TIXAGEVIMAB/CILGAVIMAB – Clinical Development Overview

Tixagevimab/Cilgavimab [TIXA/CILGA], a combination of two recombinant long-acting monoclonal antibodies administered as two separate consecutive injections, may not be approved or authorized for use in your country. AstraZeneca is providing you with this material as an information service and professional courtesy. Providing this information does not constitute any recommendation for use.

For US only: EVUSHELD™ (tixagevimab co-packaged with cilgavimab) is not FDA-approved and is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of EVUSHELD under Section 564(b)(1) of the Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

TIXA/CILGA trials for prophylaxis and treatment of COVID-19 are being conducted, with expected total enrollment in >10,000 participants globally.¹²,⁷,⁹,¹⁵,¹⁶

This document contains some information from a pre-print article which has not undergone peer-review.¹⁷

### TIXA/CILGA Trials

- **TIXA/CILGA** is being evaluated for prophylaxis in high-risk adults before and after exposure to SARS-CoV-2. It is also being evaluated for treatment of COVID-19, including in high-risk populations.²,⁷,⁹,¹⁰,¹³-¹⁵,¹⁸
- Refer to the table below for further details of the TIXA/CILGA clinical trials evaluating the safety and efficacy of TIXA/CILGA.

#### Table 1: TIXA/CILGA Trials.

<table>
<thead>
<tr>
<th>Trial Name/Details</th>
<th>Ph I (N~60)</th>
<th>PROVENT²-⁶ (N=5,197)</th>
<th>STORM CHASER⁷,⁸ (N=1,121)</th>
<th>TACKLE⁵,⁹,¹² (N=903)</th>
<th>ACTIV-2¹³,¹⁴ (N~2,000)</th>
<th>ACTIV-3¹⁵-¹⁷ (N~850)</th>
<th>DisCoVeRy¹⁸ (N~620)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention/Treatment</td>
<td>Prevention/ Treatment</td>
<td>Prevention: Exposure Pre-exposure Prophylaxis</td>
<td>Prevention: Exposure Post-exposure Prophylaxis</td>
<td>Treatment: Outpatient</td>
<td>Treatment: Outpatient</td>
<td>Treatment: Hospitalized patients</td>
<td>Treatment: Hospitalized patients</td>
</tr>
<tr>
<td>Sponsor</td>
<td>AZ</td>
<td>AZ</td>
<td>AZ</td>
<td>AZ</td>
<td>NIH</td>
<td>NIH</td>
<td>INSERM</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Trial Design</td>
<td>Phase I, randomized, double-blind, placebo-controlled, dose escalation study assessing safety, tolerability, pharmacokinetics</td>
<td>Phase III, randomized, double-blind, placebo-controlled, multicenter assessing safety and efficacy</td>
<td>Phase III, randomized, double-blind, placebo-controlled, multicenter assessing safety and efficacy</td>
<td>Phase III, randomized, double-blind, placebo-controlled, multicenter</td>
<td>Phase II/III, randomized, double-blind, placebo-controlled, multicenter</td>
<td>Phase III, randomized, double-blind, placebo-controlled, multicenter</td>
<td>Phase II, randomized, blinded, placebo-controlled, multicenter</td>
</tr>
<tr>
<td>Primary Efficacy Endpoint</td>
<td>Participants with AEs and SAEs though Day 361</td>
<td>Incidence of first case of SARS-CoV-2 RT PCR positive symptomatic illness by Day 183</td>
<td>Incidence of first case of SARS-CoV-2 RT PCR positive symptomatic illness by Day 183</td>
<td>Composite of either severe COVID-19 or death from any cause through Day 29</td>
<td>Prevention of death or hospitalization due to severe COVID-19 through Day 28</td>
<td>Sustained recovery from COVID-19: participants discharged from hospital and lived at home for 14 days</td>
<td>Percentage of subjects reporting each severity rating on a 7-point ordinal scale through Day 15³</td>
</tr>
</tbody>
</table>

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¹²,⁷,⁹,¹⁵,¹⁶

¹⁷

¹³,¹⁴

¹⁸

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<table>
<thead>
<tr>
<th>Trial Name/ Details</th>
<th>Ph I (N~60)</th>
<th>PROVENT\textsuperscript{2-6} (N=5,197)</th>
<th>STORM CHASER\textsuperscript{7,8} (N=1,121)</th>
<th>TACKLE\textsuperscript{5,9,12} (N=903)</th>
<th>ACTIV-2\textsuperscript{13,14} (N=2,000)</th>
<th>ACTIV-3\textsuperscript{15-17} (N=850)</th>
<th>DisCoVeRy \textsuperscript{18} (N=620)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing</td>
<td>TIXA/CILGA doses across five fixed-dose cohorts via IV infusions and IM injections</td>
<td>Single dose of TIXA/CILGA 300 mg (via 2 x IM injections)</td>
<td>Single dose of TIXA/CILGA 300 mg (via 2 x IM injections)</td>
<td>Single dose of TIXA/CILGA 600 mg (via 2 x IM injection) or 300 mg (via IV infusion)</td>
<td>Single dose of TIXA/CILGA 600 mg (via IV infusion)</td>
<td>Single dose TIXA/CILGA 600 mg (via IV infusion)</td>
<td>Single dose TIXA/CILGA 600 mg (via IV infusion)</td>
</tr>
<tr>
<td>Key Inclusion Criteria</td>
<td>Adults aged 18-55 years with negative serology/qRT-PCR for SARS-CoV-2</td>
<td>≥18 years of age at increased risk for SARS-CoV-2 infection or at increased risk of having inadequate response to active immunization \textsuperscript{19}</td>
<td>≥18 years of age with potential exposure, within 8 days to a specific identified individual with laboratory-confirmed SARS-CoV-2 infection, symptomatic or asymptomatic</td>
<td>≥18 years of age; non-hospitalized patients with mild to moderate COVID-19 who have been symptomatic for ≤7 days</td>
<td>≥18 years of age; non-hospitalized patients with mild to moderate COVID-19; at lower risk of progression to hospitalization or death (phase II); at higher risk for progression to hospitalization or death (phase III)</td>
<td>≥18 years of age; initially hospitalized patients for acute medical care</td>
<td>≥18 years of age; hospitalized with: • Presence of pulmonary rales/crackles on clinical exam OR • SpO2 ≤ 94% on room air OR • Requirement of supplemental oxygen including high flow oxygen devices or non-invasive ventilation</td>
</tr>
<tr>
<td>For detailed inclusion/exclusion criteria</td>
<td>Phase I</td>
<td>PROVENT</td>
<td>STORM CHASER</td>
<td>TACKLE</td>
<td>ACTIV-2</td>
<td>ACTIV-3</td>
<td>DisCoVeRy</td>
</tr>
<tr>
<td>High-Level Results</td>
<td>NA</td>
<td>Primary outcome met. Please refer to the publication for further information.</td>
<td>Primary outcome met. Please refer to the publication for further information.</td>
<td>Primary outcome met. Please refer to the publication for further information.</td>
<td>NA</td>
<td>Primary outcome not met. Please refer to the publication for further information.</td>
<td>NA</td>
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<tr>
<td>Countries</td>
<td>• UK • US • UK</td>
<td>• US • UK</td>
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<td>• UK • US</td>
<td>• US</td>
<td>• US • UK</td>
<td>• Austria • Belgium</td>
</tr>
</tbody>
</table>
The information in this response is intended to be a concise summation of representative clinical trial data, rather than being all-inclusive, so all available published literature may not be included.

**Abbreviations:**


**REFERENCE(S)**


19 In House Data, AstraZeneca Pharmaceuticals LP. Clinical study protocol D8850C00002. April 07, 2021.