# Pre-exposure treatment and prevention of SARS-COV-2.

**Nightingale Syabbalo***

Professor of Physiology and Medicine Nabanji Medical Centre, Lusaka, Zambia

## Abstract

**Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a severe pneumonia caused by an enveloped, single-stranded beta coronavirus, belonging to the coronaviridae family. SARS-CoV-2 (Covid-19) has caused several pandemic due to its ability to mutate into new subvariants of variable virulence. According to the latest report by the World Health Organization, Covid-19 has infected 664, 097, 132 cumulative cases and caused more than 6, 716, 108 deaths since the first pandemic in Wuhan, China. Covid-19 has paralyzed businesses and has been an economic burden in many countries globally due. Vaccination has been very effective in preventing Covid-19 infections. However, some individuals with immunosuppression are unable to mount adequate immunity after vaccination and others are allergic to the components of the Covid-19 mRNA vaccines. These individuals require pre-exposure prophylaxis in order to prevent them from developing SARS-CoV-2 infection and progressing to severe disease leading to death. Tixagevimab plus cilgavimab (Evusheld) are IgG1 long-acting recombinant human monoclonal antibodies (mAbs), produced using recombinant DNA technology. Both biologics bind to non-overlapping epitopes of the spike protein receptor-binding domain (RBD) of SARS-CoV-2 spike protein. They block the spike protein from attaching to its cognitive receptor the angiotensin-converting enzyme 2 (ACE2) receptor. Clinical trials have shown that evusheld treatment when administered to individuals who are at risk of Covid-19 infection, leading to severe disease result in 77% reduction in the risk of developing SARS-CoV-2. Tixagevimab plus cilgavimab pre-exposure prophylaxis is approved by the Medicines and Healthcare products Regulatory Agency in Great Britain and by the European Union. However, it is unlikely to neutralize some of the subvariants of Omicron, such as Omicron XXB.1.5 ('Kraken'). Therefore, pre-exposure treatment of Covid-19 with evusheld should be administered cautiously in countries where Omicron subvariants are endemic. Noteworthy. Pre-exposure prophylaxis should not be a substitute for the two doses of Covid-19 vaccination.**

**Keywords**: SARs-CoV-2, Pre-exposure prophylaxis, Covid-19 spike protein, Tixagevimab, Cilgavimab.

## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a severe pneumonia caused by an enveloped, single-stranded beta coronavirus, belonging to the coronaviridae family. SARS-CoV-2 (Covid-19) has caused several pandemic due to its ability to mutate into new subvariants of variable virulence. The latest report from the World Health Organization Covid-19 has infected 664, 097, 132 cumulative cases and has caused more than 6, 716, 108 deaths since the first pandemic in Wuhan City, China, in December 2019 [1]. Covid-19 has paralyzed businesses and has been an economic burden in many countries globally due to lockdowns [2]. The symptom spectrum of Covid-19 varies from mild to life-threatening disease characterized by acute respiratory distress syndrome (ARDS), hypoxaemic respiratory failure, thromboembolism and multi-organ failure. Treatment of severe SARS-CoV-2 is well established. The National Institutes of Health guidelines include treatment with high-flow nasal oxygen, remdesivir and corticosteroids [3] and most recently interlekin-6 antagonists, such as tocilizumab, or a Janus kinase inhibitor, including baricitinib [4]. Tocilizumab and baricitinib have been granted emergency use authorization by the Food and Drug Administration, USA.

The universal and effective protection against most infections is vaccination. The World Health Organization (WHO) recommended prophylaxis for SARS-CoV-2 is two Covid-19 vaccines and preferably a booster third dose. Covid-19 vaccines are now available for adults and children 5 years and older [5]. There are three vaccines which are available in most countries, including low- and middle-income countries. They include the Moderna COVID-19 (mRNA) 1273 vaccine, the Pfizer BioNTech (BNT162b2) COVID-19 vaccine and the Oxford/AstraZeneca (ChAdOx1-s [recombinant] vaccine)

***Correspondence to:** Nightingale Syabbalo. Professor of Physiology and Medicine Nabanji Medical Centre, Lusaka, zambia, E mail: nightsyab@gmail.com

***Received:** 18-Mar-2023, Manuscript No. AAIJRM-23-92156**; Editor assigned:** 20-Mar-2023, PreQC No. AAIJRM-23-92156(PQ); **Reviewed:** 03-Apr-2023, QC No. AAIJRM-23-92156; **Published:** 10-Apr-2023, DOI: 10.35841/aaijrm-8.2.136*

***Citation:** Syabbalo N. Pre-exposure treatment and prevention of SARS-COV-2. Int J Respir Med. 2022;8(2):136*

COVID-19 vaccine [5]. Table1 shows the WHO common recommended vaccines.

Covid-19 vaccines have been highly effective in preventing SARS-CoV-2, especially in preventing individuals from developing severe SARS-CoV-2, acute respiratory distress syndrome, respiratory failure, multi-organ failure (MOF) and death. Both the World Health organization and the Centers for Disease Control and Prevention (CDC) strongly recommend equity Covid-19 vaccination as a strategy for preventing SARS-CoV-2 spread.

However, pre-prophylaxis (PrEP) of Covid-19 is warranted in individuals who are immunosuppressed and in people who cannot mount adequate immunity after vaccination and in those who are allergic to the Covid-19 RNA vaccines. Notwithstanding, Covid-19 vaccination has been reported to be associated with cardiovascular complications, such as myocarditis, pericarditis, cardiac arrhythmias [6-8] and thrombotic events [9]. They have also been associated with neurological complications, such as Bell's palsy, encephalitis, meningitis, acute transverse myelitis, Gullain-Barré syndrome and cerebrovascular events [10-12]. Table 2 summarizes the reported complications associated with Covid-19 vaccination. Therefore, pre-exposure treatment is necessary in some individuals, in order to prevent them from getting Covid-19 infection and severe disease.

***Table 1***. *World Health Organization recommended COVID-19 vaccines.*

| |
|---|
| Moderna COVID-19 (mRNA) 1273 vaccine |
| Pfizer BioNTech (BNT162b2) COVID-19 vaccine |
| Oxford/AstraZeneca (ChAdOx1-s [recombinant] vaccine) COVID-19 vaccine |
| Janssen Ad26.COV2S COVIDE-19 vaccine |
| Novax vaccine against COVID-19 |
| Valnera VLA 2001 COVID-19 vaccine |
| CONAXIN |
| Covovax |
| Nuvaxovid |
| CanSino |
| Sinopharm COVID-19 vaccine |
| Sinovac-CoronaVac COVID-19 vaccine |

***Table 2***. *Complications associated with COVID-19 vaccination.*

| |
|---|
| **Systemic complication** |
| Anaphylaxis |
| Multisystem syndrome in children (MSS-C) |
| Cardiovascular complications |
| Myocarditis |
| Pericarditis |
| Cardiac arrhythmias |
| **Haematological complications** |
| Thrombosis with thrombocytopenia syndrome (TTS) |
| Cortical sinus venous thrombosis |
| Splanchnic thrombosis |
| **Neurological complications** |
| Facial (Bell's) palsy |
| Several neuropathies |
| Encephalitis |
| Meningitis |
| Acute transverse myelitis |
| Guillain-Barré syndrome (GBS) |
| Acute disseminating encephalomyelitis |
| Multiple sclerosis (MS) |
| Cerebrovascular accidents |
| Neuromyelitis optica spectrum disorder (NMOSD) |
| **Gastrointestinal complications** |
| Acute diverticulitis |
| Colon microperforation |
| **Renal complication** |
| Acute kidney injury (rare, mostly in elderly patients) |
| **Endocrine complications** |
| Adrenal haemorrhage |
| New onset type 2 diabetes mellitus |
| Subacute thyroiditis |

***Citation:*** *Syabbalo N. Pre-exposure treatment and prevention of SARS-COV-2. Int J Respir Med. 2022;8(2):136*

SARS-CoV-2 gains its access into host cells *via* the spike glycoprotein (S protein). The spike protein is composed of two functional subunits, namely S1 and S2 subunits. Tixagevimab plus cilgavimab (Evusheld) are IgG1 long-acting recombinant human monoclonal antibodies, produced using recombinant DNA technology. The two mAbs were derived from two patients who recovered from SARS-CoV-2 [13]. Tixagevimab and cilgavimab have Fc-modification which extends their half-life [14,15]. Both biologics bind to non-overlapping epitopes of the spike protein receptor-binding domain (RBD) of SARS-CoV-2 spike protein [13]. They block the spike protein from attaching to its cognitive receptor the angiotensin-converting enzyme 2 (ACE2) receptor. This prevents Covid-19 to enter human cells, such as alveolar type 2 pneumocytes and inhibits replication of the virus.

Treatment with evusheld has been shown to significantly reduce the risk of developing Covid-19 infection. In the PROVENT clinical trial which studied more than 75% adult participants with risk factors for Covid-19 infection, 8 subjects out of 3, 460 participants (0.2%) in the tixagevimab plus cilgavimab group developed symptomatic SARS-CoV-2 infection and 17 participants out of 1, 737 (1%) in the placebo arm SARS-CoV-2 symptoms [16]. Treatment with evusheld reduced the incidence of infection by 77% ($P < 0.001$). Follow-up of patient for 6 months showed a relative risk reduction of 82.8% for SARS-CoV-2 infection in the participants who received tixagevimab plus cilgavimab. None of the patients who received evusheld developed severe SARS-CoV-2 or died, but there were 5 severe Covid-d-19 cases and 2 deaths in the placebo group [16].

The TACKLE phase III clinical trial studied the efficacy and safety of tixagevimab 300 mg plus cilgavimab 300 mg in outpatients with mild to moderate Covid-19 [17]. Treatment with tixagevimab 300 mg plus cilgavimab 300 mg resulted in clinically and statistically significant protection against progression to severe SARS-CoV-2 or death compared to placebo. Evusheld reduced the risk of developing severe Covid-19 or death by 88% compared with placebo [17].

However, not all the clinical trials have reported favourable outcomes with treatment with tixagevimab 300 mg plus cilgavimab 300 mg in hospitalized patients with Covid-19 receiving the standard of care. The TICO randomized, double-blind, phase 3, multinational trial studied the efficacy and safety of intravenous (IV) tixagevimab 300 mg plus IV cilgavimab 300 mg in 1, 455 hospitalized patients [18]. The incidence of sustained recovery in 710 patients treated with tixagevimab plus cilgavimab was 89% and in 707 patients treated with placebo was 86% at day 90; ($P = 0.21$). Mortality was lower in the tixagevimab plus cilgavimab group (61 [9%]) versus placebo arm (86 [12%]). Both treatments were safe and adverse effects were similar. Adverse events were reported in 5% in the tixagevimab plus cilgavimab group and also in 5% in the placebo group [18].

Although, the PROVENT and TACKLE clinical trials demonstrated efficacy and safety of evusheld in protecting individuals from Covid-19 infection and progression to severe SARS-CoV-2 or death. Further studied are required to establish the efficacy of tixagevimab plus cilgavimab for the treatment of moderate to severe SARS-CoV-2. Currently, tixagevimab plus cilgavimab combination therapy is not recommended for the treatment of hospitalized patients with severe SARS-CoV-2.

Evusheld is effective in preventing Omicron sub variants BA.1 and BA.1.1. However, it is unlikely to be effective in neutralizing Omicron sub variants BA.2.75.2, BA.4.6, BA.5.2.6, BF.11, BQ.1, BQ.1.1 and the latest sub variant Omicron XXB.1.5 ('Kraken') [19].

Pre-exposure prophylaxis is recommended for immunocompromised individuals who cannot mount adequate immunity against Covid-19 and in those who are allergic to the vaccine in countries where Omicron sub variants are less prevalent. Evusheld was approved for the pre-exposure prophylaxis by the Medicines and Healthcare products Regulatory Agency in Great Britain on March 17, 2022. It was later approved by the European Union on September 20, 2022.

However, pre-exposure prophylaxis should not be a substitute for double-dose vaccinations. Covid-19 vaccination far outweighs the risk from the vaccine in children and adult age groups [20].

**Conclusion**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a severe pneumonia caused by an enveloped, single-stranded beta coronavirus, belonging to the coronaviridae family. SARS-CoV-2 (Covid-19) has caused endless pandemic because of its ability to mutate into new sub variants of variable virulence. Covid-19 has contributed to significant healthcare and socio-economic burden globally. Prevention of SARS-CoV-2 with two doses of vaccines has been very effective and successful in preventing Covid-19 infection and progression of the disease to respiratory failure, multi-organ failure and death. However, some immunocompromised individuals cannot develop adequate immunity after vaccination and others are allergic to the vaccine. Pre-exposure prophylaxis is necessary in this category of people. Evusheld has been shown to be effective in affording pre-exposure prophylaxis and in preventing the development and progression of Covid-19 to respiratory failure and multi-organ failure. However, PrEP should not be a substitute for double-dose Covid-19 vaccination.

## References

1. WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int/ 2022.
2. Richards F, Kodjamanova P, Chen X, et al. Economic burden of COVID-19: a systematic review. Clin Outcomes Res. 2022:293-307.
3. National Institutes of Health (NIH). COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov/

***Citation:*** *Syabbalo N. Pre-exposure treatment and prevention of SARS-COV-2. Int J Respir Med. 2022;8(2):136*

4. Syabbalo N. The role of interleukin-6 and janus kinases in the pathogenesis, and treatment of SARS-CoV-2. J Lung Pulm Respir Res. 2022;9(1):17-32.
5. World Health Organization. Global COVID-19 vaccination Strategy a Changing World. 2022.
6. Lio R, Pan J, Zhang C, et al. Cardiovascular complications of COVID-19 vaccines. Front Cardiovasc Med 2022; 9:840929.
7. Lane S, Yeomans A, Shakir S. Reports of myocarditis and pericarditis following mRNA COVID-19 vaccination: a systematic review of spontaneously reported data from the UK, Europe and the USA and of the scientific literature. BMJ Open 2022; 12(5):059223.
8. Hatziantoniou S, Anastassopoulou C, Lazaros G, et al. Comparative assessment of myocarditis and pericarditis reporting rates related to mRNA COVID-19 vaccines in Europe and the United States. Expert Rev Vaccines. 2022;21(11):1691-6.
9. Afshar ZM, Barary M, Babazadeh A, et al. SARS-CoV-2-related and Covid-19 vaccine-induced thromboembolic events: A comparative review. Rev Med Virol. 2022;32(4):2327.
10. De Michele M, Kahan J, Berto I, et al. Cerebrovascular complications of COVID-19 and COVID-19 vaccination. Circ Res. 2022;130(8):1187-203.
11. Garg RK, Paliwal VK. Spectrum of neurological complications following COVID-19 vaccination. Neurol Sci 2022; 43(1):3-40.
12. Chatterjee A, Chakravarty A. Neurological complications following COVID-19 vaccination. Curr Neurol Neurosci Rep 2023; 23(1):1-14.
13. Dong J, Zost SJ, Greaney AJ, et al. Genetic and structural basis for SARS-CoV-2 variant neutralization by a two-antibody cocktail. Nat Microbiol 2021; 6:1233-1244.
14. Oganesyan V, Damschroder MM, Woods RM, et al. Structural characterization of a human Fc fragment engineered for extended serum half-life. Mol Immunol 2009; 46:1750-1755.
15. Loo YM, McTamney PM, Arends RH, et al. The SARS-CoV-2 monoclonal antibody combination, AZD7442, is protective in nonhuman primates and has an extended half-life in humans. Sci Transl Med. 2022;14(635):l8124.
16. Levin MJ, Ustiannowski A, De Wit S, et al. Intramuscular AZD7442 (tixagevimab-cigavimab) for prevention of COVID-19. N Engl J Med 2022; 386(23):2188-2200.
17. Montgomery H, Hobbs FDR, Padilla F, et al. Efficacy and safety of intramuscular administration of tixagevimab-cilgavimab for early outpatient treatment of COVID-19 (TACKLE): a Phase 3, randomised, double-blind, placebo-controlled trial. Lancet Respir Med. 2022;10(10):985-996.
18. Ginde AA, Paredes R, Murray TA, et al. Tixagevimab–cilgavimab for treatment of patients hospitalised with COVID-19: a randomised, double-blind, phase 3 trial. Lancet Respir Med. 2022;10(10):972-84.
19. Yue C, Song S, Wang L, et al. Enhanced transmission of XBB.1.5 is contributed by both strong ACE2 binding and antibody evasion. BioRxiv 2023.
20. Hunter PR. Thrombosis after covid-19 vaccination. BMJ 2021; 373.958.

***Citation:*** *Syabbalo N. Pre-exposure treatment and prevention of SARS-COV-2. Int J Respir Med. 2022;8(2):136*