REVIEW

Cite This: Int. J. of Immun amd Microbiol. 2021, 1, 5-8

Sciforce

International Journal of Immunology and Microbiology

Journal homepage: www.sciforce.org

COVID-19 treatments and vaccines: A year in review

Joseph F. Murphy*

ImmunePCS LLC, Greater Boston Area, MA, USA.

ARTICLE INFO

Article history:
Received : 04022021
Received in revised form 04292021
Accepted : 04292021
Available online: 06022021

Keywords:
COVID-19;
Vaccines;
Year in review.

ABSTRACT

The SARS-CoV-2 coronavirus (COVID-19) pandemic has precipitated an enormous collaborative global effort within the scientific and medical community in search of therapeutic and preventative solutions. The aim of this review is to collate the key developments regarding pharmacological treatments tested and vaccine candidates that have been approved to treat and arrest the spread of COVID-19.

*Corresponding author. E-mail: joseph.murphy@immunepcs.com

Introduction

COVID-19 Transmission

The COVID-19 outbreak has caused one of the most widespread and significant public health crises in decades. It has become one of the leading causes of death internationally. The primary route of transmission from person-to-person is from airborne aerosol spread through close physical contact, particularly in enclosed, poorly ventilated areas.[(1)] Transmission through contaminated objects was originally considered a major transmission contributor; however, it is no longer considered a significant driver of the spread. Wearing masks has shown to be effective at preventing or curtailing viral transmission, especially when combined with other measures like social distancing and depopulation of indoor communal spaces.[(2)]

Mechanism of action:

The mechanism of action and entry into human physiology at a cellular level has been described previously.[(3)] Briefly, the virus binds and enters the host cell through a spike protein expressed on its surface. The infection begins when the long protruding spike proteins that latches on to the angiotensin-converting enzyme 2 (ACE-2), a receptor involved in regulating blood pressure ACE-2 protein. From this point, the spike transforms, unfolding and refolding itself, using coiled spring-like parts that start out buried at the core of the spike. The reconfigured spike hooks and docks the virus particle to the host cell. This forms a channel allowing the viral genetic material into the unsuspecting cell, in the case of COVID-19, type II lung cells. From this point onwards, most of the damage caused by COVID-19 results from the immune system going into overdrive to stop the virus from spreading.[(4)] The influx of immune cells to the infected tissue causes severe damage in the process of cleaning out the virus, infected cells, and bacterial infections with potentially lethal consequences.

Treatments

Medical therapies to treat COVI-19 evolved rapidly. Treatments include drugs that were approved by the US Food and Drug Administration (FDA) and drugs made available under FDA emergency use authorizations (EUA). The Centers for Disease Control and Prevention (CDC) has strongly encouraged clinicians, patients, and their advocates to consult the treatment guidelines published by the National Institute of Health (NIH). These guidelines are based on scientific evidence and expert opinion.[(5)] Several therapeutic modalities have been tested and deployed to treat the disease, some of which are summarized here.

Anti-virals:

Antivirals are drugs that arrest the replication of the virus. They are generally considered most effective when administered in the early phase of infection.

Remdesivir:

To date, remdesivir is currently the only antiviral approved under EUA by the FDA to treat COVID-19. The approval was based on findings that hospitalized patients who receivedremdesivir recovered faster.[(6)]Remdesivir can be administered either alone or in combination with other medications.

Molnupiravir:

An antiviral drug, previously known as EIDD-2801, appears safe and effective. Viral levels reduce to undetectable levels in COVID-19 patients after five days of administration, according

to data from a US-based Phase II clinical trial. While molnupiravir is proven to inhibit coronavirus replication in infected patients, more data is required to determine whether it can prevent severe illness.[7]

Lopinavir/ritonavir:

Lopinavir/ritonavir are anti-human immunodeficiency virus (HIV) drugs. Both have been investigated and neither drug showed any efficacy in large randomized controlled trials in hospitalized COVID-19 patients.[8]

Anti-inflammatories:

One reason for mortality in COVID-19 infected patients is an overactive response by the patient's immune system. This response leads to several inflammatory disorders, not least of which is the much publicized "cytokine storm". The following outlines agents have been tested to dampen the inflammatory response to COVID-19.

Dexamethasone:

Dexamethasone is an anti-inflammatory corticosteroid used for many years to treat autoimmune conditions and allergic reactions. It is cheap and widely available and has been shown to reduce mortality in the sickest hospitalized patients by dampening the immune response.[9] A meta-analysis study evaluating the results of seven trials shows the death rates were lower in hospitalized patients who took one of three different corticosteroids — dexamethasone, hydrocortisone, or methylprednisolone.[6]

Baricitinib:

Baricitinib is an anti-inflammatory drug used for the treatment of rheumatoid arthritis. In November 2020, the FDA issued an EUA to use baricitinib in combination with remdesivir in hospitalized adults and children two years and older requiring respiratory support. However, there is not enough evidence to support the use of this therapy with or without remdesivir.[10]

Antibody Based Treatments:

Antibodies are proteins generated by the immune system to help fight infections, such as viruses, by binding to and destroying them. Antibody-based treatments are likely most helpful soon after infection, rather than after the disease has progressed.

Monoclonal antibodies:

Monoclonal antibodies are synthesized in the laboratory. The FDA has approved two monoclonal antibody treatments, one single antibody from Eli Lilly, and a combination of two antibodies from Regeneron.

The Eli Lilly antibody, Bamlanivimab (LY-CoV555), works by blocking COVID-19 from entering and infecting human cells. Preliminary results indicated that patients with mild-to-moderate COVID-19 who received bamlanivimab were less likely to be hospitalized. Studies are still underway, both as a monotherapy and combination therapy. Regeneron's treatment utilizes a combination of two monoclonal antibodies, casirivimab and imdevimab (REGN-COV2), referred to as an antibody cocktail. Preliminary trial data reported that REGN-COV2 reduced viral load and relieved symptoms sooner in non-hospitalized patients. These treatments are available for patients under EUAs, but more data is required before becoming part of routine care.[6]

Convalescent plasma:

One of the first groups of antibody-based treatments used convalescent plasma (plasma from recovered COVID-19 patients). This treatment involves administering plasma from a recovered individual into someone infected with the virus. Theoretically, the antibodies fromthe recovered individual neutralize the virus in the infected individual. Although the FDA issued an EUA for convalescent plasma for hospitalized patients with COVID-19, the data to date has been conflicting and inconclusive.[6]

Anti-coagulants:

Because of the systemic nature of COVID-19 where the circulatory system supplies all parts of the body, some COVID-19 deaths are believed to be caused by blood clots forming in major arteries and veins. A recent study has reported that full-dose blood thinners decreased the need for life support and improved outcome in hospitalized COVID-19 patients. [11] This worldwide large clinical trial, where full dose treatments were administered to moderately ill patients hospitalized for COVID-19, reduced the requirement of vital organ support—such as the need for ventilators.

In addition to some of the FDA approved drugs cited in the previous section, multiple treatments were investigated during the early phase of the COVID crisis, with varying results.[12] In contrast to the overall trials for COVID-19 treatments, the programs initiated for vaccine development have been incredibly successful, surpassing all expectations.

Vaccines

From the outset of the COVID-19 pandemic, vaccines ultimately offer the most appealing and robust therapeutic modality as they prevent the disease from taking hold. This has led to a global vaccine R&D effort that is unprecedented in terms of scale and delivery. The urgency to create a vaccine for COVID-19 led to expedited schedules that compressed the standard vaccine development timeline from years to months.

At the time of writing, three vaccines have been authorized for emergency use by the FDA in the US, with more likely to come onstream as they progress through the development pipeline. A fourth vaccine, from Oxford-AstraZeneca, has also been approved for distribution within the European Union (EU). The three vaccines approved in the US are highly effective at preventing hospitalization, death, and severe disease. Vaccines work by triggering an immune response that generate highly specific antibodies against an antigen, in the case of COVID-19, the virus spike protein expressed on the surface of the virus. Moreover, the immune system is taught to recognize the spike protein specific to the virus. If this spike protein is encountered

in the future, an immune response is swiftly mounted, thus preventing escalation of the virus.

Two of the authorized vaccines, developed by both Pfizer/BioNTech and Moderna, have revolutionized a technology referred to as messenger RNA (mRNA) technology. This technology acts as a delivery system to cells within our bodies with specific instructions to carry out a specific task.[13]

Of importance:

- mRNA vaccines do not use live virus, but rather a portion of the message encoding for the spike protein.
- mRNA is produced by DNA, but does not enter the nucleus of the cell containing the DNA.
- Once the mRNA vaccine finishes producing the protein that is expressed on the cell surface, it is broken down and removed by normal cellular processes.

The Johnson and Johnson (J&J) and Oxford-Astra Zeneca vaccines utilize a more conventional approach, referred to as a viral vector. This vaccine utilizes a harmless modified version of a common cold virus to deliver the gene encoding for the spike protein into the cell.[13]

Vaccine comparison:

Both the Pfizer/BioNTech and Moderna vaccines have been reported to confer over 94% protection rates against symptomatic COVID-19 infection.[14,15] The single shot J&J vaccine has shown to be 85% effective at protecting against severe disease, 66% against preventing moderate to severe disease, and also appears to be effective against the South African variant of the virus (B.1.351).[16] Although superficially the single shot J&J appears less effective, it is difficult to compare all three vaccines directly because of differences in trial design and outcomes. From a logistical point of view, the J&J vaccine is advantageous as it is a single-dose regimen that can be stored for up to three months in a refrigerator. The most recent data from the AstraZeneca phase three trial reports that the vaccine is 76% effective against symptomatic cases of the virus.[17]

Several other trials are ongoing

Several other trials are ongoing. The most important point from the information collected from 7 large efficacy trials is that all vaccines confer 100% protection against severe disease, hospitalizations, and death. Moreover, it is not just the vaccinated individual who benefits from vaccination. Most vaccines also reduce transmission of infection among people, and in so doing, help protect those who fail to mount an effective immune response to vaccines or who cannot receive the vaccinate because of their age or compromised immune system.[18]

Vaccines and viral variants:

Several variants of the virus have been reported, with the two properties causing the most concern being enhanced contagion and immune response evasion. The current vaccines were developed based on the spike protein before it contained the mutations identified in the variants. A recently published study investigated the effectiveness of the FDA approved Pfizer/BioNTech vaccine against the newly-emerged variants from the United Kingdom (UK) and South Africa (SA).[19] While both variants are deemed more transmissible, the levels of antibody generated in response to the vaccine are so high that it seems unlikely that it will impact the overall efficacy of the vaccine for these strains. This preliminary study also highlights the ongoing evolution of COVID-19, necessitating continuous monitoring of the significances of viral mutations for vaccine efficacy. While research suggests that COVID-19 vaccines have lower efficacy against the variants, and further research is needed, the vaccines appear to provide protection against severe COVID-19.[20]

Vaccine manufacturing and distribution:

The development of the vaccines, from basic R&D through human clinical trials, has been carried out within a very rapid time frame. Ramping up production, however, has been slow and cumbersome. After a slow start, Pfizer/BioNTech andModerna have raised output by gaining experience, scaling up production lines, and taking other steps like making certain raw materials on their own.[21]

Of the three candidates, AstraZeneca has already struck a deal with COVAX, the global initiative to distribute COVID-19 vaccines equitably. Moderna has partnered with Lonza and Catalent Inc. to manufacture and distribute millions of doses.[22] Moreover, a recent agreement between J&J and Catalent has secured a US FDA emergency clearance that allows Catalent's facility to manufacture and distribute, thus aiding the vaccination supply.

Vaccination and reinfection:

The first large scale study investigating whether reinfection can occur recently reported that the vast majority of people who had COVID-19 are protected from catching it again, for at least six months.[23] This Danish study found that protection against repeat COVID-19 infection is both robust and detectable in the majority of individuals, 80% or more of the naturally infected population younger than 65 years. However, individuals aged 65 years and older had less than 50% protection against repeat infection, since the older age group is more susceptible serious illness. Their finding highlights the need for continued vigilance to keep themselves and others safe. This also indicates that vaccination of previously infected individuals should be done because natural protection cannot be relied upon, consistent with the general consensus that vaccines confer a level of immune response that is higher than previous COVID-19 infection. Follow-up studies will give a better idea of the duration of vaccine protection.

Conclusion

As the COVID-19 pandemic has demonstrated, it is extremely difficult to eliminate a virus from the human population once it has entered. The pandemic spread has been compounded because the virus spreads asymptomatically. That

said, the virus is manageable, similar to the manner in which vaccines have worked against other preventable communicable diseases. Monitoring the protective effects of the different vaccines will likely last for several years. For now, the outlook is positive as global cases decline, the vaccines roll out, and the momentum to investigate and repurpose drugs continues.

Acknowledgments

The author is grateful to Tara Finn for the careful reading of this manuscript.

Conflict of interest

There is no conflict of interest.

References

1. Coronavirus disease (COVID-19): How is it transmitted? **2020.**
2. Bai, N. Still Confused About Masks? Here's the Science Behind How Face Masks PreventCoronavirus. **2020.**
3. Murphy, J. F. COVID-19: An Immunological Perspective. *MOJ Immunol*. **2020**, 7(1), 10.
4. Kupferschmidt, K, Cohen, J. Science. Race to find COVID-19 treatments accelerates. **2020**.
5. Information for Clinicians on Investigational Therapeutics for Patients with COVID-19Centers for Disease Control and Prevention. **2020.**
6. Tran, J. The Latest Research on COVID-19 Treatments and Medications in the Pipeline. **2021.**
7. Drug launched at Emory reduces virus that causes COVID-19 to undetectable levels. **2021.**
8. Group, R. C. Lopinavir-ritonavir in patients admitted to hospital with COVID-19(RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. **2020.**
9. Baragona, S. Treating COVID-19 One Year In: Better, but No Breakthrough. **2021.**
10. Harvard Health Publishing. Treatments for COVID-19. **2021.**
11. NIH: National Institutes of Health. Full-dose blood thinners decreased need for life support and improved outcome in hospitalized COVID-19 patients. **2021.**
12. Lehrer, S.; Rheinstein, P. H. Ivermectin Docks to the SARS-CoV-2 Spike Receptor-binding Domain Attached to ACE2. **2020**.
13. Murphy, J. F. COVID-19 mRNA vaccines.
14. Baden, L.R. et al Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. **2021**
15. Information about the Moderna COVID-19 Vaccine. **2021**
16. Ledford, H. J&J's single-dose COVID vaccine raises hopes for faster rollout. **2021**
17. Cohen, J. AstraZeneca lowers efficacy claim for COVID-19 vaccine, a bit, after board's rebuke. **2021**
18. Emanuel, E. Take whatever COVID vaccine you can get. All of them stop death and hospitalization. **2021**
19. Xuping, X et al. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera. **2021**
20. COVID-19 vaccines: Get the facts **2021**.
21. Loftus, P. Covid-19 Vaccine Manufacturing in U.S. Races Ahead. **2021**.
22. COVAX announces additional deals to access promising COVID-19 vaccine candidates; *plans global rollout starting* Q1 **2021**.
23. Hansen, H. H et al Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: *a population-level observational study*.**2021**.