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The role of spike protein entry inhibitors in the treatment and prophylaxis of mild to moderate covid-19 in nonhospitalized patients

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Abstract

Enterobacterales a Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a life- threatening pneumonia caused by an enveloped, single-stranded RNA beta coronavirus belonging to the coronaviridae 2B lineage [1]. The SARS-CoV-2 genome is enclosed in the nucleocapsid protein, and is surrounded by three protective structural proteins, including membrane protein, envelop protein, and spike protein [5]. The structural proteins are potential targets for the development of antivirals, and vaccines for early treatment and prevention of the progression of Covid-19. Entry of SARS-CoV-2 into host cells is mediated by the spike glycoprotein [7,8], which is composed of two functional subunits, including the S1 and S2 subunits. The standard of care of severe Covid-19 includes high-flow nasal oxygen, corticosteroids, remdesivir, and anti-interleukin-6, such as tocilizumab, or Janus kinase inhibitors, including baricitinib. However, mortality due to Covid-19 is prohibitively very high. Monoclonal antibodies which bind to epitopes on the receptor binding domain (RBD) of the spike protein of SARS-CoV-2, have the potential for early treatment of Covid- 19, and in preventing progression of the disease. Bamlanivimab plus etesevimab [1-3], casirivimab plus imdevimab [4-6], and sotrovimab [7] are recombined human monoclonal antibodies that bind to different epitopes in the RBD of the spike protein. They have been shown to reduce the risk of hospitalization and death in about 70-85% of nonhospitalized patients who had mild to moderate Covid-19 symptoms [12,19-21]. Bamlanivimab- etesevimab, and casarivimab-imdevimab are still effective against Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2) variants, but they have reduced susceptibility against the Omicron (B.1.1.529) variant of concern. Therefore, these spike protein entry inhibitors should not be recommended in countries where the Omicron variant of concern prevalence exceeds 80% [17]. Sotrovimab has been demonstrated to retain vitro and in vivo activity against all currently tested variants of concern and interest of the SARS-CoV-2 virus, including Delta (B.1.617), Delta Plus (AY.1 or AY.2), and Omicron (B.1.1.529) [13-15]. Sotrovimab is recommended for the treatment of nonhospitalized patients with mild to moderate Covid-19, and for post-exposure prophylaxis in countries severely affected by the Omicron variant [16]. Other recommended antivirals include remdesivir [22], nirmatrelvir plus ritonavir [23], and molnupiravir [24], which are active against the Omicron variant.

Conclusion & Significance: Treatment of nonhospitalized patients with Covid-19 is challenging because of the emergence of SARS-CoV-2 variants which become less susceptible to novel spike entry inhibitors.

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Biography

Nightingale Syabbalo is a Pulmonologist and Clinical Respiratory Physiologist by training, and obtained his postgraduate training at St. George's Hospital Medical School, University of London, UK. He was trained by one of the international prominent Respirologist of our times. Nightingale has worked as an academician, Consultant Physician, and a Clinical Researcher in several counties, including Canada, Kuwait, Oman, South Africa, and Zambia. He has published extensively in high impact medical journals, and is an Editorial Board member of thirteen journals in Pulmonology and Respiratory Medicine; and a reviewer of four journals in Thoracic Medicine, Respiratory Research, and Internal Medicine. Prof. Syabbalo's current area of research focuses on the role of interleukins in the pathophysiology and treatment of severe asthma. He has also interest in the mechanisms of interleukins-1β in the pathogenesis and treatment of pericardial syndromes.

