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Background. Casirivimab and imdevimab (CAS/IMDEV) is authorized for emergency use in the US for outpatients with COVID-19. We present results from patient cohorts receiving low flow or no supplemental oxygen at baseline from a phase 1/2/3, randomized, double-blinded, placebo (PBO)-controlled trial of CAS/IMDEV in hospitalized patients (pts) with COVID-19.

Methods. Hospitalized COVID-19 pts were randomized 1:1:1 to 2.4 g or 8.0 g of IV CAS/IMDEV (co-administered) or PBO. Primary endpoints were time-weighted average (TWA) change in viral load from baseline (Day 1) to Day 7, proportion of pts who died or went on mechanical ventilation (MV) through Day 29. Safety was evaluated through Day 57. The study was terminated early due to low enrollment (no safety concerns).

Results. Analysis was performed in pooled cohorts (low flow or no supplemental oxygen) as well as combined treatment doses (2.4 g and 8.0 g). The prespecified primary virologic analysis was in seronegative (seroneg) pts (combined dose group n=360; PBO n=160), where treatment with CAS/IMDEV led to a significant reduction in viral load from Day 1–7 (TWA change: LS mean (SE): -0.28 (0.12); 95% CI: -0.51 to -0.05; P=0.0172; Fig. 1). The primary clinical analysis had a strong positive trend, though it did not reach statistical significance (P=0.2048), and 4.5% clinical endpoints prespecified for hypothesis testing were nominally significant (Table 1). In seroneg pts, there was a 47.0% relative risk reduction (RRR) in the proportion of pts who died or went on MV from Day 1–29 (10.3% treated vs 19.4% PBO; nominal P=0.0061; Fig. 2). There was a 55.6% (6.7% treated vs 15.0% PBO; nominal P=0.0032) and 35.9% (7.3% treated vs 11.5% PBO; nominal P=0.0178) RRR in the prespecified secondary endpoint of mortality by Day 29 in seroneg pts and the overall population, respectively (Fig. 2). No harm was seen in seropositive patients, and no safety events of concern were identified.

Figure 1: TWA daily viral load decreased from baseline (Day 1) in seronegative patients receiving low flow or no supplemental oxygen

Table 1. Primary virologic and clinical endpoints

Table 2. Proportion of patients who died or were hospitalized with COVID-19

Conclusion. Co-administration of CAS/IMDEV led to a significant reduction in viral load in hospitalized, seroneg pts requiring low flow or no supplemental oxygen. In seroneg pts and the overall population, treatment also demonstrated clinically meaningful, nominally significant reductions in 28-day mortality and proportion of pts dying or requiring MV.

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Table. Primary efficacy endpoint results: first SARS-CoV-2 RT-PCR-positive symptomatic illness - censored at unblinding and/or receipt of any COVID-19 preventive product (full pre-exposure analysis set)

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<tr>
<th></th>
<th>AZD7442 (N=2441)</th>
<th>Placebo (N=1731)</th>
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<tbody>
<tr>
<td>n (%)</td>
<td>8 (0.2)</td>
<td>17 (1.0)</td>
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<tr>
<td>RRR (95% CI)</td>
<td>77% (46.0, 90.0)</td>
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<tr>
<td>P-value</td>
<td>&lt; 0.001</td>
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CI, confidence interval; RRR, relative risk reduction; RT-PCR, real-time polymerase chain reaction.

The full pre-exposure analysis set included all study participants in the full analysis set (all randomized participants who received at least one dose of AZD7442 or placebo) without prior confirmed SARS-CoV-2 RT-PCR-positive infection.

Conclusion. The primary study endpoints were met: a one-time dose of AZD7442 demonstrated statistically significant protection against symptomatic COVID-19 and was well tolerated. AZD7442 is the first long-acting monoclonal antibody combination that represents a potential new option to augment COVID-19 prevention.

PROVENT funding statement image