

COVID-19 CADTH HEALTH TECHNOLOGY REVIEW

Ongoing Trials for Drugs in the Prevention and Treatment of COVID-19

This report is current as of October 9, 2020.

To produce this report, CADTH used a modified approach to the selection of the evidence to meet decision-making needs during the COVID-19 pandemic. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly.

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Questions or requests for information about this report can be directed to requests@cadth.ca.

The following version table will be updated as changes are made to the report.

Version	Date of publication	Summary of revisions
1.0	June 9, 2020	Information current as of May 28, 2020.
2.0	July 2, 2020	Addition of phase IV trials. Addition of new trials. Information current as of June 19, 2020.
3.0	July 8, 2020	Addition of Health Canada's Clinical Trial Database's identifier. Addition of new trials. Information current as of July 3, 2020.
4.0	July 21, 2020	Addition of new trials. Information current as of July 17, 2020.
5.0	August 6, 2020	Addition of new trials (to February 28, 2021). Information current as of July 31, 2020. Removal of all trials of chloroquine/hydroxychloroquine.
6.0	August 18, 2020	Addition of new trials. Information current as of August 14, 2020.
7.0	September 1, 2020	Addition of new trials. Information current as of August 28, 2020.
8.0	September 16, 2020	Addition of new trials (to March 31, 2021). Information current as of September 11, 2020.
9.0	September 29, 2020	Addition of new trials. Information current as of September 25, 2020.
10.0	October 16, 2020	Addition of new trials (to April 30, 2021). Information current as of October 9, 2020.

About This Document

This report provides information on the ongoing phase II/III, phase III, and phase IV randomized controlled trials (RCTs) of drugs intended to prevent or treat COVID-19. The goal is to provide an evergreen document that is regularly updated. It is important to note that this report is not a systematic review and does not include a critical appraisal of studies. It is not intended to provide any recommendations.

Objective

To describe the trial characteristics and estimated primary completion dates of the ongoing phase II/III, phase III, and phase IV RCTs evaluating drugs to prevent or treat COVID-19.

Selection Criteria and Methods

The phase II/III, phase III, and phase IV RCTs were identified from the ClinicalTrials.gov website¹ using the inclusion criteria in Table 1.

Table 1: Selection Criteria

Population	Patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (COVID-19) or at risk (pre-/post-exposure prophylaxis or prevention)
Intervention	Drugs for treatment and prevention
Comparator	No restriction
Outcomes	No restriction
Study designs	Phase III (including phase II/III) and phase IV RCTs that are: recruiting; not yet recruiting; enrolling by invitation; or active, but not recruiting
Estimated primary completion date	by April 30, 2021

Exclusion Criteria

Non-drugs (e.g., devices), natural products, nutraceuticals, plasma products, stem cell therapies, and vaccines were excluded from this report. Trials on plasma products and vaccines are provided in separate reports. Non-randomized studies and single-arm trials were excluded. All trials of chloroquine, hydroxychloroquine, and remdesivir were also excluded from this review, as their trial information is available in published CADTH reports.²

The results were tabulated according to indication (prevention and treatment) and phase of clinical development and are presented in order of estimated primary trial completion dates (with the earliest first). Health Canada's Clinical Trial Database's identifier is also noted in the tables (Health Canada [HC] Control No.).³

The tables will be updated bi-weekly or if key trial data or results become available. When a trial's status changes to "Completed," "Withdrawn," "Terminated," or "Suspended" in ClinicalTrials.gov, the information will be moved to an appendix. A separate report may be initiated to evaluate and critically appraise the evidence once results are published.

Results

As of October 9, 2020, 48 phase II/III, 80 phase III, and 30 phase IV treatment trials; one phase II/III and two phase III pre-exposure trials; and one phase II/II and eight phase III post-exposure trials met the inclusion criteria (Tables 2 and 3). The sample sizes of the included trials ranged from 20 to 12,000 patients.

Trial populations for most of the trials included hospitalized adult patients; few treatment trials included outpatients (16 trials) or children younger than 16 years (12 trials). Based on dates included in the tables, 69 trials have estimated primary completion dates by October 2020. Twelve trials with Canadian study sites were identified (as highlighted in the tables).

Trials for which the status was changed to "Completed," "Withdrawn," "Terminated," or "Suspended" in ClinicalTrials.gov are depicted in Appendix 1, Table 4.

Limitations

The information provided in this report relies on the information posted on the ClinicalTrials.gov registry. There may be reporting errors in the study records posted on ClinicalTrials.gov. Furthermore, given the rapid changes occurring with the scientific evidence related to COVID-19, the reporting of amendments to the included trial protocols may be delayed. While some trials have reached their primary completion dates, their status are still showing as "recruiting" and results have not yet been posted. Finally, not all ongoing trials are posted to the website and, as such, ClinicalTrials.gov may provide an incomplete picture of the ongoing clinical trials related to COVID-19.

We have chosen to show the earliest trial completion date, that is the "estimated primary trial completion date" (the date on which the data collection was completed for all the primary outcome measures) and not the "estimated trial completion date" (the date on which the last patient was examined or received a treatment) to be able to quickly flag trials that may have results available ahead of the completion of a trial. We have limited our search date from March 1, 2020 to April 30, 2021, as these trials address the immediate needs for evidence.

Summary

A total of 170 ongoing phase II/III, phase III, or phase IV drug trials on COVID-19 met the inclusion criteria as of October 9, 2020.¹ Their sample sizes range from 20 to 12,000 patients. Most of the trials are being conducted in hospitalized adult patients, with few trials evaluating children or outpatients. By the end of October 2020, 69 trials will have reached their estimated primary completion dates. Twelve trials have Canadian study sites (as highlighted in the tables).

The ClinicalTrials.gov registry will be monitored regularly, and tables will be updated bi-weekly or when key trial data or results become available. A separate report may be initiated to evaluate and critically appraise the evidence once results are published.

Table 2: Drugs to Treat COVID-19: Ongoing Randomized Controlled Trials — April 2021 Estimated Primary Completion Date

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Phase IV					
Tocilizumab	NA	MC, OL Israel N = 500	April 29, 2020	Hospitalized adult patients with severe COVID-19 with suspected pulmonary hyperinflammation	NCT04377750
Spironolactone	NA	DB, PC Turkey N = 60	July 21, 2020	Hospitalized adult patients with ARDS due to COVID-19	NCT04345887
Budesonide	NA	OL Spain N = 300	August 31, 2020	Hospitalized adult patients with COVID-19	NCT04355637
Ibuprofen	LIBERATE	MC, DB UK N = 230	September 25, 2020	Hospitalized adult patients with confirmed or suspected SARS-CoV-2 and acute hypoxemic respiratory failure	NCT04334629
Enoxaparin	COVI-DOSE	MC, OL France N = 602	September 2020	Hospitalized adult patients with COVID-19	NCT04373707
Cholecalciferol	COVID-VIT-D	DB Spain N = 80	September 14, 2020	Adult patients with COVID-19	NCT04552951
Bivalirudin	ANTI-CO	DB Qatar N = 100	September 28, 2020	Hospitalized adult patients with COVID-19	NCT04445935
Desferal	NA	OL Egypt N = 200	September 30, 2020	Hospitalized children and adult patients with moderate COVID-19	NCT04389801
Telmisartan	NA	OL Argentina N = 400	October 1, 2020	Hospitalized adult patients with COVID-19	NCT04355936

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Early or late dexamethasone	NA	OL Egypt N = 450	October 1, 2020	Adult patients with mild and moderate COVID-19	NCT04530409
Losartan	NA	MC, OL US N = 200	October 6, 2020	Adult patients with mild-to-moderate respiratory symptoms of COVID-19	NCT04340557
Sofosbuvir and ledipasvir or nitazoxanide	NA	OL Egypt N=240	October 30, 2020	Hospitalized patients (12- to 65-years-old) with COVID-19	NCT04498936
Nebulized heparin with or without enoxaparin	NEBUHEPA	OL Argentina N = 200	October 30, 2020	Adult patients with COVID-19	NCT04530578
Sargramostim	SARPAC	OL Belgium N = 80	October 31, 2020	Adult patients with acute hypoxic respiratory failure due to COVID-19	NCT04326920
Enoxaparin prophylactic dose and heparin SC, or enoxaparin intermediate dose and heparin infusion	IMPROVE-COVID	OL US N = 100	November 2020	Hospitalized adult patients with COVID-19	NCT04367831
Early or late dexamethasone	NA	OL Egypt N = 300	November 30, 2020	Adult patients with mild-to-moderate COVID-19	NCT04528329
Intermediate dose prophylaxis (enoxaparin sodium or unfractionated heparin or fondaparinux) or therapeutic dose anticoagulation (enoxaparin sodium or unfractionated heparin or fondaparinux or argatroban)	IMPACT	OL US N = 186	December 2020	Critically ill adult patients with COVID-19	NCT04406389
Valsartan	PRAETORIAN-COVID	DB, PC Netherlands N = 651	December 2020	Hospitalized adult patients with COVID-19	NCT04335786

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Rivaroxaban followed by enoxaparin or unfractionated heparin	ACTION	OL Brazil N = 600	December 2020	Hospitalized adult patients with COVID-19	NCT04394377
Cyclosporine	NA	OL Spain N = 120	December 2020	Hospitalized adult patients with COVID-19	NCT04392531
Vitamin D (cholecalciferol)	CARED	DB, PC Argentina N = 1,265	December 15, 2020	Hospitalized adult patients with COVID-19	NCT04411446
Heparin	NA	DB, PC US N = 50	December 31, 2020	Hospitalized adult patients with COVID-19	NCT04397510
Sodium bicarbonate	NA	OL US N = 40	January 2021	Hospitalized adult patients with COVID-19	NCT04530448
Angiotensin receptor blocker (candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, or valsartan)	CLARITY	SB Australia N = 605	January 30, 2021	Adult patients with SARS-CoV-2 infection	NCT04394117
N-acetylcysteine	NA	OL US N = 200	January 31, 2021	Adult patients with mild-to-moderate COVID-19	NCT04419025
Heparin (prophylactic dose and therapeutic dose)	ACTIV-4	OL, MC US N = 2,000	March 2021	Hospitalized adult patients with COVID-19	NCT04505774
Enoxaparin prophylactic dose or full dose, or apixaban	FREEDOM COVID	OL US N = 3,600	March 2021	Hospitalized adult patients with COVID-19	NCT04512079
Tetrandrine	TT-NPC	OL China N = 60	March 1, 2021	Adult patients with mild and severe SARS-CoV-2 pneumonia	NCT04308317

Experimental arm		Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Pioglitazone		NA	OL Spain N = 76	March 10, 2021	Adult patients with type 2 diabetes mellitus and COVID-19	NCT04535700
NEW	Prophylactic or intermediate dose enoxaparin	NA	MC, OL US N = 170	April 16, 2021	Hospitalized adult patients with COVID-19	NCT04360824
Phase III						
Budesonide		COVIDORL	MC, SB, PC France N = 120	May 18, 2020	Adult patients with persistent hyposmia related to SARS-CoV-2 infection	NCT04361474
Azithromycin		AMBU-COVID	OL France N = 64	June 2020	Adult outpatients with non-severe symptoms of COVID-19	NCT04371107
Tacrolimus and methylprednisolone		TACROVID	OL Spain N = 84	June 1, 2020	Patients with severe lung injury secondary to COVID-19	NCT04341038
Colchicine		ECLA PHRI COLCOVID	OL Argentina N = 2,500	June 30, 2020	Hospitalized adult patients with moderate-to-severe COVID-19	NCT04328480
Favipiravir		NA	MC, DB, PC Italy N = 100	July 2020	Adult patients with moderate COVID-19	NCT04336904
Neurokinin 1 receptor antagonist		NA	DB Pakistan N = 100	July 15, 2020	Hospitalized adult patients with severe or critical COVID-19 infection	NCT04468646
Bromhexine and spironolactone		BISCUIT	OL Russian Federation N = 80	July 18, 2020	Hospitalized adult patients with mild and severe COVID-19	NCT04424134
Dornase alfa (Tigerase)		NA	OL Russian Federation N = 100	July 20, 2020	Adult patients with moderate COVID-19	NCT04459325

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Favipiravir	NA	OL, MC Russian Federation N = 168	July 29, 2020	Adult patients with mild-to-moderate COVID-19 without respiratory failure	NCT04501783
Azithromycin with or without amoxicillin-clavulanate	AziA	MC, OL France N = 104	July 30, 2020	Hospitalized adult patients with COVID-19 pneumonia in a non-intensive care unit	NCT04363060
Sarilumab	NA	Adaptive, MC, DB, PC Multi-country ^b N = 420	July 30, 2020	Hospitalized adult patients with severe or critical COVID-19	NCT04327388
Favipiravir	NA	MC, DB, PC Multi-country N = 256	August 2020	Adult patients with moderate COVID-19	NCT04425460
Enoxaparin low dose or high dose	X-COVID 19	MC, OL Italy N = 2,712	August 2020	Hospitalized adult patients with SARS-CoV-2 infection	NCT04366960
Vitamin D (ergocalciferol) low dose or high dose	NA	DB Canada N = 64	August 2020	Adult inpatients and outpatients with COVID-19	NCT04385940 HC Control No. 240943
Tradipitant	ODYSSEY	DB, PC US N = 300	August 1, 2020	Adult patients with severe or critical COVID-19	NCT04326426
Tocilizumab	NA	MC, DB, PC Multi-country N = 379	August 18, 2020	Hospitalized adult patients with COVID-19 pneumonia	NCT04372186
Dornase alpha	COVIDORNASE	MC, OL France N = 100	August 21, 2020	Hospitalized adult patients with ARDS due to COVID-19	NCT04355364
Chlorpromazine	ReCoVery	MC, SB France N = 40	August 30, 2020	Hospitalized adult patients with moderate COVID-19	NCT04366739
Anakinra or siltuximab or tocilizumab or in combination	COV-AID	MC, OL Belgium N = 342	September 2020	Adult patients with acute hypoxic respiratory failure and systemic cytokine release syndrome due to COVID-19	NCT04330638

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Lenzilumab	NA	MC, DB, PC US N = 300	September 2020	Hospitalized adult patients with severe and critical COVID-19 pneumonia	NCT04351152
Imatinib mesylate	NA	OL Egypt N = 30	September 2020	Hospitalized adult patients with moderate-to-severe COVID-19–induced pneumonia	NCT04422678
Ciclesonide	NA	MC, DB, PC US N = 400	September 1, 2020	Outpatient patients (≥ 12-years-old) with symptomatic COVID-19	NCT04377711
Tocilizumab or deferoxamine	TRONCHER	MC, OL Tunisia N = 260	September 4, 2020	Hospitalized adult patients in intensive care unit	NCT04361032
Famotidine	NA	MC, DB US N = 942	September 7, 2020	Hospitalized adult patients with COVID-19	NCT04370262
Azithromycin	ATOMIC2	MC, OL UK N = 800	September 13, 2020	Adult outpatients with COVID-19	NCT04381962
Canakinumab	CAN-COVID	MC, DB, PC Multi-country N = 451	September 16, 2020	Hospitalized patients (≥ 12-years-old) with COVID-19–induced pneumonia and cytokine release syndrome	NCT04362813
Colchicine	COLCHI-COVID	OL Spain N = 1,028	September 25, 2020	Older adult outpatients (≥70-years-old) at high risk of pulmonary complications due to COVID-19 pneumonia	NCT04416334
Ruxolitinib	RUXCOVID-DEVENT	MC, DB, PC US N = 500	September 29, 2020	Patients (≥ 2-years-old) with COVID-19 who require mechanical ventilation	NCT04377620
Azithromycin	ACTION	DB, PC US N = 2,271	September 30, 2020	Adult outpatients with SARS-CoV-2	NCT04332107
Prednisone	PREDCOVID	SB Chile N = 184	September 30, 2020	Hospitalized adult patients with moderate COVID-19 pneumonia	NCT04451174

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Linagliptin with or without insulin	COVID19DPP4i	DB Mexico N = 28	September 30, 2020	Hospitalized adult patients with COVID-19 and hyperglycemia	NCT04542213
Favipiravir or oseltamivir	NA	OL Indonesia N = 100	September 30, 2020	Adult patients with COVID-19	NCT04558463
Dapagliflozin	DARE-19	MC, DB, PC Multi-country ^b N = 900	October 2020	Hospitalized adult patients with mild-to-moderate COVID-19	NCT04350593 HC Control No. 240352
Prasugrel hydrochloride	PARTISAN	MC, DB, PC Italy N = 128	October 2020	Hospitalized adult patients with severe COVID-19 pneumonia	NCT04445623
Tocilizumab	NA	MC, DB, PC US N = 243	October 1, 2020	Hospitalized adult and older adult patients with severe COVID-19	NCT04356937
Ruxolitinib	RUXCOVID	MC, DB, PC Multi-country ^b N = 402	October 16, 2020	Hospitalized patients (≥12-years-old) with COVID-19 — associated cytokine storm	NCT04362137 HC Control No: 240395
Colchicine	COL-COVID	OL Spain N = 102	October 20, 2020	Hospitalized adult patients with SARS-CoV-2 infection confirmed within the first 48 hours after hospital admission	NCT04350320
Enoxaparin low dose or high dose	HEP-COVID	MC, DB US N = 308	October 22, 2020	Hospitalized adult patients with COVID-19	NCT04401293
Intermediate dose enoxaparin/ unfractionated heparin or standard prophylactic dose enoxaparin/ unfractionated heparin or atorvastatin	INSPIRATION	MC, OL, PC Iran N = 600	October 25, 2020	Critically ill hospitalized adult patients with COVID-19 admitted to ICU	NCT04486508

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Sitagliptin	SIDIACO	OL Italy N = 170	October 30, 2020	Hospitalized adult patients with COVID-19 and type 2 diabetes	NCT04365517
Famotidine	NA	OL Bangladesh N = 200	October 30, 2020	Patients (16- to 80-years-old) with COVID-19	NCT04504240
Tocilizumab or methylprednisolone	NA	OL Malaysia N = 310	October 31, 2020	Hospitalized adult patients with moderate COVID-19 at risk for complications	NCT04345445
CD24Fc	SAC-COVID	MC, DB, PC US N = 241	October 31, 2020	Adult patients with severe COVID-19	NCT04317040
Heparin	RAPID COVID COAG	MC, OL Canada N = 462	November 2020	Hospitalized adult patients with COVID-19	NCT04362085 HC Control No: 238510
Losmapimod	LOSVID STUDY	DB, PC Multi-country N = 410	November 2020	Hospitalized adult patients (≥ 50-years-old) with COVID-19	NCT04511819
Colchicine	COLCOVID19	OL Colombia N = 128	November 2020	Hospitalized adult patients with COVID-19	NCT04539873
Dexamethasone or methylprednisolone	NA	OL Bangladesh N = 60	November 5, 2020	Hospitalized adult patients (20- to 80-years-old) with moderate-to-severe COVID-19	NCT04499313
Enoxaparin	RAPID- BRAZIL	OL Brazil N = 462	November 30, 2020	Hospitalized adult patients with COVID-19 and with low oxygen saturation	NCT04444700
Prednisone or hydrocortisone hemisuccinate	CORTICOVIDHUGO	SB France N = 210	December 2020	Hospitalized adult patients with COVID-19 pneumonia on oxygen therapy	NCT04359511
Methylprednisolone	CORTIVID	DB Spain N = 72	December 2020	Hospitalized adult patients with COVID-19	NCT04438980

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
XC221	NA	MC, DB, PC Russian Federation N = 118	December 2020	Adult patients with COVID-19	NCT04487574
Almitrine	AIRVM-COVID	DB, PC France N = 212	December 2020	Hospitalized adult patients with COVID-19	NCT04357457
Colchicine	COLCORONA	MC, DB, PC Multi-country ^b N = 6,000	December 2020	Adult patients (≥ 40-years-old) with COVID-19 and have at least one high-risk criterion	NCT04322682 HC Control No: 237317
Doxycycline	DYNAMIC	MC, DB, PC France N = 330	December 1, 2020	Adult patients (> 45-years-old) with SARS-CoV-2 infection	NCT04371952
Baricitinib	COV-BARRIER	MC, DB, PC Multi-country N = 600	December 5, 2020	Hospitalized adult patients with COVID-19	NCT04421027
Niclosamide	NICLONEX	DB, PC Turkey N = 200	December 30, 2020	Hospitalized adult patients with COVID-19	NCT04558021
Nitazoxanide and vitamin B	NA	DB, PC US N = 800	December 30, 2020	Patients (12- to 120-years-old) with mild-to-moderate COVID-19	NCT04486313
Telmisartan or vitamins	COVERAGE	MC, OL, MAMS France N = 338	December 31, 2020	Outpatient elderly patients (≥ 60-years-old) with symptomatic SARS-CoV-2 infection	NCT04356495
Colchicine or interferon-beta or Aspirin or rivaroxaban	ACTCOVID-19	OL Multi-country ^b N = 4,000	December 31, 2020	Adult patients with COVID-19	NCT04324463 HC Control No. 238157
Methylprednisolone or heparin or both in combination	NA	OL Brazil N = 268	December 31, 2020	Adult patients with COVID-19	NCT04485429
Dexamethasone (high dose)	NA	MC, OL Argentina N = 284	December 31, 2020	Adult patients with ARDS due to COVID-19	NCT04395105

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Favipiravir	NA	MC, DB, PC Kuwait N = 780	December 31, 2020	Adult patients (21- to 80-years-old) with moderate-to-severe COVID-19 hospitalized or quarantined in an institutional quarantine facility	NCT04529499
Enoxaparin	ETHIC	OL, MC Country NR N = 1,370	January 2021	Adult patients (≥ 55-years-old) with COVID-19 symptoms	NCT04492254
Apixaban (various doses) or Aspirin	NA	MC, DB, PC Country NR N = 7,000	January 2021	Adult outpatients (40- to 79-years-old) with stable COVID-19 symptoms with elevated D dimer and hsCRP	NCT04498273
Anakinra	NA	DB US N = 30	January 2021	Hospitalized adult patients with SARS-CoV-2 infection with markers of cytokine storm syndrome	NCT04362111
Vitamin D3	VIVID	DB, PC US N = 2,700	January 15, 2021	Adult patients (≥ 30-years-old) with COVID-19	NCT04536298
Tissue plasminogen activator	AtTAC	MC, DB Russia N = 50	January 15, 2021	Hospitalized adult patients with severe COVID-19	NCT04453371
Vitamin D (cholecalciferol)	NA	OL Mexico N = 40	February 2021	Pediatric patients (1-month to 17- years-old) hospitalized with COVID-19	NCT04502667
Bucillamine	NA	MC, DB, PC US N = 1,000	February 1, 2021	Adult patients with mild-to-moderate COVID-19	NCT04504734
Nintedanib	NINTECOR	DB, PC France N = 250	March 2021	Adult patients with SARS-CoV-2–induced pulmonary fibrosis and a history of hospitalization due to COVID-19	NCT04541680
Rivaroxaban	PREVENT-HD	MC, DB, PC US N = 4,000	March 3, 2021	Adults outpatients with COVID-19	NCT04508023

Experimental arm		Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Enoxaparin		NA	MC, OL Switzerland N = 1,000	March 14, 2021	Adult outpatients (≥ 50-years-old) with COVID-19	NCT04400799
Favipiravir		PIONEER	OL UK N = 450	March 31, 2021	Hospitalized adult patients with suspected or confirmed COVID-19	NCT04373733
Lopinavir-ritonavir		CORIPREV-LR	OL Canada N = 1,220	March 31, 2021	Patients (≥ 6-months-old) with COVID-19 symptoms	NCT04321174 HC Control No. 237350
Sevoflurane		SevCov	MC, DB Switzerland N = 64	March 31, 2021	Hospitalized adult patients with COVID-19 ARDS	NCT04355962
Enoxaparin high dose or low dose		COVID-HEP	OL, SB Switzerland N = 200	March 31, 2021	Hospitalized adult patients with severe COVID-19	NCT04345848
Dipyridamole and Aspirin		ATTAC-19	OL US N = 132	March 15, 2021	Hospitalized adult patients with COVID-19	NCT04410328
NEW	Aspirin, losartan, or simvastatin, each alone or combined with another	CRASH-19	OL Multi-country N = 10,000	April 2021	Hospitalized adult patients (≥ 40-years-old) with COVID-19	NCT04343001
NEW	Levilimab	CORONA	MC, PC, DB Russian Federation N = 204	April 2021	Hospitalized adult patients with severe COVID-19	NCT04397562
NEW	Rivaroxaban	COVID-PREVENT	MC, OL Germany N = 400	April 30, 2021	Hospitalized adult patients with moderate-to-severe COVID-19	NCT04416048
PHASE II/III						
Favipiravir		NA	DB, PC Bangladesh N = 50	July 2020	Adult patients with novel coronavirus	NCT04402203

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Ivermectin	NA	OL Egypt N = 100	July 30, 2020	Adult patients with COVID-19	NCT04445311
Nitazoxanide	NA	DB, PC Brazil N = 300	September 2020	Adult outpatients (≥ 50-years-old) with symptomatic SARS-CoV-2 infection	NCT04441398
Vidofludimus calcium (IMU-838)	NA	MC, DB, PC Multi-country N = 230	September 2020	Hospitalized adult patients with COVID-19	NCT04379271
Pyridostigmine	PISCO	DB, PC Mexico N = 436	September 30, 2020	Hospitalized adult patients with pneumonia secondary to SARS-CoV-2 infection	NCT04343963
Chlorpromazine	NA	SC, SB, OL Egypt N = 100	October 2020	Adult patients with COVID-19	NCT04354805
Aviptadil	AVICOVID-2	MC, DB, PC US N = 288	October 1, 2020	Patients (≥ 12-years-old) with moderate and severe COVID-19 who have not yet developed respiratory failure	NCT04360096
Ivermectin and nitazoxanide	NA	DB Egypt N = 100	October 2020	Adult patients with SARS-CoV-2 infection	NCT04360356
Sofosbuvir or daclatasvir	NA	DB Egypt N = 100	October 1, 2020	Adult patients with COVID-19	NCT04497649
Cannabidiol	CANDIDATE	SC, DB, PC Brazil N = 100	October 17, 2020	Adult patients with mild or moderate COVID-19	NCT04467918

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Metenkefalin-tridecactide	NA	OL Bosnia and Herzegovina N = 120	October 31, 2020	Hospitalized adult patients with moderate-to-severe COVID-19	NCT04374032
Ivermectin	NA	DB, PC Columbia N = 400	November 2020	Adult patients with mild SARS-CoV-2 infection within 7 days of symptoms	NCT04405843
Emapalumab or anakinra	NA	MC, OL Multi-country N = 54	November 2020	Adult patients (30- to 79-years-old) with SARS-CoV-2 infection	NCT04324021
LY3819253	ACTIV-2	DB, PC US N = 2,000	November 2020	Adult patients with COVID-19 in an outpatient setting	NCT04518410
Vitamin D (25-hydroxyvitamin D3)	NA	MC, DB, PC Iran N = 1,500	November 15, 2020	Treatment: Adult patients with COVID-19 Prevention: See Table 3	NCT04386850
Nitazoxanide	NA	SB, PC Argentina N = 135	November 15, 2020	Adult patients with mild COVID-19	NCT04463264
Olokizumab	NA	MC, DB, PC US N = 376	November 16, 2020	Hospitalized adult patients with severe SARS-CoV-2 infection	NCT04452474
Lopinavir-ritonavir alone or in combination with telmisartan or atorvastatin	INTENSE-COV	MC, OL Cote D'Ivoire N = 294	November 20, 2020	Adult patients with SARS-CoV-2 infection	NCT04466241
NEW Emtricitabine and tenofovir or colchicine or rosuvastatin	NA	OL Colombia N = 1,200	November 30, 2020	Hospitalized adult patients with COVID-19	NCT04359095
Favipiravir	Avi-Mild	MC, DB, PC Saudi Arabia N = 576	December 2020	Adult patients with mild COVID-19	NCT04464408

Experimental arm		Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Anakinra		ANA-COVID-GEAS	MC, OL Spain N = 180	December 2020	Hospitalized adult patients with severe pneumonia due to SARS-CoV-2	NCT04443881
NEW	Favipiravir	NA	OL, PC Egypt N = 90	December 1, 2020	Children, adults, and older adult patients with COVID-19	NCT04351295
ABX464		MiR-AGE	DB, PC Multi-country N = 1,034	December 30, 2020	Adult inpatients or outpatients with SARS-CoV-2 infection	NCT04393038
Angiotensin-(1,7)		ATCO	Adaptive, DB, PC Belgium N = 60	December 30, 2020	Adult patients with COVID-19 requiring mechanical ventilation	NCT04332666
Ivermectin		IVERCORCOVID19	DB, PC Argentina N = 500	December 31, 2021	Adult patients with COVID-19	NCT04529525
NA-831 alone or in combination with atazanavir or dexamethasone, and atazanavir with dexamethasone		NATADEX	DB US N = 525	December 31, 2020	Hospitalized adult patients with SARS-CoV-2	NCT04452565
Heparin		NA	OL, MC Multi-country ^b N = 3,000	January 2021	Hospitalized adult patients with COVID-19	NCT04372589 HC Control No. 238691
VIR-7831		COMET-ICE	MC, DB, PC US N = 1,360	January 2021	Adult outpatients with COVID-19	NCT04545060
Opaganib		NA	DB, PC Multi-country N = 270	January 2021	Adult patients with COVID-19 pneumonia	NCT04467840

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Lopinavir-ritonavir or losartan	COVIDMED	MC, DB, PC US N = 4,000	January 1, 2021	Hospitalized adult patients with COVID-19	NCT04328012
RESP301 (nitric oxide)	NA	MC, OL UK N = 300	January 27, 2021	Hospitalized adult patients with COVID-19	NCT04460183
Bardoxolone methyl	BARCONA	MC, DB, PC US N = 440	January 30, 2021	Hospitalized adult patients with COVID-19	NCT04494646
PTC299	FITE19	DB, PC, MC Multi-country N = 380	January 30, 2021	Hospitalized adult patients with COVID-19	NCT04439071
EB05	NA	DB, PC Country NR N = 865	February 2021	Hospitalized adult patients with moderate-to-severe COVID-19	NCT04401475 HC Control No. 239462
Mavrilimumab	NA	DB, PC Multi-country N = 573	February 2021	Hospitalized adult patients with severe COVID-19 pneumonia and hyperinflammation	NCT04447469
Dociparstat	NA	DB, PC US N = 524	February 2021	Hospitalized adult patients with severe COVID-19 and at high risk of respiratory failure	NCT04389840
XPro1595	NA	MC, DB, PC Country NR N = 366	February 2021	Adult patients with severe COVID-19 who have high-risk factors for complication	NCT04370236
EDP1815 or dapagliflozin and ambrisentan	TACTIC-E	OL UK N = 1,407	February 15, 2021	Hospitalized adult patients (pre-ICU) with COVID-19	NCT04393246
Ruxolitinib	RUXO-COVID	DB, PC Brazil N = 200	February 17, 2021	Hospitalized adult patients with COVID-19 pneumonia	NCT04477993
Ciclesonide	CONTAIN	DB, PC Canada N = 454	February 25, 2021	Symptomatic adult patients with mild COVID-19	NCT04435795 HC Control No. 239123

Experimental arm		Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Amiodarone or verapamil		ReCOVary-SIRIO	OL Poland N = 804	March 2, 2021	Hospitalized adult patients with COVID-19	NCT04351763
Sarilumab		CORIMUNO-SARI	MC, OL France N = 239	March 27, 2021	Hospitalized adult patients with moderate or severe COVID-19 pneumonia	NCT04324073
Nafamostat mesylate		NA	OL China N = 84	March 30, 2021	Hospitalized adult patients with COVID-19 pneumonia	NCT04418128
NEW	Zavegepant (BHV-3500)	NA	DB, PC US N = 120	April 2021	Hospitalized adult patients with COVID-19	NCT04346615
NEW	Azoximer bromide	NA	MC, DB, PC Russian Federation N = 394	April 2021	Hospitalized adult patients with COVID-19	NCT04381377
NEW	Nitazoxanide	C3-RCT	PC, DB South Africa N = 960	April 2021	Adult outpatients with COVID-19	NCT04523090
NEW	Molnupiravir	MK-4482-002	PC, DB Country NR N = 1,450	April 11, 2021	Adult outpatients with COVID-19	NCT04575597
NEW	Molnupiravir	MK-4482-001	PC, DB Country NR N = 1,300	April 15, 2021	Hospitalized adult patients with COVID-19	NCT04575584

ARDS = acute respiratory distress syndrome; DB = double blind; HC = Health Canada; hsCRP = high-sensitivity C-reactive protein; MC = multi-centre; OL = open label; MAMS = multi-arm multi-stage; NA = not applicable; NR = not reported; PC = placebo controlled; SARS-CoV2 = severe acute respiratory syndrome coronavirus 2; SB = single blind; SC = subcutaneous.

^a The date on which data collection is completed for all the primary outcome measures.

^b Includes Canada.

Table 3: Drugs to Prevent COVID-19: Ongoing Randomized Controlled Trials — April 2021 Estimated Primary Completion Date

Experimental arm	Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Pre-exposure prophylaxis or prevention					
Phase III					
Levamisole or isoprinosine or in combination	NA	OL Egypt N = 100	November 1, 2020	Healthy health care workers testing negative for COVID-19	NCT04360122
Emtricitabine-tenofovir alafenamide	CoviPrep	DB, PC Argentina N = 1,378	November 15, 2020	Healthy health care workers having a high transmission risk for COVID-19 and no prior diagnosis of SARS-CoV-2 infection	NCT04405271
Phase II/III					
Vitamin D (25-hydroxyvitamin D3)	NA	MC, DB, PC Iran N = 1,500	November 15, 2020	Prevention: Hospital health providers with a negative COVID-19 test Prevention: Close relative of a patient with COVID-19 Treatment: See Table 3	NCT04386850
Post-exposure prophylaxis					
Phase III					
RTB101	NA	DB, PC US N = 550	September 2020	Older adults (≥ 65-years-old) with COVID-19 residing in a nursing home in which ≥ 1 person has COVID-19	NCT04409327
Ivermectin	IverprofCovid19	MC, DB, PC Colombia N = 550	November 30, 2020	Health care workers at all levels of care	NCT04527211
Icosapent ethyl	PREPARE-IT	DB, PC Country NR N = 1,500	December 2020	Health care providers at risk of occupational exposure to COVID-19	NCT04460651

Experimental arm		Trial name	Study design, country, sample size	Estimated trial primary completion date ^a	Population	ClinicalTrials.gov reference
Nitazoxanide		NA	MC, DB, PC US N = 800	December 31, 2020	Health care workers at increased risk for direct occupational exposure to COVID-19	NCT04359680
Nitazoxanide		NA	MC, DB, PC US N = 800	December 31, 2020	Residents (≥ 55-years-old) of long-term care facilities	NCT04343248
Lopinavir-ritonavir		COPEP	OL Switzerland N = 300	March 2021	Children and adults (≥ 16-years-old) exposed to SARS-CoV-2	NCT04364022
LY3819253 (LY-CoV555)		BLAZE-2	DB, PC US N = 2,400	March 8, 2021	Residents and facility staff in a skilled nursing or assisted living facility with at least one confirmed case of SARS-CoV-2	NCT04497987
NEW	Vitamin D3	PROTECT	DB, PC Canada N = 2,414	April 1, 2021	Health care workers at high risk of COVID-19 infection (working at COVID-designated or infected installations)	NCT04483635 HC Control No.: 243196
Phase II/III						
Tenofovir and emtricitabine		NA	MC, DB, PC Colombia N = 950	December 31, 2020	Health care professionals in direct care of patients in emergency rooms, general COVID-wards, or intensive care units	NCT04519125

ARDS = acute respiratory distress syndrome; DB = double blind; MC = multi-centre; OL = open label; MAMS = multi-arm multi-stage trial; NA = not applicable; NR = not reported; PC = placebo controlled; SARS-CoV2 = severe acute respiratory syndrome coronavirus 2.

^a The date on which data collection is completed for all the primary outcome measures.

References

1. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine; 2020: <https://clinicaltrials.gov/>. Accessed 2020 Oct 9.
2. CADTH COVID-19 evidence portal. *CADTH report archives*. Ottawa (ON): CADTH; 2020: <https://covid.cadth.ca/tag/cadth-report/>. Accessed 2020 Oct 9.
3. Government of Canada. Clinical trial search. 2020; <https://health-products.canada.ca/ctdb-bdec/index-eng.jsp>. Accessed 2020 Oct 9.

Appendix 1: Trials That Are No Longer Active

Table 4: Drugs to Treat COVID-19: Completed, Withdrawn, Terminated, or Suspended Randomized Controlled Trials

Treatment groups	Trial name	Study design, country, sample size	Trial end date ^a	Population	ClinicalTrials.gov reference and status	Publication
Phase IV						
Bromhexine	NA	OL Russian Federation N = 50	August 31, 2020	Medical personnel at risk of contracting COVID-19 (assisting patients with COVID-19)	NCT04405999 Completed	Not yet published
Dexamethasone	DEXA-COVID19	MC, OL Spain N = 200	October 30, 2020	Adult patients with moderate-to-severe ARDS due to COVID-19 and who are mechanically ventilated	NCT04325061 Suspended	NA
Phase III						
Tocilizumab	COVACTA	MC, DB, PC Multi-country ^b N = 450	June 24, 2020	Hospitalized adult patients with severe COVID-19 pneumonia	NCT04320615 HC Control No: 237397 Completed	Not yet published related article
Tocilizumab	TOCIBRAS	OL Brazil N = 129	July 8, 2020	Adult patients with moderate-to-severe COVID-19	NCT04403685 Terminated	NA
Dexamethasone	CoDEX	MC, OL Brazil N = 299	July 22, 2020	Adult patients with moderate and severe ARDS due to SARS-CoV2	NCT04327401 Terminated	Published
Favipiravir	NA	OL Russian Federation N = 200	August 10, 2020	Hospitalized adult patients with moderate COVID-19	NCT04542694 Completed	Not yet published
Ivermectin and doxycycline	NA	DB, PC Bangladesh N = 400	August 22, 2020	Adult patients with mid and moderate COVID-19	NCT04523831 Completed	Not yet published Results posted on ClinicalTrials.gov

Treatment groups	Trial name	Study design, country, sample size	Trial end date ^a	Population	ClinicalTrials.gov reference and status	Publication
Mometasone furoate	NA	OL Egypt N = 50	September 3, 2020	Adult patients with COVID-19 and recent onset of anosmia or hyposmia	NCT04484493 Completed	Not yet published
Phase II/III						
Methylprednisolone	NA	MC, OL China N = 80	April 13, 2020	Hospitalized adult patients with COVID-19	NCT04244591 Completed	Not yet published
RPH-104 or olokizumab	NA	Adaptive, MC, DB, PC Russia Federation N = 372	July 10, 2020	Adult patients with severe SARS-CoV-2 infection	NCT04380519	Not yet published
Ivermectin	NA	OL Egypt N = 304	July 14, 2020	Asymptomatic family contact (≥ 6-years-old) with patients with confirmed COVID-19	NCT04422561 Completed	Not yet published
Sarilumab	NA	DB, PC US N = 1,912	July 24, 2020	Hospitalized adult patients with SARS-CoV-2	NCT04315298 HC Control No. 237332	Not yet published
Sulodexide	SuIES-COVID	OL, PC Mexico N = 243	September 7, 2020	Adult patients (40- to 80-years-old) with COVID-19 symptoms	NCT04483830 Completed	Not yet published
DAS181	STOP COVID-19	MC, DB, PC Italy N = 0	September 30, 2020	Adult patients with SARS-CoV-2 infection with lower respiratory tract infection who require supplemental oxygen	NCT04354389 Withdrawn	NA
Lopinavir-ritonavir	TRASCOV	OL Nigeria N = 928	December 31, 2020	Outpatients (≥ 12-years-old) with COVID-19	NCT04409483 Withdrawn	NA

ARDS = acute respiratory distress syndrome; MC = multi-centre; NA = not applicable, OL = open label; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

^a Actual trial completion, withdrawal, termination, or suspension date as indicated in ClinicalTrials.gov.

^b Includes Canada.