



Abatacept

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Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) is a protein receptor that is expressed by activated T cells. By mediating inhibitory signals, this receptor can decrease T cell proliferation and cytokine production.^{1,2} Abatacept (CTLA-4-Ig) is a soluble fusion protein that contains CTLA-4 linked to human immunoglobulin, and it is used to block T cell activation. Because excessive T cell stimulation and proliferation is thought to propagate the pathogenesis of COVID-19,³ modulating this response may be a potential option for the treatment of COVID-19.⁴

Abatacept is approved by the Food and Drug Administration (FDA) for the treatment of inflammatory arthritis and for the prophylaxis of acute graft-versus-host disease.⁵ It is currently not approved for the treatment of COVID-19. Abatacept has been evaluated in clinical trials for the treatment of hospitalized patients with moderate to severe COVID-19.

Recommendation

See [Therapeutic Management of Hospitalized Adults With COVID-19](#) for the COVID-19 Treatment Guidelines Panel's (the Panel) recommendations on the use of abatacept in hospitalized patients who require conventional oxygen, high-flow nasal cannula (HFNC) oxygen, or noninvasive ventilation (NIV).

Rationale

The ACTIV-1 immune modulator trial was a double-blind, multi-arm, placebo-controlled, randomized trial in moderately to severely ill adults hospitalized with COVID-19.⁶ The trial separately evaluated treatment with abatacept, cenicriviroc, and infliximab versus placebo. All arms received standard care, and the separate analyses included data from a shared placebo arm. One substudy compared the use of a single dose of intravenous abatacept 10 mg/kg to placebo. The primary endpoint was time to recovery by Day 28. Key secondary endpoints included clinical status at Day 14 and mortality through Days 28 and 60.

The study concluded that use of abatacept in patients with COVID-19 did not have a significant effect on the time to recovery. A reduction in 28-day mortality, a secondary endpoint, was found. Patients who required mechanical ventilation or extracorporeal membrane oxygenation (ECMO) did not benefit from the use of abatacept.

Clinical Data

In the ACTIV-1 trial, the modified intention-to-treat analysis for the abatacept substudy included 509 patients in the abatacept arm and 510 patients in the placebo arm. At baseline, 53% of the patients required conventional oxygen supplementation, and 33% required HFNC oxygen or NIV. As part of their standard care before or during the study, 93% of the patients received remdesivir, and 91% received corticosteroids.

Results

- The use of abatacept did not reduce the median time to recovery, which was the primary endpoint. The median time to recovery was 9 days in both the infliximab and placebo arms (recovery rate ratio 1.12; 95% CI, 0.98–1.28; $P = 0.09$), and there was no differential effect across subgroups

based on disease severity (interaction $P = 0.66$).

- Mortality by Day 28 was lower among patients who received abatacept (56 of 509 patients [11.0%]) than among those who received placebo (77 of 510 patients [15.1%]; OR 0.62; 95% CI, 0.41–0.94).
- Subgroup analyses showed reduced mortality only among patients in the abatacept arm who required HFNC oxygen or NIV (OR 0.48; 95% CI, 0.28–0.84).
- Among patients who required mechanical ventilation or ECMO, there was no difference in mortality by Day 28 (OR 1.63; 95% CI, 0.66–4.05).
- There were no differences in secondary infections or in the number or severity of serious adverse events between the abatacept and placebo arms.

Limitations

- Each of the 3 active agents was compared to a shared placebo group without adjustment for multiple comparisons.
- Mortality was a secondary endpoint. Although the treatment difference found for mortality by Day 28 was nominally significant, no adjustment was made for having considered multiple outcomes (primary outcome and mortality).
- The study was not powered to analyze differences within disease severity subgroups.

Adverse Effects and Monitoring

Most of the data on the adverse effects of abatacept come from the chronic use of the agent for the treatment of autoimmune diseases and graft-versus-host disease. When abatacept is used for the prevention of acute graft-versus-host disease, the most commonly reported adverse effects include fever, anemia, hypertension, cytomegalovirus infection (or reactivation), pneumonia, epistaxis, CD4 lymphopenia, and acute kidney injury.⁵ Concomitant use with other immunomodulatory agents may increase the risk of serious infections. Due to its immunosuppressive effects, all patients who are receiving abatacept should also be monitored for new infections. In the ACTIV-1 trial, data on the safety of short-term use of abatacept in patients with COVID-19 did not reveal significant safety concerns.

Considerations in Pregnant and Lactating People

See [Pregnancy, Lactation, and COVID-19 Therapeutics](#) for the Panel’s guidance regarding the use of abatacept during pregnancy and lactation.

Considerations in Children

The intravenous formulation of abatacept is approved by the FDA for the treatment of juvenile idiopathic arthritis and acute graft-versus-host disease in children aged ≥ 2 years. It is not approved for the treatment of COVID-19 in children, and there are no published reports on the efficacy of using abatacept in this population. No patients aged < 18 years were included in the ACTIV-1 trial.

References

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