

Monitoring International Trends

May 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. Some items of interest are reported below.

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1. Clinical experience with COVID-19

Respiratory concerns

- Researchers report that mechanically ventilated COVID-19 patients can be managed like patients with acute respiratory distress syndrome (ARDS)¹.
- Others suggest that the presentation of ARDS in critically ill COVID-19 differs from the typical presentation of ARDS².
- A report on a series of patients who recovered from COVID-19 in China said that impairment of their lung diffusion capacity, which correlated with severity of disease, appeared to be the most common lung function abnormality³.
- A study found that “among patients with COVID-19 treated during the height of the pandemic in New York City, critical illness was common and was significantly associated with invasive mechanical ventilation, extrapulmonary organ dysfunction and in-hospital mortality”⁴.
- Philips was cleared by the US Food and Drug Administration (FDA) “to market its ultrasound solutions portfolio for the management of lung and cardiac complications associated with COVID-19”⁵.
- A review found that “patients with coronavirus-related respiratory infections are often prescribed broad-spectrum empirical antimicrobials despite scarce evidence for bacterial or fungal co-infections”⁶.

Cardiovascular concerns

- Global experience has been that cardiovascular comorbidities are common in patients with COVID-19, and they are associated with a greater risk of mortality⁷.

¹ David R Ziehr et al., “Respiratory Pathophysiology of Mechanically Ventilated Patients with COVID-19: A Cohort Study”, *American Journal of Respiratory and Critical Care Medicine*, online 29 April 2020. <https://doi.org/10.1164/rccm.202004-1163LE> reported at

<https://www.medscape.com/viewarticle/930178?nlid>. See also

<https://www.medscape.com/viewarticle/929609?nlid> and

<https://pipelinereview.com/index.php/2020042774428/Small-Molecules/Santhera-and-Cold-Spring-Harbor-Laboratory-to-Investigate-Lonodelestat-POL6014-in-COVID-19-related-Acute-Respiratory-Distress-Syndrome-ARDS.html>

² https://www.healio.com/pulmonology/pulmonary-vascular-disease/news/online/%7Bebf9c253-46af-4e7d-990a-d5dc0cc8cf3f%7D/thrombolysis-a-potential-treatment-for-atypical-ards-in-covid-19?utm_source and https://thelimbic.com/haematology/abnormal-coagulation-linked-to-poorer-covid-19-prognosis/?utm_source

³ https://www.healio.com/pulmonology/practice-management/news/online/%7Bc2fc7d8e-6d11-4741-a46c-7a5c5bec64db%7D/lung-diffusion-capacity-impairment-common-among-covid-19-survivors?utm_source

⁴ https://www.healio.com/pulmonology/critical-care/news/online/%7Beb770fb8-5b1a-4d0f-8288-632221009400%7D/mortality-mechanical-ventilation-common-among-critically-ill-patients-with-covid-19-in-nyc?utm_source

⁵ https://www.healio.com/cardiology/imaging/news/online/%7Bfdf10808-b995-4a0b-8966-bab35090c32b%7D/ultrasound-systems-net-clearance-for-management-of-lung-cv-complications-of-covid-19?utm_source

⁶ https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7B8f9072f4-9386-4efe-b507-d04e731b2fb%7D/patients-with-covid-19-frequently-receive-antimicrobials-despite-low-rate-of-bacterial-coinfections?utm_source

⁷ https://www.healio.com/cardiology/chd-prevention/news/print/cardiology-today/%7Bc7417d27-5908-4c8a-892b-317ee67cdb19%7D/clinical-review-of-covid-19-and-cvd-what-the-cardiovascular-practitioner-needs-to-know?utm_source

- Studies have continued of the relationship between ACE inhibitors and COVID-19⁸.
- A brief UK report identified stroke as a COVID-19 complication, including breakthrough strokes despite therapeutic anticoagulation⁹.
- While there is a widely held view that hospitalized COVID-19 patients should be on anticoagulants, there is also substantial support for continuing this after discharge¹⁰.
- Chinese researchers say that “evaluation of right ventricular function should be implemented by investigation of right ventricular longitudinal strain for risk stratification in patients with COVID-19”¹¹.
- Imperial College London initiated a randomized controlled trial, in hospitalized COVID-19 patients with cardiovascular risk factors, to compare dual antiplatelet therapy with a direct oral anticoagulant against standard care for 30-day all-cause mortality¹².
- Doctors at Lille University Hospital in France reported twice the incidence of pulmonary embolism among COVID-19 patients in ICU compared with patients in ICU at the same time in 2019¹³.

Neurological symptoms

- Doctors in Detroit describe the first case of acute necrotizing haemorrhagic encephalopathy presumed to be linked with COVID-19¹⁴.
- Two further neurologic conditions, both rare, have arisen in hospitalized COVID-19 patients¹⁵.

The cytokine storm

- Cytokine storm is one of the factors thought to be associated with myocardial injury in COVID-19¹⁶.
- One therapy that has been suggested to inhibit inflammation is the hormone progesterone¹⁷.
- GSK is trialling its pipeline monoclonal antibody otilimab as a therapy for COVID-19 patients hit with a cytokine storm¹⁸.

⁸ <https://www.medscape.com/viewarticle/929992?nlid> see also https://www.fiercehealthcare.com/payer/unitedhealth-launching-clinical-trial-to-test-impact-ace-inhibitors-covid-19?mkt_tok

⁹ <https://www.medpagetoday.com/infectiousdisease/covid19/86285?xid>

¹⁰ https://www.medpagetoday.com/infectiousdisease/covid19/86230?utm_source

¹¹ https://www.healio.com/cardiology/imaging/news/online/%7Bb7b5c1aa-644f-4958-97bc-4a51afed862b%7D/right-ventricular-longitudinal-strain-may-predict-mortality-in-covid-19?utm_source

¹² https://www.medpagetoday.com/cardiology/prevention/86452?xid=nl_mpt_DHE_2020-05-13&eun

¹³ https://www.healio.com/cardiology/vascular-medicine/news/online/%7Bca83ec8d-7162-4caf-bf8d-5a32efbb6496%7D/pe-twice-as-prevalent-in-covid-19-in-case-series-report?utm_source

¹⁴ <https://www.medscape.com/viewarticle/928134?src>

¹⁵ <https://www.medscape.com/viewarticle/929631?nlid>

¹⁶ https://www.healio.com/cardiology/vascular-medicine/news/online/%7Bd4dc8255-02c2-42b9-9e14-5d2540b3e6cb%7D/review-identifies-possible-mechanisms-for-elevated-troponin-cardiac-injury-in-covid-19?utm_source

¹⁷ https://www.healio.com/endocrinology/hormone-therapy/news/online/%7B5c31e490-3ffe-4fa6-bc4b-c7f9c9c0e41b%7D/study-examines-progesterone-to-reduce-inflammation-in-covid-19?utm_source

¹⁸ https://www.fiercebiotech.com/biotech/gsk-taps-experimental-arthritis-antibody-to-calm-cytokine-storm-hitting-covid-19-patients?mkt_tok

Suggested disease modifying factors

- Researchers reported that haematological and lung cancers appear to be associated with poor COVID-19 outcomes¹⁹.
- It appears that patients with common haemoglobin disorders may be at risk of COVID-19 complications²⁰.
- An analysis suggests that the younger a COVID-19 patient in ICU is, the more obese that patient is likely to be²¹.
- A small study published in *Open Forum Infectious Diseases* confirms other reports that “male gender, old age and the presence of underlying conditions appear to be the most common characteristics associated with fatal COVID-19 outcomes.”²²
- Dr Shailendra Singh²³ said: “Patients with liver disease might be at increased risk of COVID-19 poor outcomes”. This can arise because “expression of receptors for COVID-19 has been suggested in the liver and liver injury is possible during the COVID-19 disease progression”²⁴.
- A US study confirmed experience elsewhere that people with underlying health conditions are at higher risk for more severe COVID-19²⁵.
- Genetics are thought to have an impact on COVID-19 severity²⁶.
- Researchers have reported that the risk of COVID-19 in expectant mothers to them and their unborn infants is not insignificant²⁷.

COVID-19 in paediatric patients

- That COVID-19 in children can trigger a condition resembling Kawasaki disease is widely accepted as plausible²⁸.

¹⁹ https://thelimbic.com/haematology/haematological-cancers-associated-with-poor-covid-19-outcomes/?mc_cid and https://www.medpagetoday.com/meetingcoverage/aacr/86201?utm_source

²⁰ https://www.hospitalhealth.com.au/content/clinical-services/news/haemoglobin-disorders-and-covid-19-what-do-we-know-so-far--859008540?utm_source

²¹ <https://www.medscape.com/viewarticle/930275?nlid>

²² https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7B21c3a3d5-6b32-4b7d-a41e-43b966575804%7D/male-gender-old-age-predominate-in-fatal-covid-19-cases?utm_source

²³ of Charleston Area Medical Center Health System, West Virginia

²⁴ <https://www.medscape.com/viewarticle/930616?nlid>

²⁵ <https://www.medscape.com/viewarticle/928130?src>

²⁶ <https://www.medscape.com/viewarticle/930369?nlid> and

https://www.healio.com/pulmonology/asthma/news/online/%7B4afc8751-73c1-4346-b5af-9a7f2adc7ec8%7D/asthma-in-certain-patients-elevates-risk-for-worse-covid-19-outcomes?utm_source

http://www.pharmatimes.com/news/new_partnership_to_sequence_human_genomes_in_fight_against_coronavirus_1340177?utm_source and

²⁷ https://www.medpagetoday.com/infectiousdisease/covid19/86261?utm_source

²⁸ https://www.healio.com/pediatrics/emerging-diseases/news/online/%7B4a39039-ea18-441c-bcf0-6cbf55d30ea4%7D/does-sars-cov-2-cause-kawasaki-disease-in-children?utm_source and

<https://time.com/5834737/new-york-children-die-syndrome-covid-19/> and <https://picsociety.uk/wp-content/uploads/2020/04/PICS-statement-re-novel-KD-C19-presentation-v2-27042020.pdf>>. and

<http://promedmail.org/post/20200430.7286479> and

<https://www1.nyc.gov/assets/doh/downloads/pdf/han/alert/2020/covid-19-pediatric-multi-system-inflammatory-syndrome.pdf> and <https://www.bmjjournals.org/doi/10.1136/bmjjm.2020.118162> and

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31103-X/fulltext?dgcid](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31103-X/fulltext?dgcid) and

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31129-6/fulltext?dgcid](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31129-6/fulltext?dgcid) and

https://www.medpagetoday.com/infectiousdisease/covid19/86393?utm_source and

<https://www.medscape.com/viewarticle/930598?nlid> and <https://www.sbs.com.au/news/concern-in-europe-as-france-confirms-more-children-have-new-disease-with-possible-coronavirus-link>

- The US Senate was told²⁹ by Dr Anthony Fauci, Director of the US National Institute of Allergy and Infectious Diseases, that “it would be a mistake to underestimate the effect that COVID-19 has on children, particularly in light of recent reports of children experiencing a serious inflammatory syndrome that has been [linked to SARS-CoV-2 infection](#).
- Researchers from Wuhan concluded that children with sickness and diarrhoea who also have a fever or history of exposure to coronavirus should be suspected of having COVID-19³⁰.
- A US study found that eleven percent of children hospitalized with COVID-19 required care in the paediatric ICU³¹.

Other issues in clinical management

- The American Society of Haematology is establishing an international panel of experts to develop clinical practice guidelines on the use of anticoagulation in patients with COVID-19³².
- Early research suggests that patients with haemoglobin disorders are more vulnerable to COVID-19³³.
- The International Society on Thrombosis and Haemostasis issued interim guidance on coagulopathy in patients with COVID-19³⁴.
- Researchers have written that COVID-19 patients treated in intensive care units are at increased risk for delirium. They recommend a strategy to modify risk factors³⁵.
- Researchers are investigating whether a greater susceptibility to psychosis is a potential secondary, long-term impact of COVID-19 infection³⁶.

²⁹ https://www.healio.com/pediatrics/emergency-medicine/news/online/%7B3be668da-0a6d-4813-8578-f394a6d97662%7D/fauci-tells-senate-not-to-underestimate-covid-19s-effect-on-children?utm_source

³⁰ Wenbin Li et al., “Clinical Characteristics of 5 COVID-19 Cases with Non-respiratory Symptoms as the First Manifestation in Children”, *Frontiers in Pediatrics*, 12 May 2020.

<https://doi.org/10.3389/fped.2020.00258> Reported in <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/stomach-ills-may-signal-covid-19-in-kids-study-says-757515.html>

³¹ https://www.healio.com/pediatrics/emerging-diseases/news/online/%7Bca1f6e5e-7a2d-4a25-8c32-44cf57dfe89b%7D/study-estimates-11-of-children-hospitalized-with-covid-19-require-picu-care?utm_source

³² https://thelimbic.com/haematology/ash-to-develop-anticoagulation-guidelines-for-patients-with-covid-19/?mc_cid Discussion of coagulation abnormalities and thrombosis in patients with COVID-19: [https://www.thelancet.com/journals/lancet/article/PIIS2352-3026\(20\)30145-9/fulltext?dgcid1](https://www.thelancet.com/journals/lancet/article/PIIS2352-3026(20)30145-9/fulltext?dgcid1) See also <https://www.medscape.com/viewarticle/930165> and <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/covid-19-tied-to-blood-clots-blood-thinners-could-boost-survival-757397.html> and https://www.medpagetoday.com/infectiousdisease/covid19/86331?xid=nl_mpt_DHE_2020-05-07&eun=g465425d0r&utm_source and https://thelimbic.com/haematology/abnormal-coagulation-linked-to-poorer-covid-19-prognosis/?utm_source

³³ https://www.hospitalhealth.com.au/content/clinical-services/news/haemoglobin-disorders-and-covid-19-what-do-we-know-so-far--859008540?utm_source

³⁴ https://transfusionnews.com/2020/05/13/coagulopathy-in-patients-with-covid-19-interim-guidance-from-the-international-society-on-thrombosis-and-haemostasis/?elq_mid

³⁵ <https://www.medscape.com/viewarticle/930472?nlid> reporting on Kotfis K et al. “COVID-19: ICU delirium management during SARS-CoV-2 pandemic”, *Critical Care*. 2020 28 April. doi: 10.1186/s13054-020-02882-x. see also https://www.the-scientist.com/news-opinion/the-unusual-symptoms-of-covid-19-67522?utm_campaign

³⁶ <https://www.medscape.com/viewarticle/930224>

- COVID-19 has been disproportionately affecting obese people in the US³⁷.
- As the pandemic has progressed, a number of cutaneous signs of infection have been recognised³⁸.
- Men who contract COVID-19 are more likely to be intubated or die than women, so researchers have begun a trial designed to determine whether a transdermal oestrogen patch can reduce symptom severity compared with standard care³⁹.
- A study of over 7,000 patients has emphasised the strong link between glucose control and COVID-19 outcomes in hospitalized patients with pre-existing type 2 diabetes⁴⁰.
- Conjunctivitis was the only presenting system of COVID-19 in five patients in Italy⁴¹.
- A review suggested that bacterial or fungal co-infection is not common in patients with coronavirus infections⁴².
- Researchers suggested that biomarkers for inflammation and thrombosis in critically ill COVID-19 patients may predict mortality⁴³.
- In the US, the Biomedical Advanced Research and Development Authority (BARDA) has expanded its partnership with Cytovale to continue development of a rapid diagnostic system for viral sepsis in patients with respiratory infections including COVID-19⁴⁴.
- Scientists found that receptors for SARS-CoV-2 are present in a wide range of human cells⁴⁵.
- The American College of Rheumatology released [guidance](#) for the rheumatology community on effectively caring for people with rheumatic diseases during the pandemic⁴⁶.
- Guidance for treating people with osteoporosis during the COVID-19 pandemic have been developed by the American Society for Bone and Mineral Research, and endorsed by the Endocrine Society, the American Association of Clinical Endocrinologists, and the European Calcified Tissue Society⁴⁷.

³⁷ https://www.healio.com/endocrinology/obesity/news/online/%7B73a6d4bb-2dbf-453d-9b05-ca7775cdd18d%7D/obesity-should-not-be-dismissed-excess-weight-drives-inflammation-hypoventilation-behind-covid-19-complications?utm_source

³⁸ <https://www.medscape.com/viewarticle/930180> and
<https://www.medscape.com/viewarticle/930128?nlid> and
<https://www.medscape.com/viewarticle/929996?nlid> and <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/more-symptoms-of-coronavirus-covid-toes-skin-rashes-757310.html>

³⁹ https://www.healio.com/endocrinology/hormone-therapy/news/online/%7B334d4dd8-cc70-4672-952f-735440eef7da%7D/study-investigates-estrogen-patch-use-to-lessen-covid-19-complications?utm_source and also

⁴⁰ <https://www.medscape.com/viewarticle/930521?nlid>

⁴¹ <https://www.medscape.com/viewarticle/930600?nlid>

⁴² <https://www.medscape.com/viewarticle/930282?nlid>

⁴³ <https://www.medscape.com/viewarticle/930804?nlid>

⁴⁴ <https://www.medicalcountermeasures.gov/newsroom/2020/cytovale-diagnostic/>

⁴⁵ https://www.the-scientist.com/news-opinion/receptors-for-sars-cov-2-present-in-wide-variety-of-human-cells-67496?utm_campaign

⁴⁶ <https://www.medpagetoday.com/acrr/generalrheumatology/86447?xid>

⁴⁷ https://www.healio.com/endocrinology/bone-mineral-metabolism/news/online/%7B526d7d8a-439a-402a-946b-de16229e0533%7D/dont-forget-osteoporosis-experts-outline-guidance-for-managing-fracture-risk-during-covid-19?utm_source Joint guidance on osteoporosis management in the era of COVID-19. Available at: <https://www.endocrine.org/-/media/endocrine/files/membership/joint-statement-on-covid19-and-osteoporosis-final.pdf>.

Testing

- The Infectious Diseases Society of America released diagnostic recommendations for both symptomatic and asymptomatic patients with COVID-19⁴⁸.
- Roche announced on 3 May that the US Food and Drug Administration (FDA) had issued an Emergency Use Authorization for the company's new Elecsys® Anti-SARS-CoV-2 antibody test. The test is designed to indicate if a person has been exposed to the SARS-CoV-2 virus and whether she or he has developed antibodies against the virus⁴⁹. Roche's test relies on an intravenous blood draw rather than a finger prick⁵⁰.
- On 8 May, the FDA published results from the first round of COVID-19 antibody diagnostics to have their accuracy assessed by federal laboratories⁵¹.
- Thermo Fisher Scientific acknowledged on 13 May that it was developing its OmniPath COVID-19 antibody test in collaboration with WuXi Diagnostics and the Mayo Clinic. It will manufacture the test in the US and Europe⁵².
- A study⁵³ of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2 underlined "the importance of stringent infection control and early use of potent antiviral agents, alone or in combination, for high-risk individuals".
- On 7 May the FDA issued an emergency use authorization for the gene-editing technology Crispr, approving a diagnostic which takes about an hour to determine whether a patient sample contains the virus that causes COVID-19⁵⁴.
- On 8 May the FDA a saliva-based coronavirus test for home use⁵⁵.
- On 9 May the FDA authorised its first antigen test for rapid point-of-care screening⁵⁶.
- In mid-May the American Medical Association issued guidance for physicians on the potential uses and limitations of serological testing (antibody testing)⁵⁷.
- A study found that "screening only for cough, shortness of breath, fever or sore throat may have missed 17 per cent of symptomatic health care personnel with COVID-19"⁵⁸.

⁴⁸ IDSA. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19.

<https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/>.

⁴⁹ <https://pipelinereview.com/index.php/2020/05/04/74526/More-News/Roches-COVID-19-antibody-test-receives-FDA-Emergency-Use-Authorization-and-is-available-in-markets-accepting-the-CE-mark.html>

⁵⁰ <https://www.reuters.com/article/us-health-coronavirus-testing-roche-hldg/roche-wins-us-nod-for-covid-19-antibody-test-aims-to-boost-output-idUSKBN22F02Q>

⁵¹ https://www.fiercebiotech.com/medtech/fda-publishes-first-validation-results-12-covid-19-antibody-tests?mkt_tok For the context of validation see https://www.the-scientist.com/news-opinion/why-the-accuracy-of-sars-cov-2-antibody-tests-varies-so-much-67513?utm_campaign and [What Do Antibody Tests For SARS-CoV-2 Tell Us About Immunity?](#)

⁵² https://www.fiercebiotech.com/medtech/thermo-fisher-wuxi-and-mayo-clinic-to-develop-open-platform-covid-19-antibody-test?mkt_tok

⁵³ [https://www.thelancet.com/journals/lancinf/article/PIIS1473-3099\(20\)30196-1/fulltext?dgcid](https://www.thelancet.com/journals/lancinf/article/PIIS1473-3099(20)30196-1/fulltext?dgcid)

⁵⁴ <https://www.forbes.com/sites/katiejennings/2020/05/07/fda-authorizes-first-ever-crispr-application-for-covid-19-coronavirus-test/#6df23f451708>

⁵⁵ https://www.fiercebiotech.com/medtech/fda-authorizes-saliva-based-coronavirus-test-for-at-home-use?mkt_tok

⁵⁶ https://www.fiercebiotech.com/medtech/fda-greenlights-its-first-coronavirus-antigen-test-for-rapid-point-care-screening?mkt_tok

⁵⁷ https://www.fiercehealthcare.com/practices/ama-issues-guidance-to-physicians-using-covid-19-antibody-tests?mkt_tok

⁵⁸ https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7B5d37b55b-7bc7-42fe-9ed7-daf8826e961f%7D/screening-for-only-common-covid-19-symptoms-may-miss-symptomatic-cases-among-hcp?utm_source

- A study reportedly found one rapid, point-of-care coronavirus test “could miss nearly half of positive cases, depending on how the samples were handled and fed into the machine”⁵⁹.
- On 29 April, the US National Institutes of Health announced an initiative to speed up innovation, development and commercialization of COVID-19 testing technologies⁶⁰. NIH is working with the FDA, the Centers for Disease Control and Prevention and the Biomedical Advanced Research and Development Authority (BARDA).

2. Developing vaccines for Covid-19

- Scientific leaders have advocated a collaborative approach to the clinical testing, scale-up and distribution of a range of candidate vaccines to prevent COVID-19⁶¹.
- Dr Anthony Fauci, director of the US Institute of Allergy and Infectious Diseases, told a US Senate hearing that with at least eight COVID-19 vaccines in human testing he was cautiously optimistic that at least one might work, although there could be no guarantee at this stage⁶².
- Dr Rick Bright, formerly chief of the US Biomedical Advanced Research and Development Authority (BARDA), told a US House of Representatives hearing that he doubted immunization could be available in 12 to 18 months. He said: “My concern is if we rush too quickly, and consider cutting out critical steps, we might not have a full assessment of the safety of the vaccine”⁶³. The Trump administration’s “Operation Warp Speed” has a goal of delivering 100 million doses of a viable COVID-19 vaccine by the end of 2020⁶⁴.
- The CEO of Novartis said a vaccine may take until the end of 2021 to reach patients⁶⁵.
- Bill Gates, whose foundation is funding a number of vaccine initiatives, has said that only 8-10 of the 115 vaccines under development globally are “promising”⁶⁶.
- In the first half of May, Moderna received fast-track designation from the FDA for its investigational COVID-19 vaccine, mRNA-1273⁶⁷.

⁵⁹ https://www.fiercebiotech.com/medtech/nyu-study-flags-false-negatives-from-abbott-s-portable-coronavirus-test?mkt_tok

⁶⁰ <https://www.nih.gov/news-events/news-releases/nih-mobilizes-national-innovation-initiative-covid-19-diagnostics>

⁶¹ Lawrence Corey et al., “A strategic approach to COVID-19 vaccine R&D”, Science, 11 May 2020. DOI: 10.1126/science.abc5312 reported in <https://www.nih.gov/news-events/news-releases/coordinated-strategy-accelerate-multiple-covid-19-vaccine-candidates-key-nih-experts-say>

⁶² https://www.fiercepharma.com/vaccines/multiple-shots-goal-niaid-director-anthony-fauci-cautiously-optimistic-about-covid-19?mkt_tok

⁶³ <https://www.fiercepharma.com/vaccines/hhs-whistleblower-bright-doubts-18-month-coronavirus-vaccine-timeline>

⁶⁴ https://www.fiercebiotech.com/biotech/chutes-ladders-gsk-vaccines-vet-slaoui-to-lead-project-warp-speed?mkt_tok and https://www.fiercepharma.com/pharma/coronavirus-tracker-hydroxychloroquine-fails-va-study-fda-approves-at-home-sample-collection?mkt_tok

https://www.fiercepharma.com/vaccines/after-sneak-peak-at-early-data-operation-warp-speed-head-slaoui-confident-covid-19-vaccine?mkt_tok

⁶⁵ https://www.fiercepharma.com/manufacturing/novartis-ceo-covid-19-vaccine-might-take-until-end-2021?mkt_tok

⁶⁶ <https://www.9news.com.au/world/coronavirus-bill-gates-predicts-covid19-vaccine-in-possibly-just-nine-months/9df35b82-6cd9-4ef8-a658-8218e7c89120> and <https://gatesnot.es/3d06cC2> and <https://www.biopharmadive.com/news/coronavirus-vaccine-herd-immunity-covid-19/577312/>

⁶⁷ https://www.fiercebiotech.com/biotech/moderna-nabs-fda-fast-track-tag-for-its-covid-19-vax?mkt_tok and https://www.fiercebiotech.com/biotech/it-s-too-soon-to-assume-success-for-moderna-s-covid-19-vaccine-analyst?mkt_tok and <https://www.reuters.com/article/us-health-coronavirus-modernas-experimental-coronavirus-vaccine-gets-fdas-fast-track-status-idUSKBN27I0JU>

- Two German biotechs, CureVac and Pfizer-partnered BioNTech, are also using mRNA technology for their COVID-19 vaccines⁶⁸.
- In early pre-clinical testing The University of Queensland's COVID-19 vaccine demonstrated the ability to raise high levels of antibodies that can neutralise the virus⁶⁹.
- A report on 13 May⁷⁰ said China's CanSino Biologics, whose coronavirus vaccine candidate is already in clinical trials, is collaborating with Canada's National Research Council. The NRC said it would scale up a production process for CanSino's vaccine at a government facility in Montreal, and that CanSino was preparing a trial application for drug regulator Health Canada.
- Chinese researchers reported they had tested a SARS-CoV-2 vaccine candidate in mice, rats and non-human primates (macaques), producing antibodies that neutralised several different SARS-CoV-2 strains⁷¹. US and UK researchers announced in *Science Advances* that a single-dose vaccine has been shown to protect rhesus macaques from MERS-CoV⁷².
- The French President sought a meeting with Sanofi⁷³ after the company's CEO said the US would get early access to COVID-19 vaccines.
- Sinovac, another Chinese company with a potential COVID-19 vaccine, is also seeking to hold trials abroad in countries where there are more cases. CEO Yin Weidong is reported to have said the US would be the ideal location⁷⁴.
- Pfizer and BioNT began dosing US participants in a vaccine trial in early May⁷⁵. Volunteers in Germany had received the RNA vaccine in a Phase I/II trial in April⁷⁶.
- Inovio completed enrolment in Phase I of its vaccine trial at the end of April⁷⁷.

[idUSKBN22O1RG](#) and https://www.fiercebiotech.com/biotech/moderna-eyes-early-summer-start-for-phase-3-covid-19-vaccine-trial?mkt_tok and <https://seekingalpha.com/news/3564957-moderna-submits-ind-application-for-phase-2-covidminus-19-study> and

<https://pipelinereview.com/index.php/2020042874463/Vaccines/Moderna-Announces-IND-Submitted-to-U.S.-FDA-for-Phase-2-Study-of-mRNA-Vaccine-mRNA-1273-Against-Novel-Coronavirus.html> and

<https://pipelinereview.com/index.php/2020050174511/Vaccines/Moderna-and-Lonza-Announce-Worldwide-Strategic-Collaboration-to-Manufacture-Moderna-Vaccine-mRNA-1273-Against-Novel-Coronavirus.html>

⁶⁸ <https://pipelinereview.com/index.php/2020050574539/Vaccines/Pfizer-and-BioNTech-Dose-First-Participants-in-the-U.S.-as-Part-of-Global-COVID-19-mRNA-Vaccine-Development-Program.html>

⁶⁹ <https://pipelinereview.com/index.php/2020043074498/Vaccines/UQ-COVID-19-vaccine-shown-to-induce-potent-protective-response-in-pre-clinical-trials.html>

⁷⁰ <https://in.reuters.com/article/health-coronavirus-canada-vaccine/chinese-coronavirus-vaccine-could-be-tested-manufactured-in-canada-idINKBN22O2F4>

⁷¹ https://www.labonline.com.au/content/life-scientist/news/coronavirus-vaccine-candidates-show-promise-in-macaques-31621822?utm_source

⁷² <https://7news.com.au/lifestyle/health-wellbeing/promising-uk-coronavirus-vaccine-is-protective-in-monkey-trial-c-1038920>

⁷³ https://www.fiercepharma.com/pharma/sanofi-chairman-steps-after-ceo-says-u-s-set-to-get-first-covid-19-vaccines?mkt_tok and https://www.fiercepharma.com/pharma/french-president-macron-seeks-meeting-after-sanofi-ceo-s-vaccine-comments?mkt_tok and <https://www.medscape.com/viewarticle/930019?nlid>

⁷⁴ <https://economictimes.indiatimes.com/industry/healthcare/biotech/pharmaceuticals/chinese-drugmaker-in-talks-to-test-virus-vaccine-globally/articleshow/75635105.cms>

⁷⁵ https://www.fiercebiotech.com/biotech/pfizer-biontech-dose-first-u-s-subject-covid-19-vaccine?mkt_tok

⁷⁶ <https://seekingalpha.com/news/3565228-inovio-completes-enrollment-in-covidminus-19-vaccine-study-shares-up-5-premarket>

⁷⁷ <https://seekingalpha.com/news/3565228-inovio-completes-enrollment-in-covidminus-19-vaccine-study-shares-up-5-premarket>

- ZYUS Life Sciences is collaborating with the Vaccine and Infectious Disease Organization-International Vaccine Centre (VIDO-InterVac) at the University of Saskatchewan to test plant produced antigens in a vaccine for COVID-19⁷⁸.
- Johnson & Johnson's goal is to deliver 1 billion doses of coronavirus vaccine in 2021⁷⁹.
- Predictive Oncology, with the acquisition of Soluble Therapeutics, and the subsequent partnership and licensing of a novel nanoparticle vaccine platform recently developed by Dr Daniel Carter, has entered the race to develop a COVID-19 vaccine⁸⁰.
- OSE Immunotherapeutics said on 5 May that its immunologists are working on the development of a prophylactic vaccine against the pandemic virus SARS-CoV-2⁸¹.
- Applied DNA Sciences and Takis Biotech announced that the first injections of their DNA vaccine candidates (against the Spike protein of the SARS-CoV-2 virus) had produced neutralizing antibodies in test animals⁸².
- Belgian manufacturing specialist Univercells company has partnered with German construction firm Excite to produce prefabricated facilities that "will enable rapid mass production and shortened time-to-market" for potential COVID-19 vaccines⁸³.
- Novavax has been awarded \$US 384 million from the Coalition for Epidemic Preparedness Innovations to finance its COVID-19 vaccine testing including phase II, plus preparatory work to scale-up manufacturing⁸⁴.
- The Coalition for Epidemic Preparedness Innovations, CEPI, is investing an initial \$US 3.5 million in a partnering agreement with Clover Biopharmaceuticals AUS Pty Ltd, a wholly-owned subsidiary of Sichuan Clover Biopharmaceuticals, Inc to support Clover Australia to initiate a Phase 1 clinical trial in Australia of its COVID-19 S-Trimer vaccine candidate⁸⁵.
- TriLink BioTechnologies and Imperial College, London, have entered into a partnership in which TriLink will manufacture self-amplifying RNA (saRNA) for COVID-19 vaccine development⁸⁶.

⁷⁸ <https://pipelinereview.com/index.php/2020050874575/Vaccines/ZYUS-Collaborates-with-USasks-VIDO-InterVac-to-Develop-a-Plant-Based-Vaccine-for-COVID-19.html>

⁷⁹ <https://thehill.com/homenews/sunday-talk-shows/497010-johnson-johnson-officer-says-goal-is-to-deliver-1-billion-vaccines>

⁸⁰ <https://pipelinereview.com/index.php/2020050674563/Vaccines/Predictive-Oncology-and-Dr.-Daniel-Carter-Collaborating-to-Develop-a-Potential-COVID-19-Vaccine-Utilizing-Novel-Nanoparticle-Vaccine-Platform-Based-on-NSP-10.html>

⁸¹ <https://pipelinereview.com/index.php/2020050674551/Vaccines/OSE-Immunotherapeutics-Announces-COVID-19-Prophylactic-Vaccine-Program.html>

⁸² <https://pipelinereview.com/index.php/2020050474524/Vaccines/Applied-DNA-and-Takis-Biotech-Announce-the-Production-of-Neutralizing-Antibodies-Against-SARS-CoV-2-After-DNA-Vaccination-in-Animals.html>

⁸³ https://www.fiercepharma.com/manufacturing/univercells-inks-deal-to-produce-prefabricated-vaccine-facilities-for-potential-covid?mkt_tok and
https://www.fiercepharma.com/manufacturing/johnson-johnson-inks-2nd-manufacturing-deal-to-boost-capacity-for-covid-19-vaccine?mkt_tok and https://www.fiercepharma.com/manufacturing/moderna-aims-for-a-billion-covid-19-shots-a-year-lonza-manufacturing-tie-up?mkt_tok and
<https://njbiz.com/catalent-enters-2nd-covid-19-vaccine-manufacturing-partnership/>

⁸⁴ <https://www.fiercepharma.com/vaccines/novavax-scores-cepi-s-largest-award-up-to-384m-to-support-covid-19-vaccine-work>

⁸⁵ <https://pipelinereview.com/index.php/2020042774445/Vaccines/CEPI-Announces-COVID-19-Vaccine-Development-Partnership-With-Clover-Biopharmaceuticals-Australian-Subsidiary.html>

⁸⁶ <https://pipelinereview.com/index.php/2020042774448/Vaccines/TriLink-BioTechnologies-and-Imperial-College-London-Announce-Collaboration-to-Produce-saRNA-for-Covid-19-Vaccine-Development.html>

- UMN Pharma, a group company of Shionogi, is seeking to develop a recombinant protein vaccine for COVID-19 utilizing its Baculovirus Expression Vector System technology⁸⁷.
- Verndari announced at the end of April that it would begin preclinical testing at the University of California, Davis, of a potential COVID-19 vaccine, administered using its patented VaxiPatch, a microneedle array dermal patch⁸⁸.

3. Potential treatments for COVID-19

Recovered plasma, hyperimmune immunoglobulin, and antibodies

- Plasma from COVID-19 survivors is being sought for three purposes: for transfusion with its antibodies into patients who are gravely ill, for producing a concentrated antibody serum (hyperimmune globulin), and for producing a monoclonal antibody therapy (which would extract antibody-producing cells from high-antibody donors and create lab-produced molecules)⁸⁹.
- The [CoV Ig-19 Plasma Alliance](#), led by Takeda and CSL Behring, will work with the US National Institute of Allergy and Infectious Diseases (NIAID) to test the safety and efficacy of hyperimmune immunoglobulins in the treatment of adults with COVID-19, as the basis for a regulatory submission⁹⁰. Takeda says a trial of its treatment TAK-888⁹¹ based on recovered patients' blood could start in July⁹². A successful trial would give all members of the alliance the right to produce the treatment, which will not have patent protection because the technology is known.
- Two randomized, placebo-controlled clinical trials at Johns Hopkins were initiated to test if convalescent blood plasma is effective as prophylaxis against COVID-19⁹³.
- In the US, the Biomedical Advanced Research and Development Authority (BARDA) entered a collaboration with the Mayo Clinic to support an expanded access program⁹⁴ to provide convalescent plasma for patients hospitalized with COVID-19⁹⁵.
- Even if one or more vaccines can be successfully developed for COVID-19 most experts consider they are unlikely to be widely available until 2021, so having therapeutic antibodies available in the interim is considered desirable as a public health measure, and offers a lucrative commercial opportunity⁹⁶.
- A number of teams have cloned antibodies to COVID-19. The antibodies come from people who have recovered from coronavirus. Researchers select the most potent

⁸⁷ <https://pipelinereview.com/index.php/2020042874475/Vaccines/Shionogi-Accelerates-Development-of-Potential-COVID-19-Treatments-and-Vaccine.html>

⁸⁸ <https://pipelinereview.com/index.php/2020042974489/Vaccines/Verndari-Inc.-Begins-Preclinical-Testing-of-COVID-19-Vaccine-at-University-of-California-Davis.html>

⁸⁹ https://www.fiercebiotech.com/medtech/covid-survivors-blood-plasma-a-sought-after-new-commodity?mkt_tok and https://seekingalpha.com/news/3566136-clinical-trial-launched-testing-convalescent-plasma-in-covidminus-19-patients?utm_medium

⁹⁰ https://www.fiercebiotech.com/biotech/takeda-csl-led-alliance-and-nih-to-test-plasma-treatment-summer?mkt_tok

⁹¹ Later designated CoV Ig-19, a plasma-based polyclonal hyperimmune globulin

⁹² <https://www.reuters.com/article/us-health-coronavirus-takeda-pharma-trea/takeda-says-coronavirus-treatment-trial-using-recovered-patients-blood-could-start-in-july-idUSKBN22P3HR>

⁹³ https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7Ba2fe84db-8b89-40b6-930f-1d98f974845c%7D/johns-hopkins-begins-trials-of-blood-plasma-for-covid-19-treatment-prophylaxis?utm_source

⁹⁴ Expanded access programs allow access to pre-approved treatments outside a clinical trial.

⁹⁵ <https://www.medicalcountermeasures.gov/newsroom/2020/mayo-clinic>

⁹⁶ <https://www.biopharmadive.com/news/coronavirus-antibody-drug-trials/577778/>

antibodies and make them into a drug⁹⁷. Regeneron Pharmaceuticals hopes to have its monoclonal antibody available as early as the end of the northern summer but there is no guarantee it could work for COVID-19. Other teams which have cloned antibodies are Vanderbilt, Lilly Pharmaceuticals and Distributed Bio.

- Scientists⁹⁸ have developed a potential treatment that links two nanobodies isolated from a llama to create an antibody that binds to the spike protein on the coronavirus that causes COVID-19, and which they hope may be able to be delivered direct to the lungs. This follows work they began in 2016, concerning SARS-CoV-1 and MERS-CoV. Then they injected a llama with spike proteins from the viruses, and six weeks later, they collected her blood and isolated antibodies that had bound to the protein.
- ProteoGenix has created a Human Immune COVID-19 library to assist the rapid discovery of potent antibodies. The library was developed using blood samples from recovered patients⁹⁹.
- AbCellera announced that the Canadian Government had awarded it over \$C 175 million to increase efforts to discover antibodies to treat COVID-19, and to develop technology and manufacturing infrastructure for antibody therapies¹⁰⁰.
- Junshi Biosciences and Eli Lilly announced on 4 May that they will co-develop therapeutic antibodies for the potential prevention and treatment of COVID-19¹⁰¹.
- Researchers at Utrecht University, Erasmus Medical Center and Harbour BioMed reported on 4 May that they had identified a fully human monoclonal antibody that prevents the SARS-CoV-2 virus from infecting cultured cells¹⁰².
- Sorrento, in collaboration with the Mount Sinai Health System, is aiming to develop an antibody cocktail that binds to three different regions of the SARS-CoV-2 virus. Henry Ji, CEO of Sorrento, said: "If one epitope mutates and one of the antibodies does not do its job anymore, the other two can do the job."¹⁰³
- Scientists at the Icahn School of Medicine at Mount Sinai, in collaboration with GenScript, are developing a synthetic antibody to SARS-CoV-2. The antibody is intended to block the virus from entering human lung cells¹⁰⁴.

⁹⁷ <https://7news.com.au/lifestyle/health-wellbeing/next-big-thing-for-covid-excitement-over-drug-inspired-by-old-treatment-c-1022913>

⁹⁸ from the University of Texas at Austin, the US National Institutes of Health and Ghent University in Belgium

⁹⁹ https://www.labonline.com.au/content/consumables/news/proteogenix-antibody-library-to-help-fight-covid-19-1085664909?utm_source

¹⁰⁰ [https://pipelinereview.com/index.php/2020050474523/Antibodies/AbCellera-Receives-\\$175.6-Million-from-the-Government-of-Canada-to-Discover-Solutions-for-COVID-19-and-Build-a-Manufacturing-Facility-for-Antibody-Drugs.html](https://pipelinereview.com/index.php/2020050474523/Antibodies/AbCellera-Receives-$175.6-Million-from-the-Government-of-Canada-to-Discover-Solutions-for-COVID-19-and-Build-a-Manufacturing-Facility-for-Antibody-Drugs.html)

¹⁰¹ <https://pipelinereview.com/index.php/2020050474528/Antibodies/Lilly-and-Junshi-Biosciences-to-Co-develop-Antibody-Therapies-for-the-Prevention-and-Treatment-of-COVID-19.html> explains that "JS016 is a recombinant fully human monoclonal neutralizing antibody that is specific to the SARS-CoV-2 surface spike protein receptor binding domain and can effectively block the binding of viruses to host cell surface receptor ACE2."

¹⁰² <https://pipelinereview.com/index.php/2020050474521/Antibodies/Utrecht-University-Erasmus-Medical-Center-and-Harbour-BioMed-Researchers-Report-Discovery-of-Antibody-that-Blocks-Novel-Coronavirus-SARS-CoV-2-Infection-in-Cells.html> and <https://www.nature.com/articles/s41467-020-16256-y>

¹⁰³ https://www.fiercebiotech.com/research/sorrento-ventures-into-covid-19-mount-sinai-antibody-pact?mkt_tok see also <https://pipelinereview.com/index.php/2020051074588/Antibodies/Sorrento-And-Mount-Sinai-Health-System-To-Jointly-Develop-COVI-SHIELD-Antibody-Therapy-Targeting-SARS-CoV-2-Infection-COVID-19.html>

¹⁰⁴ https://www.healio.com/endocrinology/bone-mineral-metabolism/news/online/%7Bf47eecec-90ac-4611-91c3-a6e8f9270b16%7D/endocrine-research-spurs-synthetic-antibody-development-for-covid-19?utm_source

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

- On 14 May in San Diego, the first participant enrolled in a clinical trial to evaluate whether the malaria drug hydroxychloroquine, given together with the antibiotic azithromycin, can prevent hospitalization and death from COVID-19¹⁰⁵. The US National Institute of Allergy and Infectious Diseases (NIAID) is sponsoring the trial. The Phase IIb trial will enrol approximately 2,000 adults across the US. Each must have confirmed infection with SARS-CoV-2, the virus that causes COVID-19, and be experiencing fever, cough and/or shortness of breath. Some will be 60 years of age or more, some will have cardiovascular disease or diabetes, some may be living with HIV, and some may be pregnant or breastfeeding.
- This is just one of many trials involving hydroxychloroquine¹⁰⁶. They have been of varying scientific rigour, and have included:
 - i) a small, uncontrolled study by French scientists where they concluded the drug was associated with reduced viral load¹⁰⁷
 - ii) An observational study in 1400 COVID-19 patients in a New York hospital which found the risk of intubation or death was not significantly higher or lower among patients who were given hydroxychloroquine than among those who were not¹⁰⁸.
 - iii) A trial in Brazil testing a high dose in severely ill patients. It was stopped early, reportedly due to toxicity and deaths¹⁰⁹.
- One criticism made of trials of hydroxychloroquine as prophylaxis for COVID-19 is that they “failed to include ECG assessment to either exclude people at the highest risk for possibly developing a life-threatening cardiac arrhythmia or to flag people who achieve a dangerous QTc interval on treatment”¹¹⁰.
- At the beginning of May, hospitals across the US updated their treatment protocols after a warning from the FDA about the risks of prescribing hydroxychloroquine and chloroquine for COVID-19¹¹¹.
- The American College of Physicians advised that current evidence does not support the use of chloroquine or hydroxychloroquine, alone or in combination with azithromycin, as prophylaxis or therapy COVID-19.
- One of hydroxychloroquine's known potential toxic effects is on the retina¹¹².
- Japan approved Gilead's antiviral drug remdesivir to treat COVID-19¹¹³. By then it had emergency use authorization for use in COVID-19 in the US¹¹⁴. The US National

¹⁰⁵ <https://www.nih.gov/news-events/news-releases/nih-begins-clinical-trial-hydroxychloroquine-azithromycin-treat-covid-19> See also [NCT04358068](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7235068/).

¹⁰⁶ <https://www.bmjjournals.org/content/369/bmjm1849>; <https://www.bmjjournals.org/content/369/bmjm1844>; <https://jamanetwork.com/journals/jama/fullarticle/2766117>

¹⁰⁷ Philippe Gautret et al., “Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial”, *International Journal of Antimicrobial Agents*, online 20 March 2020. <https://doi.org/10.1016/j.ijantimicag.2020.105949>

¹⁰⁸ <https://www.cidrap.umn.edu/news-perspective/2020/05/study-finds-no-hydroxychloroquine-effect-death-severe-covid-19>

¹⁰⁹ <https://www.medscape.com/viewarticle/929499?nlid>

¹¹⁰ <https://www.medscape.com/viewarticle/930382>

¹¹¹ <https://www.medscape.com/viewarticle/929608?nlid> see also https://www.medpagetoday.com/infectiousdisease/covid19/86246?utm_source and https://www.healio.com/cardiology/practice-management/news/print/cardiology-today/%7Be1f6ce13-e57b-442f-b14e-ee4d02e017e0%7D/covid-19-and-the-heart-knowledge-evolving-by-the-hour?utm_source

¹¹² <https://www.medscape.com/viewarticle/927954>

¹¹³ https://www.fiercepharma.com/pharma-asia/fiercepharmaasia-gilead-s-remdesivir-japan-nod-licensing-talks-lilly-junshi-covid-19?mkt_tok

¹¹⁴ <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>

Institute of Allergy and Infectious Diseases had stopped its placebo-controlled remdesivir study early based on positive effects from the drug¹¹⁵.

- Roche and Gilead Sciences have launched a Phase III clinical trial in severe COVID-19 pneumonia, testing Roche's Actemra/ RoActemra with Gilead's remdesivir¹¹⁶.
- On 8 May the US National Institutes of Health said¹¹⁷ it has started a clinical study to test a combination remdesivir and anti-inflammatory treatment baricitinib¹¹⁸ in more than 1,000 COVID-19 patients in the US.
- In a pilot study, twelve adult patients with moderate COVID-19 were given a daily dose of the rheumatoid arthritis drug baricitinib, together with an anti-HIV drug combination of lopinavir and ritonavir, for a fortnight. Another twelve were given only lopinavir and ritonavir. The first group appeared to fare better, but the study design faced criticism¹¹⁹.
- An open-label, randomised Phase II trial has assessed the efficacy and safety of combined interferon beta-1b, lopinavir–ritonavir, and ribavirin as anti-viral therapy in COVID-19¹²⁰. The authors' interpretation of their findings was that "early triple antiviral therapy was safe and superior to lopinavir–ritonavir alone in alleviating symptoms and shortening the duration of viral shedding and hospital stay in patients with mild to moderate COVID-19. Future clinical study of a double antiviral therapy with interferon beta-1b as a backbone is warranted".

¹¹⁵ https://www.fiercepharma.com/pharma/gilead-may-struggle-to-expand-remdesivir-s-market-to-moderately-ill-covid-19-patients?mkt_tok and https://www.fiercepharma.com/pharma/gilead-to-start-selling-remdesivir-coming-weeks-expects-multi-year-commercial-opportunity?mkt_tok and <https://www.medpagetoday.com/infectiousdisease/covid19/86582?xid> and <https://www.biopharmadive.com/news/gilead-coronavirus-license-global-generic/577483/> and <https://pipelinereview.com/index.php/2020042974487/Small-Molecules/Gilead-Sciences-Statement-on-Positive-Data-Emerging-From-National-Institute-of-Allergy-and-Infectious-Diseases-Study-of-Investigational-Antiviral-Remdesivir-for-COVID-19.html> and <https://pipelinereview.com/index.php/2020042974488/Small-Molecules/Gilead-Announces-Results-From-Phase-3-Trial-of-Investigational-Antiviral-Remdesivir-in-Patients-With-Severe-COVID-19.html> and <https://pipelinereview.com/index.php/2020050274517/Small-Molecules/Gileads-Investigational-Antiviral-Remdesivir-Receives-U.S.-Food-and-Drug-Administration-Emergency-Use-Authorization-for-the-Treatment-of-COVID-19.html> and <https://www.biopharmadive.com/news/gilead-license-remdesivir-generic-makers/577876/> and https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7B4042cbe2-9217-4247-b1f4-d22ae3f9179d%7D/remdesivir-is-the-best-that-we-have-right-now-for-covid-19?utm_source and https://www.healio.com/infectious-disease/emerging-diseases/news/online/%7B30f206a4-1037-4975-82bd-7936bd7714e3%7D/faucion-remdesivir-for-covid-19-this-will-be-the-standard-of-care?utm_source and <https://www.fiercebiotech.com/biotech/gilead-s-remdesivir-speeds-recovery-1st-controlled-trial-readout-but-it-s-no-silver-bullet> and Yang W, et al. *Lancet*. 2020;doi:10.1016/S0140-6736(20)31022-9. and https://www.fiercepharma.com/manufacturing/gilead-talks-to-expand-covid-19-hopeful-remdesivir-supply-chains-outside-partner?mkt_tok

¹¹⁶ <https://www.pharmalive.com/roche-and-gilead-launch-covid-19-trial/>

¹¹⁷ <https://www.reuters.com/article/us-health-coronavirus-remdesivir/nih-begins-study-of-remdesivir-with-anti-inflammatory-drug-to-treat-covid-19-idUSKBN22K2M7> and <https://www.nih.gov/news-events/news-releases/nih-clinical-trial-testing-antiviral-remdesivir-plus-anti-inflammatory-drug-baricitinib-covid-19-begins>

¹¹⁸ marketed as Olumiant by Eli Lilly and Co

¹¹⁹ Fabrizio Cantini, et al., "Baricitinib therapy in COVID-19: A pilot study on safety and clinical impact", *Infection*, published 23 April 2020. DOI:<https://doi.org/10.1016/j.jinf.2020.04.017> reported in https://www.the-scientist.com/news-opinion/ai-is-screening-billions-of-molecules-for-coronavirus-treatments-67520?utm_campaign

¹²⁰ [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31042-4/fulltext?dgcid](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31042-4/fulltext?dgcid) . For comment, see [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31101-6/fulltext?dgcid](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31101-6/fulltext?dgcid) see also <https://www.medscape.com/viewarticle/930336>

- The FDA authorized Caladrius Biosciences to begin its clinical trial of its drug CLBS119 for repair of COVID-19-induced lung damage¹²¹, in patients with severe infection who had respiratory failure.
- Novartis and Incyte are testing their JAK inhibitor Jakafi in a second Phase III trial for COVID-19 patients with acute respiratory distress syndrome (ARDS). The trial, in US patients who have needed ventilators, is testing Jakafi's safety and efficacy over standard of care¹²².
- Israeli company Pluristem Therapeutics has been awarded up to €50 million from the European Investment Bank to take its coronavirus cell therapy to Phase III¹²³.
- Exvastat (Ireland) Ltd has a 3.6 million euro grant from the Innovative Medicines Initiative to produce a reformulated version of the drug imatinib and test it in critically ill patients for the treatment of Acute Respiratory Distress Syndrome (ARDS) induced by COVID-19¹²⁴.
- Roche's Genentech launched a new study of Actemra for COVID-19 pneumonia in hospitalized patients from underserved and minority populations, while Fujifilm's Avigan was reported as having failed to show clear efficacy in mild and asymptomatic patients¹²⁵. Avigan (favipiravir) is now being trialled in India¹²⁶.
- A small retrospective study suggested the arthritis drug Anakinra (an interleukin-1 blocker) "improved respiratory symptoms and reduced signs of cytokine storm in nearly three-quarters of patients with COVID-19, acute respiratory distress and hyperinflammation"¹²⁷.
- Atea Pharmaceuticals will conduct a Phase II trial of its oral purine nucleotide prodrug¹²⁸ in hospitalized patients with moderate COVID-19. It is designed to interfere with viral RNA polymerase and inhibit replication¹²⁹.
- Amgen announced its anti-inflammatory drug Otezla will be trialled to study its effectiveness in preventing respiratory distress from COVID-19¹³⁰.

Investigational new treatments

- Vicore Pharma Holding AB received approval from the UK regulatory agency of its clinical trial application for a Phase II study of VP01 (C21) in patients with COVID-19. The trial, named ATTRACT (Angiotensin II Type Two Receptor Agonist Covid-19 Trial), is in hospitalized patients treated with basic respiratory care, but not

¹²¹ 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

¹²² https://www.fiercepharma.com/pharma/novartis-incyte-will-take-jakafi-into-2nd-trial-for-covid-19-patients-ventilators?mkt_tok

¹²³ <https://www.labiatech.eu/gene-cell-therapy/pluristem-covid-19-cell-therapy/>

¹²⁴ http://www.pharmatimes.com/news/exvastat_wins_3.6m_euro_grant_for_covid-19_trial_1340323?utm_source

¹²⁵ https://www.fiercepharma.com/pharma/coronavirus-tracker-hydroxychloroquine-fails-va-study-fda-approves-at-home-sample-collection?mkt_tok

¹²⁶ <https://www.reuters.com/article/us-glenmark-pharms-stocks/indias-glenmark-to-conduct-trials-for-potential-covid-19-drug-shares-jump-idUSKBN22C0IZ>

¹²⁷ <https://www.medscape.com/viewarticle/930311?nlid>

¹²⁸ A prodrug, once administered, is metabolized into a pharmacologically active drug. The use of a prodrug may increase the efficiency of absorption and distribution.

¹²⁹ https://www.fiercebiotech.com/biotech/atea-raises-215m-to-support-midphase-covid-19-antiviral-trial?mkt_tok

¹³⁰ https://www.fiercepharma.com/pharma/amgen-s-anti-inflammatory-otezla-makes-its-foray-into-covid-19-as-strong-sales-lift-q1?mkt_tok

mechanical ventilation. VP01 activates the “protective arm” of the renin angiotensin system¹³¹.

- On 4 May, Aridis Pharmaceuticals enrolled its first COVID-19 patient in the ongoing Phase III clinical trial of AR-301, a monoclonal antibody against *S. aureus* induced pneumonia in patients who were already on mechanical ventilators¹³².
- Molecular Partners AG announced on 7 May the satisfactory completion of *in vitro* potency assessments of its DARPin® candidates, a new class of custom-built protein therapeutics targeting live, replicating coronavirus SARS-CoV-2¹³³.
- Vir Biotechnology and Alnylam Pharmaceuticals on 4 May announced the selection as a development candidate of VIR-2703/ ALN-COV, an investigational RNAi therapeutic targeting the SARS-CoV-2 genome¹³⁴.
- Inhaled nitric oxide has been reported anecdotally as helpful in COVID-19 oxygenation¹³⁵.
- ILC Therapeutics, with the University of Oxford, is investigating if evasins – molecules derived from ticks – could offer a new treatment option for COVID_19 patients with serious lung damage¹³⁶.
- Romark is initiating two clinical trials of NT-300 (nitazoxanide extended-release tablets) for prevention of viral respiratory illnesses including COVID-19¹³⁷.

Other therapies

- Plasmapheresis uses filters to bind either the virus itself, or selected components of viral replication, and returns the “cleansed” plasma to the patient¹³⁸.

4. Managing the pandemic

- Researchers reported early in May¹³⁹ that a genetic study of virus samples from more than 7,500 COVID-19 sufferers showed the disease spread rapidly around the world after it emerged in China during the last quarter of 2019.
- Merck and the Institute for Systems Biology announced a research collaboration to investigate and define the molecular mechanisms of SARS-CoV-2 infection and

¹³¹ <https://pipelinereview.com/index.php/2020042974486/Small-Molecules/Vicore-Pharma-gets-regulatory-approval-to-start-phase-II-clinical-trial-with-VP01-C21-in-patients-with-COVID-19-SARS-CoV-2-infection.html>

¹³² <https://pipelinereview.com/index.php/2020050474533/Antibodies/Aridis-Pharmaceuticals-Enrolls-Its-First-COVID-19-Patient-in-Ongoing-Phase-3-AR-301-Clinical-Trial-in-Ventilator-Associated-Pneumonia-VAP.html>

¹³³ <https://pipelinereview.com/index.php/2020050774568/Proteins-and-Peptides/Molecular-Partners-Confirms-Ultra-Potent-Inhibition-of-SARS-CoV-2-Live-Virus-by-Anti-COVID-19-DARPin-Candidates.html>

¹³⁴ <https://pipelinereview.com/index.php/2020050474531/DNA-RNA-and-Cells/Vir-and-Alnylam-Identify-RNAi-Therapeutic-Development-Candidate-VIR-2703-ALN-COV-Targeting-SARS-CoV-2-for-the-Treatment-of-COVID-19.html>

¹³⁵ <https://www.medscape.com/viewarticle/930412?nlid> reporting on Roham T Zamanian et al., “Outpatient Inhaled Nitric Oxide in a Patient with Vasoreactive IPAH and COVID-19 Infection”, *American Journal of Respiratory and Critical Care Medicine*, accepted 5 May 2020.

<https://doi.org/10.1164/rccm.202004-0937LE>

¹³⁶ http://www.pharmatimes.com/news/researchers_assessing_use_of_tick_molecule_for_covid-19_1340147?utm_source

¹³⁷ <https://pipelinereview.com/index.php/202004277446/Small-Molecules/Romark-Initiates-Phase-3-Clinical-Trials-Of-NT-300-For-COVID-19.html>

¹³⁸ <https://www.medscape.com/viewarticle/929182?nlid>

¹³⁹ <https://www.medscape.com/viewarticle/930107>

identify targets for medicines and vaccines. The US Biomedical Advanced Research and Development Authority (BARDA) will provide funding support¹⁴⁰.

- Two significant scientific journals, *BMJ* and *Nature*, have criticised¹⁴¹ the quality of many clinical trials in the race to find new drugs and diagnostics in the pandemic.
- Chinese researchers reported that asymptomatic individuals who test positive for the virus that causes COVID-19 can carry the virus for several weeks¹⁴².
- A Chinese study found the virus in the semen of severely infected men, raising the question of whether COVID-19 could be sexually transmitted¹⁴³.
- A small study suggests patients may continue to shed the SARS-CoV-2 virus for up to six weeks after symptoms emerge¹⁴⁴.
- Researchers reported that the strain of the coronavirus now dominant globally is more contagious than the strains which spread earlier¹⁴⁵.
- An online survey launched by the US National Institutes of Health-supported [Rare Diseases Clinical Research Network \(RDCRN\)](#) is investigating how the current pandemic is affecting people with rare diseases, their families and their caregivers¹⁴⁶.
- Researchers have searched for traces of the SARS-CoV-2 virus in some wastewater treatment plants¹⁴⁷.
- With so many severely ill COVID-19 patients having previously existing comorbidities, treating physicians have to be aware of possible interactions between experimental medications for the pandemic virus with an existing drug regimen¹⁴⁸.
- One issue not yet resolved is whether a person who recovers from COVID-19 has immunity against further infection, and if so, how long this will last¹⁴⁹.
- The US Centers for Disease Control and Prevention (CDC) is undertaking a nationwide study of up to 325,000 people to track how COVID-19 is spreading across the country into 2021 and beyond¹⁵⁰.

¹⁴⁰ <https://pipelinereview.com/index.php/2020042774442/More-News/Merck-and-Institute-for-Systems-Biology-Collaborate-to-Define-Molecular-Mechanisms-of-SARS-CoV-2-Infection-and-Identify-Potential-Prognostic-Biomarkers.html>

¹⁴¹ https://www.fiercebiotech.com/cro/bmj-nature-warn-against-sabotaging-covid-19-response-poor-and-chaotic-trials?mkt_tok

¹⁴² Yanfeng Pan et al., “Epidemiological and Clinical Characteristics of 26 Asymptomatic Severe Acute Respiratory Syndrome Coronavirus 2 Carriers”, *The Journal of Infectious Diseases*, 22 April 2020. <https://doi.org/10.1093/infdis/jiaa205> reported in <https://www.medscape.com/viewarticle/929950?nlid> see also <https://blogs.bmj.com/bmj/2020/05/04/how-much-is-covid-19-spreading-via-asymptomatic-versus-symptomatic-infections/>

¹⁴³ <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/virus-found-in-semen-of-covid-19-survivors-&dash-is-it-sexually-transmittable-757467.html> and <https://www.medscape.com/viewarticle/930127>

¹⁴⁴ <https://www.medscape.com/viewarticle/929519?nlid>

¹⁴⁵ <https://www.latimes.com/california/story/2020-05-05/mutant-coronavirus-has-emerged-more-contagious-than-original> reporting on B Korber et al., “Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2”, *bioRxiv*, 30 April, 2020. See also <https://www.cnbc.com/2020/05/05/the-coronavirus-mutated-and-appears-to-be-more-contagious-now-new-study-finds.html>

¹⁴⁶ <https://www.nih.gov/news-events/news-releases/nih-supported-research-survey-examine-impact-covid-19-rare-diseases-community>

¹⁴⁷ https://www.the-scientist.com/news-opinion/countries-begin-large-scale-screening-for-sars-cov-2-in-sewage-67535?utm_campaign

¹⁴⁸ <https://www.medscape.com/viewarticle/930265>

¹⁴⁹ https://www.healio.com/primary-care/infectious-diseases/news/online/%7B84140e88-db61-428d-bbfd-fdf0e2c0e3ac%7D/qa-researchers-hope-new-covid-19-cohort-study-will-be-a-game-changer?utm_source_and

https://www.medpagetoday.com/infectiousdisease/covid19/86171?utm_source

¹⁵⁰ <https://www.reuters.com> doi: <https://doi.org/10.1101/2020.04.29.069054>

- The US National Institutes of Health initiated a study to identify the infection rate of COVID-19 in children and their families in the US¹⁵¹.
- A study of Chinese patients reports that children are as likely as adults to be infected by COVID-19¹⁵².
- Researchers are trialling the effectiveness of the interferon in stopping outbreaks of COVID-19 by reducing the infectiousness of people carrying the SARS-CoV-2 virus¹⁵³.

5. Other news

- Australia's Therapeutic Goods Administration has approved the nanobody therapy caplacizumab (Cablivi) for acquired thrombotic thrombocytopenic purpura (aTTP)¹⁵⁴.
- [Alexion Pharmaceuticals, Inc.](#) is to acquire [Portola Pharmaceuticals, Inc.](#) Portola's commercialized drug Andexxa® [coagulation factor Xa (recombinant), inactivated-zhzo], marketed as Ondexxya® in Europe, is a Factor Xa inhibitor reversal agent, and has demonstrated effectiveness in reversing the anticoagulant effects of Factor Xa inhibitors rivaroxaban and apixaban in severe and uncontrolled bleeding¹⁵⁵.
- The COVID-19 pandemic has caused healthcare systems to stock up on blood-thinning drugs¹⁵⁶.
- Roche [has launched](#) Roche v-TAC, a digital diagnostic solution that yields arterial blood gas values from patients with respiratory or metabolic abnormalities via a less invasive venous puncture, by using a digital algorithm¹⁵⁷.
- A retrospective cohort study found that starting pulmonary rehabilitation within 90 days after hospitalization for chronic obstructive pulmonary disease was associated with significantly lower mortality at year one¹⁵⁸.
- Akebia Therapeutics announced success in the first of two Phase III programs trialling its anaemia drug vadadustat in adults with damaged kidneys¹⁵⁹.
- Researchers from Japan¹⁶⁰ developed "a method that uses a high-throughput imaging process to capture thousands of various blood clot images". They then "used a convolutional neural network to identify key distinctions in their makeup". Keisuke Goda¹⁶¹ said: "Using this new tool may uncover the characteristics of different types of clots that were previously unrecognized by humans, and enable the

[/article/us-health-coronavirus-testing-cdc-exclus/exclusive-cdc-plans-sweeping-covid-19-antibody-study-in-25-metropolitan-areas-idUSKBN22U2TZ](#)

¹⁵¹ <https://www.reuters.com/article/uk-health-coronavirus-us-children/u-s-starts-study-to-find-covid-19-infection-rate-in-children-idUSKBN22G1SH>

¹⁵² <https://www.medscape.com/viewarticle/930071>

¹⁵³ https://www.labonline.com.au/content/life-scientist/news/drug-trial-to-make-covid-19-patients-less-infectious-81760250?utm_source

¹⁵⁴ https://thelimbic.com/haematology/caplacizumab-approved-for-acquired-thrombotic-thrombocytopenic-purpura/?mc_cid

¹⁵⁵ <https://pipelinereview.com/index.php/2020050574540/More-News/Alexion-to-Acquire-Portola.html> and https://www.fiercepharma.com/pharma/alexion-bags-portola-for-cool-1-4b-but-anticoagulant-andexxa-worth-it?mkt_tok

¹⁵⁶ https://www.fiercepharma.com/pharma/covid-drives-huge-demand-for-bristol-myers-blood-thinner-eliquis-but-could-dampen-mid-year?mkt_tok

¹⁵⁷ http://www.pharmatimes.com/news/roche_launches_new_blood_gas_digital_solution_1340324?utm_source

¹⁵⁸ https://www.healio.com/pulmonology/copd/news/online/%7Badb337d6-3f86-455c-8e21-d0cd0bd32241%7D/pulmonary-rehab-after-copd-hospitalization-lowers-mortality-risk?utm_source

¹⁵⁹ <https://www.biopharmadive.com/news/akebia-anemia-kidney-disease-fibrogen-data/577374/>

¹⁶⁰ <https://www.healthimaging.com/topics/advanced-visualization/machine-learning-imaging-differences-blood-clots>

¹⁶¹ A professor at the University of Tokyo's Department of Chemistry

diagnosis of clots caused by combinations of clotting agents. Information about the causes of clots can help researchers and medical doctors evaluate the effectiveness of anti-clotting drugs and choose the right treatment, or combination of treatments, for a particular patient."

- Researchers have warned against off-label use of direct oral anticoagulants in patients with left ventricular thrombi, as they carry a higher risk of stroke or systemic embolism than warfarin¹⁶².
- Pfizer and Valneva have announced a partnership to develop and commercialize Valneva's Lyme disease vaccine candidate VLA15, which is currently in Phase II clinical trials¹⁶³.
- Researchers have identified a microbe that prevents mosquitoes from being infected with malaria¹⁶⁴.
- So far this year, the number of Q fever cases reported in Australia has been significantly lower than it was in 2019¹⁶⁵.
- Chimerix has FDA clearance for a rolling submission of its New Drug Application for the approval of brincidofovir as a medical countermeasure for smallpox¹⁶⁶.
- At the American Society of Gene and Cell Therapy Conference Inovio and GeneOne Life Science announced interim data from a Phase I/Ia trial of DNA vaccine INO-4700 (GLS-5300) for MERS coronavirus (MERS-CoV). They reported that vaccine recipients demonstrated strong antibody and T cell immune responses¹⁶⁷.
- ViiV Healthcare's trial evaluating a long-acting injection for HIV prevention was halted early due to high levels of efficacy¹⁶⁸.
- Australian researchers have found that the "influenza A virus can kill key white blood cells and hide among them like a Trojan Horse to aid its spread in the body"¹⁶⁹.

¹⁶² https://thelimbic.com/haematology/caution-on-off-label-doac-use-in-lv-thrombus/?utm_source

¹⁶³ <https://www.rdworlondonline.com/130-million-pfizer-and-valneva-partnership-to-co-develop-lyme-disease-vaccine/>

¹⁶⁴ Jeremy K Herren, "A microsporidian impairs *Plasmodium falciparum* transmission in *Anopheles arabiensis* mosquitoes", *Nature Communications* volume 11, article number 2187 (2020) 4 May 2020 <https://www.nature.com/articles/s41467-020-16121-y> reported in <https://www.bbc.com/news/health-52530828>

¹⁶⁵ <https://www.abc.net.au/news/rural/2020-05-01/dramatic-drop-q-fever-cases/12199922>

¹⁶⁶ <https://pipelinereview.com/index.php/2020042974483/Small-Molecules/Chimerix-Receives-FDA-Clearance-for-Rolling-Submission-of-New-Drug-Application-for-Brincidofovir-as-a-Medical-Countermeasure-for-Smallpox.html>

¹⁶⁷ <https://pipelinereview.com/index.php/2020042974479/Vaccines/INOVIO-and-GeneOne-Life-Science-Report-Positive-Phase-1/2a-Clinical-Data-With-DNA-Vaccine-INO-4700-for-MERS-Coronavirus-at-the-American-Society-of-Gene-Cell-Therapy-ASGCT-Confer.html>

¹⁶⁸ http://www.pharmatimes.com/news/viiv_hiv_prevention_trial_stopped_early_on_efficacy_1340441

¹⁶⁹ https://www.labonline.com.au/content/life-scientist/news/influenza-and-the-trojan-horse-effect-1357851642?utm_source