NORPLASMA COVID-19

NORPLASMA MONITOR

Monitoreringsstudie for bruk av COVID-19 rekonvalesensplasma

Lise Sofie H. Nissen-Meyer
Prosjektleder NORPLASMA
Seksjonsleder/seksjonsoverlege Blodbanken, OUS

NORPLASMA COVID-19

Innhold

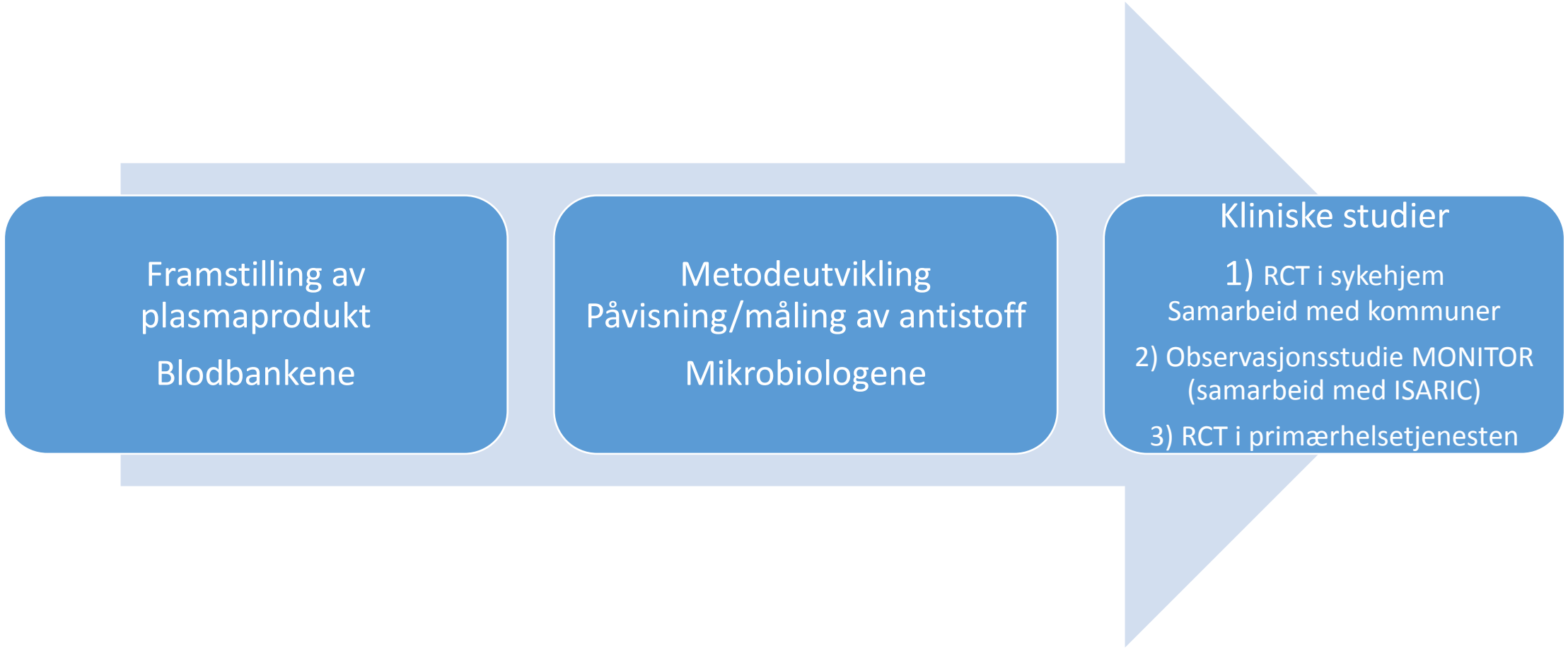
- Nasjonalt prosjekt for innsamling av rekonvalesensplasma
- Kunnskapsgrunnlag: kan rekonvalesensplasma virke mot COVID-19?
- Helsedirektoratets oppdrag
- Hvorfor monitoreringsstudie?
- Blodbankens oppgaver
- Klinikernes oppgaver
- Oppsummering
- Spørsmål

NORPLASMA COVID-19

Hvorfor norsk plasmastudie?

- Tidlig i COVID-19-pandemien: lovende kliniske data (i studier uten kontroller), → effekt bør testes i et RCT.
- Plasma nevnt i WHO-anbefalingene fra januar/februar
- Anbefalt av EU/EBA og ønsket av Helsedirektoratet
- utvikle norsk kompetanse til å evaluere og bruke plasma i behandling av COVID-19
- Tilgang på plasma, opp mot remdesivir og andre nye lovende medikamenter produsert noen få steder i utlandet og mot et globalt behov. Plasma er kortreist og tilgjengelig, om vi da får dokumentert effekt.
- Det er nå registrert >100 RCT rundt om i verden for å teste rekonvalesens-plasma

NORPLASMA COVID-19



Del 3: Kliniske studier

1. *Gjennomføring av randomisert, kontrollert behandlingsstudie (Fase 2a) for å utrede effekt og sikkerhet av behandling med rekonvalesensplasma til sykehjemspasienter med COVID-19*

   NORPLASMA PLEIE

   STUDIEN ER GODKJENT AV REK* MEN MANGLER FINANSIERING

2. *Monitoreringsstudie av COVID-19 rekonvalesensplasma brukt til behandling av pasienter i Norge*

   NORPLASMA MONITOR

   GODKJENT AV REK

   SAMARBEID med ISARIC ved OUS og samarbeidende sykehus

3. *Randomisert kontrollert behandlingsstudie som 1) men rettet mot pasienter som kontakter feberpoliklinikker/primærhelsetjeneste*

   NORPLASMA FEBER

Project organization

NORPLASMA COVID-19

Board of directors:
Leader: John Torgils Vaage, Oslo University Hospital HF/Helse Sør-Øst
Einar Kristoffersen, Haukeland University Hospital HF/Helse Vest
Svein Arne Nordbø, St. Olav Hospital HF/Helse Midt-Norge
Oddny Kristin Remlo, Nordlandssykehuset HF/Helse Nord
Øystein Flesland, Norwegian Directorate of Health
Anne-Marte Bakken Kran, Institute of Public Health
Thomas Larsen Titze, Vestre Viken HF
Børre Fevang, Clinical research representative
User representative: Tone Hansen, Blodkreftforeningen
Secretary: Project Manager

Project Management
Project manager: Lise Sofie Nissen-Meyer
Chair, transfusion team: Tor Hervig
Chair, microbiology team: Anne-Marte Bakken Kran
Clinical coordinator: Børre Fevang
Administrative support: Representatives of the Norwegian Directorate of health

Reference group
Leader: Project manager
Aim: scientific advice
NFIT-leader: Mona H. Fenstad
EBA representative: Kristin Gjerde Hagen
Other relevant partners/advisers and user representatives

Transfusion team
Chair: Tor Hervig. Co-chair: Lise Sofie Nissen-Meyer
Tasks: Process from inclusion of donors to delivery of approved plasma for clinical trials. Coordinate production and QC, distribution.

- **Recruitment/ registration of Blood donors**
- **Coordinate bloodbanks performing plasmapheresis**
- **Quality control ELISA, PRNT Plasma QC**
- **Available Plasma Logistics**

Microbiology team
Chair: Anne-Marte Bakken Kran. Co-chair: Fredrik Müller
Tasks:
RTPCR data,
ELISA, PRNT live or pseudovirus
- Screening of donors
- Plasma quality control

Clinical trials: MONITOR and CARE/FEVER
Leaders: John Torgils Vaage
Protocol MONITOR: Tor Hervig
Protocol CARE: Børre Fevang
Protocol FEVER: Børre Fevang
Tasks: Perform clinical trials according to protocols

Monitor: CTU, Oslo University Hospital

Local teams

Helse Midt-Norge	Helse Vest	Helse Sør-Øst	Helse Nord
Site leader	**Site leader**	**Site leader**	**Site leader**
Mona H Fenstad	Einar Kristoffersen	Lise Sofie Nissen-Meyer	Ingvild Hausberg Sørvoll

Local teams

NORPLASMA COVID-19

Helse Sør-Øst
Site leader
Lise Sofie Nissen-Meyer

Akershus universitetssykehus
Abid Hussain Llohn

Oslo universitetssykehus
Lise Sofie Nissen-Meyer

Sykehuset i Vestfold
Lilja Synnøve Høiback

Sykehuset Østfold
Bjørg Kari Bolstad

Vestre Viken
Thomas Larsen Titze

Sykehuset Innlandet
Karin Magnussen

Sørlandet Sykehus
Christine Torsvik Steinsvåg
Kari-Ann Nedal

Helse Vest
Site leader
Einar Kristoffersen

Helse Bergen/Haukeland
Kristin Gjerde Hagen
Torunn Apelseth

Helse Fonna
Tor Hervig
Anne Mari Hagen

Helse Stavanger
Gunn Kristoffersen

Helse Førde
Robin Andre Sørland

Helse Midt-Norge
Site leader
Mona H Fenstad

St.Olavs hospital
Mona H Fenstad

Lene Haugnæss (rekruttering)
Ingvild Ahne Teigum (biobank)
Bjørn Ståle Benjaminsen (produksjon)

Helse Nord-Trøndelag
Birgit Johanne Hoel Stubbe (Levanger, Namsos)

Gunn Mary Andersen

Helse Møre og Romsdal
Brit Valaas Viddal

Bodil Stige (Ålesund)
Katrine Rindarøy (Molde)
Randi S. Tømmervåg (Kristiansund)
Helen Sylte Tjugen (Volda)

Helse Nord
Site leader
Ingvild Hausberg Sørvoll

Universitetssykehuset Nord-Norge
Ingvild Hausberg Sørvoll

Nordlandssykehuset

https://www.ous-research.no/home/norplasma

Oslo University Hospital

Plasmaproduksjon › Informasjon til blodbankene ›

Informasjon til blodbankene

Framgangsmåte (pdf)

Informasjon fra Helsedirektoratet
Til alle landets blodbanker Informasjon om innsamling, testing og bruk av Covid19-konvalesentplasma.PDF

Oversikt over blodbanker som har fått tillatelse til å tappe og distribuere rekonvalesensplasma:
Blodbanker som tar imot Covid-19-konvalesentplasma.pdf

Informasjon til giver:

Forespørsel om deltakelse i forskningsprosjektet "Behandling av pasienter med COVID-19 med plasma fra blodgivere som har antistoff mot SARS-CoV-2 (rekonvalesensplasma)": REK-godkjent spesifikt samtykke NORPLASMA 140845.docx

FORESPØRSEL OM Å AVGI BIOLOGISK MATERIALE TIL GENERELL FORSKNINGSBIOBANK OG OPPLYSNINGER TIL FORSKNING PÅ COVID-19 (SARS-COV-2): Infoskriv_generell_Biobank_COVID19_rev.pdf

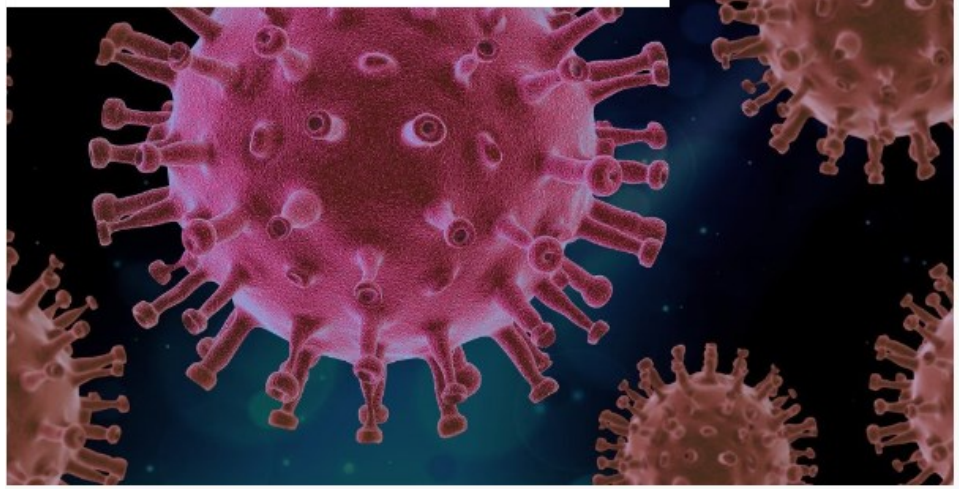
Kalkulator plasmavolum (xls)

Prøver som skal tas:
COVID19prøver-v280820.pdf

BLODBANKEN | OSLO

Blodbanken ønsker kontakt med givere som har gjennomgått COVID-19 (koronavirusinfeksjon)

NYHETER TORSDAG 13. AUGUST 2020, KL 16:53



Blodbanken ønsker å komme i kontakt med blodgivere som har blitt friske etter covid-19-infeksjon. Vi ønsker å måle antistoff mot koronavirus hos dere, med tanke på å donere plasma for bruk i pasientbehandling som en del av NORPLASMA-prosjektet.

Lise Sofie H. Nissen-Meyer
Blodbanken i Oslo

Personer som har gjennomgått infeksjon med covid-19 kan danne beskyttende antistoff mot viruset SARS-CoV2. Overføring av plasma med slike antistoffer ("passiv immunisering") kan hindre alvorlig forløp av sykdommen hos pasienter med infeksjon og kan også beskytte utsatte pasientgrupper eller personell som er utsatt for smitte.

NORPLASMA COVID-19 er et prosjekt for å produsere covid-19-rekonvalesensplasma til pasienter i Norge og innbefatter studier for å evaluere effekt av behandlingen.

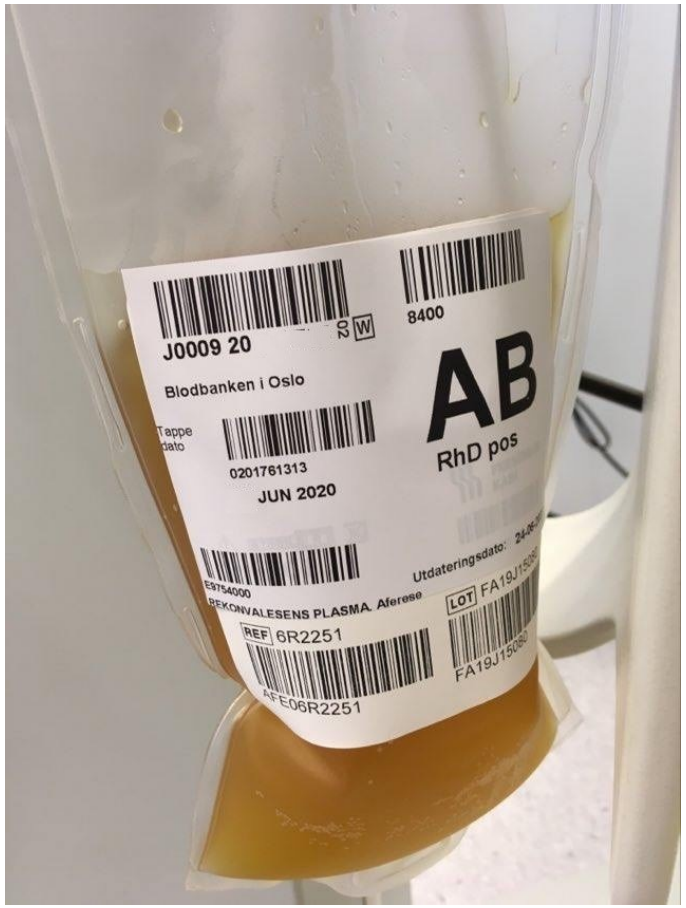
Blodbanken i Oslo ønsker at **etablerte blodgivere** som har gjennomgått

Nasjonal oversikt over rekonvalesensplasma

Blodbank	totalt antall	antall O	antall A	antall B	antall AB	Størrelse enheter (ml)	Oppdatert
BiO	410	225	133	27	25	200-300	30.12.2020
Ahus	180	44	104	24	8	200-300 ml	29.11.2020
St.Olavs	30	16	11	2	1	290	04.12.2020
Ålesund	8	0	8	0	0	290	26.06.2020
Helse Fonna	116	58	46	9	3	300	24.07.2020
Østfold	80	27	48	0	5	300	10.12.2020
UNN	202	72	94	16	20	200-300 ml	16.11.2020
Haukeland	165	64	82	9	10	200-300 ml	26.06.2020
Førde	16	16	0	0	0	300 ml	22.12.2020
SSHF	102	23	64	4	11	200-300 ml	04.01.2021
Innlandet	104	36	62	6	0	200-300 ml	16.12.2020
Stavanger	38	8	16	0	14	300	04.12.2020
Nasjonalt	1451	589	668	97	97		30.12.2020

NORPLASMA COVID-19

Hva er passiv immunisering?



- Definisjon: Overføring av antistoff
  - Hyperimmunglobulin: antiserum
  - Anti-D-profylakse
  - IVIG
  - Rekonvalesensplasma
  - (immunterapi/monoklonale antistoffer)

Paul Erlich, 1893:

1. Behandling må gis så tidlig som mulig
2. Jo mer alvorlig pasientens tilstand er, dess større dose
3. All behandling må inneholde en minimumsdose

Kan rekonvalesensplasma virke mot COVID-19?

- Erfaringer fra SARS- og MERS-epidemiene: Små studier, ikke kontrollgrupper, men lovende funn
- Flere kasuistiske meddelelser under COVID-19-pandemien: Positiv effekt av rekonvalesensplasma
- Observasjonsstudie fra New York, USA: 39 pasienter fikk plasma, 116 kontroller fikk ikke plasma:

  Betydelig positiv effekt på sykelighet og dødelighet hos pasienter som IKKE var intuberte, ingen sikker effekt hos de intuberte

(Altså gunstig å ikke vente for lenge, kfr. Også Erlich, 1893!)

Outline

Abstract
Keywords
INTRODUCTION
Reports of efficacy and safety of convalescent plasma for t...
Reports of efficacy and safety of convalescent plasma for t...
Risks of convalescent plasma therapy
Patient selection
Donor selection
Feasibility
Funding
Conflict of interest
Author's contributions
REFERENCES

Tables (3)

Table 1
Table 2
Table 3

ELSEVIER

Clinical Microbiology and Infection

Available online 11 August 2020

In Press, Journal Pre-proof

Narrative Review

Treatment of COVID-19 with convalescent plasma: lessons from past coronavirus outbreaks

Denise J. Wooding [1], Horacio Bach [2]

https://doi.org/10.1016/j.cmi.2020.0

Abstract

Background

There is currently no treat
Convalescent plasma has b
pandemics, including SAR

Objectives

To summarize the existing
and safety of convalescent
feasibility, and donor and patient selection.

"Most COVID-19 reports described a potential benefit of convalescent plasma on clinical outcomes in severe or critically ill patients with few immediate adverse events."

"… a number of limitations, including the concurrent use of antivirals, steroids, and other treatments, small sample sizes, lack of randomization or control groups, and short follow-up time."

Evidence favouring the efficacy of convalescent plasma for COVID-19 therapy

Michael J. Joyner[1*], Stephen A. Klassen[1], Jonathon W. Senefeld[1], Patrick W. Johnson[2], Rickey E. Carter[2], Chad C. Wiggins[1], Shmuel Shoham[3], Brenda J. Grossman[4], Jeffrey P. Henderson[5,6], James M. Musser[7,8,9], Eric Salazar[7,9], William R. Hartman[10], Nicole M. Bouvier[11,12], Sean T. H. Liu[11,12], Liise-anne Pirofski[13], Sarah E. Baker[1], Noud van

Abstract

To determine the effect of COVID-19 convalescent plasma on mortality, we aggregated patient outcome data from randomized clinical trials, matched control, and case-series studies. Fixed-effects analyses demontrated that hospitalized COVID-19 patients transfused with convalescent plasma exhibited a ~57% reduction in mortality rate (13%) compared to matched-patients receiving standard treatments (25%; OR: 0.43, $P < 0.001$). These data provide evidence favouring the efficacy of human convalescent plasma as a therapeutic agent in hospitalized COVID-19 patients.

The American Journal of PATHOLOGY
Discoveries in Basic and Translational Pathobiology
ASIP American Society for Investigative PATHOLOGY

REGULAR ARTICLE | ARTICLES IN PRESS

Treatment of COVID-19 Patients with Convalescent Plasma Reveals a Signal of Significantly Decreased Mortality

Eric Salazar • Paul A. Christensen • Edward A. Graviss • ... David W. Bernard • Jimmy Gollihar • James M. Musser • Show all authors

Open Access • Published: August 10, 2020 • DOI: https://doi.org/10.1016/j.ajpath.2020.08.001

ABSTRACT
INTRODUCTION
MATERIALS AND METHODS
RESULTS
DISCUSSION
Uncited reference
ACKNOWL

ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, has spread globally, and proven treatments are limited. Transfusion of convalescent plasma collected from donors who have recovered from COVID-19 is among many approaches being studied as potentially efficacious therapy. We are conducting a prospective, propensity score-matched study assessing the efficacy of COVID-19 convalescent plasma transfusion versus standard of care as treatment for severe and/or critical COVID-19. We present here the results of an interim analysis of 316 patients (n=316) enrolled at Houston Methodist hospitals from March 28 to July 6, 2020. Of the 316 transfused patients, 136 met a 28-day outcome and were matched to 251 non-transfused control COVID-19 patients. Matching criteria included age, sex, BMI, comorbidities, and baseline ventilation requirement 48 h from admission, and in a second matching analysis, ventilation status at Day 0. Variability in the timing of transfusion relative to admission and titer of antibodies of plasma transfused allowed for analysis in specific matched cohorts. The analysis showed a significant reduction ($P = 0.047$) in mortality within 28 days, specifically in patients transfused within 72 h of admission with plasma with an anti-spike protein receptor binding domain titer of ≥1:1350. These data suggest that treatment of COVID-19 with high anti-receptor binding domain (RBD) IgG titer convalescent plasma is efficacious in early-disease patients.

Am J Pathol. 2020 Nov 3;S0002-9440(20)30489-2. doi: 10.1016/j.ajpath.2020.10.008.
Online ahead of print.

Significantly decreased mortality in a large cohort of COVID-19 patients transfused early with convalescent plasma containing high titer anti-SARS-CoV-2 spike protein IgG

Eric Salazar [1], Paul A Christensen [2], Edward A Graviss [3], Duc T Nguyen [4], Brian Castillo [2], Jian Chen [2], Bevin Valdez Lopez [5], Todd N Eagar [1], Xin Yi [1], Picheng Zhao [2], John Rogers [2], Ahmed Shehabeldin [2], David Joseph [2], Faisal Masud [6], Christopher Leveque [2], Randall J Olsen [7], David W Bernard [1], Jimmy Gollihar [8], James M Musser [9]

Affiliations + expand

PMID: 33157066 PMCID: PMC7609241 DOI: 10.1016/j.ajpath.2020.10.008

Free PMC article

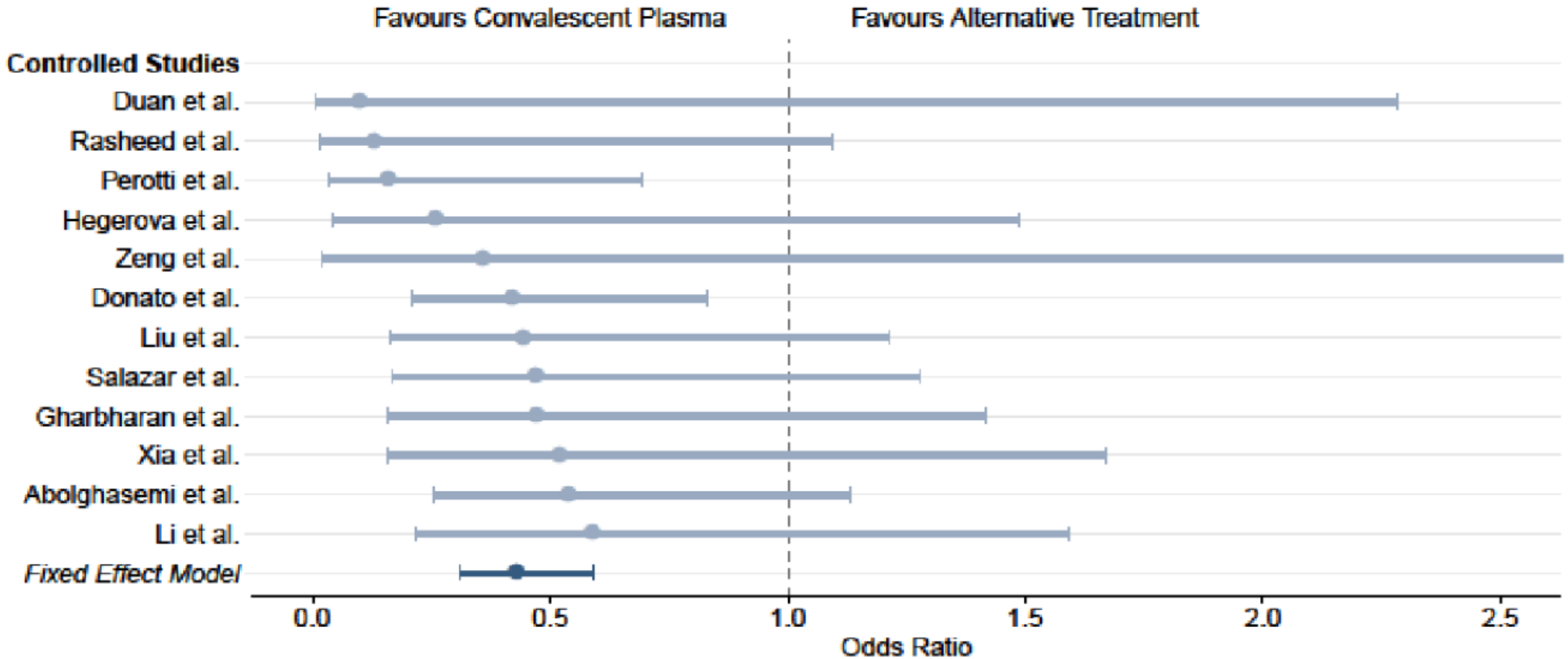
Abstract

Coronavirus disease 2019 (COVID-19) convalescent plasma has emerged as a promising therapy and has been granted emergency use authorization by the U.S. Food and Drug Administration (FDA) for hospitalized COVID-19 patients. We recently reported results from interim analysis of a propensity-score matched study suggesting that early treatment of COVID-19 patients with convalescent plasma containing high titer anti-spike protein receptor binding domain (RBD) IgG significantly decreases mortality. We here present results from 60-day follow up of our cohort of 351 transfused hospitalized patients. Prospective determination of ELISA anti-RBD IgG titer facilitated selection and transfusion of the highest titer units available. Retrospective analysis by the Ortho VITROS IgG assay revealed a median signal/cutoff (S/C) ratio of 24.0 for transfused units, a value far exceeding the recently FDA-required cutoff of 12.0 for designation of high titer convalescent plasma. With respect to altering mortality, our analysis identified an optimal window of 44 hours post-hospitalization for transfusing COVID-19 patients with high titer convalescent plasma. In the aggregate, the analysis confirms and extends our previous preliminary finding that transfusion of COVID-19 patients soon after hospitalization with high titer anti-spike protein RBD IgG present in convalescent plasma significantly reduces mortality.

Randomized controlled studies - summary

Author/ Country (reference)	Patients	Clinical status	Dose of CCP NTAb - titer	Summary finding
Li, L., et al. China, (1)	n=103; n=52 treatment n=51 control	Severe or critically ill	4 to 13 mL/kg	• Better clinical improvement only in the subgroup of severe CCP patients; • Higher clearance of viral load in all CCP patients; • No significant difference in the 28-day mortality; • Non severe allergic/febrile non-haemolytic reaction (n=1); • Possible severe transfusion-associated dyspnoea (n=1); • Early termination of the trial,(no cases for enrolment)- limited power
Gharbharan, A., et al. Netherlands (2)	n = 86 n = 43 treatment n = 43 control	Severe or critically ill	300 ml CCP 1:80	• The trial stopped early because they observed that antibody titers in the recipients were already high at the time of transfusion. • At the time of study stopping No difference in mortality, hospital stay or day-15 disease severity was observed although 14% of CCP patients had died and compared to 26% control that had died • The study may have been underpowered to detect statistically significant clinical benefit at study stopping.
Avendano-Sola, C., et al. Spain (3)	n = 81 n = 38 treatment n = 43 control	Severe	250-300 ml CCP >1:80,	• The trial was stopped after first interim analysis due to the fall in recruitment related to pandemic control. • No patients progressing to mechanical ventilation or death among CCP patients versus 6 out of 43(14%) control patients progressing. • Mortality rates were 0% vs 9.3% at days 15 and 29 for the active and control groups, respectively.
Agarwal A, et al. India (4)	n=464 n = 235 n = 229	Moderate	2x 200 mL of CCP, 24 hours apart, Median 1:40	• CCP was not associated with reduction in mortality or progression to severe COVID-19

The effect of COVID-19 convalescent plasma on mortality – meta analysis



Joyner MJ, Klassen SA, Senefeld J, Johnson PW, Carter RE, Wiggins CC, et al. Evidence favouring the efficacy of convalescent plasma for COVID-19 therapy. medRxiv. 2020:2020.07.29.20162917.

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

A potentially effective treatment for COVID-19: A systematic review and meta-analysis of convalescent plasma therapy in treating severe infectious disease

Mengyao Sun[a,1], Yinghui Xu[a,1], Hua He[a], Li Zhang[b], Xu Wang[a], Qing Qiu[c], Chao Sun[a], Ye Guo[a], Shi Qiu[a], Kewei Ma[a,*]

[a] Cancer Center, The First Hospital of Jilin University, 71 Xinmin Street, Changchun, Jilin 130021, China
[b] Radiology, The First Hospital of Jilin University, 71 Xinmin Street, Changchun, Jilin 130021, China
[c] Academy of Life Sciences, Northeast Normal University, Changchun, Jilin 130024, China

ARTICLE INFO

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Keywords:
Convalescent plasma (CP)
Coronavirus disease 2019 (COVID-19)
Infectious disease
Meta-analysis

ABSTRACT

Background: Convalescent plasma (CP) has been used successfully to treat many types of infectious disease, and has shown initial effects in the treatment of the emerging 2019 coronavirus disease (COVID-19). However, its curative effects and feasibility have yet to be confirmed by formal evaluation and well-designed clinical trials. To explore the effectiveness of treatment and predict the potential effects of CP with COVID-19, studies of different types of infectious disease treated with CP were included in this systematic review and meta-analysis.

Methods: Related studies were obtained from databases and screened according to the inclusion criteria. The data quality was assessed, and the data were extracted and pooled for analysis.

Results: 40 studies on CP treatment for infectious diseases were included. Our study found that CP treatment could reduce the risk of mortality, with a low incidence of adverse events, promote the production of antibodies, lead to a decline in viral load, and shorten the disease course. A meta-analysis of 15 controlled studies showed that there was a significantly lower mortality rate in the group treated with CP (pooled OR = 0.32; 95% CI = 0.19–0.52; $p < 0.001$, $I^2 = 54\%$) compared with the control groups. Studies were mostly of low or very low quality, with a moderate or high risk of bias. The sources of clinical and methodological heterogeneity were identified. The exclusion of heterogeneity indicated that the results were stable.

Conclusions: CP therapy has some curative effect and is well tolerated in treating infectious diseases. It is a potentially effective treatment for COVID-19.

Received: 21 July 2020 | Accepted: 4 August 2020
DOI: 10.1002/jmv.26408

RESEARCH ARTICLE

Convalescent plasma is a clutch at straws i management! A systematic review and met

Soumya Sarkar MD[1] | Kapil D. Soni MD[2] | Puneet Khar

[1]Department of Anaesthesia, Pain Medicine & Critical Care, AIIMS, New Delhi, India
[2]Department of Critical & Intensive Care, JPN Apex Trauma Centre, AIIMS, New Delhi, India

Correspondence
Puneet Khanna, MD, Department of Anaesthesia, Pain Medicine & Critical Care, AIIMS, Ansari Nagar, New Delhi-110029, India.
Email: k.punit@yahoo.com

Abstract

In the absence of definitive therapy for c valescent plasma therapy (CPT) may be a criti conducted to evaluate the impact of CPT in lications reported to date. A robust screening up to 10th July 2020. Randomized controlled series with a control group evaluating the effe with COVID-19 are included for the meta- studies, including two RCTs and five cohort st patients with COVID-19, the use of CPT red 95% CI, 0.25-0.77), increases viral clearanc improves clinically (OR, 2.06; 95% CI, 0.8 to quality (mortality reduction, and viral clea improvement). CPT may be beneficial for r improving clinical conditions in COVID-19 p control trials (RCT) are required to substantia dosage, titre and duration of CPT.

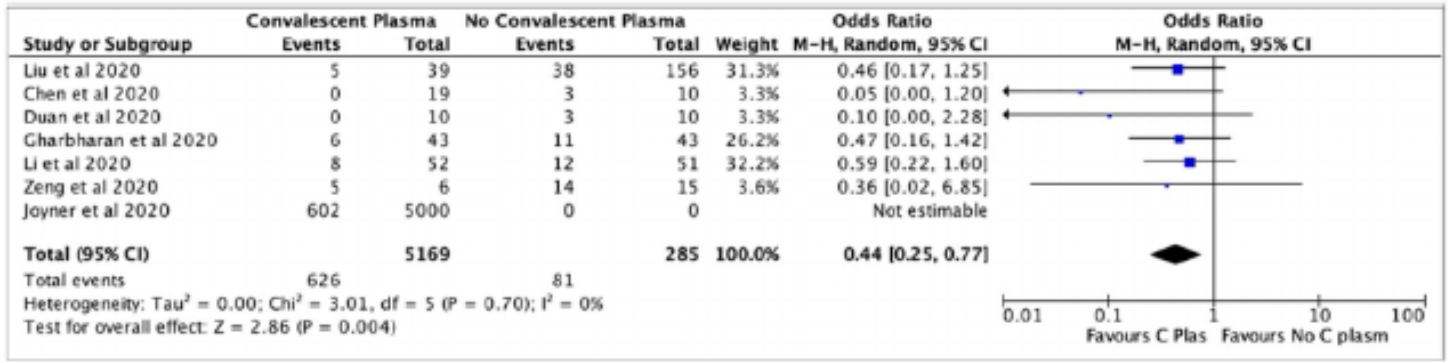

FIGURE 3 The efficacy of convalescent plasma therapy on mortality in COVID-19 patients

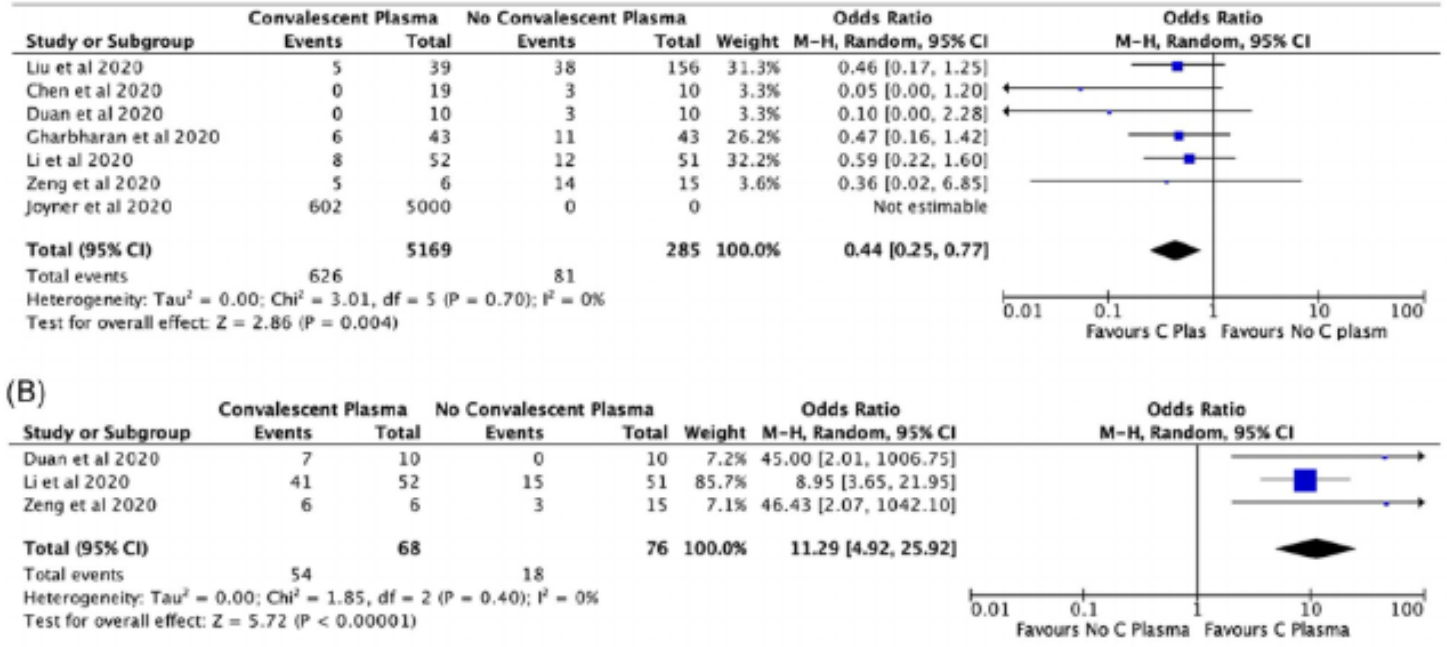

FIGURE 4 A, The impact of convalescent plasma therapy on clinical improvement in COVID-19 patients. B, The effect of convalescent plasma therapy on viral clearance in COVID-19 patients

Agarwal et al, PLACID Trial sammen med en lederartikkel i BMJ

Check for updates

FAST TRACK

Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre randomised controlled trial (PLACID Trial)

Anup Agarwal,[1] Aparna Mukherjee,[1] Gunjan Kumar,[1] Pranab Chatterjee,[1] Tarun Bhatnagar,[2] Pankaj Malhotra,[3] on behalf of the PLACID Trial Collaborators

[1]Clinical Trial and Health Systems Research Unit, Indian Council of Medical Research, V Ramalingaswamy Bhawan, PO Box 4911, Ansari Nagar, New Delhi, 110029, India
[2]ICMR School of Public Health, Indian Council of Medical Research -National Institute of Epidemiology, Chennai, Tamil, India
[3]Department of Internal Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Correspondence to: A Mukherjee, Clinical Trial and Health Systems Research Unit, Indian Council of Medical Research, V Ramalingaswamy Bhawan, PO Box 4911, Ansari Nagar, New Delhi, 110029, India
aparna.sinha.deb@icmr.gov.in
(ORCID 0000-0001-7298-5097)

ABSTRACT

OBJECTIVE
To investigate the effectiveness of using convalescent plasma to treat moderate coronavirus disease 2019 (covid-19) in adults in India.

DESIGN
Open label, parallel arm, phase II, multicentre, randomised controlled trial.

SETTING
39 public and private hospitals across India.

PARTICIPANTS
464 adults (≥18 years) admitted to hospital (screened 22 April to 14 July 2020) with confirmed moderate covid-19 (partial pressure of oxygen in arterial blood/fraction of inspired oxygen (PaO_2/FiO_2) ratio between 200 mm Hg and 300 mm Hg or a respiratory rate of more than 24/min with oxygen saturation 93% or less on room air): 235 were assigned to convalescent plasma with best standard of care (intervention arm)

RESULTS
Progression to severe disease or all cause mortality at 28 days after enrolment occurred in 44 (19%) participants in the intervention arm and 41 (18%) in the control arm (risk difference 0.008 (95% confidence interval −0.062 to 0.078); risk ratio 1.04, 95% confidence interval 0.71 to 1.54).

CONCLUSION
Convalescent plasma was not associated with a reduction in progression to severe covid-19 or all cause mortality. This trial has high generalisability and approximates convalescent plasma use in real life settings with limited laboratory capacity. A priori measurement of neutralising antibody titres in donors and participants might further clarify the role of convalescent plasma in the management of covid-19.

TRIAL REGISTRATION
Clinical Trial Registry of India CTRI/2020/04/024775.

Convalescent plasma is ineffective for covid-19

Lessons from the Placid Trial

Elizabeth B Pathak *president*

Convalescent plasma generated great enthusiasm in the earliest days of the coronavirus disease 2019 (covid-19) pandemic because of a plausible mechanism of action,[1] its 100 year history of use in the treatment of other infectious diseases,[2] and rapid availability from voluntary donors.[3]

In the linked PLACID Trial, Agarwal and colleagues (doi:10.1136/bmj.m3939) evaluated convalescent plasma for the treatment of moderate covid-19 in patients admitted to hospital in India.[4] Strengths of the study included a primary "hard" outcome meaningful to patients, "real world" patient enrollment with no exclusions for comorbidities, careful attention to donor selection and safety screening of donated plasma, post facto quantitative testing of antibody titers in all plasma samples, assessment of secondary patient outcomes, and evaluation of the efficacy of the subsample of plasma

coagulopathies.[5] Despite the presence in plasma of anticoagulation factors such as antithrombin and protein C, the net effect of plasma is prothrombotic.[5] Immunoglobulin therapy, which is derived from whole plasma, is subject to a US Food and Drug Administration warning about the risks of thrombosis, particularly in older patients, those with cardiovascular risk factors, and those with hypercoagulable conditions.[5]

It is now widely recognized that covid-19 is a life threatening thrombotic disorder.[6-8] An excellent recent pathophysiology synthesis concluded that "SARS-CoV-2 not only produces an inflammatory and hypercoagulable state, but also a hypofibrinolytic state not seen with most other types of coagulopathy."[7] Most recently, plasma from convalescent covid-19 patients has been shown to directly cause endothelial cell damage in vitro.[9]

Funn, Agarwal et al

- 464 pas med moderat covid-19 randomisert til plasma/standard of care
- 8 dager fra symptomdebut til inklusjon (6-11)
- 235 pas fikk plasma, 200 ml, 2x med 24 t mellom
- Antistoffer i plasma ikke målt på forhånd
- Ingen forskjell i progresjon til alvorlig sykdom/mortalitet v/28 dgr
- Raskere bedring av dyspnoe og fatigue på dag 7, ingen forskjell for hoste/feber
- SARS-CoV2 RNA negativ på dag 7 signifikant flere i plasmagruppen
- Ingen forskjell mellom de som hadde mottatt plasma med nøytraliserende antistoff sammenlignet med standard of care
- Ingen forskjell i ferritin, CRP, D-dimer eller LD
- Forfatterne innrømmer at deres studie er «underpowered»

Agarwal et al, antistoffanalyser:

- Nearly two thirds (n=161, 64%) of the donors had a neutralising antibody titre of more than 1:20, with a median titre of 1:40 (interquartile range 1:30-1:80).
- Neutralising antibody titres were measured in 418 trial participants; 348 (83%) had detectable neutralising antibodies at enrolment. The median neutralising antibody titre at enrolment was 1:90 (interquartile range 1:30-1:240).
- **We found that participants had higher antibody positivity and median neutralising antibody titres than the donors of convalescent plasma.**

Lederartikkel av Elizabeth B Pathak

- Omtaler PLACID-studien uten å adressere antistoffproblemet
- Går over til å diskutere plasmas protrombotiske effekt
  - Rauch et al fant at plasma fra COVID-19-pasienter ga endotelskade, men mindre med rekonvalesenstid. Plasma fra 21 ±7 dgr etter utskrivelse fra ICU var «partially restored»
  - Joyner et als rapport om sikkerhet ved 20.000 plasmatransfusjoner hadde ekskludert data om 88 % av «cardiac events» og 66 % av «thrombotic events» fordi disse ble bedømt til å ikke være relatert til transfusjon
  - Trombotiske hendelser ble ikke rapportert i PLACID-studien

Anbefalinger for videre studier av rekonvalesensplasma ved COVID-19:

1. Mulig skadeeffekt av plasma bør undersøkes, særlig protrombotisk effekt
2. Kun donorplasma med nøytraliserende antistoff bør gis i studier
3. Dobbelblindet design med «sham procedure controls» bør brukes
4. Nonimmunt plasma bør ikke brukes som kontroll-intervensjon

Men hva med antistoffnivået hos mottaker?

Kommentarer til BMJ etter Agarwal et al https://www.bmj.com/content/371/bmj.m3939/rapid-responses

- Tuccori, Focosi, Menichetti (Italia):
  - Påpeker problemet med at pasienter behandles med lavere antistoffkonsentrasjoner enn de har selv. Det er fremdeles relevant å undersøke behandling med høyere antistoffnivå enn pasientene har selv
  - Bestrider Pathaks utsagn om at «net effect of plasma is prothrombotic»
- Fisher, Pavel, Mildiner, Malnick (Israel):
  - Agarwal hadde beregnet at de trengte 226 deltakere i hver arm, men beregnet at bare 160 av deltakerne faktisk fikk nøytraliserende antistoff.
  - Antall dager til inklusjon var for høyt (8)
- Wig, Rashid, Mittal (India):
  - Påpeker at 83 % av pasientene allerede hadde nøytr. antistoffer, således for sen behandling
  - En stor andel pasienter er ikke analysert mhp dyspne/hoste/feber etter 7 dager
  - Donorene hadde for lave antistofftiter (1:40) og subgruppeanalysene er utført på for små grupper
  - Kritiserer bruken av statistiske metoder og at man forventet en effekt på 50 % reduksjon i primary outcome
  - Reagerer på at steroider ble gitt bare til 64 % i intervensjonsarmen
- Zavascki, Falci (Brasil):
  - For unge pasienter (41-60 år) til å sammenligne med andre studier; høy andel diabetes og lav BMI
  - Få pasienter fikk O2-terapi selv om de trengte det
  - Spørsmålstegn ved «standard of care» i studien
- Lipworth, Rui, Kuo, Chan (UK):
  - Påpeker de samme problemene med antistoff, underpowering og for sen behandling.

November 2020: Simonovich et al, NEJM

- Argentinsk RCT (228/105 pas) viste ingen effekt på alvorlig syke pasienter (>90 % fikk O2 og glukokortikoider ved inklusjon).
  - **54 %** av pas har antistoffer på forhånd i denne studien, median titer 1:50
  - Median tid fra symptomdebut til inklusjon også her 8 dager

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia

V.A. Simonovich, L.D. Burgos Pratx, P. Scibona, M.V. Beruto, M.G. Vallone, C. Vázquez, N. Savoy, D.H. Giunta, L.G. Pérez, M..L. Sánchez, A.V. Gamarnik, D.S. Ojeda, D.M. Santoro, P.J. Camino, S. Antelo, K. Rainero, G.P. Vidiella, E.A. Miyazaki, W. Cornistein, O.A. Trabadelo, F.M. Ross, M. Spotti, G. Funtowicz, W.E. Scordo, M.H. Losso, I. Ferniot, P.E. Pardo, E. Rodriguez, P. Rucci, J. Pasquali, N.A. Fuentes, M. Esperatti, G.A. Speroni, E.C. Nannini, A. Matteaccio, H.G. Michelangelo, D. Follmann, H.C. Lane, and W.H. Belloso, for the PlasmAr Study Group*

ABSTRACT

BACKGROUND

Convalescent plasma is frequently administered to patients with Covid-19 and has been reported, largely on the basis of observational data, to improve clinical outcomes. Minimal data are available from adequately powered randomized, controlled trials.

METHODS

We randomly assigned hospitalized adult patients with severe Covid-19 pneumonia in a 2:1 ratio to receive convalescent plasma or placebo. The primary outcome was the patient's clinical status 30 days after the intervention, as measured on a six-point ordinal scale ranging from total recovery to death.

RESULTS

A total of 228 patients were assigned to receive convalescent plasma and 105 to receive placebo. The median time from the onset of symptoms to enrollment in the trial was 8 days (interquartile range, 5 to 10), and hypoxemia was the most frequent severity criterion for enrollment. The infused convalescent plasma had a median titer of 1:3200 of total SARS-CoV-2 antibodies (interquartile range, 1:800 to 1:3200). No patients were lost to follow-up. At day 30 day, no significant difference was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale (odds ratio, 0.83 (95% confidence interval [CI], 0.52 to 1.35; P=0.46). Overall mortality was 10.96% in the convalescent plasma group and 11.43% in the placebo group, for a risk difference of −0.46 percentage points (95% CI, −7.8 to 6.8). Total SARS-CoV-2 antibody titers tended to be higher in the convalescent plasma group at day 2 after the intervention. Adverse events and serious adverse events were similar in the two groups.

CONCLUSIONS

No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo. (PlasmAr ClinicalTrials.gov number, NCT04383535.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Simonovich at the Clinical Pharmacology Section, Hospital Italiano de Buenos Aires, Juan D. Perón 4190 (C1181ACH), Ciudad Autónoma de Buenos Aires, Argentina, or at ventura.simonovich@hospitalitaliano.org.ar.

*A complete list of the PlasmAr Study Group members is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 24, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2031304

Libster et al

- Argentinsk RCT på eldre pasienter viste **signifikant redusert utvikling av alvorlig respirasjonssykdom når behandlet innen 3 døgn etter symptomdebut**.
  - 13/80 pasienter i intervensjonsgruppen mot 25/80 i kontrollgruppen
- **Høye antistofftitre**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults

R. Libster, G. Pérez Marc, D. Wappner, S. Coviello, A. Bianchi, V. Braem, I. Esteban, M.T. Caballero, C. Wood, M. Berrueta, A. Rondan, G. Lescano, P. Cruz, Y. Ritou, V. Fernández Viña, D. Álvarez Paggi, S. Esperante, A. Ferreti, G. Ofman, Á. Ciganda, R. Rodriguez, J. Lantos, R. Valentini, N. Itcovici, A. Hintze, M.L. Oyarvide, C. Etchegaray, A. Neira, I. Name, J. Alfonso, R. López Castelo, G. Caruso, S. Rapelius, F. Alvez, F. Etchenique, F. Dimase, D. Alvarez, S.S. Aranda, C. Sánchez Yanotti, J. De Luca, S. Jares Baglivo, S. Laudanno, F. Nowogrodzki, R. Larrea, M. Silveyra, G. Leberzstein, A. Debonis, J. Molinos, M. González, E. Perez, N. Kreplak, S. Pastor Argüello, L. Gibbons, F. Althabe, E. Bergel, and F.P. Polack, for the Fundación INFANT–COVID-19 Group*

ABSTRACT

BACKGROUND

Therapies to interrupt the progression of early coronavirus disease 2019 (Covid-19) remain elusive. Among them, convalescent plasma administered to hospitalized patients has been unsuccessful, perhaps because antibodies should be administered earlier in the course of illness.

METHODS

We conducted a randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in older adult patients within 72 hours after the onset of mild Covid-19 symptoms. The primary end point was severe respiratory disease, defined as a respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both. The trial was stopped early at 76% of its projected sample size because cases of Covid-19 in the trial region decreased considerably and steady enrollment of trial patients became virtually impossible.

RESULTS

A total of 160 patients underwent randomization. In the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%. A modified intention-to-treat analysis that excluded 6 patients who had a primary end-point event before infusion of convalescent plasma or placebo showed a larger effect size (relative risk, 0.40; 95% CI, 0.20 to 0.81). No solicited adverse events were observed.

CONCLUSIONS

Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19. (Funded by the Bill and

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Polack at Fundación INFANT, Gavilan 94, Buenos Aires (1406), Argentina, or at fpolack@infant.org.ar.

*The Fundación INFANT–COVID-19 Group members are listed in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Drs. Libster and Pérez Marc contributed equally to this article.

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CCP til utvalgte pasienter?

- As a proof of concept, COVID-19 convalescent plasma represents an interesting approach in B-cell–depleted patients with protracted COVID-19.
- COVID-19 convalescent plasma induce a decrease in temperature and inflammatory parameters within 1 week associated with oxygen weaning.

blood® Brief Report

CLINICAL TRIALS AND OBSERVATIONS

Convalescent plasma therapy for B-cell–depleted patients with protracted COVID-19

Thomas Hueso,[1,2] Cécile Pouderoux,[3] Hélène Péré,[4,5] Anne-Lise Beaumont,[6] Laure-Anne Raillon,[3] Florence Ader,[3,7] Lucienne Chatenoud,[8,9] Déborah Eshagh,[10] Tali-Anne Szwebel,[10] Martin Martinot,[11] Fabrice Camou,[12] Etienne Crickx,[13] Marc Michel,[13] Matthieu Mahevas,[13] David Boutboul,[14,15] Elie Azoulay,[16] Adrien Joseph,[16] Olivier Hermine,[17,18] Claire Rouzaud,[19] Stanislas Faguer,[20] Philippe Petua,[21] Fanny Pommeret,[22] Sébastien Clerc,[23] Benjamin Planquette,[23] Fatiha Merabet,[24] Jonathan London,[25] Valérie Zeller,[25] David Ghez,[1] David Veyer,[4,26] Amani Ouedrani,[8,9] Pierre Gallian,[27,28] Jérôme Pacanowski,[6] Arsène Mékinian,[29] Marc Garnier,[30] France Pirenne,[28,31] Pierre Tiberghien,[28,32] and Karine Lacombe[6,33]

[1]Hematology Department, Gustave Roussy, Villejuif, France; [2]Paris-Sud University, Paris-Saclay University, Le Kremlin-Bicêtre, France; [3]Infectious Diseases Department, Croix Rousse Hospital, Hospices Civils de Lyon, Lyon, France; [4]Laboratoire de Virologie, Hôpital Européen Georges Pompidou, Assistance Publique–Hôpitaux de Paris (AP-HP), Paris, France; [5]Université de Paris, INSERM U970, Paris Cardiovascular Research Center, Paris, France; [6]Infectious Diseases Department, Saint-Antoine Hospital, AP-HP, Paris, France; [7]Université Claude Bernard Lyon 1, INSERM 1111, Centre International de Recherche en Infectiologie UCBL1, Lyon, France; [8]Paris University, Institut Necker-Enfants Malades, CNRS UMR 8253 and INSERM UMR1151, Hôpital Necker-Enfants Malades, Paris, France; [9]Laboratoire d'immunologie Biologique, Hôpital Necker-Enfants Malades, Paris, France; [10]Internal Medicine Department, Cochin Hospital, AP-HP, Paris, France; [11]Infectious Diseases Department, Hôpitaux Civils de Colmar, Colmar, France; [12]Intensive Care and Infectious Diseases Department, Saint-André Hospital, Bordeaux, France; [13]Internal Medicine Department, Centre National de Référence des Cytopénies Auto-Immunes de l'Adulte, Centre Hospitalier Universitaire Henri-Mondor, AP-HP, Université Paris Est Créteil, Créteil, France; [14]Department of Clinical Immunology, Hôpital Saint-Louis Hospital, AP-HP, Paris, France; [15]Laboratory of Lymphocyte Activation and Susceptibility to EBV Infection, Imagine Institute, INSERM, Paris, France; [16]Intensive Care Unit, Hôpital Saint-Louis, AP-HP, Paris Diderot Sorbonne University, Paris, France; [17]Laboratory of Molecular Mechanisms of Hematologic Disorders and Therapeutic Implications, Imagine Institute, Paris, France; [18]Department of Clinical Hematology, Hôpital Necker-Enfants-Malades, Paris, France; [19]Infectious Diseases Department, Necker-Enfants Malades Hospital, AP-HP, Paris, France; [20]Département de Néphrologie et Transplantation d'Organes, Centre de Référence des Maladies Rénales Rares, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [21]Intensive Care Unit, Tarbes Hospital, Tarbes, France; [22]Oncology Department, Gustave Roussy, Villejuif, France; [23]Respiratory Diseases Intensive Care Unit, Hôpital Européen Georges Pompidou, AP-HP, Paris, France; [24]Hematology Department, Versailles Hospital, Versailles, France; [25]Department of Internal Medicine and Infectious Diseases, Hôpital Diaconesses Croix Saint-Simon, Paris, France; [26]Université de Paris and Sorbonne Université, INSERM, Centre de Recherche des Cordeliers, Functional Genomics of Solid Tumors (FunGeST), Paris, France; [27]Unité des Virus Émergents (UVE) (Aix-Marseille Université-Institut de recherche pour le développement 190-INSERM 1207-IHU Méditerranée Infection), Marseille, France; [28]Etablissement Français du Sang, La Plaine St-Denis, France; [29]Sorbonne Université, Internal Medicine Department, Inflammation-Immunopathology-Biotherapy Department (DMU i3D), Saint-Antoine Hospital, AP-HP, Paris, France; [30]Sorbonne University, GRC 29, AP-HP, DMU DREAM, Anesthesiology and Intensive Care Department, Saint-Antoine Hospital, AP-HP, Paris, France; [31]Institut Mondor de Recherche Biomédicale, Unité 955, Equipe 2: Transfusion et Maladies du Globule Rouge, INSERM, Etablissement Français du Sang, Université Paris-Est Créteil, Créteil, France; [32]UMR 1098 RIGHT INSERM Université de Franche-Comté Etablissement Français du Sang, Besançon, France; and [33]Sorbonne University, INSERM IPLESP, AP-HP, Paris, France

KEY POINTS

- As a proof of concept, COVID-19 convalescent plasma represents an interesting approach in B-cell–depleted patients with protracted COVID-19.
- COVID-19 convalescent plasma induces a decrease in temperature and inflammatory parameters within 1 week associated with oxygen weaning.

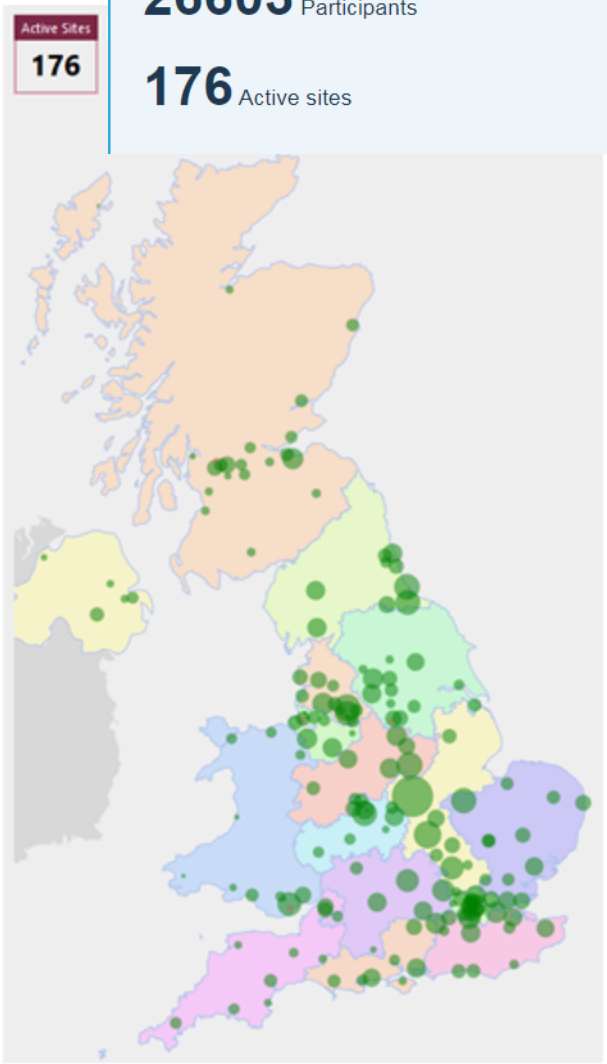
Anti-CD20 monoclonal antibodies are widely used for the treatment of hematological malignancies or autoimmune disease but may be responsible for a secondary humoral deficiency. In the context of COVID-19 infection, this may prevent the elicitation of a specific SARS-CoV-2 antibody response. We report a series of 17 consecutive patients with profound B-cell lymphopenia and prolonged COVID-19 symptoms, negative immunoglobulin G (IgG)-IgM SARS-CoV-2 serology, and positive RNAemia measured by digital polymerase chain reaction who were treated with 4 units of COVID-19 convalescent plasma. Within 48 hours of transfusion, all but 1 patient experienced an improvement of clinical symptoms. The inflammatory syndrome abated within a week. Only 1 patient who needed mechanical ventilation for severe COVID-19 disease died of bacterial pneumonia. SARS-CoV-2 RNAemia decreased to below the sensitivity threshold in all 9 evaluated patients. In 3 patients, virus-specific T-cell responses were analyzed using T-cell enzyme-linked immunospot assay before convalescent plasma transfusion. All showed a maintained SARS-CoV-2 T-cell response and poor cross-response to other coronaviruses. No adverse event was reported. Convalescent plasma with anti–SARS-CoV-2 antibodies appears to be a very promising approach in the context of protracted COVID-19 symptoms in patients unable to mount a specific humoral response to SARS-CoV-2. (*Blood*. 2020;136(20):2290-2295)

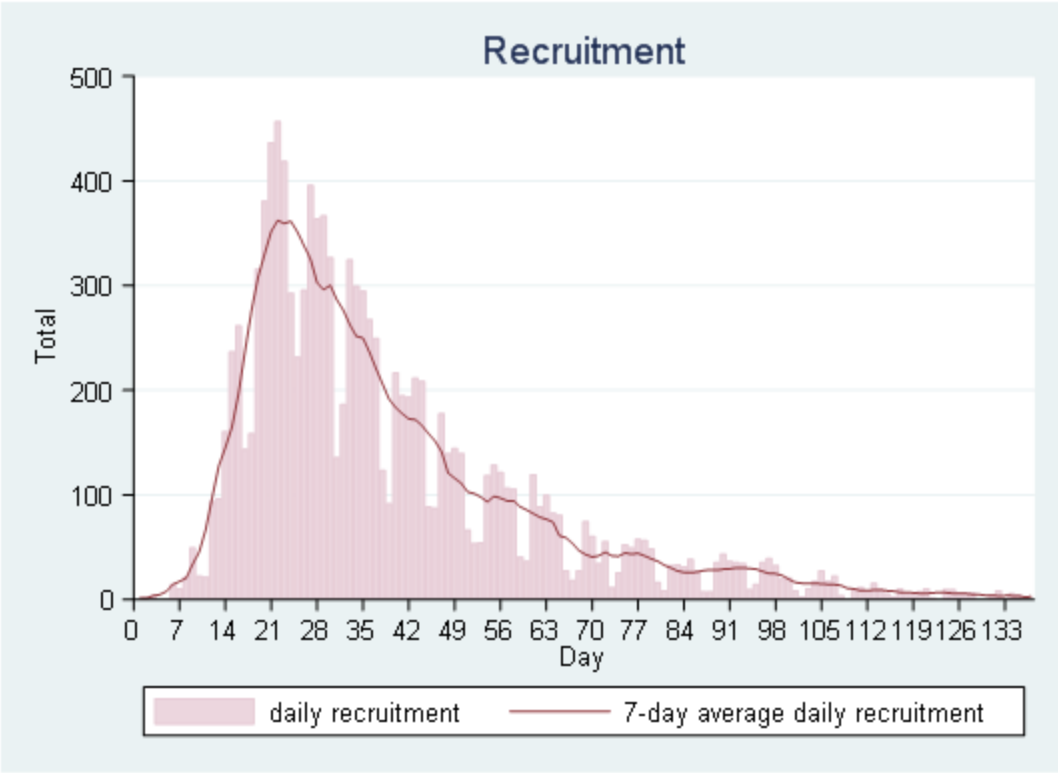
Recruitment by site and by time

RECOVERY
Randomised Evaluation of COVID-19 Therapy

26603 Participants

176 Active sites





RECOVERY trial investigators

8 January 2021

Dear Colleagues

Convalescent plasma

Recruitment of patients requiring invasive mechanical ventilation or extra-corporal membranous oxygenation (ECMO) to the convalescent plasma arm should be paused immediately. The study randomisation system now enforces this exclusion.

The Data Monitoring Committee strongly encouraged continued recruitment of all other eligible patients to the convalescent plasma comparison. Thus recruitment of patients requiring non-invasive ventilation (e.g. CPAP, high flow oxygen, other forms of non-invasive ventilation), oxygen, or no respiratory support remains open.

yesterday (7th January). We have appended a copy of their letter. The DMC will review the situation at their next meeting on 14th January.

Oppsummering litteratur per idag

- Sannsynligvis mest effekt av rekonvalesensplasma når gitt **tidlig** og med antistoffer **i høy dose**
- Pasienter som allerede selv har dannet antistoffer vil i liten grad ha nytte av det
- Kan hindre progresjon til alvorlig sykdom hos eldre
- Kan ha effekt hos pasienter med B-cellesvikt/som ikke danner antistoff selv
- Vi venter på resultatene fra Recovery Trial (> 10 000 pas i plasmaarmen)

NORPLASMA COVID-19

Er plasmatransfusjon trygt?

- Vanlige blodgiverkriterier brukes, vanlige testrutiner og tillegg av anti-HLA og a-HNA hos kvinnelige givere og mannlige transfunderte givere
- Publikasjon fra USA (20 000 pasienter) viser at sikkerhetsprofilen for transfusjon av rekonvalesensplasma er som for ordinært plasma
  - Bivirkninger i form av urticaria og andre lette plager kan forventes til 1%. TRALI eller TACO kan forventes i ca 0,1% av transfusjonene
  - NB! «Cardiac/thrombotic events» i stor grad tatt ut av regnestykket og betraktet som «ikke transfusjonsrelaterte»
- Forsiktighet hos pasienter med IgA- eller haptoglobin-mangel
- OBS! Volumoverbelastning kan gi TACO – tilpass transfusjonshastighet!
- Plasma fra friske blodgivere regnes ikke for å være protrombotisk

Dosering av rekonvalesensplasma

- Det er ingen veldefinert dosering av rekonvalesensplasma
- Ulike protokoller anbefaler fra 1-3 enheter
- De ulike enhetene har ulikt innhold av antistoff men vi er straks klare med en cut-off for antistoffinnhold
- Det må derfor vurderes utfra klinisk tilstand, pasienten høyde og vekt om man skal transfundere 1 eller 2 enheter initialt (samt volum på enhet)
- Et annet mål kan være: Dersom man ikke oppnår fjerning av virus etter en transfusjon, gi tilleggstransfusjon senere
- Kontakt gjerne lokal spesialist i immunologi og transfusjonsmedisin for forhold knyttet til transfusjon av rekonvalesensplasma

NORPLASMA COVID-19

Utfordring

Hvilke antistoff virker?

NØYTRALISERENDE ANTISTOFF

TOTALANTISTOFF

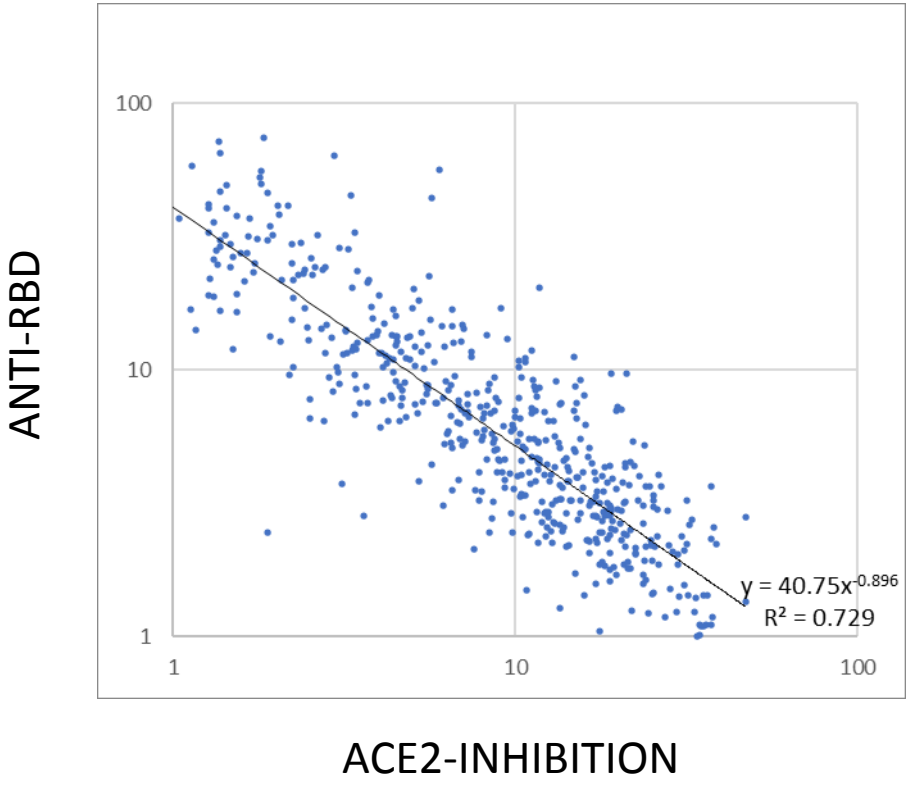
Vi vil bruke enheter med påviste nøytraliserende antistoff, men også enheter med høy evne til inhibisjon av ACE-binding og høy konsentrasjon av totalantistoff

Monitoreringsstudien kan her gi verdifull informasjon ved at alle enheter som er transfundert vil bli grundig undersøkt i ettertid med hensyn på ulike antistoff-spesifisiteter

MIK	IMM (RBD/NC)	Nøytr.AB
21,1	8,9/16,2	10/30
84,6	35,8/99,3	
30,3	grense: 6,7/9,7	0
67,1	6,2/13,7	10
131	8,7/41,2	
25	6,1/26,2	0
90,3	7,3/36/7	
32,7	14,4/17	10
81,8	19,1/75,3	
8,17	usikker: 8,5/4,5	
58,9	11,3/31,1	10/5
133	30,5/41,1	60/80
41,6	51,8/17,2	
53,5	usikker: 4,3/2,0	
70,7	42,5/14,3	
124	70,3/28,8	
44,2	30,9/10,1	

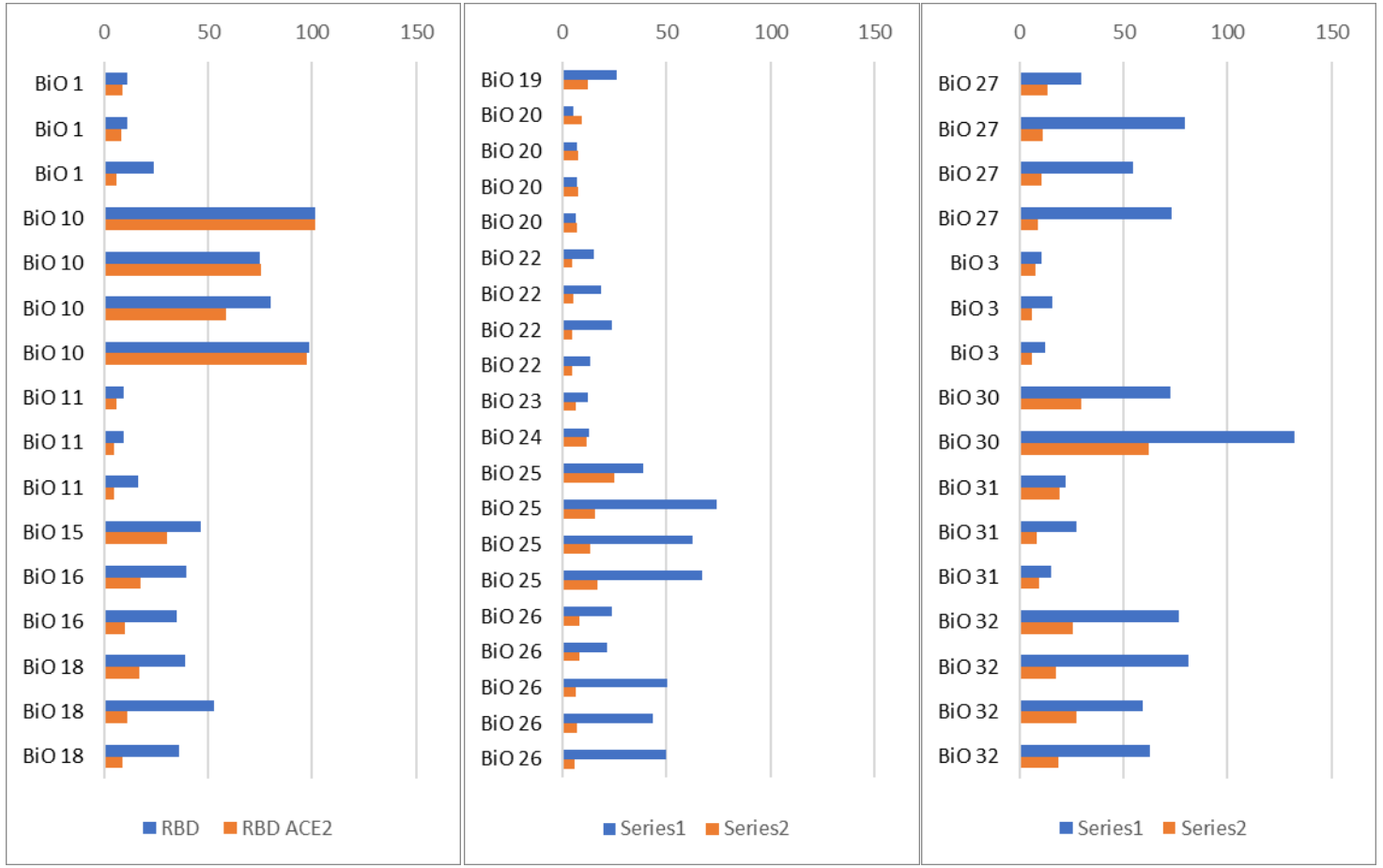
Rød skrift: utgår, blå skrift: avh av nøytralisasjon og inhibisjonsresultat

Correlation between anti-RBD and ACE2 inhibition



535 samples in one experiment
-single dilution (Ab: 1:1000/ACE2: 1:100)

Selection of donors with high titers and ACE2 inhibition capacity

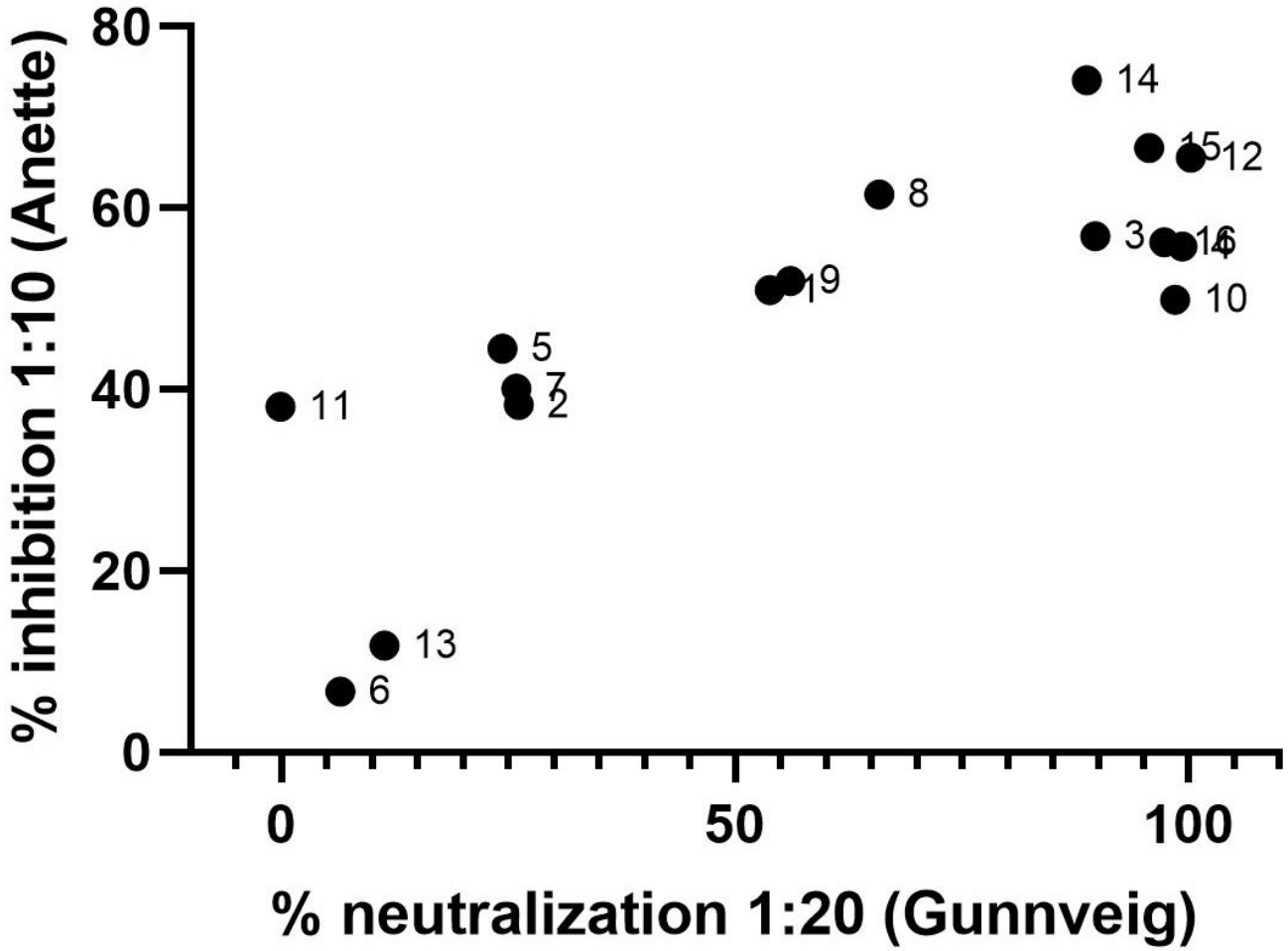


RBD antibody signal

500/ACE2 signal

Reproducible

Correlation between ACE2 inhibition and SARS-CoV-2 neutralization



The three-step procedure

1. **Anti-RBD and NP: ELISA and ARRAY**

2. **ACE2 inhibition: ELISA and ARRAY**

3. **Virus neutralization: cellular assay**

NORPLASMA COVID-19

Helsedirektoratets oppdrag

I brev av 20.04.20 og 02.07.20:

- Blodbankene skal gjøre rekonvalesensplasma tilgjengelig for pasientene
- Rekonvalesensplasma regnes som utprøvende behandling, det vil si at pasienten må samtykke og dette må journalføres
- Det oppfordres til deltakelse i kliniske studier (randomisert behandlingsstudie på utvalgte sykehjem og monitoreringsstudie for alle sykehus og sykehjem med transfusjonskompetanse)

NORPLASMA COVID-19

Monitoreringsstudie MONITOR

Monitoreringsstudien MONITOR er en studie der vi registrerer data om pasienter og rekonvalesensplasmaenhetene på en systematisk måte for å vurdere sikkerhet og effekter. Effekter påvises gjennom de tilleggsundersøkelser som tas, og ved bruk av relevant kontrollgruppe.

Intet ønske om å konkurrere med NOR Solidarity-studien.

Fra ultimo oktober samarbeid med Norwegian SARS-COV2-study (ISARIC): pasienter som får immunmodulerende behandling v/covid-19

NORPLASMA COVID-19

Status Monitor/Norw.SARS-CoV-2 study januar 2021

- Ca 25 pasienter har fått rekonvalsensplasma ved OUS, Haugesund, Ålesund, Ahus og Sørlandet sykehus.
- Muntlig hørt at de fleste pasientene er rekruttert til studiene.
- Data fra 3 pas er lagt inn i Ledidi.
- Gjennomført informasjonsmøter med Ahus, SSHF, Telemark, Østfold og Innlandet
- Signaler fra Vestre Viken, Tromsø og Vestfold at klinikerne ikke er interessert og ikke vil behandle med plasma
- Norsk Forening for Infeksjonsmedisin har tatt rekonvalesensplasma inn i sine anbefalinger: «Konvalesentplasma kan være aktuelt hos pasienter med kjent immunsvikt som ikke selv utvikler antistoff mot Covid-19»

NORPLASMA COVID-19

MONITOR-Blodbankens oppgaver

- Blodbanken utleverer rekonvalesensplasma og sammen med plasmaet vanlig transfusjonsjournal, informasjonsbrev og konvolutt med relevante papirer knyttet til deltakelse i monitoreringsstudien
- Blodbanken har lokalt lederansvar for studien, med mindre annet ikke er bestemt
- Blodbanken fører liste over alle pasienter som mottar plasma, og hvilke pasienter som deltar i studien
- Blodbanken samler inn de kliniske opplysningene og videresender disse til nasjonal studieledelse, sammen med opplysninger om enhetene som er transfundert

NORPLASMA COVID-19

MONITOR - Klinikernes oppgave

- Før studien: Rekvirere rekonvalesensplasma og sørge for å dokumentere at pasientens samtykke til transfusjon journalføres
- Rekruttere pasientene til studien og innhente samtykke
  - Samtykke fra pasient til deltakelse i studien skal ikke innhentes av den lege som har rekvirert behandlingen
- Eventuelt inkludere pasientene i ISARIC-studien istedenfor
- Fylle inn de kliniske opplysninger og sørge for at ekstraprøver blir tatt, slik det fremgår av dokumentene som leveres med plasmaet
  - Disse gjennomgås i de neste bildene:

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1. INKLUSJON:

☐ Samtykke innhentet og dokumentert i journal. Dato:

Behandlingssenter:

Blodbankens ISBT-nummer (fire første siffer):

Blodbankens løpenummer:

Fødselsdato : *(dd.mm.yyyy)*

Kjønn: Mann / Kvinne

Symptomdebut: *(dd.mm.yyyy)*

Innleggelsesdato: *(dd.mm.yyyy)*

Dokumentert SARS-CoV-2: *(dd.mm.yyyy)*

Høyde: _____ cm

Vekt: _____ kg

***Komorbiditet*:**

☐ Astma/KOLS	☐ Koronarsykdom	☐ Hjertesvikt
☐ Hypertensjon	☐ Kronisk nyresvikt	☐ Diabetes
☐ Aktiv kreftsykdom	☐ Immunsuppresjon	☐ Revmatisk sykdom
☐ Leversykdom/cirrhose		

Clinical frailty score (*Funksjonsstatus 4 uker før innleggelse*)

Se veiledning/scoringsskjema side 7

☐ **1** - Veldig sprek.	☐ **2** - Sprek	☐ **3** - Klarer seg bra
☐ **4** - Sårbar	☐ **5** - Lett skrøpelig	☐ **6** - Moderat skrøpelig
☐ **7** - Alvorlig skrøpelig	☐ **8** - Svært alvorlig skrøpelig	☐ **9** - Terminalt syk

Pågående sykdomsrettet behandling mot COVID-19

☐ Kortikosteroider Preparat/dose:

☐ Antivirale agens Preparat/dose:

☐ Immunmodulerende Preparat/dose:

☐ Inkludert annen behandlingsstudie. Spesifiser:

Ved transfusjon (dag 0), dag 1, 5 og 10

2. KLINISK EVALUERING, FØRSTE TRANSFUSJONSDAG (DAG +0)

Lokalisasjon: ☐ Sengepost ☐ Intensivavdeling

Status før transfusjon:

Temp: ___°C **Puls**: ____ bpm **Blodtrykk**: ____ /____ mmHg

SaO2: ____% **O2-tilskudd**: _____ l/min **Resp.frekv.**: ____ /min

O2-tilførsel: ☐Nasal ☐ Maske ☐ CPAP/NIV ☐ Respirator

Hvis NIV/respirator: FiO2: ____% PaO2: _____ kPa

SARS-CoV-2 mikrobiologi/serologi tatt før transfusjon:

Oropharynx	☐ Pos. ☐ Neg. ☐ Ikke utført
Blod PCR	☐ Pos. ☐ Neg. ☐ Ikke utført
Serologi	☐ IgM+ ☐ IgG+ ☐ Ikke utført

Antall plasmaenheter rekvirert:

Transfusjonskomplikasjoner: ☐ Ja ☐ Nei

(*Hvis Ja, vennligst fyll ut transfusjonsjournal*)

*Status **etter** transfusjon:*

Temp: ___°C **Puls**: ____ bpm **Blodtrykk**: ____ /____ mmHg

SaO2: ____% **O2-tilskudd**: _____ l/min **Resp.frekv.**: ____ /min

O2-tilførsel: ☐Nasal ☐ Maske ☐ CPAP/NIV ☐ Respirator

Hvis NIV/respirator: FiO2: ____% PaO2: _____ kPa

6. KLINISK STATUS, UTREISEDAG/DØD

Lokalisasjon: ☐ Sengepost ☐ Intensivavdeling

Status:

☐ Utreise hjem, selvhjulpen ☐ Utreise hjem, kommunal hjelp

☐ Utreise institusjon ☐ Død i institusjon

Dato utskrevet/død: *dd.mm.yyyy*

Status morgenvisitt, hvis målt:

Temp: ___°C **Puls**: ____ bpm **Blodtrykk**: ____ /____ mmHg

SaO2: ____% **O2-tilskudd**: _____ l/min **Resp.frekv.**: ____ /min

O2-tilførsel: ☐Nasal ☐ Maske ☐ CPAP/NIV ☐ Respirator

Hvis NIV/respirator: FiO2: ____% PaO2: _____ kPa

Oropharynx PCR	**Blod PCR**	**Serologi**
☐ Pos. ☐ Neg. ☐ Ikke utført	☐ Pos. ☐ Neg. ☐ Ikke utført	☐ IgM+ ☐ IgG+ ☐ Ikke utført

7. BIOKJEMI

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	Dag +0 (transfusjon)	Dag +1	Dag+ 5	Dag +10	Utskr./Død
Hemoglobin					
LPK (x10^6)					
Nøytrofile					
Lymfocytter					
Monocytter					
Eosinofile					
Trombocytter					
CRP					
Prokalsitonin					
INR					
APTT					
Fibrinogen					
Ferritin					
D-dimer					
ALAT					
ALP					
LD					
Kreatinin					
Na					
K					
Troponin T					

8. RADIOLOGI

Radiologiske undersøkelser utføres kun på klinisk indikasjon

	Røntgen thorax	**CT thorax**
Dato:	☐ Infiltrater Kvadranter affisert (0-4): ____ ☐ Pleuravæske	☐ Infiltrat/konsolidering ☐ Mattglassfortetninger ☐ Pleuraeffusjon
Dato:	☐ Infiltrater Kvadranter affisert (0-4): ____ ☐ Pleuravæske	☐ Infiltrat/konsolidering ☐ Mattglassfortetninger ☐ Pleuraeffusjon
Dato	☐ Infiltrater Kvadranter affisert (0-4): ____ ☐ Pleuravæske	☐ Infiltrat/konsolidering ☐ Mattglassfortetninger ☐ Pleuraeffusjon
Dato:	☐ Infiltrater Kvadranter affisert (0-4): ____ ☐ Pleuravæske	☐ Infiltrat/konsolidering ☐ Mattglassfortetninger ☐ Pleuraeffusjon

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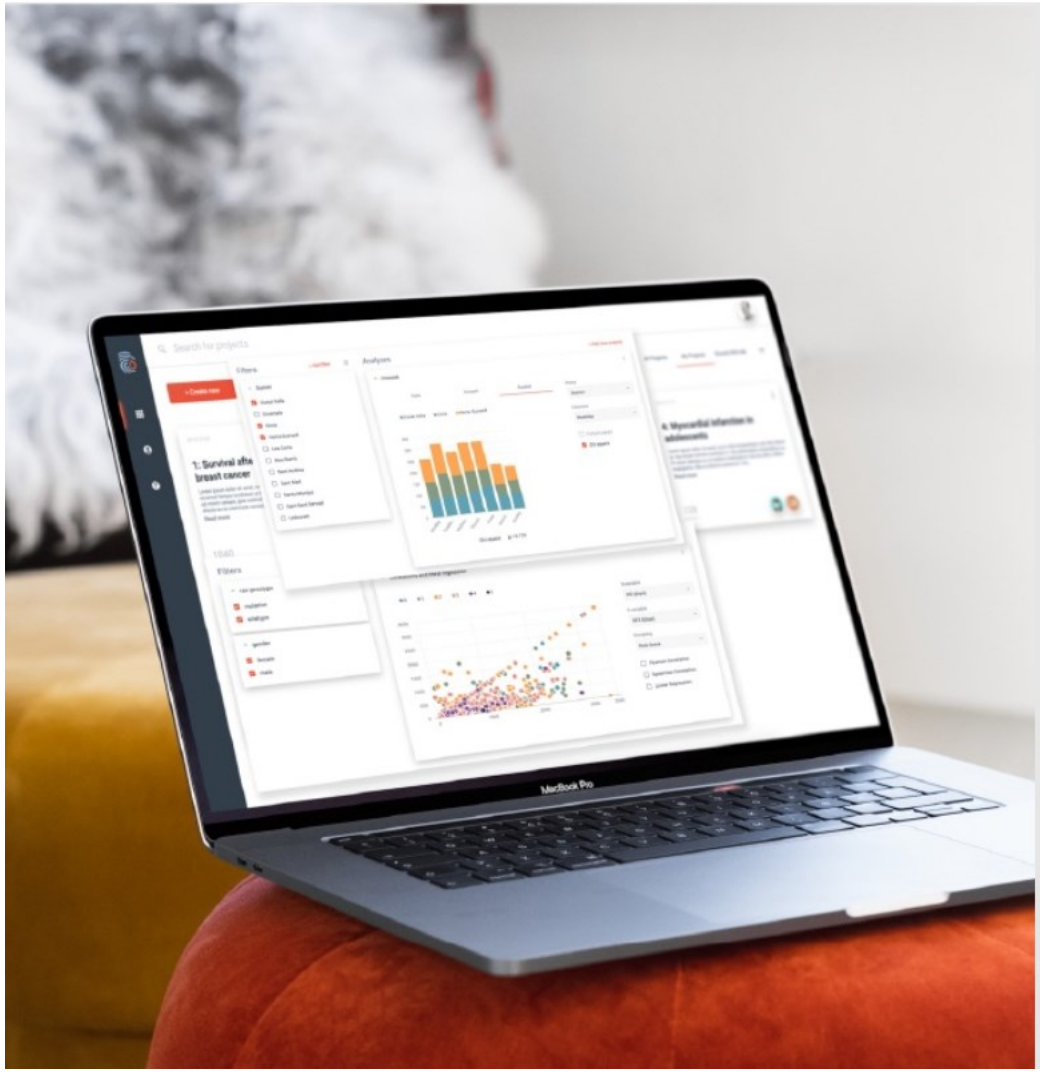

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NORPLASMA MONITOR

Analysis | Dataset | Variables | Collaborators

LN

Create entry

Pasientdata ved innleggelse

Sykehus *

ISBT-nr *

Pasientnr *

Fødselsdato *
---- / -- / --

Kjønn *
Value required

Samtykke dato *
---- / -- / --

Syk dato *
---- / -- / --

Inn dato *
---- / -- / --

PCR Dato *
---- / -- / --

Høyde *

Vekt *

Komorbiditet
No selection

Funksjon før *
Value required

Behandling

- Kortikosteroider
- Antivirale midler
- Immunmodulerende

Kliniske data dag 0, Før transfusjon

0F Lokalisasjon *
Value required

0F RR *

0F HR *

0F SaO2 *

0F Temp *

0F SBP *

0F DBP *

0F O2-tilførsel? *
Value required

0F O2-tilskudd

0F FiO2

0F PaO2

0F SARS-CoV2 LV *
Value required

0F SARS-CoV2 blod
No selection

0F anti-SARS-CoV2 *
Value required

Kliniske data dag 0, Etter transfusjon

0 antall E *

Transfusjonskomplikasjoner *
Value required

0E RR *

0E HR *

0E SaO2 *

0E Temp *

0E SBP *

0E DBP *

0E O2-tilførsel? *
Value required

0E O2-tilskudd *

0E FiO2

0E PaO2 *

0E SARS-CoV2 blod
No selection

0E anti-SARS-CoV2
No selection

Cancel

Add entry

Kliniske data dag 1 etter transfusjon

1 RR *

1 HR *

1 Temp *

1 SaO2 *

1 SBP *

1 DBP *

1 O2-tilførsel? *

Value required

1 O2-tilskudd

1 FiO2

1 PaO2 *

1 SARS-CoV2 LV *

Value required

1 SARS-CoV2 blod

No selection

1 anti-SARS-CoV2

No selection

Kliniske data ved utskrivelse

Ut RR *

Ut HR *

Ut Temp *

Ut SaO2 *

Ut SBP *

Ut DBP *

Ut O2-tilskudd? *

Value required

Ut O2-tilskudd

Ut FiO2

Ut PaO2

Ut SARS-CoV2 LV *

Value required

Ut SARS-CoV2 blod

No selection

Ut anti-SARS-CoV2 *

Value required

Fields marked with an (*) are required

Cancel

Add entry

Cancel

Add entry

NORPLASMA COVID-19

Viktige kontakter

Nasjonal prosjektleder MONITOR:
Lise Sofie Haug Nissen-Meyer lisoha@ous-hf.no T: *48284525*

Prosjektleder ISARIC: Jan Cato Holter/Anne Ma Dyrhoel Riise

Helsedirektoratets kontaktperson:
Øystein Flesland Oystein.Flesland@helsedir.no T: *45969707*

NETTSIDE der alle dokumenter finnes:
https://www.ous-research.no/home/norplasma

NORPLASMA COVID-19

Oppsummering

- COVID-19 rekonvalesensplasma er tilgjengelig ved alle store blodbanker over hele landet.
- Ordineres for transfusjon på grunnlag av klinisk vurdering. Pasienten må samtykke til transfusjon
- NB pasienter som ikke selv danner antistoff
- Blodbanken sender plasma med nødvendige dokumenter
- Motiver pasienten til å bli med i MONITOR/ISARIC
- Alle relevante dokumenter er vedlagt plasmaenheten og kan lastes ned fra https://www.ous-research.no/home/norplasma

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Spørsmål?