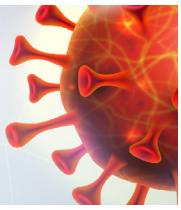
INESSS
LE SAVOIR PREND FORME

JUNE 2021

COLCHICINE

ANALYSIS OF THE COLCORONA STUDY



The COLCORONA study evaluated the effects of taking colchicine for 30 days on reducing hospitalizations or deaths in participants 40 years of age or older with a confirmed diagnosis of COVID-19[1] and at least one risk factor[2] for developing COVID-19 complications.

⚠ POSITION

Based on currently available scientific data, the epidemiological context, the status of the vaccination campaign, the vaccination status of the target population (June 2021), and the perspective of the clinicians consulted, INESSS believes that :

The current state of scientific knowledge and the uncertainty about the potential benefits and risks following colchicine use in non-hospitalized individuals with a diagnosis of COVID-19 confirmed or not by RT-PCR test, and who meet the selection criteria of the COLCORONA study (over 40 years of age with at least one risk factor), do not support the use of colchicine for this population outside of a clinical trial.

WHAT DO THE SCIENTIFIC DATA SAY?

Study endpoints	Entire intent-to-treat population N=4,488 (regardless of the method used to confirm the COVID-19 diagnosis)	RT-PCR+ subpopulation N=4,159
PRIMARY ENDPOINTS		
 **or** 	NON-statistically significant decrease of 1.16 %, absolute of **hospitalizations or deaths** (Odds ratio (OR) : 0.79 [95% confidence interval (CI95%) : 0.61-1.03], p=0.081). The results do not establish a statistical link between using colchicine for 30 days and a decrease in hospitalizations or deaths.	Statistically significant decrease of 1.4%, absolute of **hospitalizations or deaths** (OR: 0.75 [CI95%: 0.57-0.99], p=0.042). ⚠ This result is fragile because transferring one or more events from one group to the other would make it NON-statistically significant.
SECONDARY ENDPOINTS		
	NON-statistically significant decrease of 1.2 %, absolute of **hospitalizations** (Odds ratio (OR) : 0.79 [95% confidence interval (CI95%) : 0.60-1.03]) (p value not reported)).	Statistically significant decrease of 1.4%, absolute of **hospitalizations** (OR: 0.75 [CI95%: 0.57-0.99]) (p value not reported)).
	Statistically, the results do not demonstrate that taking colchicine for 30 days leads to a decrease in **deaths** or in the **use of mechanical ventilation** when these events are considered separately. The event frequencies are low, and the reductions in frequency are NOT statistically significant.	

Documented adverse events	Entire study population (reported in the preprint) N=4,412 (regardless of the method used to confirm the COVID-19 diagnosis)
 	Serious adverse events were less frequent in the colchicine group than in the placebo group, mainly because of a lower incidence of **pneumonia** (4.9% for colchicine vs. 6.3% for placebo). ⚠ Unexpectedly, more participants in the colchicine group (11) experienced a **pulmonary embolism** than those in the placebo group (2) (0.5% for colchicine vs. 0.1% for placebo).
	Adverse events, mainly **gastrointestinal** in nature, were more common in the colchicine-treated participants (24.2% vs. 15.5% for the placebo group).

1. According to an RT-PCR test or an epidemiological link within the previous 24 hrs or on the basis of a clinical algorithm.
2. Age ≥ 70 years, body mass index (BMI) ≥ 30 kg/m2, diabetes, uncontrolled hypertension (≥ 150 mm Hg), known respiratory disease, known heart failure, known coronary artery disease, fever ≥ 38.4 degrees Celsius in the 48 hours prior to recruitment, dyspnea at presentation, bicytopenia, pancytopenia, leukopenia or the combination of a low leukocyte count and a high neutrophil count.

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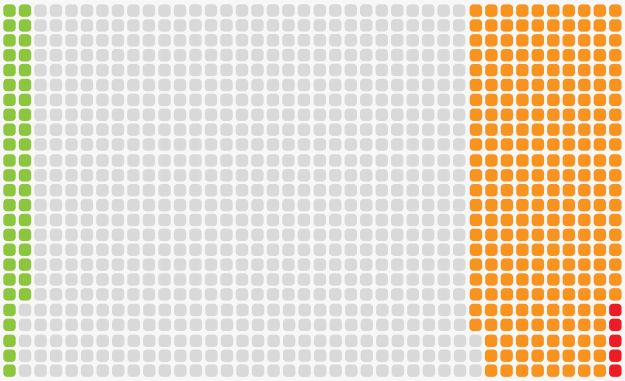
VISUAL REPRESENTATION OF THE POTENTIAL IMPACT OF THE TREATMENT

The figure below shows the potential impact of colchicine on hospitalizations and adverse events in RT-PCR-positive individuals who meet the study criteria.

⚠The criteria of the parameter hospitalization, the actual length of hospital stay beyond the predefined 24 hours, and the need for a transfer to intensive care are not reported in the publication.

30-day treatment with colchicine

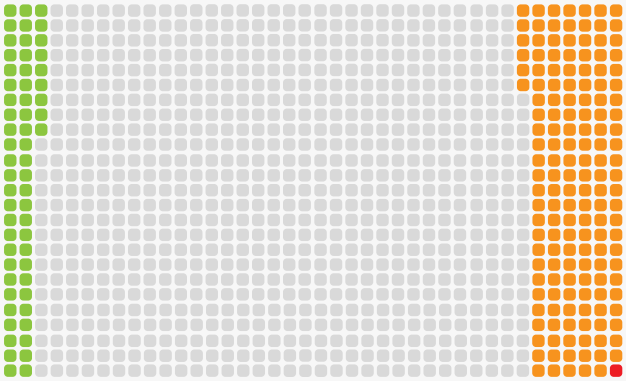
Of 1,000 individuals who tested positive for COVID-19 on RT-PCR
Not hospitalized | 40 years or older | ≥ 1 Risk factor



- **45** would be hospitalized for COVID-19 disease
- **242** would experience adverse events (mainly gastrointestinal)
- **5** would experience a pulmonary embolism

30-day treatment with placebo

Of 1,000 individuals who tested positive for COVID-19 on RT-PCR
Not hospitalized | 40 years or older | ≥ 1 Risk factor



- **59** would be hospitalized for COVID-19 disease
- **155** would experience adverse events (mainly gastrointestinal)
- **1** would experience a pulmonary embolism

Of those receiving 30 days of treatment with colchicine vs. placebo

14 more people would avoid hospitalization for COVID-19

87 more people would experience adverse events (mainly gastrointestinal)

4 more people would experience a pulmonary embolism

The study values have been rounded off for the purpose of displaying the results. The events are not necessarily mutually exclusive.

WARNINGS

It is impossible to predict who might avoid hospitalization or experience adverse effects when taking colchicine for 30 days. It is even more difficult to generalize and transfer the study results to people aged 70 or older and even less in the context of being vaccinated. Although this age group is the most likely to be hospitalized or to succumb to COVID-19 disease, such persons accounted for less than 10% of the participants recruited by the COLCORONA study.

The study and the statistical analyses were not designed to demonstrate a link between patient risk factors and the reduction in hospitalizations and deaths following the use of colchicine. The results presented in the publication regarding subgroup analyses by risk factor are thus exploratory in nature.

The study was conducted using 0.5 mg colchicine tablets, which are not commercially available at this time. Although the experts consulted did not express any particular concern about this, a certain degree of uncertainty surrounds switching to 0.6 mg tablets, which are commercially available, particularly with respect to adverse effects, since such a dose is 20% higher than that used in the study.

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