Supplementary Material for the 2025 Clinical Practice Guideline Update by the Infectious Diseases Society of America on the Treatment and Management of COVID-19: Abatacept

Table of Contents

METHODS

Panel formation and conflicts of interest

The chair and vice chair of the guideline panel were selected by the leadership of IDSA. Twenty-four additional panelists comprised the full panel. The panel included clinicians with expertise in infectious diseases, pediatric infectious diseases, critical care medicine, pulmonology, maternal fetal medicine, and pharmacology, as well as biostatistics. Guideline methodologists oversaw all methodological aspects of the guideline development, including the identification and summarization of scientific evidence for each clinical question. IDSA staff oversaw all administrative and logistic issues related to the guideline panel.

All members of the expert panel complied with the IDSA policy on conflict of interest (COI), which requires disclosure of any financial, intellectual, or other interest that might be construed as constituting an actual, potential, or apparent conflict. Evaluation of such relationships as potential conflicts of interest was determined by a review process which included assessment by the Standards and Practice Guidelines Subcommittee (SPGS) Chair, and if necessary, the Conflict of Interests Ethics Committee. This assessment of disclosed relationships for possible COI was based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an independent observer might reasonably interpret an association as related to the topic or recommendation of consideration). The reader of these

guidelines should be mindful of this when the list of disclosures is reviewed. See the Notes section at the end of the guideline for the disclosures reported to IDSA.

Practice recommendations

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care by assisting practitioners and patients in making shared decisions about appropriate health care for specific clinical circumstances. These are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options [IOM 2011]. The "IDSA Handbook on Clinical Practice Guideline Development" provides more detailed information on the processes followed throughout the development of this guideline [IDSA CPG Handbook].

Review and approval process

Feedback was obtained from two external individual peer expert reviewers as well as the endorsing organizations. The IDSA Standards and Practice Guidelines Subcommittee (SPGS) and Board of Directors reviewed and approved the guideline prior to publication.

Process for updating

IDSA guidelines are regularly reviewed for currency. The need for updates to the guideline is determined by a scan of current literature and the likelihood that any new data would impact the recommendations. Any changes to the guideline will be submitted for review and approval to the appropriate Committees and Board of IDSA.

Clinical questions

Each clinical question was formatted according to the PICO style: Patient/Population (P), Intervention/Indicator (I), Comparator/Control (C), Outcome (O). For each PICO question, outcomes of interest were identified a priori and rated for their relative importance for decision-making.

Literature search

A literature search was conducted in Ovid Medline, Embase, and Cochrane Library in August 2024. Searches were limited to studies published in English.

Search terms: abatacept OR abatacept (tiab)

Study selection

Inclusion and exclusion criteria were pre-defined. The eligibility criteria below were used.
Inclusion criteria:

- *Patient population*- Patients with severe or critical COVID-19
- *Intervention*- Abatacept
- *Comparator*- No abatacept
- *Outcomes*- Mortality, serious adverse events
- *Study design***-** RCTs

Exclusion criteria:

- *Patient population*- Patients without severe or critical COVID-19
- *Intervention*- N/A
- *Comparator*- N/A
- *Study design***-** Review articles, case reports

Data extraction and analysis

Guideline methodologists, with panelist assistance, extracted the data for each pre-determined patient-important outcome. If a relevant publication was missing raw data for an outcome prioritized by the panel, an attempt was made to contact the author(s) for the missing data.

Evidence to decision

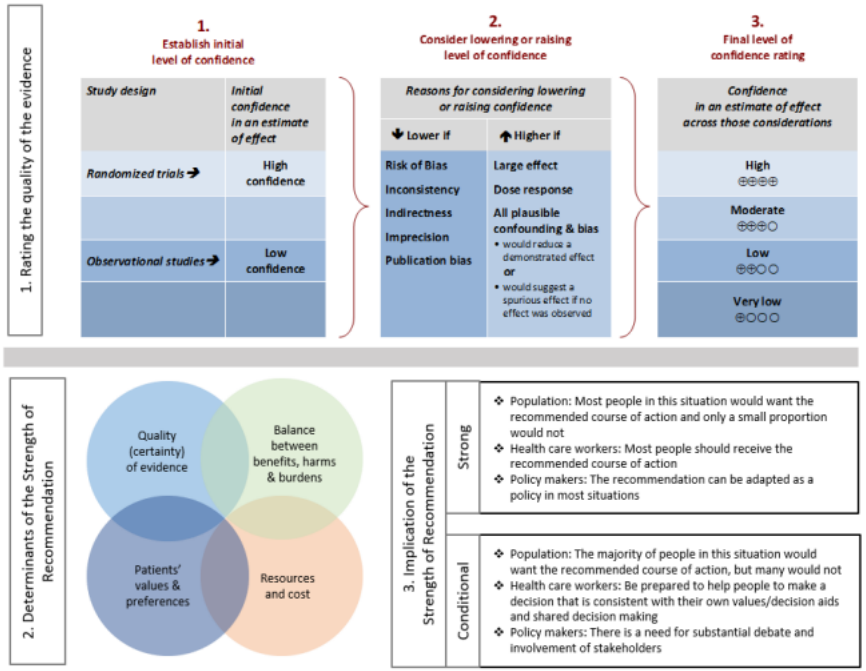
Guideline methodologists prepared the evidence summaries for each question and assessed the risk of bias and the certainty of evidence. Risk of bias was assessed by using the Cochrane Risk of Bias tool for RCTs [Higgins 2011]. The certainty of evidence was determined first for each critical and important outcome and then for each recommendation using the GRADE approach for rating the confidence in the evidence [Guyatt 2008, GRADE Handbook/Schunemann]. Evidence profiles were developed using the GRADEpro Guideline Development Tool [Guyatt 2008] and reviewed by panel members.

The Evidence to Decision framework [GRADEpro] was used to translate the evidence summaries into a practice recommendation. All recommendations are labeled as either “strong” or “conditional” according to the GRADE approach [IDSA CPG Handbook]. The words “we recommend” indicate strong recommendations and “we suggest” indicate conditional recommendations. Supplementary Figure 1 provides the suggested interpretation of strong and conditional recommendations for patients, clinicians, and healthcare policymakers. For recommendations where the comparator treatment or tests are not formally stated, the comparison of interest is implicitly referred to as “not using the intervention” (either not using a specific treatment or a diagnostic test).

All members of the panel participated in the preparation of the draft guideline and approved the recommendation.

TABLES AND FIGURES

Supplementary Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (unrestricted use of figure granted by the U.S. GRADE Network)



Supplementary Table 1. Characteristics of included studies

Study/Year	Country/ Hospital	Study design	N subjects (intervention/ comparator); % female	Age mean (SD)/ Median (IQR)	Severity of disease	Intervention (study arms)	Comparator	Co-interventions	Outcomes reported	Funding source
O'Halloran 2023 ACTIV-1	US and Latin America/95 hospitals at 85 clinical research site	RCT	1049 (Abatacept 524/ Placebo 525) Abatacept: 37.6% female Placebo 42.3% female	Abatacept: 54.8 (14.65)/55.0 (44.0-65.0) Placebo: 55.0 (14.66)/55.0 (45.0-65.0)	Hospitalized adults aged 18+ with confirmed SARS-CoV-2 infection within 14 days, anticipated hospitalization of 72 hours or more, and evidence of pulmonary involvement	Single infusion of abatacept (10 mg/kg, maximum dose 1000 mg) + Standard of care: remdesivir (93%), corticosteroids (89%), tocilizumab (3%), baricitinib (1%)	Standard of care: remdesivir (94%), corticosteroids (93%), tocilizumab (3%), baricitinib (3%)	N/A	Time to recovery by day 28 Clinical status at day 14 and day 28 All-cause mortality at day 14 and 28 SAEs grade 3 or 4	US Department of Health and Human Services NCATS of the National Institutes of Health

Supplementary Table 2. Risk of bias assessment

Study	Bias in randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result
O'Halloran 2023	Low	Low	Low	Low	Low

Low	High	Some concerns

REFERENCES

Guyatt GH, Oxman AD, Vist GE, et al.; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ **2008**; 336:924-6.

Higgins JPT, Altman DG, Gotsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomized trials. BMJ **2011**; 343:d5928.

IOM (Institute of Medicine). Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press, **2011**.

Infectious Diseases Society of America. IDSA Handbook on Clinical Practice Guideline Development. Available at: https://www.idsociety.org/practice-guideline/clinical-practice-guidelines-development-training-and-resources/. Accessed 02/10/2025.

McMaster University and Evidence Prime Inc. GRADEpro GDT. Available at: https://gradepro.org/. Accessed 02/10/2025.

O'Halloran JA, Ko ER, Anstrom KJ, et al, for the ACTIV-1 IM Study Group Members. Abatacept, cenicriviroc, or infliximab for treatment of adults hospitalized with COVID-19 pneumonia. JAMA **2023**, 330:328-39.

Schünemann H, Brożek J, Guyatt GH, Oxman A. Introduction to GRADE Handbook. Available at: https://gdt.gradepro.org/app/handbook/handbook.html. Accessed 02/10/2025.