CADTH COVID-19 PANDEMIC

COVID-19 CADTH HEALTH TECHNOLOGY REVIEW

Ongoing Trials of Plasma-Based Therapies for the Treatment of COVID-19

This report is current as of December 22, 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 control table will be updated as changes are made to the report.

Version	Date of Publication	Summary of Revisions
1.0	June 15, 2020	Information current as of June 10, 2020
2.0	June 26, 2020	Information current as of June 25, 2020. One new trial added.
3.0	July 9, 2020	Information current as of July 9, 2020. No new trials added.
4.0	July 28, 2020	Information current as of July 27, 2020. Two new trials added.
5.0	August 10, 2020	Information current as of August 6, 2020. Two new trials added.
6.0	August 24, 2020	Information current as of August 24, 2020. Two new trials added.
7.0	September 29, 2020	Information current as of September 24, 2020. Four new trials added.
8.0	October 23, 2020	Information current as of October 23, 2020. No new trials added. 1 trial published. Table 4 added.
9.0	November 26, 2020	Information current as of November 25, 2020. No new trials added. Table 5 updated.
10.0	December 22, 2020	Information current as of December 21, 2020. 1 new trial added. 2 trials published. Table 5 updated.

About This Document

This report provides information on the ongoing phase II, phase III, and phase IV studies of plasma-based therapies for 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.

Background

Plasma-based therapies include convalescent plasma, intravenous immune globulin (IVIG), and hyperimmune globulin. All three are being evaluated to prevent or treat COVID-19.

Convalescent plasma is an intervention where plasma collected from patients who have recovered from a particular disease is administered to patients with the same active disease.[1] Administering convalescent plasma to someone with COVID-19 may result in the acquisition of passive immunity because of disease-specific neutralizing antibodies present in convalescent plasma.[2,3] The CADTH report *Convalescent Plasma Therapy for the Treatment of COVID-19: Clinical Effectiveness*[4] describes a literature search and the *Convalescent Plasma Therapy for the Treatment of COVID-19: A Review of Clinical Effectiveness*[5] report examines the clinical effectiveness with critical appraisal of the literature about this intervention. These reports will be regularly updated.[4,5]

IVIG products are sterile solutions or lyophilized (i.e., freeze-dried) concentrates of human immune globulin G (IgG).[6] These products are generated from plasma from donors, processed to remove multimers and aggregates of IgG.[6] Although the mechanism of action of IVIG is unknown in many diseases, IVIG is considered to provide general IgG antibodies to help facilitate the neutralization of reactive pathogens in the setting of primary immune deficiency.[6] IVIG has been used off-label to treat patients with viral infections such as severe acute respiratory syndrome (SARS),[7] Middle East Respiratory syndrome (MERS),[8] and respiratory syncytial virus (RSV),[9] and has been proposed to be an immunomodulator in COVID-19.[10,11]

Hyperimmune globulins are fractionation products derived from pools of plasma obtained from donors. The plasma to create hyperimmune globulin is chosen for high antibody titres that have selected specificities to a particular infection.[6] For example, hyperimmune globulin products are available in Canada for hepatitis B, cytomegalovirus, and varicella-zoster.[6] Hyperimmune globulin is more concentrated than convalescent plasma and avoids the transmission of coagulation factors from convalescent plasma.[12,13] Hyperimmune globulin has been used in H1N1 influenza infection.[12]

The purpose of this report is to provide information on the ongoing phase II, phase III, and phase IV clinical trials for the plasma products IVIG and hyperimmune globulin for COVID-19. A list of ongoing trials for convalescent plasma is included in separate CADTH reports.[4,5] A list of ongoing trials for bacille Calmette-Guérin (BCG) vaccines, novel vaccines, and drugs for COVID-19 are available in separate CADTH reports, as well.[14]

Objective

To describe the trial characteristics and estimated primary completion dates of the ongoing phase II, phase III, and phase IV studies evaluating IVIG and hyperimmune globulin to treat COVID-19.

Selection Criteria and Methods

The trials were identified from ClinicalTrials.gov,[15] the Health Canada clinical trials database,[16] and the WHO International Clinical Trials Registry Platform[17] using the inclusion criteria presented in Table 1. Grey literature relating to plasma-based therapies and COVID-19 was identified by searching relevant websites from the *Grey Matters: A Practical Tool For Searching Health-Related Grey Literature* checklist[18] and CADTH COVID-19 grey literature resources,[19] which include the websites of regulatory agencies, health technology assessment agencies, and clinical guideline repositories. Google was used to search for additional internet-based materials. Results from the grey literature search will be updated every three months.

Table 1: Selection Criteria

Population	Patients with Sars-CoV2 infection (COVID-19)
Intervention	Intravenous immune globulin, IVIG, human immunoglobulin, or hyperimmune globulin, hyperimmune immunoglobulin
Comparator	No restriction
Outcomes	No restriction
Study designs	Phase II or phase III or phase IV (including phase I/II and phase II/III), randomized controlled trials

Exclusion Criteria

Trials of convalescent plasma, stem cell or other cellular therapies, and vaccines are excluded from this report.

The results of the included trials are tabulated according to the type of intervention (IVIG or hyperimmune globulin), phase of clinical development, and order of trial completion dates (earlier first). The tables of ongoing trials will be updated monthly.

Results

As of December 21, 2020, there was one phase IV, eight phase III, four phase II/III, and three phase II ongoing treatment trials of IVIG (Table 2), and one phase III, one phase II/III, one phase II, and one phase I/II treatment trials of hyperimmune globulin (Table 3) that met the inclusion criteria. Sample sizes ranged from 15 patients to 500 patients (except for one large trial of 15,000 patients, although the number of patients in the IVIG arm is not stated at this time). There were three trials published (one phase II/III, one phase III, and one phase IV; Table 4). The majority of trials are being conducted in hospitalized adult patients. No ongoing trials of IVIG or hyperimmune globulin include Canadian study sites.

Other resources from the grey literature search are presented in Appendix 1, Table 5. These resources did not meet the inclusion criteria.

Limitations

There may be reporting errors in the study records posted on the clinical trial registries.[20] Not all ongoing trials are posted to the websites and therefore clinical trial registries may provide an incomplete picture of the ongoing clinical trials in 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 is 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. For some trials not listed with clinicaltrials.gov, the meaning of the date is less clear. All dates reported on trial registries may be subject to change as trials proceed.

Additionally, given the rapid changes occurring with the scientific evidence related to COVID-19, reporting amendments to the included trial protocols may be delayed.

Summary

As of December 21, 2020, there were 20 ongoing randomized controlled trials of IVIG and hyperimmune globulin for the treatment of COVID-19 that met the inclusion criteria and three trials that have been published.

Ongoing trials will be updated monthly.

Table 2: Ongoing Trials of Intravenous Immune Globulin for the Treatment of COVID-19 (December 21, 2020)

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Estimated primary completion date[a] (other available date)	Population	Trial registry identifier	Study status
PHASE IV						
IVIG (Flebogamma) versus placebo Universidad Católica de Murcia (UCAM)	Double-blind randomized placebo-controlled clinical trial to evaluate the efficacy and safety of the use of intravenous gamma globulins in the treatment of patients with COVID-19	RCT, DB, PC, MC N = 100 Spain	June 2021 (estimated trial duration)	Adult patients with severe COVID-19	EudraCT Number: 2020-001890-56	Recruiting
PHASE III						
IVIG (Clariyg) versus placebo Centre Hospitalier Saint-Anne	Value of Early Treatment With Polyvalent Immunoglobulin in the Management of Acute Respiratory Distress Syndrome Associated With SARS-CoV-2 Infections (ICAR)	RCT, DB, PC, MC N = 138 France	June 2020	Adult patients in the intensive care unit with COVID-19, ARDS, and mechanical ventilation for less than 36 hours	NCT04350580	Recruiting
IVIG versus convalescent plasma versus standard of care (not described) Vali-e-Asr Hospital Birjand University of Medical Sciences	Comparison between the efficacy of intravenous immunoglobulin and convalescent plasma in improving the condition of patients with COVID-19: A randomized clinical trial	RCT, OL, SC N = 15 Iran	July 22, 2020 (recruitment end date)	Adult patents 18 years of age to 50 years of age hospitalized with COVID-19, and severe or critical COVID-19	IRTC47212	Recruitment complete

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Estimated primary completion date[a] (other available date)	Population	Trial registry identifier	Study status
IVIG (PrIvIgen) versus standard of care (standard regimen including hydroxychloroquine, ribavirin, and lopinavir/ritonavir) Tabriz University of Medical Sciences	To evaluate the effectiveness of intravenous immunoglobulin (IVIG) for the treatment of COVID-19-induced cytokine storm	RCT, OL, SC N = 100 Iran	July 2020 (recruitment end date)	Adult patients 18 years of age to 65 years of age hospitalized with COVID-19 and moderate to severe cytokine storm and respiratory symptoms (ARDS)	IRCT47014	Recruitment complete
IVIG versus convalescent plasma Centenario Hospital Miguel Hidalgo	Efficacy and Safety of Convalescent Plasma vs Human Immunoglobulin for the Treatment of COVID-19 Pneumonia: A Randomized Controlled Trial	RCT, DB, MC N = 500 Mexico	August 30, 2020	Adult patients age 16 years of age to 90 years of age with severe or critical COVID-19	NCT04381858	Recruitment complete
IVIG (Bioven 10%) versus placebo Biopharma Plasma LLC	An Open-label Multicenter Randomized Trial to Evaluate the Efficacy of Bioven, Manufactured by Biopharma Plasma, LLC, in Complex Therapy of Patients With Pneumonia Induced by COVID-19 / SARS-CoV-2	RCT, OL, PC, MC N = 76 Ukraine	September 30, 2020	Adult patients with severe COVID-19.	NCT04500067	Recruitment completed

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Estimated primary completion date[a] (other available date)	Population	Trial registry identifier	Study status
IVIG versus standard of care (not described) University of Health Sciences Lahore	Intravenous Immunoglobulins for the Treatment of Covid-19 Patients: a Clinical Trial	RCT, DB, SC N = 60 Pakistan	October 15, 2020	Adult patients hospitalized with COVID-19.	NCT04548557	Not yet recruiting
IVIG (Octagam 10%) versus placebo Octapharma	Efficacy and safety of Octagam 10% therapy in COVID-19 patients with severe disease progression	RCT, DB, PC, MC N = 208 US	December 30, 2020	Adult patients with severe COVID-19 requiring oxygen supplementation but not mechanical ventilation. Patients who receive anti-interleukin drug, or interferons are excluded.	NCT04400058	Recruiting
NEW **TY027 (humanized IgG) versus placebo** **Tychan Pte Ltd.**	Phase 3 Multi-Site, Randomised, Placebo Controlled, Double Blind, Single Dose Study of TY027 for Early Treatment of COVID-19	RCT, DB, PC, MC N = 1,305 Singapore	August 31, 2021	Adult patients with symptomatic COVID-19 and disease score of 6, 7, or 8 on the COVID scale.	NCT04649515	Recruiting
PHASE II/III						
IVIG versus standard of care (not described) Peking Union Medical College Hospital	A Randomized, Open-label, Controlled, Single-center Study to Evaluate the Efficacy of Intravenous Immunoglobulin Therapy	RCT, OL, SC N = 80 China	April 30, 2020	Adult patients hospitalized with severe or critical COVID-19.	NCT04261426	Not yet recruiting

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Estimated primary completion date[a] (other available date)	Population	Trial registry identifier	Study status
	in Patients With Severe 2019-nCoV Pneumonia					
IVIG with dexamethasone and interferon beta (all at admission) versus IVIG with dexamethasone and interferon beta (all at 48 hours) versus standard of care (antiviral drugs and hydroxychloroquine) Gorgan University of Medical Sciences	Efficacy of different methods of administration of combination regimen including dexamethasone, IV-IG and Interferon beta for treatment of patients with severe COVID-19: a randomized controlled trial	RCT, OL, SC N = 105 Iran	June 19, 2020	Adult patients aged 18 years to 70 years hospitalized with severe or critical COVID-19 but not intubated.	IRCT46810	Recruitment complete
IVIG versus convalescent plasma versus standard of care (without new therapeutic interventions) Ahvaz University	Comparison of The Therapeutic Effect of Convalescent Plasma and Plasma-derived Immunoglobulin-enriched solution on COVID-19 Patients: A Clinical Trial Study	RCT, single blind, SC N = 45 Iran	July 24 (expected recruitment end date), 2020	Adult patients aged 20 years to 45 years hospitalized with COVID-19	IRCT46424	Not yet recruiting

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Estimated primary completion date[a] (other available date)	Population	Trial registry identifier	Study status
IVIG versus standard of care (not described) is one of the treatment arms (also dexamethasone, lopinavir/ritonavir, hydroxychloroquine, azithromycin, tocilizumab, convalescent plasma, REGN-COV2 antibodies) University of Oxford	Randomised Evaluation of COVID-19 Therapy (RECOVERY)	RCT, OL, MC N = 15,000 (not stated in this arm)	December 2021	Children age > 44 weeks gestational age to 18 years with pediatric multisystem inflammatory syndrome temporally associated with COVID-19	NCT04381936	Recruiting
PHASE II						
IVIG (Flebogamma 5%) versus standard of care (not described) Instituto Grifols	A Multicenter, Randomized, Open-label Parallel Group Pilot Study to Evaluate Safety and Efficacy of High Dose Intravenous Immune Globulin (IVIG) plus Standard Medical Treatment (SMT) versus SMT alone in Hospitalized Subjects with COVID-19	RCT, OL, MC N = 100 Spain	December 2020	Adult patients hospitalized with COVID-19 but not requiring mechanical ventilation	NCT04432324 EudraCT Number: 2020-001696-32	Recruiting
IVIG versus standard of care (azithromycin or lopinavir/ritonavir, piperacillin/tazobactam, acetaminophen) Virchow Biotech Private Limited	A Phase II Safety and Efficacy Study on Prognosis of Moderate Pneumonia in COVID-19 Patients With Regular Intravenous Immunoglobulin Therapy	RCT, OL, MC N = 100 India	December 29, 2020	Adult patients hospitalized with severe or critical COVID-19	CTRI/2020/06/026222	Recruitment completed

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Estimated primary completion date[a] (other available date)	Population	Trial registry identifier	Study status
IVIG (Gamunex-C) versus standard of care (not described) Grifols Therapeutics LLC	A Multicenter, Randomized, Open-label Parallel Group Pilot Study to Evaluate Safety and Efficacy of High Dose Intravenous Immune Globulin (IVIG) Plus Standard Medical Treatment (SMT) Versus SMT Alone in Subjects With COVID-19 Requiring Admission to the Intensive Care Unit	RCT, OL, SC N = 100 US	April, 2021	Adult patients hospitalized with COVID-19 in the intensive care unit	NCT04480424	Recruiting

ARDS = acute respiratory distress syndrome; DB = double blind; EudraCT = European Union Drug Regulating Authorities Clinical Trials; IVIG = intravenous immune globulin; MC = multi-centre; OL = open label, PC = placebo controlled; RCT = randomized controlled trial; SC = single centre.

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

Table 3: Ongoing Trials of Hyperimmune Globulin for the Treatment of COVID-19 (December 21, 2020)

Intervention and comparator Sponsor	Trial name	Study design Locations	Trial primary completion date[a]	Population	Trial registry identifier	Study status
PHASE III						
Hyperimmune immunoglobulin to SARS-CoV-2 and remdesivir versus placebo and remdesivir University of Minnesota	An International Multicenter, Adaptive, Randomized Double-Blind, Placebo-Controlled Trial of the Safety, Tolerability and Efficacy of Anti-Coronavirus Hyperimmune Intravenous Immunoglobulin for the Treatment of Adult Hospitalized Patients at Onset of Clinical Progression of COVID-19 (ITAC)	RCT, DB, PC, MC N = 500 International (US, Denmark, Argentina, UK)	July 2021	Adult patients hospitalized for the medical management of COVID-19 without related serious end-organ failure	NCT04546581	Recruiting
PHASE II/III						
Convalescent plasma versus anti–COVID-19 human immunoglobulin versus standard therapy (may include hydroxychloroquine, chloroquine, remdesivir, azithromycin) Lifefactors Zona Franca	A Multicenter Randomized Clinical Trial to Evaluate the Efficacy and Safety of the Use of Convalescent Plasma (PC) Compared to Anti-COVID-19 Human Immunoglobulin and Standard Treatment in Hospitalized Patients	RCT, OL, MC N = 75 Colombia	December 2020	Adult patients hospitalized with COVID-19 but not requiring mechanical ventilation	NCT04395170	Not yet recruiting

PHASE II						
Hyper-immunoglobulin GC5131 versus placebo Green Cross Corporation	A Prospective, Open-label, Randomized, Multi-center, Phase 2a Study to Evaluation the Dose Response, Efficacy and Safety of Hyper-Ig (Hyper-immunoglobulin) GC5131 in Patients With COVID-19	RCT, OL, PC, MC N = 60 South Korea	December 30, 2020	Adult patients hospitalized with COVID-19 but not requiring mechanical ventilation	NCT04555148	Recruiting
PHASE I/II						
Intravenously administered immunoglobulins developed from pooled convalescent plasma of individuals who have recovered from COVID-19 versus standard of care (not described) Dow University of Health Sciences	Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) Antibodies Based Intravenous Immunoglobulin (IVIG) Therapy for Severe and Critically Ill COVID-19 Patients	RCT, single blind, SC N = 50 Pakistan	January 2021	Adult patients hospitalized with severe or critical COVID-19	NCT04521309	Recruiting

DB = double blind; MC = multi-centre; OL = open label; PC = placebo controlled, RCT = randomized controlled trial; SC = single centre.

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

Table 4: Published Trials of Intravenous Immune Globulin for the Treatment of COVID-19 (December 21, 2020)

Intervention (brand, if stated) and comparator Sponsor	Trial name	Study design, number of patients Locations	Population	Trial registry identifier	Study status
PHASE IV					
IVIG (Octagam) plus methylprednisolone versus standard of care George Sakoulas, MD; MD, Sharp HealthCare	Study of Standard of Care Plus Intravenous Immunoglobulin (IVIG) Compared to Standard of Care Alone in the Treatment of COVID-19 Infection	RCT, OL, SC N = 33 US	Adult patients hospitalized with COVID-19 but not requiring mechanical ventilation	NCT04411667	Published
PHASE III					
IVIG (Flebogamma 5%) versus placebo Oroumia University of Medical Sciences	Intravenous Immunoglobulin (IVIG) Effect on Improvement of Severe Pulmonary Damage in COVID-19 Disease	Phase III, RCT, DB, PC, SC N = 40 Iran	Adult patients hospitalized with COVID-19 and no response to at least one antiviral and chloroquine drugs	IRTC47609	Published
PHASE II/III					
IVIG (Biotest) versus standard of care (hydroxychloroquine and lopinavir ritonavir) for seven days Shahid Beheshti University of Medical Sciences	Evaluating the efficacy and safety of intravenous immunoglobulin (IVIG) in COVID-19 patients	RCT, OL, SC N = 80 Iran	Adult patients aged 18 years to 65 years hospitalized with severe COVID-19	IRCT49638	Published

Appendix 1: Other Resources

Table 5: Additional References (December 1, 2020)

Organization (date of statement or report)	Brief summary
Canadian resources	
CADTH Convalescent Plasma Therapy for the Treatment of COVID-19: Clinical Effectiveness[4] (May 15, 2020)	CADTH describes the results of a literature search on evidence to support the clinical effectiveness of convalescent plasma therapy for the treatment of COVID-19.
CADTH Convalescent Plasma Therapy for the Treatment of COVID-19: a Review of Clinical Effectiveness[5] (November 12, 2020)	CADTH summarizes the current evidence about convalescent plasma for the treatment of COVID-19. Overall, the quantity and quality of evidence was limited. There is currently a lack of sufficient-quality evidence to evaluate this intervention for the treatment of COVID-19. The report highlights the need for well-designed large randomized trials.
INESSS Thérapie passive par anticorps (plasma convalescent)[21] (March 31, 2020)	INESSS published a report on convalescent plasma and it is available in French.
Canadian Blood Services COVID-19 and Convalescent Plasma[22]	This Canadian Blood Services website contains information for patients, donors, and health professionals about blood donation, blood products, and participation in national research on convalescent plasma for the treatment of COVID-19.
Canadian Blood Services COVID-19 and transfusion medicine[23]	This Canadian Blood Services website has resources for Canadian transfusion medicine health care professionals. Resources are available for blood products inventory management, blood product conservation practices during COVID-19, COVID-19 education events, and information about the treatment of patients with COVID-19 with convalescent plasma and IVIG.
National Advisory Committee on Blood and Blood Products Fact Sheet on Convalescent Plasma and Intravenous Immune Globulin (IVIG) for Treatment of COVID-19 in Canada[24] (March 31, 2020)	The National Advisory Committee on Blood and Blood Products states that Canadian Blood Services (and Héma-Québec) will be collecting and producing convalescent plasma. Canadian patients will only be able to receive therapy with convalescent plasma for COVID-19 as part of a of a clinical trial. The organization states that there is no evidence to support the use of IVIG as an effective treatment for COVID-19 and that IVIG is not available for patients with COVID-19. Concerns include the limited supply of IVIG and the need for its use for patients with other diagnoses.
Héma-Québec COVID-19 Information[25]	The Héma-Québec website contains information for patients, donors, and health professionals about blood donation, blood products, and participation in national research about convalescent plasma for the treatment of COVID-19.

Organization (date of statement or report)	Brief summary
BC Centre for Disease Control Clinical Reference Group Recommendations: Therapies for COVID-19[26] (Update November 13, 2020)	The BC Centre for Disease Control recommends against the use of convalescent plasma or IVIG for COVID-19 outside the setting of a randomized controlled trial.
Ye Z, Guyatt G. Treatment of patients with non-severe and severe COVID-19: an evidence-based guideline[27] (May 19, 2020)	This Canadian clinical practice guideline describes the treatment of patients with COVID-19. The authors suggest not to use convalescent plasma to treat COVID-19.
International resources	
WHO Blood Regulators Network Position Paper on Use of Convalescent Plasma, Serum or Immune Globulin Concentrates as an Element in Response to an Emerging Virus[1] (September 14, 2017)	The World Health Organization Blood Regulators Network states that use of convalescent plasma is investigational in the context of an emerging virus.
International Society of Blood Transfusion COVID-19 Convalescent plasma Document library[28]	This document library is a platform for sharing protocols for collecting and processing convalescent plasma for COVID-19 from different WHO regions.
Cochrane Database Chai KL, Valk SJ, Piechotta V, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review [29] (October 12, 2020)	This living systematic review describes studies that evaluate convalescent plasma or hyperimmune immunoglobulin for COVID-19.
American resources	
National COVID-19 Convalescent Plasma Project[30] Health Care Providers	This website is from a US-based group of physicians and scientists. Information is available for health care providers about a rapid evaluation program, an exposure control study, and protocols for ongoing randomized controlled trials of convalescent plasma and hyperimmune globulin in the US.
American Society of Hematology COVID-19 and Convalescent Plasma: Frequently Asked Questions[31] (November 30, 2020)	The American Society of Hematology document describes the evidence, potential benefits, risks, and mechanisms to access treatment and assess clinical efficacy and effectiveness.
FDA Investigational COVID-19 Convalescent Plasma A Guidance Document[32] (November, 2020)	This FDA guidance describes US recommendations around pathways for the use of investigational COVID-19 convalescent plasma (clinical trials, expanded access, and single patient emergency IND), patient eligibility, collection of COVID-19 convalescent plasma, and record-keeping.

Organization (date of statement or report)	Brief summary
NIH Immune-Based Therapy Under Evaluation for Treatment of COVID-19[33] (July 17, 2020)	This National Institute of Health US-based treatment guidelines panel found insufficient data to recommend either for or against convalescent plasma or SARS-CoV-2 immunoglobulins for the treatment of COVID-19. The guidelines recommend against IVIG outside the setting of a clinical trial.
AABB AABB's Coronavirus Resources[34]	This website contains resources and information for the blood community about coronavirus, including sections on convalescent plasma, blood donation, hospitals and transfusion services, blood centres, stem cell therapy current status, resources translated into Spanish, educational resources on COVID-19, and AABB positions.
AABB Toolkit for COVID-19 Convalescent Plasma (CCP) under Emergency Use Authorization (EUA)[35] (December 2, 2020)	This tool kit produced by AABB contains resources and information intended to supplement the FDA's Emergency Use Authorization conditions for use and FDA's Guidance for Industry.
Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19[36] (December 2, 2020)	These Infectious Diseases Society of America guidelines recommend that convalescent plasma be used for COVID-19 only as part of a clinical trial.
European resources	
Heath Technology Wales Plasmapheresis of convalescent plasma to confer passive immunity[37] (April, 2020)	This Topic Exploration Report produced by Health Technology Wales did not find any evidence that convalescent plasma impacts outcomes in patients with COVID-19.
National Centre for Pharmacoeconomics (NCPE) Ireland Clinical evidence for the use of intravenous immunoglobulin in the treatment of COVID-19[38] (Version 2, May 14, 2020)	This Rapid Evidence Review by the National Centre for Pharmacoeconomics in Ireland found no robust evidence to support the use of IVIG for COVID-19 and advised that IVIG should ideally be used in a clinical trial.
Health Information and Quality Authority, Ireland Convalescent Plasma for the Treatment of COVID-19 (November 11, 2020)	This Health Technology Assessment scoping report by the Health Information and Quality Authority, Ireland, provides a preliminary assessment of the current available evidence on convalescent plasma for the treatment of COVID-19.
Other resources	
Ministry of Health Singapore Should convalescent plasma be used for COVID-19?[39] (updated May 18, 2020)	This write-up of a rapid evidence review found limited evidence on convalescent plasma for COVID-19.

Organization (date of statement or report)	Brief summary
MaHTAS — Malaysian Health Technology Assessment Section Convalescent plasma for treatment of COVID-19[40] (April 13, 2020)	This rapid evidence update by MaHTAS states that randomized controlled trials on convalescent plasma for COVID-19 are needed.
National COVID-19 Clinical Evidence Taskforce Australian guidelines for the clinical care of people with COVID-19[41] (December 16, 2020)	This Australian guideline does not recommend convalescent plasma for people with COVID-19.

AABB = American Association of Blood Banks; IND = investigational new drug; IVIG = intravenous immune globulin.

References

1. WHO Blood Regulators Network. Position paper on use of convalescent plasma serum or immune globulin concentrates as an element in response to an emerging virus. 2017: https://www.who.int/bloodproducts/brn/2017_BRN_PositionPaper_ConvalescentPlasma.pdf?ua=1.
2. Bloch EM, Shoham S, Casadevall A, et al. Deployment of convalescent plasma for the prevention and treatment of COVID-19. *J Clin Invest.* 2020;130(6):2757-2765.
3. Casadevall A, Pirofski LA. The convalescent sera option for containing COVID-19. *J Clin Invest.* 2020;130(4):1545-1548.
4. Convalescent plasma therapy for the treatment of COVID-19: clinical effectiveness. *(CADTH Rapid response report: reference list)*. Ottawa (ON): CADTH; 2020: https://covid.cadth.ca/treatment/convalescent-plasma-therapy-for-the-treatment-of-covid-19-a-review-of-clinical-effectiveness-2/. Accessed 2020 Dec 21.
5. Convalescent plasma therapy for the treatment of COVID-19: a review of clinical effectiveness. *(CADTH Technology review)*. Ottawa (ON): CADTH; 2020: https://covid.cadth.ca/treatment/convalescent-plasma-therapy-for-the-treatment-of-covid-19-a-review-of-clinical-effectiveness-2/. Accessed 2020 Dec 21.
6. Rutledge Harding S, Lazarus A. Clinical guide to transfusion: chapter 4 immune globulin products. Ottawa (ON): Canadian Blood Services; 2018: https://professionaleducation.blood.ca/en/transfusion/guide-clinique/immune-globulin-products Accessed 2020 Aug 6.
7. Wang JT, Sheng WH, Fang CT, et al. Clinical manifestations, laboratory findings, and treatment outcomes of SARS patients. *Emerg Infect Dis.* 2004;10(5):818-824.
8. Arabi YM, Arifi AA, Balkhy HH, et al. Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus infection. *Ann Intern Med.* 2014;160(6):389-397.
9. Khanna N, Widmer AF, Decker M, et al. Respiratory syncytial virus infection in patients with hematological diseases: single-center study and review of the literature. *Clin Infect Dis.* 2008;46(3):402-412.
10. Cao W, Liu X, Bai T, et al. High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with Coronavirus disease 2019. *Open Forum Infect Dis.* 2020;7(3):ofaa102.
11. Xie Y, Cao S, Dong H, et al. Effect of regular intravenous immunoglobulin therapy on prognosis of severe pneumonia in patients with COVID-19. *J Infect.* 2020;pii: S0163-4453(20)30087-6.
12. Hung IFN, To KKW, Lee CK, et al. Hyperimmune IV immunoglobulin treatment: a multicenter double-blind randomized controlled trial for patients with severe 2009 influenza A(H1N1) infection. *Chest.* 2013;144(2):464-473.
13. Valk SJ, Piechotta V, Chai KL, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a rapid review. *Cochrane Database Syst Rev.* 2020;5:CD013600.
14. CADTH. CADTH COVID-19 evidence portal. 2020; https://covid.cadth.ca/. Accessed 2020 Dec 21.
15. U.S. National Library of Medicine. Clinicaltrials.gov. 2020; https://www.clinicaltrials.gov/. Accessed 2020 Dec 21.
16. Government of Canada. Clinical trial search. 2020; https://health-products.canada.ca/ctdb-bdec/index-eng.jsp. Accessed 2020 Dec 21.
17. World Health Organization. International clinical trials registry platform (ICTRP). https://www.who.int/ictrp/en/. Accessed 2020 Dec 21.
18. Grey matters: a practical tool for searching health-related grey literature. Ottawa (ON): CADTH; 2019: https://www.cadth.ca/grey-matters. Accessed 2020 Aug 6.
19. CADTH COVID-19 grey literature resources : a curated list of evidence-based sources for health professionals, librarians, and researchers. Ottawa (ON): CADTH; 2020: https://covid.cadth.ca/literature-searching-tools/cadth-covid-19-grey-literature-resources/. Accessed 2020 Aug 6.
20. Tse T, Fain KM, Zarin DA. How to avoid common problems when using ClinicalTrials.gov in research: 10 issues to consider. *BMJ.* 2018;361:k1452.
21. Thérapie passive par anticorps (plasma convalescent). Quebec (QC): INESSS; 2020: https://www.inesss.qc.ca/covid-19/traitements-specifiques-a-la-covid-19/therapie-passive-par-anticorps-plasma-convalescent.html. Accessed 2020 Dec 21.
22. Canadian Blood Services. COVID-19 and convalescent plasma. https://blood.ca/en/convalescentplasma Accessed 2020 Nov 24.
23. Canadian Blood Services. COVID-19 and transfusion medicine. https://profedu.blood.ca/en/transfusion/covid-19-and-transfusion-medicine. Accessed 2020 Dec 21.
24. National Advisory Committee on Blood and Blood Products. Fact sheet on convalescent plasma and intravenous immune globulin (IVIG) for treatment of COVID-19 in Canada. 2020: https://www.nacblood.ca/resources/COVID%20QA_NAC%20March%2031%202020_FINAL.pdf. Accessed 2020 Dec 21.
25. Héma-Québec. Héma-Québec during the pandemic. 2020; https://www.hema-quebec.qc.ca/coronavirus/index.en.html. Accessed 2020 Dec 21.
26. BC Centre for Disease Control, BC Ministry of Health. Clinical reference group recommendations: therapies for COVID-19. 2020: http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments. Accessed 2020 Dec 21.

27. Ye Z, Rochwerg B, Wang Y, et al. Treatment of patients with nonsevere and severe coronavirus disease 2019: an evidence-based guideline. *Canadian Medical Association Journal.* 2020;192(20):E536-E545.
28. International Society of Blood Transfusion. COVID-19 convalescent plasma document library. 2020; https://isbtweb.org/covid-19resources/covid-19-convalescent-plasma-document-library/. Accessed 2020 Dec 21.
29. Chai KL, Valk SJ, Piechotta V, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. *Cochrane Database of Systematic Reviews.* 2020(10).
30. Michigan State University. National COVID-19 convalescent plasma project https://ccpp19.org/healthcare_providers/index.html. Accessed 2020 Dec 21.
31. American Society of Hematology. COVID-19 and convalescent plasma: frequently asked questions. 2020; https://www.hematology.org/covid-19/covid-19-and-convalescent-plasma Accessed 2020 Dec 21.
32. Investigational COVID-19 convalescent plasma. Silver Springs (MD): Food and Drug Administration; 2020: https://www.fda.gov/media/136798/download. Accessed 2020 Dec 21.
33. National Institutes of Health. Coronavirus Disease 2019 (COVID-19) treatment guidelines. 2020; https://www.covid19treatmentguidelines.nih.gov/. Accessed 2020 Dec 21.
34. AABB. AABB's coronavirus resources. 2020; http://www.aabb.org/advocacy/regulatorygovernment/Pages/AABB-Coronavirus-Resources.aspx. Accessed 2020 Dec 21.
35. AABB. Toolkit for COVID-19 Convalescent Plasma (CCP) under Emergency Use Authorization (EUA). 2020; https://www.aabb.org/docs/default-source/default-document-library/regulatory/toolkit-for-ccp-under-eua.pdf. Accessed 2020 Dec 21.
36. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. Arlington (VA): Infectious Diseases Society of America; 2020: https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt-v2.1.0.pdf. Accessed 2020 Dec 21.
37. Heath Technology Wales. Plasmapheresis of convalescent plasma to confer passive immunity. 2020: https://www.healthtechnology.wales/wp-content/uploads/2020/05/TER-203-CPT-v1.0.pdf. Accessed 2020 Dec 21.
38. Clinical evidence for the use of intravenous immunoglobulin in the treatment of COVID-19. Dublin (IE): National Centre for Pharmacoeconomics Ireland, The COVID-19 Evidence Review Group for Medicines Ireland; 2020: http://www.ncpe.ie/wp-content/uploads/2020/05/Intravenous-immunoglobulin-for-the-treatment-of-COVID-19-A-Rapid-Evidence-Review-V2.pdf. Accessed 2020 Dec 21.
39. Should convalescent plasma be used for COVID-19? Singapore (SG): Agency for Care Effectiveness, Ministry of Health Singapore; 2020: https://www.moh.gov.sg/docs/librariesprovider5/clinical-evidence-summaries/convalescent-plasma-infusion-for-covid-19-(updated-18-may-2020).pdf. Accessed 2020 Dec 21.
40. Convalescent plasma for treatment of COVID-19. Putrajaya (MY): Malaysian Health Technology Assessment Section; 2020: https://www.moh.gov.my/moh/resources/penerbitan/mymahtas/MaHTAS%20COVID-19%20Rapid%20Evidence/Clinical%20Management/Convalescent_Plasma_For_Treatment_Of_COVID-19.pdf. Accessed 2020 Dec 21.
41. Australian guidelines for the clinical care of people with COVID-19. Melbourne (AU): National COVID-19 Clinical Evidence Taskforce; 2020: https://app.magicapp.org/#/guideline/4615. Accessed 2020 Dec 21.