THE COVID–19 PANDEMIC AND HAEMOGLOBIN DISORDERS

VACCINATIONS & THERAPEUTIC DRUGS

An Informational Guide from the Thalassaemia International Federation (TIF)

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THALASSAEMIA INTERNATIONAL FEDERATION

Introduction

It is important to note that there are currently no FDA[1] or EMA[2]-approved or even recommended agents for the treatment of the novel coronavirus (COVID-19), for which the World Health Organization (WHO) declared as pandemic on Wednesday 11th of March 2020. Any agent being used at this time is being administered in an experimental setting under controlled conditions.

Thalassaemia International Federation (TIF) has made an effort to compile a list of studies/clinical trials for treatment and vaccines, which is by no means exhaustive as this situation is extremely labile and research in this area is dramatically intensified. New information is anticipated to be added to this guide which is prepared exclusively for TIF's global thalassemia community.

The viral genome was mapped very soon as rom early January 2020 and shared globally.

In February 2020, the WHO published an overview of the potential therapeutic candidates for the treatment of COVID-19. The document outlines 76 regimens that have been proposed (as of February 17, 2020) for the treatment of patients infected with the virus. Thirty-eight of these candidates are in the preclinical state with minimal information available on their proposed mechanism, uses, doses routes, or planned trials. Sixteen of the remaining regimens contain an interferon-based product. The rest include a variety of antimicrobials, corticosteroids, convalescent plasma, and biologics.

The Director-General of the WHO, Mr Tedros Adhanom, stated on the 10th of April 2020, that more than 70 countries have joined WHO's trial to accelerate research on effective treatments and 20 Institutions and companies 'are racing to develop a vaccine'. The Director-General will be soon announcing an initiative for the accelerated development and equitable distribution of vaccines.

Moreover, a survey by Genetic Engineering & Biotechnology News (GEN) reveals:
35 active drug development programs in North America, Europe, and China. Companies involved range from pharma giants like GlaxoSmithKline and Sanofi, to small and large biotechs such as Moderna and Gilead Sciences. Gilead has already begun clinical trials

[1] Food and Drug Administration (FDA)
[2] European Medicines Agency (EMA)

in China where 234 clinical trials are registered (Chinese Clinical Trial Registry) 50% of which (105), of which 85 registered studies focus on treatments f for COVID-19.

Many of these are included in the 60 studies listed in ClinicalTrials.gov whose descriptions include the term COVID-19, as well as the 7 studies whose descriptions include SARS-CoV-2. The U.S. website lists 331,715 trials in 209 countries.

China published Guidelines for clinical studies of drugs and vaccines intended to combat the deadly viral outbreak giving priority to drugs already marketed and whose efficacy has been proven in animal and in vitro studies.

In all the above studies and programmes, considerable effort is placed on repurposing existing drugs and assessing their effectiveness and safety in addressing COVID-19 while at the same time there is a plethora of drug developers, as seen in GEN's A-List of top 35 treatments under development and/or clinical study for COVID-19.

There are 412 published articles in the PubMed (a free full-text archive of biomedical and life sciences journal) and 312 clinical trials recruited at clinicaltrials.gov for 2020. "A global war of pharmaceutical industry and countries" with interest of over 1 trillion dollars always declaring of course "no conflict of interest".

WHAT IS MOST NEEDED TODAY, MORE THAN EVER IS:

A strong international co-ordination and co-operation is needed between the pharmaceutical industry to develop vaccines, regulatory authorities, policy makers, funders, public health agencies and governments to ensure that vaccines candidate for clinical trials would be manufactured in sufficient quantities and be accessible to all.

Candidate Vaccinations and Therapeutic Drugs

As some experimental treatments have yet to be named, or identified, most of the prospective treatment below is listed by its developer, followed by a description (the treatment name or description, the type of treatment including its mechanism, and a brief status update summarizing recent developments).

1 AbbVie

Treatment: Kaletra® (also marketed as Aluvia; lopinavir/ritonavir)

Type: HIV-1 protease inhibitor indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and children 14 days old and older.

Status: China's National Health Commission authorized Kaletra to treat pneumonia caused by SARS-CoV-2, AbbVie announced on January 27. AbbVie has donated RMB 10 million ($1.4 million) of Kaletra to Chinese authorities "as an experimental option to support this growing public health crisis."

This is one of the four drugs/drug combinations which is under review by the World Health Organisation (WHO). It was shown to be effective against severe acute respiratory syndrome (SARS) in vitro, and in some clinical trials. Like umifenovir, lopinavir/ritonavir is included in the latest Chinese guidelines using a 200 mg/50 mg capsule at a dose of 2 capsules twice a day for up to 10 days. The medication is being studied alone and in combination with other agents including ribavirin and interferon.

The combination from published information has been more currently included in French, Belgium, German, US, Singaporean and Japanese Guidelines.

2 AIM ImmunoTech

Treatment: Ampligen® (rintatolimod)

Type: Immune modulator indicated for severe chronic fatigue syndrome

Status: AIM ImmunoTech said February 27 it is partnering with ChinaGoAbroad, a matchmaking and advisory service for cross-border deals involving China, to facilitate talks with China's government to allow entry of AIM's drug candidate Ampligen into China for use as a prophylactic/early-onset therapeutic against COVID-19. The companies are pursuing approval for trials in China, and FDA authorization under regulations allowing the export of investigational drugs for use in a sudden and immediate national emergency. Through those rules, AIM won FDA authorization to import Ampligen into Argentina in 2019 as a treatment for severe chronic fatigue syndrome.

3 Airway Therapeutics

Treatment: AT-100

It is a recombinant protein used as a treatment of coronavirus. It has shown efficacy in preclinical studies in reducing inflammation and infection in the lungs, while also generating an immune response against various respiratory diseases.

4 AJ Vaccines

AJ Vaccines has launched the development of a vaccine against COVID-19. The company will use the latest technology to develop antigens that can mimic the native structures of the virus. The vaccine will be capable of inducing a strong immune response in the body thereby protecting against the infection.

5 Algernon Pharmaceuticals

Treatment: NP-120 (Ifenprodil)

Exploring the product NP-120 as a potential treatment N-methyl-d-aspartate (NDMA) receptor demonstrated efficacy in survivability in mice infected with H5N1.

6 Altimmune

Treatment: Single-dose, intranasal vaccine designed to provide systemic immunity

Type: Vaccine based on Altimmune's proprietary platform vaccine technology, which the company applied in developing NasoVAX, the company's influenza vaccine candidate that showed positive Phase IIa results.

Status: Altimmune said February 28 that it completed the design and synthesis of the vaccine, and was advancing it toward animal testing and manufacturing. Clinical testing of the vaccine could start as early as August. The company also said it was "actively engaged in discussions with a number of potential partners."

7 APEIRON Biologics

Treatment: APN01

Type: Recombinant human angiotensin-converting enzyme 2 (rhACE2) developed for the treatment of acute lung injury, acute respiratory distress syndrome, and pulmonary arterial hypertension.

Status: Vienna-based APEIRON on February 26 launched a pilot investigator-initiated clinical trial in China designed to assess APN01 as a treatment for patients with severe SARS-CoV-2 infection. The randomized, unblinded trial will treat 24 patients for seven days to obtain preliminary data on the impact of rhACE2 on biological, physiologic, and clinical outcomes, as well as safety. Suzhou-based Angalpharma is coordinating the Chinese clinical trial, with support from dMed Pharmaceutical, a CRO based in Shanghai

8 Ascletis Pharma

Treatments: Ganovo® danoprevir plus ritonavir; ASC09 and ritonavir; ASC09 and oseltamivir; ritonavir and oseltamivir;

Types: HIV protease inhibitors

Status: Ascletis stated February 26 that three COVID-19 patients treated with its combination therapy Ganovo® (danoprevir) plus ritonavir were discharged from the Ninth Hospital of Nanchang following treatment. On February 2, Ascletis said it is actively assisting "relevant medical institutions and medical researchers" in clinical trials assessing the combination of Ascletis' ASC09 and ritonavir for COVID-19, following a request they

made to the company. On January 25, Ascletis applied to the National Medical Products Administration and its Drug Evaluation Center to include ritonavir and ASC09 fixed-dose combination into the national emergency channel.

9 Bayer and numerous Chinese manufacturers

Treatment: Chloroquine phosphate (marketed by Bayer as Resochin®)

Type: Phosphate salt of chloroquine, a quinoline compound with antimalarial and anti-inflammatory properties. Resochin was discovered by Bayer and introduced into clinical practice in 1947 to treat malaria. It is also used in the clinical management of autoimmune diseases including erythematosus lupus and rheumatoid arthritis.

Status: Evaluated in clinical trials in over 10 hospitals in Beijing, as well as in south China's Guangdong Province and central China's Hunan Province, where it has "shown fairly good efficacy" according to Sun Yanrong, deputy head of the China National Center for Biotechnology Development under the Ministry of Science and Technology (MOST), the state-owned Xinhua news agency reported on February 17. Chloroquine and remdesivir (developed by Gilead) were "highly effective in the control of 2019-nCoV infection in vitro," a team of Chinese researchers reported in a study published February 4 in Cell Research. After China's National Health Commission included chloroquine phosphate in its latest treatment guidelines for COVID-19 pneumonia, eight Chinese companies sped up manufacturing and supply of the drug, Shanghai Daily reported February 20. Some clinical studies have also been undertaken in France, mostly in combination with Azithromycin (antibiotic). Most of the studies have not been used in severe cases, and in the USA there is an ongoing study to use high doses (results are anticipated shortly – NCT, 04308668, 2020).

Since adverse effects are quite limited and effectiveness satisfactory, future studies perhaps should also focus on severe cases to expand the knowledge on its effectiveness.

A large ongoing study is comparing hydroxychloroquine's clinical outcomes to carrimycin, lopinavir/ritonavir, and umifenovir, but the study is not anticipated to conclude before February 2021. The most recent Chinese guidelines on COVID-19 recommend chloroquine phosphate 500 mg twice a day for up to 10 days.

Chloroquine phosphate or hydroxychloroquine sulfate (plaquenil) is used alone or in combination with antibiotic in France, Belgium, Germany, Canada, USA, Singapore and Japan.

10 Beijing Staidson Biopharma and InflaRx

Treatment: IFX-1

Type: Anti-C5a monoclonal antibody in development for COVID-19 as well as hidradenitis suppurativa

Status: Chinese authorities approved clinical trials of IFX-1 as a COVID-19 treatment in February.

11 BenevolentAI

Treatment: Baricitinib

Potential treatment for COVID-19 identified by BenevolentAI using artificial intelligence enters randomised clinical trial.

Baricitinib enters a randomised-controlled trial with the US National Institute of Allergy and Infectious Diseases (NIAID); predicted to inhibit COVID-19 infection of human lungs and reduce inflammatory damage.

BenevolentAI, a leader in the creation and application of AI and machine learning to transform the way medicines are discovered and developed, today announced that baricitinib, which it identified this year as a potential treatment for COVID-19, will be entering late stage phase 3 clinical trials to treat the disease, the greatest medical challenge of the century. This new trial is occurring alongside a Canadian government-sponsored randomised-controlled trial already underway of baricitinib as a potential treatment. Others studies are ongoing or being set up currently.

Baricitinib is an already approved drug developed by Eli Lilly and Incyte for the treatment of rheumatoid arthritis and is being studied for other indications. The randomised trial announced by Eli Lilly today with the US National Institute for Allergies and Infectious Diseases (NIAID) will investigate the efficacy and safety of baricitinib as a potential

treatment for patients with serious COVID-19 infections. The study will begin in the US in late April with planned expansion to additional sites in Europe and Asia. Results are expected within the next two months.

12 BeyondSpring

Treatment: BPI-002

It has the ability to activate CD4+helper T cells and CD8+ cytotoxic T cells, generating an immune response

13 Biocryst

Treatment: Galidesivir (BCX4430)

Type: Nucleoside RNA polymerase inhibitor designed to disrupt the viral replication process

Status: Shown broad-spectrum activity in vitro against more than 20 RNA viruses in coronaviruses.

The drug has already shown survival benefits in patients against deadly viruses such as Ebola, Zika, Marburg, and Yellow fever.

Galidesivir is currently in advanced development stage under the Animal Rule to combat multiple potential viral threats including coronaviruses, flaviviruses filoviruses, paramyxoviruses, togaviruses, bunyaviruses, and arenaviruses.

14 BioXyTran

Treatment: BXT-25 - to treat late-stage acute respiratory distress syndrome (ARDS)

Type: Anti-necrosis drug whose glyco-polymer structure consists of hybrid molecules integrating the Hemoglobin molecule and a proprietary polymer chemical structure. BXT-25 is company's lead product candidate, designed to carry oxygen to tissues when the flow of blood is blocked.

Status: Boston-based Bioxytran said February 5 that it is exploring partnering with "international drug companies" to develop BXT-25 as a treatment for Acute Respiratory Distress Syndrome (ARDS) in end-stage patients with SARS-CoV-2.
The diffusion of oxygen to the blood is compromised in patients suffering from ARDS leading to fluid build-up in the lungs. Since BXT-25 is 5,000 times smaller than red blood cells, the drug can help in supplying oxygen to the vital organs and enable the patient to recover and survive.

The company will use MDX Life Sciences' MDX Viewer to assess the safety and efficacy of the drug.

15 CanSino Biologics and the Beijing Institute of Biotechnology

Treatment: Adenovirus type 5 Vector vaccine

This experimental vaccine is in Phase 2.

16 CEL-SCI

CEL-SCI is developing immunotherapy against COVID-19 using its proprietary LEAPS peptide technology, which utilises conserved areas of the coronavirus proteins to generate T-cell responses and reduce viral load. The technology can also be used to develop immunotherapeutic peptides with both antiviral and anti-inflammatory properties.

The peptides developed using this technology can help in reducing tissue damage from inflammation caused due to lung infection, which is a major cause of mortality in elderly patients.

17 Celularity and Sorrento Therapeutics

Treatment: CYNK-001

Type: Allogeneic, off-the-shelf, placental-derived Natural Killer (NK) cell therapy

Status: The companies on January 30 launched a clinical and manufacturing collaboration designed to expand the therapeutic use of Celularity's CYNK-001 to COVID-19. Sorrento and Celularity agreed to assess CYNK-001 as a potential novel therapy for coronaviruses, specifically SARS-CoV-2. Sorrento—which owns 25% of Celularity—agreed to use current existing capacity in its cGMP cell therapy manufacturing facilities in San Diego to supplement Celularity's new cGMP facility in Florham Park, NJ. Sorrento said it is already in contact with "leading" scientists and local Chinese experts to discuss clinical validation and logistics requirements for fast-tracking CYNK-001 in China.

18 Chugai Pharmaceutical and Zhejiang Hisun Pharmaceutical

Treatment: Tocilizumab

Type: Humanized mAb targeting interleukin-6

Status: A 94-patient trial assessing Tocilizumab has been registered with Chinese authorities by The First Affiliated Hospital of University of science and technology of China (Anhui Provincial Hospital) (ChiCTR2000029765).

19 Clover biopharmaceutical

Treatment: Recombinant Subunit vaccine

The vaccine is being developed based on the trimeric s protein (S-TRIMER) of the COVID-19 virus which is responsible for binding witj the host cell causing a viral infection. The vaccine has been produced in February 10 in a mammalian cell culture. A highly purified form is expected 6-8 weeks (from Feb 10) for pre-clinical studies.

20 Columbia University

Treatment: Drugs

Researchers at Columbia University have been awarded a $2.1m grant by the Jack Ma Foundation to develop a cure for coronavirus. Four different teams at the university will adopt various approaches towards the development of a vaccine against coronavirus.

21 CureVac

Treatment: mRNA-based vaccine

Type: Vaccine applying CureVac's mRNA vaccine development platform

Status: CureVac and the public-private Coalition for Epidemic Preparedness Innovations (CEPI) are collaborating to develop a vaccine against SARS-CoV-2, the partners said January 31, extending their existing partnership to develop a rapid-response vaccine platform. CEPI has committed up to $8.3 million in additional funding for accelerated development, manufacturing, and clinical tests. CEPI CEO Richard Hatchett said the Coalition and CureVac aspire to bring the pathogen's gene sequence to a vaccine candidate for clinical testing "within a few months."
CureVac announced successful vaccination results in its Rabies programme fully protecting humans with two doses of 1 microgram (1 million of a gram)

"The combination of mRNA science, disease understanding, formulation and production expertise make CureVac a unique player to fight against any infectious disease"[3]

22 CytoDyn

Treatment: Leronlimab (PRO 140)

Type: Humanized IgG4 monoclonal antibody. Leronlimab is CytoDyn's lead candidate, and is a CCR5 antagonist with potential for multiple therapeutic indications.

Status: CytoDyn plans to offer an update during a March 5 conference call with analysts about its planned filing of an IND and its Phase II clinical trial protocol with the FDA, as the company seeks to evaluate the leronlimab as a coronavirus treatment. CytoDyn and Longen China Group said February 12 they will begin exploring leronlimab as a potential treatment for coronavirus as well as cancer.

23 Emergent BioSolutions

[3] https://www.curevac.com/news/curevac-focuses-on-the-development-of-mrna-based-coronavirus-vaccine-to-protect-people-worldwide

Emergent BioSolutions is developing two plasma-derived product candidates or hyperimmunes using its hyperimmune platforms for the treatment of coronavirus. The hyperimmune platforms have been used previously for the development of several approved products including vaccines for smallpox, botulism, and anthrax.
The hyperimmunes are polyclonal antibodies derived from plasma, which are capable of generating an immune response and protecting against infection. Product candidate derived from human plasma is named COVID-HIG, while COVID-EIG is derived from equine plasma. Both will be explored for the treatment of patients with a severe case of infection.

24 Enanta Pharmaceuticals

Treatment: Drugs

Enanta Pharmaceuticals has announced its plans to develop antiviral drug candidates to treat COVID-19 patients. The company is testing compounds from its existing antiviral compound library for potential efficacy in treating COVID-19. It has also launched a drug discovery programme to develop direct-acting drug candidates to treat COVID-19.

25 Fujifilm Holdings and Zhejiang Hisun Pharmaceutical

Treatment: Favipiravir (marketed by Fujifilm as Avigan and by Hisun in China as Favilavir)

Type: Broad spectrum anti-viral agent that is designed to selectively and potently inhibit the RNA-dependent RNA polymerase (RdRp) of RNA viruses. Japan has approved Avigan for novel or re-emergent influenza and was previously used to treat Ebola patients in Guinea.

Status: Japan's Health Minister Katsunobu Kato said February 22 that his ministry would recommend Avigan, developed by Fujifilm-owned Toyama Chemical, for use as a coronavirus treatment after test dosages appeared effective in mild and asymptomatic cases in at least two medical institutions. In China, the National Health Commission on

February 17 approved Hisun's version of the drug as an investigational treatment for SARS-CoV-2 in an upcoming clinical trial being conducted in Shenzhen.

Currently published information shows that it is being used also in Germany. Cyprus is also participating in this trial with 20 patients. Study shown that use of 1600mg twice the first day and 600mg twice daily until the 14th day, gave positive results in combating COVID-19 as compared to LPV/RTV.
The Russian Direct Investment Fund (RDIF) with a local drug maker will start the production of a new drug designed analogue of the favipiravir drug initially developed by Fujifilm Holdings approved for the treatment of influenza in Japan in 2015 and showed effectiveness in patients with coronavirus and Shenzhen.

The trade name is AVIGAN and the plan is to produce 600.000 packages this year.

26 Generex Biotechnology

Treatment: Ii-Key peptide vaccine

Type: Vaccine based on Generex's Ii-Key immune system activation technology platform

Status: Generex said February 27 it has received a contract from the China Technology Exchange, Beijing Zhonghua Investment Fund Management Co. Ltd., Biology Institute of Shandong Academy of Sciences, and Sinotek-Advocates International Industry Development (Shenzhen) Co. Ltd. to develop a Ii-key vaccine. Generex said it would receive $1 million upfront to initiate project work in the U.S., a $5 million licensing fee for the Ii-Key technology, payment by the Chinese consortium for all costs and expenses related to the development of a COVID-19 vaccine, and a 20% royalty on each dose of vaccine produced.

27 Gilead Sciences

Treatment: Remdesivir (GS-5734). Originally under development for Ebola, remdesivir incorporates into nascent viral RNA chains, and causes premature termination.

Type: Nucleotide prodrug

Status: The NIH announced February 25 it will run the first U.S. clinical trial evaluating an experimental treatment for COVID-19, by assessing remdesivir in patients at the University of Nebraska Medical Center in Omaha, where some Americans with the disease are being cared for or are under quarantine. Remdesivir showed "no adverse events" when administered to the first American confirmed to be infected with SARS-CoV-2, members of the Washington State 2019-nCoV Case Investigation Team reported in a case study published January 31 in The New England Journal of Medicine.

In China, clinical trials of Gilead Sciences' remdesivir have begun after China's National Medical Products Administration approved applications by the China-Japan Friendship Hospital and the Chinese Academy of Medical Sciences to conduct the studies. Remdesivir and chloroquine phosphate were "highly effective in the control of 2019-nCoV infection in vitro," a team of Chinese researchers reported in a study published February 4 in Cell Research.

It is now being tested in two phase III randomised clinical trials in Asian countries.

The trials are being performed on 761 patients in a randomised, placebo-controlled, double-blind study at multiple hospitals in Wuhan, the epicentre of the novel coronavirus outbreak. The results from the trials are expected in May 2020.

A phase 2, multicenter, placebo controlled, international study is currently recruiting adult patients. Four of the study sites are located within the US. Other countries included France and Singapore. Patients randomized to remdesivir will receive 200 mg IV on day 1, and then 100 mg IV once daily for the duration of their hospitalization, up to 10 days total. The study is not scheduled to conclude until 2023.

Additionally, the U.S. Army Medical Research and Development Command is operating an expanded access program.

At this time, evaluation of an oral version of remdesivir has not been proposed and it is unknown if this antiviral would be useful for patients whose symptoms are not severe enough to warrant hospitalization.

28 GlaxoSmithKline and Clover Biopharmaceuticals

Treatment: COVID-19 S-Trimer

Type: Protein-based coronavirus vaccine

Status: GSK agreed to provide Clover with its pandemic adjuvant system for further evaluation of S-Trimer in preclinical studies, the companies said February 24, under a research collaboration. GSK reasons that Clover could rapidly scale-up and produce large-quantities of a new coronavirus vaccine since it has one of the largest in-house, commercial-scale cGMP biomanufacturing capabilities in China.

29 Heat Biologics

Heat Biologics has announced plans to develop a vaccine to treat or prevent coronavirus infection using its proprietary gp96 vaccine platform. The technology is capable of reprogramming live cells to produce antigens that can bind to the gp96 protein and generate an immune response against those antigens.

30 Hong Kong University of Science and Technology

Treatment: Vaccine

The Hong Kong University of Science and Technology has identified several vaccine targets, which can be developed as a treatment for coronavirus. Researchers at the university have identified B-cell and T-cell epitopes, which are capable of generating an immune response against the SARS virus and a similar response against the coronavirus.

Some of the epitopes identified may be capable of generating an immune response specifically against COVID-19.

31 iBio and Beijing CC-Pharming

Treatment: Vaccine

Type: Plant-derived vaccine to be manufactured using iBio's FastPharming System™

Status: The companies on February 3 disclosed plans to develop and test a COVID-19 vaccine, combining the vaccine R&D experience—including work on the MERS-

coronavirus—by CC-Pharming Chairman and chief scientific officer Kevin Wang, PhD, and iBio VP Upstream Bioprocessing Sylvain Marcel, PhD, in rapid design of manufacturing processes for biopharmaceutical production in plant-based expression systems. If successful, the research will deliver product candidates for production at iBio's *FastPharming* Manufacturing Facility, built in 2010 with funding from the Defense Advanced Research Projects Agency (DARPA), to establish facilities capable of rapid delivery of medical countermeasures in response to a disease pandemic.

32 ImmunoPrecise Antibodies

Treatments: Vaccines and coronavirus-neutralizing antibodies

Types: Prophylactic (i.e. vaccine) and therapeutic compounds (i.e. antibodies) using ImmunoPrecise's proprietary discovery platforms (including B Cell Select™ and DeepDisplay™) and ImmunoPrecise subsidiary Talem Therapeutics' access to the transgenic animal platform OmniAb® for direct generation of human antibodies.
The company has updated its research efforts and noted that it will be using the PolyTope mAb TherapyTM and EVQLV's artificial intelligence platforms to develop a COVID-19 therapy.

Status: ImmunoPrecise announced its commitment to finding COVID-19 treatments on February 20, saying it had designated Ilse Roodink, PhD, chairwoman of Talem's scientific committee, as its Coronavirus Global Project Leader.

33 Incyte, Shanghai Hengrui Pharmaceutical

Treatment: Camrelizumab and thymosin

Types: Humanized monoclonal antibody targeting PD-1 (Camrelizumab); 5-Da polypeptide hormone secreted by the thymus gland (thymosin)

Status: Chinese clinical trials assessing the combination treatment have been registered by Wuhan Jinyintan Hospital (Wuhan Infectious Diseases Hospital) (ChiCTR2000029806) and Southeast University (NCT04268537).

34 Innovation Pharmaceuticals

Treatment: Brilacidin

Type: Defensin mimetic in Phase II development in oral muscositis in Head and Neck Cancer patients

Status: Innovation said February 24 that it submitted a Material Transfer Agreement with an unidentified "leading U.S.-based virology laboratory" to study Brilacidin as a potential novel treatment for SARS-CoV-2. If lab tests prove successful, Innovation said, it will expedite research and clinical development of Brilacidin "via pharmaceutical partnerships, academic collaborations and government grants." Innovation has also submitted a preliminary summary of Brilacidin's potential for treating coronavirus to the Biomedical Advanced Research and Development Authority (BARDA).
Inovio Pharmaceuticals will begin in April at the University of Pennsylvania

35 Inovio Pharmaceuticals and Beijing Advaccine Biotechnology

Treatment: INO-4800

The investigational DNA immunotherapy, INO-4700 (GLS-5300) is being developed by Inovio in partnership with GeneOne Life Science. It is delivered as vaccine intramuscularly, using the Cellectra® delivery device.

The vaccine was well-tolerated and demonstrated high immune responses against the MERS-CoV in 94% of patients in the early-stage clinical trial in July 2019.

It also generated broad-based T cell responses in 88% of the subjects.
"Research organisations such as the National Institutes of Health (NIH), US are also developing a vaccine for the coronavirus."

Collaboration of the above, to develop the INO-4800 vaccine as a novel coronavirus vaccine. The company stated pre-clinical testing for clinical product manufacturing. The development is supported by a $9 million grant from the Coalition for Epidemic Preparedness Innovations (CEPI). Also, the company has received a $5 million grant from the Bill & Melinda Gates Foundation to accelerate the testing and development of the Cellectra® delivery device for the intradermal delivery of INO-4800.

The plan is for 3000 doses for human clinical trial in US, China and South Korea. Human trial in 30 healthy volunteers planned in April in USA followed by China and South Korea by Beijing Advaccine Biotechnology.

Inovio aims to produce 1 million dose by the end of 2020 or additional clinical trials in emergency cases.

36 Integral Molecular

Integral Molecular has launched a vaccine programme using its two technology platforms including Shotgun Mutagenesis Epitope Mapping and the Membrane Proteome Array. The technologies will help in understanding the human immune response to the coronavirus and isolate the cellular receptors that enable the virus to spread quickly.

The Shotgun technology helps in identifying more than 1,000 binding sites for antibodies, while the Membrane Proteome Array technology is capable of identifying the receptors through which viruses infect cells.

37 Janssen Pharmaceutical Cos. (Johnson & Johnson)

Treatments: Prezcobix™ (darunavir and cobicistat); Vaccine to be developed with BARDA

Types: HIV protease inhibitors (Prezcobix); vaccine type to be developed

Status: Janssen said January 29 it has donated 300 boxes of Prezcobix to the Shanghai Public Health Clinical Center and Zhongnan Hospital of Wuhan University for use in research to support efforts in finding a solution against SARS-CoV-2. Another 50 boxes have been provided to the Chinese Center for Disease Control and Prevention for laboratory-based investigations. Prezcobix is under study in a trial sponsored by Shanghai Public Health Clinical Center (NCT04252274), while a Chinese trial is assessing Precobix or the lopinavir-ritonavir combination combined with thymosin a1 (ChiCTR2000029541).

38 LineaRx (Applied DNA Sciences) and Takis Biotech

Treatment: Linear DNA vaccine

Type: To be based on PCR-produced linear DNA designed to induce antibodies that can neutralize SARS-CoV-2

The PCR technology offers several advantages including high purity, increased production speed, and absence of antibiotics and bacterial contaminants. Further, the vaccine gene developed through this technology can be effective without being inserted into the patient's genome.

The design for four DNA vaccine candidates is expected to be produced using the PCR technology for carrying out animal testing. The design of one of the vaccine candidates is based on the entire spike gene of the coronavirus, while the remaining are designed based on the antigenic portions of the protein.

Status: LineaRx, a majority-owned subsidiary of Applied DNA Sciences of Stony Brook, NY, and Rome-based Takis Biotech said February 7 they have formed a joint venture to develop the preclinical vaccine using PCR-based DNA manufacturing technology. No commercial partner to take the coronavirus vaccine to market has been identified, the companies said.

39 Mateon Therapeutics

Mateon Therapeutics has launched an antiviral response programme to develop coronavirus treatments using its therapeutic and artificial intelligence (AI) platforms. It has also established a division, which will adopt a multi-modal approach to developing COVID-19 treatments as well as other future zootonic outbreaks.

40 Medicago

Treatment: Vaccine

The company is developing antibodies against SARS-CoV-2 and is partly funded by the Canadian Institutes of Health Research (CIHR).

41 MIGAL Research Institute

Treatment: Avian coronavirus Infectious Bronchitis Virus (IBV) vaccine

Infectious Bronchitis Virus (IBV) vaccine developed to treat avian coronavirus has been modified to treat COVID-19. The IBV vaccine was developed after 4 years of research and has high genetic similarity to the human coronavirus. The Institute modified genetically the vaccine to treat COVID-19 and will be available in the oral form.

42 Modern and Vaccine Research Centre

Treatment: mRNA-1273

Type: Novel lipid nanoparticle (LNP)-encapsulated mRNA vaccine against the COVID-19 encoding for a prefusion stabilized form of the Spike (S) protein.

Status: Moderna said February 24 that it shipped the first batch of mRNA-1273 to the NIH's National Institute of Allergy and Infectious Diseases (NIAID) for use in a planned Phase I study in the U.S. The primary aim of the Phase I open-label, dose-ranging trial study (NCT04283461), which had yet to recruit patients at deadline, is to evaluate the safety and reactogenicity of a 2-dose vaccination schedule of mRNA-1273, given 28 days apart, across 3 dosages in healthy adults. Moderna designed the vaccine in collaboration with investigators at the NIAID Vaccine Research Center (VRC).

The first patient was dosed today (Mar 16). An unusual aspect is that this vaccine has NOT BEEN TESTED in laboratory animals as is the rule.

43 NanoViricides

Treatment: Antiviral therapy based on company's novel nanomedicines platform.

Type: Broad-spectrum virus-binding ligand: "It is like a 'Venus-Fly-Trap' for the virus," says Anil R. Diwan, PhD, President and Executive Chairman.

Status: NanoViricides confirmed January 30 that it was developing a COVID-19 treatment, stating that it "already found some lead candidate ligands in its chemical library" that can bind to the SARS-CoV spike protein just as it binds to cognate receptor ACE2.

44 Novartis

Treatment: Jakavi® (ruxolitinib)

New clinical trial to evaluate Jakavi® (ruxolitinib) a well-established JAK inhibitor) in patients with COVID-19 associated cytokine storm (severe immune overreaction (to date licensed for myelofribosis and polycythemia vera).

45 Novavax

Treatment: Vaccine candidate to be selected

Types: Vaccines designed to apply company's proprietary recombinant protein nanoparticle technology platform to generate antigens derived from the coronavirus spike (S) protein. Novavax said it expects to utilize its proprietary saponin-based Matrix-M™ adjuvant with COVID-19 vaccine candidates to enhance immune responses.

The candidate is designed to primarily bind to the major surface S-protein and developed using the company's recombinant nanoparticle vaccine technology. Tested along with the Novavax's proprietary adjuvant Matrix-M™, it inhibited infection by inducing immune responses in the laboratory studies.

Novavax has received $4m in funding from CEPI to advance the development of the vaccine. The company has produced several nanoparticle vaccine candidates for testing in animal models and aims to carry out human trials in 2020.

Status: Novavax developed a novel Middle East Respiratory Syndrome (MERS) coronavirus vaccine candidate in 2013, post the identification of the first MERS coronavirus ((MERS-CoV) in Saudi Arabia in 2012. It is a crucial target for vaccine development by the Coalition for Epidemic Preparedness Innovations (CEPI) and is a priority disease for the World Health Organisation (WHO).

"We are now well-positioned to advance the COVID-19 vaccine candidate to Phase I clinical testing in May or June," President and CEO Stanley C. Erck said February 26 in a statement. Novavax cited progress in its development saying it has produced and is currently assessing multiple nanoparticle vaccine candidates in animal models prior to identifying an optimal candidate for human testing.

46 Oxford University

Treatment: ChAdOx1 nCoV-19 vaccine

The Oxford University has developed the ChAdOx1 nCoV-19 vaccine which has already started clinical trials in humans on April 2020.

47 OyaGen

Treatment: OYA1

It has been found effective in inhibiting SARS-COV-2 from replicating in cell culture. OYA1 was approved earlier as an investigative drug for cancer but abandoned due to lack of efficacy

48 Pfizer

Pfizer announced that it has identified certain under development antiviral compounds that may be effective in treating coronavirus. The company is planning to partner with a third party to screen and identify potential compounds by the end of March and begin testing in April.

49 Pharmstandard

Treatment: Arbidol (umifenovir)

Type: Membrane fusion inhibitor developed as a treatment for influenza

Status: Pharmstandard is assessing Arbidol in clinical trials as monotherapy and in combinations that include AbbVie's Kaletra (See above), Ascletis Pharma's ASC09 (See above), lopinavir, ritonavir, carrimycin, and Bromhexine Hydrochloride (enrolling by invitation). Five trials including Arbidol were listed on ClinicalTrials.gov. China's Ruijin Hospital is conducting the monotherapy trial (NCT04260594), while various Chinese hospitals are investigating the combination therapies (NCT04252885, NCT04273763, NCT04261907, NCT04286503).

50 Predictive Oncology

Predictive Oncology has launched an AI Platform for the discovery and development of vaccines against coronavirus. The company has signed an agreement with InventaBioTech to acquire Soluble Therapeutics, which provides it with access to the HSCTM Technology.

Predictive will use the HSCTM Technology along with its predictive modeling platform to deploy an AI discovery platform that can screen the ideal combination of additives and excipients for protein formulations.

51 Regeneron Pharmaceuticals

Treatments: REGN3048 and REGN 3051

Types: Discovered by Regeneron, the combination of neutralising monoclonal antibodies REGN3048 and REGN3051 leveraging Regeneron's monoclonal antibody discovery platform called VelocImmune® (part of the company's VelociSuite™ technologies).

It is being studied against coronavirus infection in a first-in-human clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). The safety and tolerability of the drug will be studied in 48 patients.

Both the antibodies bind to S-protein of MERS coronavirus. The intravenous administration of the drug in the mouse model of MERS resulted in the high-level neutralisation of the MERS coronavirus in circulating blood with reduced viral loads in the lungs.

Status: On February 4, The Biomedical Advanced Research and Development Authority (BARDA) said it was expanding upon an earlier partnership agreement with Regeneron to develop "multiple monoclonal antibodies that, individually or in combination, could be used to treat new treatments." The combination completed a Phase I trial in MERS-CoV last year (NCT03301090).

52 Regeneron Pharmaceuticals & Sanofi

Treatments: Kevzara® (sarilumab)

Regeneron has partnered with Sanofi to evaluated Kevzara®, a fully-human monoclonal antibody, in a phase two/three clinical trial in patients with severe COVID-19 infection. Kevzara® is approved for the treatment of rheumatoid arthritis and is known to block the interleukin-6 (IL-6) pathway, which causes an overactive inflammatory response in the lungs of COVID-19 patients.

It will test 400 patents in about 16 US sites.

53 Roche

Treatment: Actemra

Actemra by Roche to treat coronavirus-related complications. China approved the use of Roche's Actemra for the treatment of severe complications related to coronavirus. Drugs like Actemra have the ability to prevent cytokine storms or overreaction of the immune system, which is considered as the main reason behind organ failure leading to death in some coronavirus patients.

Actemra is also being evaluated in a clinical trial in China, which is expected to enroll 188 coronavirus patients. The clinical trial is expected to be conducted until May 10.

54 Sanofi

Treatment: Unnamed vaccine

Type: Vaccine based on Sanofi's recombinant DNA platform, designed to produce an exact genetic match to proteins found on the surface of the virus. Sanofi said the DNA sequence encoding the antigen will be combined into the DNA of the baculovirus expression platform and used for rapidly producing large quantities of the coronavirus antigen, which will be formulated to stimulate the immune system to protect against the virus.

Status: Sanofi said February 18 that its Sanofi Pasteur vaccines global business unit will apply previous development work for a SARS vaccine with the aim of accelerating development of a COVID-19 vaccine through a collaboration with the Biomedical Advanced Research and Development Authority (BARDA). In non-clinical studies, the SARS vaccine candidate was immunogenic and afforded partial protection as assessed in animal challenge models, Sanofi said. That earlier work by Protein Sciences, acquired by Sanofi in 2017, "provides a head start in expediting a COVID-19 vaccine," Sanofi stated.

In addition, Sanofi produces the treatment drug (a cheap drug) Plaquenil (Hydroxychloroquine) used in China initially, now in France. Sanofi Company is authorised to produce this drug for conducting clinical trials in 3000.000 affected individuals.

55 Serum Institute of India

Treatment: Vaccine

Serum Institute of India (SII) is collaborating with Codagenix, a US-based biopharmaceutical company, to develop a cure for coronavirus using a vaccine strain similar to the original virus. The vaccine is currently in the pre-clinical testing phase, while human trials are expected to commence in the next six months. SII is expected to launch the vaccine in the market by early 2022.

56 Southwest Research Institute

Treatment: Drugs

Southwest Research Institute is using its virtual screening called Rhodium to identify potential drug candidates for treating coronavirus from more than two million drug compounds. The most promising compounds will be identified for further development.

57 Takeda Pharmaceutical Company

Takeda Pharmaceutical Company has announced plans to develop a plasma-derived therapy against coronavirus. The anti-SARS-CoV-2 polyclonal hyperimmune globulin (H-IG) therapy will be designed to treat high-risk patients. The H-IG therapy includes concentrated pathogen-specific antibodies derived from plasma of recovered patients. These antibodies have the potential to generate an immune response when injected into a new patient.

58 Tiziana Life Sciences

Treatment: TZLS-501

The company developed a monoclonal antibody named TZLS-501 which is a human anti-interleukin-6 receptor (IL-6R). It helps in preventing lung damage and elevated levels of IL-6.

59 Tonix Pharmaceuticals Holding

Treatment: TNX-1800

Type: Live modified horsepox virus vaccine for percutaneous administration

Status: Tonix said February 26 it has partnered with Southern Research to develop TNX-1800 as a vaccine treatment for COVID-19. TNX-1800 is under development as a potential smallpox preventing vaccine for the U.S. strategic national stockpile and as a monkeypox preventing vaccine.

60 Tulane University

Treatment: Vaccine

Tulane University has launched a research programme to identify a potential coronavirus medicine in the form of a vaccine. The university will utilise a grant from the Brown Foundation to carry out the research activities.

61 Vaxart

Treatment: Vaccine based on proprietary VAAST™ Platform

Type: Oral recombinant vaccine administered by tablet

Status: Vaxart said January 31 that it plans to generate vaccine candidates based on the published genome of the 2019 COVID-19 (SARS-nCoV-2) and evaluate them in preclinical models based on their ability to generate both mucosal and systemic immune responses.

62 Vir Biotechnology

Vir Biotechnology, a clinical-stage immunology company, announced on 12 February that it has identified two monoclonal antibodies that can bind to the virus that causes COVID-19. The antibodies target the spike (S) protein of the virus by entering through the cellular receptor ACE2.

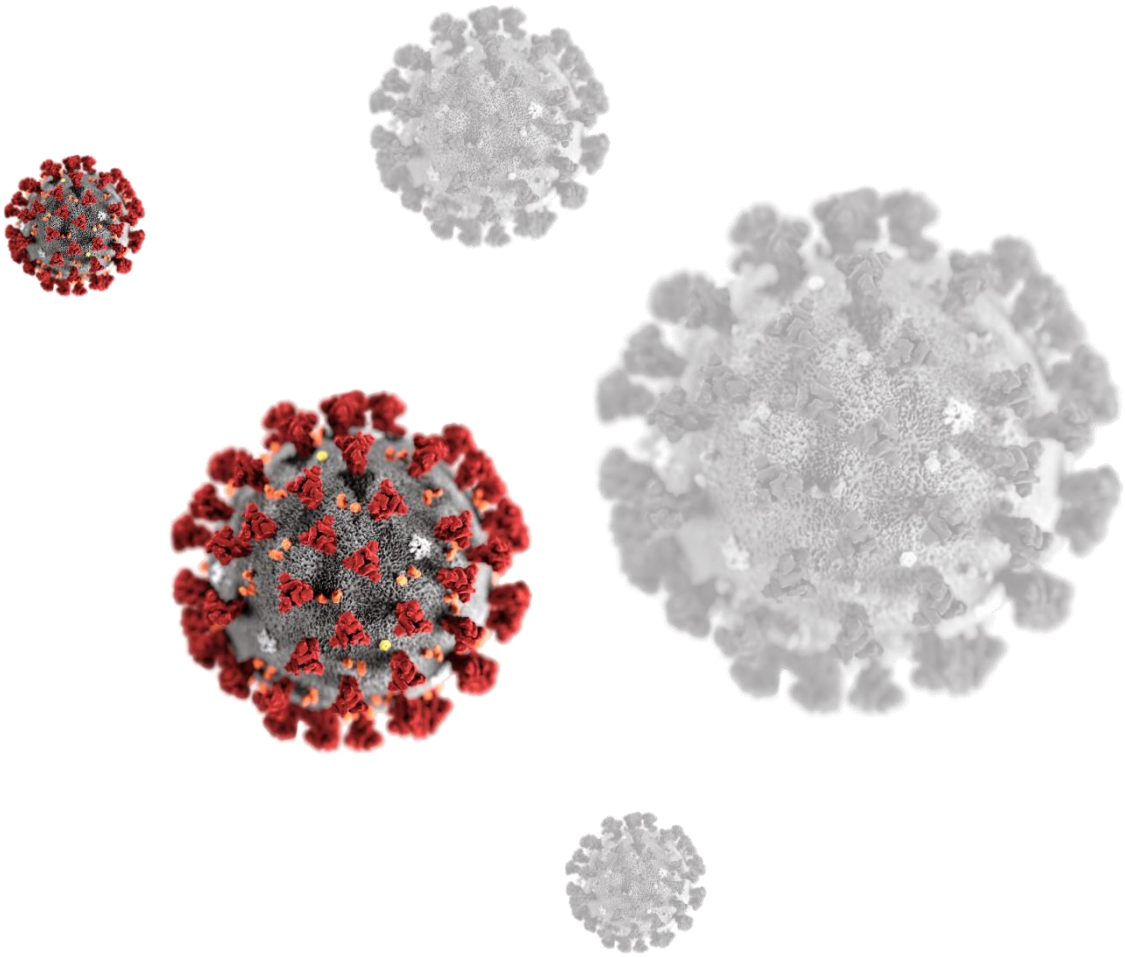
The company has formed a partnership with WuXi Biologics on 25 February to commercialise the antibodies identified to treat coronavirus. If approved, Wuxi will have the rights to market the therapies in China, while Vir will retain the marketing rights in other countries.

Vir has also partnered with Alnylam Pharmaceuticals to identify siRNA candidates targeting SARS-CoV-2. It has formed another partnership with Biogen for cell line and process development and manufacturing of the antibodies.

63 Zydus Cadila

Treatment: Vaccine

Zydus Cadila announced the launch of an accelerated research programme to develop a vaccine for COVID-19 using two novel approaches. The first approach includes the development of a DNA vaccine against the viral membrane protein of the virus, while a live attenuated recombinant measles virus (rMV) vectored vaccine will be developed in the second approach. The rMV-based vaccine works by inducing specific neutralising antibodies, which will provide protection from the coronavirus infection.



Review of the HIV drugs for coronavirus treatment

Abbvie's HIV protease inhibitor, lopinavir is being studied along with ritonavir for the treatment of MERS and SARS coronaviruses. The repurposed drug is already approved for the treatment of HIV infection under the trade name Kaletra®.
The combination is listed in the WHO list of essential medicines. Lopinavir is believed to act on the intracellular processes of coronavirus replication and demonstrated reduced mortality in the non-human primates (NHP) model of the MERS.

Lopinavir/ritonavir in combination with ribavirin showed reduced fatality rate and milder disease course during an open clinical trial in patients in the 2003 SARS outbreak.

Cipla is also reportedly planning to repurpose its HIV drug LOPIMUNE, which is a combination of protease inhibitors Lopinavir and Ritonavir, for the treatment of coronavirus.

A licensed generic of Kaletra®, LOPIMUNE is currently available in packs of 60 tablets each, containing 200mg of Lopinavir and 50mg of Ritonavir.

Janssen Pharmaceutical Companies, a subsidiary of Johnson & Johnson, donated its PREZCOBIX® HIV medication (darunavir/cobicistat) for use in research activities aimed at finding a treatment for COVID-19.

Darunavir is a protease inhibitor marketed by Janssen. Anecdotal reports suggest darunavir as potentially having antiviral activity against COVID-19. It is, however, currently approved only for use with a boosting agent, and in combination with other antiretrovirals, for the treatment of HIV-1.

Janssen has no in vitro or clinical data to support the use of darunavir as a treatment for COVID-19. The drug is in the process of being evaluated in vitro for any potential activity against the coronavirus.

Further, Janssen has partnered with the Biomedical Advanced Research and Development Authority (BARDA) to expedite the development of a COVID-19 treatment.

News & Updates

European Medicines Agency (EMA)

- The following drugs in in clinical trials in hum to assess their safety and effectiveness in combating COVID-19:
  - Remdesivir (investigational)
  - Lopinavir/Ritonavir (authorised todate for HIV infections – Kalentra®)
  - Chloroquine and Hydroxychloroquine (todate antimalarial drugs and for some autoimmune patients including lupus and rheumatoid arthritis
  - Interferon especially β (todate authorized for multiple sclerosis)
  - Monoclonal antibody (for immune system boosting)

- Chloroquine and Hydroxychloroquine are being used in USA and France under strict protocols for addressing patients with severe form for COVID-19.

- Favipiravir is also under investigation for COVID-19. A trial enrolling 80 patients in China suggested a more potent antiviral action than lopinavir–ritonavir. A phase 2 study evaluating its efficiency has started in Thailand.

The World Health Organisation (WHO)

- Four drugs or drug combinations already licensed and used for other illnesses will be tested by WHO and 10 countries have indicated their interest to take part in the trial:
  1. Remdesivir (by Gilead)
  2. Lopinavir and Ritonavir (sold as Kaletra or Aluvia by AbbVie)
  3. Lopinavir and Ritonavir plus Interferon β; and
  4. the antimalarial drug Chloroquine.

- Like Umifenovir used in China, Lopinavir/ Ritonavir use a 200gm/50mg capsule at a dose of 2 capsules twice a day for up to 10 days. The medication is studied alone or in combination with others including ribavirin and interferon.

- Corticosteroids- Interim guidance from WHO recommends against using them in patient with COVID-19 unless they have another indication.

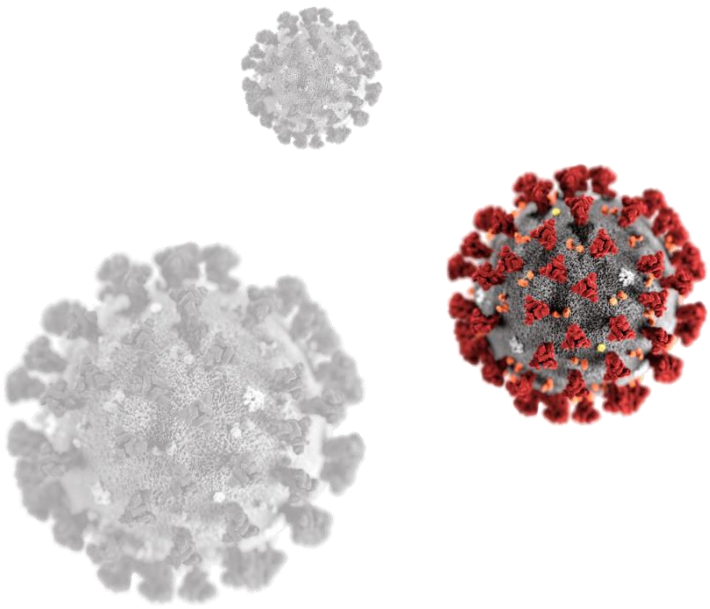
In the meantime, however, a plethora of other combinations are either under consideration or in studies/trials e.g. (i) interferon alfacon-1 with corticosteroids and (ii) ribavirin with corticosteroids

- FDA allows treatment of life threatening COVID-19 cases using blood from patients who have recovered. It is a temporary authorization under FDA's investigational NEW DRUG APPLICANTS (INDs) exemption.

  Convalescent plasma transfusion has been used against H1N1 flu, and SARS and MERS epidemic with varying results. It is not new and is relatively safe.

- Vaxart's coronavirus vaccine – a oral recombinant vaccine in tablet formulation is under development based on the published genome of 2019-nCOV.

- CytoDyn – Leronlimab. The company is examining leronlimab (PRO140 a CCRs antagonist as a potential coronavirus drug. The drug is already being investigated in phase II clinical trials as a treatment for HIV and has been awarded fast-track approval status by FDA.



CLINICAL MANAGEMENT OF COVID-19 IN SELECTED COUNTRIES

Current therapeutic practices - COVID-19			
Country	**Drugs used**	**Administration**	**Source**
France	remdesivir	people ≥ 40 kg : 200 mg/ day, then 100 mg/ day from day 2 to day 10	Haut Conseil de la santé publique, Avis relatif aux recommandations thérapeutiques dans la prise en charge du COVID-19 (complémentaire à l'avis du 5 mars 2020), p. 3 - available at https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=785
	Combination of lopinavir/ritonavir	2 pills of lopinavir/ritonavir 200/50 mg (a total of 400/100 mg) twice/day for 14 days	Haut Conseil de la santé publique, Avis relatif aux recommandations thérapeutiques dans la prise en charge du COVID-19 (complémentaire à l'avis du 5 mars 2020), p. 4 - available at https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=786
	hydroxychloroquin	400 mg twice/day in day 1, then 400 mg once/day for 9 days (Detailed guidance in Table 2, p.8)	Haut Conseil de la santé publique, Avis relatif aux recommandations thérapeutiques dans la prise en charge du COVID-19 (complémentaire à l'avis du 5 mars 2020), p. 6 - available at https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=787
Belgium	hydroxychloroquine sulphate (Plaquenil)	400mg BID on day 1, followed by 200mg BID on days 2-5 (max. 5 days) (Detailed guidance in Table 2, p.8)	Interim Clinical Guidance for Adults with suspected or confirmed COVID-19 in Belgium, p.5 - available at https://epidemio.wiv-isp.be/ID/Documents/Covid19/COVID-19_InterimGuidelines_Treatment_ENG.pdf
	chloroquine	a total of 25 mg/kg within 3 days - restricted to hospitalised patients	Interim Clinical Guidance for Adults with suspected or confirmed COVID-19 in Belgium, p.5 - available at https://epidemio.wiv-isp.be/ID/Documents/Covid19/COVID-19_InterimGuidelines_Treatment_ENG.pdf
	lopinavir/ritonavir	a second choice, when hydroxychloroquine is contraindicated / to be administered early in the course of the disease (within 12 days after symptoms onset)	Interim Clinical Guidance for Adults with suspected or confirmed COVID-19 in Belgium, p.5 - available at https://epidemio.wiv-isp.be/ID/Documents/Covid19/COVID-19_InterimGuidelines_Treatment_ENG.pdf
United Kingdom	No data		
Germany	No	Use of investigational anti-COVID-19 therapeutics (Lopinavir/Ritonavir, Hydroxychloroquin, Favirpiravir, Camostat) should be done under ethically approved, randomized, controlled trials.	Robert Koch-Institut, Notes on the detection, diagnosis and therapy of Patients with COVID-19, p.6 - available at https://www.rki.de/DE/Content/Kommissionen/Stakob/Stellungnahmen/Stellungnahme-Covid-19_Therapie_Diagnose.html
Canada	No	Use of investigational anti-COVID-19 therapeutics should be done under ethically approved, randomized, controlled trials.	Clinical management of patients with moderate to severe COVID-19 - Interim guidance - available at: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/clinical-management-covid-19.html

United States (state level)	lydroxychloroquine	400mg BID x2 doses, then 200mg PO BID for 5-10 days	Nebraska Medicine, COVID-19 Antiviral and Pharmacotherapy Recommendations - available at: https://www.nebraskamed.com/sites/default/files/documents/covid-19/covid19-antiviral-pharmacotherapy-recommendations.pdf
	lopinavir/ritonavir	400/100mg (2 tabs) BID for 5-10 days	Nebraska Medicine, COVID-19 Antiviral and Pharmacotherapy Recommendations - available at: https://www.nebraskamed.com/sites/default/files/documents/covid-19/covid19-antiviral-pharmacotherapy-recommendations.pdf
	remdesivir (compassionate use)	-	Nebraska Medicine, COVID-19 Antiviral and Pharmacotherapy Recommendations - available at: https://www.nebraskamed.com/sites/default/files/documents/covid-19/covid19-antiviral-pharmacotherapy-recommendations.pdf
Singapore	Remdesivir	200 mg IV loading, 100 mg IV daily x 5 to 10 days (as part of clinical trial)	Singapore National Center for Infectious Diseases, Interim Treatment Guidelines for COVID-19 (Version 1.0, dated 2 April 2020) - available at: https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx
	Lopinavir/ritonavir	400/100 mg BD x 14 days	Singapore National Center for Infectious Diseases, Interim Treatment Guidelines for COVID-19 (Version 1.0, dated 2 April 2020) - available at: https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx
	Interferon Beta-1B	250 microgram (8.0 million IU), contained in 1 ml of the reconstituted solution, to be injected subcutaneously every other day up to 7-14 days (3-7 doses).	Singapore National Center for Infectious Diseases, Interim Treatment Guidelines for COVID-19 (Version 1.0, dated 2 April 2020) - available at: https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx
	Hydroxychloroquine	400 mg BD x 1 day (loading dose) followed by 200 mg bd for a 4 further days	Singapore National Center for Infectious Diseases, Interim Treatment Guidelines for COVID-19 (Version 1.0, dated 2 April 2020) - available at: https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx
	Tocilizumab	To discuss with Rheumatology-Allergy-Immunology / Infectious Diseases /Intensive Care Physicians	Singapore National Center for Infectious Diseases, Interim Treatment Guidelines for COVID-19 (Version 1.0, dated 2 April 2020) - available at: https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx

China	(4) Antiviral therapy: α-interferon (5 million U or equivalent for adult, add 2ml of sterile water, 2 times daily inhalation), lopinavir/ritonavir (200 mg/50 mg/capsule, 2 capsules each time for adults, twice a day, the course of treatment should not exceed 10 days). Ribavirin (combination with interferon or lopinavir/ritonavir is recommended, 500 mg each time for adults, 2 to 3 times intravenous infusions per day, the course of treatment should not exceed 10 days), chloroquine phosphate (for adults whose weigh over 50 kg, 500 mg each time, twice daily for 7 days; for those whose weigh less than 50 kg, 500 mg each time, twice daily for day 1 and day 2, once daily for day 3- day 7), Abidol (200 mg each time, three times a day for adults, the course of treatment should not exceed 10 days) can be tried. Attention should be paid to the adverse reactions of the above drugs, contraindications (such as chloroquine should not be used in patients with heart disease), and interaction with other drugs. It is not recommended to use 3 or more antiviral drugs at the same time. The use of related drugs should be stopped when intolerable side effects occur. The treatment of pregnant women should consider the number of weeks of gestation and choose drugs that have less impact on the fetus.		Chinese Clinical Guidance for COVID-19, available at: http://kjfy.meetingchina.org/msite/main/cn
Japan	Lopinavir and Ritonavir	400 mg / 100 mg twice a day	Concept of antiviral treatment for COVID-19 1st edition (February 26, 2020), available at: http://www.kansensho.or.jp/modules/topics/index.php?content_id=31
	1) Pyrazinamide, 2) Repaglinide, 3) Theophylline 4) famciclovir, 5) sulindac	Use with caution	Concept of antiviral treatment for COVID-19 1st edition (February 26, 2020), available at: http://www.kansensho.or.jp/modules/topics/index.php?content_id=32
	Remdecib, Interferon, chloroquine	Not recommended yet	Concept of antiviral treatment for COVID-19 1st edition (February 26, 2020), available at: http://www.kansensho.or.jp/modules/topics/index.php?content_id=33

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12. **WHO R&D Blueprint** - *Nnovel Coronavirus An international randomised trial of candidate vaccines against COVID-19, 09 April 2020*