EUnetHTA Joint Action 3 WP4

"Rolling Collaborative Review" of Covid-19 treatments

CONVALESCENT PLASMA THERAPY FOR THE TREATMENT OF COVID-19

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Monitoring Report

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V 1.1	**26/08/2020**	Literature searches, Literature screening, Data extraction
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V 2.0	**15/09/2020**	Second version

Major changes from previous version

Chapter, page no.	Major changes from version 1.0
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Chapter 3 [page 9]	• Information on regulatory status updated
Chapter 3 [page 9]	• Information on level of evidence updated
Chapter 4 [page 9]	• Information on effectiveness and safety evidence from RCTs updated
Chapter 4 [page 9]	• Information on safety evidence from observational studies updated
Chapter 4 [page 10]	• Information on ongoing trials updated
Chapter 4, [page 13 to 16]	• Newly identified observational studies added to Table 4-2 to 4-5
Chapter 4, [page 50 to 54]	• Newly identified ongoing trials added to Table 4-19 and Table 4-21

Disclaimer

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Conflict of interest

All authors and co-authors involved in the production of this living document have declared they have no conflicts of interest in relation to the technology and comparator(s) assessed according to the EUnetHTA declaration of interest (DOI) form. Conflict of Interest was evaluated following the EUnetHTA Procedure Guidance for handling DOI form (https://eunethta.eu/doi).

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LIST OF ABBREVIATIONS

AE	Adverse Event
ARR	Absolute Risk Reduction
ATC	Anatomical Therapeutic Chemical [Classification System]
ATMP	Advanced therapy medicinal product
CI	Confidence Interval
COVID-19	Coronavirus disease 2019
CS	Case study/series
CT	Controlled trial
CPT	Convalescent plasma therapy
DOI	Declaration of interest
EMA	European Medicines Agency
EUnetHTA	European Network of Health Technology Assessment
FDA	Food and Drug Administration
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HR	Hazard Ratio
HRQOL	Health-related Quality of Life
ICD	International Classification of Diseases
ITT	Intention-to-treat
IQR	Interquartile Range
MD	Mean Difference
MeSH	Medical Subject Headings
NA	Not applicable
NR	Not reported
OB	Observational study
OR	Odds Ratio
PCR	Polymerase Reaction Chain
PP	Per Protocol
RCT	Randomized Controlled Trial
RCA	Rolling collaborative review
REA	Relative Effectiveness Assessment
RR	Relative Risk
SAE	Serious Adverse Event
SARS	Severe acute respiratory syndrome
SD	Standard Deviation
SMD	Standardized Mean Difference
SmPC	Summary of product characteristics
SOF	Summary of findings
SOP	Standard Operating Procedure
TRALI	Transfusion-related acute lung injury
WP4	Work Package 4

1 OBJECTIVE

The aim of this EUnetHTA Rolling Collaborative Review is

- to inform health policy at the national/regional and at the European level at an early stage in the life-cycle of therapies which interventions are currently undergoing clinical trials,
- to monitor (ongoing studies and their results) permanently - in the format of a Living Document - potential therapies against covid-19,
- to present comparative data on effectiveness and safety of potential therapies and
- to support preparations for an evidence-based purchasing of regional/ national health politicians, if necessary.

To avoid redundancies and duplication, the EUnetHTA Rolling Collaborative Review will reuse sources from international initiatives to collect information and data on Covid-19 treatments.

The scope of the Rolling Collaborative Review is of descriptive nature. These **EUnetHTA Rolling Collaborative Reviews are not meant to substitute a joint Relative Effectiveness Assessment (REA)** adhering to the agreed procedures and aiming at critical appraisal of the clinical evidence based on the Submission Dossier submitted by the (prospective) Marketing Authorization Holder (MAH).

2 METHODS

This Rolling Collaborative Review is prepared according to the project plan ("Rolling Collaborative Review (RCR) on Covid-19 treatments: Project description and planning", published on the EUnetHTA website) and will be updated monthly. Monthly updates are published on the EUnetHTA Covid-19 Website (https://eunethta.eu/services/covid-19/) and on the EUnetHTA Rolling Collaborative Review Sharepoint page each 15th of the month.

2.1 Scope

Table 2-1 Scope of the RCR

Description	Project Scope
Population	**Disease** • SARS-CoV-2 is a novel coronavirus causing a respiratory illness termed Covid-19. The full spectrum of Covid-19 ranges from mild, self-limiting respiratory tract illness to severe progressive pneumonia, multi-organ failure, and death. **ICD-Codes** (https://www.who.int/classifications/icd/covid19/en) • An emergency ICD-10 code of 'U07.1 COVID-19, virus identified' is assigned to a disease diagnosis of COVID-19 confirmed by laboratory testing. • An emergency ICD-10 code of 'U07.2 COVID-19, virus not identified' is assigned to a clinical or epidemiological diagnosis of COVID-19 where laboratory confirmation is inconclusive or not available. • Both U07.1 and U07.2 may be used for mortality coding as cause of death. See the International guidelines for certification and classification (coding) of COVID-19 as cause of death following the link below. • In ICD-11, the code for the confirmed diagnosis of COVID-19 is RA01.0 and the code for the clinical diagnosis (suspected or probable) of COVID-19 is RA01.1. **MeSH-terms** • COVID-19, Coronavirus Disease 2019 **Target population** (https://www.covid19treatmentguidelines.nih.gov/overview/management-of-covid-19/)

	• Asymptomatic or pre-symptomatic Infection: Individuals who test positive for SARS-CoV-2 by virologic testing using a molecular diagnostic (e.g., polymerase chain reaction) or antigen test, but have no symptoms. • Mild Illness: Individuals who have any of the various signs and symptoms of COVID 19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnoea, or abnormal chest imaging. • Moderate Illness: Individuals who have evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SpO2) ≥94% on room air at sea level. • Severe Illness: Individuals who have respiratory frequency >30 breaths per minute, SpO2 <94% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mmHg, or lung infiltrates >50%. • Critical Illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.
Intervention	Convalescent Plasma Treatment Convalescent plasma has been used in the past to treat conditions when no vaccine or pharmacological interventions were available. Convalescent plasma from recovered COVID-19 patients contains antibodies against SARS-CoV-2 produced by their immune system. Collecting donations of convalescent plasma from recovered COVID-19 patients and transfusing this into others could confer a degree of passive immunity. This may allow the recipient time for their own immune system to develop resistance to SARS-CoV-2.
Comparison	Any active treatment, placebo, or standard of care. **Rationale**: Since there is no gold standard treatment any comparator is acceptable as well as the above listed interventions.
Outcomes	<u>Main outcome:</u> • All-cause Mortality (Survival) <u>Additional Outcomes:</u> Efficacy: • Length of hospital stay, • Viral burden (2019-nCoV RT-PCR negativity), • Clinical progression (WHO Clinical Progression Scale measured daily over the course of the study), • Rates of hospitalization and of patients entering ICU, • Duration of mechanical ventilation, • Quality of life. Safety: • Adverse events (AE), • Serious adverse events (SAE), • Withdrawals due to AEs, • Most frequent AEs, • Most frequent SAEs. • AEs of special interest • Death as a SAE **Rationale:** We will give priority according to the Core Outcome Set for Clinical Trials on Coronavirus Disease 2019 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102592/pdf/main.pdfc) and A minimal common outcome measure set for COVID-19 clinical research from the WHO Working Group on the Clinical Characterisation and Management of COVID-19 infection.
Study design	Efficacy: randomised controlled trials (RCT) Safety: observational studies (comparative or single-arm prospective studies and registries)

2.2 Sources of information

According to the project plan, this Rolling Collaborative Review is based on three main sources of information, as described below:

1. Summary of findings (SoF) table for published RCTs related to effectiveness and safety:

This table is based on the living systematic review and Network Meta-Analysis (NMA) created by the partnering institute of DEPLazio: find the PROSPERO protocol here. DEPLazio provides updates for the SoF table on a monthly basis to the EUnetHTA partners authoring the respective Rolling CR documents who are integrating this information accordingly.

The literature search is conducted in the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library
- MEDLINE, accessed via OVID
- Embase, accessed via OVID

Population	People affected by COVID-19, as defined by the authors of the studies. No limits in terms of gender or ethnicity. SARS-CoV-2 is a novel coronavirus causing a respiratory illness termed Covid-19. It started spreading in December 2019, and was declared a pandemic by the World Health Organisation on 11th March 2020. The full spectrum of Covid-19 ranges from mild, self-limiting respiratory tract illness to severe progressive pneumonia, multi-organ failure, and death.
Intervention	Interventions for the treatment of people affected by COVID-19, including pharmacological interventions (e.g. antibiotics, antibodies, antimalarial, antiviral, antiretroviral, immune-suppressors/modulators, kinase inhibitors) and their combinations.
Comparison	Any active treatment, placebo, or standard of care.
Outcomes	All-cause mortality Additional outcomes: Length of hospital stay, 2019-nCoV RT-PCR negativity, PaO2/FiO2, Duration of mechanical ventilation, radiological imaging, Adverse events, Severe adverse events.
Study design	Randomised controlled trials (RCT); no restriction on language of publication

To identify preprints of preliminary reports of work that have not been peer-reviewed, the following sources are searched:

- medRxiv Health Sciences
- bioRxiv Biology

In addition to the sources and strategies described above, registers of ongoing studies are screened. Key conferences and conference proceedings are considered.

Data extraction, Risk of bias assessment, data synthesis:

Two reviewers from DEPLazio are screening search results, assessing full texts of studies and extract study characteristics and outcome data according to pre-defined criteria.

Risk of bias is assessed using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions [1].

Dichotomous outcomes are analysed by calculating the relative risk (RR) for each trial with the uncertainty in each result being expressed by its 95% confidence interval (CI).Continuous outcomes are analysed by calculating the mean difference (MD) with the relative 95% CI when the study used the same instruments for assessing the outcome.

The standardised mean difference (SMD) is applied when studies used different instruments. Pairwise meta-analyses is performed for primary and secondary outcomes using a random-effects

model in RevMan for every treatment comparison [2]. Network meta-analysis (NMA) is performed for the primary outcome. For rating the certainty of the evidence, the GRADE approach is being used [3].

- Sources: http://deplazio.net/farmacicovid/index.html for SoF (or https://covid-nma.com/)

2. Table(s) on published (peer reviewed) observational studies for safety results:

The literature search is conducted on a monthly basis using the following sources:

- https://www.fhi.no/en/qk/systematic-reviews-hta/map/
- https://www.ncbi.nlm.nih.gov/research/coronavirus/docsum?filters=topics.General%20Info

Population	See project Scope
Intervention	Convalescent Plasma Treatment
Comparison	Any active treatment, placebo, or standard of care.
Outcomes	See project Scope
Study design	Prospective non-randomised controlled trials, prospective case series, registries Exclusion criteria: retrospective case series, case studies

One researcher carries out title and abstract screening and assesses the full texts of all potentially eligible studies. One researcher extracts the data and assesses the risk of bias using ROBINS-I (https://training.cochrane.org/handbook/current/chapter-25).

Results are presented in tabular form for all included studies.

3. Table(s) on ongoing trials:

The following clinical trial registries are searched on a monthly basis:

- ClinicalTrials.gov: https://clinicaltrials.gov/
- ISRCTN: https://www.isrctn.com/
- European Clinical Trials Registry: https://www.clinicaltrialsregister.eu/

Inclusion criteria: Randomised controlled trials, Controlled trials

One researcher is searching and extracting the data for the eligible studies.

Data are presented in tabular form.

3 ABOUT THE TREATMENT

3.1 Mode of Action

Convalescent plasma from patients recently recovered from coronavirus disease 2019 (COVID-19) contains antibodies against SARS-CoV-2 which have been produced by their immune system. Collecting donations of convalescent plasma from recovered COVID-19 patients and transfusing this into others could confer a degree of passive immunity. This may allow the recipient time for their own immune system to develop resistance to SARS-CoV-2. Convalescent plasma therapy (CPT) has previously been used in other outbreaks such as severe acute respiratory syndrome (SARS), pandemic 2009 influenza A (H1N1), avian influenza A (H5N1), and Ebola. Studies which compare CPT to standard treatment in patients with SARS or severe influenza report inconsistent findings for overall mortality [4-8]. However, studies suggest that CPT may result in earlier discharge from hospital in SARS patients, particularly if given earlier on in treatment, and lower viral load in patients with severe influenza.

Based on evidence from other viral diseases and some recent case studies, there is potential for CPT to play an important role in the COVID-19 pandemic [9-13]. However, there is also the potential for adverse events which arise from plasma transfusions, such as allergic reactions, transfusion-related acute lung injury (TRALI), and circulatory overload [14-16]. Factors such as the levels of antibodies present in the plasma and the time point at which it is administered may also impact on its effectiveness.

3.2 Regulatory Status

CPT is not currently approved for use in COVID-19 by the European Medicines Agency. However, a number of guidelines have been produced to encourage a standardised approach. The European Commission published guidance on the use of COVID-19 CPT in April 2020 and the Italian Society for Transfusion Medicine and Immunohaematology and the Italian Society for Haemapheresis and Cell Manipulation have published a position paper on preparation of immune plasma for treatment of patients with COVID-19. In the United States, the Food and Drug Administration (FDA) issued an emergency investigational new drug (eIND) in March 2020. They further issued an emergency use authorization (EUA) in August 2020 while also stating that randomised controlled trials are needed to provide more definitive evidence of efficacy and to define optimum treatment attributes and most appropriate patient populations.

3.3 Level of Evidence

Currently the evidence for CPT for COVID-19 is in the early stages. One RCT and 15 prospective observational studies of varying size and quality have been published to date. However, there are a large number of RCTs and other trials currently being conducted. We identified 85 ongoing RCTs with estimated primary completion dates which range from pre-August 2020 to January 2023. The majority of these have estimated primary completion dates in 2020 or the first half of 2021.

4 SUMMARY

4.1 Effectiveness and Safety evidence from RCTs

To date, two RCTs with very low certainty of evidence have been published comparing standard treatment plus CPT to standard treatment alone [17, 18]. One trial was terminated early due to the containment of COVID-19 in China and did not reach the planned sample size [17]. There was no significant difference in time to clinical improvement (within 28 days), mortality at 28 days, discharge rate at 28 days, or time from hospitalisation to discharge between groups. There was a significant difference in conversion to SARS-CoV-2 negative rates at 24, 48 and 72 hours. Another trial was terminated early as a high proportion of patients were found to already have high virus neutralizing titers prior to treatment initiation [18]. There was no significant difference in overall mortality, improvement in disease severity, or time to discharge from hospital. No plasma related adverse events were observed.

4.2 Safety evidence from observational studies

Fifteen prospective observational studies were identified. Eleven had critical risk of bias, three were at serious risk of bias and one was at moderate risk of bias. Nine studies were very small (N=3 to 46), two were moderately sized (N=150 to 189) and four were large (N=1568 to 36226). Where reported, participants had severe or critical disease or were judged at risk of progressing to severe or critical disease. The overall rates for adverse events (AEs) were rarely stated. In the larger trials, transfusion-related AEs and SAEs were reported to be between 2% and below 1% . Death as a SAE ranged from 0% to 31% across varying time periods and intervention arms. The largest study reported 10.4% mortality at 7 days and 24.4% at 30 days for participants receiving CPT.

4.3 Ongoing studies

In total 85 ongoing RCTs were identified across a wide range of countries. Trials were mostly described as Phase II (33 in total) with eight described as Phase I or I/II, 12 described as Phase II/III and 13 described as Phase III. Estimated primary completion dates ranged from pre-August 2020 to the first half of 2023, with the majority expected to report in 2020 or the first half of 2021. Anticipated study size ranged from 15 to 15,000 participants.

4.4 Scientific conclusion about status of evidence generation

Currently the evidence for CPT for COVID-19 is in the early stages and it is difficult to draw reliable conclusions from it. Proxy measures such as viral conversion rates are promising but as yet there is no high quality evidence of effectiveness for clinical outcomes. With the large number of RCTs which are expected to report in 2020 or early 2021 good quality evidence is expected to be available in the near future.

Table 4-1 Summary of findings (SoF) table for published RCTs related to effectiveness and safety of Convalescent Plasma Therapy

Outcome	No. of patients		Relative effect (95% CI)	Absolute effect (95% CI)	No. of studies	Certainty of evidence
	CPT	Standard Treatment				
All-cause mortality	14/95 (14.7%)	23/94 (24.5%)	RR 0.60 (0.33 to 1.10)	98 fewer per 1,000 (from 164 fewer to 24 more)	2[17, 18]	Low
serious patients	8/23 (34.8%)	10/22 (45.5%)	RR 0.77 (0.37 to 1.58)	105 fewer per 1,000 (from 286 fewer to 264 more)	1[17]	Low
critically ill patients	0/29 (0.0%)	2/29 (6.9%)	RR 0.20 (0.01 to 3.99)	55 fewer per 1,000 (from 68 fewer to 206 more)	1[17]	Low
SARS-CoV-2 clearance	41/52 (78.8%)	15/51 (29.4%)	RR 2.67 (1.71 to 4.18)	491 more per 1,000 (from 209 more to 935 more)	1[17]	Very low
serious patients	19/23 (82.6%)	7/22 (31.8%)	RR 2.60 (1.37 to 4.92)	509 more per 1,000 (from 118 more to 1,000 more)	1[17]	Very low
critically ill patients	22/29 (75.9%)	8/29 (27.6%)	RR 2.75 (1.47 to 5.13)	483 more per 1,000 (from 130 more to 1,000 more)	1[17]	Very low
Number of patients discharged	26/52 (50.0%)	18/51 (35.3%)	RR 1.35 (1.00 to 1.84)	124 more per 1,000 (from 0 fewer to 296 more)	1[17]	Very low
serious patients	21/23 (91.3%)	15/22 (68.2%)	RR 1.34 (0.98 to 1.83)	232 more per 1,000 (from 14 fewer to 566 more)	1[17]	Very low
critically ill patients	5/29 (17.2%)	3/29 (10.3%)	RR 1.67 (0.44 to 6.34)	69 more per 1,000 (from 58 fewer to 552 more)	1[17]	Very low
Duration of hospitalisation (follow up range 28-60 days)	NA	NA	HR 1.21 (0.64 to 2.28)	NA	2[17, 18]	Very low
serious patients	NA	NA	HR 1.97 (1.00 to 3.88)	NA	1[17]	Low
critically ill patients	NA	NA	HR 1.90 (0.45 to 8.04)	NA	1[17]	Low
Number of patients with AE	2/51 (3.9%)	0/50 (0.0%)	RR 2.94 (0.32 to 27.32)	0 fewer per 1,000 (from 0 fewer to 0 more)	1[17]	Low
serious patients	1/23 (4.3%)	0/22 (0.0%)	RR 2.88 (0.12 to 67.03)	0 fewer per 1,000 (from 0 fewer to 0 more)	1[17]	Low
critically ill patients	1/28 (3.6%)	0/28 (0.0%)	RR 3.00 (0.13 to 70.64)	0 fewer per 1,000 (from 0 fewer to 0 more)	1[17]	Low
Number of patients with SAE	None reported	None reported	NA	NA	1[18]	Low

Source: Cruciani F, De Crescenzo F, Vecchi S, Saulle R, Mitrova Z, Amato L, Davoli M
Abbreviations: AE=Adverse Events; SAE=Serious Adverse Events .

Table 4-2 Summary of safety from observational studies (AE and SAE) of Convalescent Plasma Therapy

Author, year	Abolghasemi 2020[19]	Duan 2020[9]	Enzmann 2020[20]	Joyner 2020[21]	Xia 2020[22]
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Country	Iran	China	United States	United States	China
Sponsor	Baqiyatallah Medical Science University	China National Biotec Group	Sanford Research	Mayo Clinic	Nanjing University School of Medicine
Intervention/ Product	CPT	CPT	CPT	CPT	CPT
Dosage	500-1000 cc (in 1-2 units); titre >1:1	200 mL; titre >1:640	NR	200-500 mL; no minimum titre	200-1200 mL; titre NR
Comparator	Standard treatment	None	Standard treatment	None	Standard treatment
Study design	Observational	Single-arm interventional	Observational	Observational	Observational
Setting	Hospital	Hospital	Hospital	Hospital	Hospital
Number of pts	189	10	150	5,000	1,568
Inclusion criteria	COVID-19 confirmed by PCR and/or CT, aged ≥ 18 years, SPO2 ≤ 93% at rest, ≤ 7 days since onset	Diagnosed with severe COVID-19 with PCR confirmation, aged ≥18 years	COVID-19 confirmed by PCR, attended emergency department or admitted to hospital	Lab-confirmed COVID-19, admitted to hospital, aged ≥ 18 years	Diagnosed with COVID-19
Age of patients (yrs)	Mean (SD): 54.4 (13.7) & 56.8 (15.0)	Median 52.5 (IQR 45.0 to 59.5)	Median 56 (range: 1 month to 95 years)	Median: 62 (range 18 to 97)	Median 63 (IQR 54 to 71)
Disease severity	Severe	Severe	NR	Severe, life-threatening or high risk of progression to severe or life-threatening	Severe or critical
Follow-up	NR	NR	NR	7 days	NR
Loss to follow-up, n (%)	NR	NR	NR	NR	NR
Risk of Bias	Moderate	Critical	Serious	Critical	Serious
Safety – Outcomes*					
Overall AEs, n (%)	CPT, 1 vs control, NR	CPT, 1 (10%)	CPT, 0 vs Hydroxychloroquine + azithromycin, 69 vs tocilizumab, 0	NR	NR

Author, year	Abolghasemi 2020[19]	Duan 2020[9]	Enzmann 2020[20]	Joyner 2020[21]	Xia 2020[22]
Serious AE (SAE), n (%)	0	0 (0%)	Hydroxychloroquine + azithromycin: 39	At 4 hours: 36 (<1%)	NR
Most frequent AEs n (%)	NA	CPT: Evanescent facial red spot, 1 (10%)	Hydroxychloroquine + azithromycin: arrhythmia, 14 (18.7%); QT interval prolongation, 15 (20.0%)	NR	NR
Most frequent SAEs, n (%)	NA	NA	NR	NR	NR
AEs of special interest, n (%)	CPT, possible transfusion related fever, 1 (<1%)	NA	NA	At 4 hours: mortality (15, <1%); transfusion-related acute lung injury (11, <1%); transfusion-associated circulatory overload (7, <1%); severe allergic transfusion reaction (3, <1%)	Minor allergic reactions during transfusion (pruritis or erythema), 3 (2%); severe allergic reactions, 0 (0%)
Death as SAE, n (%)	CPT, 17 (15%) vs Control, 18 (24%)	CPT, 0 (0%)	CPT, 5 (31%) vs Hydroxychloroquine + azithromycin, 7 (11%) vs tocilizumab, 3 (25%) vs all hospitalised, 11 (8%)	At 4 hours: 15 (0.3%) At 7 days: 602 (14.9%)	CPT, 3 (2%) vs Control, 59 (4%)
Withdrawals due AEs, n (%)	NR	0 (0%)	NR	NR	NR

*** by arms, if available, (Robins-I): https://training.cochrane.org/handbook/current/chapter-25**

Abbreviations: AE=Adverse event, CPT=Convalescent Plasma Therapy, IQR=Interquartile Range, PCR= Polymerase Chain Reaction, pts=participants. NA=Not Applicable, NR=Not Reported SAE=Serious Adverse Event, SD=Standard Deviation

Table 4-3 Summary of safety from observational studies (AE and SAE) of Convalescent Plasma Therapy (continued)

Author, year	Bradfute 2020[23]	Chen 2020[24]	Faqihi 2020[25]	Hartman 2020[26]	Hegerova 2020[27]
Version added	V2.0, September	V2.0, September	V2.0, September	V2.0, September	V2.0, September
Country	United States	China	Saudi Arabia	United States	United States
Sponsor	University of New Mexico	The First Affiliated Hospital of Zhengzhou University	King Saud Medical City	University of Wisconsin	Swedish Medical Centre (Seattle)

Author, year	Bradfute 2020[23]	Chen 2020[24]	Faqihi 2020[25]	Hartman 2020[26]	Hegerova 2020[27]
Intervention/ Product	CPT	CPT	CPT	CPT	CPT
Dosage	200 mL; titre NR	200-400 mL transfusions with up to three repeat tranfusions available; titre NR	A dose of 1.5 plasma volumes then one plasma volume daily for five to seven doses; titre NR	NR	NR
Comparator	None	None	None	None	None
Study design	Single-arm interventional	Single-arm interventional	Single-arm interventional	Single-arm interventional	Single-arm interventional
Setting	Hospital	Hospital	Hospital	Hospital	Hospital
Number of pts	13	16	10	31	20
Inclusion criteria	Diagnosed with COVID-19 with PCR confirmation, respiratory symptoms, requiring supplemental oxygen, aged ≥18 years	Diagnosed with COVID-19 by the nucleic acid amplification (NAA) test, severe or critically ill	Diagnosed with COVID-19 with PCR confirmation, intubated and in ICU with life-threatening COVID, aged ≥18 years	Diagnosed with COVID-19 with lab confirmation, severe or life-threatening disease.	Diagnosed with COVID-19 confirmed with PCR, severe or critical illness
Age of patients (yrs)	Median 52 (Range 39 to 91)	Average 65 (Range 30 to 90)	Median 51 (IQR 45.1 to 55.9)	NR	Median 60 (Range 29 to 95)
Disease severity	NR	Severe or critically ill	Life-threatening	Severe or life-threatening	Severe or critical
Follow-up	14 days	NR	28 days	NR	14 days
Loss to follow-up, n (%)	1 (7.8%)	NR	NR	NR	0 (0%)
Risk of Bias	Critical	Critical	Critical	Critical	Critical
Safety – Outcomes*					
Overall AEs, n (%)	0 (0%)	0 (0%)	0 (0%)	NR	0 (0%)
Serious AE (SAE), n (%)	0 (0%)	0 (0%)	0 (0%)	NR	0 (0%)
Most frequent AEs n (%)	NA	NA	NA	NR	NA
Most frequent SAEs, n (%)	NA	NA	NA	NR	NA

Author, year	Bradfute 2020[23]	Chen 2020[24]	Faqihi 2020[25]	Hartman 2020[26]	Hegerova 2020[27]
AEs of special interest, n (%)	NA	NA	NA	NR	NA
Death as SAE, n (%)	2 (15.4%)	2 (12.5%)	1 (10%)	4 (12.9%)	CPT, 2 (10%) vs Control, 6 (30%)
Withdrawals due AEs, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*** by arms, if available, (Robins-I): https://training.cochrane.org/handbook/current/chapter-25**

Abbreviations: AE=Adverse event, CPT=Convalescent Plasma Therapy, IQR=Interquartile Range, PCR= Polymerase Chain Reaction, pts=participants. NA=Not Applicable, NR=Not Reported SAE=Serious Adverse Event, SD=Standard Deviation

Table 4-4 Summary of safety from observational studies (AE and SAE) of Convalescent Plasma Therapy (continued)

Author, year	Joyner 2020[28]	Liu 2020[29]	Morath 2020[30]	Perotti 2020[31]	Salazar 2020[32]
Version added	V2.0, September	V2.0, September	V2.0, September	V2.0, September	V2.0, September
Country	United States	China	Germany	Italy	United States
Sponsor	Mayo Clinic	Central Hospital of Wuhan	Heidelberg University Hospital	Fondazione IRCCS Policlinico San Matteo	Houston Methodist Hospital and Research Institute
Intervention/ Product	CPT	CPT	CPT	CPT	CPT
Dosage	NR	200 to 225 mL; titre of 160	Target dosing strategy not reported. Patients received initial dose ranging from 3.02 to 3.60 L and a subsequent dose ranging from 2.93 to 3.66 L, if applicable	Target dosing strategy not reported. Patients received between one and three doses with titres between 1:80 and 1:640	Initial dose of plasma followed by a second dose on worsening of condition, if available. No minimum and maximum titre reported.
Comparator	None	None	None	None	Standard care
Study design	Single-arm interventional	Single-arm interventional	Single-arm interventional	Single-arm interventional	Propensity score-matched observational
Setting	Hospital	Hospital	Hospital	Hospital	Hospital
Number of pts	36,226	3	5	46	2724

Author, year	Joyner 2020[28]	Liu 2020[29]	Morath 2020[30]	Perotti 2020[31]	Salazar 2020[32]
Inclusion criteria	Diagnosed with COVID-19 with lab confirmation, were or were judged to be at high risk of progression to severe or life-threatening, aged ≥18 years	Diagnosed with COVID-19 confirmed with radiographic and clinical features	NR	Diagnosed with COVID-19 confirmed with PCR, moderate to severe, on mechanical ventilation and/or CPAP, aged ≥18 years	Diagnosed with COVID-19 confirmed with PCR, severe and/or life-threatening
Age of patients (yrs)	Mode 40 to 59	Mean 52 (Range 42 to 58)	Median 67 (Range 53 to 71)	Mean 63 (SD 12)	Mode 50 to 59
Disease severity	Severe, life-threatening or high risk of progression to severe or life-threatening	NR	NR	Moderate to severe	Severe and/or life-threatening
Follow-up	30 days	NR	NR	7 days	28 days
Loss to follow-up, n (%)	904 (2.5%)	0 (0%)	0 (0%)	0 (0%)	2337 (85.8%)
Risk of Bias	Critical	Critical	Critical	Critical	Serious
Safety – Outcomes*					
Overall AEs, n (%)	NR	1 (33.3%)	NR	5 (10.8%)	NR
Serious AE (SAE), n (%)	NR	1 (33.3%)	NR	4 (8.7%)	NR
Most frequent AEs n (%)	NR	NA	NR	NA	NR
Most frequent SAEs, n (%)	NR	NA	NR	NA	NR
AEs of special interest, n (%)	NR	Suspected tranfusion related cytokine storm, 1 (33.3%)	NR	Tranfusion related fever, 1 (2.2%); Tranfusion related anaphylaxis, 1 (2.2%); Transfusion acute lung injury, 1 (2.2%); Urticaria, 1 (2.2%)	NR

Author, year	Joyner 2020[28]	Liu 2020[29]	Morath 2020[30]	Perotti 2020[31]	Salazar 2020[32]
Death as SAE, n (%)	At 7 days: 3706 (10.4%) At 30 days: 8652 ((24.4%)	0 (0%)	2 (40%)	3 (6.5%)	Transfused within 72 hours of admission: CPT, 2 (1.8%) vs. Control, 7 (6.3%) Transfused over 72 hours of admission: CPT, 4 (12.9%) vs. Control, 7 (11.5%) Transfused within 72 hours of admission with titre ≥1:1350: CPT, 1 (1.2%) vs. Control, 11 (7.0%)
Withdrawals due AEs, n (%)	NR	0 (0%)	0 (0%)	0 (0%)	NR

*** by arms, if available, (Robins-I): https://training.cochrane.org/handbook/current/chapter-25**

Abbreviations: AE=Adverse event, CPT=Convalescent Plasma Therapy, IQR=Interquartile Range, PCR= Polymerase Chain Reaction, pts=participants. NA=Not Applicable, NR=Not Reported SAE=Serious Adverse Event, SD=Standard Deviation

Table 4-5 RCTs related to convalescent plasma therapy in clinical trial registry

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Hamilton Health Sciences Corporation/ Canadian Blood Services; Héma-Québec; University of Toronto; Université de Montréal	Institute of Liver and Biliary Sciences, India	Stony Brook University	Assistance Publique - Hôpitaux de Paris/ Etablissement Français du Sang	DRK-Bluspendedienst Baden-Württemberg - Hessen gGmbH
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04348656 (CONCOR-1)	NCT04346446	NCT04344535	NCT04345991 (COVIPLASM trial, a	EudraCT 2020-001310-38 (CAPSID trial)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
				nested trial in the CORIMUNO-19 COHORT)	
Phase & Intention	Phase III study to determine the efficacy of transfusion of COVID-19 convalescent plasma to adult patients admitted to hospital with COVID-19 infection at decreasing the frequency of in-hospital mortality in patients hospitalized for COVID-19	Phase II study to evaluate the efficacy of this therapy in COVID-19 infected sick patients	Phase I / II study to find out if transfusion of blood plasma containing antibodies against COVID-19 (anti-SARS-CoV-2), which were donated from a patient who recovered from COVID-19 infection, is safe and can treat COVID-19 in hospitalized patients	Phase II study to evaluate the efficacy of convalescent plasma to treat SARS-COV2 infected patients	Phase II study to assess positive value of blood plasma from donors having built immunity against the new corona virus (SARS-CoV-2) transfused to patients suffering from SARS-CoV-2 infection To improve survival and remove criteria of severe COVID-19 (CoV-2 infection) within 21 days after randomization
Study design	**RCT**, open-label, standard of care-comparator, parallel assignment	**RCT**, open-label, active comparator, parallel assignment	**RCT**, Quadruple-blind, active comparator, parallel assignment	**RCT**, open-label, best standard of care-comparator, parallel assignment	**RCT**, open-label, best standard of care-comparator
Status trial	Recruiting, started April 27, 2020	Completed, started April 21, 2020	Enrolling by invitation, started April 8, 2020	Recruiting, started April 15, 2020	Ongoing
Duration/End of Study	Estimated Primary Completion Date: October 31, 2020 Estimated Study Completion Date: December 31, 2020	Estimated Primary Completion Date: June 30, 2020 Estimated Study Completion Date: June 30, 2020	Estimated Primary Completion Date: April 30, 2021 Estimated Study Completion Date: August 31, 2021	Estimated Primary Completion Date: May 15, 2020 Estimated Study Completion Date: June 1, 2020	Estimated Primary Completion Date: NA Estimated Study Completion Date: NA
Study details					
Number of Patients	n = 1200 (16 Years and older - Child, Adult, Older Adult)	n = 20 (Adult, Older Adult, 18 Years to 65 years)	n = 500 (Adult, Older Adult; 18 Years and older)	n = 120 (Adult, Older Adult, 18 Years and older)	n = 120 (age ≥ 18 years and ≤ 75 years)
Location/Centres	Canada	India	US	France	Germany
Intervention	500 mL of ABO compatible convalescent apheresis plasma (from one single-donor unit of 500 mL or 2 units of 250 mL from 1-2 donations) collected by apheresis from donors who have	Convalescent Plasma+Supportive Care	Convalescent Plasma (450-550 mL of plasma containing anti-SARS-CoV-2 antibody titer ideally > 1:320, but meeting minimum titer per	Transfusion of COVID-19 convalescent plasma (Two convalescent plasma units of 200 to 220 ml each will be transfused i.v. as early as possible and no later than 10 days after onset of clinical symptoms. In the	Convalescent Plasma against COVID-19 (Fresh frozen plasma (FFP) with marketing authorisation in Germany issued by PEI)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
	recovered from COVID-19 and frozen (1 year expiration date from date of collection)		FDA Guidelines for convalescent plasma)	absence of acute unforeseen adverse events in the first 3 patients, an additional 2 plasma units of 200/220 ml each will be transfused 24 hours after first 2 units: a total of 4 units / patient)	
Controls	Standard of care	Random Donor Plasma+Supportive Care	Standard Donor Plasma	Standard of care	Best supportive care
Duration of observation/Follow-up (Current Primary Outcome Measures)	Until hospital discharge or death, up to 90 days (for an individual subject, the study ends 90 days after randomization)	Up to 28 days	Up to 90 days	Up to 28 days	Up to 60 days
Endpoints (Current Primary Outcome Measures)	Intubation or death in hospital (Time Frame: Day 30) Endpoint of the need for intubation or patient death in hospital	Proportion of patients remaining free of mechanical ventilation in both groups (Time Frame: Day 7)	28 day ventilator free days (Time Frame: 28 days post randomization)	Survival without needs of ventilator utilization or use of immunomodulatory drugs [Time Frame: At day 14 after randomization] WHO progression scale ≥6 [Time Frame: at day 4 of randomization]	Composite endpoint of survival and no longer fulfilling criteria of severe COVID-19 within 21 days after randomization
Results/ Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-6 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Erasmus Medical Center/Maasstad Hospital	Artesh University of Medical Sciences	Birjand University of Medical Sciences	Ahvaz University of Medical Sciences	China-Japan friendship hospital / Union Hospital, Tongji Medical College, Huazhong university of Science and Technology /Red Cross Hospital in Wuhan of Hubei Province /

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
					Wuhan Asia Heart Hospital / Wuhan Maternal and Child Health Hospital
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04342182 (CONCOVID Study)	IRCT20200404046948N1	IRCT20200413047056N1	IRCT20200310046736N1	ChiCTR2000030702
Phase & Intention	Phase II/III study to decrease overall mortality in patients within COVID disease	Phase III study to evaluate the efficacy and safety of convalescent plasma in the treatment of patients with severe SARS-CoV-2 infection (COVID-19)	Phase III study to evaluate the efficacy of intravenous immunoglobulin and convalescent plasma in improving the condition of patients with COVID-19	Phase II/III study evaluating the therapeutic effect of Convalescent Plasma and Plasma-derived Immunoglobulin-enriched solution on COVID-19 Patients	Phase 0 study to evaluate efficacy and safety indicators of received convalescent plasma therapy

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Study design	**RCT**, single-blind, standard of care-comparator, parallel assignment	**RCT**, open-label, conventional therapy comparator, parallel assignment	**RCT**, open-label, intravenous immunoglobulin and common national protocol comparator, three arms, parallel assignment	**RCT**, single-blind, Plasma-derived Immunoglobulin-enriched solution and - routine care comparator, three arms, parallel assignment	**RCT**, open-label, conventional treatment comparator, parallel assignment
Status trial	Recruiting, started April 8, 2020	Recruitment completed, started April 13, 2020	Recruitment complete, started April 18, 2020	Not yet recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: July 1, 2020 Estimated Study Completion Date: July 1, 2020	Estimated Primary Completion Date: NA Estimated Study Completion Date: NA	NA	NA	From 2020-02-15 to 2020-08-15
Study details					
Number of Patients	n = 426 (Adult, Older Adult; 18 Years and older)	n = 60 (Adult, Older Adult, 18 Years to 70 years)	15 (From **18 years** old to **50 years** old)	45 (From **20 years** old to **45 years** old)	n = 50 (age ≥ 18 years)
Location/Centres	Netherlands	Teheran	Iran	Iran	China
Intervention	Convalescent plasma (300mL of convalescent plasma from COVID-19 recovered donors)	Convalescent plasma	Intravenous immunoglobulin therapy+ common national protocol treatments convalescent plasma therapy+ common national protocol treatments	Convalescent plasma Plasma-derived Immunoglobulin-enriched solution	Conventional treatment combined with convalescent plasma treatment
Controls	Standard of care	Conventional therapy	Common national protocol treatments	Routine care	Conventional treatment
Duration of observation/Follow-up (Current Primary Outcome Measures)	Until hospital discharge or a maximum of 60 days whichever comes first	Up to 14 days	Up to 12 days	Up to 14 days	Up to 28 days
Endpoints (Current Primary Outcome Measures)	Overall mortality until discharge from the hospital or a maximum of 60 days after admission whichever comes first [Time Frame: until hospital discharge or a maximum of 60	Clinical improvement within 14 days of admission	Lung involvement in X-ray and CT-scan, SPO2, LDH enzyme, viral load, acute phase protein, white blood cell count, ESR, length of hospital stay, duration of mechanical ventilation (from the start of the intervention for 12 days)	complete remission of clinical signs of disease; Negative result for COVID-19 RT-PCR test; Normal CT Scan	Time to clinical recovery after randomization

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
	days whichever comes first] the mortality in the 300ml convP group will be compared with the control arm				
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-7 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	The First Affiliated Hospital of Zhengzhou University	China-Japan friendship hospital	Wuhan Jinyintan Hospital (Wuhan Infectious Diseases Hospital)	Renmin Hospital of Wuhan University	Johns Hopkins University
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	
Trial Identifier	ChiCTR2000030627	ChiCTR2000029757	ChiCTR2000030010	ChiCTR2000030929	NCT04323800
Phase & Intention	Phase 0 study to evaluate the effect of convalescent plasma therapy on the efficacy, safety and prognosis of severe COVID-19 patients, in order to find an effective treatment plan for COVID-19.	Phase 0 study to evaluate the efficacy of this therapy for the treatment of severe and critical novel coronavirus pneumonia (COVID-19)	Phase NA, to evaluate the efficacy and safety of anti-SARS-CoV-2 virus inactivated plasma in the treatment of severe novel coronavirus pneumonia patients (COVID-19)	Phase NA, to evaluate the efficacy and safety of anti-SARS-CoV-2 virus inactivated plasma in the treatment of severe novel coronavirus pneumonia (COVID-19)	Phase 2 Comparing the Efficacy and Safety Human Coronavirus Immune Plasma (HCIP) vs. Control (SARS-CoV-2 Non-immune Plasma) Among Adults Exposed to COVID-19
Study design	**RCT**, routine treatment-comparator, parallel assignment	**RCT**, open-label, Conventional treatment comparator, parallel assignment	**RCT**, double-blind, ordinary plasma comparator, parallel assignment	**RCT**, double-blind, ordinary plasma comparator, parallel assignment	**RCT**, triple-blind, standard plasma comparator, parallel assignment
Status trial	Recruiting, started	Recruiting, started	Not yet recruiting	Not yet recruiting	Recruiting
Duration/End of Study	From 2020-02-01 to 2020-05-30	From 2020-02-14 to 2021-02-05	From 2020-02-19 to 2020-05-31	From 2020-03-17 to 2020-06-16	Estimated Primary Completion Date: December 31, 2022 Estimated Study Completion Date: January, 2023
Study details					
Number of Patients	n = 30	n = 200 (18 or more years old)	n = 100 (18 to 70 years old)	n = 60 (18 to 70 years old)	n = 150 (18 years and older)
Location/Centres	China	China	China	China	US
Intervention	Convalescent plasma therapy + routine treatment	Conventional treatment and convalescent plasma therapy	Anti-SARS-CoV-2 virus inactivated plasma	Anti-SARS-CoV-2 virus inactivated plasma	SARS-CoV-2 convalescent plasma
Controls	Routine treatment	Conventional treatment	Ordinary plasma	Ordinary plasma	SARS-CoV-2 non-immune Plasma (Standard plasma collected prior to December 2019)
Duration of observation/Follow-up	NA	Up to 28 days	Up to 28 days	Up to 28 days	28 (up to 90)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
(Current Primary Outcome Measures)					
Endpoints (Current Primary Outcome Measures)	Temperature, Virus nucleic acid detection	The number of days between randomised grouping and clinical improvement (Time Frame: within 28 days admission)	Improvement of clinical symptoms (Clinical improvement is defined as a reduction of 2 points on the 6-point scale of the patient's admission status or discharge from the hospital)	Improvement of clinical symptoms (Clinical improvement is defined as a reduction of 2 points on the 6-point scale of the patient's admission status or discharge from the hospital)	Cumulative incidence of composite outcome of disease severity [Time Frame: Day 28]: the presence or occurrence of at least one of the following: Death; Requiring mechanical ventilation and/or in ICU; non-ICU hospitalization, requiring supplemental oxygen;non-ICU hospitalization, not requiring supplemental oxygen;Not hospitalized, but with clinical and laboratory evidence of COVID-19 infectionNot hospitalized, no clinical evidence of COVID-19 infection, but with positive PCR for SARS-CoV-2
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-8 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Universidad del Rosario/ undación Universitaria de Ciencias de la Salud;CES University;Instituto Distrital de Ciencia Biotecnología e Innovacion en Salud	Baylor Research Institute	Thomas Benfield, Hvidovre University Hospital	Cristina Avendaño Solá, Puerta de Hierro University Hospital	Stanford University
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
	donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04332835	NCT04333251	NCT04345289	NCT04345523	NCT04355767
Phase & Intention	Phase 2/3 study to evaluate the effect of Convalescent Plasma for Patients With COVID-19	Phase 1 study Evaluating Efficacy and Safety of High-titer Anti-Sars-CoV-2 Plasma vs Best Supportive Care in Hospitalized Patients With Interstitial Pneumonia Due to COVID-19	Phase 3, to assess the safety and efficacy of novel treatment option of moderate-severe COVID-19	Phase 2, to study the efficacy and safety of passive immunotherapy with CP compared to a control of standard of care (SOC)	Phase 2, to evaluate the efficacy of treatment with high-titer Anti-SARS-CoV-2 plasma (convalescent plasma) versus control (standard plasma) in patients with COVID-19 respiratory symptoms
Study design	**RCT**, open-label, active comparator, parallel assignment	**RCT**, open-label, best supportive care comparator, parallel assignment	**RCT**, Quadruple blinded, placebo-controlled, multicenter, multi-stage study with six parallel treatment arms consisting of either convalescent plasma, sarilumab, hydroxychloroquine,	**RCT**, open-label, standard of care comparator, parallel assignment	**RCT**, double-blind, standard plasma comparator, parallel assignment

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
			baricitinib, intravenous and subcutaneous placebo, or oral placebo		
Status trial	Not yet recruiting	Not yet recruiting	Recruiting	Recruiting	Enrolling by invitation
Duration/End of Study	Estimated Primary Completion Date: August 31, 2020 Estimated Study Completion DateDecember 31, 2020	Estimated Primary Completion Date: December 31, 2022 Estimated Study Completion Date: December 31, 2022	Estimated Primary Completion Date: June 15, 2021 Estimated Study Completion Date: June 15, 2021	Estimated Primary Completion Date: July, 2020 Estimated Study Completion Date: July, 2020	Estimated Primary Completion Date: December, 2022 Estimated Study Completion Date: December, 2022
Study details					
Number of Patients	n = 80 (18 to 60 years old)	n = 115 (18 years and older)	n = 1500 (18 years and older)	n = 278 (18 years and older)	n = 206 (18 years and older)
Location/Centres	Colombia	NA	Denmark	Spain	US
Intervention	Convalescent Plasma COVID-19 + Hydroxychloroquine	Convalescent plasma	Convalescent anti-SARS-CoV-2 plasma; Sarilumab; Baricitinib; Hydroxychloroquine	Fresh plasma from donor immunized against COVID-19	SARS-CoV-2 convalescent plasma
Controls	Hydroxychloroquine	Best supportive care	Injective placebo; Oral placebo	Standard of care	Standard Plasma
Duration of observation/Follow-up (Current Primary Outcome Measures)	Up to 28 days	An average 28 days	28 days, up to 90 days	15 days, Up to 3 months	15 days
Endpoints (Current Primary Outcome Measures)	Change in Viral Load; Change in Immunoglobulin M COVID-19 Titers; Change in Immunoglobulin G COVID-19 Titers	reduction in oxygen and ventilation support [Time frame: through study completion, an average of 4 weeks]	All-cause mortality or need of invasive mechanical ventilation [Time frame: 28 days]	Category Changes in Ordinal Scale [Time frame: 15 days]	Time to disease progression [TimefFrame: 15 days]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-9 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Sponsor	Royal College of Surgeons in Ireland - Medical University of Bahrain/ Salmaniya Medical Complex; Bahrain Defence Force Royal Medical Services, Military Hospital; Mohammed Bin Khalifa Bin Sulman Al Khalifa Cardiac Centre, Awali	Hospital Universitario Dr. Jose E. Gonzalez	Max R. O'Donnell, Columbia University/ New York Blood Center	Brigham and Women's Hospital	Vanderbilt University Medical Center
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04356534	NCT04358783	NCT04359810	NCT04361253	NCT04362176
Phase & Intention	Phase NA, study to compare plasma therapy using convalescent plasma with antibody	Phase II study Evaluating the Efficacy and Safety of Plasma From Patients Cured of	Phase 2, to Evaluate the Efficacy and Safety of Human Anti-SARS-CoV-2 Convalescent Plasma	Phase 3, to determine whether the early addition of HT-CCP to standard treatment improves the	Phase 3, to Test the Safety and Efficacy of Convalescent Donor Plasma to Treat

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
	against SARS-CoV-2 to usual supportive therapy in COVID-19 patients with pneumonia and hypoxia, and to determine if the clinical course is improved	COVID-19 Compared to the Best Available Therapy in Subjects With SARS-CoV-2 Pneumonia	in Severely Ill Adults With COVID-19	clinical outcome (as assessed by the Modified WHO Ordinal Scale) of patients with COVID-19 who are hospitalized but not yet in moderate or severe ARDS	COVID-19 in Hospitalized Adults
Study design	**RCT**, open-label, routine care comparator, parallel assignment	**RCT**, Quadruple-blind, best available therapy comparator, parallel assignment	**RCT**, double-blind, non-convalescent plasma comparator, parallel assignment	**RCT**, double-blind, standard plasma comparator, parallel assignment	**RCT**, triple-blind, placebo comparator, parallel assignment
Status trial	Completed	Recruiting	Recruiting	Recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: May 3, 2020 Estimated Study Completion Date: June 30, 2020	Estimated Primary Completion Date: Estimated Study Completion Date: February 1, 2021 May 30, 2021	Estimated Primary Completion Date: December 31, 2022 Estimated Study Completion Date: April, 2021	Estimated Primary Completion Date: June, 2021 Estimated Study Completion Date: December, 2021	Estimated Primary Completion Date: April, 2021 Estimated Study Completion Date: April, 2021
Study details					
Number of Patients	n = 40 (18 or more years old)	n = 30 (18 or more years old)	n = 105 (18 or more years old)	n = 220 (12 months and older)	n = 500 (18 years and older)
Location/Centres	Bahrain	Mexico	US	NA	US
Intervention	convalescent patient plasma plus routine local standard of care	Convalescent plasma from cured COVID-19 patients and Supportive management depending on individual needs	Convalescent Plasma (anti-SARS-CoV-2 plasma	High-Titer COVID-19 Convalescent Plasma (HT-CCP	SARS-CoV-2 convalescent plasma
Controls	Routine care for COVID-19 patients	Best available therapy	Non-convalescent plasma	Standard plasma (FFP)	Placebo
Duration of observation/Follow-up (Current Primary Outcome Measures)	10 day or until discharge	14 days, up to 90 days	Up to 28 days	14 days	15 days, up to 29 days
Endpoints (Current Primary Outcome Measures)	Requirement for invasive ventilation [Time frame: 10 day or until discharge]	Early all-cause mortality [Time frame: 14 days]	Time to Improvement [Time frame: Up to 28 days]	Modified WHO Ordinal Scale (MOS) score [Time frame: Day 14]	COVID Ordinal Outcomes Scale: Day 15 [Time frame: Study Day 15]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-10 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	The First Affiliated Hospital of Nanchang University	NYU Langone Health/ Albert Einstein College of Medicine; Yale University	Andalusian Network for Design and Translation of Advanced Therapies	Direction Centrale du Service de Santé des Armées/ University Hospital, Grenoble	Lifefactors Zona Franca, SAS
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	ChiCTR2000030179	NCT04364737	NCT04366245	NCT04372979	NCT04395170
Phase & Intention	Phase NA study to evaluate the effects of novel coronavirus pneumonia rehabilitation plasma in teatment of severe novel coronavirus pneumonia infection	Phase 2 study to assess the efficacy and safety of anti-SARS-CoV-2 convalescent plasma in hospitalized patients with acute respiratory	Phase 1/2 study to Evaluate the Efficacy of Treatment With Hyperimmune Plasma Obtained From Convalescent Antibodies of COVID-19 Infection	Phase 3 study to Evaluate the Efficacy Of COVID-19 Convalescent Plasma Versus Standard Plasma In The Early Care Of COVID-19 Patients Hospitalized	Phase 2/3 study Evaluating the Efficacy and Safety of the Use of Convalescent Plasma (PC) and Human Intravenous Anti COVID-19 Immunoglobulin (IV Anti

		symptoms requiring oxygen supplementation		Outside Intensive Care Units	COVID-19 IgG) in Patients Hospitalized for COVID-19
Study design	**RCT**, routine treatment-comparator, parallel assignment	**RCT**, double-blind, placebo comparator, parallel assignment	**RCT**, open label, standard of care comparator, parallel assignment	**RCT**, triple blind, standard plasma comparator, parallel assignment	**RCT**, multicentre, open label, standard therapy comparator, parallel assignment
Status trial	Recruiting	Recruiting	Recruiting	Not yet recruiting	Not yet recruiting
Duration/End of Study	From 2020-02-24 to 2020-04-24	Estimated Primary Completion Date: January 31, 2023 Estimated Study Completion Date: April 30, 2023	Estimated Primary Completion Date: December, 2020 Estimated Study Completion Date: December, 2021	Estimated Primary Completion Date: October, 2020 Estimated Study Completion Date: May, 2021	Estimated Primary Completion Date: December, 2020 Estimated Study Completion Date: June, 2021
Study details					
Number of Patients	n = 100 (18 to 65 years)	n = 300 (18 or more years old)	n = 72 (18 years to 80 years)	n = 80 (18 years to 80 years)	N = 75 (18 years and older)
Location/Centres	China	United States	Spain	France	Colombia
Intervention	Convalescent plasma therapy + routine treatment	Convalescent plasma	Hyperimmune plasma	SARS-CoV-2 Convalescent Plasma + support therapy	Convalescent plasma; or Anti-COVID-19 human immunoglobulin
Controls	Routine treatment	Placebo: saline solution	Standard of care for SARS-CoV-2 infection	Standard plasma	Standard (specific) therapy (pharmacological)
Duration of observation/Follow-up (Current Primary Outcome Measures)	NA	14 days	21 days to 30 days	30 days	1 year
Endpoints (Current Primary Outcome Measures)	Cure rate; Mortality	Score on the WHO 11-point ordinal scale for clinical improvement at 14 days [Time Frame: 14 days post randomization]	Incidence of Adverse Events and Serious Adverse Events [30 days after enrolment]. Death; need for mechanical ventilation; IL-6> 40 pg / mL, D-dimer> 1500, ferritin> 1000ng / mL; SOFA scale [day +21 after randomization]	Survival time without needs of a ventilator [time frame: Day 30]	Admission to ICU and/or mechanical ventilation [time frame: 1 year]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-11 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Johns Hopkins University/ State of Maryland; Bloomberg Foundation; United States Department of Defense; National Institute of Allergy and Infectious Diseases (NIAID)	Max Healthcare Insititute Limited	Fondazione Policlinico Universitario Agostino Gemelli IRCCS	Fundacion Clinic per a la Recerca Biomédica	University of Pennsylvania
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04373460	NCT04374487	NCT04374526	NCT04374539	NCT04397757
Phase & Intention	Phase 2 study comparing the Efficacy	Phase 2 study Assessing the Safety and Efficacy	Phase 2/3 study evaluating the early	Phase 2 study investigating Plasma	Phase 1 Safety and Exploratory Efficacy

	and Safety of Human Coronavirus Immune Plasma (HCIP) vs. Control (SARS-CoV-2 Non-immune) Plasma Among Outpatients With Symptomatic COVID-19	of Convalescent Plasma to Limit COVID-19 Associated Complications	transfusIon of COVID-19 Convalescent Plasma in Elderly COVID-19 Patients to Prevent Disease Progression	Exchange in Patients With COVID-19 Disease and Invasive Mechanical Ventilation	Study of Convalescent Plasma for Severely Ill, Hospitalized Participants With COVID-19 Pneumonia Caused by SARS-CoV-2
Study design	**RCT**, triple blind, standard plasma comparator, parallel assignment	**RCT**, open label, standard care comparator, parallel assignment	**RCT**, open label, standard therapy comparator, parallel assignment	**RCT,** multicentre, open label, standard medical treatment comparator, parallel assignment	**RCT**, open label, standard care comparator, parallel assignment
Status trial	Recruiting	Active, not recruiting	Recruiting	Recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: December 21, 2022 Estimated Study Completion Date: January 31, 2023	Estimated Primary Completion Date: August 9, 2021 Estimated Study Completion Date: August 9, 2021	Estimated Primary Completion Date: September 30, 2020 Estimated Study Completion Date: June 30, 2021	Estimated Primary Completion Date: May 5, 2021 Estimated Study Completion Date: August 29, 2021	Estimated Primary Completion Date: September 13, 2020 Estimated Study Completion Date: November 13, 2020
Study details					
Number of Patients	N = 600 (18 years and older)	N = 100 (18 years to 85 years)	N = 182 (65 years and older)	N = 116 (18 years to 80 years)	N = 80 (18 years and older)
Location/Centres	United States	India	Italy	Spain	United States
Intervention	SARS-CoV-2 convalescent plasma	Convalescent Plasma	COVID-19 Convalescent Plasma	Plasma exchange	COVID-19 Convalescent plasma
Controls	Standard plasma (SARS-CoV-2 Non-immune)	Standard care therapy	Standard therapy	Standard medical treatment (Kaletra [lopinavir/ritonavir])	Standard care
Duration of observation/Follow-up (Current Primary Outcome Measures)	28 days, up to 90 days	28 days	1 to 14 days	28 days	29 days
Endpoints (Current Primary Outcome Measures)	incidence of hospitalization or death prior to hospitalization; serious adverse events [time frame: up to day 28]. Grade 3 or higher adverse events [time frame : up to day 90]	Progression to severe ARDS; all-cause mortality at 28 days [time Frame: depends on the total treatment time of the subjects within one year period of the trial]	Rate of COVID-19 progression (time frame: days 1 to 14]	Impact of plasma exchange (time frame: 28 days)	Serious adverse events; clinical severity score [time frame: up to 29 days from treatment]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

RCT=Randomised Controlled Trial

Table 4-12 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Pontificia Universidad Catolica de Chile/ Fundacion Arturo Lopez Perez	Ain Shams University	The Hospital for Sick Children/ C17 Council (regulatory sponsor)	Indonesia University/ Dr Cipto Mangunkusumo General Hospital; Fakultas Kedokteran Universitas Indonesia	Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh/ Dhaka Medical College
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04375098	NCT04376788	NCT04377568	NCT04380935	NCT04403477
Phase & Intention	Phase 2 study investigating the Efficacy and Safety of Early Anti-SARS-COV-2 Convalescent Plasma in	Phase 2 study investigating Exchange Transfusion Versus Plasma From Convalescent Patients	Phase 2 study investigating the Safety and Efficacy of Human Coronavirus- Immune Convalescent Plasma for	Phase 2/3 study investigating the Effectiveness and Safety of Convalescent Plasma Therapy on COVID-19	Phase 2 study investigating the tolerability, efficacy and dose-response of Convalescent Plasma

	Patients Admitted for COVID-19 Infection	With Methylene Blue in Patients With COVID-19	the Treatment of COVID-19 Disease in Hospitalized Children	Patients With Acute Respiratory Distress Syndrome in Referral Hospitals in Indonesia	Transfusion Therapy in Severe COVID-19 Patients
Study design	**RCT**, open label, parallel assignment	**RCT**, open label, parallel assignment	**RCT**, multicentre, open label, standard of care comparator, parallel assignment	**RCT,** open label, standard of care comparator, parallel assignment	**RCT**, open label, standard supportive treatment comparator, parallel assignment
Status trial	Active, not recruiting	Recruiting	Not yet recruiting	Not yet recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: December, 2020 Estimated Study Completion Date: December, 2021	Estimated Primary Completion Date: July 1, 2020 Estimated Study Completion Date: September 1, 2020	Estimated Primary Completion Date: December 1, 2021 Estimated Study Completion Date: May 1, 2022	Estimated Primary Completion Date: August 31, 2020 Estimated Study Completion Date: August 31, 2020	Estimated Primary Completion Date: July 20, 2020 Estimated Study Completion Date: October 30, 2020
Study details					
Number of Patients	N = 58 (18 years and older)	N = 15 (18 years to 65 years)	N = 100 (0 to less than 19 years)	N = 60 (18 years and older)	N = 20 (16 years and older)
Location/Centres	Chile	Egypt	Canada	Indonesia	Bangladesh
Intervention	patients with high risk of COVID19-associated respiratory failure will be randomized to early treatment with convalescent plasma (≤ 7 days from symptoms start) or at early signs of respiratory failure or prolonged hospitalization	One group will receive exchange blood transfusion from a normal donor; one group will receive plasma from convalescent patients with COVID-19, with methylene blue; one group will receive exchange blood transfusion from a normal donor, plasma from convalescent patients with COVID-19, and methylene blue	Convalescent plasma + standard of care	Convalescent plasma + standard of care	apheretic convalescent plasma + standard treatment
Controls	Not reported	Not reported	Standard of care	Standard of care	Standard supportive treatment
Duration of observation/Follow-up (Current Primary Outcome Measures)	1 year	3 to 5 days	30 days	28 days	7 days
Endpoints (Current Primary Outcome Measures)	Percentage Mechanical Ventilation, hospitalization longer	Improvement of condition [time frame: 3 to 5 days]	Clinical recovery [time frame: at day 30]	All-cause mortality [time frame: up to 28 days]	Proportion of In-hospital mortality; time to death [time frame: 7 days]

	than 14 days or death during hospitalization [Time Frame: 1 year follow up]				
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-13 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Centenario Hospital Miguel Hidalgo	University of Oxford/ UK Research and Innovation; National Institute for Health Research, United Kingdom; Wellcome; Bill and Melinda Gates Foundation; Department for International Development, United Kingdom; Health Data Research UK; Medical Research Council Population Health Research Unit; NIHR Clinical Trials Unit Support Funding	Hospital Italiano de Buenos Aires	Assiut University	Grupo Mexicano para el Estudio de la Medicina Intensiva/ Hospital General Naval de Alta Especialidad - Escuela Medico Naval; National Institute of Pediatrics, Mexico; Instituto Nacional de Enfermedades Respiratorias
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)

Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04381858	NCT04381936	NCT04383535	NCT04383548	NCT04405310
Phase & Intention	Phase 3 study investigating the Efficacy and Safety of Convalescent Plasma vs Human Immunoglobulin for the Treatment of COVID-19 Pneumonia	Phase 2/3 study investigating whether treatment with either Lopinavir-Ritonavir, Hydroxychloroquine, Corticosteroids, Azithromycin, Convalescent plasma or Tocilizumab prevents death in patients with COVID-19	Phase not applicable. Convalescent Plasma and Placebo for the Treatment of COVID-19 Severe Pneumonia	Phase not applicable. Clinical Study for Efficacy of Anti-Corona VS2 Immunoglobulins Prepared From COVID19 Convalescent Plasma Prepared by VIPS Mini-Pool IVIG Medical Devices in Prevention of SARS-CoV-2 Infection in High Risk Groups as Well as Treatment of Early Cases of COVID19 Patients	Phase 2 study investigating Plasma From Covalescent Donors With Covid-19 for the Management of Patients With SARS-COV-2
Study design	**RCT**, double blind, human immunoglobulin comparator, parallel assignment	**RCT**, open label, standard care comparator, factorial assignment	**RCT**, multicentre, double blind, placebo-controlled, parallel assignment	**RCT,** open label, single group assignment	**RCT**, double centre, double blind, placebo comparator, parallel assignment
Status trial	Recruiting	Recruiting	Recruiting	Not yet recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: August 30, 2020 Estimated Study Completion Date: September 30, 2020	Estimated Primary Completion Date: December, 2021 Estimated Study Completion Date: December 2031	Estimated Primary Completion Date: August 15, 2020 Estimated Study Completion Date: September 15, 2020	Estimated Primary Completion Date: December 1, 2020 Estimated Study Completion Date: January 1, 2021	Estimated Primary Completion Date: June 20, 2020 Estimated Study Completion Date: July 20, 2020
Study details					
Number of Patients	N = 500 (16 years to 90 years)	N = 15,000 (child, adult, older adult)	N = 333 (18 years and older)	N = 100 (21 years to 50 years)	N = 80 (18 years to 70 years)
Location/Centres	Mexico	United Kingdom	Argentina	Not provided	Mexico

Intervention	Plasma from COVID-19 convalescent patient	Lopinavir-Ritonavir; or Corticosteroid; or Hydroxychloroquine; or Azithromycin; or Convalescent plasma; or Tocilizumab	Convalescent SARS COVID-19 plasma	hyper immunoglobulins containing anti-Corona VS2 immunoglobulin	Convalescent Plasma of patients with COVID-19
Controls	Human immunoglobulin	Standard care	Placebo	Not reported	placebo (hartmann plus albumin)
Duration of observation/Follow-up (Current Primary Outcome Measures)	An average of 3 months	28 days	30 days	72 hours to 1 month	15 days
Endpoints (Current Primary Outcome Measures)	Mean hospitalization time, Mean Oxygenation index evolution, Rate of severe ARDS, Rate and time to dead, Mean time with invasive mechanical ventilation [Time Frame: Through study completion, an average of 3 months]	All-cause mortality [time frame: within 28 days after randomisation]	Clinical status [Time Frame: 30th Day since study preparation infusion (Placebo or Convalescent SARS COVID-19 plasma)]	Efficacy of COVID-19 hyper immunoglobulins for patients [time frame: 2 weeks]; Efficacy of COVID-19 hyper immunoglobulins for high-risk groups [time frame: 1 month]; percentage of adverse events [Time Frame: 72 hours]	Death [time frame: 15 days]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-14 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	University of Catanzaro/ Azienda Ospedaliera Policlinico "Mater Domini"; Azienda Sanitaria Provinciale Di Catanzaro; Annunziata Hospital, Cosenza, Italy; Azienda Ospedaliera Bianchi-Melacrino-Morelli	National Blood Center Foundation, Hemolife	Henry Ford Health System	Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran/ Hospital San Jose Tec de Monterrey; Instituto Nacional de Enfermedades Respiratorias; Instituto Nacional de Cardiologia Ignacio Chavez;	University of Sao Paulo General Hospital/ Ministério da Ciência, Tecnologia, Inovações e Comunicações; Faculty of Medicine of Ribeirão Preto (FMRP-USP); Hospital de Clínicas, Faculdade de Medicina Universidade Estadual de Campinas;

				Hospital General Dr. Manuel Gea González; Instituto Nacional de Cancerologia, Columbia; Hospital Regional de Alta Especialidad del Bajio	Hospital Sirio-Libanes; Hospital Israelita Albert Einstein
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04385043	NCT04385186	NCT04385199	NCT04388410	NCT04415086
Phase & Intention	Phase 2/3 study investigating the Efficacy and Safety of Hyperimmune Plasma Treatment in Patients With COVID-19 Severe Infection	Phase 2 study investigating Inactivated Convalescent Plasma as a Therapeutic Alternative in Patients CoViD-19	Phase 2 study investigating tolerability and efficacy of convalescent plasma in patients with COVID-19 respiratory disease	Phase 2/3 study evaluating the efficacy and safety of convalescent plasma from COVID-19 recovered individuals to treat hospitalized	Phase 2 study investigating treatment of Patients With COVID-19 With Convalescent Plasma Transfusion

				patients with severe COVID-19 disease	
Study design	**RCT**, open label, standard therapy comparator, parallel assignment	**RCT**, multicentre, single blind, best supportive treatment comparator, parallel assignment	**RCT**, open label, standard therapy comparator, parallel assignment	**RCT**, multicentre, placebo-controlled, double blinded, parallel assignment	**RCT**, open label, standard treatment comparator, parallel assignment
Status trial	Recruiting	Not yet recruiting	Recruiting	Not yet recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: October 15, 2020 Estimated Study Completion Date: May 15, 2021	Estimated Primary Completion Date: November 30, 2020 Estimated Study Completion Date: December 30, 2020	Estimated Primary Completion Date: August 1, 2020 Estimated Study Completion Date: August 1, 2020	Estimated Primary Completion Date: October 31, 2020 Estimated Study Completion Date: December 31, 2020	Estimated Primary Completion Date: April 20, 2022 Estimated Study Completion Date: May 22, 2022
Study details					
Number of Patients	N = 400 (18 years to 60 years)	N = 60 (18 years and older)	N = 30 (18 years and older)	N = 250 participants (18 years and older)	N = 120 (18 years and older)
Location/Centres	Italy	Colombia	United States	Not provided	Brazil
Intervention	plasma hyperimmune + standard therapy	Inactivated convalescent plasma + supportive treatment selected by hospital	Convalescent plasma	Convalescent plasma	Convalescent plasma + standard of care
Controls	Standard therapy	Best supportive treatment	Standard therapy	Placebo	Standard of care
Duration of observation/Follow-up (Current Primary Outcome Measures)	30 days	28 days	1 day to 28 days	28 days	28 days
Endpoints (Current Primary Outcome Measures)	Mortality [time frame: 30 days]	Mortality [time frame: over a period of 28 days]	Improvement in respiratory disease [time frame: day 1 to day 28 post transfusion]	Severity, death [time frame: 28 days]; adverse events that require study treatment interruption [time frame: during the 28 days]	Clinical improvement or hospital discharge [Time Frame: Follow up until 28 days after transfusion]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-15 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma	Convalescent plasma
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Columbia University	Hospital San Vicente Fundación/ Clínica León XIII; Grupo de Inmunodeficiencias primarias Universidad de Antioquia; Clínica Universitaria Bolivariana; Hospital Pablo Tobón Uribe; Clínica Rosario El Tesoro; Clínica Las Américas; Clínica Cardiovid	Federal Research Clinical Center of Federal Medical & Biological Agency, Russia	Azienda Ospedaliero, Universitaria Pisana	Weill Medical College of Cornell University/ Hamilton Health Sciences Corporation
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency

	investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04390503	NCT04391101	NCT04392414	NCT04393727	NCT04418518
Phase & Intention	Phase 2 study investigating the Efficacy and Safety of Human Anti- SARS-CoV-2 Plasma in Close Contacts of COVID-19 Cases	Phase 3 study investigating the Efficacy of Convalescent Plasma for the Treatment of Severe SARS-CoV-2 Infection	Phase 2 study investigating the Safety and Efficacy of Hyperimmune Convalescent Plasma in Moderate and Severe COVID-19 Disease	Phase 2 study investigating the transfusion of Convalescent Plasma for the Early Treatment of pneumonia Due to SARSCoV2	Phase 3 study investigating Convalescent Plasma for Hospitalized Adults With Acute COVID-19 Respiratory Illness
Study design	**RCT**, double blind, albumin control, parallel assignment	**RCT** with stratified patient allocation, best supportive treatment comparator, open label, parallel assignment,	**RCT**, open label, standard plasma comparator, prospective, parallel assignment	**RCT**, multicentre, open label, standard therapy comparator, parallel assignment	**RCT**, open label, standard of care comparator, parallel assignment
Status trial	Recruiting	Not yet recruiting	Recruiting	Recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: April, 2021 Estimated Study Completion Date: April, 2021	Estimated Primary Completion Date: June, 2021 Estimated Study Completion Date: September 15, 2020	Estimated Primary Completion Date: August 1, 2020 Estimated Study Completion Date: December, 2021	Estimated Primary Completion Date: September 30, 2020 Estimated Study Completion Date: October 30, 2020	Estimated Primary Completion Date: June, 2021 Estimated Study Completion Date: December, 2021
Study details					
Number of Patients	N = 200 (18 years and older)	N = 231 (18 years and older)	N = 60 (18 years to 75 years)	N = 126 (18 years and older)	N = 1,200 (18 years to 70 years)
Location/Centres	United States	Colombia	Russian Federation	Italy	United States
Intervention	Convalescent Plasma (anti-SARS-CoV-2 plasma)	Convalescent plasma	COVID-19 convalescent hyperimmune plasma	Convalescent plasma	ABO compatible convalescent apheresis plasma
Controls	Albumin	Best supportive treatment	Non-convalescent fresh frozen plasma (Standard plasma)	Standard therapy	Standard of care
Duration of observation/Follow-up (Current Primary Outcome Measures)	28 days	28 days	1 to 7 days	30 days	30 days

Endpoints (Current Primary Outcome Measures)	Rate of severe disease [time frame: up to 28 days]	Intrahospital mortality from any cause [time frame: up to 28 days]	Body temperature [Time Frame: Days 1, 2, 3, 4, 5, 6, 7]	Need for invasive mechanical ventilation [time frame: 30 days]	Intubation or death in hospital [time frame: day 30]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-16 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Priscilla Hsue, MD/ Blood Systems Research Institute; San Francisco General Hospital	Fundación Santa Fe de Bogota	Institute of Liver and Biliary Sciences, India	Azienda Ospedaliera Città della Salute e della Scienza di Torino	Universitaire Ziekenhuizen Leuven/ Federal Knowledge Centre (KCE)
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)

Trial Identifier	NCT04421404	NCT04425837	NCT04425915	NCT04428021	NCT04429854
Phase & Intention	Phase 2 study assessing the efficacy and safety of anti-SARS-CoV-2 convalescent plasma in hospitalized patients with acute respiratory symptoms up to 14 days after the onset of initial symptoms	Phase 2/3 study investigating the effectiveness and Safety of Convalescent Plasma in Patients With High-risk COVID-19	Phase 3 study investigating the efficacy of Convalescent Plasma Therapy in Patients With COVID-19	Phase 2 study investigating the Effectiveness of Adding Standard Plasma or COVID-19 Convalescent Plasma to Standard Treatment, Versus Standard Treatment Alone, in Patients With Recent Onset of COVID-19 Respiratory Failure	Phase 2 study. Proof-of-concept Clinical Trial of Donated Antibodies Working Against With COVID-19
Study design	**RCT**, triple blind, placebo-controlled, parallel assignment	**RCT**, single blind, standard care comparator, parallel assignment	**RCT**, open label, standard of care comparator, parallel assignment	**RCT**, triple blind, standard therapy comparator, parallel assignment	**RCT**, open label, standard of care comparator, parallel assignment
Status trial	Recruiting	Not yet recruiting	Recruiting	Not yet recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: April 30, 2021 Estimated Study Completion Date: April 30, 2021	Estimated Primary Completion Date: February, 2021 Estimated Study Completion Date: February, 2021	Estimated Primary Completion Date: May 30, 2021 Estimated Study Completion Date: May 30, 2021	Estimated Primary Completion Date: June 15, 2021 Estimated Study Completion Date: December 15, 2021	Estimated Primary Completion Date: November 2, 2021 Estimated Study Completion Date: November 2, 2021
Study details					
Number of Patients	N = 50 (18 years or older)	N = 236 (18 years and older)	N = 400 (18 years and older)	N = 180 (18 years and older)	483 (18 years and older)
Location/Centres	United States	Colombia	India	Not provided	Belgium
Intervention	COVID-19 Convalescent Plasma (CCP)	SARS-CoV-2 convalescent plasma treatment	Convalescent Plasma with Standard of Care	Standard plasma + standard therapy protocol; or COVID-19 Convalescent Plasma + standard therapy protocol	Convalescent plasma
Controls	Placebo	Standard care	Standard of care	Standard therapy protocol	Standard of care
Duration of observation/Follow-up (Current Primary Outcome Measures)	14 days	30 days	28 days	30 days	15 days

Endpoints (Current Primary Outcome Measures)	Mechanical ventilation or death [time frame: day 14]	Mortality [up to 30 days after study enrolment]	Time to clinical improvement (Reduction of two points in ordinal scale or live discharge from the intensive care unit, whichever is earlier [Time Frame: Day 28])	30-days survival	Patients requiring mechanical ventilation or death [time Frame: No mechanical ventilation at day 15 after hospitalization]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-17 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Deutsches Rotes Kreuz DRK-Blutspendedienst Baden-Wurttemberg-Hessen	Metro Infectious Disease Consultants	Cairo University	Alkarkh Health Directorate-Baghdad	Emory University
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category.

	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	FDA issued an emergency use authorization (EUA)	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04433910	NCT04438057	NCT04438694	NCT04441424	NCT04441996
Phase & Intention	Phase 2 study on the Use of Convalescent Plasma Compared to Best Supportive Care in Patients With Severe COVID-19	Phase 2 study Evaluating the Efficacy of Convalescent Plasma in Symptomatic Outpatients Infected With COVID-19	Phase 1/2 study investigating the Use of Convalescent Plasma for Treatment of Patients With COVID-19 Infection	Phase of study not applicable. Investigating The Therapeutic Potential of Convalescent Plasma Therapy on Treating Critically-ill COVID-19 Patients Residing in Respiratory Care Units	Phase 4 study investigating Therapeutic Plasma Exchange for COVID-19-associated Hyperviscosity
Study design	**RCT**, open label, best supportive care comparator, crossover assignment	**RCT**, open label, standard of care comparator, parallel assignment,	**RCT**, open label, standard of care comparator, single group assignment	**RCT**, open label, conventional pharmacological comparator therapy, parallel assignment	**RCT**, open label, standard of care comparator, parallel assignment
Status trial	Recruiting	Not yet recruiting	Recruiting	Completed	Enrolling by invitation
Duration/End of Study	Estimated Primary Completion Date: December, 2020 Estimated Study Completion Date: February, 2021	Estimated Primary Completion Date: July 6, 2021 Estimated Study Completion Date: July 6, 2021	Estimated Primary Completion Date: May 31, 2021 Estimated Study Completion Date: December 31, 2021	Estimated Primary Completion Date: June 1, 2020 Estimated Study Completion Date: June 1, 2020	Estimated Primary Completion Date: October, 2020 Estimated Study Completion Date: October, 2020
Study details					
Number of Patients	N = 106 (18 years to 75 years)	N = 150 (18 years and older)	N = 60 (21 years to 70 years)	N = 49 (18 years and older)	N = 20 participants (18 years and older)
Location/Centres	Germany	United States	Egypt	Iraq	United States
Intervention	Convalescent plasma	Convalescent plasma	Convalescent Plasma	Convalescent Plasma	Therapeutic plasma exchange (TPE)
Controls	Best supportive care	Standard of care	Standard of care	Conventional pharmacological therapy (Hydroxychloroquine)	Standard of care
Duration of observation/Follow-up (Current Primary Outcome Measures)	21 days	28 days	2 to 3 weeks	8 weeks	4 days

Endpoints (Current Primary Outcome Measures)	Composite endpoint of survival and no longer fulfilling criteria of severe COVID-19. [Time Frame: Day 21]	Time to resolution of symptoms; serious adverse events within 24 hours [time frame: 28 days]	Duration of hospitalization/Recovery status [Time Frame: 2-3 weeks]	Death versus survival of patients [time frame: up to 8 weeks]	Change in Plasma Viscosity [Time Frame: Baseline (Study Day 1 prior to TPE), up to Day 4 (within 24 hours of last TPE)]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-18 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	University of Illinois at Chicago	University of Melbourne/ The Peter Doherty Institute for Infection and Immunity; Australasian Society for Infectious Diseases	Bagcilar Training and Research Hospital	Hackensack Meridian Health	Hospital de Infecciosas Francisco Javier Muniz
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new

	drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	(eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	23rd, 2020, the FDA issued an emergency use authorization (EUA)	drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04442191	NCT04483960	NCT04442958	NCT04456413	NCT04468009
Phase & Intention	Phase 2 study investigating the Infusion of Convalescent Plasma for the Treatment of Patients Infected With Severe Acute Respiratory Syndrome-Coronavirus-2	Phase 3 study Assessing the Clinical, Virological and Immunological Outcomes in Patients Diagnosed With SARS-CoV-2 Infection (COVID-19)	Not applicable phase investigating the Effectiveness of Convalescent Immune Plasma Therapy in Severe COVID-19 Patients With Acute Respiratory Distress Syndrome	Phase 2 study of Convalescent Plasma From Recovered COVID-19 Donors Collected by Plasmapheresis as Treatment for Subjects With Early COVID-19 Infection	Phase 2 study investigating Treatment of Critically Ill Patients With Covid-19 With Convalescent Plasma
Study design	**RCT**, double blind, placebo-controlled, proof-of-concept study	**RCT**, open label, standard of care and pharmacological comparators, factorial assignment	**RCT**, double blind, standard critical care, crossover assignment	**RCT**, open label, best supportive care, crossover assignment	**RCT**, open label, standard of care comparator, sequential assignment
Status trial	Recruiting	Recruiting	Completed	Not yet recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: May 5, 2021 Estimated Study Completion Date: May 5, 2021	Estimated Primary Completion Date: June 12, 2021 Estimated Study Completion Date: June 12, 2022	Estimated Primary Completion Date: June 15, 2020 Estimated Study Completion Date: June 17, 2020	Estimated Primary Completion Date: July, 2021 Estimated Study Completion Date: July, 2021	Estimated Primary Completion Date: June, 2021 Estimated Study Completion Date: June, 2021
Study details					
Number of Patients	N = 50 (40 years and older)	N = 2,400 (18 years and older)	N = 60 (18 years to 90 years)	N = 306 (18 years and older)	N = 36 (18 years or more)
Location/Centres	United States	Australia	Turkey	United States	Argentina
Intervention	Convalescent plasma	Convalescent plasma	Convalescent Immune Plasma	Convalescent Plasma	Convalescent plasma
Controls	Placebo	Standard of care or pharmacological	Standard critical care treatment	Best supportive care	Standard of care
Duration of observation/Follow-up (Current Primary Outcome Measures)	8 days	28 days	7 days	10 days	30 days

Endpoints (Current Primary Outcome Measures)	Oxygen supplementation [time frame: 8 days]	Proportion of participants alive and not having required new intensive respiratory support (invasive or non-invasive ventilation) or vasopressors/inotropic support [Time Frame: 28 days]	Plasma ferritin level; Lymphocyte count; D-Dimer level; C-Reactive protein level; Plasma procalcitonin level; Plasma fibrinogen level [time frame: 7 days]	Hospitalization Rate [Time Frame: 10 Days]	Mortality [time frame: mortality at 30 days]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-19 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V1.0, August
Sponsor	Fundacion Infant	MJM Bonten/ Australian and New Zealand Intensive Care Research Centre; Medical Research Institute of New Zealand; Unity Health; Berry Consultants; Global Coalition for Adaptive Research; University of Pittsburgh Medical Center	Kashif Khan	University College London	First people's hospital of Jiangxi district, Wuhan; Sinopharm Wuhan blood products Co Ltd
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2

	antigens to the recipient, thus allowing the generation of passive immunization)	recipient, thus allowing the generation of passive immunization)		antigens to the recipient, thus allowing the generation of passive immunization)	antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04479163	NCT02735707	NCT04467151	2020-002668-29	ChiCTR2000030381
Phase & Intention	Phase not applicable. Study investigating Prevention of Severe Covid-19 in Infected Elderly by Early Administration of Convalescent Plasma With High-titers of Antibody Against SARS-CoV2	Phase 4 study evaluating the effect of a range of interventions to improve outcome of patients admitted to intensive care with community-acquired pneumonia	Phase 2 study evaluating the safety and efficacy of anti-SARS-CoV-2 convalescent plasma in COVID-19 patients	Unknown phase. Treatment of treatment of severe COVID-19 infection	Not applicable. Evaluation of the efficacy and safety of anti-SARS-CoV-2 inactivated convalescent plasma in the treatment of novel coronavirus pneumonia (COVID-19) patient
Study design	**RCT**, quadruple-masked, placebo-controlled, parallel assignment	**RCT**, open label, factorial assignment	**RCT,** triple blind, placebo-controlled, parallel assignment	**RCT**	**RCT**, open label, single centre, standard treatment and ordinary plasma comparator, parallel assignment
Status trial	Recruiting	Recruiting	Not yet recruiting	Ongoing	Not yet recruiting
Duration/End of Study	Estimated Primary Completion Date: July 30, 2020 Estimated Study Completion Date: July 30, 2020	Estimated Primary Completion Date: July 30, 2020 Estimated Study Completion Date: July 30, 2020	Estimated Primary Completion Date: October, 2021 Estimated Study Completion Date: December, 2021	Unknown completion date. Start date: 25 June, 2020	Not specified

Study details					
Number of Patients	N = 210 (65 years and older)	N = 7,100	N = 96 (18 years and older)	Not reported	N = 40 (18 years to 70 years)
Location/Centres	Argentina	France	United States	Not reported	China
Intervention	Convalescent Plasma	evaluates treatments specific to COVID-19: pharmacological; convalescent plasma; Protocolised mechanical ventilation strategy	anti-SARS-CoV-2 plasma	plasma exchange with standard of care	Conventional treatment and anti-SARS-CoV-2 virus inactivated plasma
Controls	Placebo	No treatment	Placebo	Standard of care alone	Conventional treatment and Ordinary plasma
Duration of observation/Follow-up (Current Primary Outcome Measures)	From 12 hours to 15 days	From 21 days to 90 days	Day 0 to day 28	Not reported	Not specified
Endpoints (Current Primary Outcome Measures)	Development of severe respiratory disease, defined as a respiratory rate >30 and/or an O2 sat<93% [Time Frame: From 12 hours post infusion to day 15 post infusion]	Mortality [time frame: day 90); days alive and not receiving organ support in ICU [time frame: day 21]	Disease progression measured by WHO scale [Time Frame: Day 0 through Day 28 (or hospital discharge)]	Not reported	Clinical symptom improvement rate
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-20 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V1.0, August	V1.0, August	V1.0, August	V1.0, August	V2.0, September
Sponsor	Department of Infectious Diseases, Hvidovre Hospital	Ardabil University of Medical Sciences	King Saud Medical City	Universidad Tecnológica Equinoccial	Universidad Peruana Cayetano Heredia
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows the transfer of donor	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients

	allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	2020-001367-88	IRCT20150808023559N21	ISRCTN21363594	Isrctn85216856	NCT04497324
Phase & Intention	Phase not specified. Evaluation of the efficacy and safety of convalescent anti-SARS-CoV-2 plasma, hydroxychloroquine, sarilumab and baricitinib compared with placebo in combination with standard of care (SOC) for the treatment of moderate-to-severe COVID-19 pneumonia	Phase 1/2 study Evaluating convalescent plasma therapy in the treatment of patients with COVID-19 disease	Phase not reported. Therapeutic plasma exchange (TPE) in serious SARS CoV-2 disease (COVID-19)	Phase 2/3 study investigating the use of convalescent plasma from patients who have recovered from COVID-19 in the management of Ecuadorian patients infected with SARS-CoV-2 with clinical deterioration	Phase 2 study. Trial to evaluate the safety and efficacy of the use of convalescent plasma in hospitalized patients with COVID-19 infection
Study design	**RCT**, double blind, multi-stage, placebo-controlled, adaptive, parallel assignment	**RCT**, open label, parallel assignment	**RCT**, open label , usual care comparator	RCT, triple blind, two-arm, standard care comparator	**RCT,** open label, parallel assigned
Status trial	Ongoing	Recruiting	Recruiting	Recruiting	Not yet recruiting

Duration/End of Study	Duration of study: 1 year, 2 months	Not reported	Trial start date: 01 April, 2020 Trial end date: 29 December, 2020	Trial start date: 11 March, 2020 Trial end date: 31 December, 2020	Estimated Primary Completion Date: November 30, 2020 Estimated Study Completion Date: December 31, 2020
Study details					
Number of Patients	N = 1,500 (18 years and older)	N = 60 (no age limit)	N = 40 (18 years and older)	N = 200 (18 years and older)	N = 100 (18 years and older)
Location/Centres	Denmark	Iran	Saudi Arabia	Ecuador	Peru
Intervention	anti-SARS-CoV-2 plasma, hydroxychloroquine, sarilumab and baricitinib	Convalescent plasma	Therapeutic plasma exchange	convalescent plasma from a patient who has recovered from COVID-19	Administration of 1 to 2 units of convalescent plasma (200 ml to 250 ml, each), within 48 hours, plus standard of care
Controls	Placebo	Routine treatment	Usual care	Regular plasma	Standard of care
Duration of observation/Follow-up (Current Primary Outcome Measures)	28 days	Not provided	48 hours to 28 days	21 to 28 days	3 to 30 days
Endpoints (Current Primary Outcome Measures)	All-cause mortality or need of invasive mechanical ventilation up to 28 days	All-cause mortality	28-day mortality; adverse events and serious adverse events collected as usual for TPE treatment using the Saudi FDA reporting standard during the TPE session and the following 48 h	Case fatality rate at 21 and 28 days	Transfusion-related Serious Adverse Events [Time Frame: 14 days after randomization]
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Table 4-21 RCTs related to Convalescent plasma therapy in clinical trial registry (Continued)

Active substance	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**	**Convalescent plasma**
Version added	V2.0, September	V2.0, September	V2.0, September	V2.0, September	V2.0, September
Sponsor	South African National Blood Service	Vinmec Research Institute of Stem Cell and Gene Technology	Dow University of Health Sciences	University of North Carolina, Chapel Hill	Leiden University Medical Center
Mechanism of operation	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19 convalescent patients allows	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19	Passive immunization (transfusion of apheresis frozen plasma (AFP) from COVID-19

	convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)	convalescent patients allows the transfer of donor neutralizing antibodies directed against SARS-CoV2 antigens to the recipient, thus allowing the generation of passive immunization)
Regulatory status EMA/FDA	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)	EMA: no marketing authorisation FDA: On March 25th, 2020, the FDA approved the use of convalescent plasma under the emergency investigational new drug (eIND) category. On August 23rd, 2020, the FDA issued an emergency use authorization (EUA)
Trial Identifier	NCT04516811 PROTECT-Patient Study	NCT04521036	NCT04521309	NCT04524507	NL8633
Phase & Intention	Phase III trial to assess the safety and efficacy of COVID-19 convalescent plasma as a therapeutic treatment for hospitalised patients with moderate to severe COVID-19	Phase I/II study to test the safety and efficacy of convalescent plasma therapy	Phase I/II study to assess the clinical efficacy and safety of intravenously administered Immunoglobulins for COVID-19 patients	Phase II study to find out if convalescent COVID-19 plasma is safe and to determine the safest and most effective level of anti-viral antibody when given to people admitted to the hospital with confirmed COVID-19 infection	Phase II/III comparing efficacy and safety of anti-SARS-CoV-2 convalescent plasma vs standard plasma in maximally 3 days hospitalized COVID-19 patients that are not at or bound to be referred to the ICU
Study design	**RCT**, randomised, double-blinded, placebo-controlled	**RCT,** open label, parallel assignment	**RCT,** randomised, single-blinded, sequential assignment	**RCT,** double blind, parallel assignment	**RCT, placebo controlled,** double blind, parallel assignment

Status trial	Not yet recruiting	Not yet recruiting	Recruiting	Recruiting	Recruiting
Duration/End of Study	Estimated Primary Completion Date: December 30, 2021 Estimated Study Completion Date: July 31, 2022	Estimated Primary Completion Date: June 30, 2021 Estimated Study Completion Date: October 30, 2021	Estimated Primary Completion Date: January, 2021 Estimated Study Completion Date: March, 2021	Estimated Primary and Study Completion Date: May, 2021	Not reported
Study details					
Number of Patients	N = 600 (18 years and older)	N = 44 (18 to 75 years of age)	N = 50 (above 18 years of age)	N = 56 (aged 18 and older	N = 430 (aged between 18 and 85 years)
Location/Centres	South Africa	Vietnam	Pakistan	United States	Netherlands
Intervention	A single unit of approximately 200-250 mL of CCP that contains anti-SARS-CoV-2 collected by plasmapheresis from a volunteer who recovered from COVID19 with SOC as determined by local practice and guidelines	500 mL of convalescent plasma from COVID-19 recovered donors plus standard of care	Single dose of intravenous purified immunoglobulins from convalescent plasma with standard care. Four intervention arms with dosing of 0.20 g/Kg, 0.25 g/Kg, 0.30 g/Kg, 0.35 g/Kg	High-titer Convalescent COVID-19 Plasma At least two units of CCP transfused 4-24 hours apart on Study Day 0. A third unit may be administered, if available	Convalescent thawed fresh frozen plasma 1 unit (250-325 ml)
Controls	A single unit of 200 mL normal saline with SOC as determined by local practice and guidelines	Standard of care	Standard care only	Standard-titer Convalescent COVID-19 plasma At least two units of CCP transfused 4-24 hours apart on Study Day 0. A third unit may be administered, if available.	Standard thawed fresh frozen plasma 1 unit (250-325 ml)
Duration of observation/Follow-up (Current Primary Outcome Measures)	28 days	60 days	28 days	14 to 28 days	14 days
Endpoints (Current Primary Outcome Measures)	Clinical Improvement [Time Frame: Day 28]	Change in mortality [Time Frame: until hospital discharge or a maximum of 60 days whichever comes first]	28 Days mortality [Time Frame: 28 days]; Requirement of supplemental oxygen support [Time Frame: 28 days]; Number of days on assisted ventilation [Time Frame: 28 days]; Days to step down [Time Frame: 28 days]; Days to Hospital	Cumulative Incidence of Serious Adverse Events (SAEs) at study Day 14 [Time Frame: 14 days]; Days to hospital discharge (or discharge equivalent) following first	Outcome at day 14 of all-cause mortality, mechanical ventilation, ICU admission and long duration of hospital stay (6 days or more), with less than 6 hospitalized

			Discharge [Time Frame: 28 days]; Adverse events during hospital stay [Time Frame: 28 days]; Change in C-Reactive Protein (CRP) levels [Time Frame: 28 days]; Change in neutrophil lymphocyte ratio [Time Frame: 28 days]	dose of CCP [Time Frame: 28 days]	days as reference category
Results/Publication	Not provided	Not provided	Not provided	Not provided	Not provided

Abbreviations: RCT=Randomised Controlled Trial

Source: all tables of ongoing RCTs based on AIHTA: http://eprints.aihta.at/1234/

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