WEBINAR SERIES:

:

Convalescent Plasma as an Adjunct Therapy for COVID-19 (PlaSenTer): A Phase 2/3 Clinical Trial in Indonesia

David Handojo Muljono

Webinar “One year living with SARS-CoV-2:
Progress on prevention and treatment ”
Jakarta, 4 December 2021

Outline

- **Background and Rationale**
- Study design
- Interim results
- Limitations
- Conclusion

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Disease manifestation of COVID-19 is determined by the host and viral factors.

Two distinct but overlapping pathological subsets in COVID-19, initially by the virus and later by the host

The outcome of treatment is determined by when it is administered during the disease phases, i.e. the first (mild), second (moderate), and third (severe).

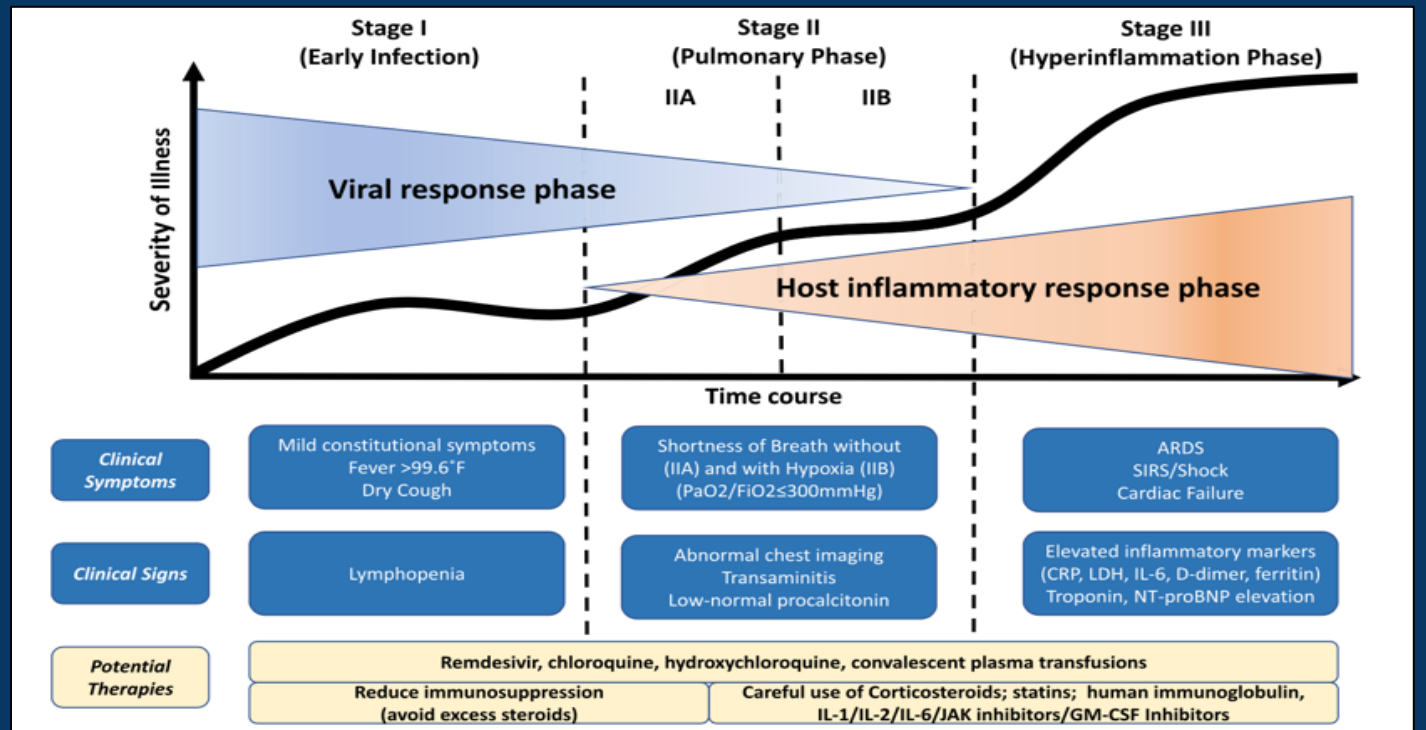


Figure 1 Classification of COVID-19 disease states and potential therapeutic targets. The figure illustrates 3 escalating phases of COVID-19 disease progression, with associated signs, symptoms, and potential phase-specific therapies. ARDS, acute respiratory distress syndrome; CRP, C-reactive protein; JAK, janus kinase; LDH, lactate dehydrogenase; NT-proBNP, N-terminal pro B-type natriuretic peptide; SIRS, systemic inflammatory response syndrome; GM-CSF, Granulocyte Macrophage Colony Stimulating Factor.

Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: A clinical-therapeutic staging proposal. *J Heart Lung Transplant* 2020; **39**(5): 405-7

3

Treatment strategies for COVID-19 (WHO)

Strategy	Category	Benefit
Antivirus	Remdesivir, Lopinavir/Ritonavir, Hidroklorokuin, Ivermectin, dll	**Depend on timing of therapy**
Immunology based therapy	Convalescent plasma	
	Specific Immunoglobulin	
	Non-specific Immunoglobulin	
	Stem-cell Therapy	
Immunomodulator	Corticosteroid	
	Interferon	
	Interleukin-inhibitor	
	Kinase inhibitor	
Adjuvant therapy	Anti-thrombotic	
	Vitamin and mineral	

Treatment strategies for COVID-19 (WHO)

Strategy	Category	
Immunology based therapy	**Convalescent plasma**	
	Specific Immunoglobulin	
	Non-specific Immunoglobulin	
	Stem-cell Therapy	
	Vaccination →	

Passive Immunotherapy

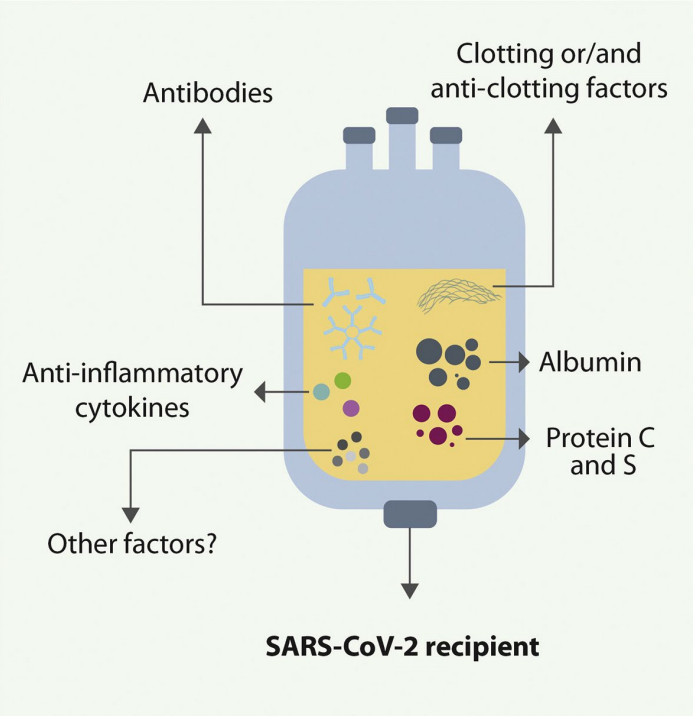
Active Immunotherapy

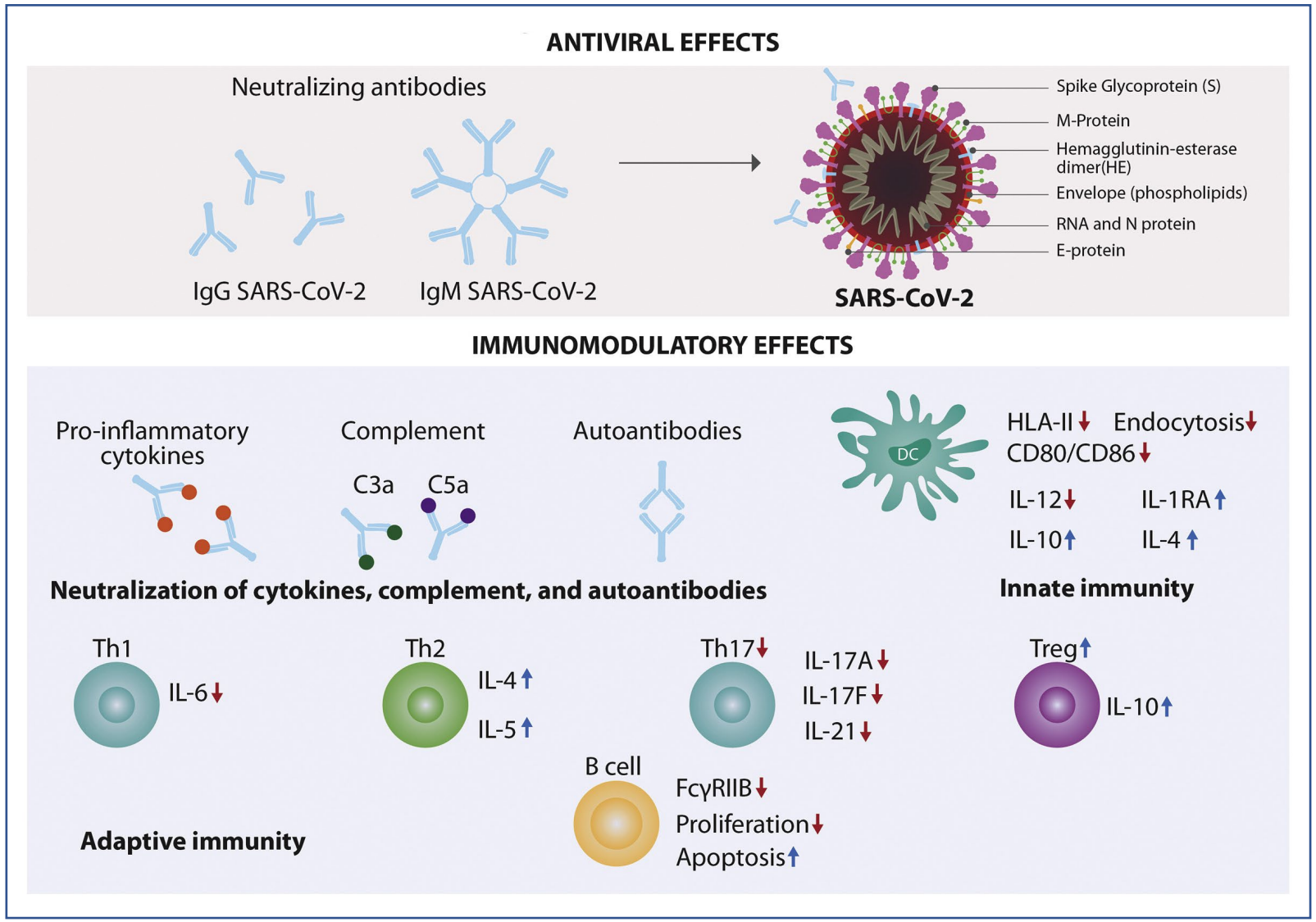
Antibody

Results of current studies

Main roles of convalescent plasma in the treatment of COVID-19

- ✓ **Antiviral property**
- ✓ **Immunomodulator**





Rojas et al. Convalescent plasma in Covid-19: Possible mechanisms of action Autoimmune reviews 2020. doi.org/ 10.1016 / j.autrev.2020.

Results of Convalescent Plasma Therapy 2020-2021

No	Peneliti	Lokasi	Design	Jumlah Subjek	Karakteristik Populasi Studi	Intervensi	Titer Plasma Donor	Ringkasan Hasil
1	Li, et.al., JAMA, 2020	China	RCT, open label	103 pasien (52 plasma, 51 kontrol)	COVID-19 derajat berat/kritis	1x200 mL, syarat titer S-RBD-spesific IgG =1:640	Tidak dirinci	**Tidak ada perbedaan perbaikan klinis dan mortalitas** secara umum pada kedua kelompok uji. **Serokonversi negatif** RNA virus lebih banyak terjadi pada **kelompok plasma**.
2	Gharbharan, et.al. medRxiv, 2020*	Belanda	RCT, open label	86 (43 terapi, 43 kontrol)	COVID-19 yang dirawat inap	Minimal 1x300 mL, dengan syarat titer antibody neutralisasi PRNT50 =1:80	Median titer PRNT50 donor 1:160	**Tidak ada perbedaan** dalam mortalitas, lama rawat inap ataupun perbaikan klinis pada hari ke-15. **84.8% subjek sudah memiliki antibodi** neutralisasi saat enrolment (medtiter 1:160)
3	Salazar, et. al., Am. J. Pathol., 2020	Amerika Serikat	Studi retrospektif, dengan *matched control*	387 (136 plasma, 251 *matched control*)	COVID-19 derajat berat/kritis	1-2 kali pemberian plasma.	90% resipien mendapatkan inisial dengan IgG anti-RBD =1:1350	Secara umum, **tidak ada perbedaan reduksi mortalitas** antar kedua kelompok, **kecuali** bila diberikan plasma dengan **titer IgG RBD > 1:1350 pada 72 jam pertama** admisi (p=0.047)
4	Liu, et.al., Nat. Med, 2020	Amerika Serikat	Studi retrospektif, dengan *matched control*	195 (39 plasma, 156 kontrol)	COVID-19 derajat berat/kritis	2x250 mL, syarat IgG Spike = 1:320, alat: MSH-ELISA	Tidak dirinci	**Perbaikan klinis** dan **peningkatan survival** lebih tampak di pemberian plasma pada pasien **non-intubasi, onset gejala dini** (<8 hari) dan menerima terapi antikoagulasi
5	Avendo-Sola, et.al., medRxiv, 2020*	Spanyol	RCT, open label	81 (38 plasma, 43 plasebo)	COVID-19 rawat inap fase awal (onset gejala <12 hari)	1x250-300 mL, kadar titer antibodi tidak diukur sebelum pemberian plasma	Median titer Antibodi netralisasi 1:292, metode: VMNT-ID50	**Tidak ada perbedaan** perburukan klinis, angka kematian dan laju kumulatif serokonversi RNA virus pada kedua kelompok UK

Results of Convalescent Plasma Therapy 2020-2021

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6	Agarwal, et.al., BMJ, 2020	India	RCT, open label	464 (235 plasma, 229 kontrol)	COVID-19 derajat sedang	2x200 mL, kadar titer antibodi tidak diukur sebelum pemberian plasma	Median titer Antibodi netralisasi 1:40, metode: VMNT	**Tidak ada perbedaan** proporsi perburukan klinis, kematian dan biomarker inflamasi. Serokonversi negative RNA virus pada hari ke 7 signifikan terjadi pada kelompok uji plasma
7	Simonovich, et.al., NEJM, 2020	Argentina	RCT dengan Placebo	333 (228 PK, 105 plasebo)	COVID-19 derajat berat	1x500 mL, syarat titer IgG Spike > 1:400	Median IgG Spike = 1:3200, alat: COVIDAR	**Tidak ada perbedaan** outcome klinis, proporsi kematian, durasi rawat inap, dan perbaikan klinis antara 2 kelompok uji.
8	Maor, *et al*, Lancet e-clinical medicine	Isreael	Kohort, prospektif , observasi	49	COVID-19 derajat ringan, sedang, dan berat. Dibagi 2 kelompok, mendapat PK dengan kadar antibodi rendah dan tinggi	2x200 mL dengan interval 24 jam	Kadar IgG <4 dan = 4 dengan ELISA (Euroimmun AG, Luebeck, Germany), setara kadar antibodi netralisasi <1:160 vs =1:160 dengan PRNT.	PK dengan kadar IgG tinggi berpotensi memberi hasil lebih baik pada kelompok pasien derajat dan berat disbanding PK dengan kadar IgG rendahKadar IgG <4.0
9	Joyner, et.al., J Clin Invest., 2020	Amerika Serikat	Studi Observasional, Open label	5000 pasien diberikan plasma konvalesen	COVID-19 derajat berat/kritis atau memiliki resiko progresifitas berat	1x200-500 mL, syarat titer antibodi plasma donor = 1:160	Tidak dirinci	**Terapi plasma konvalesen memiliki profil keamanan yang baik**, dengan SAE <1% dan kematian 0.3% pada 4 jam pertama transfusi. **Efikasi terapi plasma tidak dinilai** dalam studi.
10	Libster, et.al., NEJM, 2021	Argentina	RCT dengan Placebo	160 (80 plasma, 80 plasebo)	COVID-19 derajat ringan, onset gejala <72 jam, usia lanjut / dengan komorbid.	1x 250 mL, syarat titer IgG Spike > 1:1000	Median IgG Spike = 1:3200, alat: COVIDAR	Intervensi plasma dengan **titer tinggi** secara **dini (<72 jam** onset gejala) **dapat mencegah perburukan** penyakit COVID-19
11	Joyner, et.al., NEJM, 2021	Amerika Serikat	Kohort restrospektif,	3082	COVID-19 derajat berat / kritis (65.2%), perawatan ICU (60.6%), terpasang ventilator (33.3%)	Minimal 1x pemberian, kadar titer antibodi tidak diukur sebelum pemberian plasma	18.2% titer rendah, 65.1% titer sedang, 16.7% titer tinggi, alat: VITROS	Terapi PK **dapat menurunkan angka kematian** pada pasien yang diberikan **titer tinggi**, tidak terpasang ventilator dan diberikan pada waktu **3 hari pertama** setelah diagnosis.

Results of Convalescent Plasma Therapy 2020-2021

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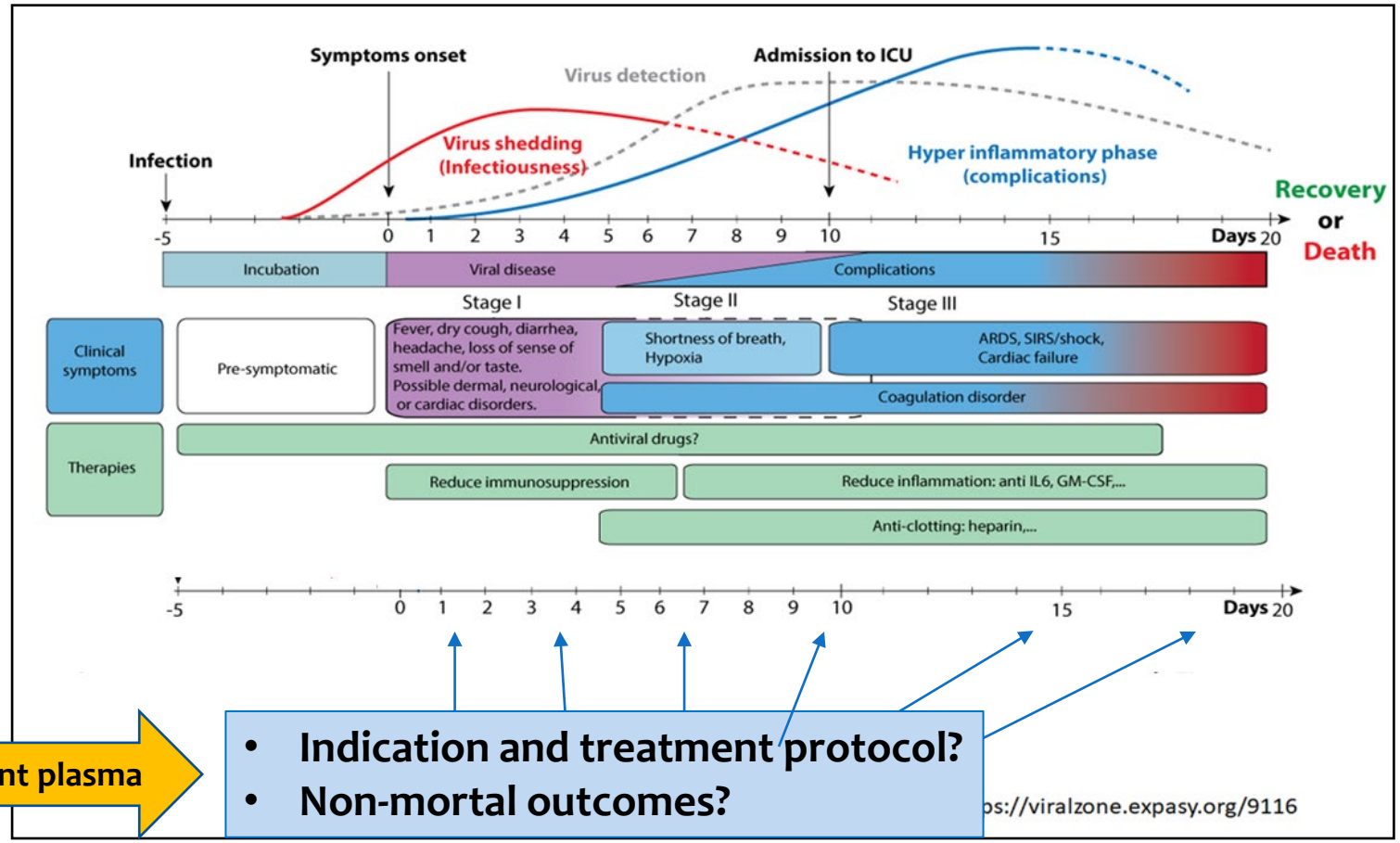
12	O'Donnel, Journal of Clin Invest 2021	Amerika Serikat, Brazil	RCT, double blind,	223 (150 terapi PK, 73 terapi Plasma normal)	Pasien COVID-19 berusia =18 tahun derajat berat dan kritis	PK 200-250 mL	Kadar IgG antibody SARS-CoV-2 = 1:400 dengan ELISA terhadap *spike protein*	PK memberikan perbaikan survival, tetapi tidak memberi perbaikan klinis bermakna, dalam periode 28 hari
13	Bégin et al,Nature Medicine, 2021	Canada, Amerika Serikat, Brazil	RCT, open label	938	Pasien dengan O2, dibagi menjadi 2: dirawat di ruang biasa (non-ICU) dan di ICU. Subjek dibagi 2: 614 mendapat PK dan 307 terapi standar	500 mL plasma	PK dengan kadar antibodi tinggi: (a) anti-RBD (OD = 500); (b) PRNT kadar = 1:500); (c) anti-S IgG = 500); atau (d) kadar antibody-dependent cellular cytotoxicity (ADCC) = 500, dibanding plasma dengan kadar rendah (dibawah kriteria a-d).	Intubasi atau kematian terjadi pada 199 (32.4%) dari kelompok terapi dan 86 (28.0%) dari 307 kelompok terapi standar (RR = 1.16, 95% CI 0.94–1.43, P = 0.18). Terapi PK dengan kadar antibodi rendah memberikan perburukan klinis pada kelompok terapi dibanding kelompok standar.
14	Horby et al, Lancet, 14 Mei 2021 (Recovery Collaborative Group)	Inggris	RCT, open label, dengan terapi standar sebagai kontrol	**11558**	COVID-19 derajat ringan (tanpa/dengan O2 nasal) dan dengan ventilasi mekanik, dibagi 2; **5795** dengan terapi PK dan **5763** dengan terapi standar	275 mL(200-350 mL), diberikan 2 kali selang 12-24 jam.	Plasma dengan kadar cut-off igG= 6 (EUROIMMUN ELISA; PerkinElmer, London, UK)	Pemberian plasma titer tinggi tidak meningkatkan survival atau outcome klinis yang bermakna
15	Korley et al, NEJM, 18 Agustus 2021	Amerika Serikat (21 negara bagian)	RCT, dengan terapi standar sebagai kontrol	**511** (257 terapi, 254 kontrol)	Subjek rawat jalan dengan risiko tinggi (berusia = 18 tahun dengan komorbiditas atau berusia = 50 tahun), dengan gejala COVID-19 **<7 hari.**	250 ml PK atau 250 NaCl 0.9%	Kadar antibody netralisasi = 1:160 dengan uji pseudovirus reporter viral particle neutralization (RVPN)	Terapi PK pada pasien rawat jalan berisiko tinggi dengan gejala <7 hari tidak mencegah perburukan penyakit.

Systematic reviews and Meta-analyses

Author	Title	Journal	Conclusion
Rajendran	Convalescent plasma transfusion for the treatment of COVID-19: Systematic review (April 2020)	Med Virol. 2020;1–9.	CP therapy in COVID-19 patients appears safe, clinically effective, and reduces mortality. Well-designed large multicenter clinical trial studies should be conducted urgently to establish the efficacy of CPT to COVID-19..
Wang et al	Convalescent plasma may be a possible treatment for COVID-19: A systematic review	International Immunopharmacology. 2021, 91(2):107262	CP **may be** a possible treatment option. High-quality studies are needed for establishing a stronger quality of evidence. Pharmacists should also be actively involved in the CP treatment process and provide close pharmaceutical care.
Szakó et al.	Convalescent plasma therapy for COVID-19 patients: a protocol of a prospective meta-analysis of randomized controlled trials	BMC Trials (2021) 22:112	CP therapy might be a good alternative to prevent the negative effects of COVID-19, but the clear benefits remain unclear. More prospective meta-analyses from randomized controlled trials are expected in terms of mortality, need and duration of intensive care unit stay, and organ failure
Janiaud et al	Association of Convalescent Plasma Treatment With Clinical Outcomes in Patients With COVID-19 A Systematic Review and Meta-analysis	JAMA 2021, 6 February 2021	Treatment with CP compared with placebo or standard of care was not significantly associated with a decrease in all-cause mortality or with any benefit for other clinical outcomes. The certainty of the evidence was low to moderate for all-cause mortality and low for other outcomes
Horby et al (Recovery)	Convalescent plasma in patients admitted to hospital with COVID-19	Lancet 2021, 14 May	In (severe) patients hospitalised with COVID-19, high-titre convalescent plasma did not improve survival or other prespecified clinical outcomes
Piechotta et al	Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review	*Cochrane Database of Systematic Reviews* 2021, Issue 5.	• The evidence on the effectiveness and safety of CP for the treatment of people hospitalised with COVID-19 is of low to very low certainty. • None of the studies assessed quality of life.
Axfors *et al*	Association between CP treatment and mortality in COVID-19: a collaborative systematic review and meta-analysis of randomized clinical trials	*BMC Infectious Diseases (2021) 21:1170*	• CP treatment of COVID-19 did not reduce all-cause mortality, and should not be used outside of randomized trials. • Evidence synthesis from collaborations among trial investigators can inform both evidence generation and evidence application in patient care.
Korley et al	Early Convalescent Plasma for High-Risk Outpatients with Covid-19	N Engl J Med 2021;385:1951-60	The administration of Covid-19 CP to high-risk outpatients within 1 week after the onset of symptoms of Covid-19 did not prevent disease progression

Gaps to fill

- Clinical trials from **different parts** of the world are yet to be finished and concluded
- Most studies investigated all-cause mortalities. Data on **non-mortal clinical outcomes are needed**



- Background and Rationale
- **Study design**
- Interim results
- Limitations
- Conclusion

Convalescent Plasma as Adjunct Therapy for COVID-19 (PlaSenTer)

Identifier: NCT04873414

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	364 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Clinical Trial of Convalescent Plasma Administration as Adjunct Therapy for COVID-19 (Uji Klinik Pemberian Plasma Konvalesen Sebagai Terapi Tambahan COVID-19)
Actual Study Start Date :	December 1, 2020
Estimated Primary Completion Date :	October 30, 2021
Estimated Study Completion Date :	December 31, 2021

Brief Summary and Rationale:

- Convalescent plasma (CP) has been the subject of increasing expectations for treating coronavirus disease 2019 (COVID-19), at least to provide a bridge to recovery for at-risk patients until vaccines become widely available
- To date, most studies focused on reporting CP treatment in patients with severe COVID-19, but only a few addressed benefits on less severe diseases. The vast majority of studies reporting COVID-19 infection and treatment have come from earlier affected countries with established health systems and research infrastructure, while very few are from low- and middle-income countries (LMICs).
- Nonetheless, CP therapy could be one of the few available options in LMICs where constraints may exist in the access to novel treatments, **even once available**. Clinical trials conducted in LMICs may differ in many respects from those in high-income countries.
- This study aims to evaluate the safety and efficacy of convalescent plasma therapy in hospitalized with moderate and severe COVID-19, to investigate the impacts of the treatment over the course of clinical illness, including non-mortal clinical outcomes.

Arm
Experimental: Treatment group Subjects in the Treatment Group are given 200 ml of Plasma collected from Convalescent Patients recovered from COVID-19 at two-day intervals in addition to standard supportive treatment
No Intervention: Control group Subjects in the Control Group are given standard supportive treatment

Intervention/treatment
Biological: Convalescent plasma treatment Convalescent Plasma collected from patients who recover from COVID-19 and have been discharged from the hospital for at least 14 days.

Outcome Measures

Primary Outcome Measures :

The mortality in COVID-19 patients treated with convalescent plasma

Number of deaths from the initiation of CP treatment until hospital discharge or death.

Secondary Outcome Measures :

- Change in clinical status category in CP-receiving patients
- Duration of hospitalization
- Duration of mechanical ventilation
- Duration of ICU stay
- Change in lung image radiography in CP-receiving patients
- Change in inflammatory parameters in CP-receiving patients
- Change in coagulation parameters in CP-receiving patients

- Change in viral load in CP-receiving patients
- Changes in anti-SARS-CoV-2 antibody levels in CP-receiving patients
- Systemic organ involvement in patients receiving CP treatment
- Time to resolution of symptoms in patients receiving CP treatment
- Treatment-related adverse events and serious adverse events (SAEs)
- Impact of anti-SARS-CoV-2 antibody levels in donors on the efficacy of CP therapy in CP-receiving patients
- Impact of anti-SARS-CoV-2 antibody levels in donors on the viral clearance in CP-receiving patients

WHO clinical progression scale

Patient State	Description	Score	
		10-point scale	6-point scale
Uninfected	Uninfected; no viral RNA detected	0	
Ambulatory mild disease	Asymptomatic; viral RNA detected	1	
	Symptomatic; independent	2	**1**
	Symptomatic; assistance needed	3	
Hospitalised: moderate disease	Hospitalised; no oxygen therapy*	4	**2**
	Hospitalised; oxygen by mask or nasal prongs	5	**3**
Hospitalised: severe diseases	Hospitalised; oxygen by NIV or high flow	6	**4**
	Intubation and mechanical ventilation, $pO_2/FiO_2 \geq 150$ or $SpO_2/FiO_2 \geq 200$	7	
	Mechanical ventilation $pO_2/FIO_2 < 150$ ($SpO_2/FiO_2 < 200$) or vasopressors	8	**5**
	Mechanical ventilation $pO_2/FiO_2 < 150$ and vasopressors, dialysis, or ECMO	9	
Dead	Dead	10	**6**

Including: **Non-mortal clinical outcomes**

WHO R&D Blue Print

Moderate COVID-19:
a disease with fever, respiratory, and pulmonary imaging findings, and at least one of the following:

i) *Abnormal coagulation parameters*:
- D-dimer >1 µg/mL
- Prothrombin time (>13.6 seconds) or International normalized ratio (INR) ≥1.8
- Thrombocyte count <100x 10^3/mL

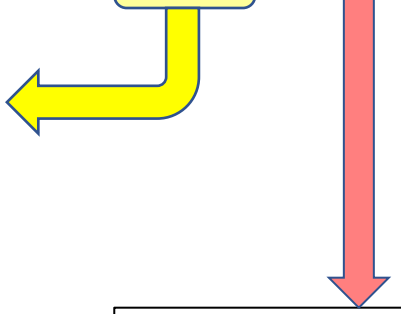
ii) *Increased pro-inflammatory markers*:
- C-reactive protein (CRP) ≥26.9 mg/L
- Procalcitonin ≥0.5 ng/mL,
- Lymphocyte count <1.5x 10^9/L) or Neutrophil/Lymphocyte ratio (NLR) >3.3

iii) *Presence of risk factors or comorbidities:*
- Age >65 years
- Type 1 Diabetes Mellitus or type 2 Diabetes Mellitus (Fasting blood glucose ≥126 mg/dl, 2-h plasma glucose ≥200 mg/dL, or random glucose ≥200 mg/dL, plus HbA1C >6.5%)
- Chronic kidney disease (creatinine >2.0 mg/dL) or with routine hemodialysis
- Chronic liver Disease with signs of liver cirrhosis; Child-Turcotte-Pugh (CTP) Class A or B or higher; or Model for End-Stage Liver Disease (MELD) score <39
- Heart failure (New York Health Association [NYHA] Class I or II)
- Bronchial asthma, chronic obstructive pulmonary disease (COPD), or pulmonary tuberculosis
- Cancer (particularly patients with chemotherapy or immunotherapy)
- Immunocompromised conditions, including HIV/AIDS, post-organ transplantation, Long-term corticosteroid use, autoimmune disease
- Sequential Organ Failure Assessment [SOFA] score ≥5.65
- Body Mass Index (BMI) ≥35 kg/m2

Criteria

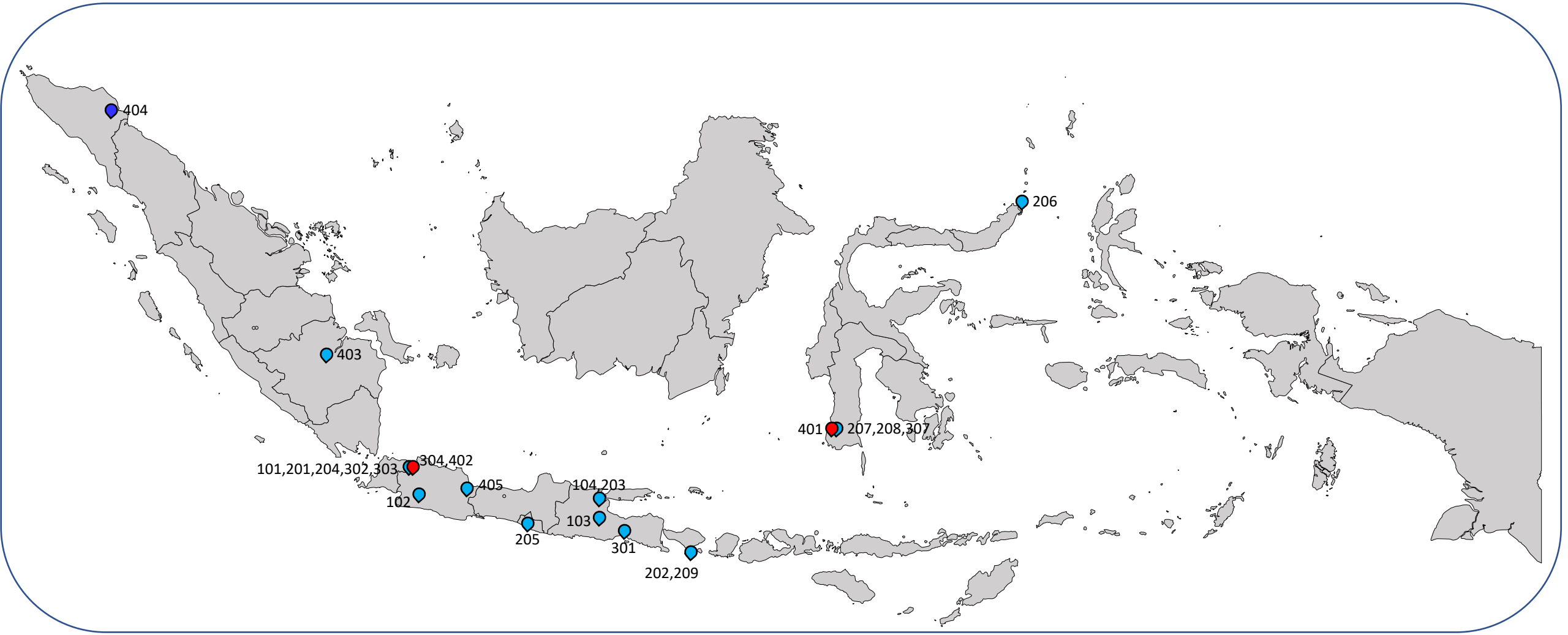
INCLUSION CRITERIA:

1. Patients with PCR-confirmed COVID-19
2. Minimal age:18 years
3. Agree to participate in the trial with written informed consent
4. Moderate or Severe COVID-19 at the time of enrollment



Severe Covid-19
a disease with Moderate COVID-19 criteria plus one of the following:
- respiratory rate ≥30 breaths/min,
- oxygen saturation <90%
- oxygenation index (PaO2/FiO2) ≤300 mmHg,
- lung infiltrates >50% within 24-48 h

Study sites: 25 hospitals



101 RSUP Fatmawati, Jakarta
102 RSUP Dr. Hasan Sadikin, Bandung
103 RSUD Sidoardjo, Sidoardjo
104 RSAL Dr. Ramelan, Surabaya

201 RSPI Sulianti Saroso, Jakarta
202 RSUP Sanglah, Denpasar
203 RSUD Dr. Soetomo, Surabaya
204 RSPAD Gatot Subroto, Jakarta
205 RS Dr. Soeradji Tirtonegoro, Klaten

206 RSUP Prof. Dr. R.D. Kandou, Manado
207 RSUP Dr. Wahidin Sudirohusodo, Makasar
208 RS Universitas Hasanuddin, Makassar
209 RS Universitas. Udayana, Bali
301 RSUD Dr. Haryoto, Lumajang

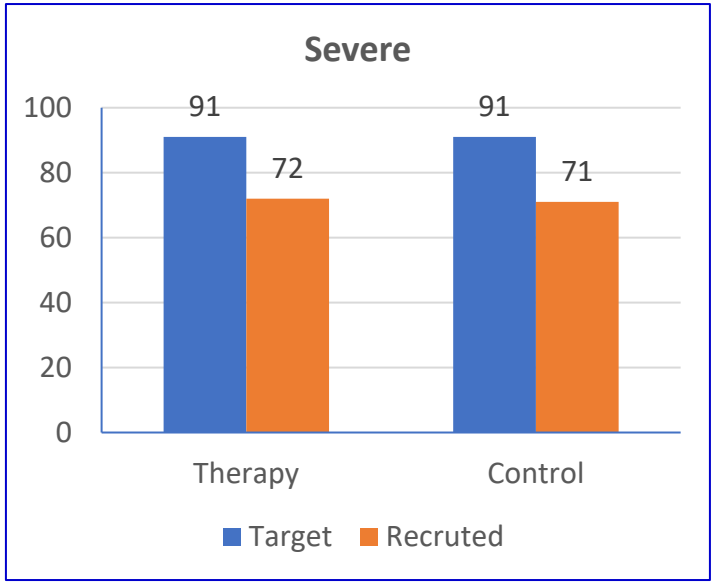
302 RSUD Pasar Minggu
303 RS Dr. Suyoto, Jakarta
307 RSUP dr. Tadjuddin Chalid, Makassar
403 RSUP Dr. M. Hoesin, Palembang
405 RSD Gunung Jati, Cirebon

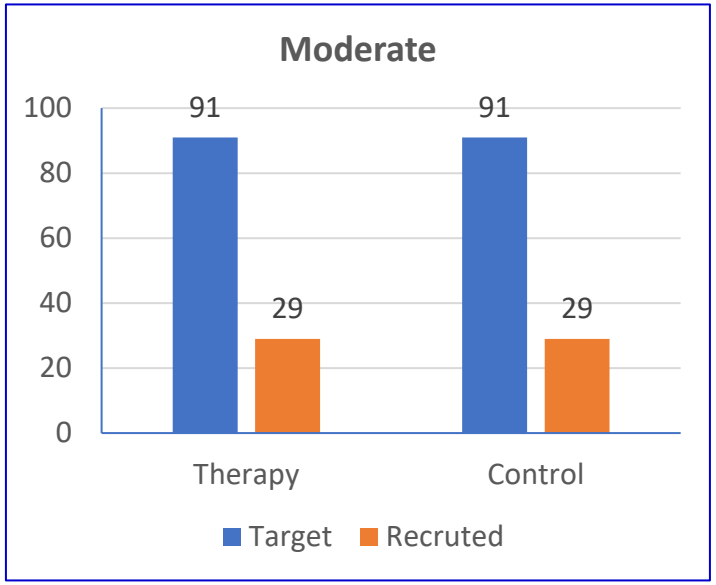
304 RS YARSI, Jakarta
401 RSKD Dadi, Makassar
402 RSUP Persahabatan, Jakarta
404 RSUD Aceh Tamiang, Aceh

- Background and Rationale
- Study design
- **Interim results**
- Limitations
- Conclusion

Number of participants recruited and randomization result

Hospital	Severe (143)		Moderate(58)	
	Control (72)	Plasma (71)	Kontrol (29)	Plasma (29)
101 - RSUP Fatmawati, Jakarta	2	5	0	1
102 - RSUP Dr. Hasan Sadikin, Bandung	4	3	0	0
103 - RSUD Sidoardjo, Sidoardjo	5	7	0	4
104 - Rumkital Dr. Ramelan, Surabaya	14	15	0	0
201 - RSPI Prof. Dr. Sulianti Saroso, Jakarta	2	3	0	0
202 - RSUP Sanglah, Denpasar	6	6	0	0
203 - RSUD Dr. Soetomo, Surabaya	10	4	1	1
204 - RSPAD Gatot Subroto, Jakarta	1	7	10	3
205 - RSUD Soeradji, Klaten	2	2	2	3
206 - RSUP Prof. Dr. R.D. Kandou, Manado	5	0	0	0
207 - RSUP Dr. Wahidin Sudirohusodo, Makassar	4	5	3	0
208 - RS Universitas Hasanuddin, Makassar	1	1	0	0
209 - RS Universitas Udayana. Jimbaran	2	4	0	0
301 - RSUD Dr. Haryoto, Lumajang	2	3	1	1
302 - RSUD Pasar Minggu, Jakarta	1	0	0	0
303 - RS Dr. Suyoto, Jakarta	2	0	0	0
305 - RSUPN Dr. Cipto Mangunkusumo, Jakarta	0	0	0	1
307 - RSUP dr. Tadjuddin Chalid, Makassar	1	2	0	0
403 - RSUP Dr. M. Hoesin, Palembang	2	2	0	0
404 - RSUD Aceh Tamiang, Aceh	1	0	0	0
405 - RSD Gunung Jati, Cirebon	2	2	0	2
406 - RSDC Wisma Atlit, Jakarta	2	0	12	11
502 - RSUD K.R.M.T Wongsonegoro	1	0	0	2

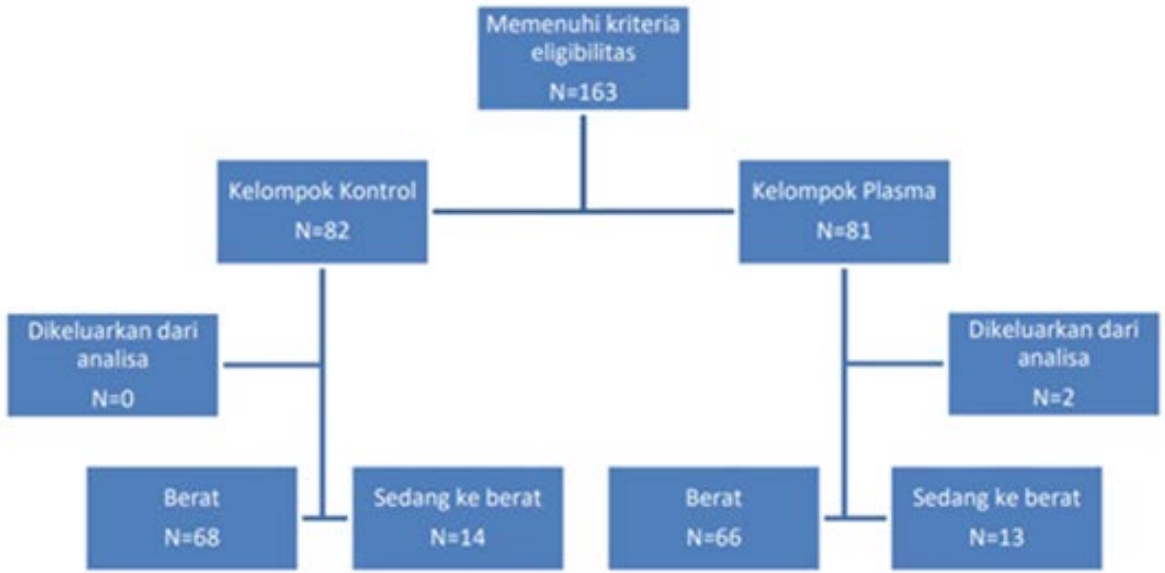




Status of participants (as of November 2021)

Hospital	Death	End of Study	loss to follow-up	on going	subyek pindah/dirujuk	withdrawn	Total Subyek
101 - RSUP Fatmawati, Jakarta	1	7					8
102 - RSUP Dr. Hasan Sadikin, Bandung	3	1	1			2	7
103 - RSUD Sidoardjo, Sidoardjo	2	12				2	16
104 - Rumkital Dr. Ramelan, Surabaya	7	18				4	29
201 - RSPI Prof. Dr. Sulianti Saroso, Jakarta	1	3		1			5
202 - RSUP Sanglah, Denpasar		11	1				12
203 - RSUD Dr. Soetomo, Surabaya	3	8		1	1	3	16
204 - RSPAD Gatot Subroto, Jakarta	1	18			1	1	21
205 - RSUP Soeradji, Klaten		7	1	1			9
206 - RSUP Prof. Dr. R.D. Kandou, Manado		3	2				5
207 - RSUP Dr. Wahidin Sudirohusodo, Makassar		7	2	1		2	12
208 - RS Universitas Hasanuddin, Makassar		2					2
209 - RS Universitas Udayana. Jimbaran	1	2		2	1		6
301 - RSUD Dr. Haryoto, Lumajang		4		2		1	7
302 - RSUD Pasar Minggu, Jakarta			1				1
303 - RS Dr. Suyoto, Jakarta	2						2
305 - RSUPN Dr. Cipto Mangunkusumo, Jakarta				1			1
307 - RSUP dr. Tadjuddin Chalid, Makassar		1	1			1	3
403 - RSUP Dr. M. Hoesin, Palembang	2	1				1	4
404 - RSUD Aceh Tamiang, Aceh		1					1
405 - RSD Gunung Jati, Cirebon	1	5					6
406 - RSDC Wisma Atlit, Jakarta		7		17		1	25
502 - RSUD K.R.M.T Wongsonegoro		1	1			1	3
Total	**24**	**119**	**10**	**26**	**3**	**19**	**201**

INTERIM ANALYSIS 2 (27 MEI 2021)



Gambar 1. Alur perekrutan subjek dan analisis

Tabel 9. Tabel evaluasi luaran Uji Klinik terhadap parameter "Kematian"

Keluaran	Semua subjek				Subjek kategori berat			
	n	OR/ HR	95% CI	p	n	OR/ HR	95% CI	p
Kematian (OR)	161	0,77	0,32 – 1,87	0,56	134	0,76	0,31 – 1,87	0,54
Waktu hingga terjadi kematian (HR)	151	0,75	0,31 – 1,81	0,51	125	0,72	0,3 – 1,73	0,45

Catatan
OR : odds ratio
HR : Hazard ratio

- Background and Rationale
- Study design
- **Interim results**
- **Limitations**
- Conclusion

Limitations/restrictions

- More severe cases were hospitalized
- Unwillingness to participate as controls
- Existing regulation in Indonesia: CP treatment can be given outside the trial
  - The scheme for using Covid-19 convalescent plasma is as follows:
    a. Clinical trial
    b. Use with specific monitoring
- Delay in obtaining consent to participate
  - Decision-making to accept medical interventions is envisioned as a communal/familial rather than an individualistic process
- Delayed availability of convalescent plasma in some occasions
  - Particularly during the surge of cases in (June – August 2020).

- Background and Rationale
- Study design
- **Interim results**
- **Limitations**
- **Summary**

Summary

- Convalescent plasma has been regarded as a modality for COVID-19 treatment, at least to provide a bridge to recovery for at-risk patients until the host (*individual or community*) immunity is achieved
- This study aims to evaluate the safety and efficacy of convalescent plasma therapy in hospitalized patients with moderate and severe COVID-19, to investigate the impacts of the treatment over the course of clinical illness, including non-mortal clinical outcomes.
- Interim analysis showed no significant difference in the survival of patients treated with Convalescent Plasma
- Most of the patients recruited are severe cases; efforts have been made to involve mild-to-moderate cases
- Study is still ongoing and to be finished and concluded

World Health Organization

Main outcomes of the meeting of the Expert Committee on Biological Standardization held from 18 to 22 October 2021

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3. There is currently little evidence to support the use of COVID-19 convalescent plasma in the treatment of moderate to severe COVID-19, and uncertainty exists regarding its potential utility in treating mild or asymptomatic COVID-19 infection. The ECBS was presented with the conclusions of a recently published Cochrane living systematic review and noted that this was a developing field with many studies still ongoing and firm conclusions on the efficacy of this approach in different subgroups of patients yet to be reached.

Thank you