Technoleg Iechyd Cymru
Health Technology Wales

# Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

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| **Topic:** | Plasmapheresis of convalescent plasma to confer passive immunity. |
| **Topic exploration report number:** | TER203 |

## Introduction and aims

Health Technology Wales researchers searched for evidence on the use of convalescent plasma (CP) to confer passive immunity by plasmapheresis or other methods. Evidence of the effectiveness of CP as an intervention specifically for COVID-19 patients was of particular interest.

CP from recovered COVID-19 patients contains antibodies against SARS-CoV-2 produced by their immune system. Collecting donations of CP 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.

Collection of CP during whole blood donation yields approximately 250ml and the donor is unable to donate again for three months. Plasmapheresis is an alternative which removes whole blood, collecting the plasma component whilst returning the remaining blood products to the donor. This approach typically yields over 500ml and can be repeated every 2 weeks as red and white cells are not depleted in the donor and they do not risk becoming anaemic.

## Summary of evidence


**Summary:**

We did not identify any evidence specifically about the effectiveness of plasmapheresis of convalescent plasma (CP) to confer passive immunity in patients with COVID-19, however, this may be due to lack of prominent reporting regarding the plasma collection method. Broadening the evidence search to the effectiveness of CP (collected by any method) as an intervention for COVID-19, we identified four case series. All patients were critically ill when they received CP and subsequent improvements in their condition were reported, but the design of the studies means this improvement cannot be attributed specifically to the intervention.

One protocol for a systematic review of CP for COVID-19 has been published and a number of studies are currently recruiting to look at CP for COVID-19.

A number of studies have been published on the effectiveness of CP for other viral diseases: clinical outcomes were reported for SARS and severe influenza patients (see clinical effectiveness section below). Studies which compare CP to standard treatment in patients with SARS or severe influenza report inconsistent findings for overall mortality. However, studies suggest that CP 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.

There are a number of protocols for systematic reviews and trials of CP for COVID-19 currently published. This suggests that the evidence base is likely to increase in future in this area.

## Evidence for convalescent plasma to confer passive immunity to COVID-19 patients

*Secondary evidence*

No systematic reviews or health technology assessments of convalescent plasma to confer passive immunity to COVID-19 patients were identified.

Zhang & Liu (2020) published the findings of a review of all treatment options relating to COVID-19 and reported that CP should be given to all COVID-19 patients if it is available. However, CP was only referred to in the abstract and conclusions, where reference was made to the study by Arabi et al. (2015) in MERS patients, and the studies by Cheng et al. (2005) and Soo et al. (2004) in SARS patients (see below). No studies on CP were included in the results and the search methodology was not systematic in nature.

*Primary evidence*

The only primary evidence identified which specifically looked at CP for use in patients with COVID-19 were four case series. Patient numbers ranged from 2 to 10 and all patients were critically ill when they received CP. Shen et al. (2020) found viral loads to be negative within 12 days of CP in five patients, three of whom were discharged and the remaining two stable at time of publication. Zhang et al. (2020) reported all four patients to be PCR-negative 3-22 days after CP and all to have recovered (three discharged and one transferred to an unfenced ICU). Duan et al. (2020) reports that of ten patients, symptoms had improved or disappeared 1-3 days after CP. Of those that were PCR-positive before CP was given, all were PCR-negative at 2-6 days. Ahn et al. (2020) reported that two patients had improved symptoms after CP and were PCR-negative at days 24 and 26. It should be noted that without a comparator group it is not possible to say whether improvements were due to CP.

*Published guidance*

The U.S. Department of Health and Human Services: Food and Drug Administration (FDA) published Guidance for Industry on the use of investigational COVID-19 convalescent plasma in April 2020. This includes guidance on the pathway, patient eligibility, collection of CP (including donor eligibility), and record-keeping. In addition, the European Commission published guidance on collection, testing, processing, storage, distribution and monitored use

of COVID-19 convalescent plasma in April 2020 with an aim of facilitating a common approach across EU Member States.

*Ongoing studies and protocols*

One protocol for a systematic review of CP for COVID-19 and three protocols for systematic reviews of all treatments for COVID-19 have been published.

Two ongoing trials of interest were identified, the REMAP-CAP study and the RECOVERY trial. The REMAP-CAP trial is a large randomised control trial taking place across 16 countries to assess the effectiveness of a range of treatments for community acquired pneumonia. The convalescent plasma arm of REMAP-CAP was added to the protocol on 19th April. Convalescent plasma is compared to no intervention for patients post 48 hours in ICU. The reported study completion is December 2023, however, preliminary results may be reported earlier in response to the current COVID-19 situation. Wales has multiple active sites and, at the date of writing, there is an ongoing collection of plasma through the full blood process. The RECOVERY trial focusses on therapies for the treatment of people hospitalised with COVID-19. RECOVERY trial is assessing a wide range of possible treatments, whilst it doesn't currently include convalescent plasma there is the possibility there will be a convalescent plasma arm added to the study.

Three international studies into CP for COVID-19 were identified in addition to REMAP-CAP and the RECOVERY trials. One cohort study was identified as currently recruiting to look at clinical effectiveness of CP for COVID-19 and two studies were identified which have not yet begun recruiting. The former is expected to complete in April 2021 (US, N=55). Of the latter, one is due to complete in July 2020 (Italy, N=10) and the other in April 2021 (Hungary, N=20). Clinical experts consulted as part of producing this TER were also able to share seven further international trial protocols. The majority are in patients with severe COVID-19, whilst one looks at use of CP as prophylaxis in adults exposed to COVID-19. Where the information is available, these began in April 2020 or are currently recruiting. The CAPSID trial in Germany will have a 10-month duration once it has begun. Two studies in the US (CSSC-001 and CSSC002) are expected to complete in December 2022.

## Evidence for convalescent plasma to transfer immunity to non-COVID-19 patients

*Secondary evidence*

We identified some secondary evidence on the use of convalescent plasma to confer passive immunity in conditions other than COVID-19. Mair-Jenkins et al. (2015) undertook a systematic review and meta-analysis of the effectiveness of CP and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections (SARIs) of viral etiology. They identified 32 studies of SARS coronavirus and severe influenza which provided consistent evidence in the narratives of a reduction in mortality. Exploratory meta-analysis combining studies from a range of conditions found a statistically significant reduction in mortality compared to placebo or no therapy (OR 0.25 95% CI 0.14 to 0.45). However, this analysis used outcome data from non-randomised studies, many of which were assessed by the review authors as being at high risk of bias, and so should be interpreted with caution.

Mo & Fisher (2016) undertook a literature review on treatment of MERS-CoV and SARS-CoV. In addition to the systematic review by Mair-Jenkins et al. (2015), they found two case reports

and a study protocol for intravenous immunoglobulin to treat MERS-CoV and four studies of CP in SARS-affected patients. The latter demonstrated that use of CP led to earlier discharge, rapid decrease in viraemia, and survival benefits.

Stockman et al. (2006) undertook a systematic review of treatments for SARS. Amongst other treatments, they identified seven studies of CP or intravenous immunoglobulin of which the results were inconclusive.

A Cochrane review (CD010056) looked at post-exposure passive immunisation for preventing measles. This assessed intramuscular injection, or intravenous infusion of polyclonal immunoglobulins derived from human sera of plasma to confer passive immunity. However, these were exposed, susceptible individuals and not patients hospitalised with infection. When given within seven days of exposure, convalescent serum was found to be effective at preventing measles.

*Primary evidence*

Multiple studies using convalescent plasma were identified across a range of disease areas. Hung et al. (2011) looked at the use of CP for patients with severe H1N1 2009 infection requiring intensive care, harvested by apheresis from recovering patients. They found lower mortality among the 20 patients receiving CP compared to controls who declined CP (OR 0.20 95% CI 0.06 to 0.69; p=0.011) and a lower viral load in patients receiving CP at day 3, 5 and 7 ($p<0.05$).

Wong et al. (2010) assessed the practicalities of collecting CP in pandemic preparation using plasmapheresis and reported on the potential limitations. They found that of around 9,100 recovered patients invited to be screened for donating plasma, 8.6% attended screening, and of these, 38.3% (3.3% of all invited) could donate by plasmapheresis. Reasons why patients could not donate included failure to meet donation criteria, failed laboratory tests, insufficient neutralisation antibody titres, and inability to make the appointment.

In addition to the studies by Hung et al. (2011) and Wong et al. 2010) using apheresis, three studies and one case report were identified which looked at the use of CP for severe influenza. Hung et al. (2013) undertook an RCT using CP fractionated to hyperimmune IV immunoglobulin compared to normal IV immunoglobulin in patients requiring intensive care (N=35). The intervention was associated with reduced mortality when given within 5 days of symptom onset (OR 0.14 95% CI 0.02 to 0.92; p=0.04) and a lower viral load in patients receiving CP at day 5 and 7 (p=0.04 and p=0.02 respectively). Davey et al. (2019) undertook a multi-country placebo-controlled RCT of patients hospitalised for influenza A or B (N=308). They found no statistically significant difference in the proportion (30%) which had a composite safety outcome of death, serious adverse event, or grade 3-4 adverse event at 28 days. Wu et al. (2011) presented a feasibility model of using CP for a population-wide passive immunotherapy programme during an influenza pandemic, using Hong Kong as a case study and based on the assumption of clinical effectiveness. Wu et al. (2015) reported that a patient who received CP on day 10 of their illness was discharged on day 24.

Two studies and one case series were identified which looked at CP for SARS. Cheng et al. (2005) found a higher day-22 discharge rate among SARS patients who received CP before day 14 of illness compared to those who received it later ($p<0.001$; N=80) and an overall mortality rate of 12.5% in patients given CP with no difference in mortality by the day at which the infusion was given. Soo et al. (2004) found no significant difference in mortality between patients receiving CP or further methylprednisolone after previous treatment with ribavirin and methylprednisolone. However, those who received CP had a shorter hospital stay

(p<0.001) than those who received further methylprednisolone (N=40). Yeh et al. (2005) saw improvements in healthcare workers with SARS following CP. One case series was identified which found that two of three MERS patients showed neutralising activity after receiving CP (Ko et al. 2018).

Two studies and two case reports were identified which looked at CP for Ebola virus disease (EVD). Van Griensven (2018) published a protocol for a study comparing CP with supportive care to supportive care alone in Guinea. Another protocol compares CP to placebo in Sierra Leone. One study looked at CP for MERS-CoV - Arabi et al. (2016) undertook a survey of physicians in Saudi Arabia to assess whether an RCT of CP for MERS-CoV would be feasible. One case report of a patient given Brincidofavir and CP at day 8 of illness was discharged on day 20, while the other found that the patient given CP on days 9, 10, 11 and 12 was discharged on day 34.

*Ongoing studies and protocols*

There are four protocols of systematic reviews of CP for SARS published. One is a review of CP for SARS or MERS resulting from coronavirus infection (with direct reference to COVID-19); one is a review of SARS resulting from viral infection with coronavirus or influenza; and two look at CP for SARS resulting from any viral infection.

## Areas of uncertainty

It is not clear as to how transferable research on the effectiveness of CP from outside of COVID-19 is to our research question.

## Conclusions

There is some evidence available on the effectiveness of CP to confer passive immunity for COVID-19 which is supported by research on other viral infections which may be useful. CP for COVID-19 currently lacks a mature evidence base, however, there are a number of active trials. Research into related conditions may help inform the development of research and use of CP. The systematic review and meta-analysis of CP in SARS patients which was published in 2015 was identified as particularly useful.

## Brief literature search results

| Resource | Results |
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| HTA organisations | |
| Healthcare Improvement Scotland | No relevant evidence identified. |
| Health Technology Assessment Group | No relevant evidence identified. |
| Health Information and Quality Authority | No relevant evidence identified. |
| UK guidelines and guidance | |
| SIGN | No relevant evidence identified. |
| NICE | No relevant evidence identified. |
| International Guidance | |
| FDA | U.S. Department of Health and Human Services. Food and Drug Administration. April 2020. Investigational COVID-19 Convalescent Plasma: Guidance for Industry. |
| EC | European Commission. An EU programme of COVID-19 convalescent plasma collection and transfusion: Guidance on collection, testing, processing, storage, distribution and monitored use. April 2020. |
| Secondary literature and economic evaluations | |
| ECRI | No relevant evidence identified. |
| EUnetHTA | No relevant evidence identified. |
| Cochrane library | Convalescent plasma to confer passive immunity to measles:<br>Young MK, Nimmo GR, Cripps AW, Jones MA. Post-exposure passive immunisation for preventing measles. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD010056. DOI: 10.1002/14651858.CD010056.pub2<br>https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010056.pub2/epdf/full<br><br>Platelet rich plasmapheresis (blood is returned to the donor):<br>Carless PA, Rubens FD, Anthony DM, O'Connell D, Henry DA. Platelet-rich-plasmapheresis for minimising peri-operative allogeneic blood transfusion. Cochrane Database of Systematic Reviews 2011, Issue 3. Art. No.: CD004172. DOI: 10.1002/14651858.CD004172.pub2<br>https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004172.pub2/epdf/full |

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| | There are also Cochrane reviews which look at treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) (where the plasma is returned to the same patient); and given concomitantly with alkylating agents for Waldenstrom's macroglobulinaemia. |
| PubMed | Mair-Jenkins J et la. (2015). The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis 211(1): 80-90. https://www.ncbi.nlm.nih.gov/pubmed/25030060<br>Zhang L & Liu Y (2020). Potential interventions for novel coronavirus in China: A systematic review. J Med Virol. 92(5): 479-490. https://www.ncbi.nlm.nih.gov/pubmed/32052466<br>Mo Y & Fisher D (2016). A review of treatment modalities for Middle East Respiratory Syndrome. J Antimicrob Chemother. 71(12): 3340-3350. https://www.ncbi.nlm.nih.gov/pubmed/27585965<br>Stockman LJ et al. (2006). SARS: systematic review of treatment effects. PLoS Med 3(9): e343. https://www.ncbi.nlm.nih.gov/pubmed/16968120 |
| Primary studies | |
| Cochrane library | CP by apheresis for severe influenza:<br>Hung IFN et al. (2011). Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1) 2009 virus infection. Clinical infectious diseases 52(4): 447-456. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00891926/full?highlightAbstract=plasmaphaeresis%7Cplasmapheresi%7Cplasmaphaeresi%7Cplasmapheresis%7Cpandem%7Cpandemic<br><br>CP for severe influenza:<br>Hung IFN et al. (2013). Hyperimmune IV immunoglobulin treatment: a multicentre double-blind randomized controlled trial for patients with severe 2009 influenza A (H1N1) infection. Chest 144(2) 464-473 https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00965115/full?highlightAbstract=convalescent%7Cplasm%7Cpandem%7Cconvalesc%7Cplasma%7Cpandemic<br>Davey et al. (2019). Anti-influenza hyperimmune intravenous immunoglobulin for adults with influenza A or B infection (FLU-IVIG): a double-blind randomised, placebo-controlled trial. The lancet respiratory medicine 7(11): 951-963. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02006066/full?highlightAbstract=convalescent%7Cplasm%7Cpandem%7Cconvalesc%7Cplasma%7Cpandemic<br><br>CP for Ebola:<br>Cochrane Central Register of Controlled Trials (CENTRAL). Convalescent plasma for early Ebola virus disease in Sierra Leone: an open-label, non-randomized, controlled clinical trial. CN-01811568. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01811568/full?highlightAbstract=convalescent%7Cconvalesc%7Cplasm%7Cplasma<br>Van Griensven J (2015). Emergency evaluation of convalescent plasma for ebola virus disease (EVD) in guinea. American Journal of Tropical Medicine and Hygiene 93(4): 387. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01249874/full?highlightAbstract=convalescent%7Cconvalesc%7Cplasm%7Cplasma |

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| | There are a wide array of trials for the use of plasmapheresis for other conditions e.g. Guillain-Barre syndrome; lupus nephritis; progressive MS; cardiac surgery; pemphigus; myasthenia gravis; rheumatoid vasculitits. |
| PubMed | CP for COVID-19 (case series/n<10 with not control):<br>Shen C et al. (2020). Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA doi: 10.1001/jama.2020.4783 [Epub ahead of print]<br>https://www.ncbi.nlm.nih.gov/pubmed/32219428<br>Zhang B et al. (2020). Treatment with convalescent plasma for critically ill patients with SARS-CoV-2 infection. Chest doi: 10.1016/j.chest.2020.03.039 [Epub ahead of print]<br>https://www.ncbi.nlm.nih.gov/pubmed/32243945<br>Duan K et al. (2020). Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U.S.A 117(17): 9490-9496<br>https://www.ncbi.nlm.nih.gov/pubmed/32253318<br>Ahn JY et al. (2020). Use of convalescent plasma therapy in two COVID-19 patients with acute respiratory distress syndrome in Korea. J Korean Med Sci 35(14): e149<br>https://www.ncbi.nlm.nih.gov/pubmed/32281317<br><br>CP for severe influenza:<br>Wu JT et al. (2012). Logistical feasibility and potential benefits of a population-wide passive immunotherapy program during an influenza pandemic. Influenza Other Respi Viruses 5(Suppl 1): 226-229.<br>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3357494/<br>Wong HK et al. (2010). Practical limitations of convalescent plasma collection: a case scenario in pandemic preparation for influenza A (H1N1) infection. Transfusion 50(9): 1967-71.<br>https://www.ncbi.nlm.nih.gov/pubmed/20412524<br><br>CP for MERS-CoV:<br>Arabi YM et al. (2016). Feasibility of a randomized controlled trial to assess treatment of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection in Saudi Arabia: a survey of physicians. BMC Anesthesiol. 16(1): 36.<br>https://www.ncbi.nlm.nih.gov/pubmed/27405596<br><br>CP for SARS:<br>Cheng Y et al. (2005). Use of convalescent plasma therapy in SARS patients in Hong Kong. Eur J Clin Microbiol Infect Dis 24(1): 44-46.<br>https://www.ncbi.nlm.nih.gov/pubmed/15616839<br>Soo YO et al. (2004). Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. Clin Microbiol Infect 10(7): 676-8.<br>https://www.ncbi.nlm.nih.gov/pubmed/15214887 |
| Ongoing primary or secondary research | |
| PROSPERO database | Systematic review protocol for CP for COVID-19:<br>Cao et al. The effectiveness of convalescent plasma for the treatment of Novel Corona Virus Disease 2019 (COVID-19): a systematic review and meta-analysis. PROSPERO 2020 CRD42020177511. |

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| | https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=177511<br><br>Systematic review protocol for CP for SARS and MERS:<br>Wang L & Li J. A systematic review of convalescent plasma treatment for SAR coronavirus and MERS coronavirus: a possible reference for a 2019 novel coronavirus (COVID-19) treatment option. PROSPERO 2020 CRD42020173350.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=173350<br><br>Systematic review protocol for CP for SARS:<br>Estcourt L et al. A systematic review of the safety and efficacy of convalescent plasma or immunoglobulin treatment for people with severe respiratory viral infections due to coronaviruses or influenza. PROSPERO 2020 CRD42020176392.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=176392<br>Ribeiro CJN et al. Efficacy of convalescent plasma in the treatment of critically ill patients with severe acute respiratory syndromes caused by viruses. PROSPERO 2020 CRD42020178643.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=178643<br>Shao S et al. Effect of convalescent blood products for patients with severe acute respiratory infections of viral etiology: a systematic review, meta-analysis and meta-regression. PROSPERO 2020 CRD42020172940.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=172940<br><br>Systematic review protocol for treatments for COVID-19:<br>Zou K et al. Efficacy, effectiveness and safety of treatments for COVID-19 in trials and real healthcare settings: a protocol of systematic review. PROSPERO 2020 CRD42020179660.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=179660<br>Al-Moraissi E & Alslman W. Effectiveness and safety of different therapies agents in the treatment of Covid-19: a systematic review and meta-analysis. PROSPERO 2020 CRD42020178822.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=178822<br>Lee HW et al. Efficacy and safety of antiviral therapies in COVID-19 patients. PROSPERO 2020 CRD42020179494.<br>https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=179494 |
| Clinicaltrials.gov | Plasmapheresis for COVID-19:<br>A Pilot Study to Explore the Efficacy and Safety of Rescue Therapy With Antibodies From Convalescent Patients Obtained With Double -Filtration Plasmapheresis (DFPP) and Infused in Critically Ill Ventilated Patients With Coronavirus Disease 2019 (COVID-19). ClinicalTrials.gov Identifier: NCT04346589<br>https://clinicaltrials.gov/ct2/show/NCT04346589?term=plasmapheresis&draw=3&rank=62<br>Anti COVID-19 Convalescent Plasma Therapy. ClinicalTrials.gov Identifier: NCT04345679<br>https://clinicaltrials.gov/ct2/show/NCT04345679?term=plasmapheresis&draw=4&rank=152<br>REMAP-CAP clinical trial<br>https://clinicaltrials.gov/ct2/show/NCT02735707<br>REMAP-CAP protocol summary<br>https://static1.squarespace.com/static/5cde3c7d9a69340001d79ffe/t/5e82b60d225239559569ff77/1585624604501/REMAP-CAP+Protocol+Summary+V3+-+11+Sep+2019_WM.pdf<br>Convalescent plasma arm of REMAP-CAP |

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| | https://static1.squarespace.com/static/5cde3c7d9a69340001d79ffe/t/5ea3fddb1de102540e627663/1587805670273/REMAP-CAP+COVID-19+Immunoglobulin+Therapy+Domain-Specific+Appendix+V1-+19+April+2020_WM.pdf<br><br>RECOVERY trial:<br>https://www.recoverytrial.net/files/recovery-protocol-v5-0-2020-04-24.pdf<br><br>CP for COVID-19:<br>Phase IIa Study Exploring the Safety and Efficacy of Convalescent Plasma From Recovered COVID-19 Donors Collected by Plasmapheresis as Treatment for Hospitalized Subjects With COVID-19 Infection. ClinicalTrials.gov Identifier: NCT04343755<br>https://clinicaltrials.gov/ct2/show/NCT04343755?term=plasmapheresis&draw=4&rank=113 |
| Other | |
| Clinical experts | Convalescent plasma to limit coronavirus associated complications: a randomized open label, phase 1 study comparing the efficacy and safety of high-titre anti-SARS-CoV-2 plasma vs. placebo in hospitalized patients with interstitial pneumonia due to COVID-19 (CSSC-002).<br>Covid-19 convalescent plasma collection in the Netherlands.<br>Convalescent plasma to stem coronavirus: a randomized, blinded phase 2 study comparing the efficacy and safety human coronavirus immune plasma (HCIP) vs. control (SARS-CoV-2 non-immune plasma) among adults exposed to COVID-19 (CSSC-001).<br>A randomized, prospective, open label clinical trial of convalescent plasma compared to best supportive care for treatment of patients with severe COVID-19 infections (CAPSID).<br>Plasma from donors cured of the disease caused by the novel coronavirus 2019 (COVID-19) as a treatment for critical patients suffering from COVID-19. Proof of concept study.<br>Nested trial in corimmuno-19. Efficacy of hyperimmune plasma for patients with COVID-19. The COVIPLASM trial. |

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| **Date of search:** | April 2020 |
| **Concepts used:** | Convalescent plasma; plasmapheresis<br>For primary evidence the additional terms were used to enhance specificity: pandemic; SARS; COVID; coronavirus |