

BC COVID THERAPEUTICS

Memorandum

Date: January 29, 2021

To: BC Physicians, Family Medicine Specialists, & Pharmacists

From: BC COVID-19 Therapeutics Committee

Re: Colchicine for Treatment of Non-Hospitalized COVID-19 Patients

On January 27, 2021, the pre-print manuscript of the COLCORONA (colchicine) trial was released. Even though the study has not been officially published in a peer-reviewed journal, the BC COVID-19 Therapeutics Committee (CTC) has conducted an expedited review in order to provide appropriate guidance to prescribing clinicians. Based on these findings, the CTC recommends the following and will make updates as new data become available.

Recommendation:

For Mildly Ill COVID-19 Non-Hospitalized Patients: The CTC does **not** recommend the routine use of colchicine at this time. In patients aged 40 years or older with PCR-confirmed COVID-19 who have at least one risk factor* and no contraindications[#], **colchicine 0.6 mg PO BID x 3 days, then 0.6 mg daily x 27 days** may be considered on a case-by-case basis in discussion with the patient by clearly highlighting the uncertainty in the benefit of treatment, and the risks and potential adverse effects. Informed consent should be obtained and treatment initiated as soon as possible.

Possible Benefit = Colchicine may prevent hospitalization in 1 out of 71 patients (4.5% colchicine vs. 5.9% placebo).

Possible Harms = Side-effects include diarrhea (14% colchicine vs. 7% placebo) and nausea (2% colchicine vs. 2% placebo), and pulmonary embolism (0.5% colchicine vs. 0.1% placebo).

Colchicine is not recommended for prophylaxis or treatment of hospitalized COVID-19 patients outside of approved randomized-controlled trials.

*Age ≥ 70 years, obesity (BMI ≥ 30 kg/m²), diabetes, hypertension (systolic ≥ 150 mmHg), respiratory or coronary disease, heart failure, fever $\geq 38.4^\circ\text{C}$, or dyspnea.

[#]Contraindications – GFR < 30 mL/min, inflammatory bowel disease, chronic diarrhea or malabsorption, neuromuscular disease, severe liver disease, chemotherapy, current colchicine treatment, hypersensitivity to colchicine, or concurrent medications that interact with colchicine (e.g. amiodarone, azoles, carvedilol, cyclosporine, estradiol, macrolides, propafenone, protease inhibitors, quinidine, quinine, verapamil).

Evidence used for this recommendation:

In the COLCORONA randomized, double-blind, placebo-controlled trial of non-hospitalized patients with probable or proven COVID-19, colchicine 0.5 mg PO BID x 3 days, then 0.5 mg daily x 27 days did not have a statistically significant reduction in a composite primary endpoint of hospitalization or mortality at 30 days when compared to placebo (**4.7% colchicine [n=2235] vs. 5.8% placebo [n=2253]; OR 0.79; 95% CI 0.61 to 1.03; p<0.08**). However, when only COVID-19-confirmed patients were included, results were statistically significant (**4.6% colchicine [n=2075] vs. 6.0% placebo [n=2084]; OR 0.75; 95% CI 0.57 to 0.99; p<0.04**). Of these patients, the odds ratio was statistically significant for reduction in hospitalization 0.75 (95%CI, 0.57 to 0.99), but not for mechanical ventilation 0.50 (95%CI, 0.23 to 1.07) or death 0.56 (95%CI, 0.19 to 1.66). Serious adverse events were 4.9% in colchicine vs. 6.3% in placebo groups (p=0.05), pneumonia 2.9% vs. 4.1% (p=0.02), pulmonary embolism 0.5% vs. 0.1% (p=0.01), and diarrhea 13.7% vs. 7.3% (p<0.0001), respectively.

Several limitations exist. The intent-to-treat analysis did not show statistical significance in the primary endpoint, yet after removal of 329 patients without PCR-confirmed COVID-19, significance was observed. The absolute difference of 1.4% for the primary endpoint provides a relatively minor benefit corresponding to a number-needed-to-treat of 71, and odds ratios had wide confidence intervals. Median age was young at 54.7 years with only 9.9% who were 70 years or older. Additionally, the trial was terminated early due to logistical issues and intent for early publication, attaining 4506 out of the intended sample of 6000 patients.

The CTC will continue to update the “Clinical Practice Guidance for Antimicrobial and Immunomodulatory Therapy in Adult Patients with COVID-19” document based on any new studies and relevant data. Please refer to the BCCDC website for the most updated information:

<http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments>