatment for COVID-19, with a mortality rate of 0.5%, in elderly patients. It avoids worsening and clears virus persistence and contagiousity in most cases.