Poster 1918

Impact of the SARS-CoV-2–Neutralizing Antibody Combination AZD7442 (Tixagevimab/Cilgavimab) on the Severity and Progression of COVID-19 Symptoms in the Phase 3 TACKLE Trial

Jesus Abraham Simón Campos,[1] Douglas Arbetter,[2] Hugh Montgomery,[3] F.D. Richard Hobbs,[4] Francisco Padilla,[5] Kenneth Kim,[6] Katie Streicher,[7] Alison Templeton,[8] Rolando M. Viani,[7] Mark T. Esser[7]

[1]Köhler & Milstein Research/Hospital Agustín O'Horán, Mérida, Yucatán, Mexico; [2]Vaccines and Immune Therapies, BioPharmaceuticals R&D, AstraZeneca, Boston, MA, USA; [3]Department of Medicine, University College London, London, UK; [4]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK; [5]Centro de Investigación en Cardiología y Metabolismo, Guadalajara, Jalisco, Mexico; [6]ARK Clinical Research, Long Beach, CA, USA; [7]Vaccines and Immune Therapies, BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, USA; [8]Vaccines and Immune Therapies, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK

Introduction

- AZD7442 comprises two extended-half-life neutralizing monoclonal 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 and was well tolerated in the Phase 3 TACKLE study primary analysis (NCT04723394).[2]
- AZD7442 administered earlier in the disease course (≤3 vs ≤7 days) led to more favorable outcomes in TACKLE (88.0% vs 50.5% reduction in severe disease or death) and has the potential to prevent COVID-19 hospitalizations and reduce hospital burden.[2]

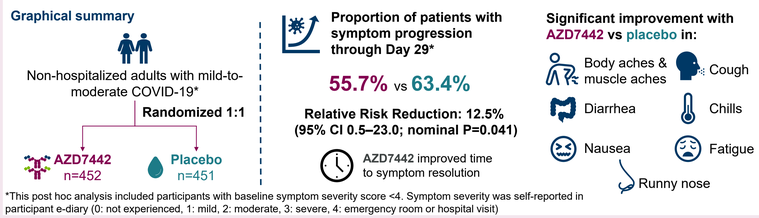
Objective

- We report a post hoc analysis of the benefit of AZD7442 in reducing self-reported COVID-19 symptom severity, symptom progression, and time to symptom resolution through Day 29.

Conclusions

- For the treatment of mild-to-moderate COVID-19, a single 600-mg intramuscular dose of AZD7442 was associated with reductions in progression of COVID-19 symptom severity and may hasten symptom improvement through Day 29.
- These results suggest that AZD7442 treatment may help outpatients with mild-to-moderate COVID-19 recover and return to normal activities faster, with less chance of disease progression.

Graphical summary



*This post hoc analysis included participants with baseline symptom severity score <4. Symptom severity was self-reported in participant e-diary (0: not experienced, 1: mild, 2: moderate, 3: severe, 4: emergency room or hospital visit)

Supplementary Content

Poster and video slides

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Results and interpretation

Baseline characteristics

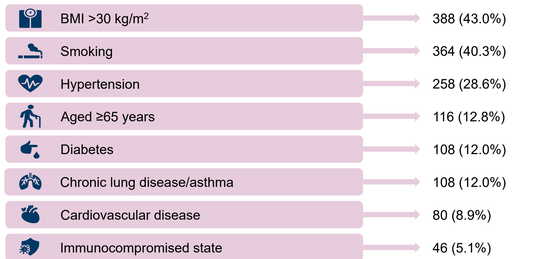
- Baseline clinical characteristics were similar between the AZD7442 and placebo groups (**Table 1**). Overall, the TACKLE study was enriched with individuals (88.7%) at high risk of progression to severe COVID-19 (**Figure 2**).

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)
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)
Range of baseline symptom severity scores	0–4	0–4
Baseline symptom severity score <4, n (%)*	305 (73.8)	322 (76.5)

BMI, body mass index; SD, standard deviation. *Among participants in modified full analysis set[2] (denominator: N=413 AZD7442, N=421 placebo) eligible for the present analysis.

Figure 2. Comorbidities considered risk factors for severe COVID-19

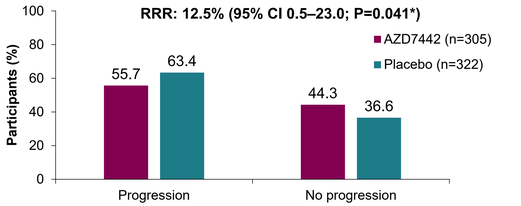


Comorbidities were assessed at baseline for the overall trial population (N=903).

Symptom progression

- AZD7442 reduced the progression of COVID-19 symptom severity versus placebo (**Figure 3**).

Figure 3. Proportion of participants with symptom progression through Day 29



*Nominally significant. CI, confidence interval; RRR, relative risk reduction.

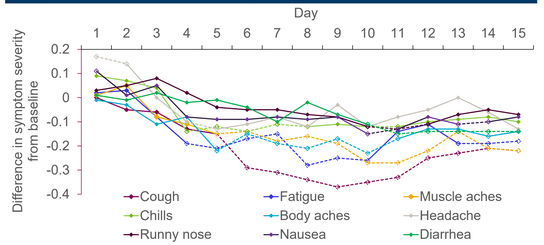
Symptom resolution

- Time to symptom resolution was improved with AZD7442 vs placebo, Kaplan-Meier (KM) failure probability at Day 29: 75.6 (70.4–80.5) vs 69.2 (63.9–74.5); Hazard Ratio: 1.17 [0.97–1.42]; KM Median (days): 11 [10–13] vs 13 [11–15].

Symptom severity

- Over 29 days, the overall mean improvement from baseline in severity of body aches, chills, cough, diarrhea, fatigue, headache, muscle aches, nausea, and runny nose was significantly greater with AZD7442 versus placebo (**Figure 4**).
- AZD7442 was associated with accelerated symptom improvement through Day 29 versus placebo.
- Most symptoms significantly improved with AZD7442 versus placebo within 1–2 weeks post dose (**Figure 5**).

Figure 5. Daily least squares mean difference in symptom severity from baseline through Day 15 with AZD7442 versus placebo



LSM, least squares mean. Open circles and dashed lines indicate P<0.05 vs placebo.

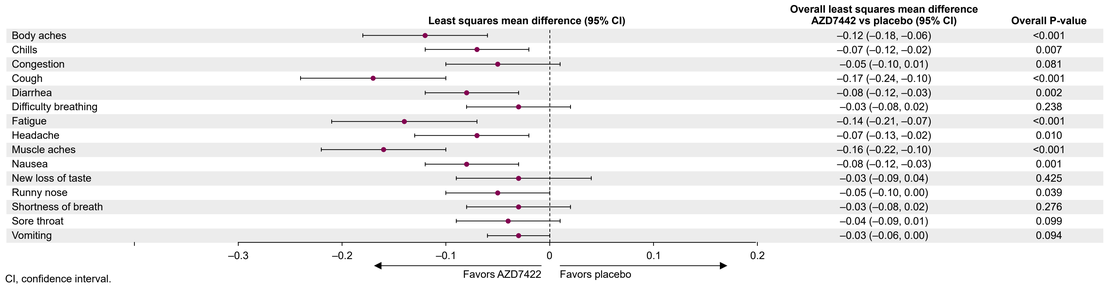
Duration of fever

- Among participants with fever at baseline (n=42 AZD7442; n=38 placebo), no difference was observed in duration of fever with AZD7442 versus placebo (median 2.0 vs 1.5 days, respectively).

Limitations

- Individuals previously vaccinated against COVID-19 were excluded from this study.
- Symptom severity was self-reported by participants and not clinically assessed.

Figure 4. Overall least-squares mean difference in symptom severity change from baseline with AZD7442 versus placebo through Day 29



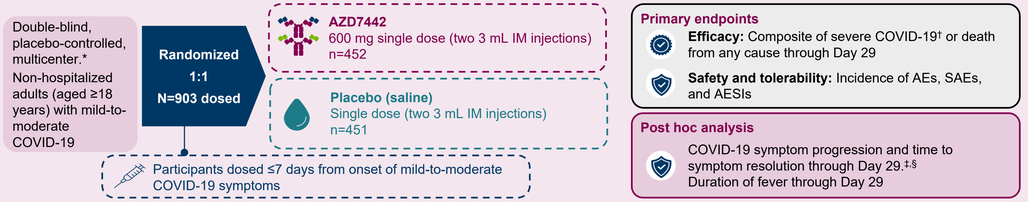
	Overall least squares mean difference AZD7442 vs placebo (95% CI)	Overall P-value
Body aches	−0.12 (−0.18, −0.06)	<0.001
Chills	−0.07 (−0.12, −0.02)	0.007
Congestion	−0.05 (−0.10, 0.01)	0.081
Cough	−0.17 (−0.24, −0.10)	<0.001
Diarrhea	−0.08 (−0.12, −0.03)	0.002
Difficulty breathing	−0.03 (−0.08, 0.02)	0.238
Fatigue	−0.14 (−0.21, −0.07)	<0.001
Headache	−0.07 (−0.13, −0.02)	0.010
Muscle aches	−0.16 (−0.22, −0.10)	<0.001
Nausea	−0.08 (−0.12, −0.03)	0.001
New loss of taste	−0.03 (−0.09, 0.04)	0.425
Runny nose	−0.05 (−0.10, 0.00)	0.039
Shortness of breath	−0.03 (−0.08, 0.02)	0.276
Sore throat	−0.04 (−0.09, 0.01)	0.099
Vomiting	−0.03 (−0.06, 0.00)	0.094

CI, confidence interval.

Methods

- Non-hospitalized adults with mild-to-moderate COVID-19 were randomized 1:1 and dosed ≤7 days from symptom onset with a single 600-mg dose of AZD7442 (300 mg of each antibody; n=452) or placebo (n=451; **Figure 1**).
- Symptom severity was self-reported daily by participants via e-diary using protocol-defined scoring system (0: not experienced, 1: mild, 2: moderate, 3: severe, 4: emergency room or hospital visit)
- The proportion of participants with progression, through Day 29, of ≥1 COVID-19-associated symptom to worse status than recorded in the symptom diary prior to start of treatment was compared between the AZD7442 and placebo groups. Only those with a baseline severity score <4 were included in the analysis.
- COVID-19 symptom severity assessments were based on symptom severity scores over time through Day 29, including the day of dosing with AZD7442 or placebo (**Figure 1**). Least Squares Mean differences were calculated using a Mixed Model for Repeated Measures
- Time to symptom resolution was compared using Kaplan-Meier and Cox proportional hazards methods.
- Duration of fever through Day 29 was defined as the last day >37.8°C was recorded. Differences were compared using Wilcoxon rank sum test.

Figure 1. Study design



*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, tachypnoea, 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; ‡Symptom progression was compared using a stratified Cochran-Mantel-Haenszel test, and time to symptom resolution was compared using Kaplan-Meier and Cox proportional hazards methods; §Missing symptom data for those who were hospitalized or died were imputed as failures or as severity scores of ER or hospital visit. AE, adverse event; AESI, adverse event of special interest; ER, emergency room; IM, intramuscular; SAE, serious adverse event; WHO, World Health Organization.

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Disclosures

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1. Loo YM et al. *Sci Transl Med*. 2020;14:635.
2. Montgomery H et al. *Lancet Respir Med*. 2022;22:S2213–S2600.