Sample Landscape Study

# Covid-19: Prophylaxis and Treatment

May 2020

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# 1. Coronavirus Disease 2019 (Covid-19)

## 1.1. Overview

On 31st December 2019, the National Health Commission of China reported a cluster of cases of pneumonia with a novel virus in Wuhan, Hubei province, China. The Chinese scientist's successfully isolated novel virus strain from the patient, pursuant to which its genome sequence was made publicly available on 12th January 2020. The novel virus strain was eventually identified as belonging to coronavirus family and was termed as SARS-CoV-2. The disease caused by SARS-CoV-2 was named COVID-19 by World Health Organization (WHO). On 11 March 2020, WHO declared COVID-19 as a pandemic disease. The novel strain of coronavirus family causes illness as mild as the common cold, and also has the potential to cause severe damage to a human body by causing pneumonia, severe acute respiratory syndrome (SARS), kidney failure and in extreme cases, death.

As per the latest data#, more than 5 million people have been infected and more than 0.33 million people have succumbed to COVID-19 disease globally.


#WHO data as of May 22, 2020 (https://covid19.who.int/)

It has been observed that most COVID-19 infected patients have shown a pattern of mild to moderate symptoms of dry cough, sore throat and fever. A majority of cases were resolved with the help of mild medication. However, not all cases are resolvable by mild medication, some patients that develop fatal

complications such as organ failure, septic shock, pulmonary edema, severe pneumonia, and Acute Respiratory Distress Syndrome (ARDS)1 require intensive treatment. People with low or compromised immunity i.e. patients with co-morbidities like cancer and/ or people who have undergone an organ transplant are at a much higher -risk at catching COVID-19 infection. Through study patterns, it has been found that age has a key role in recovery. The younger a person, the higher chances of recovery, and the older a person lessen the chances. It been reported that there is a high rate of mortality in older patients aged above 60 years.2

To limit the spread of this fatal disease, most countries shut down their economies, solely to focus on the healthcare of their people. Several countries shut down and started conducting tests and, contact tracing, and wherever necessary the citizens were put into either quarantine zones or forced into self-isolation at their respective residences. Fearing the spread of the virus due to close human proximity in crowding places, large gatherings, associations, schools, markets etc. were called off. Further, masks, gloves and other gear were made mandatory to control the transmission of the virus.

With the rapid spread of the COVID-19 pandemic, the race to bring a vaccine and suitable treatment into existence caught pace. The academicians, universities, healthcare providers and companies across the globe have started fueling their energies in search of a vaccine /drug candidates for the prophylaxis and treatment of the COVID-19 disease altogether.

## 1.2. Coronavirus

Corona viruses are a group of viruses having a crown-like appearance due to the presence of surface projections on the virus surface as visualized by electron microscopy. Corona viruses are enveloped with positive strand of RNA viruses that infect vertebrates.3.

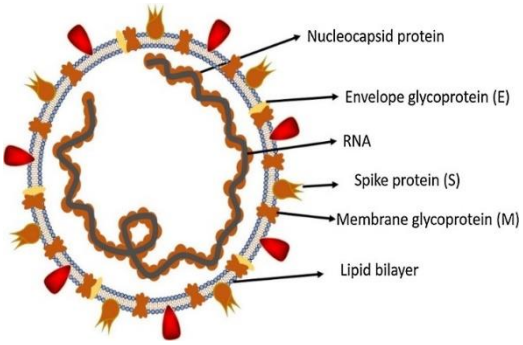



Fig.1. Novel Coronavirus (SARS-Cov-2)

The present disease pandemic is the third encounter we had with a newly emerging corona virus which seems to be transmitted from animals to people. The first of these three episodes started as an epidemic of severe respiratory disease that emerged in November 2002 in Foshan, Guangdong Province, China. The emerging epidemic was subsequently named severe acute respiratory syndrome (SARS), and, was diagnosed in 8,422 patients which caused 774 deaths in 26 countries. The etiological agent of SARS was identified as a novel coronavirus 33, the SARS coronavirus (SARS-CoV), a member of the species severe acute respiratory

syndrome-related coronavirus in the genus β-coronavirus. The SARS epidemic ended on 5 July 2003, and since 2005, no human cases of SARS have been reported.

An adult patient in Jeddah, in the month June, year 2012, in Saudi Arabia, died of a progressive respiratory and renal failure 11 days after hospital admission for respiratory symptoms. A novel corona virus was subsequently isolated from that patient and was named Middle East respiratory syndrome coronavirus (MERS-CoV) by the Coronaviridae Study Group, International Committee on Taxonomy of Viruses (CSG-ICTV). By 31 May 2015 after the appearance of the first MERS patient, 1,180 total cases of MERS and 483 deaths had been reported to the WHO. By the end of 2019, 2,499 MERS cases and 858 deaths had been reported to the WHO, from a total of 27 countries.4

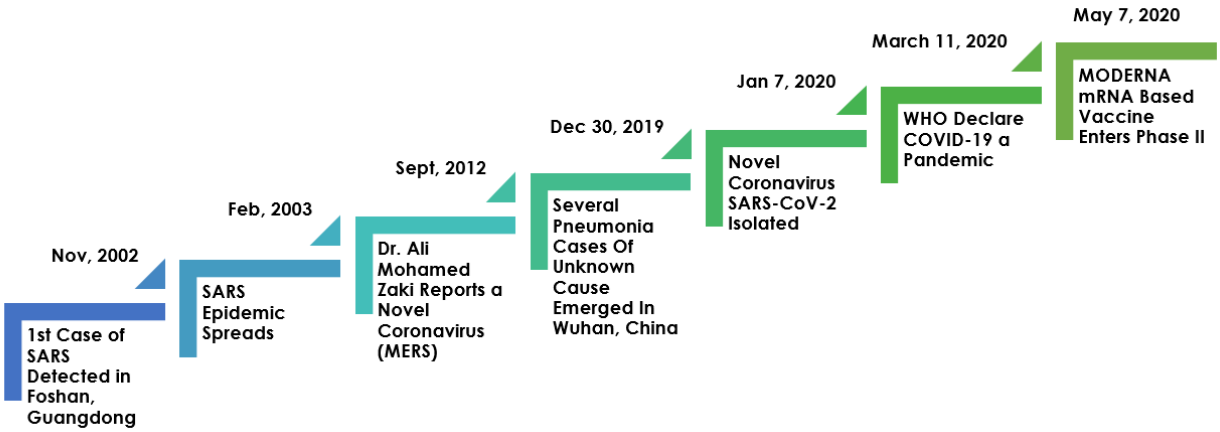
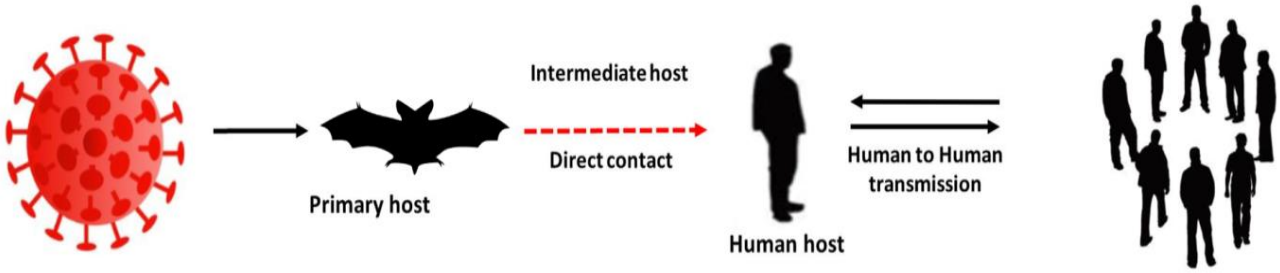



Fig.2. Coronavirus Timeline

## 1.3. Pathophysiology of Covid-19

### 1.3.1. Transmission

Person-to-person spread: The virus spread mainly from person-to-person. When a person sneeze or cough, respiratory droplets are produced which remain suspended in the air for some time. These droplets can enter in the mouths or nostrils of people who are nearby or possibly be inhaled into the lungs. Some recent studies have suggested that COVID-19 may be spread by people who are asymptomatic (not showing symptoms). Maintaining good social distance (about 6 feet) is very important in preventing the spread of COVID-19.5



Spread from contact with contaminated surfaces or objects: It is possible, that a person can get infected by COVID-19 by simply touching a contaminated surface or an object that has the virus's presence on it. The infection can be caught by a human body if the virus enters the human body via the mouth, nose or possibly the eye.

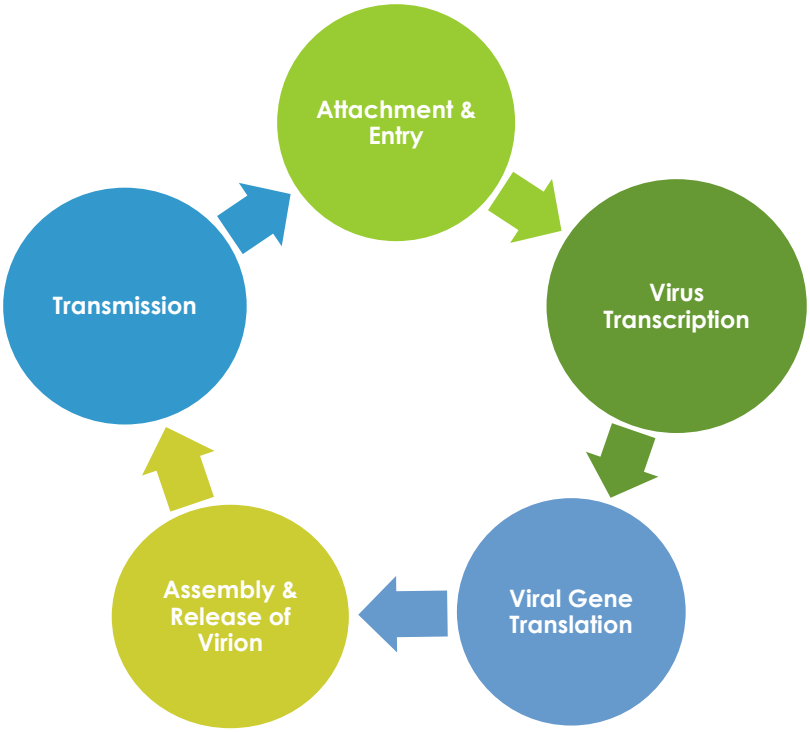
### 1.3.2. Life cycle

The attachment of the viral particle to the host is mediated by the S-protein complex. The binding domain of the S-protein shows presence and affinity to host receptors. Angiotensin Converting Enzyme (ACE2) is believed to assist viral attachment to the ciliary epithelial cells of a human lung.

Transcription of the viral genome is dependent on the formation of RTC; several Nsp are involved as cofactors for the RNA polymerase. Transcription of RNA genome also involves the synthesis of mRNA coding structural genes, following which the structural proteins start accumulating in the cytosol.

Translation of viral genes starts with the Replicase gene. A replicase is a complex compound of two polyproteins, which regulates host cytosol to enable transcription of the viral RNA genome. Accumulation of Nsp (1-15) in the cytosol signals formation replicase-transcriptase complex (RTC) enables transcription of the virus genome.

Assembly and release of virions are initiated by the Nucleocapsid protein in the presence of structural proteins. The M protein anchors the viral membrane components and accelerates the virion formation. The mature viral particles are released from the endoplasmic reticulum through budding. The viral particles are then released from the affected cells by exocytosis.6



### 1.3.3. Sign and Symptoms

The COVID-19 virus affects different people in different ways, it has an average incubation period of 14 days.7 COVID-19 causes respiratory disease

Common symptoms:

- Fever
- Tiredness
- Dry cough

Other symptoms include:

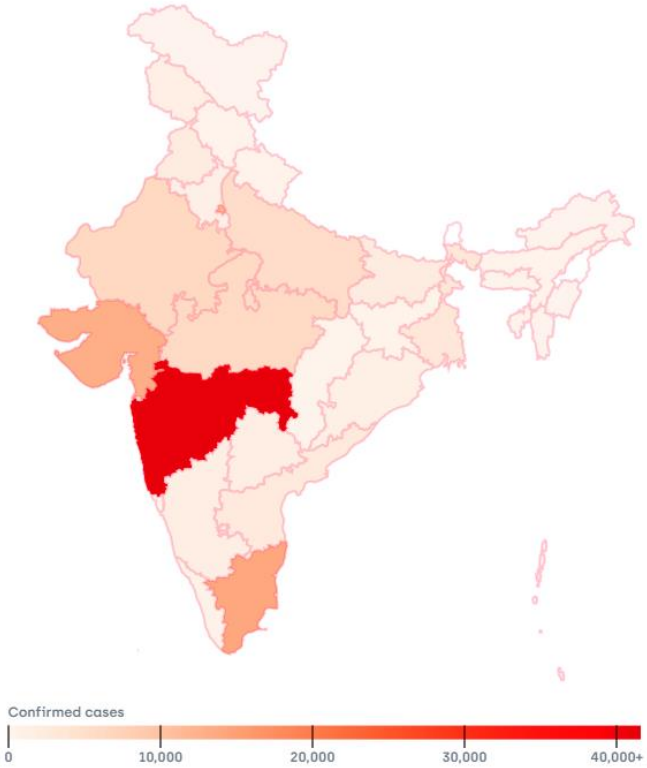
- Shortness of breath
- Aches and pains
- Sore throat
- Diarrhea, nausea, or a runny nose

Less common symptoms

- Loss of taste or smell
- Purple/blue lesions on feet and toes (COVID toes)

## 1.4. Indian Scenario

The novel SARS-CoV-2 coronavirus has its origin in the city of Wuhan, China. The first case was reported last year, eventually growing into a pandemic as announced by the WHO on 12th January 2020. History of COVID-19 in India began with a positive case in Kerala recorded on 30th January of 2020 caused by students who came from Wuhan, China. Cases grew from hundreds to thousands in less than two months, leading the government to call for timely lockdowns on 25 March 2020 as a preventive measure to contain the spread of the virus. The government had announced lockdowns in four installments; lockdown 1.0 from 25th March to 14th April; lockdown 2.0 from 15th April to 03rd May; lockdown 3.0 from 04th May to 17th May; lockdown 4.0 from 18th May to 30th May. As of 22 May 2020, the Ministry of Health and Family Welfare has confirmed a total of 118,447 cases, 48,534 recoveries, and 3,583 deaths in the country.

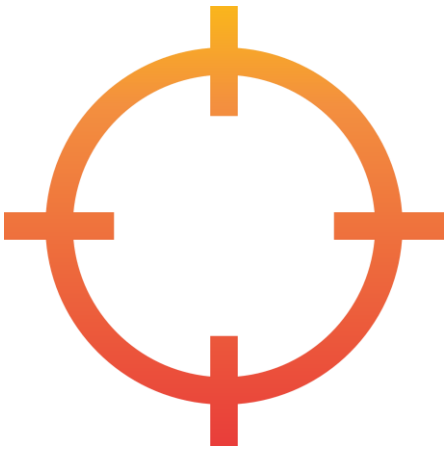


In India, four vaccine candidates are under early phases of development and may enter the clinical trial stage soon. Antimalarial drug hydroxychloroquine alone or in combination with other drugs is being used by frontline healthcare workers on severely affected patients but its efficacy and safety for COVID-19 is not yet established. Some state governments have tried convalescent plasma therapy, but the results are not very encouraging. Recently, Gilead Sciences antiviral drug remdesivir has shown positive results on the COVID-19 patient in a study and Gilead has signed non-exclusive royalty free voluntary licensing agreements with India based drug manufacturers Cipla, Jubilant Lifesciences and Mylan to manufacture and supply remdesvir to 127 countries.

Apart from modern medicines, conventional ayurvedic medicines, homeopathic medicines and herbs are also been used and tested to treat COVID-19. Recently, Dabur India's largest ayurvedic consumer goods firm has launched clinical trials to assess whether its Chyawanprash can boost immunity against the COVID-19.8 Kerala based Pankajakasthuri Herbal Research Foundation medicine, Zingivir-H used for treating respiratory infections, has got the approval from the Clinical Trial Registry of India for clinical trials on adults who have been tested positive for COVID-19. The Naiminath Homoeopathic Medical College is conducting studies to test the effects of the homeopathic medicine's arsenic album, bryonia alba, gelsemium, antimonium tartaricum and crotalus horridus.9

# 2. Objectives

- To perform detailed analysis of ongoing clinical trials with respect to new drugs, treatment regimen and vaccine candidates pertaining to Covid-19 pandemic.
- In depth analysis of clinical trials, to categorize them in accordance to study-based material and the treatment used. to understand the focus areas of lead sponsors.
- Graphical representation of trends (study type, clinical trial stage, etc.) from the mined data of relevant clinical trials.



# 3. Search Methodology

The first step is to create and define a clinical trial data set that will serve as the basis of this study. The clinical trial data was extracted from the US registry of clinical trials "Clinicaltrial.gov". Keyword based searches were carried out in the search field "condition" and "disease" on Clinicaltrial.gov.

# 4. Prophylaxis and Treatment

Currently, no pharmacologic therapies are available to treat COVID-19. A large number of clinical trials are ongoing to assess the suitability of several vaccine candidates such as synthetic chemical molecules, biological drugs, monoclonal antibodies, stem cells and plasma therapy etc. against the novel coronavirus treatment. In several cases, the old drugs are being repurposed to treat COVID-19 patients.

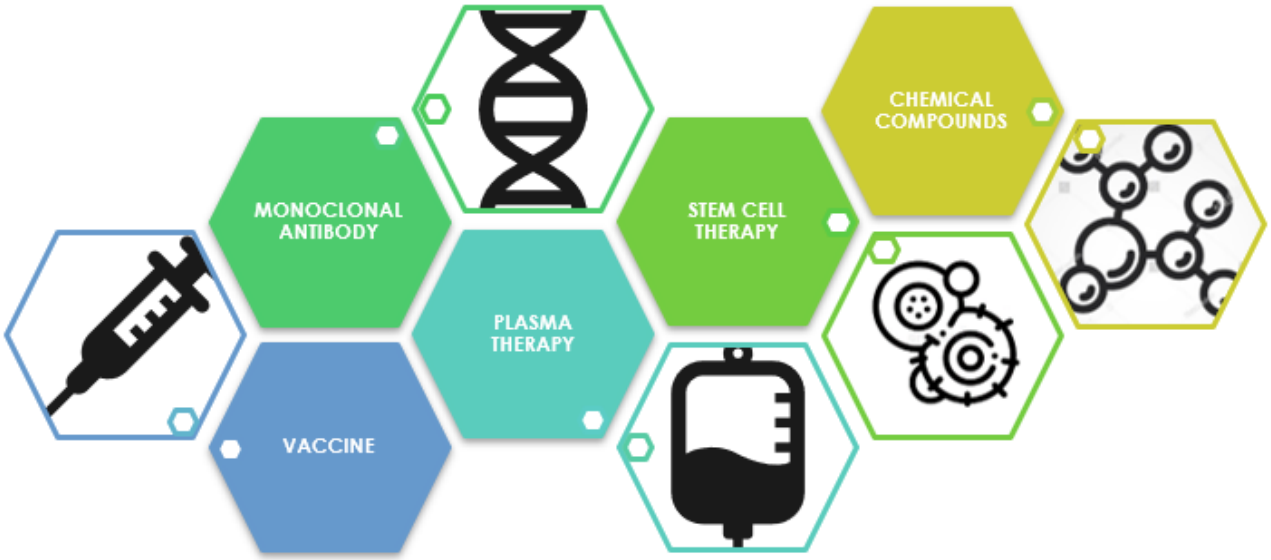



Fig.5. Therapeutic Strategies for COVID-19

## 4.1. Vaccine

The genetic sequence of SARS-CoV-2 was published on 12 January 2020, triggering enormous global R&D activity to develop a vaccine against COVID-19. Availability of next generation vaccine technology platforms accelerated the development and the first COVID-19 vaccine candidate entered human clinical testing on 16 March 2020. Vaccines including parts or whole inactivated viruses are commonly used in providing long term immunity due to the high level of protein expression and long-term stability. Developing inactivated or attenuated viral-based vaccines against coronavirus is challenging due to the variability of the strains. The list of the ongoing clinical trials of various vaccine candidates is provided below.10

| S. NO. | SOURCE | VACCINE CANDIDATE | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04299724 | Pathogen-Specific Aapc | SHENZHEN GENO IMMUNE MEDICAL INSTITUTE | Phase 1 |
| 2. | NCT04313127 | Recombinant Adenovirus Type 5 Vector | CANSINO BIOLOGICS | Phase 1 |
| 3. | NCT04276896 | LV-SMENP-DC, Antigen specific CTLs | SHENZHEN GENO-IMMUNE MEDICAL INSTITUTE | Phase 1 |
| 4. | NCT04352608 | Inactivated SARS-CoV-2 | SINOVAC BIOTECH | Phase 2 |
| 5. | ChiCTR2000031781 | Adenovirus Type 5 Vector | CANSINO BIOLOGICAL | Phase 2 |
| 6. | ChiCTR2000032459 | Inactivated | BEIJING INSTITUTE OF BIOLOGICAL PRODUCTS | Phase 2 |
| 7. | ChiCTR2000031809 | Inactivated | WUHAN INSTITUTE OF BIOLOGICAL PRODUCTS | Phase 2 |
| 8. | NCT04324606 | ChAdOx1 nCoV-19, MenACWY | UNIVERSITY OF OXFORD | Phase 2 |
| 9. | NCT04283461 | mRNA-1273 | MODERNA | Phase 2 |
| 10. | BNT162-01 | 3 LNP-mRNAs | BIONTECH/PFIZER | Phase 2 |
| 11. | NCT04327206 | BCG Vaccine | MURDOCH CHILDRENS RESEARCH INSTITUTE | Phase 3 |
| 12. | NCT04328441 | BCG Vaccine | UMC UTRECHT | Phase 3 |
| 13. | NCT04348370 | BCG Vaccine | ANDREW DINARDO | Phase 4 |

#As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

Inactivated SARS-CoV-2 by Sinovac Biotech, Adenovirus Type 5 Vector by Cansino Biological, mRNA-1273 by Moderna and ChAdOx1 nCoV-19, MenACWY by University of Oxford are some of the potential vaccine candidates which have already into phase II of clinical trials.

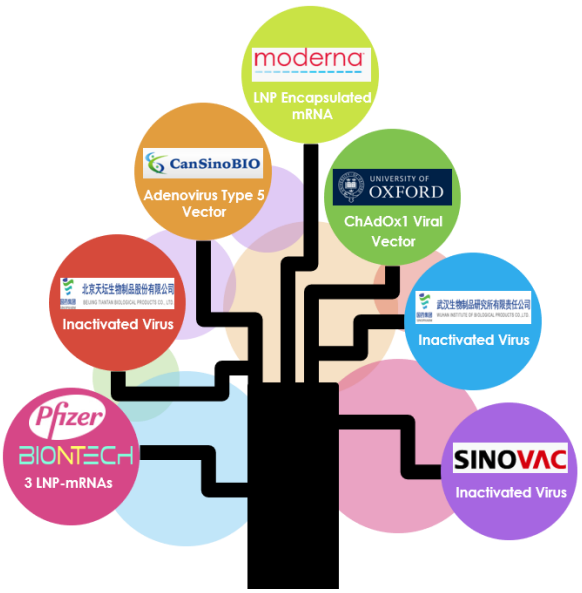



Fig.6. Vaccine Candidates in Phase II

## 4.2. Chemical Compounds

Several synthetic chemical compounds are being tested against the novel coronavirus. Intensive research and clinical trials are underway to assess the efficacy of new drugs and potential therapeutic targets for new drug development to treat COVID-19 patients. The ongoing clinical trials of new drug candidates are listed below.10

New Drug Candidates:

| S. NO. | SOURCE | NEW DRUG APPLICATION | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04324489 | DAS181 | RENMIN HOSPITAL OF WUHAN UNIVERSITY | Early Phase 1 |
| 2. | NCT04285190 | T89 | TASLY PHARMACEUTICALS | Early Phase 1 |
| 3. | NCT04341116 | TJ003234 | I-MAB BIOPHARMA | Phase 1 |
| 4. | NCT04350736 | TD-0903 | THERAVANCE BIOPHARMA | Phase 1 |
| 5. | NCT04056689 | DNL151 | DENALI THERAPEUTICS | Phase 1 |
| 6. | NCT04268784 | DNL343 | DENALI THERAPEUTICS | Phase 1 |
| 7. | NCT04335136 | RhACE2 APN01 | APEIRON BIOLOGICS | Phase 2 |

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| **8.** | **NCT04354389** | DAS181 | ANSUN BIOPHARMA | Phase 2 |
| **9.** | **NCT04313023** | PUL-042 Inhalation | PULMOTECT | Phase 2 |
| **10.** | **NCT04312997** | PUL-042 Inhalation | PULMOTECT | Phase 2 |
| **11.** | **NCT04347226** | BMS-986253 | MATTHEW DALLOS | Phase 2 |
| **12.** | **NCT04342897** | LY3127804 | ELI LILLY AND COMPANY | Phase 2 |
| **13.** | **NCT04334460** | BLD-2660 | BLADE THERAPEUTICS | Phase 2 |
| **14.** | **NCT04345614** | CM4620 Injectable | CALCIMEDICA | Phase 2 |
| **15.** | **NCT04298060** | DAS181 | ANSUN BIOPHARMA | Phase 2 |
| **16.** | **NCT03808922** | DAS181 | ANSUN BIOPHARMA | Phase 3 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

**Drug Repurposing:**

Many clinical trials are now conducting drug repurposing trials, i.e., new use of known therapeutic molecules for the treatment of COVID-19. Some of the important ongoing clinical trials for repurposing known antiviral, antimalarial and other therapeutic agents are enlisted below:

Antiviral Drugs:

| S. NO. | SOURCE | DRUG | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| **1.** | **NCT04275388** | Lopinavir | JIANGXI QINGFENG PHARMACEUTICAL | Early Phase 1 |
| **2.** | **NCT04261907** | Ritonavir | FIRST AFFILIATED HOSPITAL OF ZHEJIANG UNIVERSITY | Early Phase 1 |
| **3.** | **NCT03891420** | Galidesivir | BIOCRYST PHARMACEUTICALS | Phase 1 |
| **4.** | **NCT04349241** | Favipiravir | AIN SHAMS UNIVERSITY | Phase 3 |
| **5.** | **NCT04343248** | Nitazoxanide | ROMARK LABORATORIES | Phase 3 |
| **6.** | **NCT04292730** | Remdesivir | GILEAD SCIENCES | Phase 3 |
| **7.** | **NCT04345276** | DanopreviR | HUOSHENSHAN HOSPITAL | Phase 4 |

Antimalarial Drugs:

| S. NO. | SOURCE | DRUG | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04342169 | HCQ, Placebo oral tablet | UNIVERSITY OF UTAH | Phase 2 |
| 2. | NCT04342650 | CQ Diphosphate, Placebo oral tablet | FUNDAÇÃO DE MEDICINA TROPICAL DR HEITOR VIEIRA DOURADO | Phase 2 |
| 3. | NCT04349371 | CQ, Placebo oral tablet | COLUMBIA UNIVERSITY | Phase 2 |
| 4. | NCT04334148 | HCQ, Placebo oral tablet | DUKE UNIVERSITY | Phase 3 |
| 5. | NCT04349228 | HCQ, Placebo oral tablet | ABDERRAHMANE MAMI HOSPITAL | Phase 3 |
| 6. | NCT04346329 | HCQ, Placebo oral tablet | UNIVERSIDAD NACIONAL DE COLOMBIA | Phase 3 |
| 7. | NCT04325893 | HCQ, Placebo oral tablet | UNIVERSITY HOSPITAL ANGERS | Phase 3 |
| 8. | NCT04316377 | HCQ | UNIVERSITY HOSPITAL AKERSHUS | Phase 4 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

Miscellaneous Drugs:

| S. NO. | SOURCE | MISCELLANEOUS DRUGS | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04293887 | Recombinant Human Interferon A1β | TONGJI HOSPITAL | Early Phase 1 |
| 2. | NCT04312243 | Nitric Oxide Gas | MASSACHUSETTS GENERAL HOSPITAL | Phase 2 |
| 3. | NCT04343976 | Pegylated Interferon Lambda | RAYMOND CHUNG | Phase 2 |
| 4. | NCT04350320 | Colchicine | FUNDACION PARA LA FORMACION E INVESTIGACION SANITARIAS DE LA REGION DE MURCIA | Phase 3 |
| 5. | NCT04348305 | Hydrocortisone | SCANDINAVIAN CRITICAL CARE TRIALS GROUP | Phase 3 |

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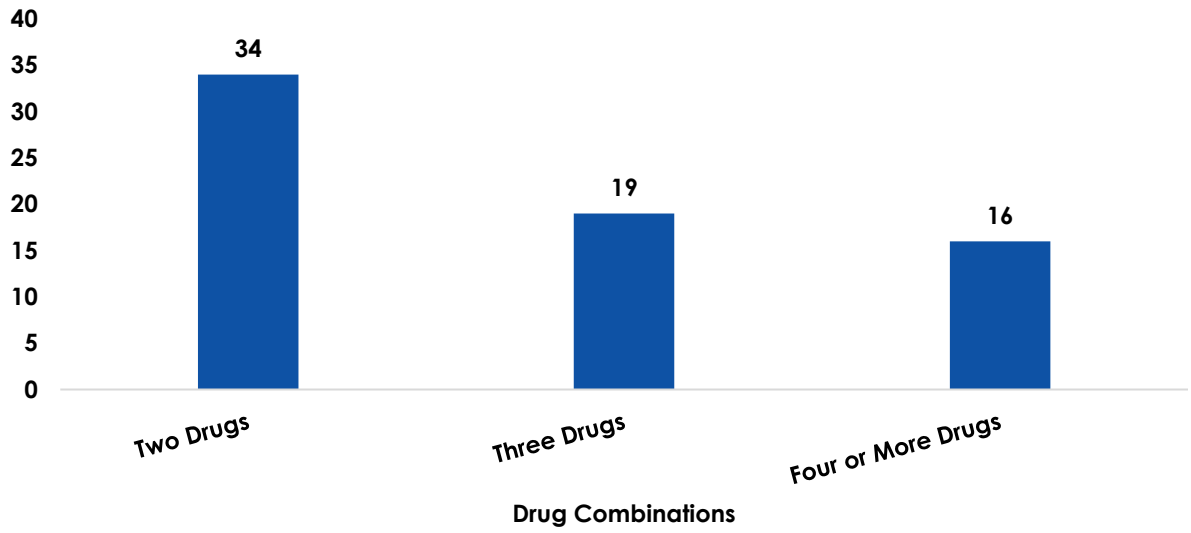
| **6.** | **NCT04325061** | Dexamethasone | DR. NEGRIN UNIVERSITY HOSPITAL | Phase 4 |
| **7.** | **NCT04263402** | Methylprednisolone, Methylprednisolone | TONGJI HOSPITAL | Phase 4 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

Combination of Drugs:

Due to multiple complications caused by COVID-19 infection, such as pulmonary tract infection, organ failure and other complications owing to patient previous health ailment, a combination of drugs are been extensively studied and tested. Some of combinations are giving good results. One such example is a two-week triple drug combination therapy of interferon with beta-1b, lopinavir–ritonavir and ribavirin, which had shown promising results. The test reduced the duration of viral shedding in patients with mild to moderate illness.11 The different ongoing clinical trials of various drug combinations are listed below.10



Combination of Two Drugs:

| S. NO. | SOURCE | COMBINATION DRUGS | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04340349 | Hydroxychloroquine, Bromhexine | INSTITUTO NACIONAL DE REHABILITACION | Early Phase 1 |
| 2. | NCT04295551 | Lopinavir/Ritonavir, Xiyanping Injection | JIANGXI QINGFENG PHARMACEUTICAL | Early Phase 1 |
| 3. | NCT04343092 | Ivermectine, Hydroxychloroquine | UNIVERSITY OF BAGHDAD | Phase 1 |
| 4. | NCT04339712 | Anakinra, Tocilizumab | HELLENIC INSTITUTE FOR THE STUDY OF SEPSIS | Phase 2 |
| 5. | NCT04339426 | Atovaquone, Azithromycin | HONORHEALTH RESEARCH INSTITUTE | Phase 2 |
| 6. | NCT04330586 | Ciclesonide, Hydroxychloroquine | KOREA UNIVERSITY GURO HOSPITAL | Phase 2 |
| 7. | NCT04347915 | Clevudine, Hydroxychloroquine | BUKWANG PHARMACEUTICAL | Phase 2 |
| 8. | NCT04328961 | Hydroxychloroquine, Ascorbic Acid | UNIVERSITY OF WASHINGTON | Phase 2 |
| 9. | NCT04350281 | Interferon Beta-1b, Hydroxychloroquine | THE UNIVERSITY OF HONG KONG | Phase 2 |
| 10. | NCT04330690 | Lopinavir, Ritonavir | SUNNYBROOK HEALTH SCIENCES CENTRE | Phase 2 |
| 11. | NCT04307693 | Lopinavir/Ritonavir, Hydroxychloroquine | ASAN MEDICAL CENTER | Phase 2 |
| 12. | NCT04329650 | Siltuximab, Methylprednisolone | JUDIT PICH MARTÍNEZ | Phase 2 |
| 13. | NCT04261270 | Asc09f, Oseltamivir | TONGJI HOSPITAL | Phase 3 |
| 14. | NCT04339816 | Azithromycin, Hydroxychloroquine | ST. ANNE'S UNIVERSITY HOSPITAL BRNO | Phase 3 |

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| **15.** | NCT04252274 | Darunavir, Cobicistat | SHANGHAI PUBLIC HEALTH CLINICAL CENTER | Phase 3 |
| **16.** | NCT04355052 | Hydroxychloroquine, Amostat Mesylate | SHEBA MEDICAL CENTER | Phase 3 |
| **17.** | NCT04345445 | Tocilizumab, Methylprednisolone | UNIVERSITY OF MALAYA | Phase 3 |
| **18.** | NCT04254874 | Abidol Hydrochloride, Interferon | TONGJI HOSPITAL | Phase 4 |
| **19.** | NCT04338906 | Camostat Mesilate, Hydroxychloroquine | HEINRICH-HEINE UNIVERSITY | Phase 4 |
| **20.** | NCT04341493 | Nitazoxanide, Hydroxychloroquine | HUGO MENDIETA ZERON | Phase 4 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

Combination of Three Drugs:

| S. NO. | SOURCE | COMBINATION DRUGS | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| **1.** | **NCT04273763** | Bromhexine Hydrochloride, Arbidol Hydrochloride, Recombinant Human Interferon A2b | SECOND AFFILIATED HOSPITAL OF WENZHOU MEDICAL UNIVERSITY | Early Phase 1 |
| **2.** | **NCT04344457** | Hydroxychloroquine, Indomethacin, Zithromax | PERSEVERANCE RESEARCH CENTER, LLC | Phase 1 |
| **3.** | **NCT04351347** | Chloroquine, Nitazoxanide, Ivermectin | TANTA UNIVERSITY | Phase 2 |
| **4.** | **NCT04328012** | Lopinavir/Ritonavir, Hydroxychloroquine Sulfate, Losartan | BASSETT HEALTHCARE | Phase 2 |
| **5.** | **NCT04341870** | Sarilumab, Azithromycin, Hydroxychloroquine | ASSISTANCE PUBLIQUE - HÔPITAUX DE PARIS | Phase 2 |
| **6.** | **NCT04332094** | Tocilizumab, Hydroxychloroquine, Azithromycin | FUNDACIÓ INSTITUT DE RECERCA DE L'HOSPITAL DE LA SANTA CREU I SANT PAU | Phase 2 |
| **7.** | **NCT04338698** | Hydroxychloroquine, Oseltamivir, Azithromycin | SHEHNOOR AZHAR | Phase 3 |

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| **8.** | NCT04328285 | Hydroxychloroquine, Lopinavir, Ritonavir | CENTRE HOSPITALIER UNIVERSITAIRE DE SAINT ETIENNE | Phase 3 |
| **9.** | NCT04330638 | Anakinra, Siltuximab, Tocilizumab | UNIVERSITY HOSPITAL, GHENT | Phase 3 |
| **10.** | NCT04350671 | Interferon Beta-1a, Lopinavir/Ritonavir, Hydroxychloroquine | SHAHID BEHESHTI UNIVERSITY OF MEDICAL SCIENCES | Phase 4 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

Combination of Four or More Drugs:

| S. NO. | SOURCE | COMBINATION DRUGS | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| **1.** | NCT04333407 | Aspirin, Clopidogrel, Rivaroxaban, Atorvastatin, Omeprazole | IMPERIAL COLLEGE LONDON | Early Phase 1 |
| **2.** | NCT04251871 | Oxygen Therapy, Alfa Interferon, Lopinavir/Ritonavir, Traditional Chinese Medicines | BEIJING 302 HOSPITAL | Early Phase 1 |
| **3.** | NCT04354428 | Ascorbic Acid, Folic Acid, Hydroxychloroquine Sulfate, Folic Acid, Hydroxychloroquine Sulfate, Azithromycin | UNIVERSITY OF WASHINGTON | Phase 2 |
| **4.** | NCT04351724 | Chloroquine/Hydroxychloroquine, Lopinavir/Ritonavi, Rivaroxaban, Thromboprophylaxis, Candesartan, Non-RAS Blocking Antihypertensives, Clazakizumab | MEDICAL UNIVERSITY OF VIENNA | Phase 2 |
| **5.** | NCT04345419 | Chloroquine, Favipiravir, Nitazoxanide, Ivermectin, Niclosamide | TANTA UNIVERSITY | Phase 2 |
| **6.** | NCT04331470 | Levamisole, Budesonide, Formoterol Inhaler, Lopinavir/Ritonavir, Hydoxychloroquine | FASA UNIVERSITY OF MEDICAL SCIENCES | Phase 2 |
| **7.** | NCT04321993 | Lopinavir/Ritonavir, Hydroxychloroquine Sulfate, Baricitinib, Sarilumab | LISA BARRETT | Phase 2 |

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|---|---|---|---|---|
| **8.** | NCT04347031 | Mefloquine, Hydroxychloroquine, Mefloquine, Azithromycin, Tocilizumab, Hydroxychloroquine, Azithromycin, Tocilizumab | BURNASYAN FEDERAL MEDICAL BIOPHYSICAL CENTER | Phase 2 |
| **9.** | NCT04303299 | Protease Inhibitors, Oseltamivir, Favipiravir, Hydroxychloroquine | RAJAVITHI HOSPITAL | Phase 3 |
| **10.** | NCT04255017 | Abidol Hydrochloride, Oseltamivir, Lopinavir, Ritonavir | TONGJI HOSPITAL | Phase 4 |
| **11.** | NCT04286503 | Carrimycin, Lopinavir/Ritonavir, Arbidol, Chloroquine Phosphate | BEIJING YOUAN HOSPITAL | Phase 4 |
| **12.** | NCT04343768 | Hydroxychloroquine, Lopinavir/Ritonavir, Interferon Beta-1a, Interferon Beta-1b | SHAHID BEHESHTI UNIVERSITY OF MEDICAL SCIENCES | Phase 4 |
| **13.** | NCT04350684 | Umifenovir, Interferon-B 1a, Lopinavir / Ritonavir, Hydroxychloroquine | SHAHID BEHESHTI UNIVERSITY OF MEDICAL SCIENCES | Phase 4 |

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## 4.3. Monoclonal Antibody

Monoclonal antibodies (mAb or moAb) are made of identical immune cells that are clones of a unique parent cell. Like the antibodies, mAbs can recognize specific targets of a virus. Recently, Israel Institute for Biological Research (IIBR) has completed the development phase of coronavirus antibody or passive vaccine.12 Italian researcher developed a vaccine which has antibodies generated in mice that works on human cells.13 Some of the important ongoing clinical trials testing various mAbs are listed below.10

| S. NO. | SOURCE | MONOCLONAL ANTIBODY | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| **1.** | NCT04305106 | Bevacizumab | QILU HOSPITAL OF SHANDONG UNIVERSITY | Early Phase 1 |
| **2.** | NCT04275245 | Meplazumab | TANG DU HOSPITAL | Phase 1 |
| **3.** | NCT04331795 | Tocilizumab | UNIVERSITY OF CHICAGO | Phase 2 |

| | | | | |
|---|---|---|---|---|
| **4.** | **NCT04348500** | Clazakizumab | CEDARS SINAI MEDICAL CENTER | Phase 2 |
| **5.** | **NCT04315298** | Sarilumab | REGENERON PHARMACEUTICALS | Phase 2 |
| **6.** | **NCT04347239** | Leronlimab | CYTODYN | Phase 2 |
| **7.** | **NCT04335071** | Tocilizumab | UNIVERSITY HOSPITAL INSELSPITAL | Phase 2 |
| **8.** | **NCT04344782** | Bevacizumab | ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS | Phase 2 |
| **9.** | **NCT04343144** | Nivolumab | ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS | Phase 2 |
| **10.** | **NCT04346797** | Eculizumab | ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS | Phase 2 |
| **11.** | **NCT04351243** | Gimsilumab | KINEVANT SCIENCES | Phase 2 |
| **12.** | **NCT04343651** | Leronlimab | CYTODYN | Phase 2 |
| **13.** | **NCT04275414** | Bevacizumab | QILU HOSPITAL OF SHANDONG UNIVERSITY | Phase 2 |
| **14.** | **NCT04335305** | Tocilizumab, Pembrolizumab | MEDSIR | Phase 2 |
| **15.** | **NCT04324021** | Emapalumab | SWEDISH ORPHAN BIOVITRUM | Phase 2 |
| **16.** | **NCT04327388** | Sarilumab | SANOFI | Phase 2 |
| **17.** | **NCT04324073** | Sarilumab | ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS | Phase 2 |
| **18.** | **NCT04315480** | Tocilizumab | UNIVERSITÀ POLITECNICA DELLE MARCHE | Phase 2 |
| **19.** | **NCT04320615** | Tocilizumab | ROCHE | Phase 3 |
| **20.** | **NCT04351152** | Lenzilumab | HUMANIGEN | Phase 3 |
| **21.** | **NCT04158648** | Emicizumab | ROCHE | Phase 3 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

## 4.4. Plasma Therapy

Along with various vaccine and chemical compound trials, plasma therapy is also one of the treatments which is being tried. Convalescent plasma obtained from COVID-19 survivors is intravenously administrated to patients requiring hospitalization for symptomatic "high risk" COVID-19 disease.11 Plasma

therapy is found to be helpful in free viral clearance, blocking the new infection and accelerating the infected cell clearance, which suppress viraemia.12

| S. NO. | SOURCE | PLASMA THERAPY | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04355897 | Convalescent COVID-19 Plasma | THE CHRIST HOSPITAL | Early Phase 1 |
| 2. | NCT04353206 | Multiple Doses of Anti-Sars-Cov-2 Convalescent Plasma | JOHNS HOPKINS UNIVERSITY | Early Phase 1 |
| 3. | NCT04340050 | Anti-Sars-Cov-2 Convalescent Plasma | UNIVERSITY OF CHICAGO | Early Phase 1 |
| 4. | NCT04346589 | Antibodies Obtained with DFPP From Convalescent Patients | AFERETICA | Early Phase 1 |
| 5. | NCT04264858 | Immunoglobulin of Cured Patients | WUHAN UNION HOSPITAL | Early Phase 1 |
| 6. | NCT03042143 | Human Umbilical Cord Derived Cd362 Enriched Mscs, Placebo (Plasma-Lyte 148) | BELFAST HEALTH AND SOCIAL CARE TRUST | Phase 1 |
| 7. | NCT04332380 | Plasma | UNIVERSIDAD DEL ROSARIO | Phase 2 |
| 8. | NCT04332835 | Plasma | UNIVERSIDAD DEL ROSARIO | Phase 2 |
| 9. | NCT04345991 | Transfusion of COVID-19 Convalescent Plasma | ASSISTANCE PUBLIQUE - HÔPITAUX DE PARIS | Phase 2 |
| 10. | NCT04354831 | Anti-Sars-Cov-2 Convalescent Plasma | MEDICAL COLLEGE OF WISCONSIN | Phase 2 |
| 11. | NCT04323800 | Anti- Sars-Cov-2 Plasma, Sars-Cov-2 Non-Immune Plasma | JOHNS HOPKINS UNIVERSITY | Phase 2 |
| 12. | NCT04343755 | Convalescent Plasma | HACKENSACK MERIDIAN HEALTH | Phase 2 |
| 13. | NCT04345523 | Blood and Derivatives | PUERTA DE HIERRO UNIVERSITY HOSPITAL | Phase 2 |
| 14. | NCT04350580 | Human Immunoglobulin | CENTRE HOSPITALIER ST ANNE | Phase 3 |

# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home)

## 4.5. Mesenchymal Stem Cells

Mesenchymal stem cells (MSCs) have regenerative properties and the ability to differentiate into diverse cell lineages. The beneficial effect of MSCs treatment is principally due to the immunomodulation and regenerative potential of these cells. MSCs can help in reducing the pathological changes of lungs and inhibit the cell-mediated immune-inflammatory response, induced by the influenza virus.

| S. NO. | SOURCE | STEM CELLS | LEAD SPONSOR | STUDY PHASE# |
|---|---|---|---|---|
| 1. | NCT04302519 | Dental pulp mesenchymal stem cells | CAR-T (SHANGHAI) BIOTECHNOLOGY | Early Phase 1 |
| 2. | NCT04273646 | UC-MSCs | WUHAN UNION HOSPITAL | Early Phase 1 |
| 3. | NCT04313322 | WJ-MSCs | STEM CELLS ARABIA | Phase 1 |
| 4. | NCT04341610 | Stem Cell Product | RIGSHOSPITALET | Phase 1 |
| 5. | NCT04252118 | MSCs | BEIJING 302 HOSPITAL | Phase 1 |
| 6. | NCT04315987 | NestCell® MSCs | AZIDUS BRASIL | Phase 1 |
| 7. | NCT04346368 | BM-MSCs | GUANGZHOU INSTITUTE OF RESPIRATORY DISEASE | Phase 1 |
| 8. | NCT04331613 | CAStem | CHINESE ACADEMY OF SCIENCES | Phase 1 |
| 9. | NCT04276987 | MSCs-derived exosomes | RUIJIN HOSPITAL | Phase 1 |
| 10. | NCT04288102 | MSCs | BEIJING 302 HOSPITAL | Phase 2 |
| 11. | NCT04348435 | HB-adMSCs | HOPE BIOSCIENCES | Phase 2 |
| 12. | NCT04349631 | HB-adMSCs | HOPE BIOSCIENCES | Phase 2 |
| 13. | NCT04299152 | Treated Mononuclear Cells Apheresis | TIANHE STEM CELL BIOTECHNOLOGIES | Phase 2 |
| 14. | NCT04269525 | UC-MSCs | ZHIYONG PENG | Phase 2 |

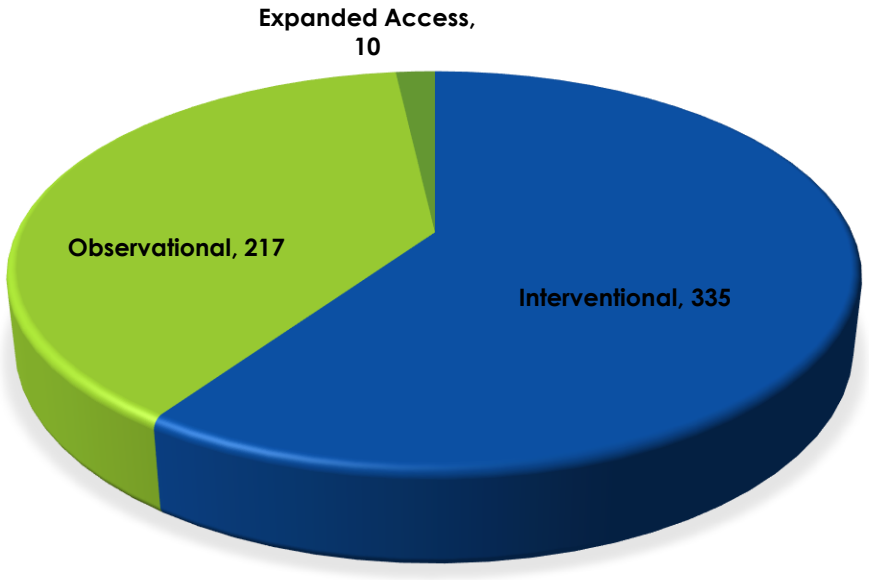
# As of 22 May 2020 (https://clinicaltrials.gov/ct2/home )

# 5. Trend Analysis

In response to the global COVID-19 pandemic, clinical trial research evaluating the efficacy and safety of suitable candidates to treat COVID-19 are emerging at an exceptional pace. Close to 1,300 clinical trials have been registered globally.

## 5.1. Study Type

Below graph represents the type of ongoing clinical trial studies.




Definition:

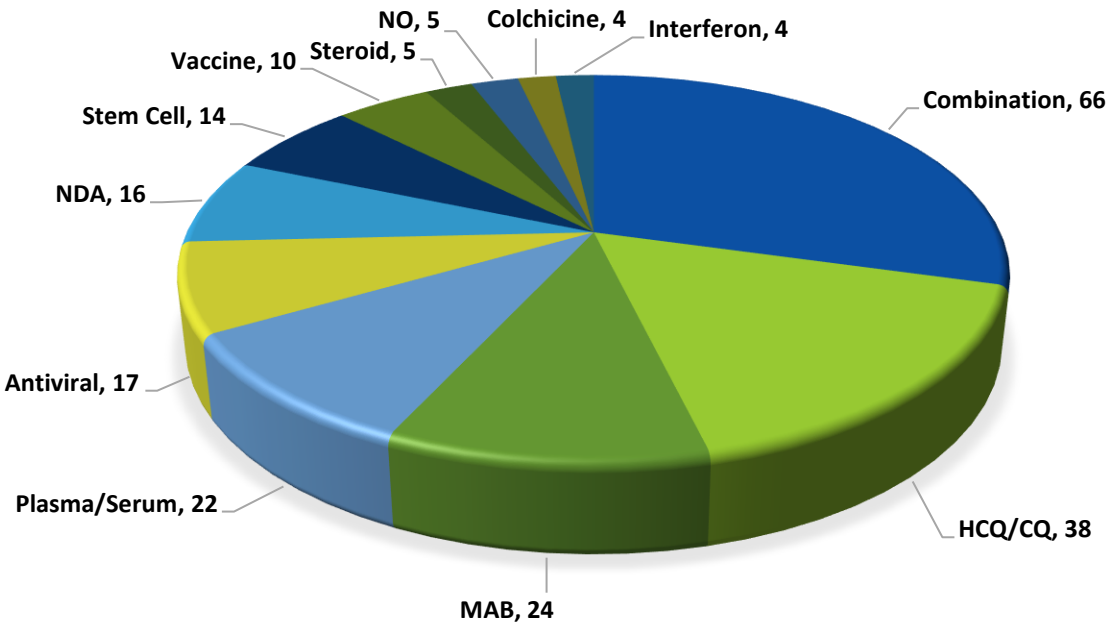
**Expanded access**: Expanded access is the use of an unapproved drug under special forms of investigational new drug applications (IND), outside of a clinical trial, by people with serious or life-threatening conditions who do not meet the enrolment criteria for the clinical trial in progress.

**Observational**: In observational studies, the investigator makes no intervention, and patients are allocated treatment based on clinical decisions.

**Interventional**: An interventional study is one in which the patient receives some kind of intervention, such as a new medicine, to evaluate it.

## 5.2. Interventional Therapy

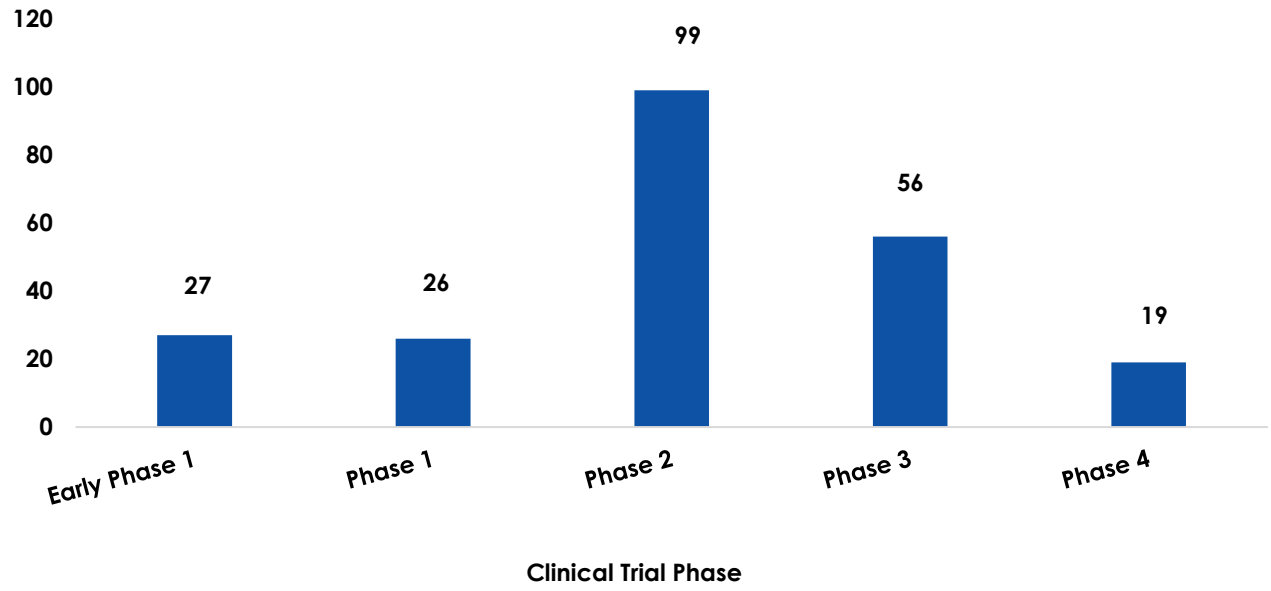
The below graph represents major interventional therapies currently been evaluated in various ongoing clinical trials.




A large number of clinical trials are focused on combination of drugs for the treatment of COVID-19 infection. Further, several clinical trials are ongoing for repurposing hydroxychloroquine, a well-known antimalarial drug. Trials for several vaccines are also underway for prophylaxis of COVID-19. Plasma therapy and monoclonal antibody treatment are also being prominently tested along with stem cell therapy to reverse the damage to the patient's body by utilizing the regeneration properties of stem cells.

## 5.3. Clinical Trial Stage

The below graph represents the status of interventional therapies in the clinical trial phase.




For almost half of the ongoing clinical trials, the vaccine/drug candidates have entered in to the phase 2 wherein they are being tested on patients to assess their efficacy and side effects.

Definitions:

**Early Phase 1**: Pharmacokinetics; particularly, oral bioavailability and half-life of the drug.

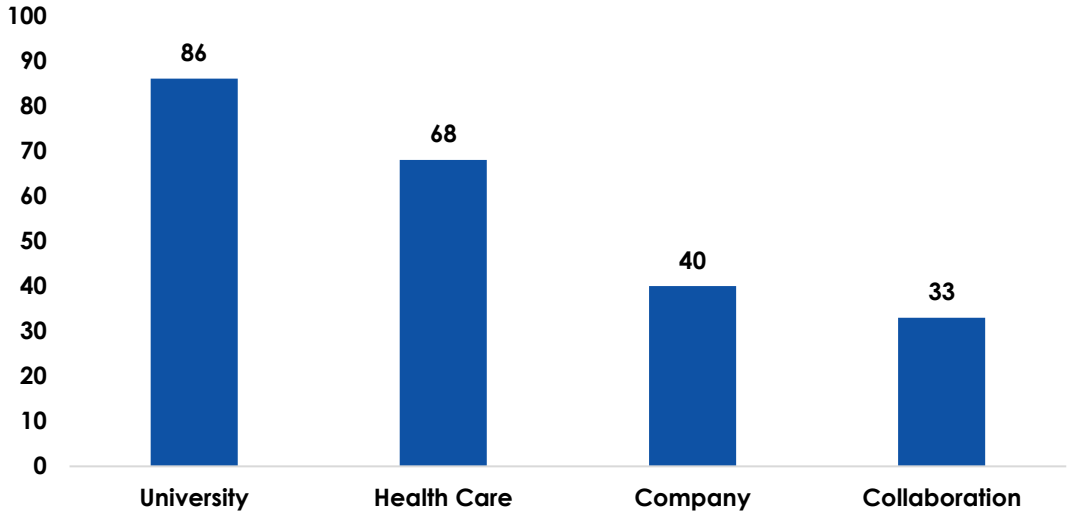
**Phase 1**: Testing of a drug on healthy volunteers for safety; involves testing multiple doses (dose-ranging).

**Phase 2**: Testing of a drug on patients to assess efficacy and side effects.

**Phase 3**: Testing of a drug on patients to assess efficacy, effectiveness, and safety.

**Phase 4**: Post marketing surveillance i.e. watching drug use in public.

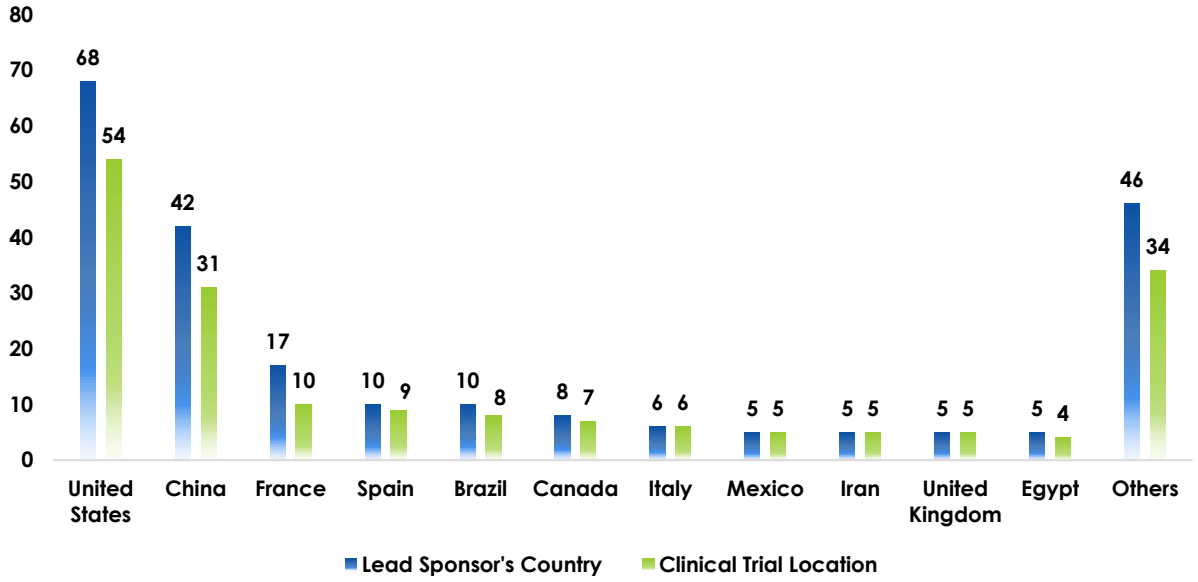
## 5.4. Lead Sponsor Type




Universities are ahead in the race of clinical trial studies followed by healthcare organizations and companies. Moreover, universities, healthcare organizations and companies are also collaborating and synchronizing their efforts to fight this pandemic.

## 5.5. Clinical Trial Location Vs Lead Sponsor's Country

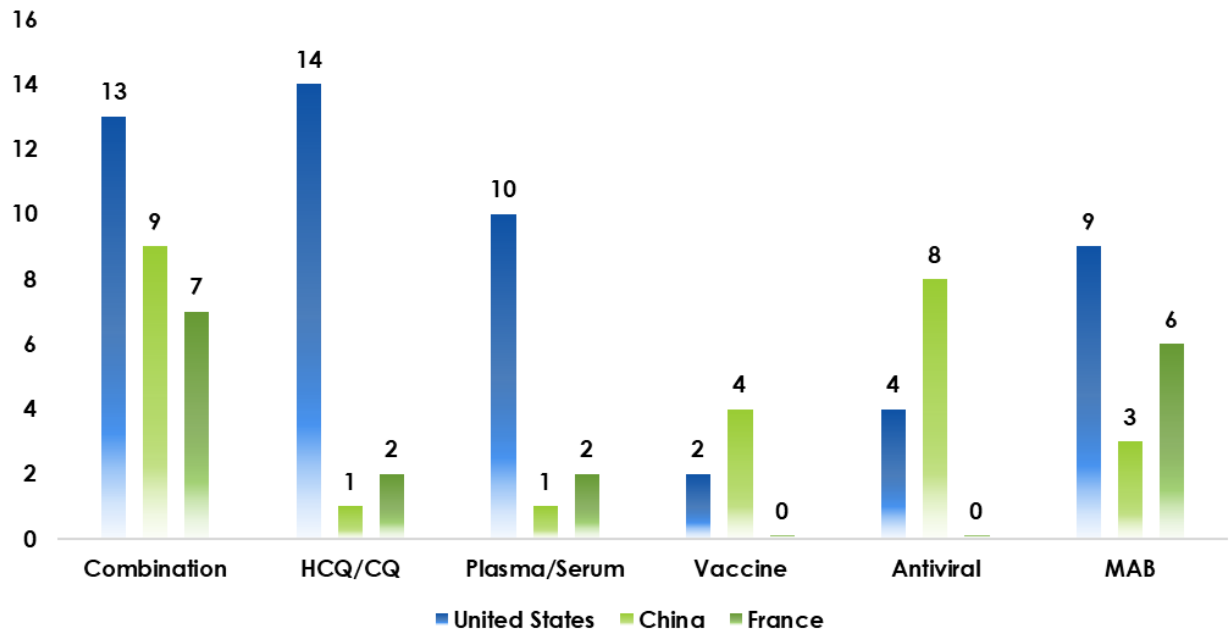
The below graph represents the top location of ongoing clinical trials Vs the lead sponsor's country of origin.




United States is the seat for highest numbers of ongoing clinical trials followed by China and France. A similar trend is observed with lead sponsor's country origin. Lead sponsors based on United States are not only conducting clinical trials in the United States but also sponsoring clinical trials in other countries.

## 5.6. Lead Sponsor's Country Vs Interventional Drugs

The below graph represents the lead sponsor's country origin Vs type of Interventional drugs in the clinical trials.




The top three lead sponsors based out of United States, China and France are sponsoring clinical trials focusing on use of combination of drugs for the treatment of COVID-19. China is ahead of United States in terms of clinical trials on vaccine development and repurposing of antiviral drugs.

# 6. Summary

The academicians, universities, healthcare providers and companies across the globe are fueling their energies in search of a vaccine and drug candidate for prophylaxis and the treatment of COVID-19 disease. Several hundreds of clinical trials are underway to establish evidence around investigational drugs and to identify a suitable vaccine candidate.

Developing inactivated or attenuated viral-based vaccines against coronavirus is challenging due to the variability of the strains. Moderna mRNA vaccine candidate for COVID-19 has shown protective antibodies production in a group of healthy volunteers in phase II of clinical trials. Oxford University vaccine candidate "ChAdOx1 nCoV-19" initial tests on rhesus macaques' monkeys had shown symptoms of fighting the virus, the tests have now entered phase II of clinical trials.

A large number of ongoing clinical trials are focused on interventional studies wherein drugs/biologics are being used to treat the patient. Clinical trials based on combination of drugs for the treatment of COVID-19 are the most studied trials along with the trials for repurposing hydroxychloroquine to treat COVID-19. Plasma therapy, monoclonal antibody and stem cell therapy are being extensively tested in clinical trials as an option for treatment of COVID-19.

Most of the clinical trials are headed by Universities and healthcare organization owing to the current situation of pandemic and the large influx of patients with COVID-19. The clinical trial race is preceded by the USA and China, with two-third of the total ongoing clinical trials being sponsored/conducted in USA and China.

With no approved vaccine or treatment available for COVID-19, Moderna vaccine candidate and Gilead Sciences antiviral drug remdesivir have shown a ray of hope. In this modern era of next generation technologies, we are able to develop multiple vaccine candidates in matter of few months, but the clinical efficacy, human safety testing and if approved, the mass production of vaccine are some of the hurdles which we need to tackle in order to develop a successful vaccine for the prophylaxic of COVID-19 pandemic.

# 7. References & Credits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