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 September 24, 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.

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 September 24, 2020, there were two phase IV, eight phase III, five phase II/III, and three phase II treatment trials of IVIG (Table 2); and one phase III, one phase II/III, one phase II and one phase I/II treatment trial of hyperimmune globulin (Table 3) that met the inclusion criteria. Sample sizes range 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). All of the included 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 4. 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 September 24, 2020, there were 22 ongoing randomized controlled trials of IVIG and hyperimmune globulin for the treatment of COVID-19 that met the inclusion criteria. Ongoing trials will be updated monthly.

Table 2: Ongoing Trials of Intravenous Immune Globulin for the Treatment of COVID-19 (September 24, 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 (Octagam) versus standard of care (not described) 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 = 40 US	November 1, 2020	Adult patients hospitalized with COVID-19 but not requiring mechanical ventilation	NCT04411667	Recruiting
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	Ongoing
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	RCT, DB, PC, SC N = 40 Iran	June 9, 2020 (recruitment end date)	Adult patients hospitalized with COVID-19 and no response to at least one antiviral and chloroquine drugs	IRTC47609	Recruitment complete
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

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 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
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	Recruiting
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	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
NEW 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	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 before enrolment or plan to receive this treatment during the study are excluded.	NCT04400058	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 in Patients With Severe 2019-nCoV Pneumonia	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
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)	Adult patients aged 20 years to 45 years hospitalized with COVID-19	IRCT46424	Not yet recruiting
IVIG (Biotest) versus standard of care (hydroxychloroquine and lopinavir ritonavir) times 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	August 9, 2020 (expected recruitment end date)	Adult patients aged 18 years to 65 years hospitalized with severe COVID-19	IRCT49638	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
NEW 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	Recruitment ongoing
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	July 2020	Adult patients hospitalized with COVID-19 but not requiring mechanical ventilation	NCT04432324 EudraCT Number: 2020-001696-32	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 (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	December 2020	Adult patients hospitalized with COVID-19 in the intensive care unit	NCT04480424	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	Not yet 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 (September 24, 2020)

Intervention and comparator Sponsor	Trial name	Study design Locations	Trial primary completion date[a]	Population	Trial registry identifier	Study status
PHASE III						
NEW 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	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	Not yet 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						
NEW 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

Intervention and comparator Sponsor	Trial name	Study design Locations	Trial primary completion date[a]	Population	Trial registry identifier	Study status
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.

Appendix 1: Other Resources

Table 4: Additional References (August 6, 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] (July 23, 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 August 10, 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 Piechotta V, Chai KL, Valk SJ, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review[29] (July 10, 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] (last updated June 8, 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] (May, 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.
Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19[35] (August 20, 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	
National Health Services Specialty guides for patient management during the coronavirus pandemic. Clinical guide for the management of patients requiring immunoglobulin treatment during the coronavirus pandemic and management of supply[36] (March 27, 2020)	This National Health Services guide indicates that the Immunology and Allergy Clinical Reference Group does not recommend IVIG for COVID-19.
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.
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.
ASCIA — Australasian Society of Clinical Immunology and Allergy Position Statement Immunoglobulin Therapies for COVID-19[40]	This position statement by ASCIA on immunoglobulin therapies for COVID-19 states that there is low-grade circumstantial evidence for convalescent plasma for COVID-19. The organization states that there is no evidence for the efficacy of IVIG and has concerns that it may worsen COVID-19.

Organization (date of statement or report)	Brief summary
MaHTAS — Malaysian Health Technology Assessment Section Convalescent plasma for treatment of COVID-19[41] (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[42] (July 22, 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.

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