NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
May 2023

AZD3152 for preventing COVID-19

Company/Developer	AstraZeneca UK Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 36632	NICE TSID: Not Available	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

AZD3152 is currently in clinical development for the prevention of COVID-19. COVID-19 is an infectious respiratory disease caused by the severe acute respiratory syndrome-coronavirus 2, SARS-CoV-2. The main symptoms of COVID-19 infection are fever, a new continuous cough, and loss of taste or smell. In some patients, COVID-19 may result in severe complications such as acute respiratory distress syndrome, blood clotting, acute heart or kidney injury and sepsis. Hospitalisation and death rates amongst COVID-19 patients remains high. Patients with conditions that cause immune impairment, who are less likely to mount an adequate protective response after COVID-19 vaccination, are at high risk of developing severe COVID-19 if they were to become infected. There is a need to develop additional therapeutics to protect these vulnerable patients and reduce the risk of poor outcomes from exposure to COVID-19.

AZD3152 is a monoclonal antibody, a type of protein that has been designed to recognise and attach to the spike protein of SARS-CoV-2 and stops it from entering human cells. AZD3152 is administered intramuscularly. If licenced, AZD3152 will provide a new therapeutic option to prevent COVID-19 in vulnerable patients.

Proposed Indication

For pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older who are less likely to mount an adequate protective immune response after vaccination and thus are at high risk of developing severe COVID-19.[1]

Technology

Description

AZD3152 is a new long-acting monoclonal antibody derived from B-cells donated by convalescent patients after SARS-CoV-2 infection.[2,3] AZD3152 has been shown in in vitro studies to have broad and potent neutralising activity across all known SARS-CoV-2 variants.[3] Monoclonal antibodies against COVID-19 target a predetermined target - the spike protein of the coronavirus - which the virus uses to enter host cells, thus blocking viral attachment and entry into human cells.[4]

AZD3152 is currently in clinical development for the pre-exposure prophylaxis of COVID-19. In the phase III clinical trial (SUPERNOVA, NCT05648110), participants receive a 300 mg single dose of AZD3152 administered intramuscularly (IM) in the thigh on day 1 and a second dose of their original randomised study intervention 6 months after visit 1 (day 181).[1]

Key Innovation

While vaccines remain the cornerstone of active immunisation, vulnerable populations that cannot build an immune response with vaccination can benefit from protection from a monoclonal antibody.[5] AZD3152 was optimised with the same half-life extension, reduced Fc effector function and complement C1q binding as its predecessor, conferring protection from COVID-19 for six months. It is based on B-cells donated by convalescent patients after SARS-CoV-2 infection, and it has been shown to have a broad activity against all known variants of SARS-CoV-2 to date.[3] In addition, the reduced Fc effector function 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.[3]

If licenced, AZD3152 will provide a new therapeutic option for preventing all variants of COVID-19 in immunocompromised patients.

Regulatory & Development Status

AZD3152 does not currently have marketing authorisation in the EU/UK for any indication.

AZD3152 is not currently in clinical development for any other indication.

Patient Group

Disease Area and Clinical Need

Coronaviruses are a large family of related viruses that cause diseases in animals and humans. Some cause less severe disease, such as the common cold, and others cause more severe disease.[6] COVID-19 is an infectious coronavirus disease caused by the virus SARS-CoV-2.[7] COVID-19 transmission occurs when an infected person breathes out droplets and small particles that contain the virus. These droplets and

particles spread to other people through the eyes, nose or mouth. Transmission can also occur by touching surfaces contaminated with the virus.[8] The main symptoms of COVID-19 include: fever; a new and continuous cough; anosmia (loss of smell); and ageusia (loss of taste). Other symptoms may include: shortness of breath; loss of appetite; myalgia (muscle ache); sore throat; headache; nasal congestion; diarrhoea, nausea and vomiting.[6] In some patients, the infection may result in severe disease with complications including acute respiratory distress syndrome, venous thromboembolism, acute myocardial or kidney injury, and sepsis.[9] The risk of severe disease and death from COVID-19 is higher in people who are older, male, from deprived areas, or from certain non-white ethnic backgrounds. Certain underlying health conditions, as well as obesity, may also increase the risk of severe disease and deaths in adults.[6]

As of 11 May 2023, there have been 20,814,571 confirmed cases of COVID-19 in England, of which 19,260,634 are thought to be first episodes, and 1,553,937 are possible reinfection cases. In the 7-day period ending on 6 May 2023, there were 9,675 COVID-19 cases in England which resulted in an infection rate of 17.1 per 100,000 of the population.[10] In the week ending 19 March 2023, the hospital admission rate in England for patients with confirmed COVID-19 was 10.62 per 100,000.[11] In the week ending 17 March 2023 there were 512 registered deaths in England involving COVID-19, and in the same week COVID-19 accounted for 4.5% of registered deaths in the UK.[12]

Recommended Treatment Options
NICE currently recommends casirivimab plus imdevimab for the prophylaxis and treatment of acute COVID-19 infection.[13]

Clinical Trial Information

Trial	**SUPERNOVA;** NCT05648110; A Phase I/III Randomized, Double Blind Study to Evaluate the Safety and Neutralizing Activity of AZD5156/AZD3152 for Pre Exposure Prophylaxis of COVID 19 in Participants With Conditions Causing Immune Impairment **Phase III:** Recruiting **Location:** Two EU countries, UK, USA, and other countries. **Primary completion date:** November 2023
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 3256 (estimated); adults and adolescents 12 years and older; subjects weighing at least 40 kg with conditions causing immune impairment and are at high risk of developing severe COVID-19
Intervention(s)	300 mg single doses of AZD3152 (IM) on Visit 1 Day 1 and on Visit 5 Day 181
Comparator(s)	600 mg single doses of AZD7442 (IM) on Visit 1 Day 1 and on Visit 5 Day 181
Outcome(s)	Primary outcome measures: • To compare neutralizing antibody responses (nAb) in serum following AZD3152 and AZD7442 administration to the SARS-CoV-2 Alpha variant in serum [Time frame: GMT ratio of SARS-CoV-2 nAbs between the treatment arms at Visit 3 (Day 29). Descriptive statistics of SARS-CoV-2 nAb titers will be made by visit.] • To evaluate the safety of AZD3152 and AZD7442 [Time frame: adverse events will be collected from Investigational Medicinal Product (IMP)

	administration for the following 90 days. Adverse events of special interest will be collected from IMP administration through to Visit 10 (Day 451). Serious Adverse Events and Medically Attended Adverse Events will be collected up to Visit 10 (Day 451)]. See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of AZD3152 is not yet known.

Relevant Guidance

NICE Guidance

- NICE guidance in development. Tixagevimab plus cilgavimab for preventing COVID-19 (ID6136). Expected date of issue June 2023.
- NICE COVID-19 rapid guideline. Managing COVID-19 (NG191). March 2023.
- NICE COVID-19 rapid guideline. Vitamin D (NG187). July 2022.

NHS England (Policy/Commissioning) Guidance

- NHS England. Next steps on infection prevention and control (IPC) C1657. June 2022.

Other Guidance

- World Health Organisation (WHO). Therapeutics and COVID-19: Living guideline. 2020 (Updated January 2023).[14]
- World Health Organisation (WHO). Drugs to prevent COVID-19: Living guideline. 2023.[15]
- Centres for Disease Control and Prevention. Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic. 2022.[16]
- Infectious Diseases Society of America. Infectious Diseases Society of America Guidelines on Infection Prevention for Healthcare Personnel Caring for Patients with Suspected or Known COVID-19. 2020 (Updated November 2021).[17]

Additional Information

References

1 Clinicaltrials.gov. *Study Understanding Pre-Exposure pRophylaxis of NOVel Antibodies (SUPERNOVA)*. 2023. Available from: https://clinicaltrials.gov/ct2/show/NCT05648110 [Accessed 13 April 2023].

2 AstraZeneca. *First participant dosed in SUPERNOVA Phase I/III trial evaluating AZD5156, a next-generation long-acting antibody combination, for prevention of COVID-19*. 2022. Available from: https://www.astrazeneca-us.com/media/statements/2022/first-participant-dosed-in-supernova-phase-I-III-trial-evaluating-azd5156-a-next-generation-long-acting-antibody-combination-for-prevention-of-covid-19.html [Accessed 13 April 2023].

3 AstraZeneca. *ECCMID data reinforces AstraZeneca's commitment to transform protection for the most vulnerable by advancing science in vaccines and immune therapies*. 2023. Available from: https://www.astrazeneca.com/media-centre/press-releases/2023/eccmid-data-reinforces-astrazenecas-commitment-to-transform-protection-for-the-most-vulnerable-by-advancing-science-in-vaccines-and-immune-therapies.html [Accessed 25 April 2023].

4 Infectious Diseases Society of America. *Anti-SARS-CoV-2 Monoclonal Antibodies*. 2023. Available from: https://www.idsociety.org/covid-19-real-time-learning-network/therapeutics-and-interventions/monoclonal-antibodies/ [Accessed 13 April 2023].

5 LifeArc Ventures. *LifeArc portfolio company RQ Bio's antibody enters clinical trials*. 2023. Available from: https://www.lifearc.org/news/2023/rq-bio-antibody-enters-clinic-as-part-of-astrazeneca-combination-study/ [Accessed 13 April 2023].

6 UK Health Security Agency. *COVID-19: epidemiology, virology and clinical features*. 2022. Available from: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-background-information/wuhan-novel-coronavirus-epidemiology-virology-and-clinical-features [Accessed 28 March 2023].

7 World Health Organisation (WHO). *Coronavirus disease COVID-19)*. 2023. Available from: https://www.who.int/health-topics/coronavirus#tab=tab_1 [Accessed 28 March 2023].

8 Centre for Disease Control and Prevention. *How COVID-19 spreads*. 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html [Accessed 28 March 2023].

9 National Institute for Health and Care Excellence (NICE). *Coronavirus - COVID-19*. 2023. Available from: https://cks.nice.org.uk/topics/coronavirus-covid-19/ [Accessed 04 April 2023].

10 GOV.UK. *Coronavirus (COVID-19) cases in the UK*. 2023. Available from: https://coronavirus.data.gov.uk/details/cases?areaType=nation&areaName=England [Downloaded 13 April 2023].

11 Office for National Statistics. *Coronavirus (COVID-19) latest insights*. 2023. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19/latestinsights [Downloaded 28 March 2023].

12 Office for National Statistics. *Coronavirus (COVID-19) latest insights: Deaths*. 2023. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19latestinsights/deaths [Downloaded 28 March 2023].

13 National Institute for Health and Care Excellence (NICE). *Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19*. 2023. Available from: https://www.nice.org.uk/guidance/ta878 [Accessed 25 April 2023].

14 World Health Organisation (WHO). *Therapeutics and COVID-19: Living guideline*. 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1 [Accessed 05 April 2023].

15 World Health Organisation. *Drugs to prevent COVID-19: Living guideline*. 2023. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-prophylaxes-2023.1 [Accessed 25 April 2023].

16 Centres for Disease Control and Prevention. *Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic*. 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html [Accessed 25 April 2023].

17 Infectious Diseases Society of America. *Infectious Diseases Society of America Guidelines on Infection Prevention for Healthcare Personnel Caring for Patients with Suspected or Known COVID-19*. 2021. Available from: https://www.idsociety.org/practice-guideline/covid-19-guideline-infection-prevention/ [Accessed 25 April 2023].

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.