

Current advancements on Covid-19 potential treatments: Learning from literature review

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ABSTRACT

The coronavirus disease hit the world in December 2019 in Wuhan, China. A lot of developments towards the treatment of the disease have risen but no therapy has been scientifically proven successful up to date. However, regardless of current vaccines under clinical trials, much attention has been brought to repurposing old drugs as thousands of studies discuss their potential effectiveness against COVID-19. The present review discusses recent advancements in possible novel treatment and preventive therapeutics that are in ongoing trials. All the reviewed therapeutics in this article, regardless of their promising outcomes on the treatment and prophylaxis of COVID-19, have demonstrated no support to their efficacy regardless of other therapeutics such as convalescent plasma which has shown some potentiality for use. However, all the discussed interventions need thorough drug repositioning and advanced trial levels for them to be proved ready for clinical use.

Keywords: Clinical trials; Coronavirus infection; Virus diseases; Drug repurposing

1. INTRODUCTION

COVID-19 is a respiratory syndrome disease caused by a virus from a large family of viruses called coronaviruses, which can infect humans or animals [1-3]. There are seven known types of coronavirus, four types (NL63, OC43, KHU1, and 229E) are common, they cause mild to moderate respiratory infections such as a common cold. The other three

can cause severe respiratory infections; these are Severe Acute Respiratory Syndrome coronavirus (SARS-Cov), Middle East Respiratory Syndrome Coronavirus (MERS-Cov), and 2019 novel coronavirus [4-6]. Based on the current findings COVID-19 virus is transmitted from person to person through respiratory droplets and contact routes. Furthermore, according to current publications, there is no evidence of airborne

transmission of the COVID-19 virus in normal circumstances, but airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are conducted, this is according to the WHO [7]. Globally, as of the 27th of August 2020, there have been 24,021,218 confirmed cases of COVID-19, including 821,462 deaths, reported to WHO [8]. Since January 2020 tremendous developments on trying to find potential therapeutics for COVID-19 are on their steep upsurge. This review summarizes the recently published studies that evaluate current therapeutic advancements that seemingly show potentiality for COVI-19. Most of the treatments that show ongoing efficacy are repurposed drugs such as remdesivir, Corticosteroids, Lopinavir/ritonavir, Chloroquine or hydroxychloroquine, Oseltamivir, Ribavirin and interferon, Colchicine, Ascorbic acid, Tocilizumab or Sarilumab and other therapies such as Convalescent plasma.

2. DISCUSSION

The SARS-CoV-2 has been identified as one of the worst groups of coronavirus family since it emerged 20 years ago. It has led to an involving pandemic that urgently requires advanced developments on its therapeutics. Globally, a lot of developments on possible novel therapeutics have risen since January 2020 in the eradication of the virus. However, much attention has been brought to repurposing old drugs as thousands of clinical studies since January 2020, discuss their potential effectiveness against COVID-19. In this review, we have summarized recent potential advancements on possible novel treatment and preventive therapeutics that are in ongoing trials (Table 1). Several case reports have confirmed that therapeutic strategies should follow a two-phased immune response to COVID-19 [9]. Firstly, the treatment should be able to strengthen the host

immune system. Secondly, it should inhibit viral replication. Studies discussing Dexamethasone (Corticosteroids) states that it has been one of the most widely used therapy since the emergence of the virus that it mainly essential for patients requiring extra oxygen (RECOVERY trial). Dexamethasone is mainly an anti-inflammatory drug used to treat various allergic reactions such as arthritis. However current studies have reported that it does not still show specific efficacy. Corticosteroids are currently on trial expected to run for 10 months. The trial started on 3 April 2020 and was expected to end on 3 February 2021[10].

Studies discussing Lopinavir/ritonavir have concluded that the therapy may not be recommended for patients with mild pneumonia as it still requires further observational studies should be conducted [11]. Lopinavir/ritonavir is normally used with other medications to treat human immunodeficiency virus (HIV) infection. A recent trial on Lopinavir/ritonavir found that the Ct increase value for patients who received LPV/r was 0.9 per day for 2 patients, 1.0 per day for 3 patients not received the medication for 1 to 10 days which indicated that the treatment did not shorten the duration of SARS-CoV-2 shedding [12].

Studies on Remdesivir have shown that the therapy has demonstrated potential results in a controlled trial in patients with severe COVID-19 conditions [13]. Remdesivir was originally made for the treatment of Ebola. However, no studies have been proven for patients with moderate disease. A recent randomized clinical trial which investigated the effect of remdesivir against standard care on clinical status at 11 days in patients with moderate covid-19 concluded that patients with moderate COVID-19 condition did not show any specific efficacy after a 10-day treatment with remdesivir as compared to

Table 1. Summarizes current main drugs that seemingly show potentiality against SARS-CoV-2 and their ongoing clinical trials

Therapeutic Intervention	Current Trial Phase	Drug Category	The recommendation inconsistent with guidelines from the World Health Organization (WHO)
Corticosteroids	2	Anti-inflammatory	Dexamethasone is strongly recommended for patients requiring mechanical ventilation and recommended for hospitalized patients requiring supplemental oxygen (RECOVERY trial).
Lopinavir/Ritonavir	3	Anti-viral and Anti-malarial	It is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.
Remdesivir	3	Anti-viral	It has received conditional approval for the treatment of Covid-19 as it shortened time to clinical recovery.
Chloroquine or Hydroxychloroquine	3	Anti-malarial and anti-inflammatory	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials.
Oseltamivir	3	Anti-viral	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials.
Ribavirin and Interferon	1	Anti-viral	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials.
Colchicine	1	Anti-inflammatory	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials.
Ascorbic acid	2	Anti-oxidant	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials.
Tocilizumab or Sarilumab	2	Anti-inflammatory	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials.
Convalescent plasma	2	Immunomodulatory	It is not recommended for treatment or prophylaxis of COVID-19 outside approved clinical trials, however, the FDA has recently issued an Emergency Use Authorization to be used.

patients with standard care on treatment for 11 days [14].

However, it received a conditional approval as it managed to reduce the recovery period [15]. Studies discussing Chloroquine or hydroxychloroquine have found that it is more effective when used in combination with azithromycin [16]. Chloroquine is mainly useful for the treatment of malaria. A recent

prospective observational study comprised of 80 patients resulted in improvement in all the patients except one patient aged 86 who died [17]. Therefore, no recommendation has been granted for the treatment of COVID-19 outside approved clinical trials [15].

Studies discussing Oseltamivir show that it has been one of the most used treatments, especially in

Chinese hospitals. Oseltamivir is mainly intended to treat some symptoms caused by flu virus (influenza). A recent study conducted in china concluded that Oseltamivir is not recommended for treating COVID-19 as there is no enough proof for its efficacy in COVID-19 therapy [18].

Studies discussing the use of Ribavirin/interferon, Colchicine, Ascorbic acid, and Tocilizumab or Sarilumab are still disapproved for therapeutics use on treatment of COVID-19. Recent clinical trials have concluded that the therapeutics does not indicate any credible difference among patients with mild COVID-19 condition as compared to standard care patients [9, 17, 19]. Furthermore, other studies have also stated that there is also an insignificant difference between COVID-19 negative and positive patients that received the treatments [11]. However, another recent study on Tocilizumab indicated that the therapy reduced mortality rate as well as a respiratory failure as compared to supportive care [20-22]

Convalescent plasma is one of the outstanding intervention for COVID-19 that has brought much more interest to the scientists regarding its ongoing efficacy [13, 23, 24]. All recent clinical trials on the efficacy of Convalescent plasma have come up with positive results as at least all patients who participated in the trials ended up with total improvements [25-28]. Several studies have suggested that Convalescent plasma can come up with a great achievement if to be used in this pandemic as no specific therapy or vaccine has yet emerged [29,30]. Currently, the FDA has issued an Emergency Use Authorization to the use of Convalescent plasma because of its precise efficacy [31]

World Health Organization (WHO) general recommendation

The World Health Organization has up to date not approved the use of any discussed interventions as they lack enough data to support their precise efficacy regardless of their potentiality in the treatment and prophylaxis of COVID-19.

3. CONCLUSION

This literature review and analysis were conducted based on recently published studies on the treatment of COVID-19 disease. All the reviewed therapeutics in this article, regardless of their potential outcomes on the treatment and prophylaxis of COVID-19 have demonstrated no support to their efficacy except Convalescent plasma which has shown some potentiality to be used against COVID-19 as no specific therapy or vaccine has emerged yet. However, all the discussed therapies need thorough drug repositioning and advanced trial levels for them to be proved ready for clinical use as they demonstrate that the available data is not sufficient to suggest their potentiality for the eradication of COVID-19.

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5. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

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7. REFERENCES

1. Amponsah, R., & Frimpong, I. A. (2020). Ghana in the Face of COVID-19: Economic Impact of Coronavirus (2019-NCOV) Outbreak on Ghana. *Open Journal of Business and Management*, **08**(04), 1404–1411.
2. Munthali, G. N. C., & Xuelian, W. (2020b). Covid-19 Outbreak on Malawi Perspective. *Electronic Journal of General Medicine*, **17**(4), em210.
3. Rahman, A., & Sathi, N. J. (2020). Knowledge, Attitude, and Preventive Practices toward COVID-19 among Bangladeshi Internet Users. *Electronic Journal of General Medicine*, **17**(5), em245.
4. *Coronavirus*. (n.d.). Retrieved August 28, 2020, from https://www.who.int/health-topics/coronavirus#tab=tab_1
5. Munthali, G. N. C., & Xuelian, W. (2020a). COVID-19 Lockdown Measures on Least Developing Economies in Africa-a case of Malawi Economy. *Technium Social Sciences Journal*, **7**(7), 295–301.
6. Xuelian, W. (2020). The Future of Tobacco Industry Amidst of COVID-19 -A Case of Malawi Producing Country. *Biomedical Journal of Scientific & Technical Research*, **27**(5), 21104–21109.
7. *Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations*. (n.d.). Retrieved August 28, 2020, from <https://www.who.int/news-room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations>
8. *WHO Coronavirus Disease (COVID-19) Dashboard | WHO Coronavirus Disease (COVID-19) Dashboard*. (n.d.). Retrieved August 28, 2020, from <https://covid19.who.int/>
9. Fragkou, P. C., Belhadi, D., Moschopoulos, C. D., Lescure, F., Janocha, H., Karofylakis, E., Yazdanpanah, Y., Mentr, F., & Tsiodras, S. (2020). *Review of trials currently testing treatment and prevention of COVID-19*. **26**, 988–998.
10. Villar, J., Añón, J. M., Ferrando, C., Aguilar, G., Muñoz, T., Ferreres, J., Ambrós, A., Aldecoa, C., Suárez-Sipmann, F., Thorpe, K. E., Jüni, P., Slutsky, A. S., & DEXA-COVID19 Network. (2020). Efficacy of dexamethasone treatment for patients with the acute respiratory distress syndrome caused by COVID-19: study protocol for a randomized controlled superiority trial. *Trials*, **21**(1), 717.
11. Dalili, N., Dalili, N., Kashefzadeh, A., Nafar, M., Nafar, M., Poorrezagholi, F., Poorrezagholi, F., Firouzan, A., Firouzan, A., Samadian, F., Samadian, F., Samavat, S., Samavat, S., Ziaie, S., & Fatemizadeh, S. (2020). Adding Colchicine to the Antiretroviral Medication - Lopinavir/Ritonavir (Kaletra) in Hospitalized Patients with Non-Severe Covid-19 Pneumonia: A Structured Summary of a Study Protocol for a Randomized Controlled Trial. In *Trials*, **21**(1).
12. Cheng, C.-Y., Lee, Y.-L., Chen, C.-P., Lin, Y.-C., Liu, C.-E., Liao, C.-H., & Cheng, S.-H. (2020). Lopinavir/ritonavir did not shorten the duration of SARS CoV-2 shedding in patients with mild pneumonia in Taiwan. *Journal of Microbiology, Immunology and Infection*, **53**(3), 488–492.
13. Beigel, J. H., Tomashek, K. M., Dodd, L. E., Mehta, A. K., Zingman, B. S., Kalil, A. C., Hohmann, E., Chu, H. Y., Luetkemeyer, A., Kline, S., Lopez de Castilla, D., Finberg, R. W., Dierberg, K., Tapson, V., Hsieh, L., Patterson, T. F., Paredes, R., Sweeney, D. A.,

- Short, W. R., Lane, H. C. (2020). Remdesivir for the Treatment of Covid-19 — Preliminary Report. *New England Journal of Medicine*.
14. Spinner, C. D., Gottlieb, R. L., Criner, G. J., Arribas López, J. R., Cattelan, A. M., Soriano Viladomiu, A., Ogbuagu, O., Malhotra, P., Mullane, K. M., Castagna, A., Chai, L. Y. A., Roestenberg, M., Tsang, O. T. Y., Bernasconi, E., Le Turnier, P., Chang, S.-C., SenGupta, D., Hyland, R. H., Osinusi, A. O., GS-US-540-5774 Investigators. (2020). Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. *JAMA*.
 15. Covid-, T. B. C., & Committee, T. (2020). *Clinical Reference Group Recommendations : Therapies for COVID-19 Position Statement on Therapies for COVID-19 :*
 16. *Comparison of effectiveness of various treatment strategies in COVID-19 patients: A Systematic Review | Journal of Rawalpindi Medical College.* (n.d.). Retrieved August 27, 2020, from <http://journalrmc.com/index.php/JRMC/article/view/1431>
 17. Hussain, M. S., Haider, A., Yousaf, U. A., Laraib, W., Dildar, F., & Hussain, H. A. (2020). Comparison of effectiveness of various treatment strategies in COVID-19 patients: A Systematic Review. *Journal of Rawalpindi Medical College*, **24**(1), 108–117.
 18. Munir, M. A., Kuganda, H., & Basry, A. (2020). The Efficacy and Safety of Antivirus Drugs for COVID-19: A Systematic Review. In *Systematic Reviews in Pharmacy*, **11**(7)
 19. Sonja A. Rasmussen, MD, MS, J. C. S. (2020). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-. *Ann Oncol*, *January*, 19–21.
 20. Gritti, G., Raimondi, F., Ripamonti, D., Riva, I., Landi, F., Alborghetti, L., Frigeni, M., Damiani, M., Micò, C., Faggioli, S., Cosentini, R., Luca Lorini, F., Gandini, L., Novelli, L., Morgan, J. P., Owens, B. M. J., Kanhai, K., Tonkovic Reljanovic, G., Rizzi, M., ... Rambaldi, A. (2020). IL-6 signalling pathway inactivation with siltuximab in patients with COVID-19 respiratory failure: an observational cohort study. *MedRxiv*, 20048561.
 21. *Tocilizumab in COVID-19 Pneumonia (TOCIVID-19) - Full Text View - ClinicalTrials.gov.* (n.d.). Retrieved August 27, 2020, from <https://clinicaltrials.gov/ct2/show/NCT04317092>
 22. *Tocilizumab treatment in COVID-19: A single center experience - Luo - 2020 - Journal of Medical Virology - Wiley Online Library.* (n.d.). Retrieved August 25, 2020, from <https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25801>
 23. Li, L., Li, L., Zhang, W., Zhang, W., Hu, Y., Tong, X., Zheng, S., Yang, J., Kong, Y., Kong, Y., Ren, L., Ren, L., Wei, Q., Mei, H., Hu, C., Tao, C., Tao, C., Yang, R., Wang, J., ... Liu, Z. (2020). Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients with Severe and Life-threatening COVID-19: A Randomized Clinical Trial. *JAMA - Journal of the American Medical Association*, **324**(5), 460–470.
 24. Psaltopoulou, T., Sergentanis, T. N., Pappa, V., Politou, M., Terpos, E., Tsiodras, S., Pavlakis, G. N., & Dimopoulos, M. A. (2020). The Emerging Role of Convalescent Plasma in the Treatment of COVID-19. *HemaSphere*, **4**(3), e409.

Saleh B. Alghamdi. (2020). Inhibition of Candida infections by synthesized Zinc oxide nanoparticles and mechanism thereof. *International Journal of Applied Chemical and Biological Sciences*, 1(4), 13-19.

25. Mucha, S. R., & Quraishy, N. (2020). Convalescent plasma for COVID-19. *Cleveland Clinic Journal of Medicine*.
26. Piechotta, V., Chai, K. L., Valk, S. J., Doree, C., Monsef, I., Wood, E. M., Lamikanra, A., Kimber, C., McQuilten, Z., So-Osman, C., Estcourt, L. J., & Skoetz, N. (2020). Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. In *Cochrane Database of Systematic Reviews* (7).
27. Sabando Vélez, B. E., Plaza Meneses, C., Felix, M., Vanegas, E., Mata, V. L., Romero Castillo, H., Oliveros Alvear, J. W., Boloña, E., Alejandra Posligua, M., Layedra Bardi, L. R., Vera Paz, C., & Chérrez-Ojeda, I. (2020). A practical approach for the compassionate use of convalescent plasma in patients with severe COVID-19 in developing countries. *Journal of Infection in Developing Countries*, 14(7), 737–741.
28. Shurville, S., Browne, T., & Whitake, M. (2009). ORE Open Research Exeter. *Campus-Wide Information Systems*, 26(3), 201–231.
29. *Convalescent plasma: A potential therapeutic option for COVID-19 patients* Ng SL, Soon TN, Yap WH, Liew KB, Lim YC, Ming LC, Tang YQ, Gob BH, - *Asian Pac J Trop Med*. (n.d.).
30. Joyner, M. J., Wright, R. S., Fairweather, D., Senefeld, J. W., Bruno, K. A., Klassen, S. A., Carter, R. E., Klompas, A. M., Wiggins, C. C., Shepherd, J. R. A., Rea, R. F., Whelan, E. R., Clayburn, A. J., Spiegel, M. R., Johnson, P. W., Lesser, E. R., Baker, S. E., Larson, K. F., Ripoll, J. G. Casadevall, A. (2020). Early safety indicators of COVID-19 convalescent plasma in 5000 patients. *Journal of Clinical Investigation*.
31. *FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement in Administration's Fight Against Pandemic | FDA*. (n.d.). Retrieved August 28, 2020, from <https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment>