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Short Title: **Colchicine in COVID-19**

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Introduction

The CHOICE-19 study was proposed to evaluate the effect of colchicine on the need on hospitalization in patients with early diagnosis of SARS-CoV-2 infection and mild disease who were followed at home. Given a series of preliminary promising data on the effect of colchicine on hospitalized patients and that a dysregulated activation and inflammatory activity of myeloid cells is one the main pathogenic events characterizing the infection by SARS-CoV-2, this strategy seemed to be promising. Indeed, colchicine has known broad anti-inflammatory effects, anti-viral properties and it is not hampered by an immunosuppressant effect suggesting a potential effect on COVID-19. Unlike other proposed treatments, colchicine is inexpensive and with known side effects.

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1.2 Objectives and endpoints

Primary	
To evaluate the efficacy of colchicine by describing:	
Rate of hospitalization (30 days)	Need for hospitalization (at 30 days after randomization)
Secondary	
To describe:	
1. Hospital-free days 2. Death 3. Clinical remission 4. Toxicity of Colchicine	1. Hospital-free days (at 30 days after randomization). 2. Rate of death (at 30 days after randomization) 3. Rate of disappearance of symptoms and two consecutive negative swabs at 24 hours (at 30 days after randomization) 4. Rate of adverse events codified by Common Terminology Criteria for Adverse Events (CTCAE) v5.0

Design

The trial was designed as an interventional, multicenter, double-arm, randomized, open-label, phase 3 study, enrolling patients with COVID-19 disease. One-month rate of hospitalization was the primary endpoint.
From available data (http://www.salute.gov.it/imgs/C_17_notizie_4640_0_file.pdf), with the ancestral strain of SARS-CoV-2, it was assumed that 1-month rate of hospitalization for the population defined by the selection criteria was around 18.4% (P0). To verify the hypothesis that the experimental drug may produce a halving of the rate of entering the critical stage (from 18.4% to 9.2%, P1), 438 patients were planned to be enrolled with an 80% power and a 5% bilateral alpha error. The two arms would have been randomized with 219 patients treated with current care and 219 with colchicine added to the current care.

Results

Twenty-one patients from 8 different centers in Italy were recruited.
The patients were recruited between 18/02/2021 and 20/05/2021. Median age was 60 years (range 36-82), there were 13 males and 8 females.
All patients signed informed consent.
At baseline 2 patients were taking azithromycin, 4 patients steroids, 2 patients LMWH. 3 patients were previously smokers, two patients were active smokers.
Eight patients had history of hypertension, 1 of cardiovascular disease, 1 of lung diseases, 3 of upper gastrointestinal disease, 1 history of cancer (breast).
COVID-19 related sign and symptoms included fever in 17/21 patients, nasal congestion in 11/21, dysgeusia 2/21, headache 10/21, sore throat in 2/21, cough in 13/21, diarrhea in 4/21, musculoskeletal pain in 9/21, mean SpO2 was 96.7%, only one patient had significantly reduced SpO^2 (93%), mean T max was 37.0 °C, only 5 patients had temperature ≥38.0°C.

11 patients were randomized to colchicine, 10 to SOC. Colchicine dosage was 1.54 mg (range 1-3)
One patient randomized to colchicine exit the trial since he refused to take the drug.

At 30 days of follow-up 4/11 patients on colchicine worsened or did not improve, 5/10 patients on SOC did not improve (P=ns). Three patients required hospitalization (one on colchicine and 2 on SOC).
Two adverse events were reported, one case of diarrhea with colchicine and one case of high blood pressure with dexamethasone used as SOC. In all cases the adverse event solved with the interruption of the drug administration.
The trial was prematurely interrupted due to the flattening of the pandemic curve, the vaccination campaigns and the rise of new virus variants.

Conclusions
A definitive conclusion could not be drawn given the small number of patients recruited and the non-significant differences among the study groups. A larger population would have been required to test the study hypothesis.