Poster 1924

Outpatient Treatment With the SARS-CoV-2–Neutralizing Antibody Combination AZD7442 (Tixagevimab/Cilgavimab) for Preventing COVID-19 Hospitalizations in the Phase 3 TACKLE Trial

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Introduction

- AZD7442 comprises two human, extended-half-life neutralizing antibodies (tixagevimab/cilgavimab) that bind to distinct epitopes on the SARS-CoV-2 spike protein receptor-binding domain.[1]
- Outpatient treatment with AZD7442 in adults with mild-to-moderate COVID-19 significantly reduced progression to severe disease or death through Day 29 and was well tolerated in the Phase 3 TACKLE study primary analysis (**NCT04723394**).[2]
- AZD7442 administered earlier in the disease course led to more favorable outcomes (88.0% and 50.5% reduction in severe disease or death when dosed ≤3 and ≤7 days after symptom onset, respectively) and has the potential to prevent COVID-19 hospitalizations and reduce hospital burden.[2]

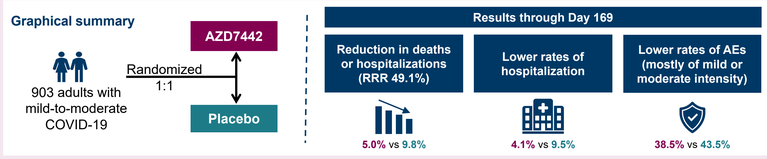
Objective

- We report key secondary efficacy results with longer term safety data from TACKLE over 6 months.

Conclusions

- A single 600-mg intramuscular dose of AZD7442 given within 7 days of symptom onset in outpatients with mild-to-moderate COVID-19 provided statistically significant protection against death from any cause or hospitalization for COVID-19 complications or sequelae through 6 months.
- AZD7442 was well tolerated through 6 months, with no new safety signals arising compared with the primary analysis.
- Overall, these data further support the administration of AZD7442 in an outpatient treatment setting to reduce hospitalization and hospital burden associated with COVID-19.

Graphical summary



Supplementary Content

Poster and video slides

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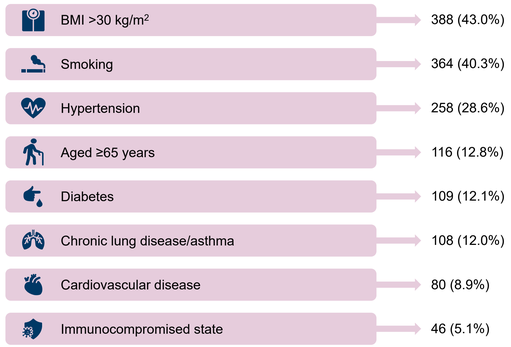
Results and interpretation

- In TACKLE, 88.7% of participants were at high risk of progression to severe COVID-19 (**Figure 1**).
- Baseline clinical characteristics were similar between the AZD7442 and placebo groups (**Table 1**).

Figure 1. Risk factors for severe COVID-19*



*These comorbidities are considered risk factors for severe COVID-19.
BMI, body mass index.

Table 1. Baseline characteristics

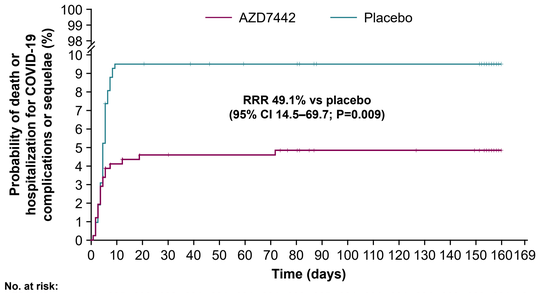
Characteristic	AZD7442 (n=452)	Placebo (n=451)
Age, years, mean (SD)	46.3 (15.4)	45.9 (15.0)
Sex, female, n (%)	239 (52.9)	216 (47.9)
Hispanic/Latino ethnicity, n (%)	230 (50.9)	238 (52.8)
Race, n (%)		
White	285 (63.1)	274 (60.8)
American Indian/Alaska Native	100 (22.1)	115 (25.5)
Asian	30 (6.6)	21 (4.7)
Black or African American	16 (3.5)	20 (4.4)
Not reported	21 (4.6)	21 (4.7)
BMI, kg/m^2, mean (SD)	28.9 (5.5)	29.2 (6.6)
Time from symptom onset to randomization, days, mean (SD)	4.9 (1.6)	5.0 (1.6)

BMI, body mass index; SD, standard deviation.

Efficacy

- AZD7442 treatment significantly reduced the incidence of death from any cause or hospitalization for COVID-19 complications or sequelae. These occurred in 20 (5.0%) and 40 (9.8%) participants receiving AZD7442 and placebo, respectively (**Figure 2**).
  - Relative risk reduction (RRR) was 58.6% (95% CI 27.6–76.4; P=0.001) among baseline seronegative participants, excluding unblinded participants for vaccine considerations, through Day 169.
  - A sensitivity analysis excluding unblinded participants showed 20 (6.8%) and 40 (13.7%) events in the AZD7442 and placebo groups, respectively; RRR was 50.7% versus placebo (95% CI 17.5–70.5; P=0.006).
- Reductions in all hospitalization types were observed with AZD7442 (**Figure 3**).

Figure 2. Probability of death or hospitalization for COVID-19 complications or sequelae through Day 169

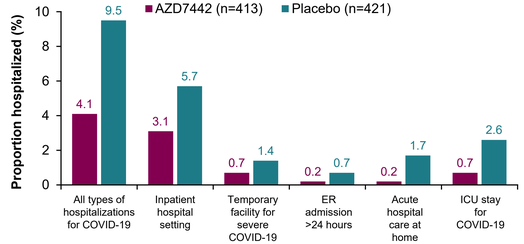


No. at risk:

AZD7442	413	395	392	392	391	391	391	391	389	385	384	384	384	384	383	383	381	0
Placebo	421	380	380	379	379	376	376	375	375	373	371	371	371	371	371	371	369	0

CI, confidence interval; RRR, relative risk reduction.

Figure 3. Hospitalizations through Day 169

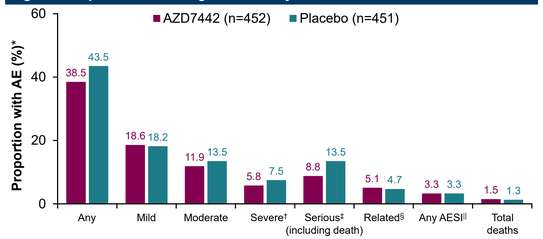


ER, emergency room; ICU, intensive care unit.

Safety and tolerability

- Median (range) safety follow-up in this analysis was 170 (1–330) days in the AZD7442 group and 170 (1–326) days in the placebo group.
- Most adverse events (AEs) were mild or moderate in severity (**Figure 4**). The proportion of serious AEs was 8.8% with AZD7442 versus 13.5% with placebo.
- The most common AE in both groups was COVID-19 pneumonia (**Table 2**).
- There were 7 (1.5%) deaths in the AZD7442 group and 6 (1.3%) in the placebo group.
  - Investigators reported 3 (0.7%) COVID-19–related deaths in the AZD7442 group versus 6 (1.3%) in the placebo group.

Figure 4. Reported AEs through at least Day 169



*Each participant is counted only once (based on maximum reported intensity) within treatment groups; †Severity is a measure of intensity. ‡Includes events leading to death, hospitalization or disability, life-threatening events, or that require medical intervention to prevent these outcomes. §Possibly related to study intervention according to the investigator (no deaths or SAEs were considered related); ‖Includes anaphylaxis, hypersensitivities, injection site pain, injection site erythema, and injection site discomfort. AE, adverse event; AESI, adverse event of special interest.

Table 2. Most common AEs through at least Day 169

Participants, n (%)	AZD7442 (n=452)	Placebo (n=451)
Any AE	174 (38.5)	163 (43.5)
Most common AEs		
COVID-19 pneumonia	26 (5.8)	49 (10.9)
Diarrhea	8 (1.8)	5 (1.1)
Injection site pain	8 (1.8)	11 (2.4)
Type 2 diabetes mellitus	8 (1.8)	5 (1.1)
COVID-19*	7 (1.5)	15 (3.3)
Vaccination complication	7 (1.5)	9 (2.0)
Headache	7 (1.5)	4 (0.9)
Diabetes mellitus inadequate control	7 (1.5)	4 (0.9)

*COVID-19 events likely resulting from reinfections after resolution of initial COVID-19. AE, adverse event.

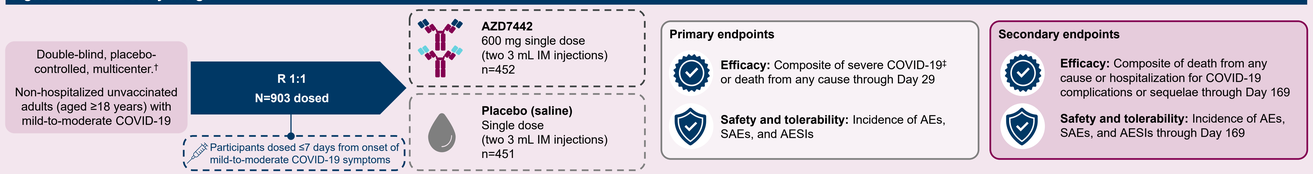
Limitations

- Only ~10% of the study population was Asian or Black/African American, even though COVID-19 has been shown to disproportionally affect these populations.[3]
- The TACKLE study excluded people who had received a COVID-19 vaccine, and there was a low proportion of immunocompromised individuals and older adults.

Methods

- TACKLE was a Phase 3 outpatient treatment study in adults with mild-to-moderate COVID-19 who were randomized 1:1 and dosed ≤7 days from symptom onset with a single 600-mg AZD7442 dose (300 mg of each antibody; n=452) or placebo (n=451; **Figure 5**).[2]
- Key secondary endpoint was analyzed using Cochran–Mantel–Haenszel test stratified by time from symptom onset (≤5 vs >5 days) and risk of progression to severe COVID-19 (high vs low).

Figure 5. TACKLE study design[2,*]



*NCT04723394; †Conducted across 95 sites in the US, Latin America, Europe, and Japan; ‡Severe COVID-19 was defined as a minimum of either pneumonia (fever, cough, tachypnea, or dyspnea, and lung infiltrates) or hypoxemia (oxygen saturation <90% in room air and/or severe respiratory distress), plus a WHO Clinical Progression Scale score of ≥5.
AE, adverse event; AESI, adverse event of special interest; IM, intramuscular; R, randomized; SAE, serious adverse event; WHO, World Health Organization.

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Disclosures

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3. Phiri P et al. *JMIR Public Health and Surveillance*. 2021;7.2:e22581.