

Monitoring International Trends

April 2020

The NBA monitors international developments that may influence the management of blood and blood products in Australia. Our focus is on:

- Potential new product developments and applications;
- Global regulatory and blood practice trends;
- Events that may have an impact on global supply, demand and pricing, such as changes in company structure, capacity, organisation and ownership; and
- Other emerging risks that could put financial or other pressures on the Australian sector.

In the period covered by this posting, the emphasis within the health sector worldwide has been on the COVID-19 pandemic. Clinical trials for non-related treatments have in many cases been paused, launches of recently approved drugs have been postponed, and the emphasis of research and product development in both the public and private sectors has been on COVID-19 testing, vaccine development and identification of potential therapies. Clinical discourse too has been extensively refocussed on how best to manage COVID-19 patients.

Selected items of interest are reported below.

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1. Clinical experience with COVID-19

We follow current issues in patient safety and achieving favourable patient outcomes.

Respiratory concerns

- The American Thoracic Society released guidance on treatment of the respiratory aspects of COVID-19¹.
- A US review² has suggested that secondary infections are common in hospitalized, severely ill COVID-19 patients, in up to 30 per cent of cases, with the highest frequency in the ICU setting. Severely ill patients are much more likely to have bacterial/fungal secondary infections than viral secondary infections.
- A retrospective case series³ found that one-third of patients hospitalized at the outset of the COVID-19 coronavirus outbreak in New York City required invasive mechanical ventilation, higher than that reported in China.
- Mechanical ventilation in COVID-19 patients has been a matter for discussion and debate amongst clinicians⁴.
- UK doctors reported that COVID-19 patients in the early phase of respiratory failure were presenting with problems with the vasculature of the lungs and microvascular thrombosis⁵.
- Clinicians have noted that COVID-19 patients may have severe hypoxaemia but the ability of their lungs to take in air is normal, which is different from patients who have acute respiratory distress syndrome⁶.
- Doctors have warned that normal chest X-rays don't necessarily rule out COVID-19⁷.
- The US Centers for Disease Control reported that COVID-19 symptoms of cough, fever, and shortness of breath are less common in children than adults. In patients younger than 18 years in the US, 73 per cent had at least one of those three symptoms, compared with 93 per cent of adults aged 18-64⁸.

¹ <https://www.thoracic.org/professionals/clinical-resources/disease-related-resources/covid-19-guidance.pdf>.

² <https://www.medpagetoday.com/infectiousdisease/covid19/86192?xid> and https://www.healio.com/pulmonology/practice-management/news/online/%7B7f22944d-bf5f-4de1-8cf5-27e9961af1f7%7D/coinfections-may-be-more-common-in-covid-19-than-previously-reported?utm_source

³ "Clinical Characteristics of COVID-19 in New York City", *NEJM*, 17 April 2020 <https://www.nejm.org/doi/full/10.1056/NEJMc2010419> and

<https://www.medpagetoday.com/infectiousdisease/covid19/86024?xid>
⁴ <https://www.medpagetoday.com/infectiousdisease/covid19/85909?xid> and <https://apnews.com/8ccd325c2be9bf454c2128dcb7bd616d> and

<https://www.medscape.com/viewarticle/928236?nliid>
⁵ https://thelimbic.com/haematology/microvascular-thrombosis-seen-in-early-phase-of-respiratory-failure-in-covid-19/?utm_source

⁶ https://www.medpagetoday.com/infectiousdisease/covid19/86046?xid=nl_mpt_DHE_2020-04-21&eun

⁷ <https://www.medscape.com/viewarticle/928946?nliid> and <https://www.medscape.com/viewarticle/928935?nliid>

⁸ <https://www.medscape.com/viewarticle/928305>

Cardiovascular concerns

- Some treatments being used in COVID-19 have prompted arrhythmia concerns⁹.
- Researchers report evidence of myocardial injury in COVID-19¹⁰.
- Some patients have developed a myriad of small blood clots, which doctors have tried treating with tissue plasminogen activator or with heparin¹¹.
- The [International Society on Thrombosis and Haemostasis recently recommended](#) that all hospitalized COVID-19 patients should be given prophylactic-dose low molecular weight heparin, unless they have contraindications (active bleeding and platelet count <25×10⁹/L). [Recommendations from Britain](#) also called for use of low molecular weight heparin in high risk patients¹².
- Cardiologists from the American Heart Association, the Heart Failure Society of America, and the American College of Cardiology, in a [joint statement](#), advised patients taking ACE inhibitors¹³ and ARBs¹⁴ who contract COVID-19 to continue treatment unless otherwise advised by their physician. The [European Society of Cardiology](#) agreed. Suddenly discontinuing these could result in heart failure and [uncontrolled hypertension](#)¹⁵.

Gastroenterology

- Results from two studies published in *Gastroenterology* discussed manifested gastrointestinal symptoms and possible faecal-oral transmission in patients with COVID-19¹⁶.
- A US study¹⁷ compared the rates of gastrointestinal symptoms between 278 patients who tested positive for COVID-19, and 238 patients who tested negative for the virus. Significantly more patients who tested positive (61 per cent) than who tested negative (39 per cent) had gastrointestinal symptoms such as diarrhoea, nausea, and vomiting. In a multivariable model, the presence of gastrointestinal symptoms was associated with 70 per cent greater odds of testing positive.
- A study¹⁸ in China found that diarrhoea [may be the first or only symptom some COVID-19 patients experience](#).

⁹ https://www.healio.com/cardiology/arrhythmia-disorders/news/online/%7B7cbafb2c-e397-4ec7-8caa-40cfd20fbf3%7D/some-covid-19-treatments-prompt-arrhythmia-concerns-management-strategy-needed?utm_source

¹⁰ <https://www.medscape.com/viewarticle/928863?nlid> and Nianguo Dong, et al., “End-stage Heart Failure with COVID-19: Strong Evidence of Myocardial Injury by 2019-nCoV”, *JACC Heart Failure*, 7 April 2020. <http://heartfailure.onlinejacc.org/content/early/2020/04/07/j.chf.2020.04.001> and <https://www.medpagetoday.com/infectiousdisease/covid19/86031?xid>

¹¹ <https://www.statnews.com/2020/04/16/blood-clots-coronavirus-tpa/> and https://www.medscape.com/viewarticle/928653?nlid=135065_1842&src and https://thelimbic.com/haematology/caution-on-off-label-doac-use-in-lv-thrombus/?utm_source

¹² https://www.medpagetoday.com/infectiousdisease/covid19/85865?utm_source

¹³ angiotensin-converting enzyme inhibitors

¹⁴ angiotensin-receptor blockers

¹⁵ <https://www.medscape.com/viewarticle/928099?nlid>

¹⁶ [Xiao F, et al. *Gastroenterology*. 2020;doi:10.1053/j.gastro.2020.02.055.](#)

[Gu J, et al. *Gastroenterology*. 2020;doi:10.1053/j.gastro.2020.02.054.](#)

¹⁷ Gastrointestinal Symptoms and COVID-19: Case-Control Study from the United States
Yael R. Nobel, et al., “Gastrointestinal Symptoms and COVID-19: Case-Control Study from the United States”, *Gastroenterology* (2020), doi: <https://doi.org/10.1053/j.gastro.2020.04.017>.

¹⁸ Chaoqun Han, Brennan Spiegel, et al, “Digestive Symptoms in COVID-19 Patients with Mild Disease Severity: Clinical Presentation, Stool Viral RNA Testing, and Outcomes”
https://journals.lww.com/ajg/Documents/COVID19_Han_et_al_AJG_Preproof.pdf

Neurological symptoms

- Dr Camille Vaughan, section chief of geriatrics and gerontology at Emory University, reported that seniors with COVID-19 might appear apathetic or confused, disoriented and dizzy. They may stop speaking, they may fall or collapse. Dr Sam Torbati, of Cedars-Sinai Medical Center, has described treating seniors who appear weak and dehydrated, or who appear to have had strokes, but who when tested are found to be exhibiting the effect of COVID-19 on their central nervous system.
- One estimate suggested that 40 per cent of people with COVID-19 have neurological symptoms¹⁹.

The cytokine storm

- For severely ill patients, a common pathology appears to be an explosion of the immune response, of the sort observed in sepsis, known as cytokine release syndrome or cytokine storm. A Chinese pilot study used intravenous infusions of donor mesenchymal stem cells (MSCs) and this treatment has been approved in the US by the FDA for the sickest patients. The use of MSCs does not have universal support. Both China and the US have approved the use in severe COVID-19 of the monoclonal antibody tocilizumab, already in trials for dealing with cytokine storms²⁰.

Suggested disease modifying factors²¹

- French research suggested nicotine may offer some protection against COVID-19 infection²², although researchers warned that smokers who became infected with coronavirus would develop more severe respiratory symptoms than non-smokers.
- Research suggests that cancer patients are at greater risk of severe disease and death, especially those with lung and blood cancers or those with late-stage cancer²³. The American Society of Haematology (ASH) Research Collaborative has launched an international registry of patients who test positive for COVID-19 and have been or are currently being treated for a haematologic malignancy²⁴.
- An international panel published recommendations for managing diabetes in COVID-19 patients²⁵.

¹⁹ https://www.upi.com/Health_News/2020/04/10/40-of-people-with-severe-COVID-19-experience-neurological-complications/2491586526495 and <https://www.medscape.com/viewarticle/928848?nlid> and Ling Mao et al., "Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China", *JAMA Neurology*. 10 April 2020. doi:10.1001/jamaneurol.2020.1127

²⁰ https://www.the-scientist.com/news-opinion/are-mesenchymal-stem-cells-a-promising-treatment-for-covid-19--67402?utm_campaign

²¹ https://www.healio.com/endocrinology/diabetes/news/online/%7B5632bfd5-7a25-4c1d-b532-356f7d71150d%7D/pneumonia-uncontrolled-inflammation-more-common-in-covid-19-with-diabetes?utm_source and https://www.healio.com/infectious-disease/practice-management/news/online/%7B0f7f3dd3-0a60-4141-b260-026d617a7dd5%7D/lsquounmasking-covid-19rsquo-healio-launches-new-podcast-for-front-line-clinicians?utm_source

²² Jean-Pierre Changeux et al., "A nicotinic hypothesis for COVID-19 with preventive and therapeutic implications", *Qeios*, 22 April 2020. <https://doi.org/10.32388/FXGQSB.2>

²³ <https://www.medpagetoday.com/meetingcoverage/aacr/86201?xid>

²⁴ https://thelimbic.com/haematology/covid-19-registry-set-up-for-haematologic-malignancies-prof-jeff-szer/?utm_source

²⁵ Stefan R Bornstein et al., "Practical recommendations for management of diabetes in patients with COVID-19", *The Lancet: Diabetes and Endocrinology*, 23 April [https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(20\)30152-2/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30152-2/fulltext) and <https://www.medscape.com/viewarticle/929558?nlid> and <https://www.healio.com/endocrinology/diabetes/news/online/%7B5632bfd5-7a25-4c1d-b532->

- Patients being treated for chronic pain may be particularly susceptible to COVID-19 and may face different consequences from others²⁶.
- At 2 April, 1.7 per cent of confirmed US cases were in children, with testing low²⁷.

Alert over multi-system hyperinflammatory state in paediatric patients

- NHS England raised an alert about a number of cases in children who were admitted to ICU in “a multi-system inflammatory state with overlapping features of [toxic shock syndrome](#) and atypical [Kawasaki disease](#), with blood parameters consistent with severe COVID-19. The symptoms have been seen in children who test positive for the virus, and those with negative tests. Abdominal pain and gastrointestinal symptoms have been a common feature as has cardiac inflammation.”²⁸

Other issues in clinical management

- The American Academy of Pediatrics has recommended temporarily separating newborns from mothers with COVID-19²⁹.
- Discussion continues on how best to manage severely ill patients with diabetes and coronavirus infections³⁰.
- There is evidence of association between rheumatologic conditions and Covid-19.³¹
- A study³² found cotton and surgical masks did not prevent COVID-19 spread.
- Acute kidney injury has been found in some ICU patients with COVID-19, creating resource issues as well as health challenges³³.
- Scientists are studying whether a patient’s genes determine how seriously ill they will become with COVID-19³⁴. Researchers from Monash University’s Central Clinical School and Alfred Health in Melbourne are working on a test they say will be able to predict the severity of symptoms in COVID-19 patients, telling them how hard the virus will hit them after they contract it and what their immunity will be when they recover³⁵.

[356f7d71150d%7D/pneumonia-uncontrolled-inflammation-more-common-in-covid-19-with-diabetes?utm_source](#) and <https://news.yahoo.com/covid-19-study-shows-more-120100977.html> and https://www.medscape.com/viewarticle/928962?nlid=135154_5404&src

²⁶ https://www.medpagetoday.com/clinical-challenges/pain-management/85857?utm_source and <https://www.asra.com/page/2903/recommendations-on-chronic-pain-practice-during-the-covid-19-pandemic>

²⁷ https://www.healio.com/pediatrics/emerging-diseases/news/online/%7B4d3d680d-33d4-4c4e-b5cf-5c22c8509947%7D/in-us-17-of-covid-19-cases-occur-in-children?utm_source

²⁸ <https://www.medscape.com/viewarticle/929415?nlid>

²⁹ Puopolo KM, et al. Initial guidance: Management of infants born to mothers with COVID-19. <https://downloads.aap.org/AAP/PDF/COVID%2019%20Initial%20Newborn%20Guidance.pdf>

³⁰ https://www.healio.com/endocrinology/diabetes/news/online/%7B4d9e4140-af42-46ab-98ac-fb164875ad15%7D/insufficient-evidence-to-recommend-dpp-iv-inhibitor-treatment-in-type-2-diabetes-with-covid-19?utm_source

³¹ https://www.healio.com/rheumatology/infection/news/online/%7B6d42e6d4-a65f-449b-8227-235beacc7e54%7D/rheumatologists-move-front-and-center-in-fight-against-covid-19?utm_source

³² https://www.healio.com/primary-care/practice-management/news/online/%7B10c2a1dc-3f55-401d-bf11-5246153357ff%7D/small-study-questions-efficacy-of-cotton-surgical-masks-at-stopping-spread-of-sars-cov-2?utm_source

³³ <https://www.medscape.com/viewarticle/929073?nlid> and <https://www.medscape.com/viewarticle/928929?nlid>

³⁴ https://www.the-scientist.com/news-opinion/dna-could-hold-clues-to-varying-severity-of-covid-19-67435?utm_campaign

³⁵ <https://www.abc.net.au/news/2020-04-08/scientists-developing-test-for-coronavirus-severity-in-patients/12124402>

- Research from the University of Hong Kong found that the coronavirus can remain on the outer layer of a face mask for a week³⁶.
- Researchers reported possible vertical transmission of COVID-19³⁷.

Issues in testing

- On 25 January 2020, the Wuhan Blood Centre began screening for severe acute respiratory syndrome coronavirus 2 RNA in real-time and retrospectively and found plasma samples positive for viral RNA from 4 asymptomatic donors³⁸.
- Researchers have raised issues over the proportion of COVID-19 tests giving a false negative result³⁹.
- Patients may continue to shed the SARS-CoV-2 virus for up to six weeks after symptoms emerge, a small study⁴⁰ of recovered COVID-19 patients suggests. Dr. Sheng Zhang of Huazhong University of Science and Technology in Wuhan wrote: "In the convalescence period, a trace of virus may still be detected. However, as with other virus infections, this is not indicative of the transmission ability of the infected individual."
- A study⁴¹ in Zhejiang, China, found the coronavirus is able to linger in COVID-19 patients' stools longer than their respiratory system. The research team found the RNA, or the genetic material, of the virus in the stool samples of 55 out of 96 patients, and the blood serum of 39. One urine sample tested positive for the coronavirus. The virus could be detected in stool samples for an average of 22 days, in respiratory samples for an average of 18 days, and 16 days for serum. For patients classified as severely ill, the virus was detectable for 21 days on average, in mild patients for an average of 14 days.
- The World Health Organization (WHO) said it was investigating reports of individuals who appeared to have recovered from COVID-19, and who tested negative for COVID-19 using PCR (polymerase chain reaction) testing, who then after some days tested positive again⁴².
- A number of serological tests have been developed to test for COVID-19 antibodies⁴³, though some vendors are careful to emphasise that the detection of

³⁶ <https://www.9news.com.au/world/coronavirus-covid19-sticks-to-face-mask-for-week-hong-kong-university-study-says/49c9ef0b-38a5-4313-8630-3397568b47b2>

³⁷ <https://www.healio.com/pediatrics/neonatal-medicine/news/online/%7Bf0bfd06b-f08c-41d9-a4a4-b076ea340d72%7D/researchers-report-possible-vertical-transmission-of-sars-cov-2-in-china>

³⁸ https://wwwnc.cdc.gov/eid/article/26/7/20-0839_article?deliveryName=USCDC_333-DM25050&fbclid

³⁹ https://www.medpagetoday.com/infectiousdisease/covid19/86047?xid=nl_mpt_DHE_2020-04-21&eun=g465425d0r&utm_source

⁴⁰ <https://bit.ly/358QIJc> *Clinical Infectious Diseases*, online April 19, 2020; and <https://www.medscape.com/viewarticle/929519?nlid>; see also Sheng Zhang et al., "Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: A descriptive study" in *Journal of Clinical Virology*, online 11 April 2020, <https://doi.org/10.1016/j.jcv.2020.104346> and <https://www.sciencedirect.com/science/article/pii/S1386653220300883>

⁴¹ Shufa Zheng et al., "Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study", *BMJ* 2020; 369 doi: <https://doi.org/10.1136/bmj.m1443> (Published 21 April 2020) see also https://www.healio.com/pulmonology/practice-management/news/online/%7B071c6a27-2c50-458f-9558-19b9f501df05%7D/patients-with-covid-19-may-shed-virus-after-symptom-resolution?utm_source

⁴² <https://www.medscape.com/viewarticle/928567?nlid> and <https://www.medscape.com/viewarticle/928749>

⁴³ https://www.fiercebiotech.com/medtech/quest-labcorp-launch-nationwide-covid-19-antibody-testing-pharmacies-and-online?mkt_tok and <https://homelandprepnews.com/stories/47422-barda-diasorin->

antibodies does not confirm immunity, and the tests have been of varying quality. In the US, the FDA at first adopted a relaxed attitude to marketing of these tests, until Congress urged a more rigorous stance⁴⁴.

- In the US, Quest Diagnostics launched [the first consumer-ordered test](#) for antibodies. The price is around \$US 120. The [U.S. Food and Drug Administration](#) says it does not yet know if antibodies protect from reinfection, and if so for how long. This launch occurred a week after Quest [announced the launch](#) of its COVID-19 antibody test service for healthcare providers to order on behalf of patients: a market where there are multiple providers.
- The FDA approved an oral fluid test developed by Curative Medical⁴⁵.
- The WHO said it is not sure if the presence of antibodies to COVID-19 in the blood gives full protection against reinfection⁴⁶.
- The US National Institutes of Health on 29 April announced an initiative to speed innovation, development and commercialization of COVID-19 testing technologies⁴⁷.
- The Infectious Diseases Society of America announced it believed the term “asymptomatic” in COVID-19 should be replaced with “presymptomatic”, as some people develop symptoms later and transmit the virus before then⁴⁸.
- Researchers have described a method for using CRISPR to quickly spot the coronavirus in samples from nose or throat swabs⁴⁹.
- Sanofi began working with Luminostics to build an at-home test which would use a sample reader powered by a personal smartphone⁵⁰.
- While the WHO recommended self-isolation for fourteen days after symptoms have resolved, The UK government said people who develop symptoms of COVID-19 need isolate for only seven days⁵¹.
- Researchers identified three distinct strains of COVID-19 globally, with two of them in Australia including one closest to the “root of the outbreak”⁵².
- Swiss researchers have developed a way of detecting the virus that causes COVID-19 as it floats through the air⁵³.

[enter-public-private-partnership-to-create-fully-automated-serology-test-for-sars-cov-2/](#) and <https://www.roche.com/media/releases/med-cor-2020-04-17.htm> and <http://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html>

⁴⁴ <https://www.fiercebiotech.com/medtech/congress-urges-fda-to-better-police-evaluate-covid-19-antibody-tests> and https://www.fiercebiotech.com/medtech/fda-cdc-nih-to-begin-validating-covid-19-antibody-tests-as-more-enter-market?mkt_tok and https://www.fiercebiotech.com/medtech/current-covid-19-antibody-tests-aren-t-accurate-enough-for-mass-screening-say-oxford?mkt_tok

⁴⁵ https://www.fiercebiotech.com/medtech/fda-greenlights-oral-fluid-test-for-covid-19?mkt_tok

⁴⁶ https://www.medscape.com/viewarticle/928910?nlid=135154_5404&src and <https://www.usatoday.com/story/news/health/2020/04/19/coronavirus-herd-immunity-vaccines-determine-covid-second-wave/5151957002/>

⁴⁷ <https://www.nih.gov/news-events/news-releases/nih-mobilizes-national-innovation-initiative-covid-19-diagnostics>

⁴⁸ <https://www.mdedge.com/familymedicine/article/220702/coronavirus-updates/presymptomatic-or-asymptomatic-id-experts-shifting>

⁴⁹ <https://www.statnews.com/2020/04/16/coronavirus-test-crispr-mammoth-biosciences/>

⁵⁰ https://www.fiercebiotech.com/medtech/sanofi-taps-luminostics-to-develop-a-smartphone-based-covid-19-test?mkt_tok

⁵¹ <https://www.bmj.com/content/369/bmj.m1574?>

⁵² <https://www.news.com.au/world/coronavirus/australia/coronavirus-australia-three-different-strains-of-virus-identified-by-cambridge-university-researchers/news-story/e6fbac027ba79e83aa1df80517>

⁵³ https://www.fiercebiotech.com/medtech/swiss-researchers-develop-methods-to-sniff-out-coronavirus-air?mkt_tok

- COVID-19 has been identified in members of the cat family – domestic cats, tigers⁵⁴ in reserves and zoos. It is so far presumed to have been transmitted from humans.

2. Developing vaccines for COVID-19

- Johnson and Johnson towards the end of April signed a deal with Emergent BioSolutions to boost manufacturing of a COVID-19 vaccine candidate which it will move into phase I trials in September⁵⁵. The company signed a \$US 1 billion deal with the US Biomedical Advanced Research and Development Authority (BARDA).
- Pfizer's CEO [told The Wall Street Journal](#) that the company could be ready for emergency vaccine distribution in the northern hemisphere autumn, and be prepared for a large-scale rollout by the end of this calendar year⁵⁶. It is also collaborating with BioNTech on a vaccine based on messenger RNA technology. Pfizer will pay BioNTech \$US185 million upfront to develop the vaccine, with additional payments if certain milestones are achieved⁵⁷.
- CEPI (Coalition for Epidemic Preparedness Innovation) in January 2020 [engaged CSIRO](#) to work on the virus which causes COVID-19. Its early tasks included pre-clinical trials of vaccine candidates from [The University of Oxford](#) and [Inovio Pharmaceuticals Inc.](#)
- Oxford University's Jenner Institute in conjunction with Oxford Vaccine Group is initiating a 6,000-participant vaccine trial. It is working with drug manufacturers in Europe and Asia to have up to 1 billion doses available quickly if the vaccine is approved.
- Inovio announced on 6 April that the FDA had accepted its Investigational New Drug application for its DNA vaccine candidate INO-4800 to enter Phase I clinical testing, and dosing human patients was to begin that day. The company said preclinical data had shown promising immune response results across multiple animal models⁵⁸.
- The University of Queensland's COVID-19 vaccine has shown in pre-clinical (laboratory) tests it can produce high levels of antibodies that can neutralise the virus. This vaccine's development is being funded by CEPI (Coalition for Epidemic Preparedness Innovation), the federal and Queensland governments and philanthropic donors.
- In the US, scientists funded by the National Institutes of Health (NIH) working on the SARS-CoV-2 virus [produced a detailed picture of the part of the virus](#), called the spike protein, that allows it to infect human cells. Then scientists⁵⁹ with experience in trying to develop vaccines for other coronaviruses adapted the system they already had⁶⁰ to produce quickly an experimental vaccine using the SARS-CoV-2 spike

⁵⁴ <https://www.freepressjournal.in/bhopal/madhya-pradesh-pench-forest-staff-qurantined-after-death-of-corona-positive-tiger-is-fit-now>

⁵⁵ https://www.fiercepharma.com/manufacturing/johnson-johnson-sets-stage-for-covid-19-vaccine-rollout-emergent-manufacturing-tie-up?mkt_tok

⁵⁶ See also <https://pipelinereview.com/index.php/2020041074294/Vaccines/Pfizer-and-BioNTech-Announce-Further-Details-on-Collaboration-to-Accelerate-Global-COVID-19-Vaccine-Development.html> and https://www.fiercebiotech.com/biotech/pfizer-biontech-pfizer-finish-dosing-covid-19-vax-test-emergency-use-could-start-fall?mkt_tok

⁵⁷ [22UAY.F](#) and https://www.fiercebiotech.com/biotech/pfizer-finds-covid-19-drug-candidate-plots-summer-testing?mkt_tok

⁵⁸ <https://pipelinereview.com/index.php/2020040674247/Vaccines/INOVIIO-Initiates-Phase-1-Clinical-Trial-Of-Its-COVID-19-Vaccine-and-Plans-First-Dose-Today.html>

⁵⁹ Led by Dr Louis Faló, Jr. and Dr Andrea Gambotto from the University of Pittsburgh

⁶⁰ designed to produce a MERS vaccine

protein.⁶¹ The vaccine was delivered to mice through a microneedle patch and resulted in robust antibody production within a fortnight. The longevity of the immune response, and the reaction of the mice to a SARS-CoV-2 challenge are the next challenge. The researchers say the vaccine could be made quickly and at large scale, and that it doesn't require refrigeration. They have begun the process of seeking FDA approval for a Phase I trial within the next few months, with clinical trials in humans to follow.

- Moderna expects to begin its Phase II trial of its mRNA vaccine before mid-year. It will evaluate the safety, reactogenicity and immunogenicity of two vaccinations of mRNA-1273 given four weeks apart. In the US, BARDA is committing up to \$US 483 million to fund late-stage clinical trials and scale up manufacturing for Moderna's COVID-19 vaccine candidate.
- In the US, the Trump administration wants to speed up vaccine development through collaboration between biotech interests, pharmaceutical companies and federal agencies, with the national government taking on financial risks⁶².
- US health agencies including the FDA and the National Institutes of Health, the European Medicines Agency, and 16 pharmaceutical manufacturers⁶³ will collaborate on vaccine and drug development efforts to fight the pandemic. The partnership will be known as ACTIV (the Accelerating COVID-19 Therapeutic Interventions and Vaccines). It will co-ordinate regulatory decisions, prioritize developments and provide funding to expedite clinical trials⁶⁴.
- The UK government has established a pandemic vaccine task force⁶⁵.
- China's National Medical Products Administration has allowed two inactivated COVID-19 vaccines to begin human trials. They are made by Sinovac and state-owned Sinopharm's Wuhan Institute of Biological Products. CanSino Bio has advanced a COVID-19 vaccine into phase II testing, based on the preliminary safety data of the phase I clinical trial.
- Germany's CureVac and BioNTech, which are to trial an mRNA vaccine in humans, have called for global drug regulators to "abbreviate" the regulatory path during the pandemic.
- Other companies and partnerships hoping to make a vaccine available include:
 - I. Dynavax and Sinovac⁶⁶
 - II. Novavax, planning a human Phase I clinical trial for NVX-CoV2372 from mid-May with preliminary results in July⁶⁷
 - III. Sanofi and GSK, proposing a recombinant DNA vaccine, to enter clinical testing before the end of 2020⁶⁸
 - IV. Sanofi and Translate Bio working on a new mRNA vaccine for COVID-19

⁶¹ Eun Kim et al., "Microneedle array delivered recombinant coronavirus vaccines: Immunogenicity and rapid translational development", *EBio Medicine*. 2 April 2020. DOI: <https://doi.org/10.1016/j.ebiom.2020.102743>

⁶² <https://www.bloomberg.com/news/articles/2020-04-29/trump-s-operation-warp-speed-aims-to-rush-coronavirus-vaccine>

⁶³ Including Pfizer Inc, Johnson & Johnson and GlaxoSmithKline Plc.

⁶⁴ <https://bit.ly/34HYTfk>. See also <https://www.nih.gov/news-events/news-releases/nih-launch-public-private-partnership-speed-covid-19-vaccine-treatment-options> and <https://www.biopharmadive.com/news/coronavirus-nih-drugmakers-fda-partnership/576283/>

⁶⁵ https://www.fiercebiotech.com/biotech/british-government-enlists-astrazeneca-bia-for-new-pandemic-vaccine-taskforce?mkt_tok

⁶⁶ <https://www.bloomberg.com/press-releases/2020-04-16/dynavax-technologies-corporation-dynavax-and-sinovac-announce-collaboration-to-develop-a-coronavirus-covid-19-vaccine>

⁶⁷ <https://pipelinereview.com/index.php/2020040874282/Vaccines/Novavax-Identifies-Coronavirus-Vaccine-Candidate-Accelerates-Initiation-of-First-in-Human-Trial-to-Mid-May.html>

⁶⁸ <https://www.cnbc.com/2020/04/17/if-sanofis-coronavirus-vaccine-works-ceo-says-it-can-produce-up-to-600-million-doses-next-year.html>

- V. VBI Vaccines and the National Research Council of Canada, aiming for a pan-coronavirus vaccine candidate targeting COVID-19, SARS and MERS.
 - VI. OncoSec Medical and Providence Cancer Institute, with a first-in-human Phase I clinical trial of OncoSec's novel DNA-encodable, investigational vaccine, CORVax12⁶⁹
 - VII. Akers Biosciences and Premas Biotech⁷⁰
 - VIII. GSK and Vir Biotechnology⁷¹
 - IX. EpiVax and GAIA Vaccine Foundation⁷²
 - X. Immunomic Therapeutics, collaborating with EpiVax and Pharmajet⁷³
 - XI. ERC⁷⁴
 - XII. Arcturus⁷⁵
 - XIII. HaloVax⁷⁶
 - XIV. Genex, Vaxart, Imperial College(London), Medicago , Altimune are working on individual vaccine projects while Takis Biotech(Italy) is working with Applied DNA Sciences (US)⁷⁷
 - XV. Axon Neuroscience is developing a peptide vaccine⁷⁸
- Scientists showed⁷⁹ that a vaccine based on the parainfluenza virus 5 believed to cause the canine respiratory disease could be useful against COVID-19 after the drug protected all trial mice from the MERS virus.
 - An investigational vaccine called ChAdOx1 MERS protected two groups of rhesus macaques from disease caused by Middle East respiratory syndrome coronavirus (MERS-CoV). NIH scientists and colleagues are pursuing similar studies with ChAdOx1 SARS2, a vaccine candidate against SARS-CoV-2⁸⁰.
 - Several groups are tracking clinical trials of both vaccines and therapeutics for COVID-19, including the [Milken Institute COVID-19 tracker](#), the [Oxford Trials Tracker on COVID-19](#), and the Centre for Evidence-Based Medicine ([CEBM COVID-19 Registered Trials Tracker](#)). For treatment only websites, see below.

⁶⁹ <https://pipelinereview.com/index.php/2020040674249/Vaccines/OncoSec-Collaborates-with-Providence-Cancer-Institute-to-Conduct-First-in-Human-Trial-of-OncoSecs-CORVax12-an-Investigational-Vaccine-to-Prevent-COVID-19-Combining-an-Enhanced-S.html>

⁷⁰ <https://pipelinereview.com/index.php/2020040674251/Vaccines/Akers-Biosciences-and-Premas-Biotech-Announce-Progress-in-its-Vaccine-Development-for-Covid-19.html>

⁷¹ <https://pipelinereview.com/index.php/2020040674252/Vaccines/GSK-and-Vir-Biotechnology-enter-collaboration-to-find-coronavirus-solutions.html>

⁷² <https://pipelinereview.com/index.php/2020040874272/Vaccines/EpiVax-Partners-with-GAIA-Vaccine-Foundation-to-Make-COVID-19-Vaccine-License-Free-to-Developing-Countries.html>

⁷³ <https://pipelinereview.com/index.php/2020041074292/Vaccines/Immunomic-Therapeutics-Forms-Collaboration-with-EpiVax-and-PharmaJet-to-Develop-Novel-Vaccine-Candidate-Against-COVID-19-Using-Its-Investigational-UNITE-Platform.html>

⁷⁴ <https://pipelinereview.com/index.php/2020041074304/Vaccines/ERC-Launches-Development-Program-for-Novel-Cell-Based-Therapeutic-and-Prophylactic-SARS-CoV-2-Vaccine.html>

⁷⁵ <https://pipelinereview.com/index.php/2020041074305/Vaccines/Arcturus-Therapeutics-Announces-Clinical-Trial-Timeline-for-its-COVID-19-Vaccine.html>

⁷⁶ https://www.fiercebiotech.com/research/researchers-harness-new-technology-for-rapid-covid-19-vaccine-development?mkt_tok Also details partnership between scientists at Flinders University, with Oracle and Vaxine; plus Amgen teaming with Adaptive Technologies.

⁷⁷ https://www.the-scientist.com/news-opinion/covid-19-vaccine-frontrunners-67382?utm_campaign

⁷⁸ <https://pipelinereview.com/index.php/2020041074298/Small-Molecules/Axon-Neuroscience-Has-a-Promising-Peptide-Vaccine-Against-COVID-19-in-Development.html>

⁷⁹ Kun Li et al, "Single-Dose, Intranasal Immunization with Recombinant Parainfluenza Virus 5 Expressing Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Spike Protein Protects Mice from Fatal MERS-CoV Infection", *mBio*, DOI: 10.1128/mBio.00554-20

⁸⁰ <https://www.nih.gov/news-events/news-releases/investigational-chimp-adenovirus-mers-cov-vaccine-protects-monkeys>

3. Potential treatments for COVID-19

On 1 April, Cytel had launched an open-access global [COVID-19 Clinical Trial Tracker](#) to help facilitate collaboration. At 4 April, Medscape listed almost 60 randomized control trials of COVID-19 treatments which were planned, recruiting or in progress⁸¹.

Recovered plasma, hyperimmune immunoglobulin, antibodies

- On 25 March, the US Food and Drug Administration (FDA) said it is allowing access to COVID-19 convalescent plasma for use in serious COVID-19 patients through the pathway of emergency investigational new drug applications (eINDs) for individual patients⁸². The FDA and European Commission released guidance on convalescent plasma collected from patients who have recovered from COVID-19 and which may potentially be used as a treatment for COVID-19⁸³.
- On 26 March Emergent BioSolutions⁸⁴ said it was exploring plasma-based treatments.
- On 30 March GigaGen announced⁸⁵ it was working on recombinant anti-coronavirus 19 hyperimmune gammaglobulin, made from the plasma of recovered patients.
- Kamada will [collaborate](#) with Kedrion Biopharma⁸⁶ on the development, manufacture and distribution of a polyclonal immunoglobulin product for the potential treatment of COVID-19. The plasma-derived anti-SARS-CoV-2 IgG product will be based on Kamada's proprietary immunoglobulin platform technology. Kedrion will collect the plasma from donors who have recovered from the virus. It will be responsible for commercialization in Australia, the US, Europe, and South Korea. Kamada will be responsible for product development, manufacturing, clinical development (with Kedrion support) and regulatory submissions. It will be responsible for commercialization in all ex-Kedrion territories other than China which will be shared.
- On 6 April, Biotest, BPL, LFB and Octapharma announced they had formed an alliance formed by CSL Behring and Takeda⁸⁷ to develop a plasma-derived therapy for COVID-19⁸⁸.
- On 29 April Montefiore Health System, Albert Einstein College of Medicine and NYU Langone announced a clinical trial of convalescent plasma in COVID-19 patients⁸⁹. The randomized trial will involve 300 patients who have had respiratory symptoms for less than a week, and who require some supplemental oxygen or who have been hospitalized for fewer than four days. Half will receive plasma containing anti-SARS-CoV-2 antibodies and half will receive a placebo.

⁸¹ <https://www.medscape.com/viewarticle/928094?nlid>

⁸² <https://www.fiercebiotech.com/medtech/fda-to-allow-covid-19-treatments-blood-from-survivors> and <https://www.prnewswire.com/news-releases/fda-approves-first-plasma-therapy-for-houston-methodist-covid-19-patient-301031772.html>

⁸³ <https://www.raps.org/news-and-articles/news-articles/2020/4/fda-ec-offer-guidance-on-covid-19-convalescent-pla> and [FDA Guidance: Investigational COVID-19 Convalescent Plasma](#) and [EC Guidance on the collection and transfusion of convalescent COVID-19 plasma](#) and

<https://www.fiercebiotech.com/biotech/plasma-therapy-trial-delays-u-k-extremely-disappointing>

⁸⁴ <https://techcrunch.com/2020/03/25/how-one-company-is-fast-tracking-development-of-potential-plasma-based-treatments-for-the-coronavirus/>

⁸⁵ <https://www.fiercebiotech.com/biotech/gigagen-jumps-into-covid-19-arena-polyclonal-antibodies>

⁸⁶ <https://pipelinereview.com/index.php/2020040774268/Antibodies/Italian-Biotech-Leader-Hopes-to-Be-Ready-With-Plasma-based-Treatment-for-COVID-19-by-Late-Summer-of-2020.html>

⁸⁷ <https://www.fiercebiotech.com/biotech/takeda-csl-led-plasma-players-band-together-covid-19>

⁸⁸ <https://pipelinereview.com/index.php/2020040674244/Antibodies/Global-Plasma-Leaders-Collaborate-to-Accelerate-Development-of-Potential-COVID-19-Hyperimmune-Therapy.html>

⁸⁹ <https://seekingalpha.com/pr/17852923-clinical-trial-begins-to-see-convalescent-plasma-can-treat-covidminus-19>

- A number of researchers are endeavouring to discover COVID-19 -neutralising antibodies⁹⁰.

Drugs approved in some jurisdictions for other uses, or tested for other uses

- Novartis announced⁹¹ that it planned to study its immunology medication Ilaris (canakinumab) in a phase III trial to test whether it can reverse severe immune overreactions in patients with COVID-19. It is already approved to treat some inflammatory diseases such as juvenile idiopathic arthritis. It is under investigation in non-small cell lung cancer, with enrolment of newly diagnosed patients in a phase III clinical trial completed in January.
- Novartis said it was also examining its cancer drug Jakavi and its multiple sclerosis drug Gilenya for their potential to mitigate COVID-19 complications.
- Scientists at the NIH and Gilead have reported⁹² results from an animal trial of remdesivir, involving 12 rhesus macaques, showing that early antiviral treatment reduced COVID-19 symptoms and lung damage. The trial replicated dosing schedules in an ongoing human trial. Six macaques were treated with the drug, six were not⁹³. The researchers wrote: “Data from clinical trials in humans are pending, but our data in rhesus macaques indicate that remdesivir treatment should be considered as early as clinically possible to prevent progression to severe pneumonia in COVID-19 patients.”
- Gilead is expected to report in late May the results of Phase III trials, one of which is comparing remdesivir to the standard of care in treating COVID-19.
- A number of studies of remdesivir, of varying rigour, have reported⁹⁴.
- Gilead has speeded up the manufacture of remdesivir⁹⁵.
- US President Trump in a press conference promoted the generic malaria drug hydroxychloroquine for possible use against COVID-19. It is also used to treat lupus and rheumatoid arthritis. The President’s endorsement was followed quickly by

⁹⁰ <https://pipelinereview.com/index.php/2020040874275/Antibodies/Researching-antibodies-to-target-COVID-19.html> and <https://pipelinereview.com/index.php/2020040874279/Antibodies/CSL-Behring-and-SAB-Biotherapeutics-Join-Forces-to-Deliver-New-Potential-COVID-19-Therapeutic.html> and https://www.fiercebiotech.com/biotech/celltrion-plans-july-covid-19-trial-advances-super-antibody?mkt_tok and <https://www.foxbusiness.com/markets/eli-lilly-developing-potential-coronavirus-treatment>

⁹¹ <https://www.novartis.com/news/novartis-announces-plan-initiate-clinical-trial-canakinumab-patients-covid-19-pneumonia>

⁹² Brandi N Williamson et al., “Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2”, *bioRxiv* 15 April 2020. doi: <https://doi.org/10.1101/2020.04.15.043166> A preliminary report which was not peer-reviewed.

⁹³ This is in contrast with two other favourable reports where there was no control group: the University of Chicago Medical Center reported that remdesivir swiftly subdued fever and respiratory symptoms in severe Covid-19 patients, and Gilead had provided results from 53 other patients to the *New England Journal of Medicine*.

⁹⁴ https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7B30f206a4-1037-4975-82bd-7936bd7714e3%7D/fauci-on-remdesivir-for-covid-19-this-will-be-the-standard-of-care?utm_source; and Yang W, et al. *Lancet*. 2020;doi:10.1016/S0140-6736(20)31022-9; and <https://www.fiercebiotech.com/biotech/gilead-s-remdesivir-speeds-recovery-1st-controlled-trial-readout-but-it-s-no-silver-bullet>; and https://seekingalpha.com/article/4338423-why-gileads-covid-drug-may-be-magic-bullet-need?utm_medium=email&utm_source; and the *New England Journal of Medicine* on 10 April, 2020 published [Compassionate Use of Remdesivir for Patients with Severe Covid-19](#) by Grein *et al.*; and [Antiviral remdesivir prevents disease progression in monkeys with COVID-19](#); and [Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2](#)

⁹⁵ <https://www.statnews.com/pharmalot/2020/04/05/gilead-covid19-coronavirus-remdesivir/>

trials⁹⁶. On 30 March Novartis announced that its Sandoz unit had donated 20,000 doses of hydroxychloroquine to the University of Washington for a new COVID-19 clinical trial. The study, funded in part by the Bill & Melinda Gates Foundation, would enrol around 2,000 patients with a 14-day post-exposure regimen. On 20 April Novartis announced it had agreed with US regulators to hold a randomized Phase III trial in 440 hospitalised patients⁹⁷. The drug had by then received FDA emergency use authorization for coronavirus disease. The European Medicines Agency limited use of chloroquine and hydroxychloroquine to clinical trials and emergency use programs for patients with COVID-19. Studies so far had yielded mixed results⁹⁸. Some cardiologists had spoken out against widespread use in COVID-19⁹⁹.

- On 24 April, the FDA issued a warning¹⁰⁰ against use of hydroxychloroquine or chloroquine for COVID-19 outside a hospital setting or within a clinical trial, due to risk of heart rhythm problems.
- Alexion is conducting a Phase III study of Ultomiris in COVID-19¹⁰¹, and is planning a Phase II study of Soliris in the disease¹⁰².
- In a recent commentary¹⁰³, a University of Miami researcher argued that DPP-4 enzyme-inhibiting diabetes medication might fight COVID-19¹⁰⁴. Several DPP-4 inhibitors are already on the market, including Boehringer Ingelheim and Eli Lilly's Tradjenta and Merck's Januvia.
- Other existing drugs suggested or being trialled for use in COVID-19 are:
 - i. Eli Lilly's JAK inhibitor (for rheumatoid arthritis) Olumiant, being tested in conjunction with the US National Institute of Allergy and Infectious Diseases (NIAID)
 - ii. arthritis drugs Kevzara (Sanofi and Regeneron), Actemra¹⁰⁵ (Roche), and Xeljanz (Pfizer)
 - iii. Astra Zeneca's blood cancer drug, BTK inhibitor Calquence
 - iv. BeiGene's BTK inhibitor Brukinsa
 - v. Bausch Health's RSV drug Virazole
 - vi. AbbieVie's HIV Kaletra

⁹⁶ <https://www.nih.gov/news-events/news-releases/nih-clinical-trial-hydroxychloroquine-potential-therapy-covid-19-begins>

⁹⁷ The trial will divide patients into three groups: hydroxychloroquine alone, hydroxychloroquine plus antibiotic azithromycin, and placebo.

⁹⁸ e.g. <https://www.medscape.com/viewarticle/928798?nlid>; and

Mayla Gabriela Silva Borba et al., "Chloroquine diphosphate in two different dosages as adjunctive therapy of hospitalized patients with severe respiratory syndrome in the context of coronavirus (SARS-CoV-2) infection: Preliminary safety results of a randomized, double-blinded, phase IIb clinical trial (CloroCovid-19 Study)", *medRxiv*, (not certified by peer review) 16 April 2020

<https://www.medrxiv.org/content/10.1101/2020.04.07.20056424v2>; and

Zhaowei Chen et al., "Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial" in *medRxiv* (not certified by peer review)

<https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2.full.pdf>; and

<https://www.latimes.com/business/story/2020-04-01/trump-chloroquine-coronavirus-bad-science-hiltzik-column>

⁹⁹ Roden DM et al. in *Circulation*. 8 April 2020 [doi:10.1161/CIRCULATIONAHA.120.047521](https://doi.org/10.1161/CIRCULATIONAHA.120.047521)

¹⁰⁰ <https://www.fda.gov/media/137250/download>

¹⁰¹ https://www.fiercepharma.com/pharma/citing-early-results-alexion-says-it-s-time-run-phase-3-study-ultomiris-severe-covid-19?mkt_tok

¹⁰² <https://www.fiercepharma.com/pharma/alexion-plans-phase-2-study-soliris-covid-19-coming-days-report>

¹⁰³ [https://www.diabetesresearchclinicalpractice.com/article/S0168-8227\(20\)30375-2/fulltext](https://www.diabetesresearchclinicalpractice.com/article/S0168-8227(20)30375-2/fulltext)

¹⁰⁴ <https://www.fiercebiotech.com/research/can-a-class-diabetes-drugs-help-treat-covid-19>

¹⁰⁵ BARDA is paying \$US 25 million for a Phase III trial in COVID--19

- vii. BioCryst's antiviral drug galidesivir¹⁰⁶
- viii. Viriom's el sulfavirine, approved for treating HIV infection in Russia and Kazakhstan¹⁰⁷
- ix. Fujifilm, with its antiviral Avigan, approved in Japan for influenza in certain conditions¹⁰⁸
- x. Riovant Sciences with gimsilumab, a drug which targets a protein called granulocyte-macrophage colony stimulating factor (GM-CSF) which belongs to a class of proteins called cytokines¹⁰⁹.

Investigational new drugs

- CytoDyn is testing its viral entry inhibitor leronlimab in COVID-19. A Phase II study in mild-to-moderately ill patients and a Phase IIb/III trial in severely and critically ill patients are underway in the US. The drug binds to a protein on the surface of certain immune cells which play a key role in modulating immune cell trafficking in sites of inflammation. CytoDyn has completed the [rolling submission](#) of its US marketing application seeking approval to use leronlimab, combined with highly active antiretroviral therapy, in treatment-experienced HIV patients, an indication in which it has Fast Track designation from the US Food and Drug Administration (FDA)¹¹⁰.
- Pfizer said it has preliminary data that "suggest" its lead protease inhibitor "shows antiviral activity against SARS-CoV-2," the virus causing COVID-19. It plans to move to preclinical studies¹¹¹.
- Mesoblast announced on 1 April that it had received clearance from the FDA for an Investigational New Drug application to treat patients with acute respiratory distress syndrome caused by COVID-19 with intravenous infusions of its allogeneic mesenchymal stem cell product candidate remestemcel-L¹¹².
- Hope Biosciences announced on 1 April that FDA had approved a Phase II clinical trial evaluating efficacy and safety of the company's autologous, adipose-derived mesenchymal stem cells to provide immune support against COVID-19¹¹³.

¹⁰⁶ https://www.fiercebiotech.com/biotech/biocryst-starts-covid-19-trial-broad-spectrum-antiviral?mkt_tokVir

¹⁰⁷ <https://pipelinereview.com/index.php/2020040874280/Small-Molecules/Viriom-Initiates-Phase-2-Clinical-Study-of-El sulfavirine-for-Treatment-of-COVID-19.html>

¹⁰⁸ <https://pipelinereview.com/index.php/2020041074307/Small-Molecules/Fujifilm-announces-the-start-of-a-phase-II-clinical-trial-of-its-influenza-antiviral-drug-Avigan-Tablet-for-COVID-19-patients-in-the-U.S.html>

¹⁰⁹ <https://www.reuters.com/article/us-health-coronavirus-roivant/roivant-begins-giving-experimental-covid-19-drug-to-first-u-s-patients-idUSKCN21X2YA>

¹¹⁰ <https://pipelinereview.com/index.php/2020040674256/Antibodies/First-Two-Patients-Enrolled-in-Randomized-Phase-2-COVID-19-Trial-with-Leronlimab-Five-More-Severely-Ill-COVID-19-Patients-Treated-Under-Emergency-IND-and-Two-Patients-Have-Alr.html>

¹¹¹ <https://www.fiercebiotech.com/biotech/pfizer-restarts-trial-recruitment-speeds-up-antiviral-work-against-covid-19>

¹¹² <https://pipelinereview.com/index.php/2020040674237/DNA-RNA-and-Cells/FDA-clears-investigational-new-drug-application-for-mesoblast-to-use-remestemcel-L-in-patients-with-acute-respiratory-distress-syndrome-caused-by-COVID-19.html>

¹¹³ <https://pipelinereview.com/index.php/2020040674241/DNA-RNA-and-Cells/Hope-Biosciences-Receives-FDA-Approval-to-Commence-First-Stem-Cell-Clinical-Trial-for-Protection-Against-COVID-19.html>

- The FDA authorized Caladrius Biosciences, to begin a clinical trial of CLBS119¹¹⁴ — an autologous CD34+ cell therapy — in patients with severe SARS-CoV-2 infection who [had respiratory failure](#).
- Oncolmmune has FDA approval for a Phase III clinical trial testing the safety and efficacy of CD24Fc for the treatment of hospitalized COVID-19 patients¹¹⁵.
- Other companies directing research efforts towards a COVID-19 treatment are
 - i. CalciMedica with its inflammation-targeting drug CM4620-IE¹¹⁶
 - ii. Vir Biotechnology with two novel antibodies¹¹⁷
 - iii. RedHill Biopharma with opaganib¹¹⁸
 - iv. Ridgeback Therapeutics with its antiviral EIDD-2801¹¹⁹
 - v. Leading Biosciences with its broad-spectrum serine protease inhibitor LB1148¹²⁰
 - vi. FirstWave Bio with its proprietary form of niclosamide¹²¹
 - vii. Theravance with its lung-selective nebulized Janus kinase inhibitor TD-0903¹²²
 - viii. Biohaven with its intranasal, high-affinity calcitonin gene-related peptide receptor antagonist, vazegepant¹²³
 - ix. Cytovia Therapeutics, partnering with Macromoltek to develop natural killer immunotherapy against COVID-19¹²⁴.
 - x. Tiziana with its investigational new technology which directly delivers anti-IL-6 receptor (anti-IL-6R) monoclonal antibodies into the lungs using a handheld inhaler or nebulizer¹²⁵.
 - xi. Anixa Biosciences and OntoChem hoping to develop new antivirals¹²⁶

¹¹⁴ https://www.healio.com/hematology-oncology/cell-therapy/news/online/%7Bf66052b0-9169-4c05-9c04-d09cd1216250%7D/fda-clears-ind-application-for-cell-therapy-to-treat-covid-19-related-lung-damage?utm_source

¹¹⁵ <https://pipelinereview.com/index.php/2020040974285/Antibodies/Oncolmmune-Receives-FDA-Approval-for-COVID-19-Clinical-Trial.html>

¹¹⁶ https://www.fiercebiotech.com/biotech/-moves-inflammation-targeting-covid-19-drug-into-phase-2?mkt_tok

¹¹⁷ https://www.fiercepharma.com/manufacturing/vir-inks-deal-samsung-to-scale-up-covid-19-antibody-manufacturing?mkt_tok

¹¹⁸ <https://seekingalpha.com/news/3558482-redhill-bio-doses-first-covidminus-19-patient-opaganib-in-israel-shares-up-9-premarket>

¹¹⁹ <https://pipelinereview.com/index.php/2020040774260/Small-Molecules/FDA-Clears-the-Way-for-Ridgeback-Biotherapeutics-to-begin-Human-Testing-of-a-Promising-Potential-Treatment-for-COVID-19.html>

¹²⁰ <https://pipelinereview.com/index.php/2020040774270/Small-Molecules/Leading-BioSciences-Announces-Potential-for-Investigational-Drug-LB1148-to-Treat-Multiple-Organ-Dysfunction-Syndrome-in-COVID-19-Patients.html>

¹²¹ <https://pipelinereview.com/index.php/2020041074293/Small-Molecules/FirstWave-Bio-to-Initiate-Phase-2a/2b-Study-of-FW-1022-a-Proprietary-Form-of-Niclosamide-to-Treat-COVID-19.html>

¹²² <https://pipelinereview.com/index.php/2020041074299/Small-Molecules/Theravance-Biopharma-Responds-to-COVID-19-Pandemic-by-Advancing-TD-0903-to-Treat-Hospitalized-Patients-with-Acute-Lung-Injury.html>

¹²³ <https://pipelinereview.com/index.php/2020041074303/Small-Molecules/Biohaven-Receives-FDA-May-Proceed-Letter-to-Begin-Phase-2-Trial-of-Intranasal-Vazegepant-to-Treat-Lung-Inflammation-After-COVID-19-Infection.html>

¹²⁴ <https://pipelinereview.com/index.php/2020040774269/DNA-RNA-and-Cells/CYTOVIA-Therapeutics-and-MACROMOLTEK-to-Develop-Dual-Acting-Natural-Killer-Immunotherapy-Against-SARS-CoV2-COVID-19.html>

¹²⁵ <https://pipelinereview.com/index.php/2020040974289/Antibodies/Tiziana-Lifesciences-Develops-Novel-Investigational-Treatment-For-Patients-Infected-with-COVID-19-Utilizing-Direct-Delivery-of-Anti-Interlukin-6-Receptor-Monoclonal-Antibodies.html>

¹²⁶ <https://www.fiercebiotech.com/biotech/cancer-startup-anixa-teams-up-machine-learning-firm-to-look-out-covid-19-hopefuls>

Other therapies

- Scientists are divided on whether intravenous infusions of donor mesenchymal stem cells are an appropriate treatment¹²⁷.
- Antonio Bertoletti from Duke-NUS' emerging infectious diseases research program suggests that CAR/TCR-T cell therapy might be useful in treating SARS-CoV-2, the virus causing the current pandemic. He said: "We demonstrated that T cells can be redirected to target the coronavirus responsible for SARS¹²⁸. Our team has now begun exploring the potential of CAR/TCR T cell immunotherapy for controlling the COVID-19-causing virus, SARS-CoV-2, and protecting patients from its symptomatic effects."¹²⁹
- Plasmapheresis uses modified dialysis filters to bind key components of viral replication or the virus itself, with the goal of returning uninfected plasma to the patient¹³⁰.
- The FDA granted an emergency authorization to a blood purification system to treat patients with the most severe cases of COVID-19¹³¹, and followed this closely with an authorization for a second blood filtering device for use in COVID-19¹³².

4. Company news not included above

- Cerus amended its contract with the US Biomedical Advanced Research and Development Authority (BARDA). It now has a further \$US 14M in available funding, increasing the total value of the contract to \$US 214M. This includes additional funding for RedeS, the company's Phase III study evaluating the safety and efficacy of INTERCEPT red blood cells in patients receiving transfusions in the acute and chronic setting, and to further evaluate the INTERCEPT Blood System in inactivating the SARS-CoV-2 virus in all three blood components¹³³.
- Sobi [reported](#) better-than-expected first-quarter results. The company cited strong growth for haemophilia products partly due to "advance purchases to secure access to treatment for a longer period than normal" amid the pandemic.

¹²⁷ https://www.the-scientist.com/news-opinion/are-mesenchymal-stem-cells-a-promising-treatment-for-covid-19-67402?utm_campaign

¹²⁸ Hsueh-Ling Janice Oh, Antonio Bertoletti et al., "Engineering T Cells Specific for a Dominant Severe Acute Respiratory Syndrome Coronavirus CD8 T Cell Epitope", *Journal of Virology*, October 2011; 85(20): 10464–10471. doi: [10.1128/JVI.05039-11](https://doi.org/10.1128/JVI.05039-11)

¹²⁹ <https://www.duke-nus.edu.sg/allnews/using-own-immune-cells-to-target-infectious-diseases-including-covid-19>

¹³⁰ <https://www.medscape.com/viewarticle/929182?nlid> and Claudio Ronco and Thiago Reis, "Kidney involvement in COVID-19 and rationale for extracorporeal therapies", *Nature Reviews Nephrology* (2020) 9 April.

¹³¹ https://www.fiercebitech.com/medtech/fda-greenlights-blood-detox-device-to-combat-covid-19-s-cytokine-storms?mkt_tokj

¹³² https://www.fiercebitech.com/medtech/fda-quickly-authorizes-its-second-blood-filtering-device-for-covid-19?mkt_tok

¹³³ https://seekingalpha.com/news/3562473-cerus-expands-barda-funding-additional-14m?utm_medium