National COVID-19 Science Task Force (NCS-TF)

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Vaccines and Treatments for Sars-CoV2/COVID-19

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Sources used/searched:
WHO COVID-19 pages, ClinicalTrial.gov, www.clinicaltrialsregister.eu, www.kofam.ch, Coronavirus Treatment tracker by Damian Garde, SwissEthics, PubMed, BioRvix and MedRvix selected search for neutralizing antibodies and screens for new antiviral drugs and news articles regarding research in Switzerland (especially University press releases).

Overall situation - global

There is a vast amount of data and planned trials. The database ClinicalTrial.gov lists a total of 1050 studies for COVID-19 and many more are listed in the BMC Trial database (21 trials) and the European Trial database (35 trials). Kofam.ch, the Swiss trial registry, has 10 entries. There is an interactive resource on ongoing and completed studies, which also assesses the quality of the study based on pre-defined criteria. The site for COVID19-treatments is: https://www.covid-nma.com/dataviz/ and the site also contains a summary for vaccination studies: https://covid-nma.com/observational_studies/index.php?intervention=5.

Table 1:

Terms	Search Results*	Entire Database**
Synonyms		
COVID-19	1,050 studies	1,050 studies
SARS-CoV-2	367 studies	367 studies

Terms	Search Results*	Entire Database**
Synonyms		
2019-nCoV	34 studies	34 studies
severe acute respiratory syndrome coronavirus 2	28 studies	28 studies
2019 novel coronavirus	20 studies	20 studies
Wuhan coronavirus	1 studies	1 studies

As reflected in the respective websites cited above, a majority of completed treatment studies suffer from biases and/or are of very small sample sizes.

Overall situation - Switzerland

A regularly updated list of ongoing clinical trials as well as pending trials is released by SwissEthics (https://swissethics.ch/covid-19/approved-projects). A list of Swiss start-up implication in the fight against Coronavirus can be found at venturelab.ch. The version from 30.4.2020 is attached. As of April 30st 2020, 93 clinical studies have been approved by SwissEthics on COVID in Switzerland. 60 additional ones are submitted and currently under evaluation (see attached list). The list below is not exhaustive and we might have missed important preclinical work.

There are many research projects already ongoing in Switzerland, with little visibility of all work (Note: we did not find any good summary on ongoing Swiss research). Different Universities are publishing press releases. This information also includes these press-releases from academia. It would be very helpful to have a list of ongoing studies in Switzerland.

Vaccines/Vaccination (active and passive)

In Switzerland, we could find information on the following studies on vaccines; passive vaccination and monoclonal antibodies are currently ongoing – still all in preclinical stage; except for the passive immunization with convalescent plasma:

Key developments:

⇒ The University Hospital Basel has used INTERCEPT treated coronavirus convalescent plasma (CCP) as experimental therapy as early as the beginning of April and was one of the first places outside of China to do so.

⇒ Swissmedic has approved the first COVID-19 therapy study with convalescent plasma on April 7st, which is led by the University Hospital of Zurich. In a first phase, 30 patients will be included (https://www.kofam.ch/en/snctp-portal/search/80826/study/50562)
⇒ A small study is ongoing in Locarno with 10 patients (https://www.kofam.ch/en/snctp-portal/search/80826/study/50686)

⇒ Martin Bachmann, Department of Immunology at the University Hospital in Berne has developed a vaccine directed against the crown protein of Sars-CoV2 engineered on cucumber virus. He could already test in animals.
⇒ Peter Burkhard, an immunologist with a private laboratory, AOPeptides, in Basel has a nanoparticle-based vaccine candidate that he already successfully tested on animals and also applied a single dosis to himself.
⇒ InnoMedica (Stefan Halbheer et al), Marly/Berne/Zug, is working on a liposome-based vaccine
⇒ Several studies on neutralizing antibodies are ongoing including a project by Humabs Biomed and VIR Bellinzona, a study by NeurImmune AG, a study by researchers from the Moncucco Hospital in Lugano and a study by the ETH spin-off Memo Therapeutics in collaboration with ETH Zürich (Sven Panke, trial not found in the Swiss Ethics database). Memo Therapeutics has also launched a hackaton called the HACK CORONA INITIATIVE.
⇒ Several groups, including the one of Sai Reddy of DBSSE, ETH Basel and the Laboratory of Protein Design and Immunoengineering at EPFL are using computational methods to try and predict good antibodies.
⇒ Emma Wetter Slack, Tim Keys and Markus Aebi from ETH Zürich are working on a glyocvaccine they hope to make easy-to-produce, affordable and storable and therefore potentially a good candidate to be used in low- and middle income countries.

Drugs / Biologicals

The most common treatments currently are:

- Antiviral drugs, especially HIV, Ebolavirus, Influenza drugs
- Monoclonal antibodies directed against different inflammatory targets
- Anti-inflammatory drugs/biologicals
- Antimalarial drugs; 4-aminoquinolines
- Most recently also drugs to prevent thrombosis
- Some treatments include: Rentioids, low-dose radiation therapy, broad spectrum immunoglobulins, anti-oxidants, Vitamin C

Specific Information:

Several Swiss drug companies and SpinOffs are first front in providing potential medication against COVID.

- Relief Therapeutics in Zurich has the drug Aviptadil, for which it is seeking FDA approval in collaboration with NeuroRx. A study is planned and registered (https://clinicaltrials.gov/ct2/show/NCT04360096).

- Roche has Actemra (also called RoActemra, Tocilizumab), a monoclonal antibody against IL-6 tested in several clinical trials (see table).
- Novartis is currently testing a monoclonal antibody against IL-1beta (Canakinumab, Can-Covid trial, see Table).
- Novartis is also planning a trial for Jakavi® (ruxolitinib) in collaboration with Incyte and several other trials are ongoing for this drug (https://clinicaltrials.gov/ct2/show/NCT04359290, https://clinicaltrials.gov/ct2/show/NCT04338958,

Several trials are registered, foreseen or ongoing in Switzerland (see attached Excel sheets from SwissEthics and the corresponding link https://swissethics.ch/covid-19/approved-projects). There are trials using Remdesivir, C1 esterase inhibitors, thrombosis prophylaxis, monoclonal antibodies including Tocilizumab and Hydroxychloroquine. A trial to prevent household spread and re-admission to the hospital using hydroxychloroquine is also planned. It is the largest of its kind in Europe so far.

Table 2: Drugs Current Randomized Controlled Trials (RCTs) in Switzerland

The following table 2 lists the current RCTs in Switzerland (The table was compiled by Oiriol Manuel and Manuel Battegay, University Hospital Basel)

Name	Arms	Sponsor	Sites	PI	Status	Open to other centers
Solidarity	HCQ, LPVr+/- IFNB, remdesivir, SOC	BAG/ Lausanne	17 in Switzerland	O. Manuel	Recruiting	Potentially
COPEP	HCQ, LPVr or surveillance as PEP	Geneva	Geneva, Basel	A. Calmy	Recruiting	Potentially
CoronACT	Tocilizumab, Placebo	Bern	Bern, Zurich, Lausanne, Ticino	P.Villiger	Recruiting	Potentially
Stay Home	HCQ vs. placebo for outpatients	Lausanne	Lausanne, Sion, Fribourg, Bern, Aargau	B. Genton	Not recruiting yet	Yes
Gilead 5773 and 5774	remdesivir 10 vs 5d vs SOC	Gilead	Locarno, Zurich, Geneva	E. Bernasconi	Recruiting	No
Gilead expanded acces	Remdesivir	Gilead	6 sites in Switzerland	-	Recruiting	Yes
Anticoagulation in Covid	Prophylaxis vs. anticoagulation	Geneva	Geneva	M. Blandon	Recruiting	Potentially
Sevoflurane in COVID-19 ARDS	Sevoflurane vs. standard sedation	Zurich	Zurich	M. Schläpfer	Recruiting	Unknown

List of the Swiss centers involved in the WHO Solidarity trial:

1. CHUV, Lausanne
2. HUG, Genève
3. Réseau hospitalier neuchâtelois Neuchâtel
4. Hôpital cantonal de Fribourg (HFR), Fribourg
5. Hôpital Rivera-Chablais, Rennaz
6. Hôpital du Valais Sion

7. Hôpital du Jura, Delémont
8. Universitätsspital Basel
9. Inselspital Bern
10. Lindenhof Bern
11. Kantonsspital Aarau
12. Hirslanden Klinik Aarau
13. Kantonsspital Baden
14. Spital Thurgau AG, Kantonsspital Frauenfeld
15. Spital Thurgau AG, Kantonsspital Münsterlingen
16. Bürgerspital Solothurn
17. Kantonsspital Olten

Further, Swiss researchers are participating in the Global PCHF-COVICAV Registry (https://clinicaltrials.gov/ct2/show/NCT03078166 and the Swiss Ethics Excel sheet for approved studies) as well as the EPICENTRE (ESPNIC Covid pEdiatric Neonatal Registry) initiative (https://espnic-online.org/News/Latest-News/More-than-100-units-willing-to-join-EPICENTRE-EsPnIc-Covid-paEdiatric-NeonaTal-Registry and Swiss Ethics Ethics sheet https://swissethics.ch/covid-19/approved-projects). Zürich, Geneva and Lugano are also participating in an international trial to test Remesdivir (https://www.kofam.ch/en/snctp-portal/search/80826/study/50547).

Development of new drugs in Switzerland

Switzerland has several ongoing projects to find new drugs against Sars-CoV2. Roland Riek and his group from ETHZ are using in silico modeling and NMR spectroscopy to find substances interacting with the spike proteins of the virus using drugs approved by the FDA. Dario Neri and his group from ETHZ is testing a chemical library in vitro. Shana Sturla and her group, also from ETH with Gisert Schendier use the platform Nexus to find drug candidates against the viral RNA polymerase and Martin Fussenegger and his group from ETHZ search for inhibitors of Sars-CoV2 proteases using chemical libraries as well.
Groups from ETH Basel (Randall Platt) and Jeffrey Bode and the Friederich Miescher Institute are focusing on host proteins important in the virus entry and try to block this. A collaborative effort was set up 5 years ago between the group of F. Stellacci, nanomaterial scientist at EPFL, and the group of C. Tapparel, virologist at UNIGE, to develop broad-spectrum cidal antivirals.

Antibody surveillance/ Natural immunity

There are several surveillance projects currently ongoing in Lausanne, Geneva, St. Gallen and Basel. The Swiss School of Public Health announced a joint action (Corona Immunitas) to test 25'000 Swiss residents and cohorts of special groups like school children, production plants, nursing homes) and provide reliable data on the number of antibody carriers / exposure to SARS-COV2. A study registered in SwissEthics aims at defining T cell epitopes that drive antibody mediated recovery and protection from COVID-19 (CoHelp study).

Project ideas submitted to the first call of the Swiss National Science Foundation COVID funding

There are 284 applications submitted to the SNF for the first COVID specific call. The majority is biomedical, but there are also 80 projects from the humanities and social sciences.

"Researchers are working overtime to find ways of overcoming the Covid-19 pandemic. In this context, the SNSF's special call for coronavirus research has met with great interest, with 284 applications being submitted in all. Of these, 96 study viruses and infections, 35 the immune response in humans and 40 the spread of the disease. 19 projects address communication issues and 60 the psychological, social, legal and economic consequences of the crisis. In 34 projects, the researchers will focus on vaccines and therapeutic substances. "

Key studies and results taking place worldwide

Active vaccinations: Clinical trials and vaccine candidates (preclinical and phase 1)

The most updated WHO list is of 26 April (https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf).

Monoclonal, potentially neutralizing antibodies against SARS-COV2:

There are several ongoing studies to isolate neutralizing, monoclonal antibodies against SARS-COV2, some registered as clinical trials, others not:

- ⇒ Lyon on 10 subjects, goal to get immortalized cell lines: https://clinicaltrials.gov/ct2/show/NCT04354766
- ⇒ Columbia University Irving Medical center on 12 subjects, https://clinicaltrials.gov/ct2/show/NCT04342195
- ⇒ Baylor College of Medicine in collaboration with AlloVir
- ⇒ Amgen with Adaptive Biotechnologies
- ⇒ Astra Zeneca with Vandebilt University Medical Center
- ⇒ Celltrion with Korea Centres for Disease Control
- ⇒ AbCellera with Eli Lilly company
- ⇒ Grifols with US government
- ⇒ Neurimmuneand Ethris (Swiss companies)
- ⇒ Regeneron (using humanized mice, successful during the Ebola outbreak to make an antibody cocktail with some protection)
- ⇒ Takeda, Behring, Biotest, BPL, LFB, Octapharma announced a collaboration

- ⇒ **SAB Biotherapeutics together with CLS Behring seems to have a polyclonal candidate (SAB-185), which was produced on their DiversitAb platform. Clinical trials are imminent.**

There are very few recent scientific articles claiming to have identified monoclonal antibodies (see attachments):

Structural Basis for Potent Neutralization of Beta-coronaviruses by Single-domain Camelid Antibodies

Daniel Wrapp, Dorien De Vlieger, Kizzmekia S. Corbett, Gretel M. Torres, WanderVan Breedam, Kenny Roose, Loes van Schie, VIB-CMB COVID-19 Response Team, Markus Hoffmann, Stefan Pöhlmann, Barney S. Graham, Nico Callewaert, BertSchepens, Xavier Saelens, Jason S. McLellan

bioRxiv 2020.03.26.010165; doi: https://doi.org/10.1101/2020.03.26.010165

"Here we report the isolation of two potently neutralizing VHHs directed against the 69 SARS-CoV-1 and MERS-CoV RBDs. These VHHs were elicited in response to immunization of 70 a llama with prefusion-stabilized SARS-CoV-1 and MERS-CoV S proteins."

A human monoclonal antibody blocking SARS-CoV-2 infection

Chunyan Wanga,**, Wentao Lia,**, Dubravka Drabekb,c,**, Nisreen M.A. Okbad, Rien van 4 Haperenb,c, Albert D.M.E. Osterhause, Frank J.M. van Kuppevelda, Bart L. Haagmansd, 5 Frank Grosveldb,c,$ and Berend-Jan Boscha,*,$

Supposedly the first article to show a monoclonal antibodiy to SARS-COV2. "47D11 binds a conserved epitope on the spike receptor binding domain explaining its ability to cross-neutralize SARS-CoV and SARS-CoV-2, 104 using a mechanism that is independent of receptor binding inhibition."

Note: the article has been cited 8 times, but is not yet published (since 6 weeks!)

Human monoclonal antibodies block the binding of SARS-CoV-2 spike protein to angiotensin converting enzyme 2 receptor

Xiangyu Chen1, Ren Li2,3, Zhiwei Pan1, Chunfang Qian4, Yang Yang1, Renrong You5, Jing Zhao6, Pinghuang Liu5, Leiqiong Gao1, Zhirong Li1, Qizhao Huang7, Lifan Xu1, Jianfang Tang1, Qin Tian1, Wei Yao1, Li Hu1, Xiaofeng Yan4, Xinyuan Zhou 1, Yuzhang Wu1, Kai Deng 8, Zheng Zhang9, Zhaohui Qian10, Yaokai Chen4 and Lilin Ye 1

Cellular & Molecular Immunology; https://doi.org/10.1038/s41423-020-0426-7

"Human monoclonal antibodies block the SARS-CoV-2 RBD protein-hACE2 protein interaction. We found that both 311mab-31B5 and 311mab-32D4 could efficiently block SARS-CoV-2 RBD hACE2 interaction (IC50 = 0.0332, and 0.0450 μg/ml, respectively), while 311mab–31B9 clone failed to inhibit such an interaction (Fig. 1g). The 31B5- and 32D4- mediated inhibition of RBD-hACE2 interaction was also evidenced by flow cytometry analysis (Fig. 1h, i). Furthermore, we determined the neutralization of these three mAbs using a SARS-CoV-2 S pseudotyped lentiviral particle.22 In line with ELISAand flow cytometry-based blockade results, both 311mab-31B5 and 311mab-32D4 effectively neutralized pseudovirus entry to host cells ectopically expressing hACE2 (IC50 = 0.0338, and0.0698 μg/ml, respectively). As expected, 311mab-31B9 clone failed to show any neutralization activities (Fig. 1j)."

Neutralizing Antibodies against SARS-CoV-2 and Other Human Coronaviruses

Shibo Jiang,[1,2] Christopher Hillyer,[1] and Lanying Du1,*

Trends in Immunology, in press, review

This is a recent review, which is in press. However, the data seems to be already to some extent outdated as they claim that there is no monoclonal antibody available. While there are some reports, the quality of these should be validated. All of these were only tested in vitro and not yet in animal models.

Several scientific pre-prints and articles show that there are neutralizing antibodies in patients who are infected by SARS-Cov2. It is however also evident that not all patients are mounting an immune response to the same extent. There are several ongoing trials for

Table 3: Passive immunization (registered trials on clinicaltrials.gov)					
Platform	**Vaccination**	**Developper/Sponsor**	**Reported Phase**	**Location and target size**	**Reference/ Link**
Convalescent plasma	passive	Hilton Pharma	N/A	Pakistan n=2000 patients; target number of donors is not specified	https://clinicaltrials.gov/ct2/show/NCT04352751 expected inclusion start: April 20 Single group assignment
Convalescent plasma	passive	Erasmus Medical Center Rotterdam Maasstad Ziekenhuis Rotterdam	Phase 2/3	Netherlands Target number of patients: 426 Target number of donors: 100	https://clinicaltrials.gov/ct2/show/NCT04342182 Recruiting since April 8, 2020 randomized, comparative trial passive, single blinded (patient) immunization vs. standard care Concovid study
Convalescent plasma	passive	King Fahad Specialist Hospital Dammam + collaborating Institutions	Phase 2	South Arabia Target number of patients: 40 Number of donors is not specified	https://clinicaltrials.gov/ct2/show/NCT04347681 Recruiting (since April 12?) non-randomized, experimental and control arm, open label
Convalescent plasma	passive	University of Alberta Edmonton, Alberta, Canada Vancouver General Hospital Vancouver, British Columbia, Canada + 24 more hospitals	Phase 3	Canda-wide 1200 participants	https://clinicaltrials.gov/ct2/show/NCT04348656 not yet Recruiting, estimated start Arpil 27 randomized, open label experimental vs. standard of care Concor-1 study
Convalescent plasma	passive	Medical College of Wisconsin Froedtert Hospita	Phase 2	USA 131 participants	https://clinicaltrials.gov/ct2/show/NCT04354831 Non-randomized open label with two cohorts: ICU and non-ICU hospitalized No control group Not yet Recruiting

passive immunization. The ones registered on ClinicalTrials.gov are listed in Table 3 below. There are likely more clinical trials ongoing, which are not (yet) registered on these platforms.

Global: Current treatments in clinical testing

Specific for Switzerland: see above sections and table 2

Below, table 4, is a selection of international key studies. The list is not exhaustive! (there are 1050 registered trials!) except for the monoclonal antibody-related trials, where we did a specific search. They are highlighted in bold (full search of the ClinicalGov.org database, BMC database and European Clinical Trial database using the keywords “antibody” and “COVID” / “Sars-CoV2”)

Results of finished studies are summarized here: https://covid-nma.com/living_data/index.php
A more or less updated study on clinical trials can be found here: https://laegemiddelstyrelsen.dk/da/nyheder/temaer/ny-coronavirus-covid-19/~/media/5B83D25935DF43A38FF823E24604AC36.ashx

Table 4: Treatments in clinical trials (registered trials on clinicaltrials.gov, www.clinicaltrialsregister.eu or the BMC trial repository)

Name of treatment	Developer/ sponsor	Type of treatment/ proposed mode of action	Repurposed or new drug?	Clinical trial In vitro In vivo	Study site	References/ Links
Solidarity trial - Remdesivir - Lopinavir/Ritonavir - Interferon beta-1a - Chloroquine/ Hydroxychlorquine	WHO		All Repurposed	Clinical trial	100 countries across the World	http://www.isrctn.com/ISRCTN83971151
Hydroxychloroquine, Telmisartan and Azithromycin	Hôpitaux Universitaires de Strasbourg		All Repurposed	Randomized, Multi-Centre, Adaptive, Blinded Study 1600 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001303-16/FR Vidoc-19 trial Recruiting
Hydroxychloroquine plus azithromycin versus hydroxychloroquine	University Hospital of Montpellier		Repurposed	Controlled, randomized, open label 120 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001406-27/FR Recruiting
Hydroxychloroquine/ Lopinavir / Ritonavir Pill / Azithromycin	Hospital Universitario de	Anti-inflammatory, HIV Inhibitors	Repurposed	Randomized, open label pragmatic trial	Columbia	https://clinicaltrials.gov/ct2/show/NCT04359095 Not yet Recruiting

	Neiva Neiva, Huila, Colombia And other partners in Colubmia			1600 participants		
Favipiravir	Asst Fatebenefratelli Sacco Milano, Italy	Antiviral, RNA Polymerase Inhibitor		Clinical trial, randomized, N=100 Double-blinded	Italy	https://clinicaltrials.gov/ct2/show/NCT04336904 Started March 25
Remdesivir	National Institute of Allergy and Infectious Diseases (NIAID)	Antiviral	Repurposed	Multi-center, adaptive, randomized, double-blind, placebo-controlled trial 800 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04280705 Recruiting
Galidesivir	Clinical Research Unit and Department of Infectious and Parasitic Diseases Hospital das Clínicas, School of Medicine, USP	RNA Polymerase Inhibitor	Repurposed	Double-blind, Placebo-controlled, Dose-ranging Study 66 participants	Brazil	https://clinicaltrials.gov/ct2/show/NCT03891420
Bemcentinib (synonym: BGB324 or R428)	University Hospital Southampton NHS Foundation Trust	Inhibits the AXL kinase		Multicentre, Seamless, Phase 2 Adaptive Randomisation Platform Study 825 participants	UK	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001736-95/GB ACCORD-2 trial Recruiting
Ruxolitinib plus simvastatin		Janus Kinase Inhibitor/ Inhibitor of HMG-CoA-Reductase	Repurposed	Randomized phase II clinical trial 94 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001405-23/ES Recruiting

Hydroxychloroquine together with baricitinib, imatinib or early lopinavir / ritonavir	Hospital Universitario de Fuenlabrada		Repurposed	randomized, open-label, parallel group study 165 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001321-31/ES Recruiting
Hydroxychloroquine (HCQ) / Azithromycin (Azithro)/	National Institute of Allergy and Infectious Diseases (NIAID)	Anti-inflammatory, antiviral	Repurposed	Randomized, Double-blind, Placebo-controlled Trial 2000 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04358068 Not yet Recruiting
Hydroxychloroquine (HCQ) / Azithromycin (Azithro)/	Instituto Investigación Sanitario Biocruces Bizkaia	Anti-inflammatory, antiviral	Repurposed	Randomized, open label controlled trial 132 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001606-33/ES Recruiting
Hydroxychloroquine	sanofi-aventis recherche & développement	Antiviral, antimalarial	Repurposed	Multicenter, double blinded, placebo-controlled, randomized clinical trial 350 participants	Denmark Czech Republic UK France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001270-29/DK https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001270-29/CZ https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001270-29/GB https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001270-29/FR Recruiting
Hydroxychloroquine	Massachusetts General Hospital	Antiviral, antimalarial	Repurposed	Multicenter, double blinded, placebo-controlled, randomized clinical trial 510 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04332991 Recruiting ORCHID study
Lopinavir-Ritonavir Dexamethasone	Oxford University			Randomised adaptive trial	UK	http://www.isrctn.com/ISRCTN50189673 https://www.recoverytrial.net

Hydroxychloroquine				5000 participants		RECOVERY trial Recruiting
AZITHROMYCIN Lopinavir-Ritonavir	Groupe Hospitalier Paris Saint Joseph		Repurposed	randomized trial of efficacy and safety 640 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001723-13/FR OUT-COV study Recruiting
Dexamethasone associated with hydroxychloroquine vs. hydroxychloroquine	Groupe Hospitalier Paris Saint Joseph	Antimalarial, anti-inflammatory	Repurposed	Open-label, randomized controlled 122 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001333-13/FR Recruiting
Hydroxychloroquine	Oxford University	Antimalarial/ antiviral	Repurposed	3000 participants; to reduce hospital admission	UK	https://doi.org/10.1186/ISRCTN86534580 https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001209-22/GB PRINCIPAL trial
Colchicine	FFIS	anti-inflammatory	Repurposed	Controlled, randomized, open label 102 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001511-25/ES Recruiting
Imatinib	Amsterdam UMC	Inhibitor of protein kinase	Repurposed	Single-blinded, randomized controlled 304 participants	Netherlands	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001236-10/NL COUNTER COVID study Recruiting
Canakinumab	Novartis Farmacéutica S.A.	Monoclonal antibody against IL-1beta		Multicenter, randomized, double-blind, placebo-controlled study 450 participants	France Germany Italy Spain United Kingdom United States	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001370-30/ES CAN-COVID trial Recruiting

Tocilizumab	Universitätskliniku m Freiburg	blockade of IL-6R, monoclonal AB		randomized, double blinded placebo-controlled trial 200 participants	Germany	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001408-41/DE Recruiting
Tocilizumab	Emory University Hospital/Winship Cancer Institute	blockade of IL-6R, monoclonal AB		Randomized, open label controlled trial 180 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04361552 Recruiting
Tocilizumab / Methylprednisolone	University Malaya Medical Centre Kuala Lumpur, Malaysia	Anti-inflammatory blockade of IL-6R, monoclonal AB (Tocilizumab)	Both Repurposed	Clinical trial, 310 participants, Open label, randomized crossover assignment	Malaysia	https://clinicaltrials.gov/ct2/show/NCT04345445 Not yet Recruiting
Tocilizumab	Assistance Publique - Hôpitaux de Paris	Monoclonal to IL-6R		Multiple Randomized Controlled Trials Open-label 228 participants	France	https://clinicaltrials.gov/ct2/show/NCT04331808 Corimuno-Toc trial
RoActemra (other name for Tocilizumab)	CHU AMBROISE PARE	Monoclonal to IL-6R		Randomized, open-label controlled trial 60 participants	Belgium	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001770-30/BE Recruiting
RoActemra (other name for Tocilizumab)	Bispebjerg-Frederiksberg Hospital Copenhagen, Denmark	Monoclonal to IL-6R		Open-Label, Multicenter Sequential and Cluster Randomized Trial 200 participants	Denmark	https://clinicaltrials.gov/ct2/show/NCT04322773 Recruiting

Anti-CD14 AB	IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University	Monoclonal antibody against CD14	Repurposed	Compassionate Use Open-Label Anti-CD14 Treatment Patient number not clear	Italy	https://clinicaltrials.gov/ct2/show/NCT04346277 Recruiting?
Lenzilumab **(Humaneered® anti-human GM-CSF monoclonal antibody)**	Humanigen, Inc.	GM-CSF targeted monoclonal antibody	Repurposed	Randomized, double blind, parallal assignment 238 participants	USA?	https://clinicaltrials.gov/ct2/show/NCT04351152 Not yet Recruiting
TJ003234	I-Mab Biopharma Co. Ltd.	GM-CSF targeted monoclonal antibody		randomized, double-blind, placebo-controlled, multi-center trial	USA	https://clinicaltrials.gov/ct2/show/NCT04341116 Recruiting
Emapalumab **Anakinra**	Swedish Orphan Biovitrum	Anti-interferon Gamma (Anti-IFNγ) monocloncal antibody (Emapalumab) Interleukin-1(IL-1) Receptor Antagonist (Anakinra)	Repurposed	open label, controlled, parallel group, 3-arm, multicenter study 54 participants	Lombardy, Italy	https://clinicaltrials.gov/ct2/show/NCT04324021 Recruiting
Leronlimab	Montefiore Medical Center Bronx, New York, United States	Anti CCR5 monoclonal antibody		Randomized, Double Blind, Placebo Controlled Study 75 participants follow-up with 390 participants	New York	https://clinicaltrials.gov/ct2/show/NCT04343651 Recruiting https://clinicaltrials.gov/ct2/show/NCT04347239

Bevacizumab	Qilu Hospital of Shandong University Jinan, Shandong, China	Monoclonal antibody to VEGF-A	Repurposed (Avastin)	Multicenter Randomized Controlled Clinical 140 participants	China/ Wuhan	https://clinicaltrials.gov/ct2/show/NCT04305106 Recruiting
Sarilumab	Rosario García de Vicuña	IL-6R monoclonal AB	Repurposed	Randomised, open-label, single-center, comparative trial 30 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001634-36/ES
Sarilumab	VA Boston Healthcare System Boston, Massachusetts, United States	blockade of IL-6R monoclonal AB	Repurposed	Randomized, open label, parallel assignment 120 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04359901 Recruiting
Sarilumab	Clínica Universidad de Navarra/Universidad de Navarra	blockade of IL-6R monoclonal AB	Repurposed	Open label, non controlled 60 participants	Spain	Repurposed Recruiting
Sarilumab	Fundación de Investigación Biomédica - Hospital Universitario de La Princesa	IL-6R monoclonal AB	Repurposed	Randomised, open-label, single-center, comparative trial of sarilumab plus standard of care vs. standard of care in a 2:1 ratio 30 particiants	Spain	https://clinicaltrials.gov/ct2/show/NCT04357808 Recruiting
Sarilumab / Azithromycin / Hydroxychloroquine	Assistance Publique - Hôpitaux de Paris	Anti-inflammatory, antiviral, monoclonal to IL6R	Repurposed	Bayesian open labelled randomized clinical trial 60 participants	France, Multi-Center	https://clinicaltrials.gov/ct2/show/NCT04341870 Recruiting

Sarilumab	Assistance Publique - Hôpitaux de Paris	monoclonal to IL6R	Repurposed	Multiple Randomized Controlled Trials Open-label 239 participants	Paris, France, Multi-Center	https://clinicaltrials.gov/ct2/show/NCT04324073 Recruiting Corimuno-19 study
polyvalent immunoglobulins Clairyg	GHU PARIS PSYCHIATRIE ET NEUROSCIENCES	Normal human immunoglobulins	Repurposed	Randomized, placebo controlled, double-blinded 126 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001570-30/FR Recruiting
inhaled corticoids (Pulmicort)	Fundació Clinic per a la Recerca Biomèdica	Corticoids anti-inflammatory	Repurposed	Controlled, randomized, open label 300 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001616-18/ES Recruiting TACTIC-COVID study
Prednisone	Hospices civiles de Lyon	anti-inflammatory	Repurposed	Controlled, randomized, open label 304 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001553-48/FR Recruiting
METHYLPREDNISOLONE PULSES AND TACROLIMUS	Dr. Xavier Solanich Moreno. Servei Medicina Interna. Hospital de Bellvitge	anti-inflammatory	Repurposed	Randomized, open label controlled 84 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001445-39/ES BELL-COVID study Recruiting
Leukine®	University Hospital Ghent	immunestimulatory	Repurposed	randomized, open-label, interventional study 80 participants	Belgium	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001254-22/BE Recruiting
Aldesleukin	Assistance Publique - Hôpitaux de Paris	Interleukin 2	Repurposed	Double-blinded, randomized controlled trial 30 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001571-32/FR LILIADE-COVID study Recruiting

Valsartan	Radboudumc	AT_1 -Antagonist	Repurposed	double-blind, placebo-controlled randomized clinical trial 641 participants	Netherlands	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001320-34/NL PRAETORIAN study Recruiting
Isotretinoin	Tanta University	Retinoid	Repurposed	Randomized, open label 300 participants	Egypt	https://clinicaltrials.gov/ct2/show/NCT04361422
L-ascorbic acid	Hunter Holmes Mcguire Veteran Affairs Medical Center	Anoxia	Repurposed	Non randomized, open label, single group assignment 20 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04357782 Recruiting
Low Dose Radiation Therapy	Emory University Hospital Midtown/ Winship Cancer Institute	To inhibit cytokine storm	Repurposed	Non randomized, open label, single group assignment 10 participants	USA	https://clinicaltrials.gov/ct2/show/NCT04366791 Recruiting
MSV®-allo	CITOSPIN S.L.	allogeneic mesenchymal stem cells		Double-blind, placebo-controlled phase I/II clinical tria 24 participantsl	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001682-36/ES Recruiting
Actilyse	University College London	recombinant tissue plasminogen activator (rt-PA)		pilot, open label, phase II clinical trial 24 participants	UK	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001640-26/GB Recruiting
Malatonin	Fundación para la Investigación Biomédica del Hospital La Paz (FIBHULP)	anti-inflammatory and anti-oxidative		Randomized multicenter clinical trial 450 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001530-35/ES Recruiting

Trials for COVID prophylaxis in clinicaltrialsregister.eu & ISRCTN						
Name of treatment	**Developer/ sponsor**	**Type of treatment/ proposed mode of action**	**Repurposed or new drug?**	**Clinical trial** **In vitro** **In vivo**	**Study site**	**References/ Links**
Hydroxychlorquine	University Health Network	Antimalaria As prophylaxis in hospital personnel	Repurposed	Multicentre double-blinded randomized placebo-controlled trial 988 participants	Canada	https://doi.org/10.1186/ISRCTN14326006 Recruiting
Azithromycin and Hydroxychloroquine	Videnskabsetisk Komite	Anti-inflammatory/ Antimalaria with antiviral property As prophylaxis in patients upon admission to hospital	Repurposed	Multicenter 226 participants	Denmark	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001198-55/DK Recruiting
vaccination with Bacillus Calmette and Guérin (BCG)	Assistance Publique Hopitaux de Paris	As prophylaxis in patients upon admission to hospital	Repurposed	Randomized controlled trial 1120 participants	France	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001678-31/FR Recruiting
Hydroxychloroquine	ISGlobal	Antimalaria with antiviral property As prophylaxis in patients upon admission to hospital	Repurposed	Single center, double-blinded randomized	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001565-37/ES PrEP_COVID trial Recruiting

				controlled trial 440 participants		
Hydroxychloroquine		Antimalaria with antiviral property As prophylaxis in health professionals	Repurposed	controlled trial 300 participants	Spain	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001536-98/ES PrepSars study Recruiting
Hydroxychloroquine	Unisanté	Antimalaria with antiviral property As prophylaxis to reduce secondary hospital admission and household transmission	Repurposed	single representative population of residents of Switzerland across several Cantons 800 participants	Switzerland	Document UniSanté https://www.kofam.ch/en/snctp-portal/search/80826/study/50571

Screens to identify new repurposed drugs with activity against SARS-Cov2 as well as new drugs

Internationally, there are several screens ongoing to identify new compounds with antiviral properties in cell-culture based assays. Only a handful have been published as pre-prints to date.

A recent preprint used the commercial library of 1,280 pharmacologically active compounds LOPAC®1280 and the ReFRAME (Repurposing, Focused Rescue, and Accelerated Medchem) drug collection (see attached, A Large-scale Drug Repositioning Survey for SARS-CoV-2 Antivirals, Riva et al.).

*"Validation studies previously approved by the FDA (**clofazimine, acitretin, tretinoin, and astemizole**) or registered outside the US (**tamibarotene**). Dose response studies have thus far characterized 7 compounds that exhibit a range of effective concentrations (EC50) that are consistent with potential clinical efficacy. These include a PIKfyve kinase inhibitor that has reached Phase II clinical trials (**Apilimod**), and **cysteine protease inhibitors** (MDL-28170, Z LVG CHN2, VBY-825, and ONO 5334) that are in various phases of*

preclinical and clinical development. In addition, the preclinical ***ion channel blocker AMG-2674*** *and the ion channel blocker and antimalarial drug* ***hanfangchin A****, the* ***phase I proton pump inhibitor YH-1238****, as well as the* ***G-protein receptor antagonists MLN****-activity against SARS-CoV-2. "*

Touret et al. (see attached) screened Prestwick Chemical Library® composed of 1,520 approved drugs.

"Several drugs, such as ***Azithromycine, Opipramol, Quinidine or Omeprazol*** *present antiviral potency with 2<EC50<20µM. nterestingly, based on the SARS-Cov-2 infection cycle, one can infer that some of the identified molecules may inhibit specific steps of the virus replication cycle. This is illustrated for example by* ***Candesartan, Olmesartan and Ambrisentan*** *which interfer with angiotensin pathways, that play a key role in virus entry as the SARS-CoV2 Spike protein is known to bind to the cellular Angiotensin Converting Enzyme 2 receptor (ACE2). We also noted that 4 compounds (****Omeprazole, Vonoprazan, Chloroquine diphosphate and Hydroxychloroquine sulfate****) have been demonstrated to increase the pH of endosomial/golgian pathway either by inhibiting ATPase proton pomp, or by buffering the pH. We can thus expect that such endosomial pH modification would limit the processing of the Spike protein by endosomal proteases and in turn bloke the virus entry mediated by membrane fusion process. Finally, we also identified* ***Darunavir****, a HIV protease inhibitor might interfere with viral polyprotein processing during the replication cycle. This analysis identified at least three possible steps of the viral infection that can be targeted by approved drugs."*

Xia et al. describe new **lipopeptides**, which seems to inhibit membrane fusion of the SARS-Cov2 (see attached, Inhibition of SARS-CoV-2 (previously 2019-nCoV) infection by a highly potent pan-coronavirus fusion inhibitor targeting its spike protein that harbors a high capacity to mediate membrane fusion). The article also found some protection against infection in mice.

A nice (not scientific) summary of the mediatized drugs and developments can be found here:
https://www.biotechniques.com/coronavirus-news/covid-19-vaccine-and-drug-development-updates/