Neutralizing Antibodies for Pre-exposure and Post-exposure Prophylaxis

Section last reviewed and updated 12/23/2021
Last literature search conducted 11/30/2021

Resources:

- **CDC**: SARS-CoV-2 variants
- **FDA**: Qualifications for SARS-CoV-2 exposure
- **FDA**: EUA for Evusheld™ (tixagevimab co-packaged with cilgavimab)
- **NIH**: National Center for Advancing Translational Science

Recommendation 1 (NEW): In moderately or severely immunocompromised individuals* at increased risk for inadequate immune response to COVID-19 vaccine or for whom COVID-19 vaccine is not recommended due to a documented serious adverse reaction to the vaccine, the IDSA guideline panel suggests pre-exposure prophylaxis with tixagevimab/cilgavimab rather than no tixagevimab/cilgavimab. (Conditional recommendation, Low certainty of evidence)

Remarks:

- Dosing for tixagevimab/cilgavimab is 150 mg of tixagevimab & 150 mg of cilgavimab administered as two separate consecutive intramuscular injections once.
- Local SARS-CoV-2 variant susceptibility should be considered.

*See Figure 1 below
Figure 1. FDA EUA criteria for the use of tixagevimab/cilgavimab for pre-exposure prophylaxis of COVID-19 in moderately or severely immunocompromised patients 1

According to the FDA Emergency Use Authorization of Evusheld, medical conditions or treatments that may result in moderate to severe immune compromise include but are not limited to:

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200mm³, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, chancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

Reference

Figure 2. FDA EUA criteria for the use of tixagevimab/cilgavimab for pre-exposure prophylaxis of COVID-19 1

This EUA for the use of the unapproved products tixagevimab and cilgavimab for pre-exposure prophylaxis in adults and pediatric individuals (12 years of age and older weighing at least 40 kg) who are:

- Not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 AND:
  - have moderate to severe immune compromise due to a medical condition OR receipt of immunosuppressive medications or treatments AND may not mount an adequate immune response to COVID-19 vaccination OR
  - For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or a COVID-19 vaccine component(s).

Reference
Recommendation 2: In persons exposed to COVID-19 who are at high risk of progression to severe COVID-19, the IDSA guideline panel suggests post-exposure casirivimab/imdevimab rather than no casirivimab/imdevimab. (Conditional recommendation, Low certainty of evidence)

Remarks:
- Dosing for casirivimab/imdevimab is casirivimab 600 mg & imdevimab 600 mg IV or SC once.
- In the trial considered for this recommendation, participants were enrolled within 96 hours after a household contact received a diagnosis of SARS-CoV-2 infection.
- Local SARS-CoV-2 variant susceptibility should be considered.

Figure 3. FDA EUA criteria for the use of casirivimab/imdevimab for post-exposure prophylaxis of COVID-19

This EUA is for the use of the unapproved products casirivimab and imdevimab for post-exposure prophylaxis of COVID-19 in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:

- Not fully vaccinated OR who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (e.g., individuals with immunocompromising conditions including those taking immunosuppressive medications) AND
  - Have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per CDC criteria OR
  - Who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (e.g., nursing homes, prisons).

Reference
Why are neutralizing antibodies considered for prophylaxis?

Neutralizing antibodies directed at the receptor-binding domain of SARS-CoV-2 spike protein have been evaluated as prophylactic agents for COVID-19. In animal models there is evidence that antibody therapy may more rapidly reduce viral load in the upper and lower airways of infected animals resulting in reduced viral-induced pathology, demonstrating in vivo prophylactic and treatment efficacy [1, 2]. Additionally, antibody mediated enhancement of disease has not been detected in animal models [2] but this potential phenomenon should be closely monitored in the future studies. In a large, randomized study of unvaccinated nursing home patients and staff where there was at least one confirmed case of COVID-19 at the facility, a single dose of either bamlanivimab appeared to significantly reduce the incidence of “mild or worse” COVID-19 amongst the nursing home residents [3].

Potential advantages of neutralizing antibodies include the ability to standardize the amount of neutralizing activity and the possibility of conferring protection more rapidly than with vaccine-induced immune responses (which generally take several weeks).

Summary of the evidence

Tixagevimab/cilgavimab

Our search identified one RCT reporting on pre-exposure prophylaxis (PrEP) with a single dose of intramuscular tixagevimab/cilgavimab administration in adults ≥18 years of age who are at increased risk of inadequate response to COVID-19 vaccination or SARS-CoV-2 infection [4, 5]. Patients included were those that were either age ≥60 years, immunocompromised, had severe renal or liver impairment, COPD, or those who had an increased risk of exposure including those working in healthcare or living in congregate living settings. All participants had a negative SARS-CoV-2 serology test result at screening, had no history of SARS-CoV-2 infection, and had not received vaccine or biologic indicated for prevention of SARS-CoV-2 or COVID-19. Study participants received a single combined 300 mg intramuscular dose of the combination of tixagevimab (150 mg) /cilgavimab (150 mg).

Casirivimab/imdevimab

Our search identified one RCT reporting on post-exposure prophylaxis (PEP) with neutralizing antibodies (combination of casirivimab/imdevimab) for patients exposed to COVID-19 who are at high risk of progression to severe disease [6] (Table 2).

One RCT reported on 1,505 persons testing negative for SARS-CoV-2 infection (by reverse-transcriptase-quantitative polymerase-chain-reaction assay [RT-qPCR]) within 96 hours following household contact with a diagnosis of SARS-CoV-2 infection [6]. Of those included in the trial, 30.5% participants were categorized as having a high risk of COVID-19 (e.g., ≥65 years of age, body mass index [BMI] ≥35, chronic kidney disease, etc.). Participants in the treatment group received a total dose of 1200 mg of casirivimab/imdevimab subcutaneously.
**Benefits**

**Tixagevimab/cilgavimab**

PrEP with tixagevimab/cilgavimab appears to have little or no effect on mortality through a median of 6 months (RR: 0.50; 95% CI: 0.13, 2.0; absolute risk reduction: 1 fewer per 1,000 [from 2 fewer to 2 more]; moderate CoE). Symptomatic COVID-19 infection within six months after administration was reduced in those who received tixagevimab/cilgavimab compared to placebo (RR: 0.18; 95% CI: 0.09, 0.35; moderate CoE).

**Casirivimab/imdevimab**

Persons receiving PEP with casirivimab/imdevimab demonstrated an 81% relative risk reduction in development of symptomatic SARS-CoV-2 infection (RR: 0.19; 95% CI: 0.10, 0.35; moderate CoE). Of the 70 persons who developed symptomatic infection, those who received casirivimab/imdevimab rather than placebo experienced a shorter duration of symptoms (mean difference [MD]: -2.0 weeks; 95% CI: -2.91, -1.09; low CoE).

**Harms**

**Tixagevimab/cilgavimab**

Serious adverse events were not meaningfully different in those that received PrEP with tixagevimab/cilgavimab compared to placebo (RR: 1.09; 95% CI: 0.67, 1.78; moderate CoE).

**Casirivimab/imdevimab**

Serious treatment-emergent adverse events may be less frequent among persons receiving casirivimab/imdevimab compared to those receiving placebo; however, this may not be meaningfully different from those receiving placebo (RR: 0.66; 95% CI: 0.30, 1.47; low CoE).

**Other considerations**

**Tixagevimab/cilgavimab**

The panel agreed that the overall certainty of evidence for PrEP with tixagevimab/cilgavimab was low due to concerns with the generalizability of the trial population to the FDA-authorized indications (e.g., immunocompromised persons) and low number of events (fragility of results). The panel noted concerns with feasibility at different centers given the large number of potentially eligible individuals and supply constraints.

**Casirivimab/imdevimab**

The panel agreed that the overall certainty of evidence for post-exposure prophylaxis with casirivimab/imdevimab was low due to low number of events (fragility of results). The panel notes some indirectness between the trial participants (30.5% with any high-risk factor for COVID) and the current approved indications for post-exposure prophylaxis within the EUA.
Conclusions and research needs for this recommendation

Tixagevimab/cilgavimab

The guideline panel suggests PrEP with tixagevimab/cilgavimab in moderately or severely immunocompromised individuals at increased risk for inadequate immune response to COVID-19 vaccine or for whom COVID-19 vaccine is not recommended due to documented severe reactions to the COVID-19 vaccine. Data on the efficacy of pre-exposure prophylaxis specifically in immunocompromised individuals who have received COVID-19 vaccines are needed.

Casirivimab/imdevimab

The guideline panel suggests PEP using casirivimab/imdevimab in persons exposed to COVID-19, who are at high risk of progression.
**IDSA Guideline on the Treatment and Management of COVID-19**

*Neutralizing Antibodies for Pre-Exposure and Post-Exposure Prophylaxis*

Table 1. GRADE evidence profile, Recommendation 1

**Question:** Tixagevimab/cilgavimab compared to no tixagevimab/cilgavimab for pre-exposure prophylaxis in adults at increased risk for inadequate immune response to COVID-19 vaccine or for whom COVID-19 vaccine is not recommended

*New evidence profile developed 12/23/2021*

<table>
<thead>
<tr>
<th>Certainty assessment</th>
<th>№ of patients</th>
<th>Effect</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All-cause mortality (follow-up: median 6 months)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,2 randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>serious</td>
<td>serious</td>
</tr>
<tr>
<td><strong>Symptomatic COVID-19 (follow-up: median 6 months; assessed with: RT-PCR-positive symptomatic illness)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,2 randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>serious</td>
<td>serious</td>
</tr>
<tr>
<td><strong>Serious adverse events (follow-up: median 83 days)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,2 randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>serious</td>
<td>serious</td>
</tr>
</tbody>
</table>

**GRADE Working Group grades of evidence**

- **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect
- **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
- **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
- **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

- **Risk of bias:** Study limitations
- **Inconsistency:** Unexplained heterogeneity across study findings
- **Indirectness:** Applicability or generalizability to the research question
- **Imprecision:** The confidence in the estimate of an effect to support a particular decision
- **Publication bias:** Selective publication of studies

*NB: Certainty ratings may be derived from evidence that includes pre-print articles, which have not been peer reviewed or published.*

**CI:** Confidence interval; **HR:** Hazard ratio; **RR:** Risk ratio

**Explanations**
a. Possible misclassification bias due to unequal rate of drop-outs after unblinding.
b. 2 deaths in the control arm were attributed to COVID-19.
c. Trial population indirect to the population indicated within the FDA EUA (e.g., immunocompromised).
d. Small number of events; fragility present.

References
Table 2. GRADE evidence profile, Recommendation 2

Question: Prophylactic casirivimab/imdevimab compared to no prophylactic casirivimab/imdevimab for persons exposed to COVID-19 at high risk for progression to severe disease

Developed 8/17/2021; last reviewed 9/19/2021

<table>
<thead>
<tr>
<th># of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>No prophylactic casirivimab/imdevimab</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic SARS-CoV-2 infection (1200 mg SC) (follow-up: 28 days; assessed with: RT-qPCR plus broad-term definition)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (^1) randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>not serious</td>
<td>serious (^a)</td>
<td>none</td>
<td>prophylactic casirivimab/imdevimab</td>
<td>11/753 (1.5%)</td>
<td>59/752 (7.8%)</td>
<td>RR 0.19 (0.10 to 0.35)</td>
<td>64 fewer per 1,000 (from 71 fewer to 51 fewer)</td>
<td>⬤⬤⬤◯</td>
</tr>
<tr>
<td>Duration of symptomatic infection (1200 mg SC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (^1) randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious (^b)</td>
<td>none</td>
<td>-</td>
<td>11</td>
<td>59</td>
<td>MD 2 weeks fewer (2.91 fewer to 1.09 fewer)</td>
<td>⬤⬤⬤◯</td>
<td>LOW</td>
</tr>
<tr>
<td>COVID-19 related hospitalizations or ER visits (1200 mg SC) (follow-up: 28 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (^1) randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious (^a,c)</td>
<td>none</td>
<td>no prophylactic casirivimab/imdevimab</td>
<td>0/753 (0.0%)</td>
<td>4/752 (0.5%)</td>
<td>RR 0.11 (0.01 to 2.06)</td>
<td>5 fewer per 1,000 (from 5 fewer to 6 more)</td>
<td>⬤⬤⬤◯</td>
</tr>
<tr>
<td>Serious treatment-emergent adverse events (1200 mg SC) (follow-up: 28 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (^1) randomized trials</td>
<td>not serious</td>
<td>not serious</td>
<td>serious (^d)</td>
<td>serious (^a,c)</td>
<td>none</td>
<td>-</td>
<td>10/1311 (0.8%)</td>
<td>15/1306 (1.1%)</td>
<td>RR 0.66 (0.30 to 1.47)</td>
<td>4 fewer per 1,000 (from 8 fewer to 5 more)</td>
<td>⬤⬤⬤◯</td>
</tr>
</tbody>
</table>

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Risk of bias: Study limitations
Inconsistency: Unexplained heterogeneity across study findings
Indirectness: Applicability or generalizability to the research question
Imprecision: The confidence in the estimate of an effect to support a particular decision
Publication bias: Selective publication of studies
IDSA Guideline on the Treatment and Management of COVID-19

Neutralizing Antibodies for Pre-Exposure and Post-Exposure Prophylaxis

NB: Certainty ratings may be derived from evidence that includes pre-print articles, which have not been peer reviewed or published.

CI: Confidence interval; MD: Mean difference; RR: Risk ratio

Explanations

a. Small number of events; fragility present
b. COVID-19 related hospitalizations is a surrogate for ICU admission, mechanical ventilation and death. Not rated down.
c. 95% CI cannot exclude meaningful harm
d. Serious treatment emergent adverse events reported for entire study population (including symptomatic and asymptomatic) and may not be generalizable to seronegative population.

Reference

References


Supplementary Materials

Study characteristics

- **Table s1.** Pre-exposure prophylactic tixagevimab/cilgavimab vs. no tixagevimab/cilgavimab in adults at risk for inadequate immune response to COVID-19 vaccine or for whom COVID-19 vaccine is not recommended

- **Table s2.** Post-exposure prophylactic casirivimab/imdevimab vs. no casirivimab/imdevimab for persons exposed to COVID-19 at high risk of progression to severe disease

Risk of bias

- **Table s3.** Randomized controlled studies, pre-exposure prophylaxis (tixagevimab/cilgavimab vs. no tixagevimab/cilgavimab)

- **Table s4.** Randomized controlled studies, post-exposure prophylaxis (casirivimab/imdevimab vs. no casirivimab/imdevimab)
Table s1. Should tixagevimab/cilgavimab vs. no tixagevimab/cilgavimab be used for pre-exposure prophylaxis in adults at risk for inadequate immune response to COVID-19 vaccine or for whom COVID-19 vaccine is not recommended?

<table>
<thead>
<tr>
<th>Study/year</th>
<th>Country/hospital</th>
<th>Study design</th>
<th>N subjects (intervention/comparator)</th>
<th>% female</th>
<th>Age mean (SD)/median (IQR)</th>
<th>Severity of disease</th>
<th>Intervention (study arms)</th>
<th>Comparator</th>
<th>Co-interventions</th>
<th>Outcomes reported</th>
<th>Funding source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levin/2021 ³</td>
<td>87 sites in Belgium, France, Spain, UK and US</td>
<td>RCT</td>
<td>5197 (3461/1736)</td>
<td>46.1</td>
<td>53.5 (15.0)</td>
<td>Adult patients at increased risk for inadequate COVID-19 vaccine response or increased risk of SARS-CoV-2 infection with negative SARS-CoV-2 serology</td>
<td>Tixagevimab/cilgavimab 300 mg x 1 dose</td>
<td>Placebo</td>
<td>None</td>
<td>Mortality, PCR positive symptomatic illness occurring post dose through day 183, Serious adverse events</td>
<td>AstraZeneca, US Department of Health and Human Services, US Biomedical Advanced Research and Development Authority</td>
</tr>
</tbody>
</table>
### Table s2. Should persons exposed to COVID-19 who are at high risk of progression to severe disease receive post-exposure casirivimab/imdevimab vs. no casirivimab/imdevimab?

<table>
<thead>
<tr>
<th>Study/year</th>
<th>Country/Hospital</th>
<th>Study design</th>
<th>N subjects (intervention/comparator)</th>
<th>% female</th>
<th>Age mean (SD) / Median (IQR)</th>
<th>Severity of disease</th>
<th>Intervention (study arms)</th>
<th>Comparator</th>
<th>Co-interventions</th>
<th>Outcomes reported</th>
<th>Funding source</th>
</tr>
</thead>
<tbody>
<tr>
<td>O’Brien/2021² Part A</td>
<td>United States (110 sites) Romania (1 site) Moldova (1 site)</td>
<td>RCT</td>
<td>1505 (753/752)</td>
<td>54.1</td>
<td>Mean: 42.9 (range of 12-92)</td>
<td>Previously and currently uninfected (RT-PCR negative) household contacts of persons with SARS CoV-2 infection</td>
<td>REGEN-COV 1200 mg (casirivimab 600 mg /imdevimab 600 mg) x 1 subcutaneous injection</td>
<td>Placebo</td>
<td>None</td>
<td>Symptomatic RT-PCR confirmed SARS-CoV-2 infection within 28 days Symptomatic and asymptomatic RT-PCR confirmed infection within 28 days Number of weeks of symptoms present Number of weeks of high viral load COVID-19 related hospitalization or ER visit Safety</td>
<td>Regeneron Pharmaceuticals F. Hoffman-La Roche COVID-19 Prevention Network grant, which is funded by cooperative awards from National Institute of Allergy and Infectious Diseases and National Institutes of Health</td>
</tr>
<tr>
<td>O’Brien/2021³ Part B</td>
<td>United States (110 sites) Romania (1 site) Moldova (1 site)</td>
<td>RCT</td>
<td>314 (155/156)</td>
<td>55</td>
<td>Mean: 40.9 (18)</td>
<td>RT-PCR positive for SARS CoV-2 and asymptomatic</td>
<td>REGEN-COV 1200 mg (casirivimab 600 mg /imdevimab 600 mg) x 1 subcutaneous injection</td>
<td>Placebo</td>
<td>None</td>
<td>Proportion of patients who developed signs and symptoms of COVID-19 within 14 days of positive RT-PCR Number of weeks of symptomatic</td>
<td>Regeneron Pharmaceuticals F. Hoffman-La Roche COVID-19 Prevention Network grant, which is funded</td>
</tr>
<tr>
<td>Study/year</td>
<td>Country/Hospital</td>
<td>Study design</td>
<td>N subjects (intervention/comparator)</td>
<td>% female</td>
<td>Age mean (SD) / Median (IQR)</td>
<td>Severity of disease</td>
<td>Intervention (study arms)</td>
<td>Comparator</td>
<td>Co-interventions</td>
<td>Outcomes reported</td>
<td>Funding source</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------</td>
<td>--------------</td>
<td>---------------------------------------</td>
<td>----------</td>
<td>-------------------------------</td>
<td>---------------------</td>
<td>-------------------------</td>
<td>------------</td>
<td>------------------</td>
<td>-------------------</td>
<td>----------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SARS CoV-2 infection</td>
<td>by cooperative awards from National Institute of Allergy and Infectious Diseases and National Institutes of Health</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Number of weeks of high viral load over 28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>COVID-19 related hospitalization or ER visit</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Safety</td>
<td></td>
</tr>
</tbody>
</table>

SARS CoV-2 infection
Number of weeks of high viral load over 28 days
COVID-19 related hospitalization or ER visit
Safety

by cooperative awards from National Institute of Allergy and Infectious Diseases and National Institutes of Health
Table s3. Risk of bias for randomized controlled studies (pre-exposure tixagevimab/cilgavimab vs. no tixagevimab/cilgavimab in adults at risk for inadequate immune response to COVID-19 vaccine or for whom COVID-19 vaccine is not recommended)

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of participants and personnel</th>
<th>Blinding of outcome assessment</th>
<th>Incomplete outcome data</th>
<th>Selective reporting</th>
<th>Other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levin 2021¹</td>
<td>Low</td>
<td>High</td>
<td>Unclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table s4. Risk of bias for randomized controlled studies (post-exposure casirivimab/imdevimab vs. no casirivimab/imdevimab for persons exposed to COVID-19 at risk of progression to severe disease)

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of participants and personnel</th>
<th>Blinding of outcome assessment</th>
<th>Incomplete outcome data</th>
<th>Selective reporting</th>
<th>Other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>O’Brien 2021 (Part A)²</td>
<td>Low</td>
<td>High</td>
<td>Unclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O’Brien 2021 (Part B)³</td>
<td>Low</td>
<td>High</td>
<td>Unclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
References for Supplementary Materials

