

LITERATURE REVIEW SARS-CoV 2 Treatment

By: Keerthi Thallapureddy, Roma Ahuja, Derrick Draeger, Elise Lasker, Cory Nunn, Anjali Prasad, Brian Seegmiller, Michelle Sutanto, and Saraaga

Tamirisa; Peer reviewed by: Dr. Kristi Traugott and Dr. Elizabeth Hand

updated 05/30/2021



SUPPORTIVE CARE

IMMUNOSUPPRESSANTS

- Long duration and excessive doses of steroids may adversely affect recovery due to the inhibition of antiviral immunity and may also result in other side effects related to steroids.
- Discontinuation of immunosuppressants and steroid treatment might help faster recovery from COVID-19 pneumonia.
- The risks and benefits of continuing or discontinuing immunosuppressants should be weighed for each individual case.
 - A lower than standard dose of immunosuppressants could be tried in patients requiring immunosuppressants to facilitate and shorten duration of disease with COVID-19.
- However, steroids are still considered standard of care in the management of patients who progress to ARDS

VENTILATION

- Though mostly anecdotal, there is some evidence on the ventilator settings and differing characteristic of COVID-19 associated ARDS. Ventilator setting recommendations include:
 - Low TV, less than or equal to 4-8 mL/kg ideal body weight
 - Plateau pressures <30 cm H2O
 - PEEP >10 cm H2O
 - Oxygen administration at an SpO2 < 90% - 96%
 - Starting RR of 16 breaths/min.
 - Early prone positioning
 - If prone positioning fails, use recruitment maneuvers and high PEEP strategies, pulmonary vasodilators, neuromuscular blocking agents, and/or ECMO.
- The most experienced team member should perform intubation with as few assistants as possible to reduce exposure. Bag-mask ventilation generates aerosols and should be minimized by performing prolonged pre-oxygenation. Rapid sequence induction with muscle relaxants will reduce coughing.
- In patients who develop hypercapnia, increase VT to ~7.7.
- For timing of intubation:
 - If a patient is on nasal high-flow oxygen therapy, the ROX index [SpO2/(FiO2 x RR)] can be used. If after 12 hours, patients have a ROX index of <3.85, initiate intubation.
 - For NCP patients, if PaO2/FiO2 is <150 mmHg (1 mmHg = 0.133 kPa), initiate intubation if receiving more than 2 hours of nasal high-flow therapy or non-invasive ventilation.
- Two recent studies found that self-proning improved oxygenation parameters in adults with COVID-19 with noninvasive ventilation
 - Some patients may be unable to tolerate this or sustain higher oxygenation parameters upon returning to the supine position.

ANTICOAGULATION

- D-dimer and FDP levels may progressively increase with COVID-19 exacerbation, resulting in acro-ischemia.
- The existence of hypercoagulation status in critical COVID-2019 patients should be monitored closely, and anticoagulation therapy with LMWH is recommended for all hospitalized adults with COVID-19. Fondaparinux is recommended in cases of HIT.
- Anticoagulant therapy mainly with LMWH appears to be associated with better prognosis in severe COVID-19 patients meeting SIC criteria or with markedly elevated D-dimer.
- Antiplatelet agent Dipyridamole has been found to suppress SARS-CoV-2 replication in vitro. A proof of concept trial involving 31 patients with COVID-19 found that dipyridamole supplementation was associated with decreased D-Dimer concentration, improved platelet and lymphocyte counts, and improved clinical outcomes compared to control patients.

ECMO

- ECMO should be considered if mortality rate approaches 50%, initiate if 80%.
- ECMO should be considered if one following criteria are met:
 1. PaO2/FiO2 <100mmHg
 2. P(A-a) O2 >600mmHg
 3. pH <7.2 and plateau pressure >30 cmH2O with respiratory rate > 35 breaths per minute
 4. <65 years old
 5. NO contraindications
 6. Severe air leak syndrome
 7. Complicated by cardiogenic shock or cardiac arrest
- Contraindications include: multi-organ failure, contraindication to anticoagulation, high mechanical vent for more than 7 days



OUTPATIENT MANAGEMENT OF COVID-19

FIRST STEPS

- Reduce COVID-19 transmission
- Advise patients on when to seek health care provider and treatment
- Triage patients with COVID-19 symptoms via tele-health visits prior to receiving in-person care

MANAGEMENT OF DYSPNEA

- Patients with dyspnea should be referred to in-person evaluation by health care provider and then monitored closely for a few days to assess for worsening respiratory status

Therapy for Mild to Moderate COVID-19

Use one of the following anti-SARS-CoV-2 monoclonal antibodies per EUA criteria:

- **Bamlanivimab 700 mg + Etesevimab 1,400 mg * OR**
- **Casirivmmab 1,200 mg + Imdevimab 1,200 mg**

*patients with mild to moderate COVID-19 infection who are at high risk of progressing to severe disease and/or hospitalization. They recommend against the use of this combination treatment in hospitalized COVID-19 patients, with exceptions for those in clinical trial

THERAPIES NOT APPROVED FOR OUTPATIENT MANAGEMENT OF COVID-19

- Chloroquine/Hydroxychloroquine with or without Azithromycin
- Dexamethasone or other systemic glucocorticoids in the absence of other indications
- Antibacterial therapy (e.g. azithromycin, doxycycline) in the absence of other indications
- Anticoagulants and antiplatelet therapy should not be initiated for prophylaxis in outpatient setting unless patient has other indications for therapy

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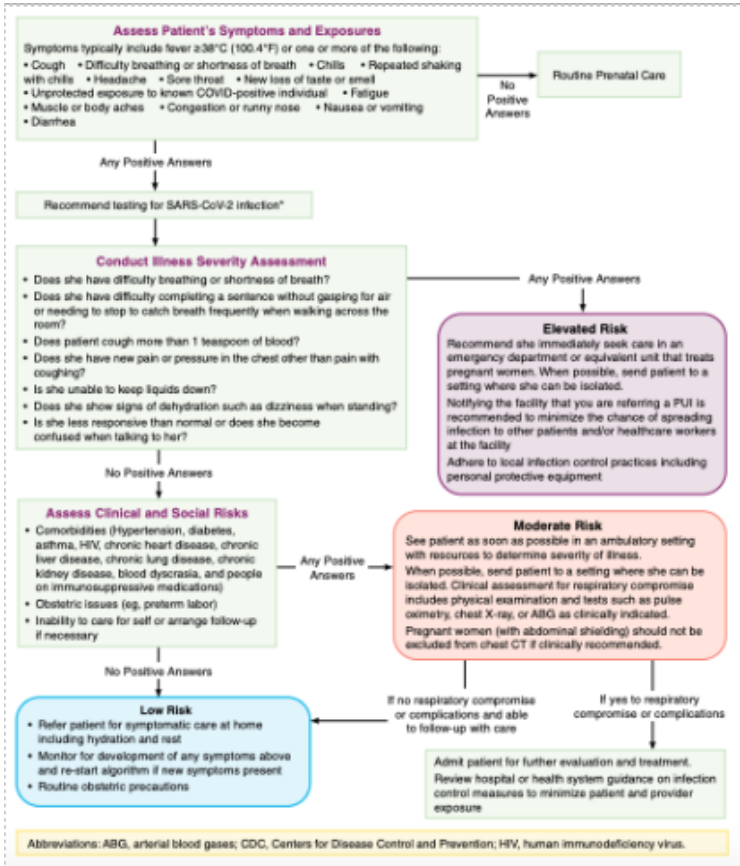
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COVID-19 MANAGEMENT IN SPECIAL POPULATIONS

PREGNANCY

- The American College of Obstetricians and Gynecologists (ACOG) has developed an algorithm in the outpatient management of COVID-19 in pregnant women



CHILDREN

- Most children with mild or moderate COVID-19, even with risk factors, will recover without specific therapy
- Bamlanivimab plus etesevimab or casirivimab plus imdevimab may be considered on a case-by-case basis for nonhospitalized children who meet the EUA criteria, especially those who meet more than one criterion or are aged ≥ 16 years
- Remdesivir is recommended for
 - Hospitalized children aged ≥ 12 years with COVID-19 who have risk factors for severe disease and have an emergent or increasing need for supplemental oxygen
 - Hospitalized children aged ≥ 16 years with COVID-19 who have an emergent or increasing need for supplemental oxygen regardless of whether they have risks factors for severe disease
- Dexamethasone for hospitalized children with COVID-19 is recommended for those who require high-flow oxygen, noninvasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation
- Convalescent plasma is recommended against for hospitalized children with COVID-19 who do not require mechanical ventilation, except in clinical trial
- Sarilumab is recommended against for hospitalized children with COVID-19 or MIS-C, except in clinical trial
- IVIg and/or corticosteroids are the first-line therapies for children with MIS-C
 - Interleukin-1 antagonist has been used for refractory cases



MEDICAL AGENTS

DIRECT ACTING ANTIVIRALS

REMEDESIVIR

- Remdesivir is the only FDA approved COVID treatment as of 10/26/2020
- Remdesivir shows promise for improved clinical outcomes in one compassionate-use cohort study. Study limitations: lack of control group, lack of uniformity of supportive care, small sample size (n=53).
- In a preliminary report of a multinational trial of >1000 patients of patients with COVID-19 and pulmonary involvement, remdesivir resulted in faster recovery time.
- Preliminary results from randomized control trial (ACTT-1, n = 1063) show 31% faster median recovery (11 vs 15 days) and improved mortality (8% vs 11.6%). Use is recommended in hospitalized patients requiring supplemental oxygen. Benefit is most evident in patients who were hypoxic but not intubated.
- The current dose regimen for remdesivir is an IV loading dose of 200mg on the first day of treatment, followed by IV maintenance doses of 100mg for 4 days. However, one study found that this would not achieve adequate plasma concentrations. It is suggested that a combination of IV and pulmonary delivery regimen may be more effective.
- A study comparing the efficacy of 5 days of remdesivir treatment vs. 10 days demonstrated no benefit in a longer treatment duration. Therefore, the current recommended dosing regimen is 5 days.
- Adverse events occur more commonly in ventilated patients. Most common adverse events: increased hepatic enzymes, diarrhea, rash, renal impairment, hypotension.
- On March 5, 2021, the COVID-19 Treatment Panel updated its recommendations on the use of remdesivir and dexamethasone in hospitalized patients requiring conventional oxygen therapy.
 - They recommend using one of the following options: remdesivir, dexamethasone + remdesivir, or dexamethasone alone

IVERMECTIN

- According to the COVID-19 Treatment Panel, There is insufficient evidence and more clinical trials are needed to understand the role of ivermectin in the treatment of COVID-19
- ivermectin has been shown to inhibit replication of the SARS-CoV-2 virus

NONSPECIFIC ANTI-INFLAMMATORIES

DEXAMETHASONE

- The RECOVERY trial (n=2104) has shown that dexamethasone reduces mortality in ventilated patients by one-third and in patients solely on oxygen by one-fifth.
 - 6 mg PO or IV QD dexamethasone was given to all patients (n=2104) for 10 days and compared to a randomized control group (n=4321) receiving usual care. The compared treatment arms were Lopinavir-Ritonavir, Hydroxychloroquine (discontinued), Azithromycin, Tocilizumab, and Convalescent plasma.
- Dexamethasone has not shown reduction in mortality of patients not using respiratory support
- Preliminary results of the RECOVERY trial have been released, but the study has not been published as of 6/18/2020.
- The primary short-term adverse effect of corticosteroids are hypoglycemia
- Adverse events associated with prolonged use include glaucoma, cataracts, fluid retention, hypertension, psychological effects, weight gain, or increased risk of infections and osteoporosis
- Dexamethasone has shown to be a moderate inducer of CYP3A4 and thus its use must be monitored for drug interactions
- According to the NIH recommendations released on April 21, 2021, dexamethasone is not recommended for outpatient management of COVID-19

METHYLPREDNISONE

- A Brazilian study evaluated the use of short-term methylprednisone as adjunct therapy for hospitalized patients, over the course of 28-days. (Prado Jeronimo, C.M. et al, 2020)
- Methylprednisone was given to one group (n=194), dosed for 5 days with twice-daily 0.5 mg/kg IV, and then compared to a randomized control group (n=199). Mortality was not different at day 28 between the two groups; however, mortality among patients over the age of 60 was decreased in the MP group.
- As a caution, insulin should be monitored in patients receiving MP.

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MEDICAL AGENTS CONTINUED

COLCHICINE

- A press release from the Montreal Heart Institute announced on Jan. 22, 2021 the preliminary results of a clinical trial using Colchicine to treat COVID-19. The results showed that Colchicine reduced the risk of death or hospitalizations by 21% compared to placebo. The colchicine was effective at preventing the cytokine storm.
 - The trial (n=4488) included people who had tested positive via naso-pharyngeal PCR, and randomly assigned them to colchicine or placebo cohorts. The colchicine was shown to reduce hospitalizations by 25%, the need for ventilation by 50%, and deaths by 44%.
 - This would be a good candidate for an oral treatment for non-hospitalized patients.
 - On April 21, 2021, the NIH panel recommends against the use of colchicine in hospitalized patients, except for clinical trial purposes. There is insufficient evidence to recommend either for or against use of colchicine in non-hospitalized COVID-19 patients.

FLUVOXAMINE

- An SSRI approved by FDA for treatment of Obsessive-Compulsive Disorder (OCD) and used for depression therapy
- Research has shown the anti-inflammatory effect of fluvoxamine in its ability to bind to the sigma-1 receptor in immune cells, resulting in decreased inflammatory cytokine production
- There is insufficient evidence to recommend either for or against use of fluvoxamine in COVID-19 treatment

MONOCLONAL ANTIBODIES

BAMLANIVUMAB+ ETESIVIMAB

- On February 23, 2021, Emergency Use Authorization was given for the use of Bamlanivimab 700 mg and Etesevimab 1,400 mg combo for outpatient treatment of patients with mild to moderate COVID-19 infection who are at high risk of progressing to severe disease and/or hospitalization
 - They recommend against the use of this combination treatment in hospitalized COVID-19 patients, with exceptions for those in clinical trial
- On March 2021, the Panel recommended AGAINST the use of Bamlanivimab monotherapy
- Bamlanivimab and etesevimab are not authorized for use in patients:
 - who are hospitalized due to COVID-19, OR
 - who require oxygen therapy due to COVID-19, OR
 - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Treatment with bamlanivimab and etesevimab has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation

REGEN-COV ANTIBODY COCKTAIL

- The REACH Trial (COVPN 3502/REGN 2069) is testing the ability to prevent the acquisition of SARS-COV-2 through the combination treatment of casirivimab and imdevimab antibody cocktail.
- This cocktail is designed to bind the SARS-COV-2 virus and prevent the virus from entering into healthy cells
- Study enrollment consists of ~3,500 adults and adolescents who share a household with a person who recently tested positive for COVID-19
- Preliminary results from Regeneron show decreased viral loads and decreased disease burden, measured by fewer weeks of viral shedding, fewer weeks of high viral load shedding, and fewer total symptomatic weeks.

KINASE INHIBITORS

BARICITINIB

- Baricitinib has received EUA approval for treatment of COVID-19 in patients 2 years of age or older as of 11/23/2020
- The ACTT-2 trial was published on Dec. 11, 2020, which showed that Baricitinib in combination with Remdesvir was more effective in reducing recovery time and accelerating recovery time than Remdesvir alone. The trial group (n=1033) compared using a 4-mg dose of Baricitinib in combination with Remdesvir, versus Remdesvir alone. Investigators found a 1-day reduction in median time overall in recovery. They defined recovery as either coming off supplemental oxygen or being discharged.
- Patients receiving combination therapy on high-flow oxygen or non-invasive ventilation at enrollment recovered faster (within 10 days versus 18 for control) and there were fewer serious adverse events and infections in the combo cohort. The 28-day mortality was 5.1% in the combination cohort and 7.8 in the control. Baricitinib received EUA for a 4-mg dose for COVID patients.

ADVANCED THERAPY MEDICINAL PRODUCTS (ATMP)

TOCILIZUMAB

- A study reviewing clinical trials in China and by the FDA suggest that Tocilizumab may be indicated in patients with cytokine release syndrome (CRS) and diffuse lung injury. The clinical trial found reduction in lung lesions, improvements in oxygen level and respiratory function, and reduction in fever to normal temperature.
 - Study limitations: small sample size (n = 14), all patients treated with methylprednisolone concomitantly
- A multicenter study (n = 63) in showed significant improvement in COVID patients with a pro-thrombotic, pro-inflammatory profile (classified as having 3 of the following: Ferritin >1000 ng/mL, CRP, D-Dimer 10x normal, LDH 2x normal). Administration of TCZ within 6 days of admission was associated with a higher chance of survival. (Sciascia et al. 05/26/2020)
 - TCZ was administered either IV (8 mg/kg) or SC (324 mg), with a 2nd dose in 52 out of 63 patients.
- Another retrospective study by the University of Maryland confirmed similar improvements in COVID patients with CRS due to Tocilizumab treatment combined with lopinavir, methylprednisolone, and oxygen therapy.
 - Both studies reviewed 1-hour infusion of tocilizumab up to 800 mg (max dosage) with some adverse effects including gastrointestinal perforations in patients with diverticulitis and concomitant high dosage corticosteroid use.
- Tocilizumab should not be used in pregnant patients and has not been found to be hepatotoxic or nephrotoxic thus far.
- According to COVID-19 treatment guidelines, patients who require ICU-level care are recommended against the use of tocilizumab or sarilumab for the treatment of COVID-19, except for clinical trials
- On February 2021, a New England Journal of Medicine paper revealed that the use of tocilizumab did not result in significantly better clinical status or lower mortality.
- On March 5, 2021, the COVID-19 Treatment Panel updated its recommendations on the use of tocilizumab:
 - They recommend the use of tocilizumab + dexamethasone in certain hospitalized COVID patients who are in rapid respiratory decompensation. These patients include:
 - ICU patients admitted within 24 hours and require respiratory support
 - Recently hospitalized patients (not ICU) with increasing oxygen requirements and have significantly increased markers of inflammation

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DIRECT ACTING AGENTS CONTINUED

CONVALESCENT PLASMA

- Convalescent plasma is FDA approved for use in clinical trials, patients with severe or immediately life-threatening laboratory confirmed COVID-19, and single patient emergency IND approval (FDA 5/1/2020)
- A study performed at Houston Methodist hospitals (n = 25) found that 36% of patients improved from baseline after 7 days and 76% improved after 14 days after 300 mL convalescent plasma obtained from 9 healthy donors who had recovered from COVID-19 was transfused (Salazar et al 5/27/2020)
 - Study limitations: n = 25, no control group, all patients were treated with HQ +azithromycin, 2 patients were treated with remdesvir, some with ribavarin, and some with tocilizumab and methylprednisone
 - Overall decrease in CRP and no increase in LFTs; 20 out of 25 patients were discharged, all but 2 patients on ventilation and ECMO were weaned off
 - Further study is needed to assess efficacy of convalescent plasma as a stand-alone treatment
 - No adverse effects related to transfusion were observed in the study
- Another randomized clinical trial from 7 medical centers in Wuhan, China compared a standard treatment group (n = 51) to a standard treatment plus convalescent plasma group (n=52)
 - 98.3% of patients in the experimental group with severe disease recovered within 28 days compared to the control group (68.2%)
 - There was no statistical difference for recovery within 28 days between the control and experimental group for patients with life-threatening disease
 - No statistically significant decrease in time to clinical improvement between the experimental and control groups

AGENTS NO LONGER RECOMMENDED FOR USE

HYDROXYCHLOROQUINE

IVERMECTIN

TENOFOVIR

BAMLANIVIMAB MONOTHERPAY

NIH RECOMMENDATIONS



VACCINE DEVELOPMENT

AUTHORIZED AND RECOMMENDED COVID-19 VACCINES

Vaccine*	Number of Doses	FDA Status	Efficacy	Age	Side Effects	Allergies
Pfizer Vaccine	2 shots 21 days apart	In use	95%	16+	Pain, swelling, redness at injection site, chills, tiredness, headaches, fever, chills	Polyethylene glycol
Moderna Vaccine	2 shots 28 days apart	In use	94.1%	18+	Pain, swelling, redness at injection site, chills, tiredness, headaches, fever	Polysorbate, Polyethylene glycol
Johnson & Johnson Vaccine	1 shot	In use	66.3%	18+	Rare blood clot in women younger than 50, Pain, swelling, redness at injection site, chills, tiredness, headaches, fever	Polysorbate

* all vaccines should not be given until 90 days after monoclonal antibody administration.

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VACCINE DEVELOPMENT

AUTHORIZED AND RECOMMENDED COVID-19 VACCINES

PFIZER VACCINE

- BioNTech, Pfizer, and Fosun Pharma have developed a two-dose mRNA vaccine that has recently expanded to testing the vaccine on children as young as 12 years old. They have also reported results stating that individuals who received the first dose experienced mostly mild to moderate side effects. On 12/11/2020, the FDA gave the Pfizer vaccine EUA in the United States. The vaccine is recommended for people aged 16 years and older. Side effects have been mild to moderate, and start within 1-2 after getting the vaccine, but should go away in a few days. Most common side effects reported include pain, swelling, and redness in the injection site and chills, tiredness, and headaches. Side effects such as fevers, chills, tiredness, and headaches are more common after the 2nd dose of the vaccine. The vaccine is reported by the NIH to be 95% effective in preventing symptomatic COVID-19. As of 4/1/21 an analysis performed on 927 symptomatic COVID-19 cases found the vaccine to be 91.3% effective against COVID-19 from seven days to six months after the second dose. New data suggests the vaccine is 87-89.5 percent effective at preventing disease with the B.1.1.7/UK variant and 72.1-75 percent effective at preventing disease with the B.1.135/South African variant in people that were at least two weeks past their second dose. Overall, the vaccine is 100 percent effective at preventing severe, critical, or fatal disease cause by the UK and South African variants.

MODERNA VACCINE

- Moderna has developed an mRNA-based vaccine that has progressed to Phase 3 testing. On 09/17/2020, Moderna shared their protocol for determining if their vaccine was safe and effective. It may take until early 2021 to evaluate this. On 11/16/2020, Moderna announced that preliminary data demonstrates that the vaccine is 94.5% effective. Data analysis also indicates that the vaccine may protect against severe disease. On 12/2/2020, Moderna registered a trial to test the vaccine on adolescents 12-18 years of age. On 12/18/2020, the FDA gave the Moderna vaccine EUA in the United States. The vaccine is recommended for people aged 18 years and older. People who are allergic to polyethylene glycol or polysorbate should not get this vaccine. Side effects have been mild to moderate and more common after the 2nd dose. Most common side effects reported include pain, swelling, and redness in the injection site, and chills, tiredness, and headaches. Based on clinical trials, the Moderna vaccine was 94.1% effective. A study performed by the CDC tracked front-line workers, first responders, and essential workers who had completed their second dose over 13 weeks found the vaccine to be 90% effective against protecting from COVID-19 in current conditions.

JOHNSON&JOHNSON VACCINE

- On February 27, 2021, the FDA announced the emergency use authorization (EUA) of the single-dose COVID-19 vaccine developed by Johnson&Johnson. The vaccine is recommended for people aged 18 years and older. The vaccine was 66.3% effective in clinical trials. People had most protection 2 weeks after getting the vaccine. This vaccine had high efficacy in preventing hospitalizations and death in people who did not get sick. This vaccine may provide protection against asymptomatic infection. The FDA and CDC have temporarily paused the use of Johnson&Johnson vaccines as of 4/13/21 due to a small percentage of women receiving the vaccine developing a severe and rare blood clot. The blood clot has been found in fifteen women and over 6.8 million doses of the vaccine have been given thus far. The blood clot occurred in women between the ages of 18 and 59. They reported that their symptoms began 6-15 days after vaccination. On 4/23/21 the CDC and FDA lifted the pause on Johnson&Johnson vaccines. Now, women under the age of 50 must be notified of the potential risk for blood clots and be made aware of other COVID-19 vaccines available.

For details and references please visit <https://oume.uthscsa.edu/longco/>

COVID-19 VACCINES IN PHASE 3 CLINICAL TRIALS

Vaccine	Number of Doses	FDA Status	Efficacy	Age	Side Effects	Allergies
Vaxzevria (AstraZeneca)	2 shots 4-12 weeks apart	Not in use	82%	18+	Vomiting, diarrhea, swelling, redness at the injection site and low levels of blood platelets occurred in less than 1 in 10 people.	Polysorbate
Novavax *	2 shots 1 month apart	Not in use	- *	18+	- *	- *

***Novavax is currently still being studied.**

VAXZEVRIA (ASTRAZENECA) VACCINE

- AstraZeneca and the University of Oxford have developed a vaccine called ChAdOx1. After halting global trials in September due to a volunteer who had developed transverse myelitis, the FDA authorized the restart of the trial on October 23. Analysis of the phase III US trials demonstrated a 76% efficacy against symptomatic COVID-19 after the first dose and 82% efficacy after the second. It has been 100% effective against development of severe COVID-19 symptoms and hospitalizations. In participants 65 and older, the vaccine has been found to be 85% effective. The AstraZeneca vaccine has been found to produce a rare form of blood clot in a small percentage of those vaccinated. As of 4/4/21 there were 222 cases out of the 34 million vaccinated with this formula in the European Union and United Kingdom. As of 4/14/2021 the Pharmacovigilance Risk Assessment Committee (PRAC) concluded that a causal relationship between vaccination with Vaxzevria and very rare cases of thrombosis together with thrombocytopenia, sometimes accompanied by bleeding, is plausible. Although rare, the cases of cerebral venous sinus thrombosis, splanchnic vein thrombosis and arterial thrombosis exceed what is observed in the general population. Most of these cases occurred 14 days after vaccination and mostly in women under 60 years of age. PRAC agreed that the product information for Vaxzevria should be updated with this assessment and specify thrombocytopenia as a new common side effect (occurring in less than 1 in 10 persons) and thrombosis in combination with thrombocytopenia as a new very rare side effect (occurring in less than 1 in 10,000 persons).

NOVAVAX VACCINE

- Novavax is a vaccine based on the genetic sequence of the SARS-CoV-2 and does not contain any live or inactivated virus. It was created using Novavax's nanoparticle technology and contains a patented adjuvant (Matrix-MTM) for immune boosting and neutralizing antibody stimulation, allowing a stronger immune response at a lower vaccine dose. In November 2020, they recently started Phase 3 trials in adults 18 years and older in the United States and Mexico. The trial has also been opened at UT Health Antonio, and study participants will be followed for 2 years. An analysis of the United Kingdom and South African trials showed the vaccine was effective in providing protection against variant strains. In the UK, the vaccine proved to be 96.4% effective against the original COVID-19 strain, 100% effective against the severe strain, and 86.3% against the UK variant. In South Africa, the vaccine in trial Phase 2b and has been found to be 100% protective against severe disease and 48.6% effective against the South African variant.

INTERNATIONAL COVID-19 VACCINE STUDIES

- The Murdoch Children's Research Institute is conducting a Phase 3 trial in Australia to see if the BCG vaccine partly protects against COVID-19.
- CanSinoBIO, the Gamaleya Research Institute, Bektov, Sinovac, Sinopharm, and the Wuhan Institute of Biological Products have developed vaccines that are approved for limited use in international countries. None are approved in the U.S. as of 5/31/2021.

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