Title: # Abatacept for Treatment of Adults Hospitalized with Moderate or Severe Covid-19.

Source: *MedRxiv : the Preprint Server for Health Sciences. 2022 Sep 26.*

Status: *PubMed-not-MEDLINE*

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Abstract:

Background: We investigated whether abatacept, a selective costimulation modulator, provides additional benefit when added to standard-of-care for patients hospitalized with Covid-19.

Methods: We conducted a master protocol to investigate immunomodulators for potential benefit treating patients hospitalized with Covid-19 and report results for abatacept. Intravenous abatacept (one-time dose 10 mg/kg, maximum dose 1000 mg) plus standard of care (SOC) was compared with shared placebo plus SOC. Primary outcome was time-to-recovery by day 28. Key secondary endpoints included 28-day mortality.

Results: Between October 16, 2020 and December 31, 2021, a total of 1019 participants received study treatment (509 abatacept; 510 shared placebo), constituting the modified intention-to-treat cohort. Participants had a mean age 54.8 (SD 14.6) years, 60.5% were male, 44.2% Hispanic/Latino and 13.7% Black. No statistically significant difference for the primary endpoint of time-to-recovery was found with a recovery-rate-ratio of 1.14 (95% CI 1.00-1.29; p=0.057) compared with placebo. We observed a substantial improvement in 28-day all-cause mortality with abatacept versus placebo (11.0% vs. 15.1%; odds ratio [OR] 0.62 [95% CI 0.41- 0.94]), leading to 38% lower odds of dying. Improvement in mortality occurred for participants requiring oxygen/noninvasive ventilation at randomization. Subgroup analysis identified the strongest effect in those with baseline C-reactive protein >75mg/L. We found no statistically significant differences in adverse events, with safety composite index slightly favoring abatacept. Rates of secondary infections were similar (16.1% for abatacept; 14.3% for placebo).

Conclusions: Addition of single-dose intravenous abatacept to standard-of-care demonstrated no statistically significant change in time-to-recovery, but improved 28-day mortality.

Trial registration: ClinicalTrials.gov (NCT04593940).

Publication Type: Preprint.

Year of Publication: 2022

Link https://www.medrxiv.org/content/10.1101/2022.09.22.22280247v1