The Therapeutic Roles for Convalescent Plasma- COVID-19 FDA Approval to Future Use

David Sullivan MD
dsulliv7@jhmi.edu
Johns Hopkins Bloomberg School of Public Health
School of Medicine Infectious Diseases

"Whatever you do, always give 100%—
unless you're donating blood"
Bill Murray

Guggenheim
Art sculpture

Disclosure Information

Faculty Johns Hopkins Bloomberg School of Public Health-David Sullivan MD

I have no relevant commercial interests to the presentation topic of COVID-19 convalescent plasma

I do have commercial interests related to malaria drugs and diagnostics
Stock ownership-
1. AliquantumRX for malaria cethromycin preclinical drug development. 33% founding stock ownership and also Chair of Board with AliquantumRX which is a Johns Hopkins Technology Ventures (JHTV) licensed start-up company. AliquantumRx has not started the FDA regulatory process.

Consulting role-
2. Hemex Health- malaria blood diagnostic test

Today I will be discussing the use of convalescent plasma to treat COVID-19, FDA approved under a Biologic License Application with CBER

Hit Virus Early With High Amounts of Therapy

1.Prophylaxis

2.Outpatient to reduce hospitalizations

3.Inpatient to reduce deaths

4.Inpatient and newly intubated to reduce deaths

5.Impact on long COVID-19

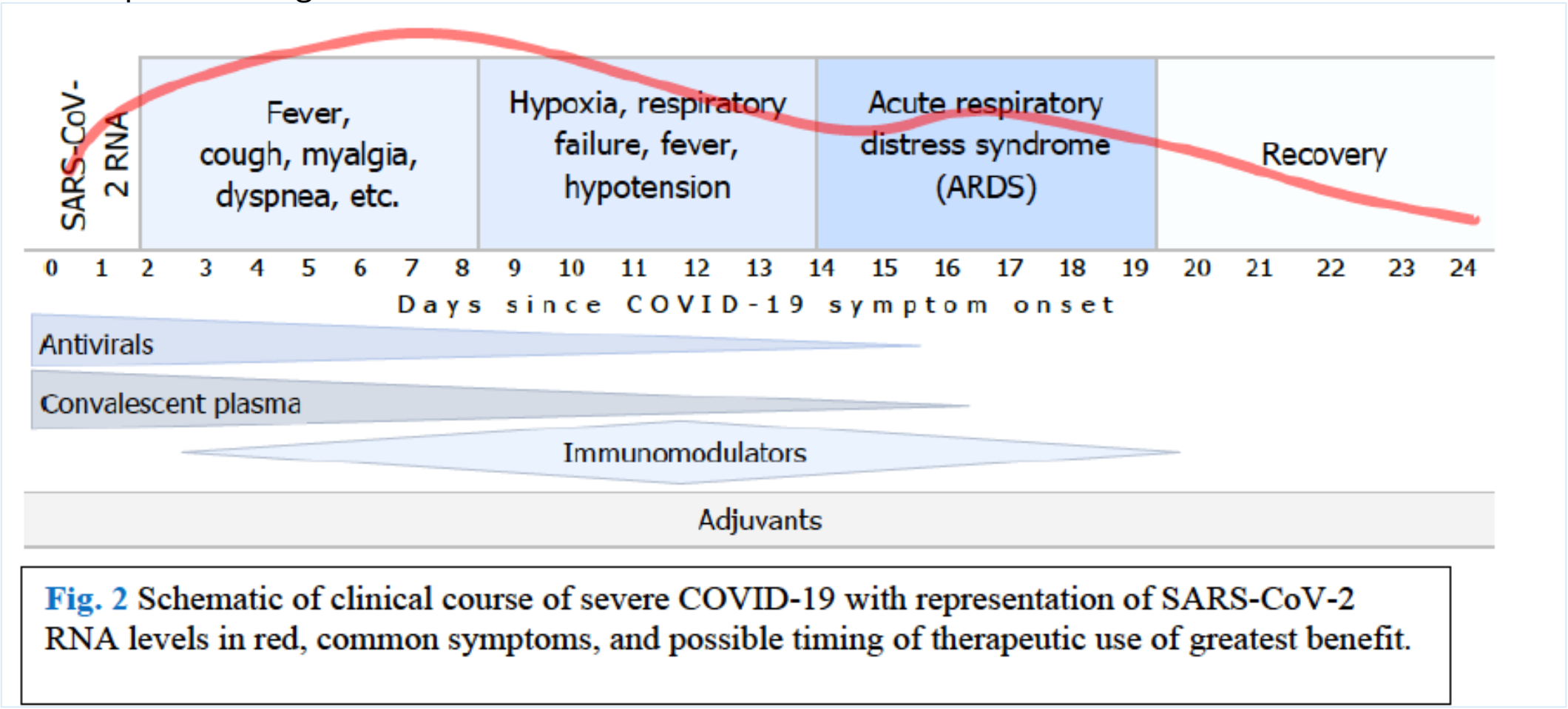


Fig. 2 Schematic of clinical course of severe COVID-19 with representation of SARS-CoV-2 RNA levels in red, common symptoms, and possible timing of therapeutic use of greatest benefit.

Source: COVID-19 Treatment Guidance Writing Group of the Johns Hopkins University and The Johns Hopkins Hospital COVID-19 Treatment Guidance Working Group. (May 19, 2020; replaces document of May 11, 2020.)

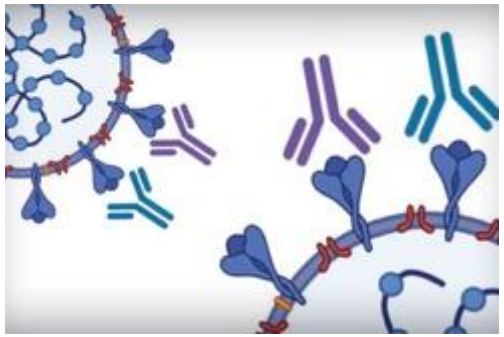
Antiviral Antibodies Work!

Passive Immediate immunity

COVID-19 Convalescent Plasma
Outpatient and hospital

1 month

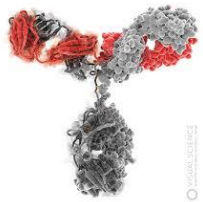
1-2 months
Inpatient Jan 2020
Outpatient June 3 2020



HyperImmune Globulin from 1000+ Donors
No RCT efficacy

4-8 months

8 months
Inpatient Oct 8, 2020
Outpatient August 6, 2021



Single Monoclonal antibodies

Multiple Monoclonal antibodies

Prophylaxis and outpatient but not once in hospital

4-8 months

4 months
Inpatient August 5, 2020
Outpatient June 10, 2020

Active Delayed immunity

Vaccines
Works for Prophylaxis, outpatient
And reduced death

2 months

6 months
Outpatient July 27, 2020
Moderna
Outpatient July 27, 2020 Pfizer-BioNTech

Time to production

Time to Phase III efficacy trial

EUA **hospitalized** Aug 23, 2020
EUA **outpatient** Dec 27, 2021
FDA BLA Approval Dec 10, 2024

IVIG **No efficacy**
No EUA or FDA approval

EUA Nov 21, 2020 outpatient (not hospital) EUA revoked 4/21(BAM)
EUA revoked Dec 13, 2024 (all Tx mAb)

EUA Dec 14, 2020 11 months
FDA approval August 23, 2021

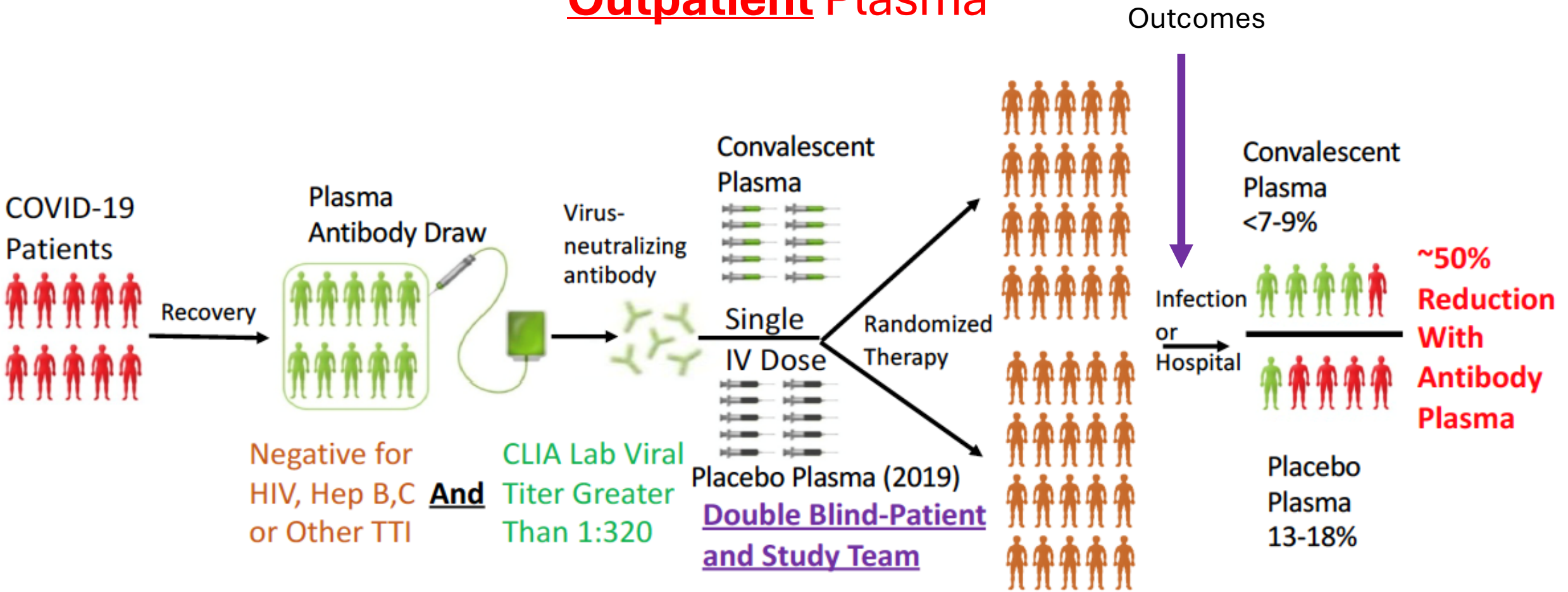
Drugs and antibodies-Duration and calendar months of the RCT in context of dominant variants of concern. Study start and end for enrollments with approximate time periods for variants of concern

TYPE	Setting	Study	Partic-ipant #	Study months	JAN-20	FEB	MAR-20	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN-21	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN-22	FEB	MAR
Vaccine	Outpatient	RNA	43,548	9	Design	1	2	3	4	5	6	7	8	9		FDA EUA															
Ab-CCP	Outpatient	CCP-Argentina	160	5						1	2	3	4	5																	
Ab-CCP	Outpatient	CCP-CSSC-004	1,181	16				Design		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16			FDA EUA			
Ab-MONO	Outpatient	Bamlanivimab-BLAZE-1	452	3									1	2	FDA EUA																
Ab-MONO	Outpatient	Casirivimab/imdevimab-REGEN-COV Ph 3	2,696	4										1	2	3	4														
Ab-MONO	Outpatient	Casirivimab/imdevimab-REGEN-COV Ph 1/2	799	3	Cloning			Selec-tion	Manu-facture		1	2	3		FDA EUA																
DRUG-AV	Outpatient	Molnupiravir-MOVe-OUT	1,408	6																	1	2	3	4	5	6		FDA EUA			
DRUG-AV	Outpatient	Nirmatrelvir/ritonavir-EPIC-HR	2,085	6																			1	2	3	4	5	FDA EUA			
DRUG-AV	Outpatient	Remdesivir-PINETREE	562	8									1	2	3	4	5	6	7	8									FDA EUA		
Ab-CCP	Inpatient	CCP-EAP	3,082	4	1st dose in China			1	2	3	4	FDA EUA																FDA EUA			
Ab-CCP	Inpatient	CCP-ColumbiaU	223	8				1	2	3	4	5	6	7	8																
Ab-CCP	Inpatient	CCP-PennCCP2	80	9					1	2	3	4	5	6	7	8	9														
Ab-CCP	Inpatient	CCP-IMV-Belgium	475	19									1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Ab-hIVIG	Inpatient	hIVIG-ITAC	593	5									1	2	3	4	5														
Ab-MONO	Inpatient	LY-CoV555	314	3								1	2	3																	
Ab-MONO	Inpatient	Tix-cig	1,455	8														1	2	3	4	5	6	7	8						
Ab-MONO	Inpatient	Strov-BRII	546	3												1	2	3													
DRUG-AV	Inpatient	Remdesivir-ACTT-1	1,062	4		1	2	3	FDA EUA																						
DRUG-AV	Inpatient	Steroids-RECOVERY	6,425	3			1	2	3	Allowed																					
Variant		614G					614G	614G	614G	614G	614G	614G	614G	614G	614G	614G	614G	614G	614G	614G											
Variant		Alpha															α	α	α	α	α	α									
Variant		Beta																β	β	β	β										
Variant		Delta																					δ	δ	δ	δ	δ	δ	δ		
Variant		Omicron																										o	o	o	o

Sullivan CTMI 2024 https://doi.org/10.1007/82_2024_273

Study Design: Double-Blind Randomized Controlled Trial

Outpatient Plasma



COVID-19 PLASMA TRIALS
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Convalescent plasma is mostly water

200 mL unit delivers ~ 2000 mg total antibody.

CCP= 2 to 20 mg viral specific dose

Monoclonals deliver

200 to 2000 mg dose!! (100 times)

Plasma

90% water

1% salts

Total protein 60-80 mg/mL

5% albumin 34-54 mg/mL

3.5% Globulins

1% Alpha- liver proteins for transport and osmotic function

1% beta liver proteins for transport and osmotic pressure

Gamma immune function

1% IgG =11 mg/mL

0.16% IgA =1.5 mg/mL

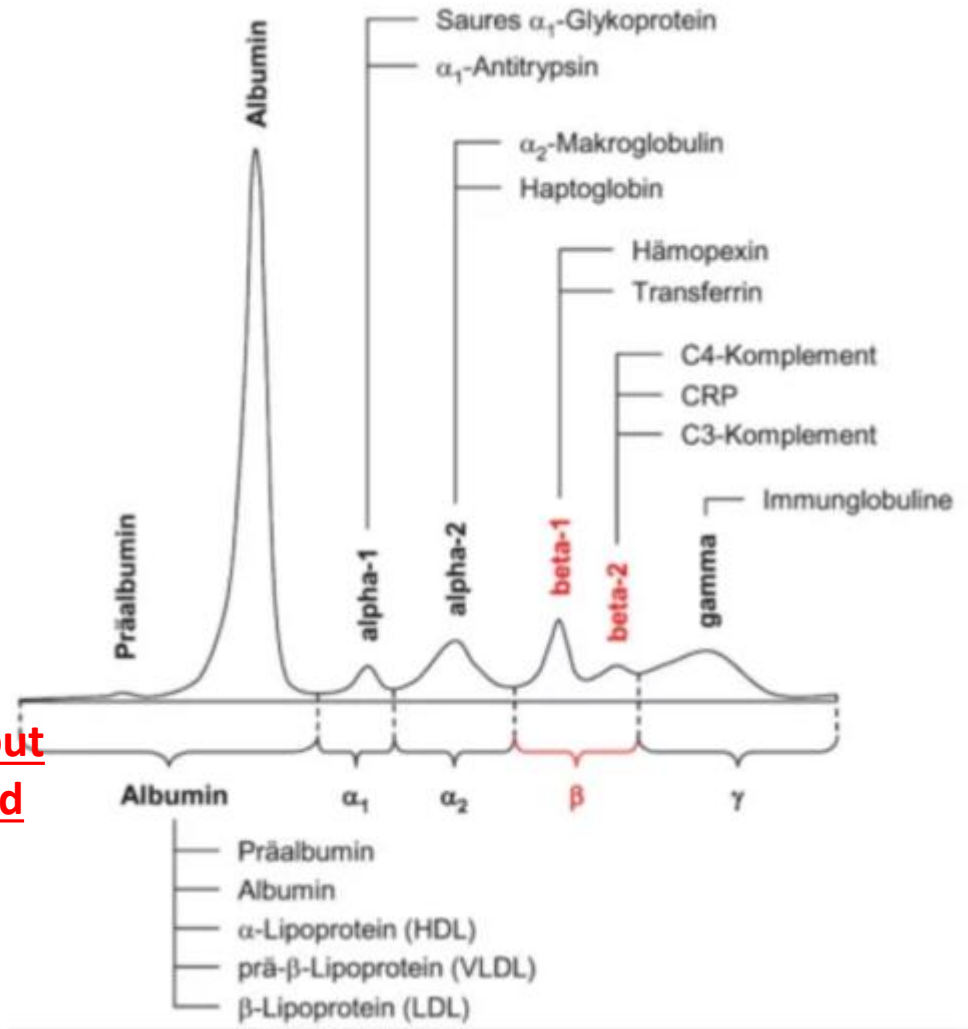
0.08% IgM = 0.8 mg/mL

0.5% fibrinogen 2-4 mg/mL

Donor viral specific antibodies about 10 to 100 mcg per mL (Hospitalized BARDA plasma=50 mcg/mL-mBio)

doi/10.1128/mbio.03523-22

Clotting factors in alpha and beta fractions



The Plasma units numbers for two outpatient trials

3,159 Units Inventoried

1,351 CCP & Control Transfusions

29 Donor centers
29 Study blood banks
26 Transfusions sites

J Clin Transl Sci. 2024 Nov 14;8(1):e200. doi: 10.1017/cts.2024.642.

AAMC, Annapolis, MD

ARC DC

NYBC Delmarva

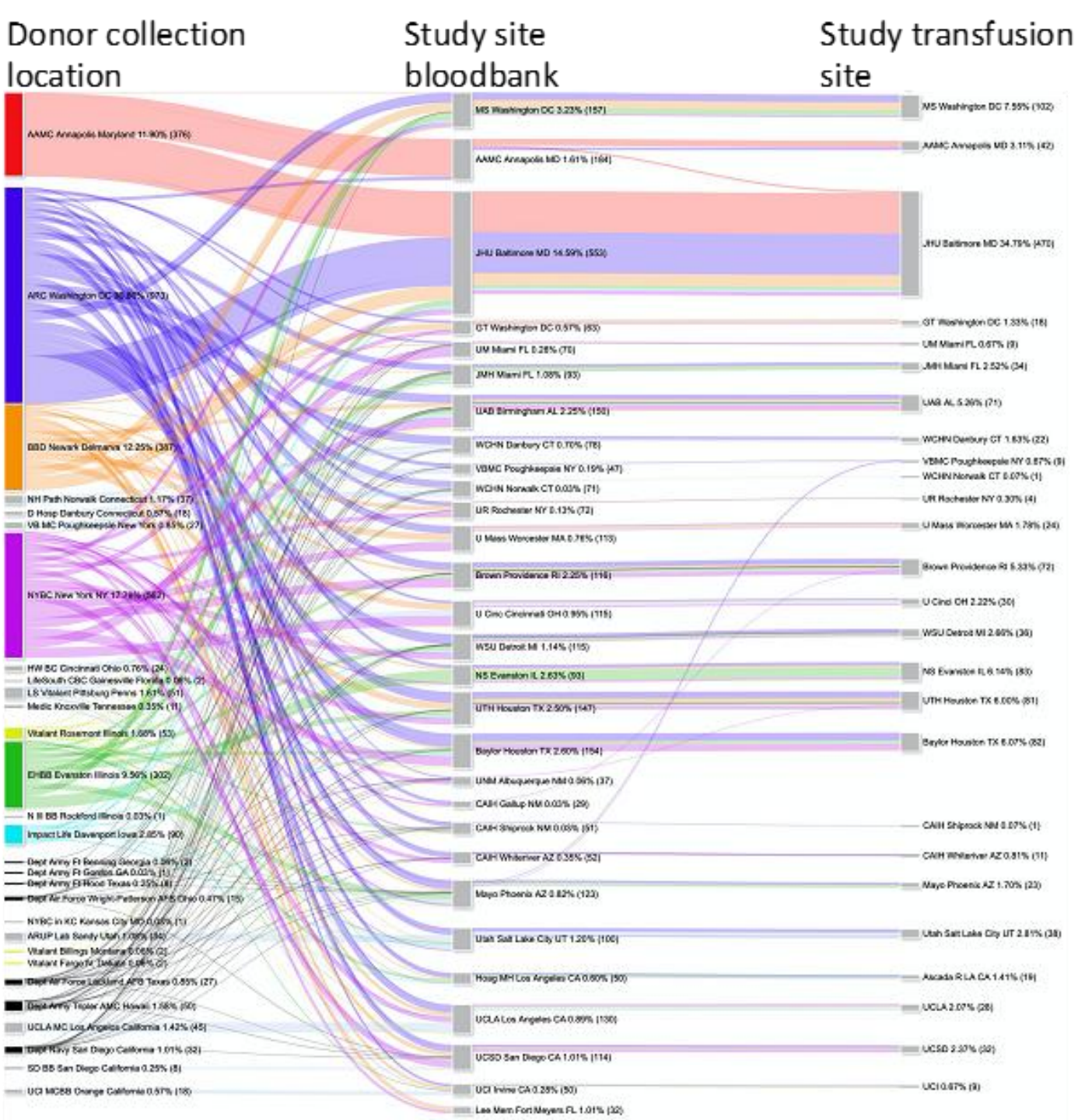
NYBC NYC

Vitalant, Rosemont IL

Northshore, Evanston, IL

Impact Life, Iowa

Assorted Military Blood Centers



COVID-19 PLASMA TRIALS
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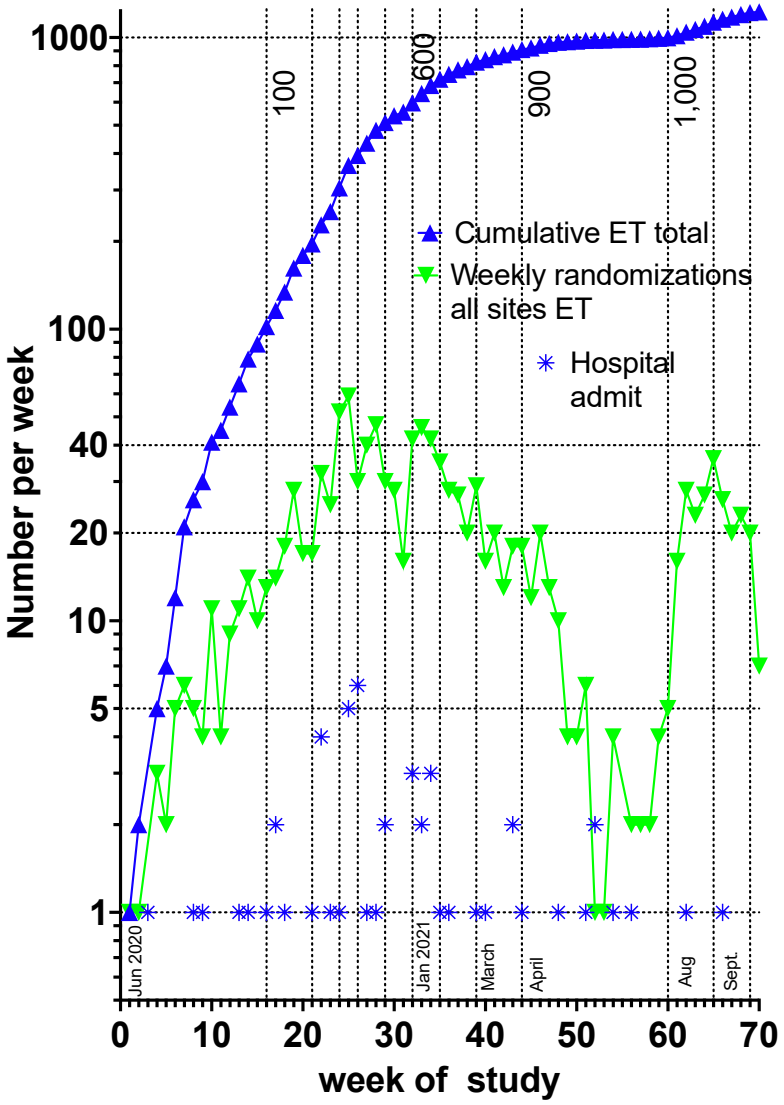
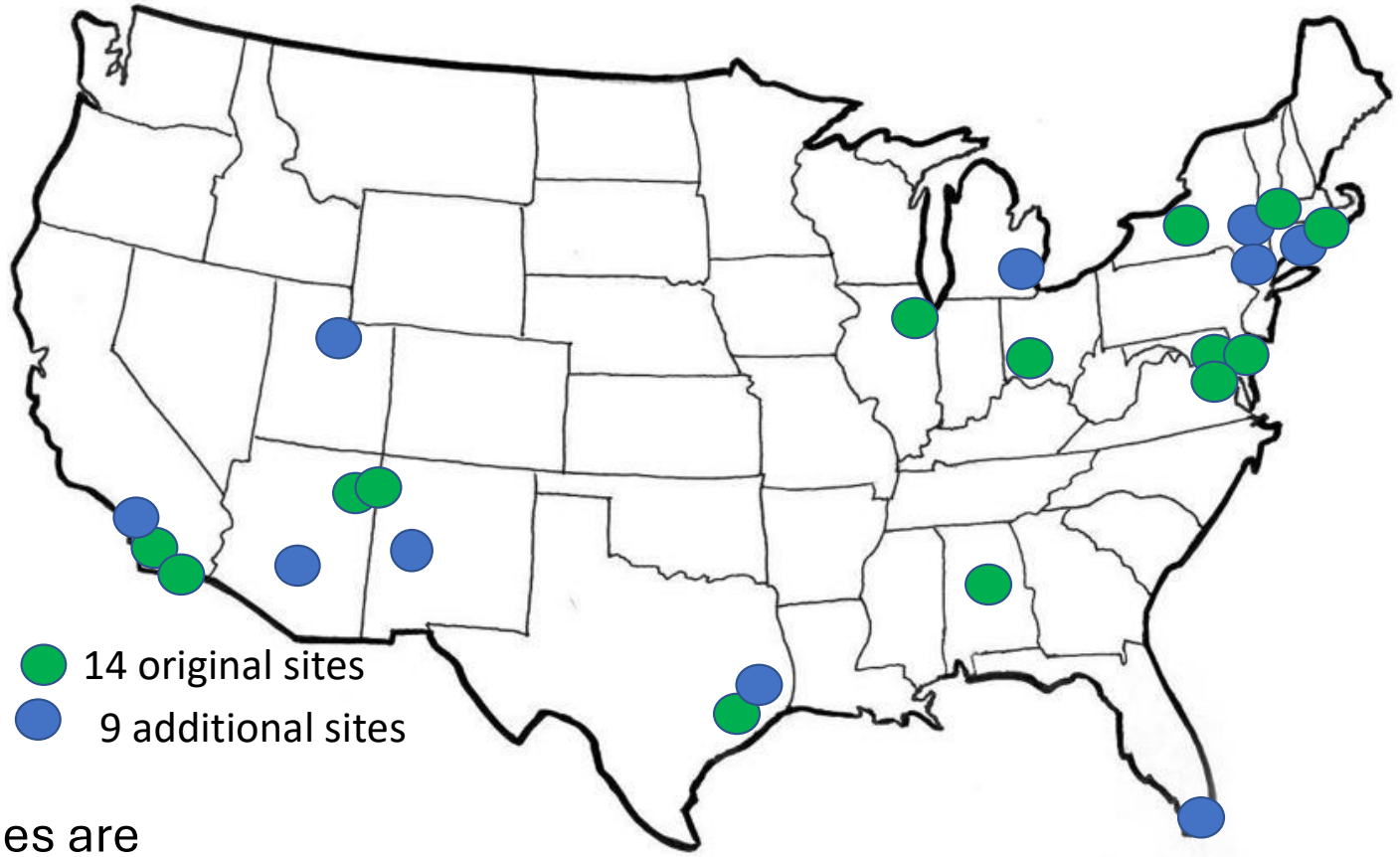
Fast and slow pace of enrollments during pandemic

Early treatment 1181 Transfusions



Sites Were Selected in Diverse Hotspots

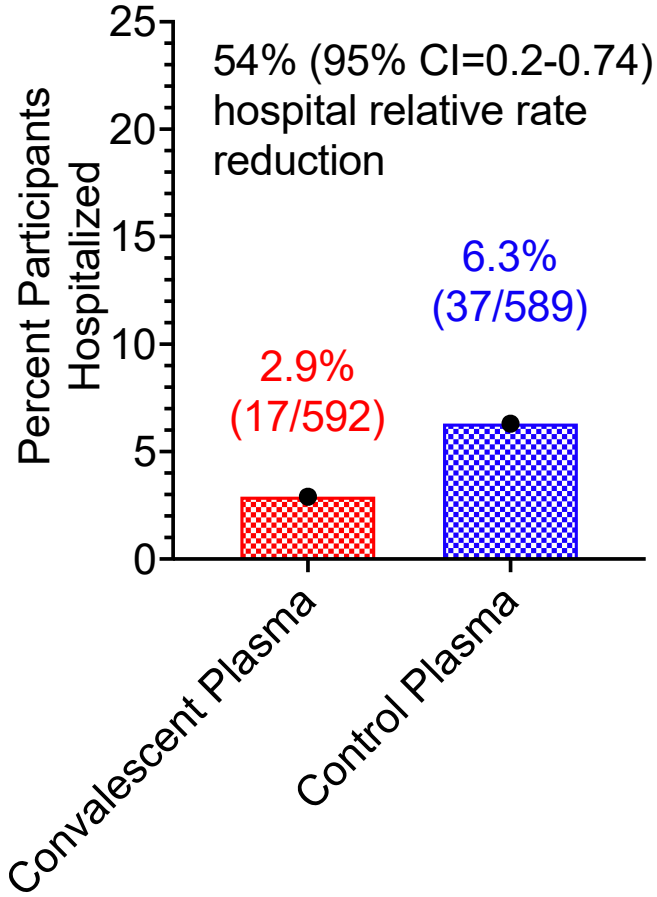


Vertical lines are successive weeks of 100 randomizations

Outpatient COVID-19 Convalescent Plasma is Safe and Effective

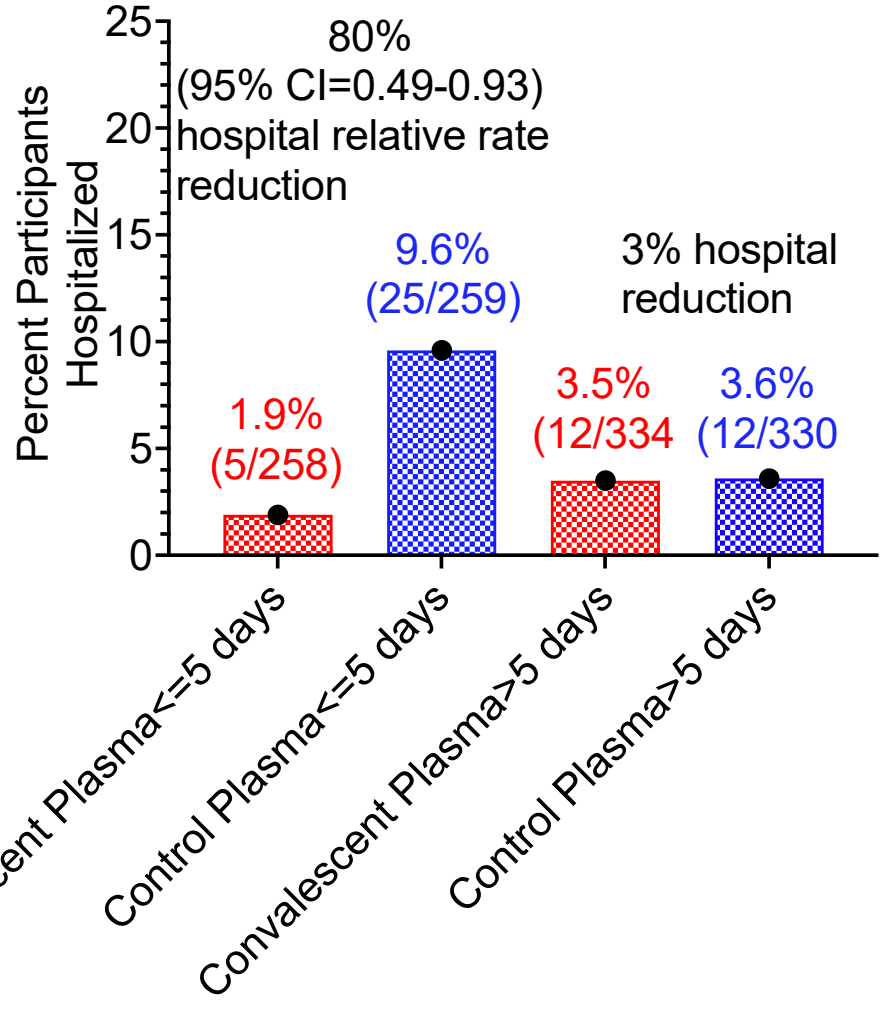
Primary Endpoint

All Participants



Subgroup point estimate

Early or Late Transfusion



EFFICACY RESULTS: The primary outcome hospitalization occurred in 17 of 592 participants (2.9%) who received convalescent plasma and 37 of 589 participants (6.3%) who received control plasma (absolute risk reduction, 3.4 percentage points; 95% confidence interval, 1.0 to 5.8; P = 0.005), which corresponded to a relative risk reduction of 54%.

SAFETY RESULTS: A total of 16 grade 3 or 4 adverse events (7 in the convalescent-plasma group and 9 in the control-plasma group) occurred in participants who were not hospitalized.

COVID-19 PLASMA TRIALS
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N England J Med. 2022 March 30 DOI: 10.1056/NEJMoa2119657

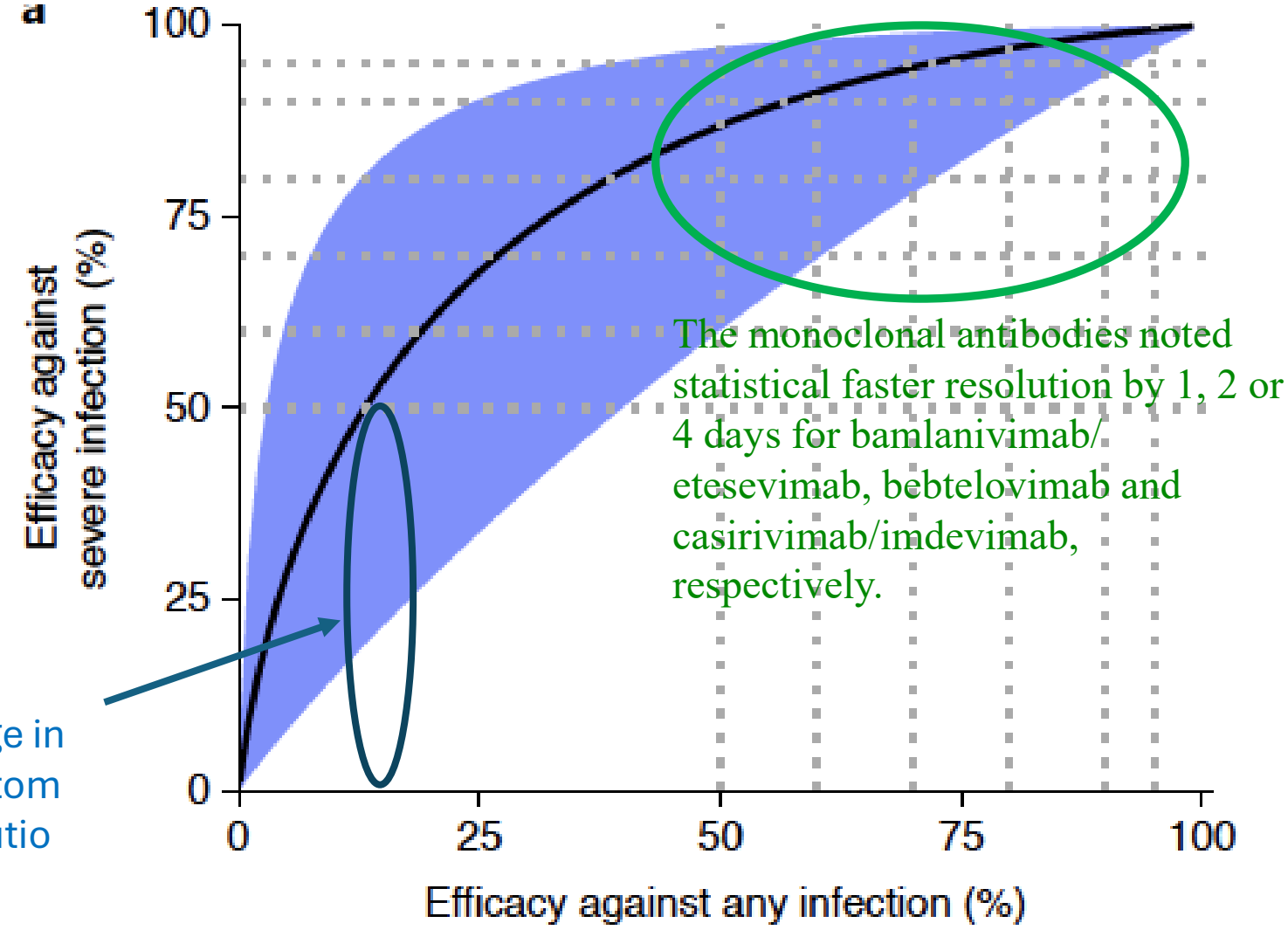
Upper 2 quintiles of CCP Dose Response

50% prevent hospitalizations

10-15% infection prevention

No effect on symptoms

Infection prevention requires more antibodies
Same antibody pools used in both trials



https://doi.org/10.1101/2022.03.21.22272672;

5 outpatient Convalescent Plasma Trials

High-titre methylene blue-treated convalescent plasma as an early treatment for outpatients with COVID-19: a randomised, placebo-controlled trial

Lancet Respir Med 2022; 10: 278–88

Andrea Alemany*, Pere Millat-Martinez*, Marc Corbacho-Monné, Pierre Malchair, Dan Ouchi, Anna Ruiz-Comellas, Anna Ramírez-Morros, Joana Rodríguez Codina, Rosa Amado Simon, Sebastian Videla, Gèlia Costes, Mar Capdevila-Jáuregui, Pamela Torrano-Soler, Alba San José, Glòria Bonet Papell, Jordi Puig, Aurema Otero, Jose Carlos Ruibal Suarez, Alvaro Zarauza Pellejero, Ferran Llopis Roca, Orlando Rodriguez Cortez, Vanesa Garcia Garcia, Josep Vidal-Alaball, Anna Millan, Enric Contreras, Joan-Ramon Grifols, Àgueda Ancochea, Ivan Galvan-Femenia, Francini Piccolo Ferreira, Mireia Bonet, Jordi Cantoni, Núria Prat, Jordi Ara, Anna Forcada Arcarons, Magí Farré, Edwards Pradenas, Julià Blanco, Miquel Àngel Rodriguez-Arias, Gema Fernández Rivas, Michael Marks, Quique Bassat, Ignacio Blanco, Bàrbara Baro*, Bonaventura Clotet*, Oriol Mitjà, for the CONV-ERT Group†

The NEW ENGLAND JOURNAL of MEDICINE

Early Convalescent Plasma for High-Risk Outpatients with Covid-19

DOI: 10.1056/NEJMoa2103784

F.K. Korley, V. Durkalski-Mauldin, S.D. Yeatts, K. Schulman, R.D. Davenport, L.J. Dumont, N. El Kassar, L.D. Foster, J.M. Hah, S. Jaiswal, A. Kaplan, E. Lowell, J.F. McDyer, J. Quinn, D.J. Triulzi, C. Van Huysen, V.L.W. Stevenson, K. Yadav, C.W. Jones, B. Kea, A. Burnett, J.C. Reynolds, C.F. Greineder, N.L. Haas, D.G. Beiser, R. Silbergleit, W. Barsan, and C.W. Callaway, for the SIREN-C3PO Investigators*

Clinical Microbiology and Infection

Outpatient convalescent plasma therapy for high-risk patients with early COVID-19: a randomized placebo-controlled trial

Arvind Gharbharan [1, **], Carlijn Jordans [1], Lisa Zwaginga [2], Grigorios Papageorgiou [3], Nan van Geloven [4], Peter van Wijngaarden [5], Jan den Hollander [6], Faiz Karim [7], Elena van Leeuwen-Segarceanu [8], Robert Soetekouw [9], Jolanda Lammers [10], Douwe Postma [11], Linda Kampschreur [12], Geert Groeneveld [13], Francis Swaneveld [14], C. Ellen van der Schoot [15], Hannelore Götz [16, 17], Bart Haagmans [18], Marion Koopmans [18], Susanne Bogers [18], Corine Geurtsvankessel [18], Jaap Jan Zwaginga [2], Casper Rokx [1], Bart Rijnders [1, *], on behalf of the CoV-Early study group

Clinical Microbiology and Infection 29 (2023) 208–214

The NEW ENGLAND JOURNAL of MEDICINE

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

DOI: 10.1056/NEJMoa2033700

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*

The NEW ENGLAND JOURNAL of MEDICINE

Early Outpatient Treatment for Covid-19 with Convalescent Plasma

DOI: 10.1056/NEJMoa2119657

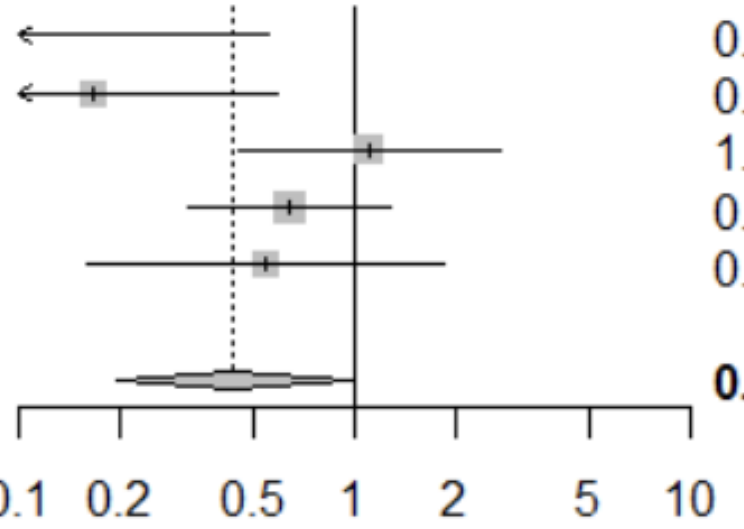
D.J. Sullivan, K.A. Gebo, S. Shoham, E.M. Bloch, B. Lau, A.G. Shenoy, G.S. Mosnaim, T.J. Gniadek, Y. Fukuta, B. Patel, S.L. Heath, A.C. Levine, B.R. Meisenberg, E.S. Spivak, S. Anjan, M.A. Huaman, J.E. Blair, J.S. Currier, J.H. Paxton, J.M. Gerber, J.R. Petrini, P.B. Broderick, W. Rausch, M.-E. Cordisco, J. Hammel, B. Greenblatt, V.C. Cluzet, D. Cruser, K. Oei, M. Abinante, L.L. Hammitt, C.G. Sutcliffe, D.N. Forthal, M.S. Zand, E.R. Cachay, J.S. Raval, S.G. Kassaye, E.C. Foster, M. Roth, C.E. Marshall, A. Yarava, K. Lane, N.A. McBee, A.L. Gawad, N. Karlen, A. Singh, D.E. Ford, D.A. Jabs, L.J. Appel, D.M. Shade, S. Ehrhardt, S.N. Baksh, O. Laeyendecker, A. Pekosz, S.L. Klein, A. Casadevall, A.A.R. Tobian, and D.F. Hanley

Both early treatment and high titer improve outcome even more

The risk reduction in patients receiving high antibody titer CCP AND within 5 days of symptom onset was higher for the combined studies at 7.6% (95%CI: 4.0%-11.1%) ARR, NNT of 13, and 51.7% (95%CI: 28.3%-67.1%) RRR

Study	CCP Events	CCP Total	Placebo Events	Placebo Total	Odds Ratio	OR	95%-CI	Weight
CSSC-004	1	127	25	259		0.07	[0.01; 0.55]	10.8%
CCP-Argentina	3	46	23	78		0.17	[0.05; 0.59]	18.5%
CONV-ERT	8	58	18	142		1.10	[0.45; 2.70]	24.0%
C3PO	13	93	39	192		0.64	[0.32; 1.26]	27.5%
CoV-Early	4	82	9	104		0.54	[0.16; 1.82]	19.2%
Random effects model	**29**	**406**	**114**	**775**		**0.44**	**[0.20; 0.97]**	**100.0%**

Heterogeneity: $I^2 = 59\%$, $\tau^2 = 0.4842$, $p = 0.05$
Test for overall effect: $z = -2.03$ ($p = 0.04$)



COVID-19 PLASMA TRIALS
SPONSORED BY JOHNS HOPKINS UNIVERSITY

Clin Infect Dis. 2023 Jun 16;76(12):2077-2086

Patient and donor antibody profiles in early COVID-19 convalescent plasma therapy in the COnV-ert trial

Andrea Alemany[1,2,3,4*], Dan Ouchi[1,3], Edwards Pradenas[5], Ruth Aguilar[3], Marta Vidal[3], Alfons Jimenez[3], Pere Millat-Martinez[3,4], Marc Corbacho-Monné[1,2,6], Clara Suñer[3], Quique Bassat[3,4,7,8,9,10], Bàrbara Baro[3,4], Gemma Moncunill[3,11], Oriol Mitjà[1,2,12], COnV-ert Group of Authors, Julià Blanco[5,11,12,13†] and Carlota Dobaño[3,11†]

Front Immunol . 2025 Sep 25:16:1647488

Methylene Blue was associated with a **significant decrease in cytophilic subclasses IgG1 and IgG3** to S and S2, and IgA to RBD, S and S2 in CCP units, **without a reduction in neutralization titer** and with a modest increase in IgG2 to RBD and S

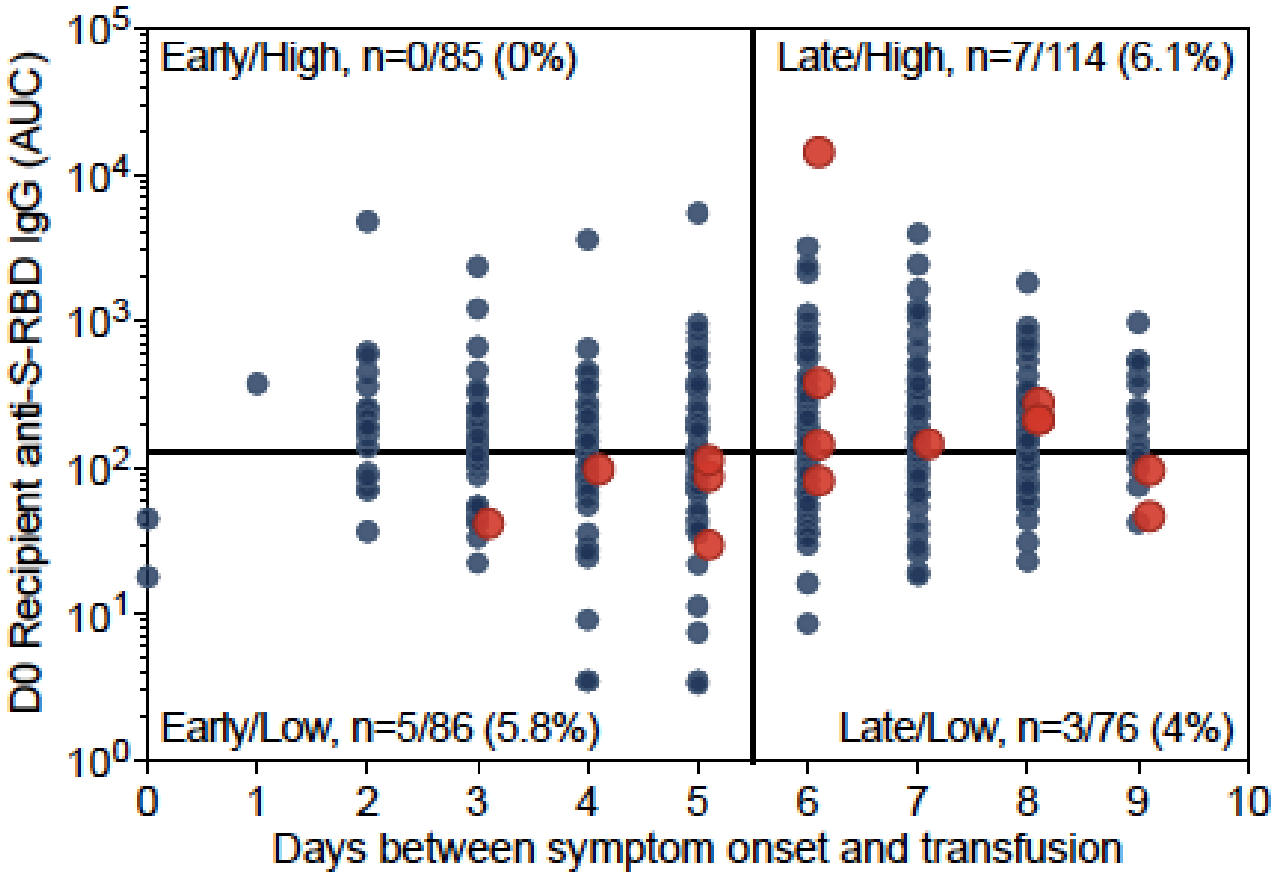
CCP units							
Ratios	**Antigens**	**Overall**	**After MB**	**Before MB**	**After – Before MB**	***P* value**	**p.sign**
Ratio IgA/IgG	N CT	0.043 (0.058)	0.043 (0.055)	0.045 (0.062)	-0.002	0.875	ns
	N FL	0.032 (0.057)	0.027 (0.058)	0.036 (0.063)	-0.009	0.005	**
	RBD	0.057 (0.095)	0.044 (0.091)	0.07 (0.13)	-0.026	0.078	ns
	S	0.091 (0.144)	0.075 (0.109)	0.101 (0.191)	-0.026	0.005	**
	S2	0.19 (0.226)	0.171 (0.186)	0.25 (0.271)	-0.079	<0.001	***
Ratio IgG1+IgG3 / IgG2+IgG4	N CT	4.588 (8.253)	3.679 (6.524)	6.042 (8.58)	-2.363	0.050	ns
	N FL	31.677 (31.013)	32.232 (31.892)	30.747 (32.048)	1.485	0.198	ns
	RBD	93.078 (89.822)	76.133 (57.272)	129.42 (99.532)	-53.287	<0.001	***
	S	153.748 (148.425)	122.629 (86.379)	231.98 (174.529)	-109.351	<0.001	***
	S2	100.772 (119.725)	100.404 (107.783)	101.502 (132.009)	-1.098	0.198	ns

Early Transfusion Early (symptom onset within 5 days) with the upper portion of antibody levels results in zero (nada) hospitalization

Strikingly, Early treatment with high post-transfusion antibody levels reduced hospitalization risk-0/102 (0%) compared to all other CCP recipients-17/370 (4.6%; Fisher exact p=0.03) and to all control plasma recipients-35/461 (7.6%; Fisher exact p=0.001).

We selected the upper 60% of donors for study qualification and by all antibody measurements for stratified analysis, the upper half of qualified donors which equals the upper 30%, had similar impact on hospitalization risk reduction.

CCP recipients stratified early/late and high/low



https://insight.jci.org/articles/view/178460
Open Access | 10.1172/jci.insight.178460

COVID-19 PLASMA TRIALS
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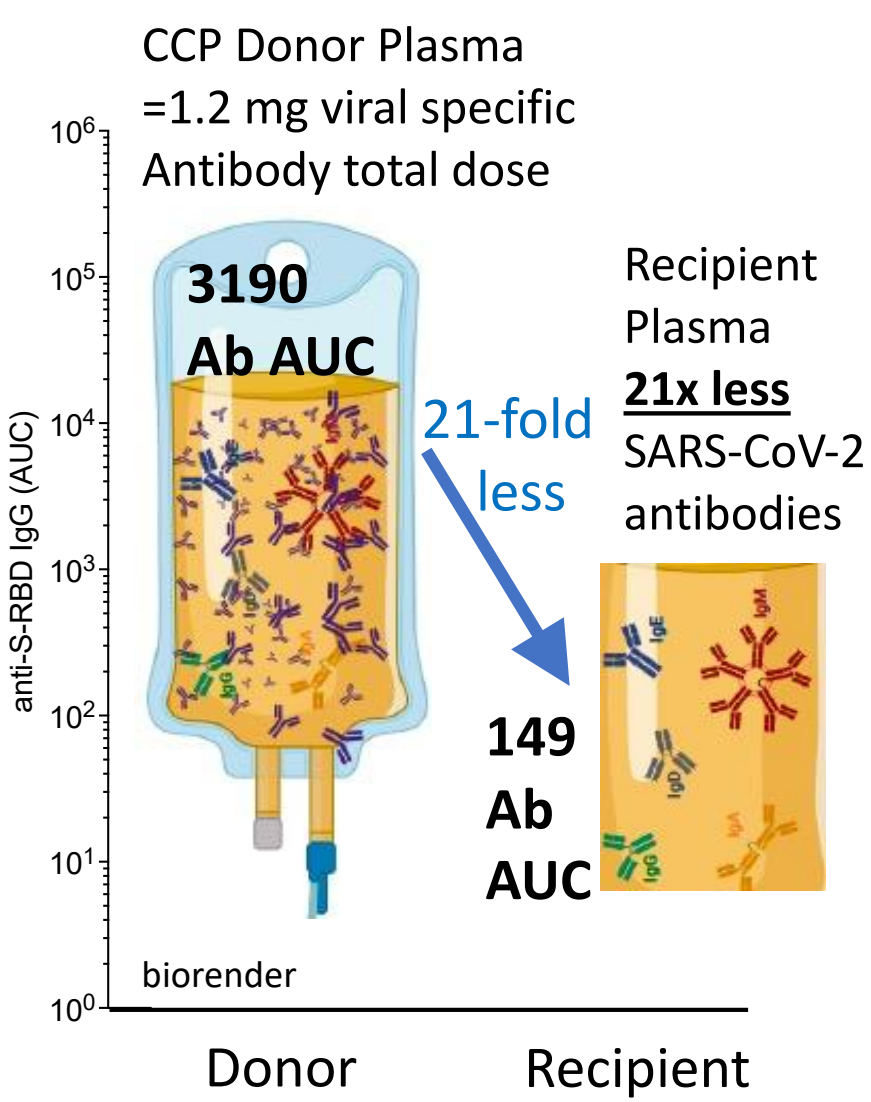
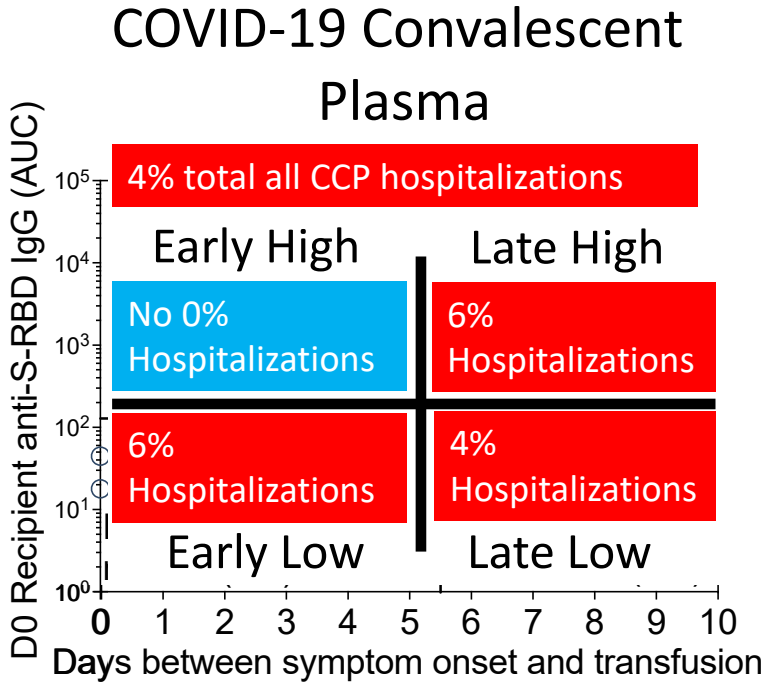
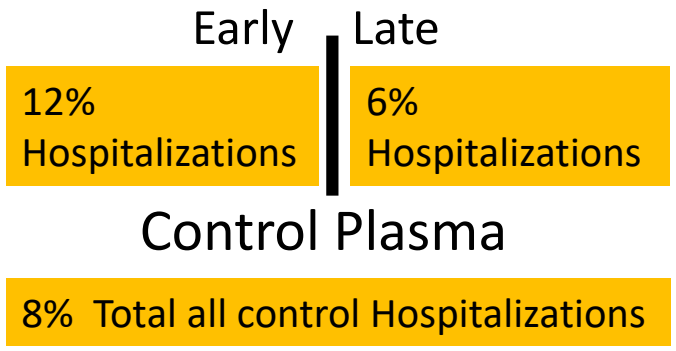
Therapeutic CCP should comprise the upper 30% of donor antibody levels to provide effective early outpatient use for immunocompromised and immunocompetent outpatients.

Outpatient COVID-19 convalescent plasma recipient antibody thresholds correlated to reduced hospitalizations within a randomized trial







COVID-19 PLASMA TRIALS
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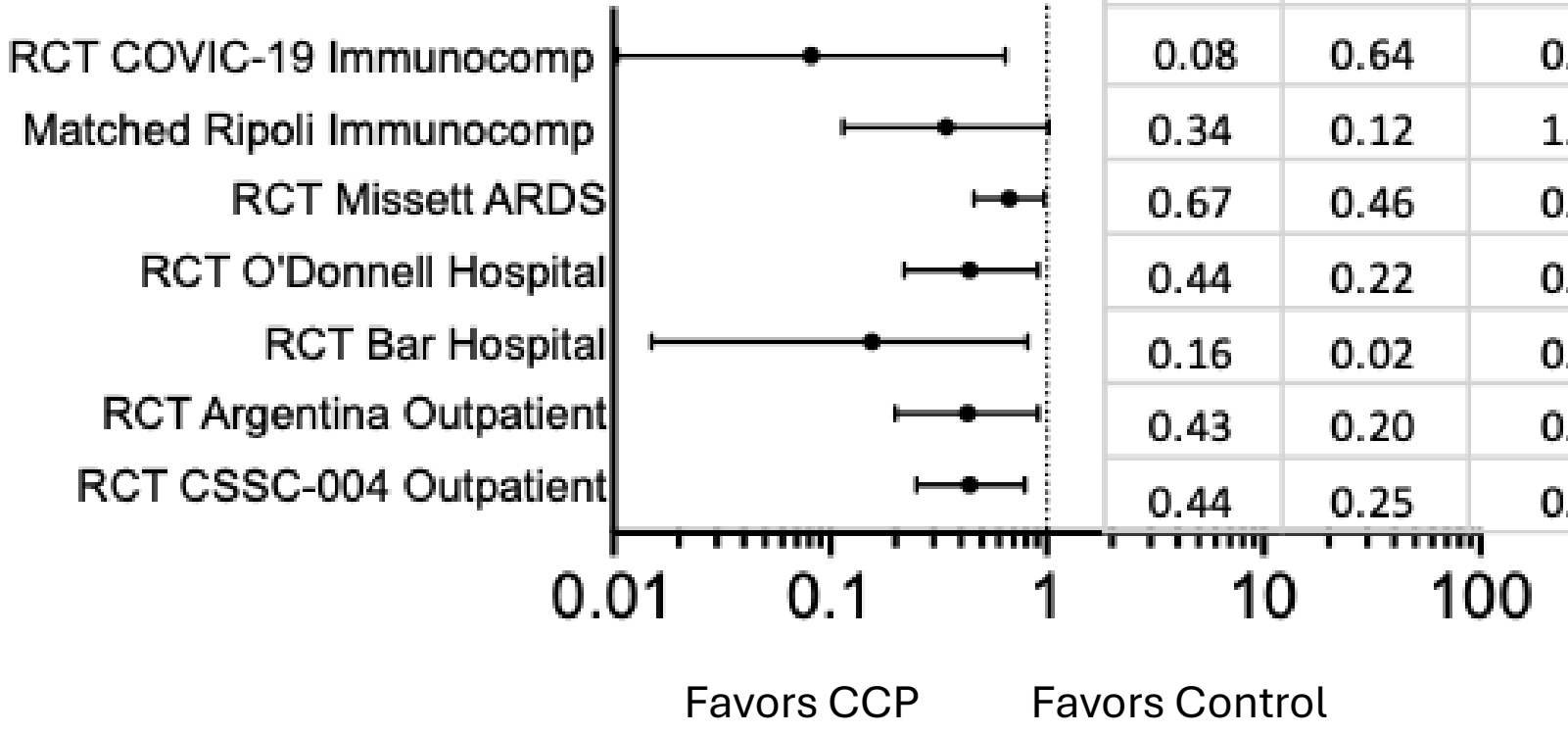
https://insight.jci.org/articles/view/178460
Open Access | 10.1172/jci.insight.178460

Robust randomized control trials established efficacy in four distinct disease stages-outpatient, inpatient, newly mechanically ventilated and in those immunocompromised to prevent acute disease progression or eliminate persistent viral carriage.

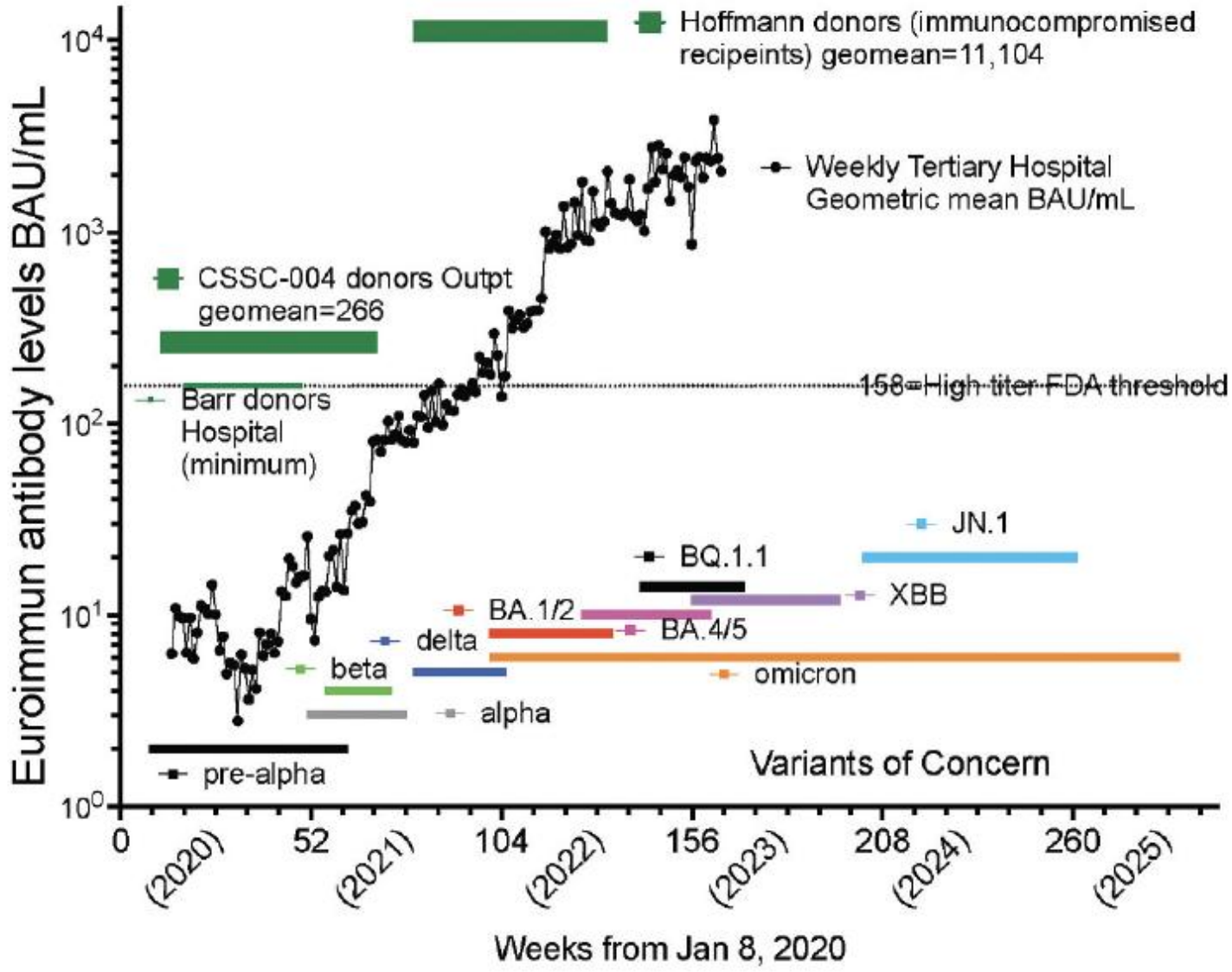


OR	95%CI	95%CI	event ccp	total ccp	event cont	total cont
0.08	0.64	0.01	0	59	5	58
0.34	0.12	1.02	5	225	10	161
0.67	0.46	0.97	84	237	107	238
0.44	0.22	0.91	19	150	18	73
0.16	0.02	0.81	2	40	10	39
0.43	0.20	0.91	13	80	25	80
0.44	0.25	0.79	17	592	37	589

COVID-19 PLASMA TRIALS
SPONSORED BY JOHNS HOPKINS UNIVERSITY

Expert Rev Anti Infect Ther. 2026 Jan;24(1):97-111. doi: 10.1080/14787210.2026.2623136.

Weekly geometric mean Euroimmun BAU/mL in 15,000 patients samples over three years with a 100-fold increase in total Spike 1 antibody levels from 14 BAU/mL to over 2000 BAU/mL in February 2023.



Donor antibody levels from two RCTs-the outpatient CSSC-004 (CCP) and the Hoffmann immunocompromised outpatient (vaccination and infection) measured mean antibody levels at 266 and 11,104 BAU/mL. The Barr hospital study noted 85% of donor plasma over a minimum threshold for FDA high titer in 2021 without a geometric mean measured.

COVID-19 PLASMA TRIALS
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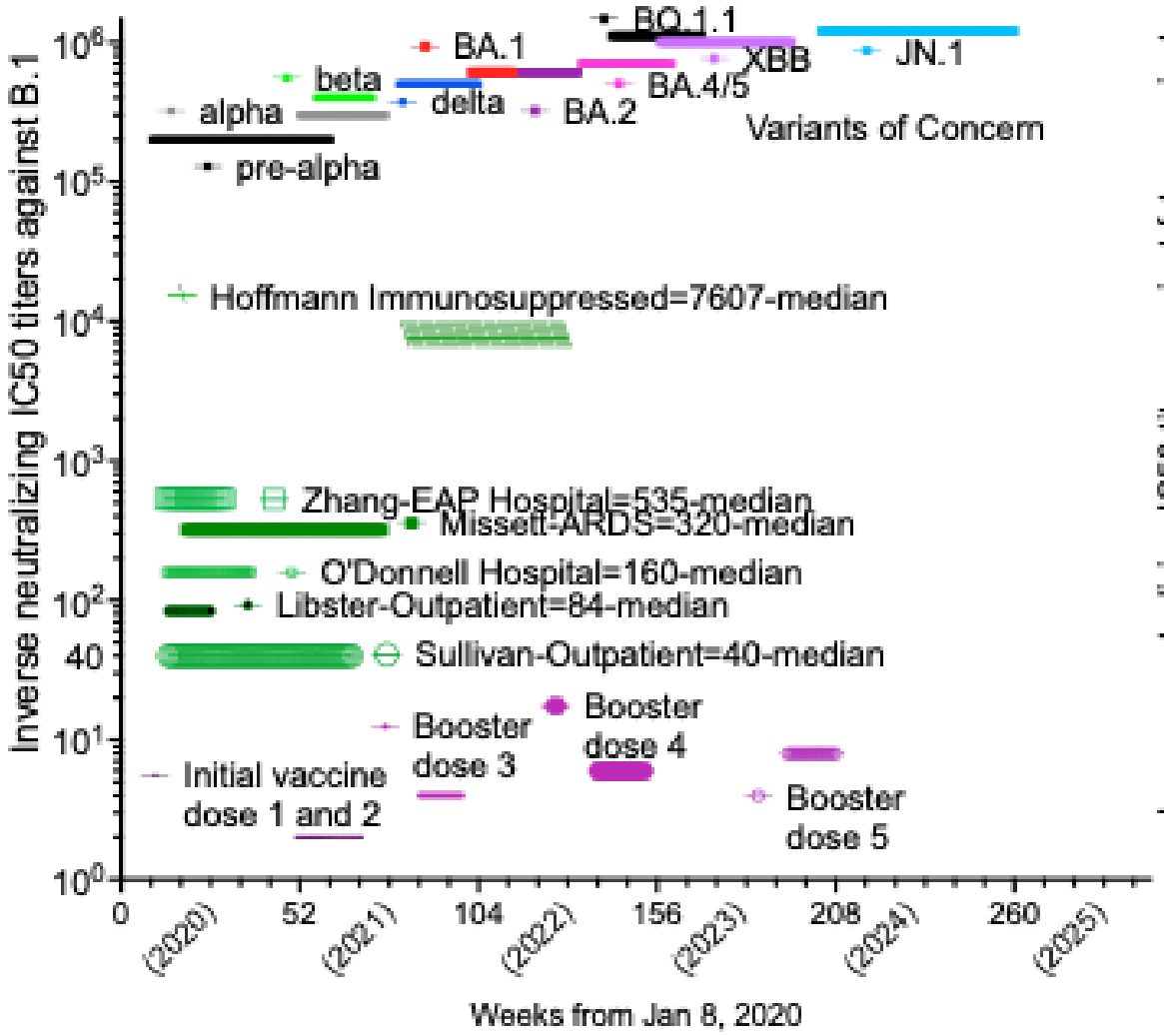
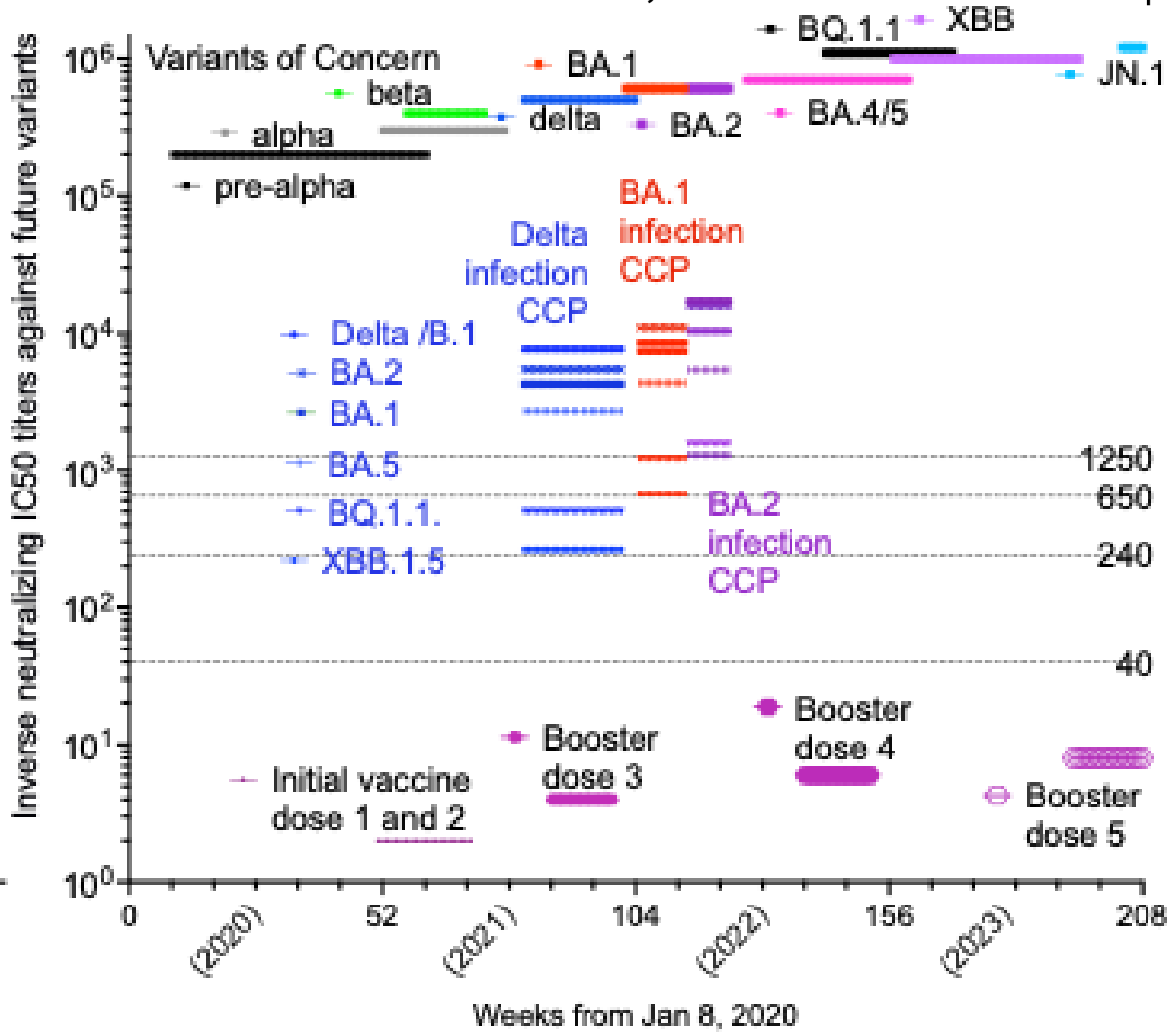
Expert Rev Anti Infect Ther. 2026 Jan;24(1):97-111. doi: 10.1080/14787210.2026.2623136.

Comparison of COVIC-19 SARS-CoV-2 plasma neutralizations titers in the context of other efficacious CCP trials, vaccinations and periods for SARS-CoV-2 variants of concern

A Donor median plasma neutralizations



B The COVIC-19 donor pool delineated most recent SARS-CoV-2 infection in the delta, omicron BA.1 and BA.2 periods.

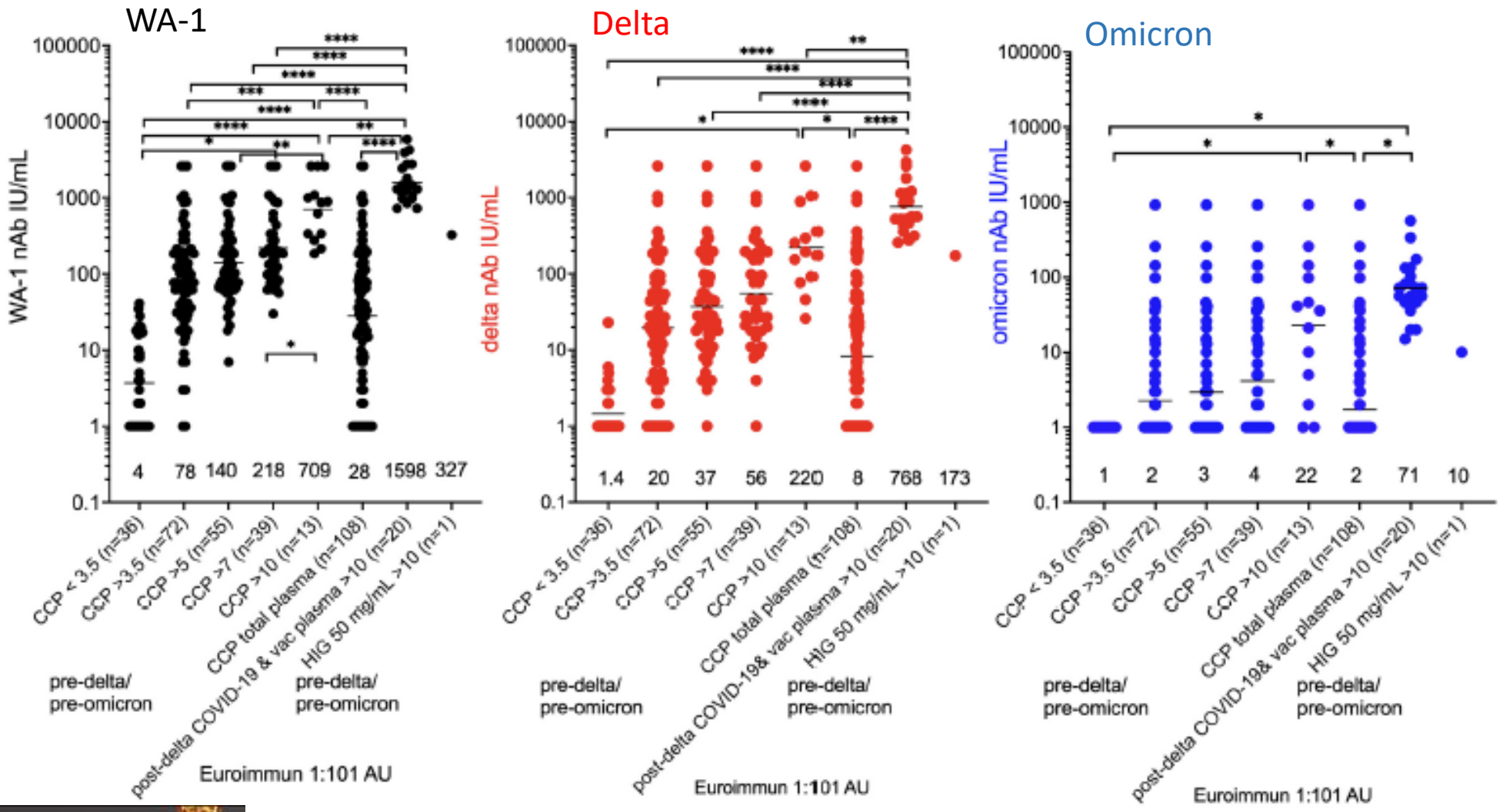


High levels of antibodies in the top deciles still retain therapeutic neutralization against future variants.

High titer mismatch equals medium titer variant match in neutralization efficacy

Sorting higher Euroimmun categories indicates virus neutralization to WA-1, delta and omicron

WA-1, delta and omicron virus microneutralization measured in CCP, post-delta COVID-19/post-vaccination and hyperimmune globulin (HIG) sorted for viral-specific antibody levels by Euroimmun arbitrary units (AU) at 1:101 dilution. IU/mL geometric means are shown above x-axis.



Blood Adv. 2022 Jun 28;6(12):3678-3683.

Therapeutic Convalescent Plasma Niche

Antibodies work best when delivered early in disease in high antibody levels

Efficacy will be unique to different microbes

Antibody naïve or predominate seronegative

Two phase disease with mild disease before severe disease

High (above 1%) case fatality to warrant convalescent donor pools

Lack of efficacious small molecule antivirals

No vaccine or monoclonal antibody therapy

Availability of rapid molecular diagnostic outpatient test

Potential candidates-RSV in adult immunosuppressed, Bird flu, West Nile Virus, Andes Hantavirus, CCHF, fungal infections, *Staph. aureus*, *Candida auris*, *Acinetobacter baumanii*

COVID-19 PLASMA TRIALS
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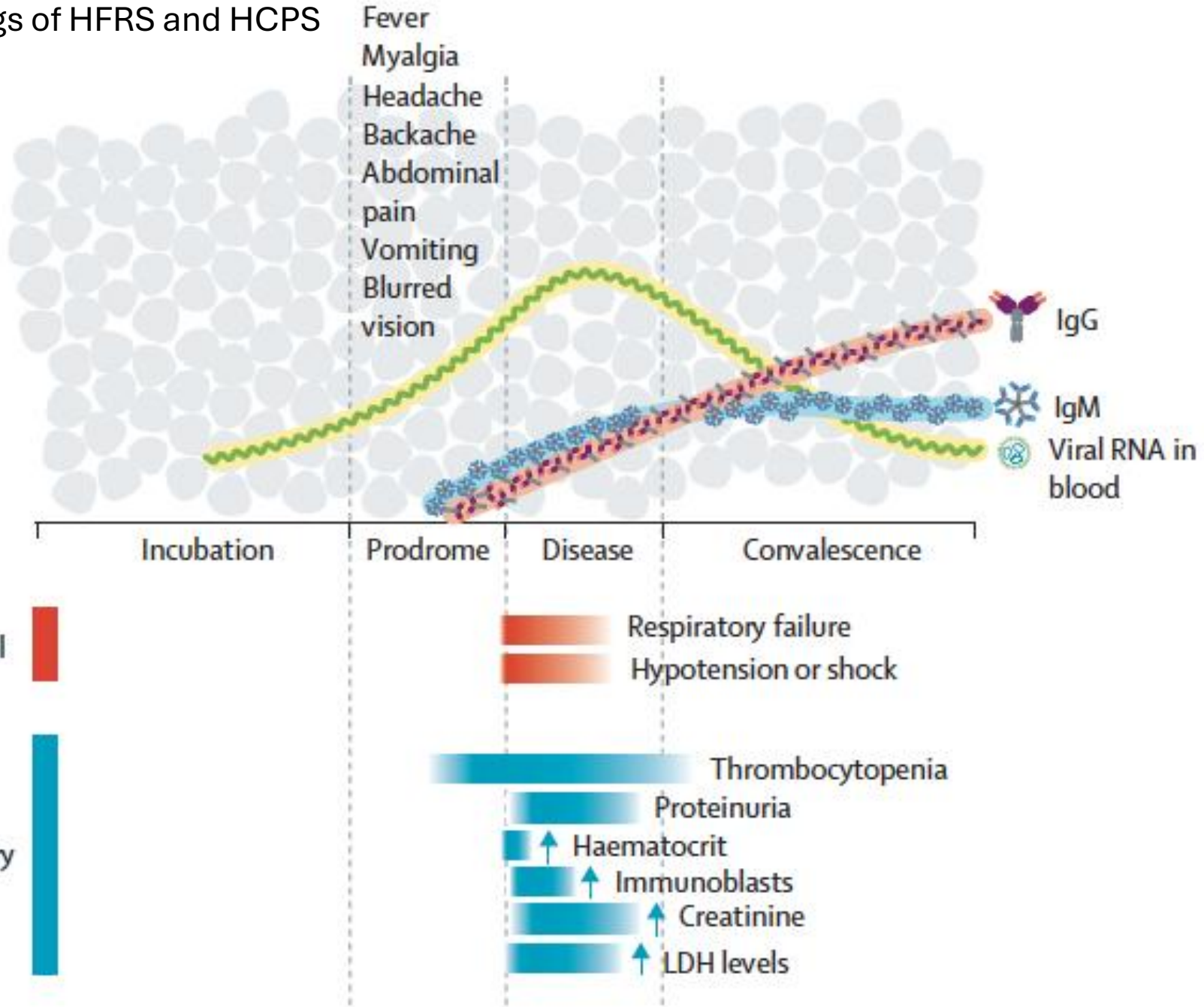
Main clinical and laboratory findings of HFRS and HCPS



HCPS=hantavirus cardiopulmonary syndrome.

Lancet Infect Dis 2023; 23: e371–82

	HFRS	HPS
incubation period	3 weeks (1.5-6 weeks)	2 weeks (1.3-5 weeks)
phases	febrile,	fever
	hypotensive	dyspnea cough
	oliguric	hypotensive/shock
	polyuric	
	convalescent	convalescent
Case fatality rate	1-15%	20-40%
pos IgM and IgG Ab to N pro	symptom onset	symptom onset
NAT	symptom onset	symptom onset
Treatment		
ribavarin	7 fold drop in deaths	inconclusive
immunotherapy	no RCT	no RCT
vaccine	phase 1/2	phase 1/2

CLINICAL MICROBIOLOGY REVIEWS, Apr. 2010, p. 412–441
0893-8512/10/$12.00 doi:10.1128/CMR.00062-09

A non-randomized multicentre trial of human immune plasma for treatment of hantavirus cardiopulmonary syndrome caused by Andes virus

- **Intervention:** Immune plasma from ANDV-convalescent donors (collected ≥6 months post-HCPS via plasmapheresis), administered intravenously at a neutralizing antibody (NAb) dose of **5,000 U/kg**.
- **Results:** From 2008-2012, Among 29 confirmed HCPS cases treated with immune plasma, the **case fatality rate (CFR) was 14% (4/29)**, compared to:
  - 32% (63/199) in untreated cases nationally during the same period (P = 0.049, OR 0.35)
  - 27% (18/66) at the same study sites from 2005–2012 (P = 0.15)
  - 33% (20/60) in a prior methylprednisolone trial (P = 0.052)
- **Safety:** No serious adverse events were associated with plasma infusion.
- **Limitations:** The study was non-randomized, and plasma NAb titers achieved in recipients were variable. **Viral load remained stable despite treatment,** raising questions about the mechanism of benefit.

Antivir Ther . 2015;20(4):377-86. doi: 10.3851/IMP2875. Epub 2014 Oct 15

The Convalescent Plasma Path Forward

Maintain a registry of confirmed recovered survivors who may be eligible to donate high-titer investigational immune plasma if requested under an authorized clinical/regulatory pathway for many pathogens of pandemic potential

Core components (Public/Private Sponsorship for Investigational program)
Confirmed survivor registry
Permission-to-contact consent
Neutralizing antibody testing pathway
Donor classification system
Apheresis collection SOP
Investigational labeling/storage/release SOP
IND/expanded access template
Public health and hospital referral network

The model is a public-health–linked warm registry of confirmed hantavirus (other potential pandemic microbe) survivors, prequalified by neutralizing antibody testing, with rapid apheresis activation under IND/expanded access or trial protocol.

AABB Plasma Antibody Network (PLAN)-Reik, Lanteri, Casadevall, Sullivan, Hanley

The clinical trial engine is built to shine bench data on equipoise.

FDA approvals rely on multiple trials in multiple phases of disease for safety and efficacy as well as potency.
FDA approval on Dec 10 2024 with safety, efficacy and potency against variants of concern generated much of this JHU work. **The CSSC manuscripts were all crafted to generate the FDA evidence base for approval.**

PUBLISHED MANUSCRIPTS (#=61) March 2020 to March 2025

A. Papers testing safety and efficacy in diverse clinical populations (#=5)

Efficacy in Infection outpatient prevention (no), Early outpatient treatment (yes), Pediatric pharmacokinetics (yes), death reduction in both outpatients and inpatients (yes) and in those newly mechanically ventilated (yes).

B. Papers characterizing donor convalescent plasma (#=16)

Age, sex and hospitalizations increase convalescent antibody levels, Fragment crystallizable portion contributes to CCP efficacy function, CCP has remnant elevated cytokines and heterogeneity of T-cell responses contributes to durable immunity

C. Papers describing novel biologic properties of convalescent plasma recipients and variant activity (#=11)

CCP catalyzes (degrades) SARS-C0V-2 spike protein, CCP neutralizes future variants appearing months after infection or vaccination, dual vaccination and infection raise high the antibodies.

D. Papers characterizing secondary outcomes of clinical studies (#=10)

Early transfusion of plasma units in the upper 30% of study donors' antibody levels reduced outpatient hospitalizations. High antibody level plasma units, given early, should be reserved for therapeutic use. Outpatient convalescent plasma is safe. A Meta-Analysis of Individual Participant Data from 5 diverse outpatient trials noted early high titer effectiveness.

E. Guidance and perspectives (#=19)

Meta-analysis perspective on convalescent plasma compared to monoclonals, antiviral drugs and repurposed drugs in the outpatient setting to prevent hospitalizations. Guidance on the use of CCP to treat immunocompromised COVID-19 patients. When transfused within 7 days from symptom onset, CCP significantly reduced the risk of death in those already hospitalized.

Heroes of the Study

Amy Gawad
Karen Lane
Nichol McBee
Jamie Braun
Lisa Walborn
Joe Trolio
Cecilia Pessoa Gingrich
Shannon Hillery
Marianne Gildea
Nathan Walborn
Daniel Amirault
Megan Clark
Yvonne Higgins
Steph Katz
Mark Sulkowski
Dan Ford
Megan Singleton
Craig Hendrix
Howard Lederman
Carol Ann Huf
Jeanne Keruly
Gill Wylie
Cindy McInnis
Christi Marshall
Sandra Thoman
Melissa Nealy
Rivcah Davis
Leigh Smith
Eric Gehrie
Emily Blair
Lisa Walborn
Joe Troilo

Kim Kafka
Cynthia Sparks
Mikaela Olsen
Alana Yoffa
Ali Otto
Amanda Penna
Jennifer Clinin
Ann Folmer
Joanne Harkness
Shelby Brumback
Bilenda Vazanian
Angie VanTassel
Belinda Overstreet
Vicky Virina
Charissa Hariston
Donna Boone
Kat Wren
Ishear Townes
Nicky Karlens
Diane Lanham
Sonali Thapa
Smita Khati
Atika Singh
Bukola Adeosunoe
Amrita Raj
Jessica Coleman
Thuy Anderson
Eugene Bosworth
Mont Brownlee
Sherilyn Brinkley
Marie Radinsky

Site PIs

Shweta Anjan University of Miami
Patrick Broderick Danbury Hospital
Lalo Cachay UCSD
Valerie Cluzet Vassar Brothers Hospital
Judy Currier UCLA
Donald Forthal UC Irvine
Yuriko Fukuta Baylor University
Jonathan Gerber University of MA, Worcester
Jean Hammel Wester CT Health Network
Laura Hammitt JHSPH CAIH
Sonya Heath University of Alabama
Moises Huaman University of Cincinnati
Seble Kassaye MedStar Georgetown
Adam Levine Brown University
Barry Meisenberg Anne Arundel Med Center
Giselle Mosnaim NorthShore University
James Paxton Wayne State University
Bela Patel Univ Texas, Houston
Aarthi Shenoy MedStar Washington
Emily Spivak University of Utah
Martin Zand University of Rochester

Thomas Gniadek Northshore University

Bryan Lau
Stephan Erhart
David Shade
Sheriza Baksh
Molly Duan
Ying Wang
Manusha Thakar
Irina Shats

Evan Bloch
Aaron Tobian
Dan Hanley
Arturo Casadevall
Adriano Franco
Brett Dietz
Isaiah Hoffland
San Suwanmanee

Larry Appel
Shmuel Shoham
Kelly Gebo
Oren Gordon
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Sanjay Jain
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Dan Ford

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Bloomberg Philanthropies
COVID-19 RESPONSE

NIH National Institute of Allergy and Infectious Diseases

NIH National Center for Advancing Translational Sciences

The Moriah Fund Est 1985

MARYLAND Department of Health

Mental Wellness Foundation
8171 Maple Lawn Boulevard
Fulton, MD 20759

TRIAL INNOVATION NETWORK

octapharma plasma

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