

# The Medical Letter<sup>®</sup>

## on Drugs and Therapeutics

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# The Medical Letter®

## on Drugs and Therapeutics

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### COVID-19 UPDATE

#### NIH Recommends Against Ivermectin

On April 29, the NIH recommended against use of the antiparasitic drug ivermectin for treatment of COVID-19 outside of a clinical trial. The recommendation was made because recent randomized, placebo-controlled trials of ivermectin have produced negative results and because alternative drugs that have been shown to be effective for treatment of COVID-19 are available.<sup>1</sup>

**IVERMECTIN** – Ivermectin has been used for years for treatment of infections caused by parasitic organisms such as *Strongyloides stercoralis* and *Onchocerca volvulus*. *In vitro*, high concentrations of ivermectin inhibit SARS-CoV-2 replication,<sup>2</sup> but achieving comparable concentrations of the drug in lung tissue or plasma would require doses much higher than those typically used in humans.<sup>3</sup>

**CLINICAL STUDIES** – In a randomized, double-blind trial, 1358 outpatient adults with COVID-19 and at least one risk factor for disease progression whose symptoms had begun  $\leq 7$  days previously received ivermectin 400 mcg/kg or placebo once daily for 3 days. The proportion of patients who required emergency department observation lasting  $>6$  hours or hospitalization due to COVID-19 within 28 days, the primary endpoint, did not differ significantly between the ivermectin and placebo groups (14.7% vs 16.3%; HR 0.90 [95% CI 0.70-1.16]).<sup>4</sup>

In another double-blind trial (IVERCOR-COVID19), 501 nonhospitalized adults in Argentina who had tested positive for SARS-CoV-2 infection  $\leq 48$  hours previously were randomized to receive ivermectin (12-24 mg based on weight) or placebo once daily for 2 days. The rate of hospitalization for any cause lasting  $\geq 24$  hours, the primary endpoint, did not differ significantly between the ivermectin and placebo groups (5.6% vs 8.4%; HR 0.65 [95% CI 0.32-1.31]). Time to hospitalization was also not significantly different between the two groups.<sup>5</sup>

In a third double-blind trial, 400 adults in Columbia with mild COVID-19 whose symptoms had begun  $\leq 7$  days previously were randomized to receive ivermectin 300 mcg/kg or placebo once daily for 5 days. The median time to symptom resolution, the primary endpoint, did not differ significantly between the ivermectin and placebo groups (10 vs 12 days; HR for resolution 1.07 [95% CI 0.87-1.32]).<sup>6</sup>

In an open-label trial in Malaysia (I-TECH), 490 adults  $\geq 50$  years old with mild to moderate COVID-19 whose symptoms had begun  $\leq 7$  days previously were randomized to receive ivermectin 400 mcg/kg or placebo once daily for 5 days. The rate of progression to severe disease (defined as a need for supplemental oxygen to maintain  $SpO_2 \geq 95\%$ ), the primary endpoint, did not differ significantly between the ivermectin and placebo groups (21.6% vs 17.3%; RR 1.25 [95% CI 0.87-1.80]).<sup>7</sup>

**RECOMMENDATIONS** – The NIH recommends that nonhospitalized adults with COVID-19 be treated with either oral ritonavir-boosted nirmatrelvir (*Paxlovid*) or IV remdesivir (*Veklury*); ritonavir-boosted nirmatrelvir is preferred.<sup>8</sup> Both of these therapies decreased the risk of hospitalization or death significantly more than placebo in large, randomized, double-blind trials.<sup>9,10</sup> If these drugs are inappropriate or unavailable, use of molnupiravir (*Lagevrio*) or bebtelovimab (both available under FDA Emergency Use Authorization) is recommended.<sup>8</sup> ■

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