Interferons

Interferons are a family of cytokines with in vitro and in vivo antiviral properties. Interferon beta-1a has been approved by the Food and Drug Administration (FDA) to treat relapsing forms of multiple sclerosis, and pegylated formulations of interferon alfa-2a and interferon alfa-2b have been approved by the FDA to treat hepatitis B and hepatitis C virus infections. Several interferons, including interferon alfa, beta, and lambda, have been evaluated for the treatment of COVID-19. Interferon lambda is not currently approved or authorized by the FDA for any use.

Recommendations

• For nonhospitalized patients with mild or moderate COVID-19, the COVID-19 Treatment Guidelines Panel (the Panel) recommends against the use of interferon alfa or beta, except in a clinical trial (AIIa).

• For hospitalized patients with COVID-19, the Panel recommends against the use of systemic interferon alfa (AIIa), except in a clinical trial.

• For hospitalized patients with COVID-19, the Panel recommends against the use of systemic interferon beta (AI).

• The Panel is unable to recommend either for or against the use of interferon lambda because this product is not currently available for clinical use.

Rationale

Interferon Alfa and Beta

Many of the early studies that evaluated the use of systemic interferons for the treatment of hospitalized adults with COVID-19 were conducted in early 2020, before the widespread use of remdesivir, corticosteroids, and other immunomodulators. In addition, these studies administered interferons with other drugs that have since been shown to have no clinical benefit in people with COVID-19, such as lopinavir/ritonavir and hydroxychloroquine.1-3

More recent studies have shown no benefit of using interferon beta-1a to treat patients with COVID-19, and some of the trials have suggested that interferon beta-1a can cause harm in patients with severe disease, such as those who require high-flow oxygen, noninvasive ventilation, or mechanical ventilation.4,5 In a large randomized controlled trial of hospitalized patients with COVID-19, the combination of interferon beta-1a plus remdesivir showed no clinical benefit when compared to remdesivir alone.4 Similarly, the World Health Organization Solidarity trial did not show a benefit for interferon beta-1a when this drug was administered to hospitalized patients, approximately 50% of whom were on corticosteroids.5

Systemic interferon alfa and inhaled interferons have also been evaluated in patients with COVID-19. The trials that have evaluated interferon alfa have generally been small or moderate in size and have not been adequately powered to assess whether this agent provides a clinical benefit for patients with COVID-19.6-8

Interferon Lambda

Pegylated interferon lambda was studied in a randomized, double-blind adaptive clinical trial that
enrolled nonhospitalized patients with COVID-19 in Brazil and Canada. A total of 1,941 patients with risk factors for severe COVID-19 were randomized to receive either a single subcutaneous injection of pegylated interferon lambda 180 mcg or placebo. Eighty-three percent of these patients had received at least 1 dose of COVID-19 vaccine. The primary outcome was a composite of observation in an emergency department for > 6 hours or hospitalization, and 1 of the secondary outcomes was a composite of hospitalization or death. By Day 28 after randomization, the use of interferon lambda was associated with a 51% decrease in the occurrence of the primary outcome and a 39% decrease in the occurrence of this secondary outcome. Patients with a high baseline SARS-CoV-2 viral load who received interferon lambda were more likely to have cleared the virus by Day 7 than those who received placebo.

The drug was generally well tolerated. However, since pegylated interferon lambda is an investigational agent that is not currently available for clinical use, the Panel cannot make a recommendation for its use at this time.

Summaries of the studies that informed the Panel’s recommendations can be found in Table 4d.

**Clinical Trials**

See ClinicalTrials.gov for a list of clinical trials that are evaluating the use of interferons for the treatment of COVID-19.

**Monitoring, Adverse Effects, and Drug-Drug Interactions**

The most common adverse effects of systemic interferons are flu-like symptoms, nausea, fatigue, weight loss, hematological toxicities, elevated transaminases, and psychiatric problems (e.g., depression, suicidal ideation). Interferon beta is better tolerated than interferon alfa, but it can cause similar types of adverse effects. Additive toxicities may occur when systemic interferons are used concomitantly with other immunomodulators and chemotherapeutic agents.

**Considerations in Pregnancy**

According to analyses of data from several large pregnancy registries, exposure to interferon beta-1b prior to conception or during pregnancy does not lead to an increased risk of adverse birth outcomes (e.g., spontaneous abortion, congenital anomaly). Exposure to interferon beta-1b during pregnancy did not influence birth weight, height, or head circumference.

**Considerations in Children**

There are insufficient data on the use of interferons to treat respiratory viral infections in children to make any recommendations for treating children with COVID-19.

**References**


