Update on AZD7442 STORM CHASER trial

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Update on AZD7442 STORM CHASER trial in post-exposure prevention of symptomatic COVID-19

AstraZeneca today announced results from the STORM CHASER trial assessing the safety and efficacy of AZD7442, a long-acting antibody (LAAB) combination, for the prevention of symptomatic COVID-19 in participants recently exposed to the SARS-CoV-2 virus. The trial did not meet the primary endpoint of post-exposure prevention of symptomatic COVID-19 with AZD7442 compared to placebo.

Trial participants were unvaccinated adults 18 years and over with confirmed exposure to a person with a case of the SARS-CoV-2 virus within the past eight days. In the overall trial population, AZD7442 reduced the risk of developing symptomatic COVID-19 by 33% (95% confidence interval (CI): -26, 65) compared to placebo, which was not statistically significant (Table 1).

The trial included 1,121 participants in a 2:1 randomisation AZD7442 to placebo, with 23 cases of symptomatic COVID-19 accrued in the AZD7442 arm (23/749) and 17 cases accrued in the placebo arm (17/372). All participants had a negative SARS-CoV-2 antibody test on the day of dosing to exclude prior infection, and a nasopharyngeal swab was also collected and subsequently analysed for SARS-CoV-2 by RT-PCR to detect virus.

Given the importance of finding therapies for COVID-19 and to help interpret trial results during the pandemic, additional analyses were performed and are being communicated (Table 1).

In a pre-planned analysis of SARS-CoV-2 PCR positive (detectable virus) and PCR negative (no detectable virus) participants, AZD7442 reduced the risk of developing symptomatic COVID-19 by 73% (95% CI: 27, 90) compared with placebo, in participants who were PCR negative at time of dosing. In a post-hoc analysis, in participants who were PCR negative at baseline, AZD7442 reduced the risk of developing symptomatic COVID-19 by 92% (95% CI: 32, 99) versus placebo more than seven days following dosing, and by 51% (95% CI: -71, 86) up to seven days following dosing.

Myron J. Levin, MD, Professor of Pediatrics and Medicine, University of Colorado School of Medicine, US, and principal investigator on the trial, said: "The results of STORM CHASER suggest that AZD7442 may be useful in preventing symptomatic COVID-19 in individuals not already infected. The PROVENT trial will give us more clarity in this patient population. While COVID-19 vaccination efforts have been successful, there is still a significant need for prevention and treatment options for certain populations, including those unable to be vaccinated or those who may have an inadequate response to vaccination."

Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, said: "While this trial did not meet the primary endpoint against symptomatic illness, we are encouraged by the protection seen in the PCR negative participants following treatment with AZD7442. We await results from PROVENT, our pre-exposure prevention trial and TACKLE, our treatment trial in preventing more severe disease, to understand the potential role of AZD7442 in protecting against COVID-19."

Table 1: STORM CHASER analyses				
Baseline subgroup	**Onset of case post dose**	**Number of cases / number of participants**		**Relative risk reduction (95% confidence interval)**
		AZD7442	**Placebo**	

		(300mg IM)		
All participants (Primary analysis)	All cases	23 / 749	17 / 372	33% reduction [a] (-26 to 65)
PCR-negative [b] (Pre-planned subgroup analysis)	All cases	6 / 715	11 / 358	73% reduction (27 to 90)
PCR-negative [b] (Post hoc subgroup analysis)	≤7 days	5 / 715	5 / 358	51% reduction (-71 to 86)
	>7 days	1 / 710	6 / 353	92% reduction (32 to 99)
a: Not statistically significant. b: Includes 974 participants (15 cases) confirmed PCR negative at baseline and 99 participants (2 cases) with PCR status missing at baseline.48 participants were confirmed PCR positive at baseline with 23 cases (AZD7442: 17/34; placebo: 6/14).				

AZD7442 was well tolerated in the trial. Preliminary analyses show similar adverse events in the placebo and treatment arms.

Full results from STORM CHASER will be submitted for publication in a peer-reviewed medical journal and presented at a forthcoming medical meeting.

Financial considerations
On 16 March 2021, AstraZeneca announced an extended agreement with the US Government to supply up to 500,000 additional doses of AZD7442 for $205m, contingent on AZD7442 receiving Food and Drug Administration Emergency Use Authorisation in post-exposure prophylaxis. Discussions regarding next steps with the US Government are ongoing.

STORM CHASER

STORM CHASER is a Phase III, randomised, double-blind, placebo-controlled, multi-centre trial assessing the safety and efficacy of a single 300mg dose of AZD7442 compared to placebo for the post-exposure prevention of COVID-19. The trial was conducted in 59 sites in the UK and US. 1,121 participants were randomised in a 2:1 ratio to receive a single intramuscular (IM) dose of either 300mg of AZD7442 (n=749) or saline placebo (n=372), administered in two separate, sequential IM injections. The primary efficacy endpoint is the first case of SARS-CoV-2 RT-PCR-positive symptomatic illness occurring post dose to Day 183. The primary analysis was to be conducted 30 days after 25 events meeting the primary efficacy endpoint definition had occurred. This primary analysis includes data and additional events accumulated up to 7 April 2021, 30 days after the symptom assessment date of the 25th event; participants will continue to be followed for 15 months.

The post hoc analysis looked at cases of symptomatic COVID-19 in the PCR-negative group occurring seven days or less after dosing and more than seven days after dosing. This was based on the known incubation period of SARS-CoV-2. Cases occurring more than seven days after dosing are likely to be due to infection that occurred after dosing rather than before.[1]

Participants were adults 18 years and over with potential exposure, within eight days, to a specific identified individual with laboratory-confirmed SARS-CoV-2 virus, symptomatic or asymptomatic, and who were therefore assessed at the time of enrolment to be at appreciable risk of imminently developing COVID-19. Such individuals included, but were not limited to, those who shared a household, those living in institutional residences (military lodging, dormitories, etc.), health care workers, long-term care facility workers, and workers in occupational or industrial settings in which close contact is common.

AZD7442
AZD7442 is a combination of two LAABs - tixagevimab (AZD8895) and cilgavimab (AZD1061) - derived from B cells donated by convalescent patients after SARS-CoV-2 virus. Discovered by Vanderbilt University Medical Center and licensed to AstraZeneca in June 2020, the human monoclonal antibodies bind to distinct sites on the SARS-CoV-2 spike protein[2] and were optimised by AstraZeneca with half-life extension and reduced Fc receptor binding. The half-life extension approximately triples the durability of its action compared to conventional antibodies and could afford six to 12 months of protection from COVID-19 following a single

administration.[3-6] The reduced Fc receptor binding aims to minimise the risk of antibody-dependent enhancement of disease - a phenomenon in which virus-specific antibodies promote, rather than inhibit, infection and/or disease.[7]

AZD7442 is currently being tested in several additional COVID-19 prevention and treatment trials: PROVENT[8] Phase III trial of over 5,000 participants in pre-exposure prophylaxis; TACKLE COVID-19[9] Phase III treatment trial in outpatient setting; and collaborator treatment trials in outpatient and hospitalised settings. AZD7442 is being assessed in both IM and intravenous administration routes.

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.

Preliminary 'in vitro' findings from investigators at Oxford University and Columbia University also demonstrate that AZD7442 neutralises recent emergent SARS-CoV-2 viral variants.[10-14]

Data published in *Nature* in July 2020 showed that in pre-clinical experiments, the LAABs were able to block the binding of the SARS-CoV-2 virus to host cells and protect against infection in cell and animal models of disease.[15]

Under the terms of the licensing agreement with Vanderbilt, AstraZeneca will pay single-digit royalties on future net sales.

AstraZeneca

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Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

References

1. Guan WJ, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020;382(18):1708. Epub 2020 Feb 28.

2. Dong J, et al. Genetic and structural basis for recognition of SARS-CoV-2 spike protein by a two-antibody cocktail. *bioRxiv*. 2021; doi: 10.1101/2021.01.27.428529.

3. Robbie GJ, et al. A novel investigational Fc-modified humanized monoclonal antibody, motavizumab-YTE, has an extended half-life in healthy adults. *Antimicrob Agents Chemother*. 2013;57:6147-53.

4. Griffin MP, et al. Safety, Tolerability, and Pharmacokinetics of MEDI8897, the Respiratory Syncytial Virus Prefusion F-Targeting Monoclonal Antibody with an Extended Half-Life, in Healthy Adults. *Antimicrob Agents Chemother.* 2017;61:e01714-16.

5. Yu XQ, et al. Safety, Tolerability, and Pharmacokinetics of MEDI4893, an Investigational, Extended-Half-Life, Anti-Staphylococcus aureus Alpha-Toxin Human Monoclonal Antibody, in Healthy Adults. *Antimicrob Agents Chemother.* 2016;61:e01020-16.

6. Domachowske JB, et al. Safety, Tolerability and Pharmacokinetics of MEDI8897, an Extended Half-life Single-dose Respiratory Syncytial Virus Prefusion F-targeting Monoclonal Antibody Administered as a Single Dose to Healthy Preterm Infants. *Pediatr Infect Dis J*. 2018;37:886-892.

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7. van Erp EA, et al. Fc-Mediated Antibody Effector Functions During Respiratory Syncytial Virus Infection and Disease. *Front Immunol*. 2019; 10: 548.

8. Clinicaltrials.gov. Phase III Double-blind, Placebo-controlled Study of AZD7442 for Pre-exposure Prophylaxis of COVID-19 in Adult. (PROVENT). Available at: https://clinicaltrials.gov/ct2/show//NCT04625725. [Last accessed: 7 April 2021].

9. Clinicaltrials.gov. Phase III Study of AZD7442 for Treatment of COVID-19 in Outpatient Adults (TACKLE). Available at: https://clinicaltrials.gov/ct2/show//NCT04723394. [Last accessed: 7 April 2021].

10. Zhou D, et al. Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine induced sera. *Cell*. 2021; 184 (9): 2348-2361.e6.

.

12. Wang P, et al. Antibody resistance of SARS-CoV-2 variants B.1.351 and B.1.1.7. *Nature* 2021;593:130-135.

13. Chen RE, et al. Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies. *Nat Med* 2021; 27, 717-726. https://doi.org/10.1038/s41591-021-01294-w.

14. Wang P, Nair MS, Liu L. et al. Antibody resistance of SARS-CoV-2 variants B.1.351 and B.1.1.7. *Nature* 2021 Mar 8. doi: 10.1038/s41586-021-03398-2. Epub ahead of print. PMID: 33684923.

15. Zost SJ, et al. Potently neutralizing and protective human antibodies against SARS-CoV 2. *Nature*. 2020;584:443-449.

Adrian Kemp
Company Secretary
AstraZeneca PLC