Supplementary Material for the 2024 Clinical Practice Guideline Update by the Infectious Diseases Society of America on the Management of COVID-19: Anti-SARS-CoV-2 Neutralizing Antibody Pemivibart for Pre-Exposure Prophylaxis

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-one 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
The U.S. Food and Drug Administration's Emergency Use Authorization for pemgarda (pemivibart) for pre-exposure prophylaxis of COVID-19 was downloaded from the FDA's website. Additionally, a literature search was conducted in Ovid Medline, Embase, and Cochrane Library in May 2024. Searches were limited to studies published in English.

Search terms: pemivibart OR pemgarda (tiab)

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

- *Patient population*- Immunocompromised persons 12 years or older
- *Intervention*- Pemivibart
- *Comparator*- No pemivibart
- *Outcomes*- Mortality, symptomatic infections, anaphylaxis
- *Study design***-** RCTs and observational studies

Exclusion criteria:

- *Patient population*- Persons <12 years
- *Intervention*- N/A
- *Comparator*- N/A
- *Study design***-** Review articles

Data extraction and analysis

Guideline methodologists, in conjunction with panelists, 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

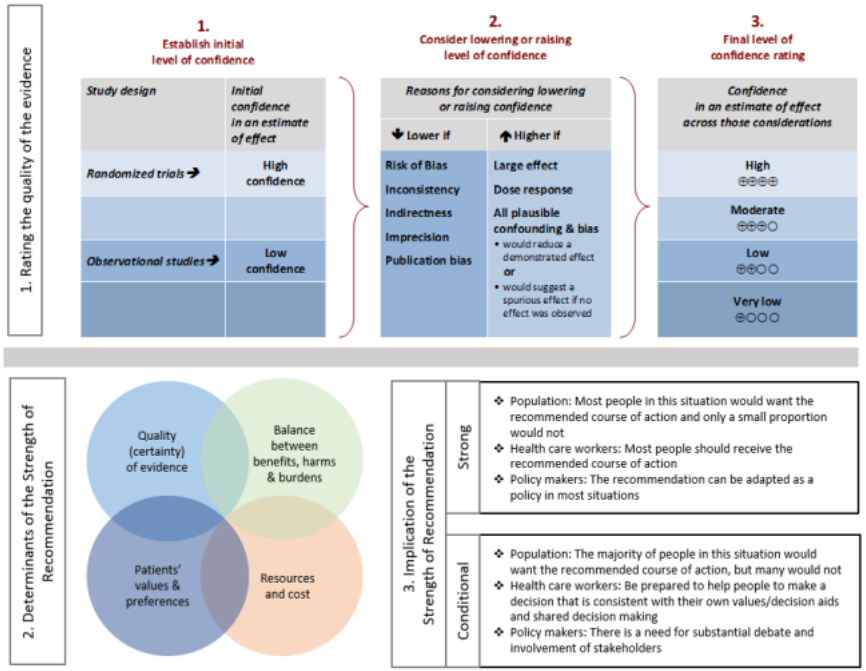
Guideline methodologists prepared the evidence summaries for each question and assessed the risk of bias and the certainty of evidence. Risk of bias was assessed by using the Cochrane Risk of Bias tool for RCTs and ROBINS-I for non-randomized studies [Higgins, Sterne]. The certainty of evidence was determined 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]. 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 for pemivibart

Study/year; design	Country/ Hospital	N subjects (intervention/ comparator); % female	Age, mean (SD)/ median (IQR)	Severity of disease	Intervention (study arms)	Comparator	Outcomes reported	Funding source
Ison 2023 RCT	Argentina, Czech Republic, Georgia, Moldova, Poland, Romania, Ukraine, USA	1831 (from pre-Omicron efficacy analysis) (PEP (351): Adintrevimab 175/Placebo 176 PrEP (1480): Adintrevimab 752/Placebo 728 52.2% female	Median (IQR): PEP: 47 (17-86) PrEP: 47 (12-87)	Unvaccinated adults and adolescents whose circumstances placed them at risk of acquiring SARS-CoV-2 infection; immunocompromised individuals were eligible but did not comprise much of the study population. *PEP group:* participants with reported recent exposure to an individual testing positive for SARS-CoV-2 (index case) *PrEP group:* no known recent exposure but did have occupational, housing, recreational, or social circumstances that increased their risk of exposure	Single 300-mg intramuscular injection of adintrevimab No cointerventions	Single 300-mg intramuscular injection of placebo	Proportion of participants with RT-PCR-confirmed symptomatic COVID-19 through day 28 (PEP cohort) and through month 3 (PrEP cohort) Time from randomization to first RT-PCR-confirmed symptomatic COVID-19 Incidence of RT- PCR-confirmed symptomatic COVID-19 through 6 months in who were considered PrEP-like participants Safety (e.g. treatment emergent and serious adverse events, vital signs and clinical laboratory assessments)	Invivyd, Inc
Pemgarda/ Pemivibart Fact Sheet 2024; RCT	USA/18 INVIVYD Investigative Sites	623 *Cohort A:* At least one dose: PEM GARDA 306/ 0 placebo,	Median: 59	Adults with immune compromise and in participants aged 12 years or older who are at risk of exposure to SARS-CoV-2 *Cohort A:* has significant immune compromise from causes including solid	*Cohort A:* 4500 mg of IV VYD222 given three months after initial dose (approx 90 days)	*Cohort B:* 4500 mg of placebo given three months after initial dose (approx 90 days)	*Cohort A:* Incidence of treatment emergent adverse events through month 12 Ratio of SARS-CoV-2 sVNA titer against a relevant variant following VYD222	Invivyd, Inc.

		Second dose: PEMGARDA 296/ 0 placebo *Cohort B:* At least one dose: PEM GARDA 317/ 162 placebo, Second dose: Total of 450 participants received either PEMGARDA or placebo 61% female		tumor or hematologic malignancies, chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant, primary immunodeficiency, advanced HIV, or receiving qualifying immunosuppressive therapies. *Cohort B:* at risk of acquiring SARS-CoV-2 due to regular unmasked face-to-face interactions in indoor settings.	*Cohort B:* 4500 mg of IV VYD222 given three months after initial dose (approx. 90 days) No cointerventions		administration at Day 28 compared to a prespecified SARS-CoV-2 sVNA titer sVNA titer by timepoint following VYD222 administration through month 12 Proportion of participants with sVNA titer against a relevant variant following VYD222 administration above a minimum SARS-CoV-2 sVNA threshold by timepoint through month 12 ADAs against VYD222 through month 12 Serum concentrations (PK) of VYD222 through month 12 Proportion of participants with RT-PCR-confirmed symptomatic COVID-19 through month 12 *Cohort B:* Incidence of treatment emergent adverse events through month 12 RT-PCR-confirmed symptomatic COVID-19 through month 3, 6 and 12. Ratio of SARS-CoV-2 sVNA titer against a relevant variant following VYD222	

							administration at Day 28 compared to a prespecified SARS-CoV-2 sVNA titer threshold sVNA titer by timepoint following VYD222 administration through month 12 Proportion of participants with sVNA titer against a relevant variant following VYD222 administration above a minimum SARS-CoV-2 sVNA threshold by timepoint through month 12 COVID-19-related hospitalization or death within 28 days of symptom onset through month 12 COVID-19-related death through month 12 Serum concentrations (PK) of VYD222 through month 12 ADAs against VYD222 through month 12	

Supplementary Table 2. Risk of bias for included studies (PrEP in adults at risk for inadequate immune response)

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
Ison 2023, RCT	**Low**	**Low**	**Low**	**Low**	**Low**
Pemgarda/Pemivibart Fact Sheet 2024	**High**	**N/A**	**Low**	**Low**	**Low**

Low	Some Concerns	High

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