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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.[1]

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,[2] but achieving comparable concentrations of the drug in lung tissue or plasma would require doses much higher than those typically used in humans.[3]

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 ≤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]).[4]

In another double-blind trial (IVERCOR-COVID19), 501 nonhospitalized adults in Argentina who had tested positive for SARS-CoV-2 infection ≤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 ≥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.[5]

In a third double-blind trial, 400 adults in Columbia with mild COVID-19 whose symptoms had begun ≤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]).[6]

In an open-label trial in Malaysia (I-TECH), 490 adults ≥50 years old with mild to moderate COVID-19 whose symptoms had begun ≤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 ≥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]).[7]

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.[8] Both of these therapies decreased the risk of hospitalization or death significantly more than placebo in large, randomized, double-blind trials.[9,10] If these drugs are inappropriate or unavailable, use of molnupiravir *(Lagevrio)* or bebtelovimab (both available under FDA Emergency Use Authorization) is recommended.[8] ■

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