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LB4. Casirivimab and Imdevimab for Treatment of Hospitalized Patients With COVID-19 Receiving Low Flow or No Supplemental Oxygen

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COVID-19 Phase 2/3 Hospitalized Trial Team

Session: 55. Late Breaker Abstracts: COVID-19 Treatment & Prophylaxis
Thursday, September 30, 2021: 6:00 PM

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, -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 4/6 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

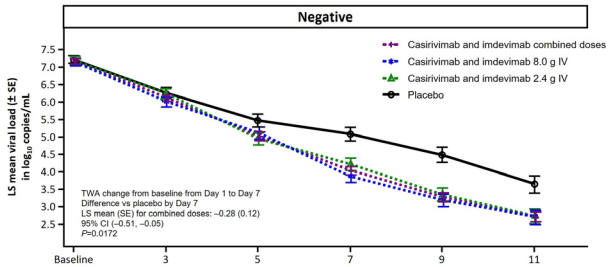
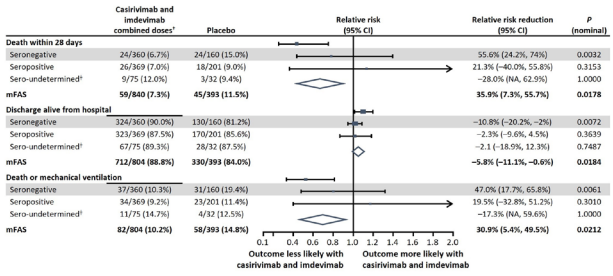


Table 1. Primary virologic and clinical endpoints

Hierarchy	Endpoint	Placebo	Casirivimab and Imdevimab Combined Doses
Primary virologic endpoint			
1.	**Time-weighted average change in viral load from baseline (day 1) to day 7 in seronegative mFAS**		
	No. of patients	131	310
	Least-squares mean change (SE) — log_{10} copies/mL	-1.03 (0.10)	-1.31 (0.06)
	95% CI	-1.22, -0.84	-1.43, -1.18
	Difference vs. placebo at day 7 — log_{10} copies/mL		
	Least-squares mean (SE)	-	-0.28 (0.12)
	95% CI	-	-0.51, -0.05
	P value	-	0.0172
Primary clinical endpoints			
2.	**Proportion of patients who died or went on mechanical ventilation from day 6 to day 29 in high viral load mFAS**		
	No./total no. (%)	28/211 (13.3)	44/445 (9.9)
	Relative risk reduction — %	-	25.5
	95% CI — %	-	-16.2, 52.2
	P value	-	0.2048*
3.	**Proportion of patients who died or went on mechanical ventilation from day 6 to day 29 in seronegative mFAS**		
	No./total no. (%)	22/147 (15.0)	27/341 (7.9)
	Relative risk reduction — %	-	47.1
	95% CI — %	-	10.2, 68.8
	P value		0.0195*
4.	**Proportion of patients who died or went on mechanical ventilation from day 6 to day 29 in overall mFAS**		
	No./total no. (%)	39/367 (10.6)	62/770 (8.1)
	Relative risk reduction — %	-	24.2
	95% CI — %	-	-10.9, 48.2
	P value		0.1486*
5.	**Proportion of patients who died or went on mechanical ventilation from day 1 to day 29 in high viral load mFAS**		
	No./total no. (%)	43/229 (18.8)	57/467 (12.2)
	Relative risk reduction — %	-	35.0
	95% CI — %	-	6.6, 54.8
	P value		0.0249*
6.	**Proportion of patients who died or went on mechanical ventilation from day 1 to day 29 in seronegative mFAS**		
	No./total no. (%)	31/160 (19.4)	37/360 (10.3)
	Relative risk reduction — %	-	47.0
	95% CI — %	-	17.7, 65.8
	P value		0.0061*
7.	**Proportion of patients who died or went on mechanical ventilation from day 1 to day 29 in overall mFAS**		
	No./total no. (%)	58/393 (14.8)	82/804 (10.2)
	Relative risk reduction — %	-	30.9
	95% CI — %	-	5.4, 49.5
	P value		0.0212*

*nominal P-value
CI, confidence interval; mFAS, modified full analysis set; SE, standard error.

Figure 2: Clinical outcomes in hospitalized patients receiving low flow or no supplemental oxygen*



* Pooled cohorts (low flow or no supplmental oxygen), Day 1 through Day 29
† 2.4 g IV and 8.0 g IV
‡ Sero-undetermined indicates missing or inconclusive serology results.

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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LB5. PROVENT: Phase 3 Study of Efficacy and Safety of AZD7442 (Tixagevimab/Cilgavimab) for Pre-exposure Prophylaxis of COVID-19 in Adults

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Session: 55. Late Breaker Abstracts: COVID-19 Treatment & Prophylaxis
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Background. Vaccines effectively prevent COVID-19, but some individuals have medical comorbidities or receive therapies that impair their immune response to vaccination, or are ineligible for vaccination. For such individuals who remain at risk of COVID-19, monoclonal antibodies may provide additional rapid protection. AZD7442 comprises 2 fully human extended half-life SARS-CoV-2–neutralizing antibodies that bind distinct epitopes of the viral spike protein receptor binding domain. AZD7442 is in development for the prevention and treatment of COVID-19. Here, we report primary Phase 3 study results of AZD7442 for pre-exposure prophylaxis of symptomatic COVID-19.

Methods. PROVENT (NCT04625725) is a Phase 3, 2:1 randomized, double-blind, placebo-controlled study of a single 300-mg AZD7442 dose (2 intramuscular injections; 150 mg each of tixagevimab and cilgavimab) for symptomatic COVID-19 prevention. Participants were unvaccinated adults (≥ 18 years old) without prior SARS-CoV-2 infection, who may benefit from immunoprophylaxis with antibodies due to an increased risk of either inadequate response to vaccination or SARS-CoV-2 exposure. The primary study endpoints were first case of SARS-CoV-2 RT-PCR-positive symptomatic illness post dose and prior to Day 183 (efficacy), and safety of AZD7442.

Results. In total, 5197 participants (mean age 53.5 years, 46% female) were randomized and dosed (safety analysis set): AZD7442 n=3460; placebo n=1737. In the primary efficacy analysis (full pre-exposure analysis set, n=5172), AZD7442 reduced the risk of developing symptomatic COVID-19 by 77% (95% confidence interval 46.0, 90.0) vs placebo (P< 0.001) (Table). Adverse events occurred in 35% and 34% of participants administered AZD7442 and placebo, respectively, and injection site reactions occurred in 2.4% and 2.1% of participants, respectively (safety analysis set). There was 1 case of severe/critical COVID-19 and 2 COVID-19–related deaths in the placebo arm.

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)

	AZD7442 (N=3441)	Placebo (N=1731)
n (%)	8 (0.2)	17 (1.0)
RRR (95% CI)	77% (46.0, 90.0)	
P-value	< 0.001	

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 ≥1 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

Funding statement

AZD7442 is being developed with support from the US Government, including federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority in partnership with the Department of Defense; Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense, under Contract No. W911QY-21-9-0001.

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LB11. Preliminary Findings from a HIV Self-Testing Program among People Who Use Drugs

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Session: 132. Late Breaker Abstracts
Saturday, October 2, 2021: 1:15 PM

Background. People who use drugs (PWUD) remain at significantly high risk for HIV infection. It is estimated that the majority of all new HIV infections are through injection drug use, with an estimated 2,500 new infections occurring annually among people who inject drugs. Although new HIV infections have been quickly rising over the past year, the Center for Disease Control and Prevention (CDC) preliminarily reported a 50% to 70% intra-pandemic decline in HIV testing. Within Kentucky, an ultra-high-risk state, multiple health departments reported all HIV testing stopped during the early stages of the COVID-19 pandemic (March-July 2020). Once testing resumed, appointments were sparse.