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Commentary

n-Covid Drugs and their Relevance in Present Day Scenario

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Abstract

This commentary briefly discusses the necessity of utilizing repurposed drugs/vaccines to combat against evil covid-19. As new variants are (such as Omicron) emerging out due to undergoing mutations by virus, urge of developing more efficient drugs is necessary both in terms of efficacy and safety.

Keywords: n-Covid; Vaccines; Efficacy; Safety; Mutations; Variants; Drugs; Repurpose

The outbreak of novel corona virus (2019-nCov) was first observed in the Wuhan city of Central China around 12th December 2019 [1] which has become pandemic, confirming 260 million cases including 5.2 million deaths across the world as on 26th November 2021 based on the data from World Health Organization (WHO) [2]. As on today, there is no specific drug or vaccine to effectively treat COVID-19. Varala and others [2-7], have already given glimpse of the n-covid origin, transmission and on the importance of medical diagnosis. In this regard, this pandemic has created worldwide urge to repurpose the present acceptable drugs (Old Weapon for New Enemy). It is a novel methodology for the development of drugs to explore potential therapeutic advantages in clinical trials [8].

Obviously, a pandemic needs trustable protocol for the drug development which should be available early in order to save money and time in conventional drug development. In reality, one among ten thousand drug candidates comes out of potent drug candidate with efficacy and safety during clinical trials, involving huge amounts of financial utilization and longer time. In this regard, during pandemic such as covid-19, pharmaceutical companies prefer to explore repurposing of drugs. There are constraints too, such as technology related and regulatory needs for their immediate utilization. The greater advantages of drug repurposing are a) already set as safe drug; b) economical viability; c) existing market potential; d) completion of toxicity studies; e) out-licensing potential.

The coronavirus disease 2019 (COVID-19) pandemic has disrupted global healthcare and economic systems throughout 2020 with no clear end in sight. While the pandemic continues to have deleterious effects across the globe, mechanisms for disrupting disease transmission have relied on behavioral controls (e.g., social distancing, masks, and hygiene) as there are currently no vaccines approved for use and limited therapeutic options. Despite mass vaccination, presently utilizing vaccines need information on their utility in kids, infants and pregnant women. Another biggest hindrance is covid keeps undergoing mutations. One cannot guarantee the existing vaccines, offer protection over such mutations. In addition, larger section of population is still hesitant to take the available vaccines (Figure 1).

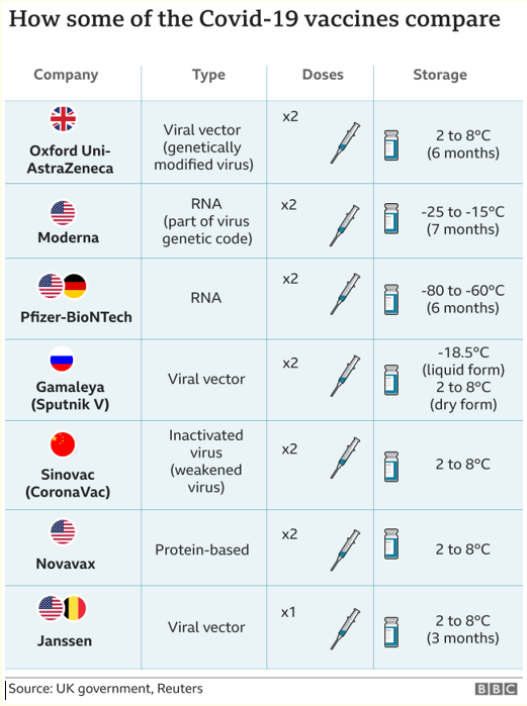

Figure 1: Available Vaccines in combating SARS Covid-2.

Since the COVID-19 pandemic first began in December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has continuously evolved with many variants emerging across the world. These variants are categorized as the variant of interest (VOI), variant of concern (VOC), and variant under monitoring (VUM). As of November 8, 2021, there are four SARS-CoV-2 lineages designated as the VOC (alpha, beta, gamma, and delta variants). VOCs have increased transmissibility compared to the original virus, and have the potential for increasing disease severity. In addition, VOCs exhibit decreased susceptibility to vaccine induced and infection-induced immune responses, and thus possess the ability to reinfect previously infected and recovered individuals. Given their ability to evade immune responses, VOC are less susceptible to monoclonal antibody treatments. VOCs can also impact the effectiveness of mRNA and adenovirus vector vaccines, although the currently authorized COVID-19 vaccines are still effective in preventing infection and severe disease. Current measures to reduce transmission as well as efforts to monitor and understand the impact of variants should be continued. On November 24, 2021, a new mutant called 'Omicron' (B. 1.1.529) has been confirmed as VUM and the frequency of mutating capacity of this new variant is presently becoming a global threat and WHO has warned all countries to be cautious to treat this as VOC.

Possible antiviral treatments, antimalarial treatments, immunosuppressants/immunomodulators, cell and plasma based therapy or alternative treatment strategies are being given to patients on trial and error basis, subject to FDA's approval (Table 1) and observing safety as well as efficacy protocol.

Mechanism of action and targets	Drugs
Inhibition of the RNA-dependent RNA polymerase	Remdesivir/+Baricitinib Favipiravir Ribavirin Molnupiravir
Inhibition of spike protein on SARS-CoV 2 (non-endosomal pathway) -TMPRSS2 inhibitor	Camostat mesylate, Nafamostat α-Ketobenzothiazole
Inhibition of endosomal acidification (early endosomal pathway)	Chloroquine, hydroxychlorquine (azithromycin is reported to greatly enhance the anti-SARS-COV-2 activity of hydroxychloroquine)
Inhibition of viral exocytosis	Interferon-α 2a Interferon-β 1b
Inhibition of papain-like protease and 3C-like protease	Lopinavir/Ritonavir
Inhibition of cathepsin L and cathepsin B in host cells (late endosomal pathway)	Teicoplanin (other glycopeptides including dalbavancin, oritavancin, and telavancin)
Enhancement of the anti-SARS-CoV-2 activity of hydroxychloroquine	Azithromycin
Inhibition against the SARS-CoV-2 target proteins: ACE2, RdRp, Spike Glycoprotein, Mpro and PL-pro	Rilpivirine
Strong anti-LCMV effects (Lymphocytic choriomeningitis virus)	Mycophenolic acid, Benidipine hydrochloride, Clofazimine, Dabrafenib, and Apatinib
pro-inflammatory activity of interleukin-6 (IL-6)	Tocilizumab
Suppresses SARS-CoV-2 Spike Protein-Mediated Cell-Cell Fusion by a Dihydroceramide D4-Desaturase 1-Independent Mechanism	N-(4-Hydroxyphenyl) Retinamide

Table 1: Mechanisms of action and targets of potential treatment agents for SARS-CoV-2 infections.

Conclusion

In this commentary, up to date information on variants of covid-19 undergoing continuous mutations and urge of developing new drug candidates in terms of safety and efficacy.

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Conflict of interest

None.

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