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]](#footnote-1).
* Others suggest that the presentation of ARDS in critically ill COVID-19 differs from the typical presentation of ARDS[[2]](#footnote-2).
* 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 abnormality[[3]](#footnote-3).
* 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]](#footnote-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]](#footnote-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]](#footnote-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 mortality[[7]](#footnote-7).
  + Studies have continued of the relationship between ACE inhibitors and COVID-19[[8]](#footnote-8).
  + A brief UK report identified stroke as a COVID-19 complication, including breakthrough strokes despite therapeutic anticoagulation[[9]](#footnote-9).
  + 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 discharge[[10]](#footnote-10).
  + 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]](#footnote-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](https://storage.googleapis.com/videos-for-inspirion/C-19-ACS-video.mp4) against standard care for 30-day all-cause mortality[[12]](#footnote-12).
  + 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 2019[[13]](#footnote-13).

Neurological symptoms

* + Doctors in Detroit [describe](https://www.medscape.com/viewarticle/928069) the first case of acute necrotizing haemorrhagic encephalopathy presumed to be linked with COVID-19[[14]](#footnote-14).
  + Two further neurologic conditions, both rare, have arisen in hospitalized COVID-19 patients[[15]](#footnote-15).

The cytokine storm

* + Cytokine storm is one of the factors thought to be associated with myocardial injury in COVID-19[[16]](#footnote-16).
  + One therapy that has been suggested to inhibit inflammation is the hormone progesterone[[17]](#footnote-17).
  + GSK is trialling its pipeline monoclonal antibody otilimab as a therapy for COVID-19 patients hit with a cytokine storm[[18]](#footnote-18).

Suggested disease modifying factors

* + Researchers reported that haematological and lung cancers appear to be associated with poor COVID-19 outcomes[[19]](#footnote-19).
  + It appears that patients with common haemoglobin disorders may be at risk of COVID-19 complications[[20]](#footnote-20).
  + An analysis suggests that the younger a COVID-19 patient in ICU is, the more obese that patient is likely to be[[21]](#footnote-21).
  + 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]](#footnote-22)
  + Dr Shailendra Singh[[23]](#footnote-23) 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]](#footnote-24).
  + A US study confirmed experience elsewhere that people with underlying health conditions are at higher risk for more severe COVID-19[[25]](#footnote-25).
  + Genetics are thought to have an impact on COVID-19 severity[[26]](#footnote-26).
  + Researchers have reported that the risk of COVID-19 in expectant mothers to them and their unborn infants is not insignificant[[27]](#footnote-27).

COVID-19 in paediatric patients

* + That COVID-19 in children can trigger a condition resembling Kawasaki disease is widely accepted as plausible[[28]](#footnote-28).
  + The US Senate was told[[29]](#footnote-29) 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](https://www.healio.com/pediatrics/emerging-diseases/news/online/%7B4a390309-ea18-441c-bcf0-6cbf55d30ea4%7D/does-sars-cov-2-cause-kawasaki-disease-in-children).
  + 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-19[[30]](#footnote-30).
  + A US study found that eleven percent of children hospitalized with COVID-19 required care in the paediatric ICU[[31]](#footnote-31).

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-19[[32]](#footnote-32).
  + Early research suggests that patients with haemoglobin disorders are more vulnerable to COVID-19[[33]](#footnote-33).
  + The International Society on Thrombosis and Haemostasis issued interim guidance on coagulopathy in patients with COVID-19[[34]](#footnote-34).
  + 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 factors[[35]](#footnote-35).
  + Researchers are investigating whether a greater susceptibility to psychosis is a potential secondary, long-term impact of COVID-19 infection[[36]](#footnote-36).
  + COVID-19 has been disproportionately affecting obese people in the US[[37]](#footnote-37).
  + As the pandemic has progressed, a number of cutaneous signs of infection have been recognised[[38]](#footnote-38).
  + 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 care[[39]](#footnote-39).
  + 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 diabetes[[40]](#footnote-40).
  + Conjunctivitis was the only presenting system of COVID-19 in five patients in Italy[[41]](#footnote-41).
  + A review suggested that bacterial or fungal co-infection is not common in patients with coronavirus infections[[42]](#footnote-42).
  + Researchers suggested that biomarkers for inflammation and thrombosis in critically ill COVID-19 patients may predict mortality[[43]](#footnote-43).
  + 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-19[[44]](#footnote-44).
  + Scientists found that receptors fir SARS-CoV-2 are present in a wide range of human cells[[45]](#footnote-45).
  + The American College of Rheumatology released [guidance](https://onlinelibrary.wiley.com/doi/10.1002/art.41301) for the rheumatology community on effectively caring for people with rheumatic diseases during the pandemic[[46]](#footnote-46).
  + 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 Society[[47]](#footnote-47).

Testing

* + The Infectious Diseases Society of America released diagnostic recommendations for both symptomatic and asymptomatic patients with COVID-19[[48]](#footnote-48).
  + 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 virus[[49]](#footnote-49). Roche’s test relies on an intravenous blood draw rather than a finger prick[[50]](#footnote-50).
  + On 8 May, the FDA published results from the first round of COVID-19 antibody diagnostics to have their accuracy assessed by federal laboratories[[51]](#footnote-51).
  + 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 Europe[[52]](#footnote-52).
  + A study[[53]](#footnote-53) 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-19[[54]](#footnote-54).
  + On 8 May the FDA a saliva-based coronavirus test for home use[[55]](#footnote-55).
  + On 9 May the FDA authorised its first antigen test for rapid point-of-care screening[[56]](#footnote-56).
  + In mid-May the American Medical Association issued guidance for physicians on the potential uses and limitations of serological testing (antibody testing)[[57]](#footnote-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]](#footnote-58).
  + 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]](#footnote-59).
  + On 29 April, the US National Institutes of Health announced an initiative to speed up innovation, development and commercialization of COVID-19 testing technologies[[60]](#footnote-60). NIH is working with the FDA, the Centers for Disease Control and Prevention and the Biomedical Advanced Research and Development Authority (BARDA).

1. 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-19[[61]](#footnote-61).
   * 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 stage[[62]](#footnote-62).
   * 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]](#footnote-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 2020[[64]](#footnote-64).
   * The CEO of Novartis said a vaccine may take until the end of 2021 to reach patients[[65]](#footnote-65).
   * 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]](#footnote-66).
   * In the first half of May, Moderna received fast-track designation from the FDA for its investigational COVID-19 vaccine, mRNA-1273[[67]](#footnote-67).
   * Two German biotechs, CureVac and Pfizer-partnered BioNTech, are also using mRNA technology for their COVID-19 vaccines[[68]](#footnote-68).
   * 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 virus[[69]](#footnote-69).
   * A report on 13 May[[70]](#footnote-70) 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 strains[[71]](#footnote-71). US and UK researchers announced in [Science Advances](https://advances.sciencemag.org/content/early/2020/04/30/sciadv.aba8399) that a single-dose vaccine has been shown to protect rhesus macaques from MERS-CoV [[72]](#footnote-72).
   * The French President sought a meeting with Sanofi[[73]](#footnote-73) 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 location[[74]](#footnote-74).
   * Pfizer and BioNT began dosing US participants in a vaccine trial in early May[[75]](#footnote-75). Volunteers in Germany had received the RNA vaccine in a Phase I/II trial in April[[76]](#footnote-76).
   * Inovio completed enrolment in Phase I of its vaccine trial at the end of April[[77]](#footnote-77).
   * 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-19[[78]](#footnote-78).
   * Johnson & Johnson’s goal is to deliver 1 billion doses of coronavirus vaccine in 2021[[79]](#footnote-79).
   * 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 vaccine[[80]](#footnote-80).
   * OSE Immunotherapeutics said on 5 May that its immunologists are working on the development of a prophylactic vaccine against the pandemic virus SARS-CoV-2[[81]](#footnote-81).
   * 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 animals[[82]](#footnote-82).
   * Belgian manufacturing specialist Univercells company has [partnered](https://www.univercells.com/newsroom/exyte-univercells-technologies-partner-for-vaccine-production-plants-covid-19-pandemic/) with German construction firm Excyte to produce prefabricated facilities that "will enable rapid mass production and shortened time-to-market" for potential COVID-19 vaccines[[83]](#footnote-83).
   * 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 manufacturing[[84]](#footnote-84).
   * 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 candidate[[85]](#footnote-85).
   * TriLink BioTechnologies and Imperial College, London, have entered into a partnership in which TriLink will manufacture self-amplifying RNA (saRNA) for COVID-19 vaccine development[[86]](#footnote-86).
   * UMN Pharma, a group company of Shionogi, is seeking to develop a recombinant protein vaccine for COVID-19 utilizing its Baculovirus Expression Vector System technology[[87]](#footnote-87).
   * 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 patch[[88]](#footnote-88).
2. 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]](#footnote-89).
  + The [CoVIg-19 Plasma Alliance](https://www.covig-19plasmaalliance.org/en-us#recruitment), 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 submission[[90]](#footnote-90). Takeda says a trial of its treatment TAK-888[[91]](#footnote-91) based on recovered patients’ blood could start in July[[92]](#footnote-92). 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-19[[93]](#footnote-93).
  + In the US, the Biomedical Advanced Research and Development Authority (BARDA) entered a collaboration with the Mayo Clinic to support an expanded access program[[94]](#footnote-94) to provide convalescent plasma for patients hospitalized with COVID-19[[95]](#footnote-95).
  + 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 opportunity[[96]](#footnote-96).
  + 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 antibodies and make them into a drug[[97]](#footnote-97). 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.
  + Scientists[[98]](#footnote-98) 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](https://www.proteogenix.science/) 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 patients[[99]](#footnote-99).
  + 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 therapies[[100]](#footnote-100).
  + Junshi Biosciences and Eli Lilly announced on 4 May that they will co-develop therapeutic antibodies for the potential prevention and treatment of COVID-19[[101]](#footnote-101).
  + 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 cells[[102]](#footnote-102).
  + 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]](#footnote-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 cells[[104]](#footnote-104).

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-19[[105]](#footnote-105). 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 hydroxychloroquine[[106]](#footnote-106). They have been of varying scientific rigour, and have included:
    1. a small, uncontrolled study by French scientists where they concluded the drug was associated with reduced viral load[[107]](#footnote-107)
    2. 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 not[[108]](#footnote-108).
    3. A trial in Brazil testing a high dose in severely ill patients. It was stopped early, reportedly due to toxicity and deaths[[109]](#footnote-109).
  + 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]](#footnote-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-19[[111]](#footnote-111).
  + **The American College of Physicians** advised that current evidence [does not support](https://www.acponline.org/acp-newsroom/acp-evidence-does-not-support-chloroquine-or-hcq-use-alone-or-in-combination-with-azithromycin-as) 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 retina[[112]](#footnote-112).
  + Japan approved Gilead’s antiviral drug remdesivir to treat COVID-19[[113]](#footnote-113). By then it had emergency use authorization for use in COVID-19 in the US[[114]](#footnote-114). The US National Institute of Allergy and Infectious Diseases had stopped its placebo-controlled **remdesivir** study early based on positive effects from the drug[[115]](#footnote-115).
  + [Roche](https://www.biospace.com/employer/547147/roche/) and [Gilead Sciences](https://www.biospace.com/employer/399098/gilead-sciences-inc-/) have launched a Phase III clinical trial in severe COVID-19 pneumonia, testing Roche’s Actemra/ RoActemra with Gilead’s remdesivir[[116]](#footnote-116).
  + On 8 May the US National Institutes of Health said[[117]](#footnote-117) it has started a clinical study to test a combination remdesivir and anti-inflammatory treatment baricitinib[[118]](#footnote-118) 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 criticism[[119]](#footnote-119).
  + 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-19[[120]](#footnote-120). 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”.
  + The FDA authorized Caladrius Biosciences to begin its clinical trial of its drug CLBS119 for repair of COVID-19-induced lung damage[[121]](#footnote-121), in patients with severe infection who [had respiratory failure](https://www.healio.com/pulmonology/critical-care/news/online/%7Bea8986c8-be3c-486a-9e60-3ae99ee58c2f%7D/qa-critical-care-and-the-covid-19-pandemic).
  + 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 care[[122]](#footnote-122).
  + Israeli company Pluristem Therapeutics has been awarded up to €50 million from the European Investment Bank to take its coronavirus cell therapy to Phase III[[123]](#footnote-123).
  + 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-19[[124]](#footnote-124).
  + 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 patients[[125]](#footnote-125). Avigan (favipiravir) is now being trialled in India[[126]](#footnote-126).
  + 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]](#footnote-127).
  + Atea Pharmaceuticals will conduct a Phase II trial of its oral purine nucleotide prodrug[[128]](#footnote-128) in hospitalized patients with moderate COVID-19. It is designed to interfere with viral RNA polymerase and inhibit replication[[129]](#footnote-129).
  + Amgen announced its anti-inflammatory drug Otzela will be trialled to study its effectiveness in preventing respiratory distress from COVID-19[[130]](#footnote-130).

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 mechanical ventilation. VP01 activates the “protective arm” of the renin angiotensin system[[131]](#footnote-131).
  + On 4 May, Aridis Pharmaceuticals enrolled its first COVID-19 patient in the congoing Phase III clinical trial of AR-301, a monoclonal antibody against S. aureus induced pneumonia in patients who were already on mechanical ventilators[[132]](#footnote-132).
  + 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-2[[133]](#footnote-133).
  + 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 genome[[134]](#footnote-134).
  + Inhaled nitric oxide has been reported anecdotally as helpful in COVID-19 oxygenation[[135]](#footnote-135).
  + 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 damage[[136]](#footnote-136).
  + Romark is initiating two clinical trials of NT-300 (nitazoxanide extended-release tablets) for prevention of viral respiratory illnesses including COVID-19[[137]](#footnote-137).

Other therapies

* + Plasmapheresis uses filters to bind either the virus itself, or selected components of viral replication, and returns the “cleansed” plasma to the patient[[138]](#footnote-138).

1. Managing the pandemic

* Researchers reported early in May[[139]](#footnote-139) 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 identify targets for medicines and vaccines. The US Biomedical Advanced Research and Development Authority (BARDA) will provide funding support[[140]](#footnote-140).
* Two significant scientific journals, *BMJ* and *Nature*, have criticised[[141]](#footnote-141) 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 weeks**[[142]](#footnote-142)**.
* A Chinese study found the virus in the semen of severely infected men, raising the question of whether COVID-19 could be sexually transmitted[[143]](#footnote-143).
* A small study suggests patients may continue to shed the SARS-CoV-2 virus for up to six weeks after symptoms emerge[[144]](#footnote-144).
* Researchers reported that the strain of the coronavirus now dominant globally is more contagious than the strains which spread earlier[[145]](#footnote-145).
* An online survey launched by the US National Institutes of Health-supported [Rare Diseases Clinical Research Network (RDCRN)](https://ncats.nih.gov/rdcrn) is investigating how the current pandemic is affecting people with rare diseases, their families and their caregivers[[146]](#footnote-146).
* Researchers have searched for traces of the SARS-CoV-2 virus in some wastewater treatment plants[[147]](#footnote-147).
* With so many severely ill COVID-19 patients having previously existing co-morbidities, treating physicians have to be aware of possible interactions between experimental medications for the pandemic virus with an existing drug regimen[[148]](#footnote-148).
* 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 last[[149]](#footnote-149).
* The US Centers for Disease Control and Prevention (CDC) is undertaking a nationwide study of up to 325,000 people to track how COVIFG-19 is spreading across the country into 2021 and beyond[[150]](#footnote-150).
* The US National Institutes of Health initiated a study to identify the infection rate of COVID-19 in children and their families in the US[[151]](#footnote-151).
* A study of Chinese patients reports that children are as likely as adults to be infected by COVID-19[[152]](#footnote-152).
* 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 virus[[153]](#footnote-153).

1. Other news

* Australia’s Therapeutic Goods Administration has approved the nanobody therapy caplacizumab (Cablivi) for acquired thrombotic thrombocytopenic purpura (aTTP)[[154]](#footnote-154).
* [Alexion Pharmaceuticals, Inc.](https://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.alexion.com%2F&esheet=52213580&newsitemid=20200505005333&lan=en-US&anchor=Alexion+Pharmaceuticals%2C+Inc.&index=1&md5=cf782074a959c4d58d45dd963e136b80) is to acquire [Portola Pharmaceuticals, Inc.](https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.portola.com%2F&esheet=52213580&newsitemid=20200505005333&lan=en-US&anchor=Portola+Pharmaceuticals%2C+Inc.&index=2&md5=5cac3e5e12f17f12573a2e916854ef96) 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 bleeding[[155]](#footnote-155).
* The COVID-19 pandemic has caused healthcare systems to stock up on blood-thinning drugs[[156]](#footnote-156).
* 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 algorithm[[157]](#footnote-157).
* 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 one[[158]](#footnote-158).
* Akebia Therapeutics announced success in the first of two Phase III programs trialling its anaemia drug vadadustat in adults with damaged kidneys[[159]](#footnote-159).
* Researchers from Japan[[160]](#footnote-160) 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 Goda[[161]](#footnote-161) said: "Using this new tool may uncover the characteristics of different types of clots that were previously unrecognized by humans, and enable the 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 warfarin[[162]](#footnote-162).
* 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 trials[[163]](#footnote-163).
* Researchers have identified a microbe that prevents mosquitoes from being infected with malaria[[164]](#footnote-164).
* So far this year, the number of Q fever cases reported in Australia has been significantly lower than it was in 2019[[165]](#footnote-165).
* Chimerix has FDA clearance for a rolling submission of its New Drug Application for the approval of brincidofovir as a medical countermeasure for smallpox[[166]](#footnote-166).
* At the American Society of Gene and Cell Therapy Conference Inovio and GeneOne Life Science announced interim data from a Phase I/IIa 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 responses[[167]](#footnote-167).
* ViiV Healthcare's trial evaluating a long-acting injection for HIV prevention was halted early due to high levels of efficacy[[168]](#footnote-168).
* 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]](#footnote-169).

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