NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
February 2024

Sarconeos for treating severe COVID-19 in people aged 45 years and over

Company/Developer	Biophytis SA

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 32780	NICE ID: Not available	UKPS ID: N/A

Licensing and Market Availability Plans

Sarconeos is currently in phase II/III clinical development.

Summary

Sarconeos is currently in clinical development for treating adults aged 45 or over who are hospitalised with 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 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. 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.

Sarconeos is an orally administered small molecule. Based on results from cellular and animal studies, it is believed that sarconeos stimulates muscle metabolism and strength through activation of the MAS receptor. This may have the potential to improve muscle function, mobility and respiratory capacity in age-related, muscular wasting and respiratory conditions, including severe COVID-19. If licensed, sarconeos will offer a new treatment option for adults hospitalised with severe COVID-19.

Proposed Indication

Prevention of respiratory deterioration in adults aged 45 or over who are hospitalised with severe COVID-19.[1]

Technology

Description

Sarconeos (BIO101) is an investigational new drug, which is an oral preparation of immediate-release 20-hydroxyecdysone (20E).[1] The Coronavirus SARS-CoV-2 (COVID-19) can cause Acute Respiratory Distress Syndrome (ARDS) by disrupting the renin angiotensin system (RAS), which has a key role in regulating respiratory function. It is believed that COVID-19 enters the lung cells using the Angiotensin 2 Converting Enzyme (ACE-2), a key enzyme in the RAS, inhibiting the system's protective arm. Sarconeos activates the MAS receptor, a key component of the protective arm of the RAS, and has been shown to significantly improve respiratory function in several preclinical models.[2]

Sarconeos is currently in clinical development for treating adults aged 45 and over who are hospitalised with severe COVID-19. In a phase II/III trial (COVA, NCT04472728), participants are given 350mg sarconeos orally twice a day.[1]

Key Innovation

SARS-CoV-2 binding to ACE2 is potentially associated with severe pneumonia due to COVID-19. It was thought that MAS-receptor activation by 20-hydroxyecdysone (Sarconeos) could restore the Renin-Angiotensin System equilibrium and limit the frequency of respiratory failure and mortality in adults hospitalized with severe COVID-19.[3] If licensed, sarconeos will offer an additional treatment option for these patients.

Regulatory & Development Status

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

Sarconeos is currently in phase 2 clinical development for the treatment of age-related sarcopenia.[4]

Patient Group

Disease Area and Clinical Need

Coronaviruses are a large family of viruses that cause diseases in both animals and humans; some coronaviruses cause severe disease.[5] COVID-19 is an infectious coronavirus disease caused by the virus SARS-CoV-2.[6] It is transmitted when an infected person breathes out droplets and small particles containing the virus, which spread to other people through the eyes, nose or mouth. COVID-19 can also be transmitted by touching surfaces contaminated with the virus.[7] The main symptoms of COVID-19 include: fever; a new and continuous cough; loss of smell; and loss of taste. Other symptoms may include: shortness of breath; loss of appetite; fatigue; muscle ache; sore throat; headache; nasal congestion; diarrhoea, nausea; and vomiting.[5,8] 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 COVID-19 and death is higher in people who are older, male, from deprived areas, or from certain non-white ethnic backgrounds. Certain underlying health conditions and obesity may also increase this risk in adults.[5]

As of 14 December 2023, there have been 21,024,823 confirmed cases of COVID-19 in England, of which 19,384,397 are thought to be first episodes and 1,640,426 are possible reinfection cases. In the seven-day period ending on 9 December 2023, there were 5975 COVID-19 cases in England, which resulted in an infection rate of 10.6 per 100,000 of the population.[10] According to the December 2023 COVID-19 daily situation report, there were 2,371 hospital admissions with COVID-19 in November 2023.[11]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommended treatment options for COVID-19 infections in adults include: nirmatrelvir plus ritonavir; sotrovimab; dexamethasone (or either hydrocortisone or prednisolone when dexamethasone cannot be used or is unavailable); and tocilizumab.[12]

Clinical Trial Information

Trial	**COVA,** NCT04472728, EudraCT 2020-001498-63; Adaptive Design Phase 2 to 3, Randomized, Double-blind, to Evaluate Safety, Efficacy, Pharmacokinetics and Pharmacodynamics of BIO101 in the Prevention of the Respiratory Deterioration in Hospitalized COVID-19 Patients. **Phase II/III –** terminated (lack of eligible patients due to lower number of COVID-19 cases in all involved sites) **Locations:** two EU countries, USA, Brazil and Puerto Rico **Study completion date:** September 2022
Trial Design	Randomised, sequential assignment, placebo controlled, quadruple-blind.
Population	N = 238 (actual). Adults aged 45 and older (55 and older in France) with a confirmed diagnosis of COVID-19 infection within the last 28 days and hospitalised or planned to be hospitalised due to COVID-19 symptoms anticipated to last ≥ 3 days.
Intervention(s)	Sarconeos capsules (350 mg bid (twice daily))
Comparator(s)	Placebo administered orally
Outcome(s)	Current primary outcomes: • End-of-part-1 interim analysis: proportion of subjects with all-cause mortality or with respiratory failure [Time frame: up to 28 days] • For part-2-sample size interim analysis: proportion of subjects with all-cause mortality or with respiratory failure [Time frame: up to 28 days] • For the final analysis: proportion of subjects with all-cause mortality or respiratory failure [Time frame: up to 28 days] See trial record for full list of outcomes.
Results (efficacy)	The COVA trial results demonstrated statistically significant efficacy of BIO101 on the primary endpoint (43.8% RR reduction of proportion of death or respiratory failure, p = 0.0426).[3]
Results (safety)	A lower proportion and number of serious treatment emergent adverse effects were reported in the BIO101 group (32 subjects [25.0%]), 59 serious events), vs. the placebo group (32 subjects, [30.8%], 64 serious events). Physical examination findings were also aligned to the underlying COVID-19 condition in most subjects indicating a very good safety profile of BIO101.[3]

Estimated Cost

The cost of sarconeos is currently unknown.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Remdesivir for treating COVID-19 (ID3808). Expected TBC.
- NICE technology appraisal in development. Remdesivir and tixagevimab plus cilgavimab for treating COVID-19 (ID6261). Expected TBC.
- NICE technology appraisal in development. AZD 3152 for preventing COVID-19. (ID6282). Expected TBC.
- NICE technology appraisal. Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 (TA878). June 2023.
- NICE technology appraisal. Tixagevimab plus cilgavimab for preventing COVID-19 (TA900). June 2023.
- NICE COVID-19 rapid guideline. Haematopoietic stem cell transplantation (NG164). September 2023.
- NICE COVID-19 rapid guideline. Managing COVID-19 (NG191). June 2023.
- NICE COVID-19 rapid guideline. Vitamin D (NG187). July 2022.
- NICE COVID-19 rapid guideline. Managing the long-term effects of COVID-19 (NG188). November 2021.

NHS England (Policy/Commissioning) Guidance

- NHS England. Next steps on infection prevention and control (IPC) C1657. June 2022.
- NHS England. Interim Clinical Commissioning Policy: Remdesivir for patients hospitalised due to COVID-19. 2022.

Other Guidance

- World Health Organization (WHO). Drugs to prevent COVID-19: Living guideline. 2023.[13]
- World Health Organization (WHO). Therapeutics and COVID-19: Living guideline. 2022 (updated January 2023).[14]
- Centres for Disease Control and Prevention. Infection Control Guidance. 2022 (updated May 2023).[15]
- Bartoletti M, Azap O, Barac A, Bussini L, Ergonul O, et al. ESCMID COVID-19 living guidelines: drug treatment and clinical management. 2022.[16]
- Lynch JB, Davitkov P, Anderson DJ, Bhimraj A, Chi-Chung Cheng V, Guzman-Cottrill J, et al. 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.[17]

Additional Information

Biophytis SA did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

1 ClinicalTrials.gov. *Adaptive Design Phase 2 to 3, Randomized, Double-blind, to Evaluate Safety, Efficacy, Pharmacokinetics and Pharmacodynamics of BIO101 in the Prevention of the Respiratory Deterioration in Hospitalized COVID-19 Patients*. *Trial ID: NCT04472728*. 2020. Status: Terminated. Available from: https://clinicaltrials.gov/study/NCT04472728 [Accessed 12 December 2023].

2 Biophytis. *COVID-19: COVA CLINICAL PROGRAM*. Available from: https://www.biophytis.com/en/pipeline/covid19-programme-clinique-cova/ [Accessed 05 January 2024].

3 Lobo SM, Plantefève G, Nair G, Joaquim Cavalcante A, Franzin de Moraes N, Nunes E, et al. Efficacy of oral 20-hydroxyecdysone (BIO101), a MAS receptor activator, in adults with severe COVID-19 (COVA): a randomized, placebo-controlled, phase 2/3 trial. *eClinicalMedicine*. 2024:102383. https://www.sciencedirect.com/science/article/pii/S2589537023005606.

4 ClinicalTrials.gov. *A Double-blind, Placebo Controlled, Randomized INTerventional Clinical Trial (SARA-INT) (SARA-INT)*. *Trial ID: NCT03452488*. 2018. Status: Completed. Available from: https://clinicaltrials.gov/study/NCT03452488?intr=BIO101&aggFilters=phase:2%203&rank=2 [Accessed 05 January 2024].

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13 World Health Organization. *Drugs to prevent COVID-19: living guideline*. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-prophylaxes-2023.1 [Accessed 03 January 2024].

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15 Center of disease control and prevention. *Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic*. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html [Accessed 03 January 2024].

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