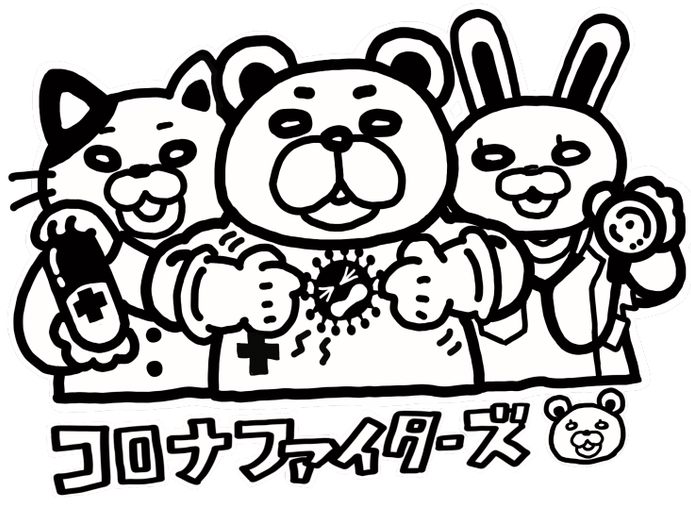
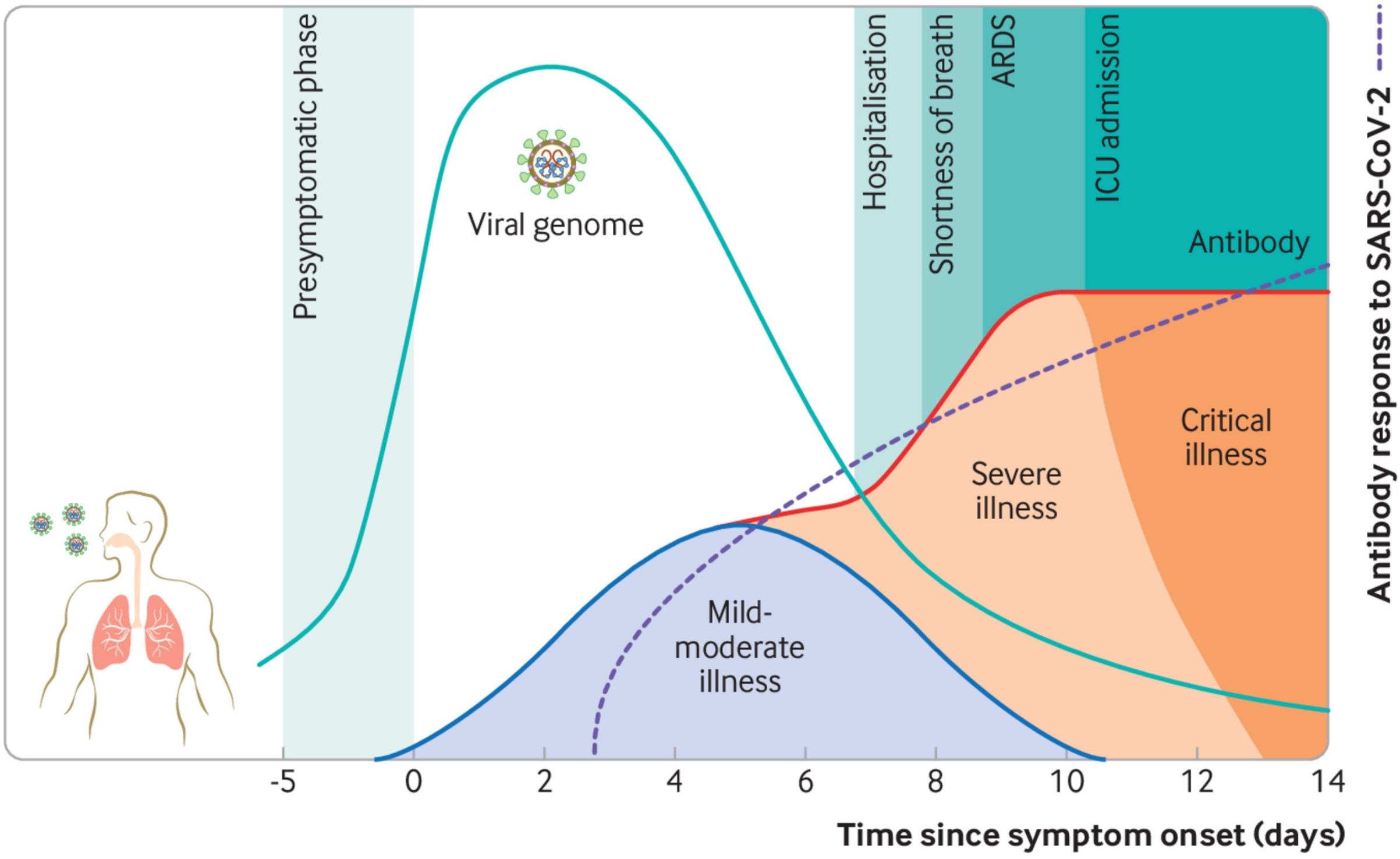
# Forefront of COVID-19 treatment: Effectiveness of antiviral and plasma neutralizing antibody therapy



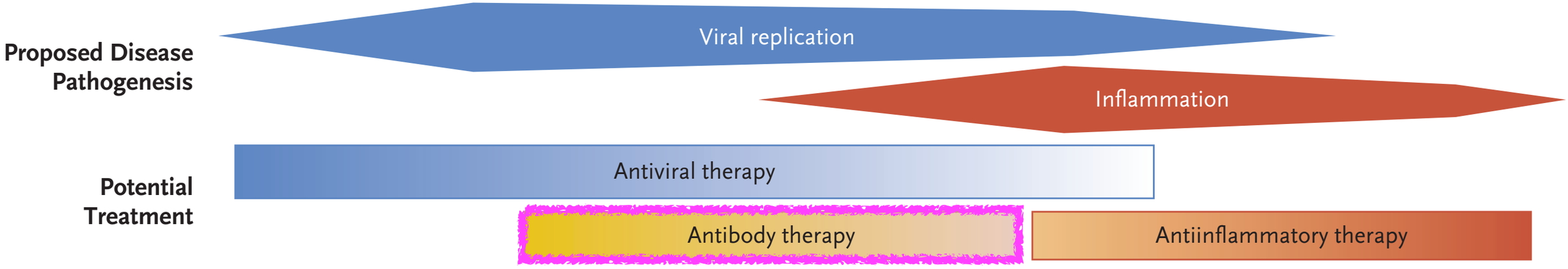

2021/06/07

The 12th NCGM International Infectious Diseases Forum




BMJ 2020;371:m3862

| | Asymptomatic or Presymptomatic | Mild Illness | Moderate Illness | Severe Illness | Critical Illness |
|---|---|---|---|---|---|
| **Features** | Positive SARS-CoV-2 test; no symptoms | Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea | Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94% | Oxygen saturation <94%; respiratory rate ≥30 breaths/min; lung infiltrates >50% | Respiratory failure, shock, and multiorgan dysfunction or failure |
| **Testing** | Screening testing; if patient has known exposure, diagnostic testing | Diagnostic testing | Diagnostic testing | Diagnostic testing | Diagnostic testing |
| **Isolation** | Yes | Yes | Yes | Yes | Yes |



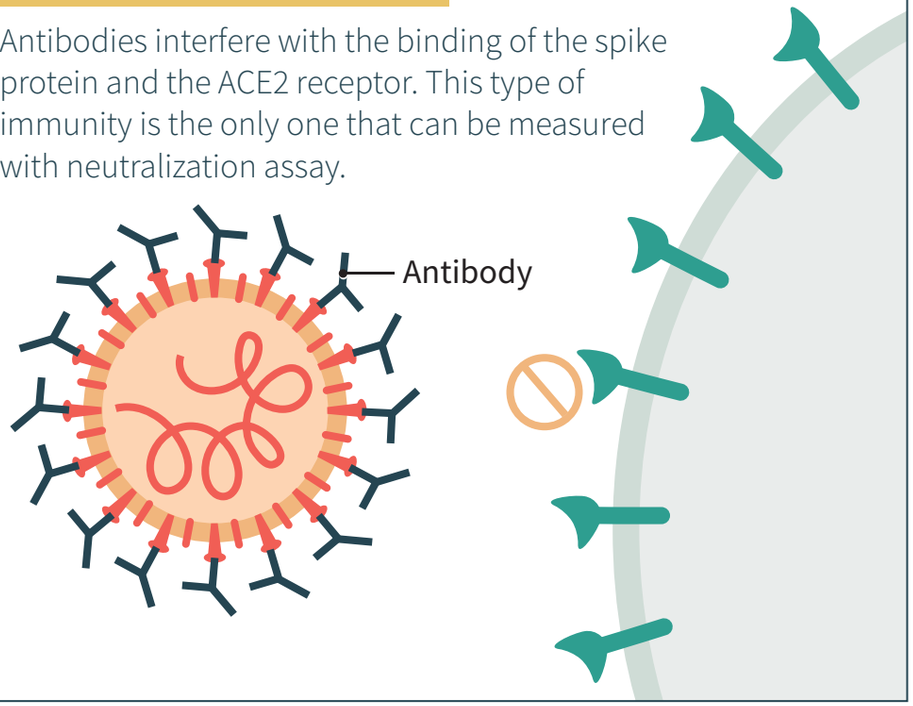

| | | | | | |
|---|---|---|---|---|---|
| **Management Considerations** | Monitoring for symptoms | Clinical monitoring and supportive care | Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir | Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone) | Critical care and specific therapy (dexamethasone, possibly remdesivir) |

DOI: 10.1056/NEJMcp2009249

# Potential mechanisms of action of anti–SARS-CoV-2 antibodies in COVID-19.

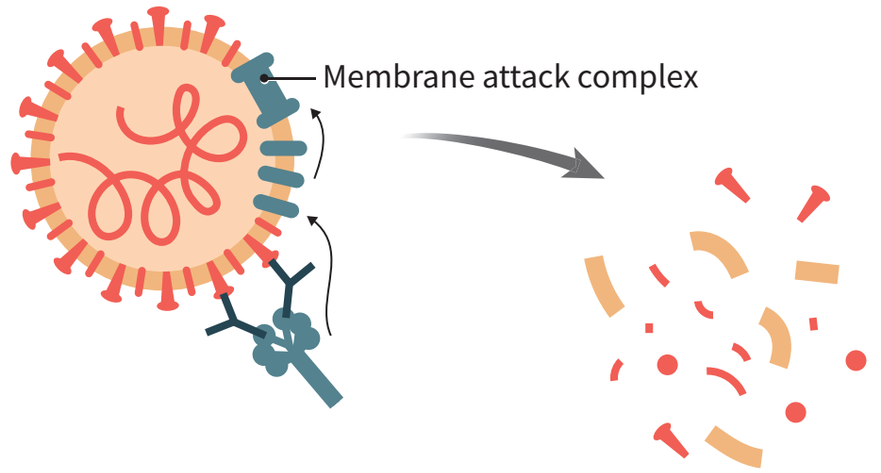
## A. Virus neutralization

Antibodies interfere with the binding of the spike protein and the ACE2 receptor. This type of immunity is the only one that can be measured with neutralization assay.



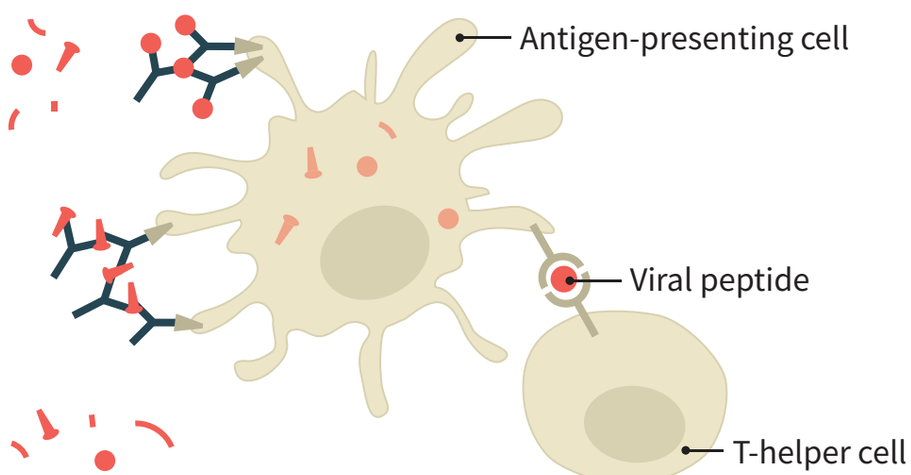

## B. Antibody-dependent virolysis

Antibodies can activate the classical pathway of complement and virolysis. This type of immunity cannot be measured with neutralization assay.



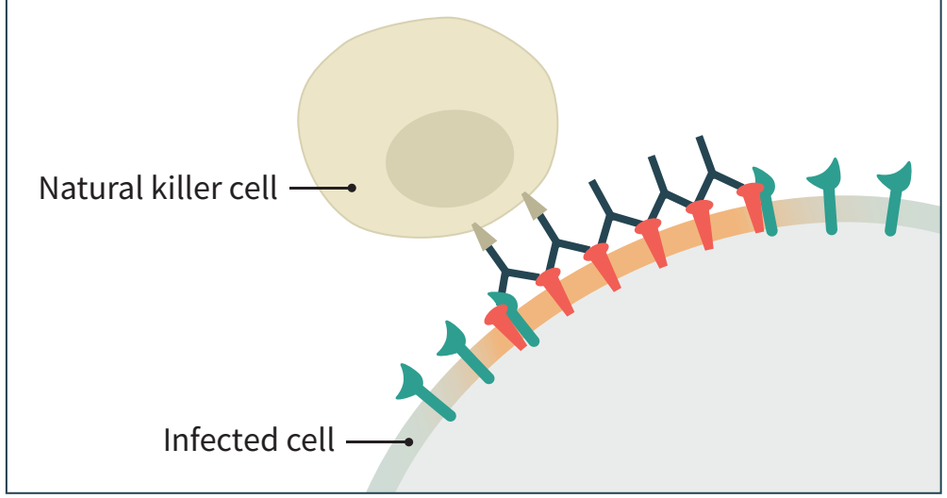

## C. Antibody-mediated presentation of antigen

Antibodies combine with viral particles, which promotes uptake by antigen-presenting cells and activates a cellular-mediated immune response. This type of immunity cannot be measured with neutralization assay.




## D. Antibody-dependent cell cytotoxicity

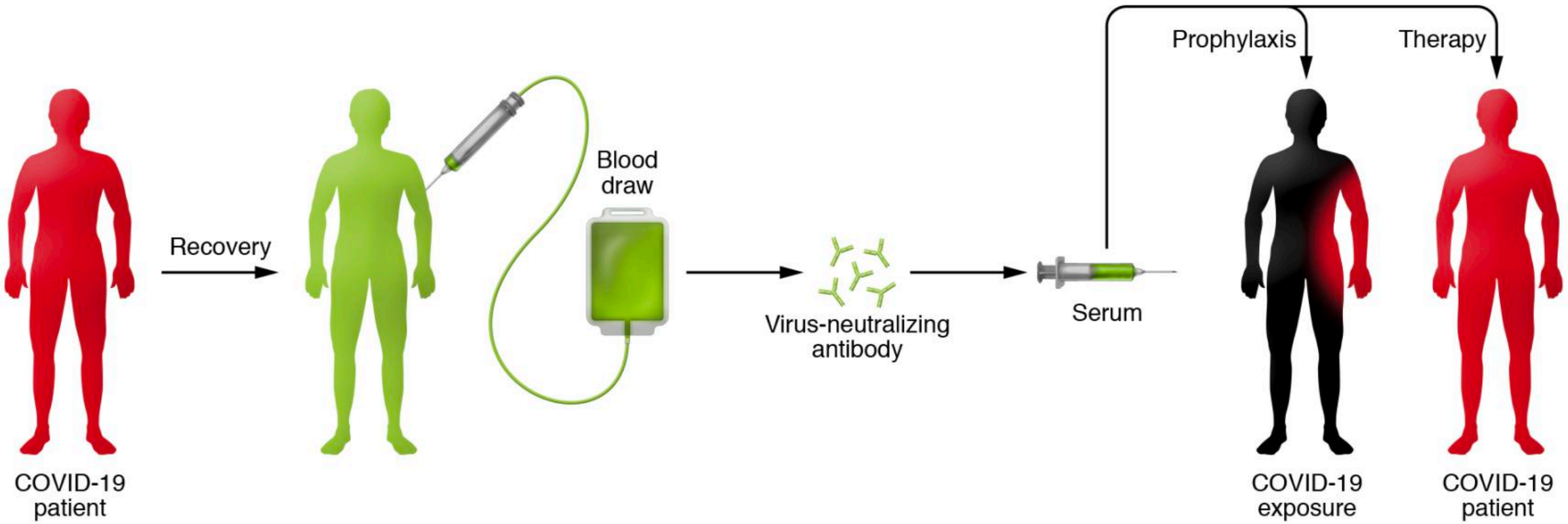
Antibodies on the host cell membrane allow natural killer cells to target infected cells for apoptosis. This type of immunity cannot be measured with neutralization assay.




CMAJ July 06, 2020 192 (27) E745-E755

# Convalescent Plasma Therapy

# Schematic of the use of convalescent plasma for COVID-19

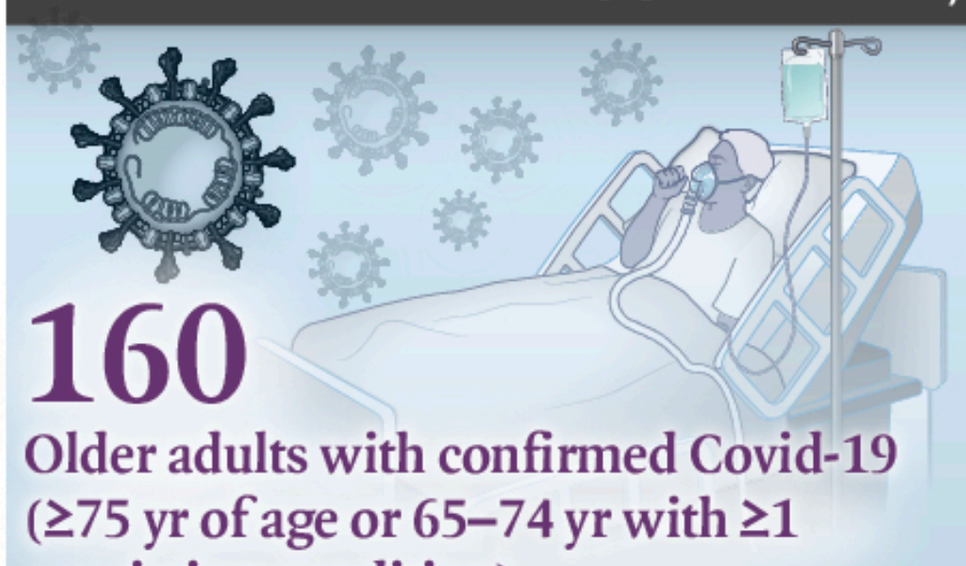



J Clin Invest. 2020;130(4):1545-1548.

The NEW ENGLAND JOURNAL of MEDICINE

# Early High-Titer Plasma to Prevent Severe Covid-19

**DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL**



**160**

**Older adults with confirmed Covid-19 (≥75 yr of age or 65–74 yr with ≥1 coexisting condition)**

## Convalescent plasma
**(IgG titer >1:1000)**

N=80

## Placebo
**(0.9% normal saline)**

N=80

**Severe respiratory disease (≥30 breaths per min, oxygen saturation <93% while breathing ambient air, or both)**

| Convalescent plasma | Placebo |
|---|---|
| 13 patients (16%) | 25 patients (31%) |

Relative risk, 0.52; 95% CI, 0.29 to 0.94; P=0.03

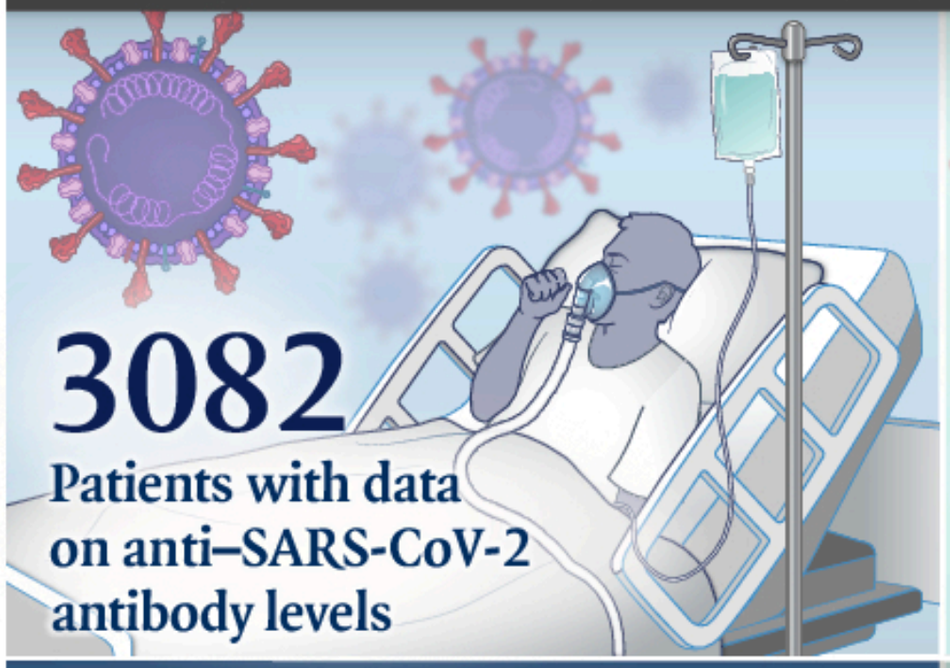
**High-titer convalescent plasma administered to older adults within 72 hours after the onset of mild Covid-19 reduced progression to severe disease.**

R. Libster et al. 10.1056/NEJMoa2033700

The NEW ENGLAND JOURNAL of MEDICINE

# Convalescent Plasma Antibody Levels and Covid-19 Mortality

RETROSPECTIVE STUDY BASED ON A U.S. NATIONAL REGISTRY



**3082**
Patients with data on anti–SARS-CoV-2 antibody levels

| | High Antibody Level | Medium Antibody Level | Low Antibody Level |
|---|---|---|---|
| | N=515 | N=2006 | N=561 |
| Death within 30 days after plasma transfusion | 22.3% (115 patients) | 27.4% (549 patients) | 29.6% (166 patients) |

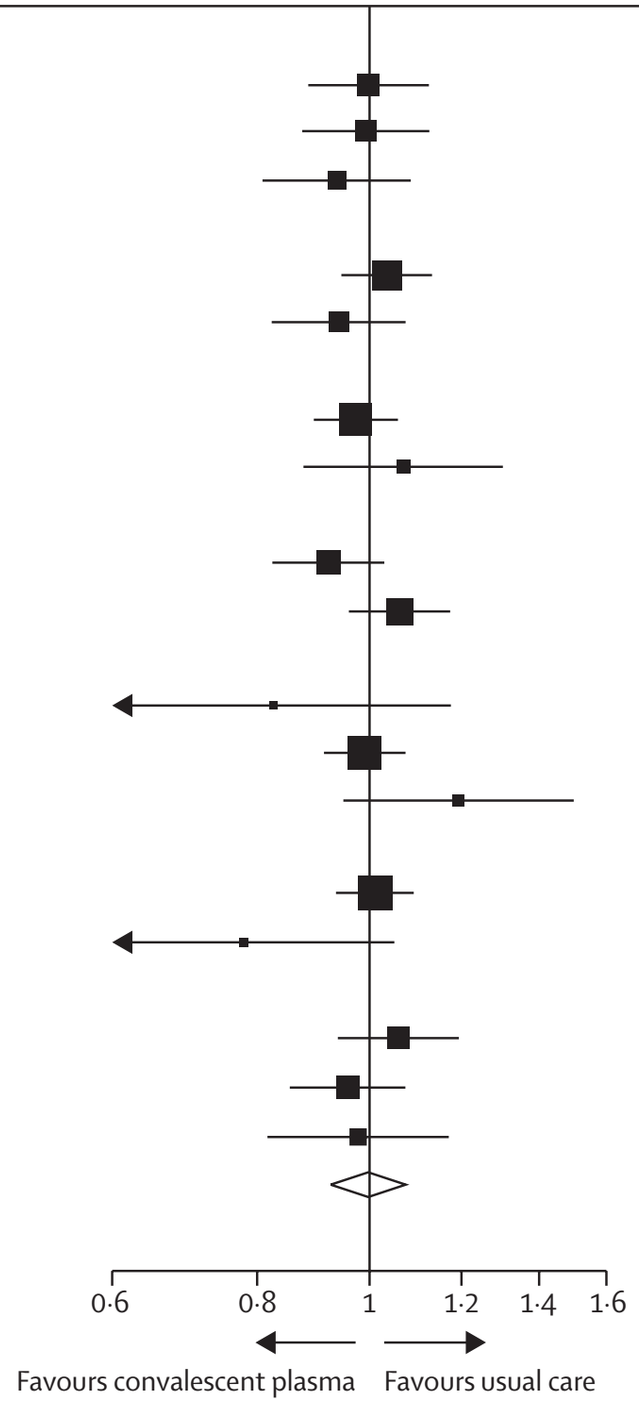
Relative risk (high vs. low), 0.66; 95% CI, 0.48 to 0.91

**In patients not receiving mechanical ventilation, transfusion of plasma with higher antibody levels was associated with a lower risk of death.**

M.J. Joyner et al. 10.1056/NEJMoa2031893

# Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial

| | Convalescent plasma group | Usual care group | RR (95% CI) |
|---|---|---|---|
| **Age, years ($\chi^2_1$=0·4; p=0·53)** | | | |
| <70 | 534/3705 (14%) | 545/3748 (15%) | 1·00 (0·89–1·13) |
| 70–79 | 495/1310 (38%) | 494/1281 (39%) | 0·99 (0·87–1·13) |
| ≥80 | 370/780 (47%) | 369/734 (50%) | 0·94 (0·81–1·09) |
| **Sex ($\chi^2_1$=1·3; p=0·25)** | | | |
| Men | 953/3643 (26%) | 972/3787 (26%) | 1·03 (0·95–1·13) |
| Women | 446/2152 (21%) | 436/1976 (22%) | 0·94 (0·82–1·07) |
| **Ethnicity ($\chi^2_1$=0·8; p=0·37)** | | | |
| White | 1111/4493 (25%) | 1129/4421 (26%) | 0·97 (0·90–1·06) |
| Black, Asian or minority ethnic | 198/833 (24%) | 199/887 (22%) | 1·07 (0·88–1·31) |
| **Days since symptom onset ($\chi^2_1$=3·4; p=0·06)** | | | |
| ≤7 | 606/2226 (27%) | 660/2240 (29%) | 0·92 (0·82–1·03) |
| >7 | 790/3564 (22%) | 748/3522 (21%) | 1·06 (0·96–1·17) |
| **Respiratory support received ($\chi^2_1$=3·5; p=0·06)** | | | |
| No oxygen received | 56/442 (13%) | 69/455 (15%) | 0·83 (0·58–1·18) |
| Oxygen only | 1185/5051 (23%) | 1194/4993 (24%) | 0·99 (0·91–1·07) |
| Invasive mechanical ventilation | 158/302 (52%) | 145/315 (46%) | 1·19 (0·95–1·50) |
| **Use of corticosteroids ($\chi^2_1$=2·7; p=0·10)** | | | |
| Yes | 1314/5370 (24%) | 1299/5311 (24%) | 1·01 (0·94–1·09) |
| No | 74/391 (19%) | 100/413 (24%) | 0·78 (0·58–1·05) |
| **Patient SARS-CoV-2 antibody test result ($\chi^2_1$=1·4; p=0·23)** | | | |
| Positive | 575/3078 (19%) | 501/2810 (18%) | 1·06 (0·94–1·19) |
| Negative | 642/2016 (32%) | 558/1660 (34%) | 0·96 (0·85–1·07) |
| Not done | 182/701(26%) | 349/1293 (27%) | 0·98 (0·82–1·17) |
| **All participants** | **1399/5795 (24%)** | **1408/5763 (24%)** | **1·00 (0·93–1·07)** |
| | | | **p=0·95** |




https://doi.org/10.1016/S0140-6736(21)00897-7

MAYO CLINIC



# Safety Update: COVID-19 Convalescent Plasma in 20,000 Hospitalized Patients

**TABLE 2. SAE Characteristics in Patients Transfused With COVID-19 Convalescent Plasma (N=20,000)[a]**

| SAE: Transfusion reactions | Reported | Related | % Estimate[b] (95% CI) |
|---|---|---|---|
| Mortality within four hours of transfusion | 63 | 10 | 0.05 (0.03-0.09) |
| TACO | 36 | 36 | 0.18 (0.13-0.25) |
| TRALI | 21 | 21 | 0.10 (0.07-0.16) |
| Severe allergic transfusion reaction | 21 | 21 | 0.10 (0.07-0.16) |
| 7-day SAE reports | | | |
| Thrombolic or thromboembolic complication | 113 | 38 | 0.19 (0.14-0.26) |
| Sustained hypotension[c] | 457 | 54 | 0.27 (0.21-0.35) |
| Cardiac events[d] | 677 | 80 | 0.40 (0.32-0.50) |
| 7-day mortality | Reported | | |
| Crude Estimate | 2592 | | 12.96 (12.50-13.44) |
| Clinical status | | | |
| No ICU admission (n=8323) | 772 | | 9.28 (8.67-9.92) |
| ICU admission (n=11,560) | 1806 | | 15.62 (14.97-16.30) |
| No mechanical ventilation (n=12,147) | 1220 | | 9.85 (9.34-10.38) |
| Mechanical ventilation (n=6864) | 1258 | | 18.33 (17.43-19.26) |
| Clinical symptoms | | | |
| No MOF or septic shock (n=17,081) | 1952 | | 11.45 (10.98-11.94) |
| MOF or septic shock (n=2919) | 640 | | 21.72 (20.27-23.24) |

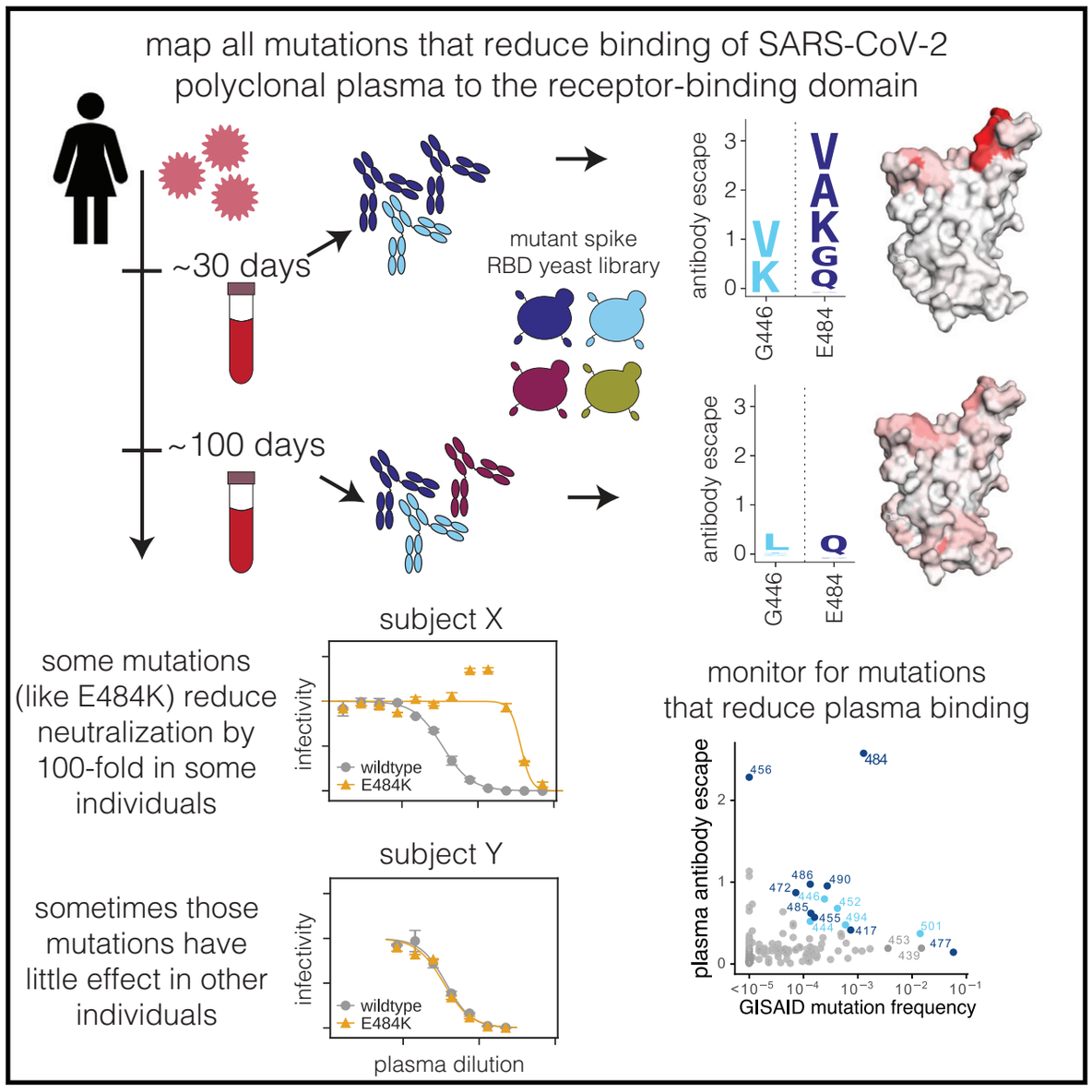
Safety report of 20000 patients who received convalescent plasma: the incidence of all serious adverse events was low and included allergic reactions (n=78, <1%), thromboembolic events (n=113, <1%), and cardiac events (n=677, ~3%). There was no ADE (antibody-dependent immune enhancement) and the safety was concluded to be high.

**Mayo Clin Proc. 2020 Sep; 95(9): 1888–1897.**

Cell Host & Microbe

# Comprehensive mapping of mutations in the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human plasma antibodies

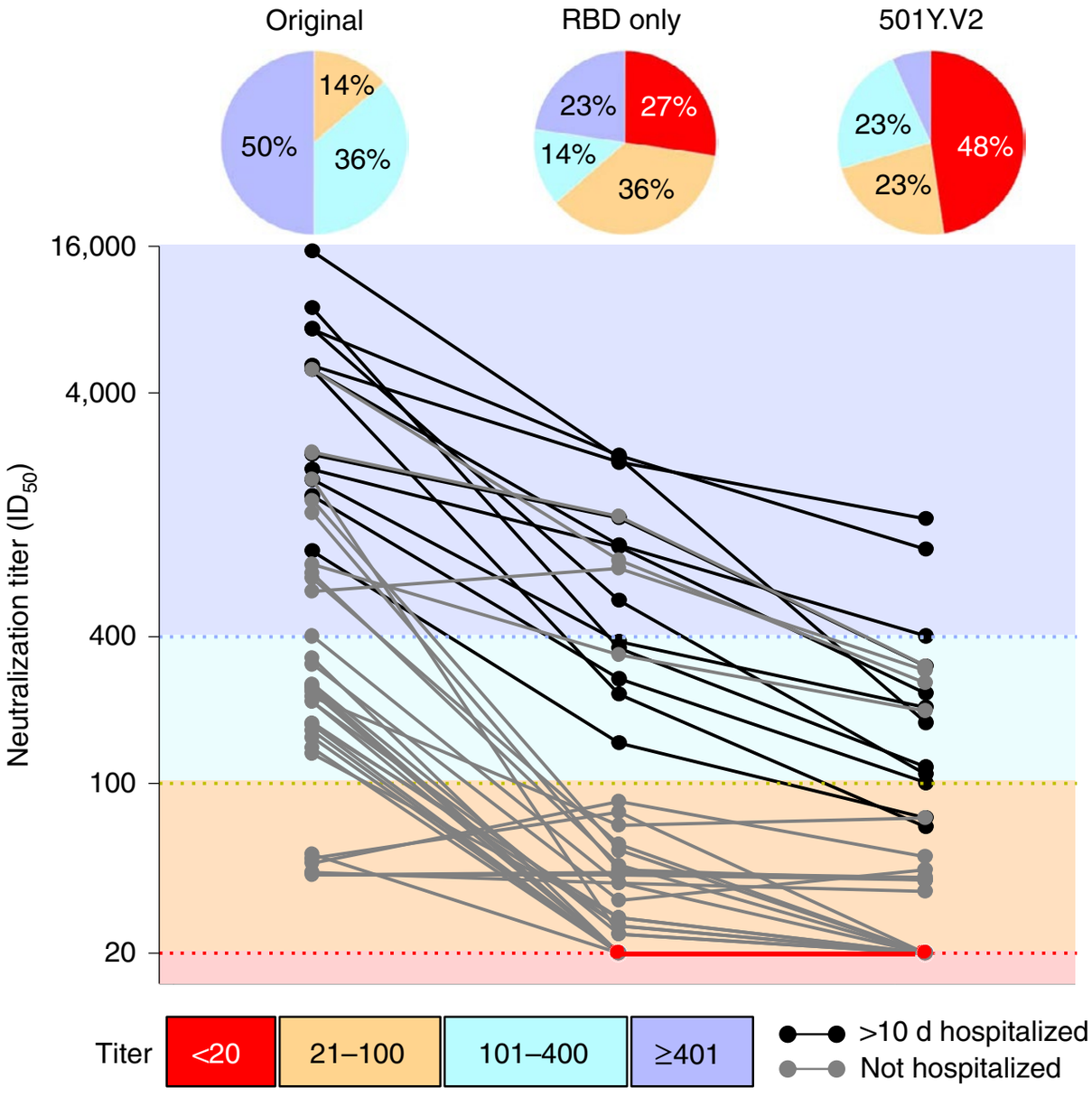
## Graphical Abstract




Cell Host Microbe. 2021;29(3):463.

BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-021-01285-x
nature medicine
Check for updates

# SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma

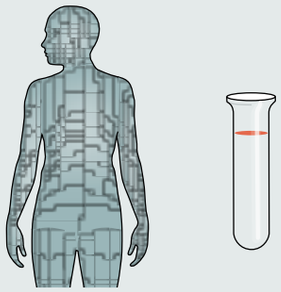



Nat Med . 2021 Apr;27(4):622-625.

# Neutralizing Monoclonal Antibody

**Process**
Source material

Convalescent patient



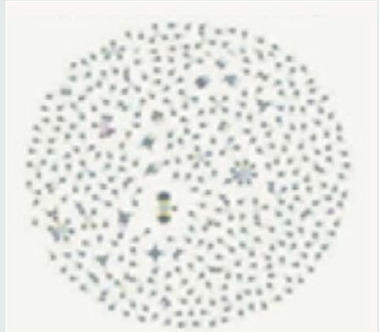
Humanized mouse that received target antigen

**Search**
Screening for RBD-specific single B cells

- Multiplexed bead-based assay
- Live cell-based assay
- Fluorescence-activated single-cell sorting

**Sequence and identity**
Cloning and expression

High-confidence sequences clustered by sequence identity

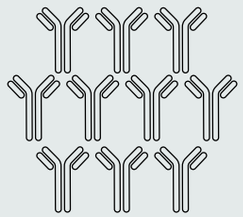


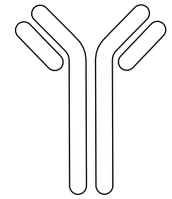
Clonal families

**Analyse**
Validate and characterize

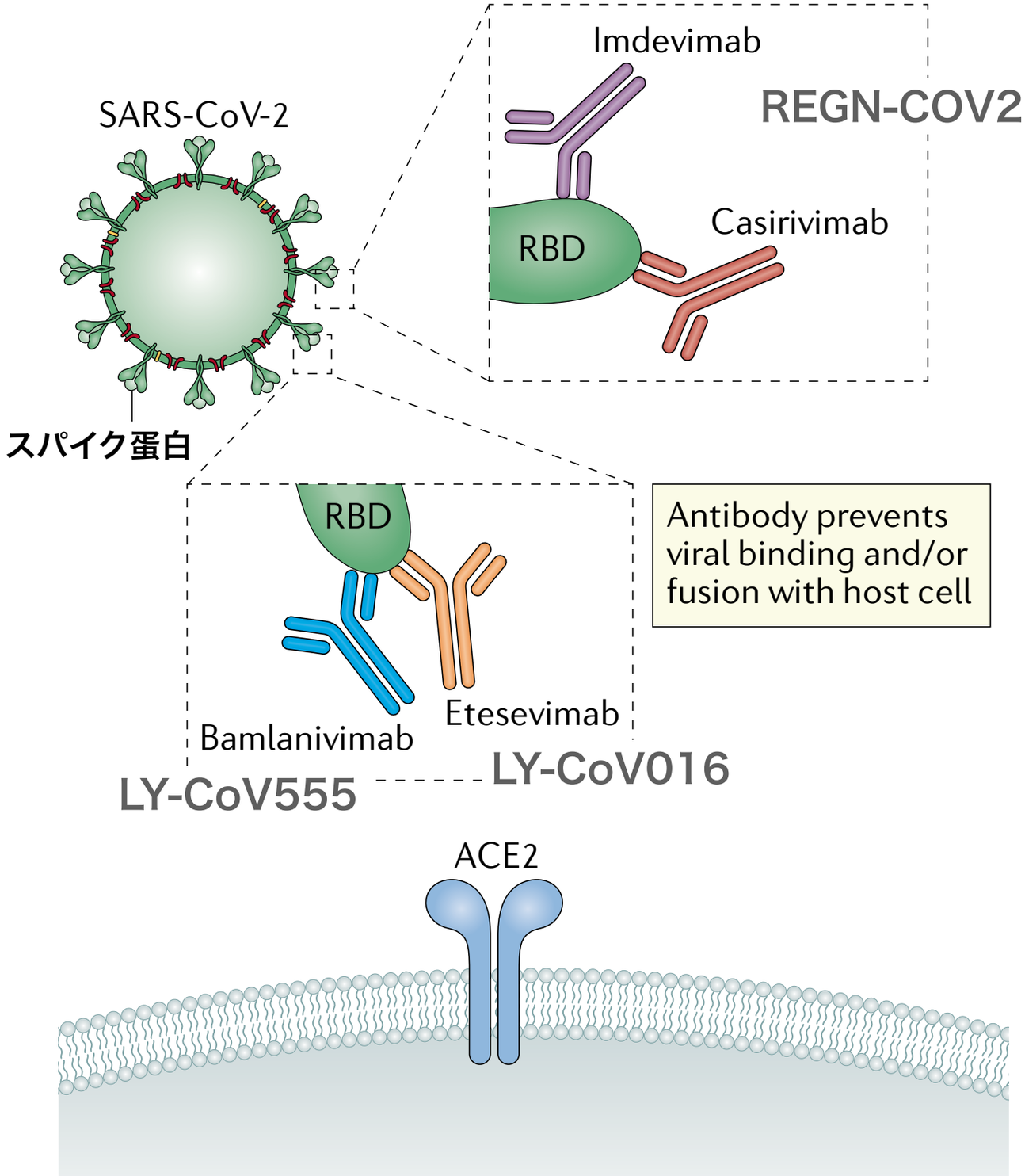
- Binding validation
- Functional validation
- Stability
- Organization
- Affinity

**Select**





https://doi.org/10.1038/s41577-021-00542-x



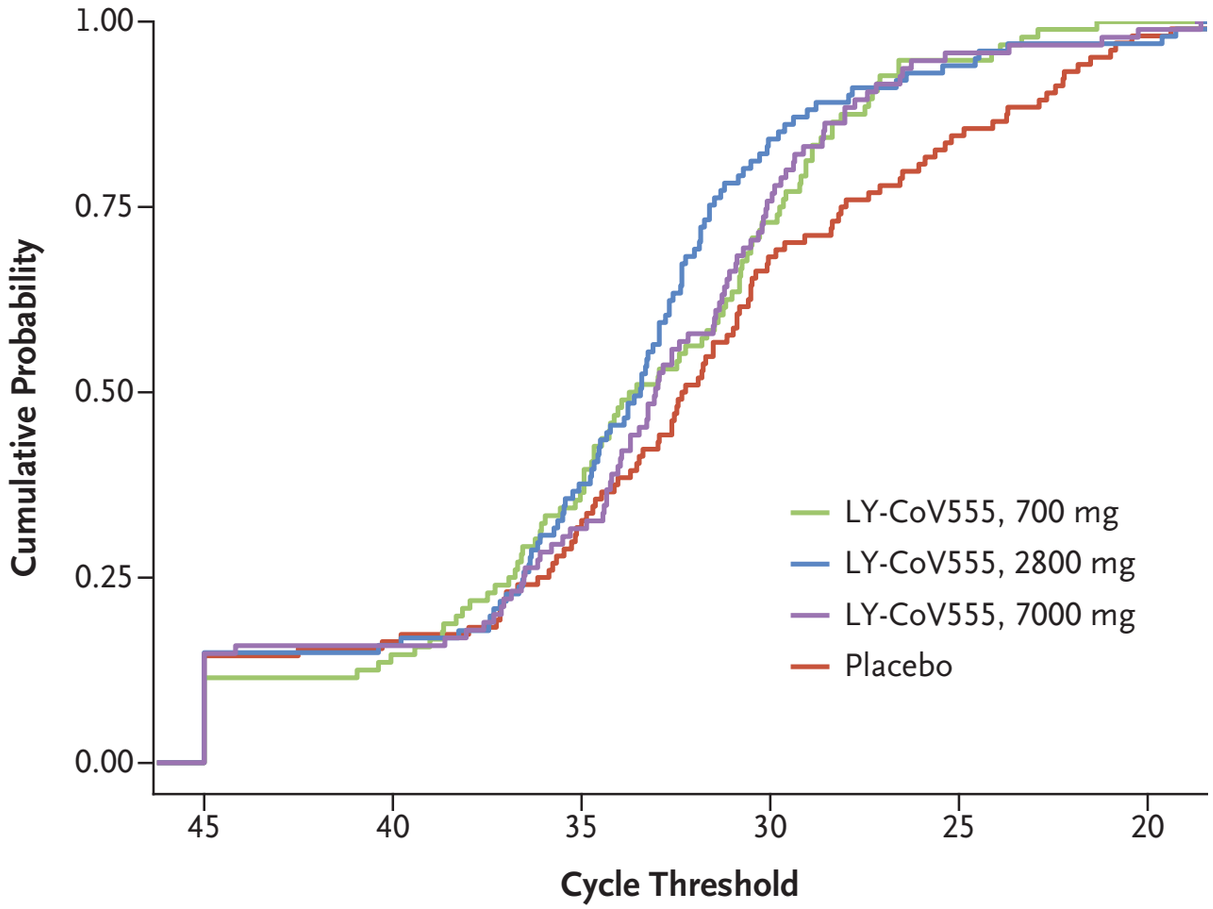

https://doi.org/10.1038/s41577-021-00542-x

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

**B** Viral Load on Day 7 in Each Trial Group



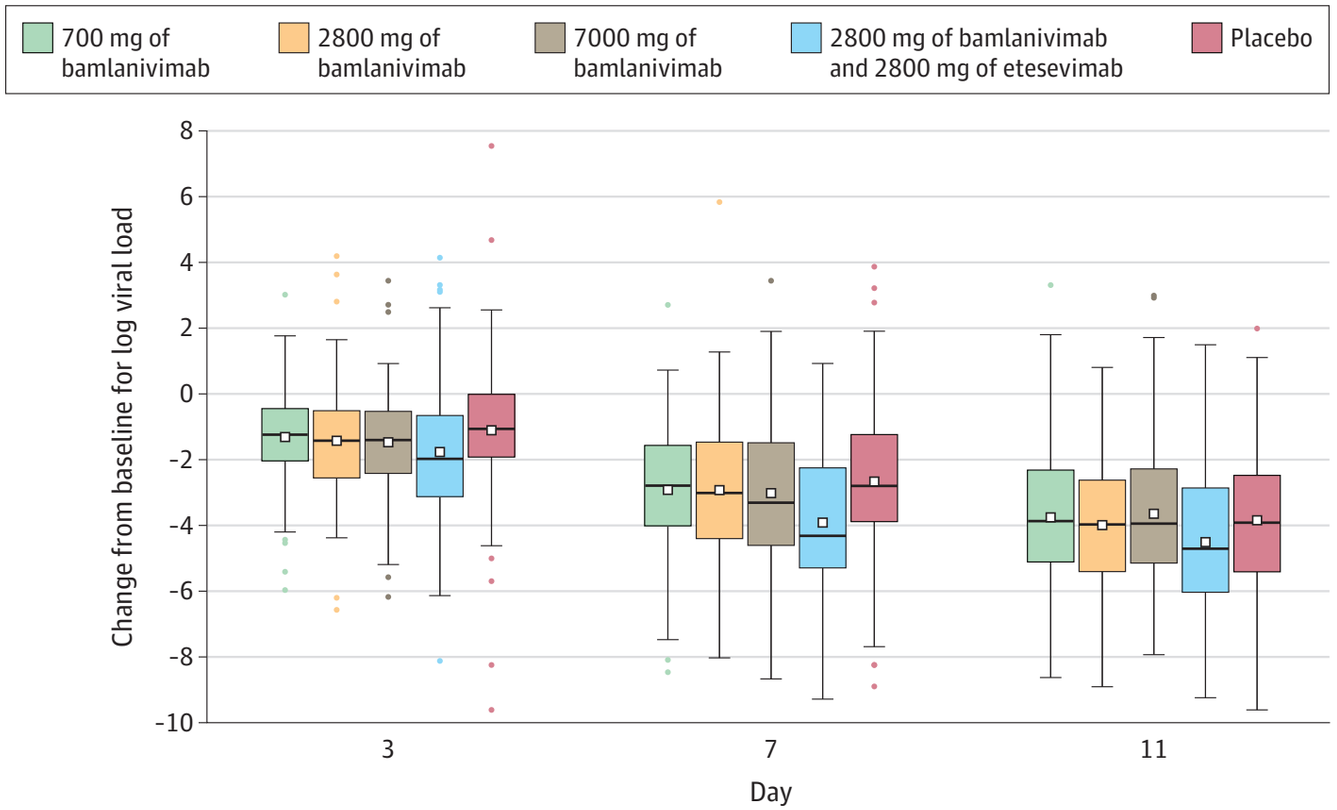

Bamlanivimab, a monoclonal antibody
Administered to outpatients
(Median time from onset to administration: 4 days)
Patients who received the monoclonal antibody had faster viral load decrease and fewer hospitalizations compared to the placebo group

DOI: 10.1056/NEJMoa2029849

JAMA | Original Investigation

# Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19
## A Randomized Clinical Trial

A Box plot for change from baseline to log viral load




| Treatment, No. | | | |
|---|---|---|---|
| 700 mg of bamlanivimab | 96 | 98 | 91 |
| 2800 mg of bamlanivimab | 98 | 101 | 99 |
| 7000 mg of bamlanivimab | 93 | 95 | 90 |
| 2800 mg of bamlanivimab and 2800 mg of etesevimab | 97 | 95 | 99 |
| Placebo | 141 | 142 | 134 |

Monoclonal Antibody Cocktail Bamlanivimab/Etesevimab Administered to outpatients (Median time from onset to administration: 4 days)

Statistically significant reduction in SARS-CoV-2 viral load at day 11 in patients treated with bamlanivimab/etesevimab compared with placebo

No significant difference between bamlanivimab alone and placebo group

JAMA. 2021;325(7):632-644.

FDA NEWS RELEASE

# Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Monoclonal Antibody Bamlanivimab

*Alternative monoclonal antibody therapies authorized to treat patients with COVID-19 remain available*



**For Immediate Release:** April 16, 2021

Español

Today, the U.S. Food and Drug Administration revoked the emergency use authorization (EUA) that allowed for the investigational monoclonal antibody therapy bamlanivimab, *when administered alone*, to be used for the treatment of mild-to-moderate COVID-19 in adults and certain pediatric patients. Based on its ongoing analysis of emerging scientific data, specifically the sustained increase of SARS-CoV-2 viral variants that are resistant to bamlanivimab alone resulting in the increased risk for treatment failure, the FDA has determined that the known and potential benefits of bamlanivimab, when administered alone, no longer outweigh the known and potential risks for its authorized use. Therefore, the agency determined that the criteria for issuance of an authorization are no longer met and has revoked the EUA.

ORIGINAL ARTICLE

# REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19

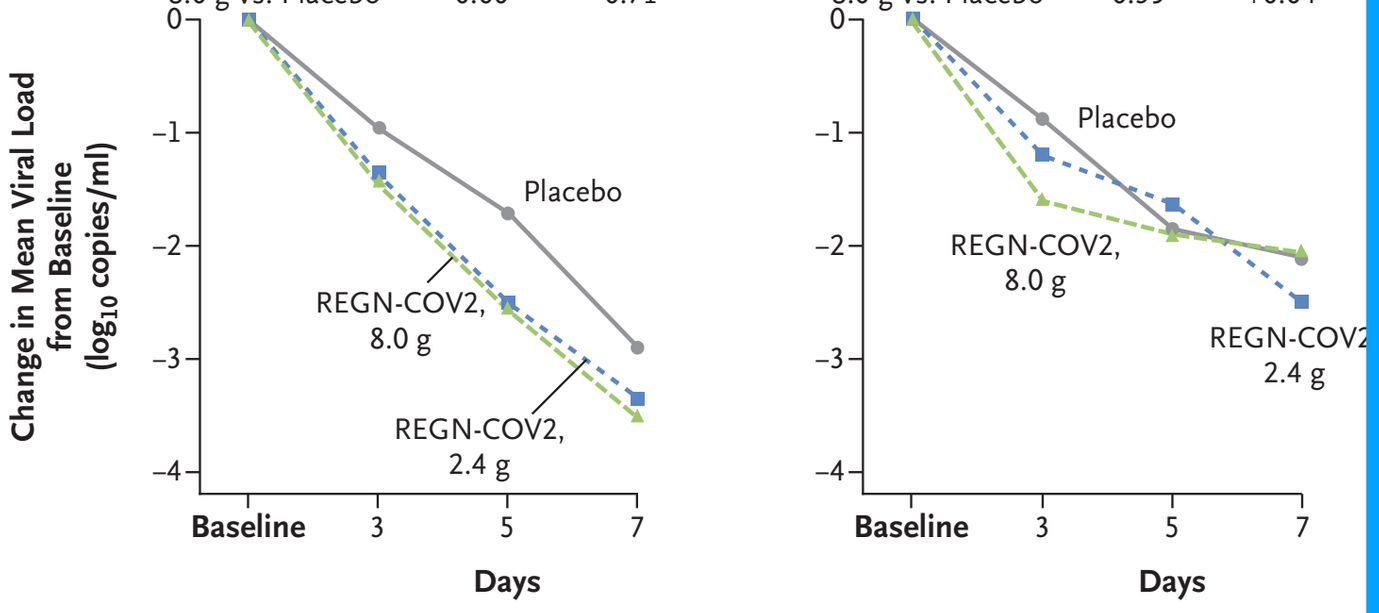
**B** Viral Load over Time According to Baseline Antibody Status

**Serum Antibody–Negative**

| | Difference in Change from Baseline, Day 7 | |
|---|---|---|
| | TWA LS mean | Mean |
| 2.4 g vs. Placebo | –0.52 | –0.59 |
| 8.0 g vs. Placebo | –0.60 | –0.71 |

**Serum Antibody–Positive**

| | Difference in Change from Baseline, Day 7 | |
|---|---|---|
| | TWA LS mean | Mean |
| 2.4 g vs. Placebo | 0.00 | –0.45 |
| 8.0 g vs. Placebo | –0.39 | +0.04 |




| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo | 30 | 23 | 28 | 28 | 38 | 35 | 37 | 37 |
| REGN-COV2, 2.4 g | 35 | 32 | 34 | 34 | 27 | 26 | 27 | 27 |
| REGN-COV2, 8.0 g | 36 | 34 | 35 | 35 | 29 | 38 | 29 | 29 |

Monoclonal Antibody Cocktail Casirivimab/Imdevimab Administered to outpatients (Median time from onset to administration: 3 days) Patients who were antibody-negative at the time of monoclonal antibody administration had a particularly high viral reduction

DOI: 10.1056/NEJMoa2035002

The NEW ENGLAND JOURNAL of MEDICINE

# Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

MULTIGROUP, MULTISTAGE, DOUBLE-BLIND, CONTROLLED TRIAL

**314**
Hospitalized adults with Covid-19 and no organ failure

| | LY-CoV555 (7000 mg) + Remdesivir N=163 | Matching Placebo + Remdesivir N=151 |
|---|---|---|
| Discharged or hospitalized without supplemental oxygen | 50% | 54% |
| | OR, 0.85; 95% CI, 0.56 to 1.29; P=0.45 | |
| Composite of death, serious adverse events, or incident grade 3 or 4 adverse events through day 5 | 19% | 14% |
| | OR, 1.56; 95% CI, 0.78 to 3.10; P=0.20 | |
| Sustained recovery among 167 patients followed over a 90-day period | 82% | 79% |
| | Rate ratio, 1.06 ; 95% CI, 0.77 to 1.47 | |

**LY-CoV555 + remdesivir did not demonstrate efficacy as compared with placebo + remdesivir.**

ACTIV-3/TICO LY-CoV555 Study Group 10.1056/NEJMoa2033130

Newsroom

News Releases

NIAID Now Blog

Media Contacts

Dr. Fauci in the News

NIAID-Funded Research News

Congressional Testimony

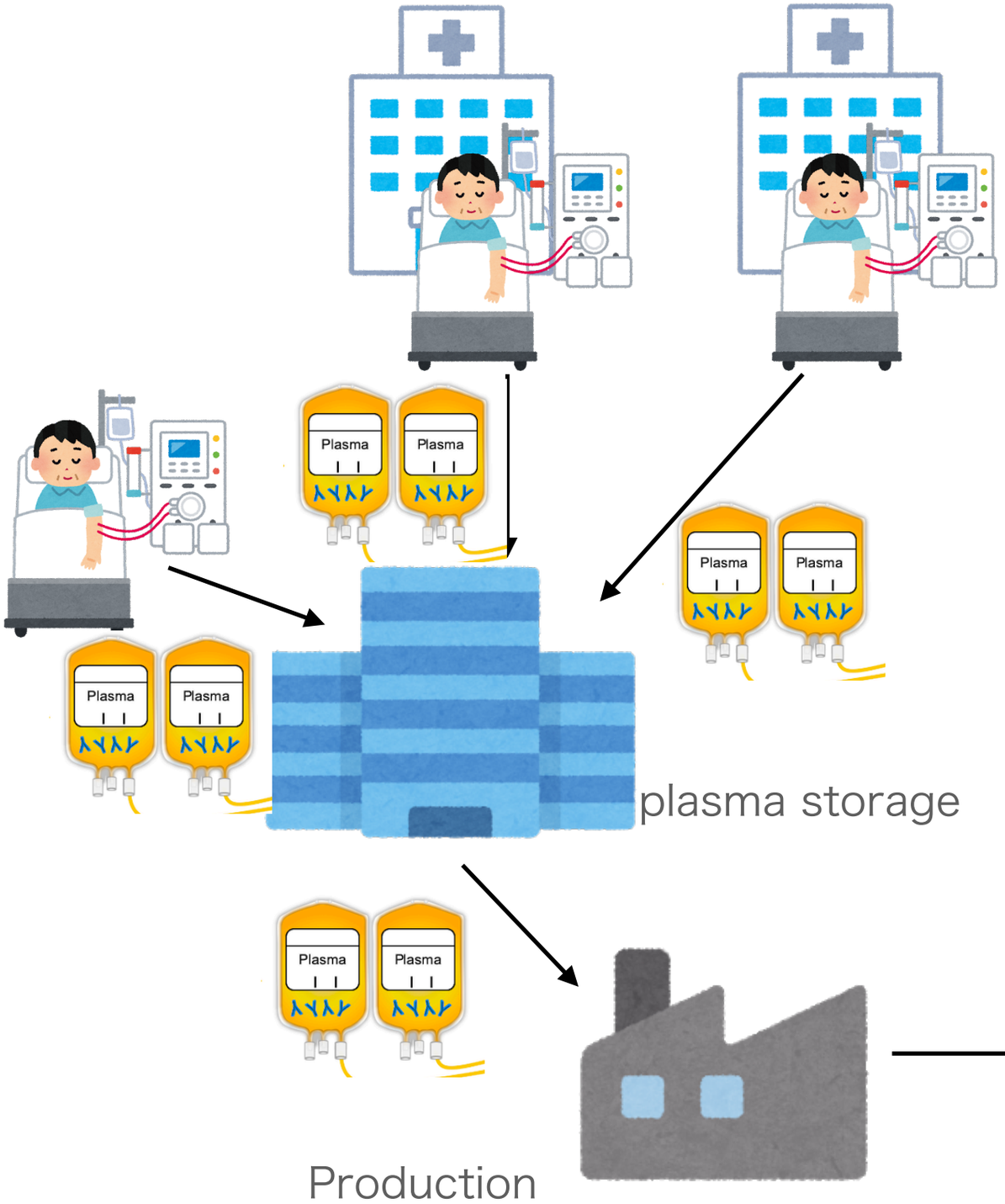
News & Events > Newsroom > News Releases

# Statement—NIH-Sponsored ACTIV-3 Trial Closes LY-CoV555 Sub-Study

October 26, 2020

The ACTIV-3 clinical trial evaluating the investigational monoclonal antibody LY-CoV555 in hospitalized patients with COVID-19 will not enroll more participants into this sub-study following a recommendation from the independent Data and Safety Monitoring Board (DSMB). The trial is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

# Anti-coronavirus Hyperimmune Intravenous Immunoglobulin


Plasma
Plasma
Plasma
Plasma
Plasma
Plasma
Plasma
Plasma
plasma storage
Production
IVIG

# CoVIg-19 Plasma Alliance Announces Topline Results from NIH-Sponsored Clinical Trial of Investigational COVID-19 Hyperimmune Globulin Medicine

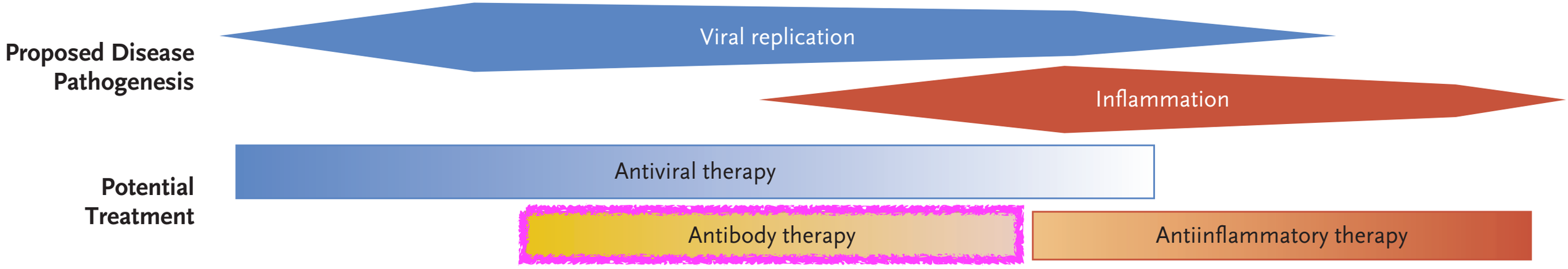


Osaka, JAPAN and King of Prussia, Pa., USA

Phase 3 Inpatient Treatment with Anti-Coronavirus Immunoglobulin (ITAC) clinical trial sponsored and funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), did not meet its endpoints to show efficacy in adults hospitalized with COVID-19

02 Apr 2021

| | Asymptomatic or Presymptomatic | Mild Illness | Moderate Illness | Severe Illness | Critical Illness |
|---|---|---|---|---|---|
| **Features** | Positive SARS-CoV-2 test; no symptoms | Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea | Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94% | Oxygen saturation <94%; respiratory rate ≥30 breaths/min; lung infiltrates >50% | Respiratory failure, shock, and multiorgan dysfunction or failure |
| **Testing** | Screening testing; if patient has known exposure, diagnostic testing | Diagnostic testing | Diagnostic testing | Diagnostic testing | Diagnostic testing |
| **Isolation** | Yes | Yes | Yes | Yes | Yes |

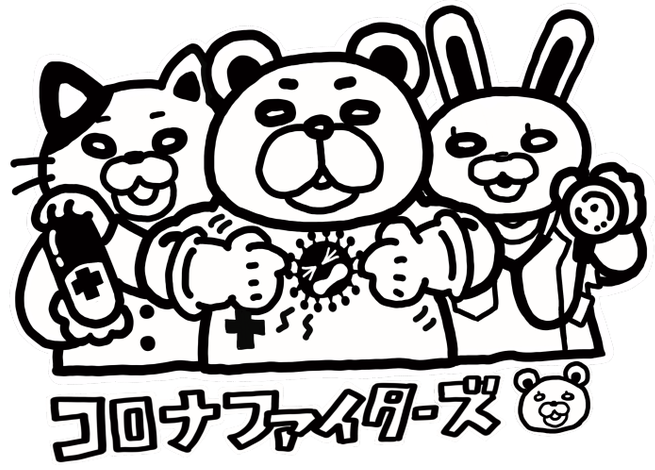



| | | | | | |
|---|---|---|---|---|---|
| **Management Considerations** | Monitoring for symptoms | Clinical monitoring and supportive care | Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir | Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone) | Critical care and specific therapy (dexamethasone, possibly remdesivir) |

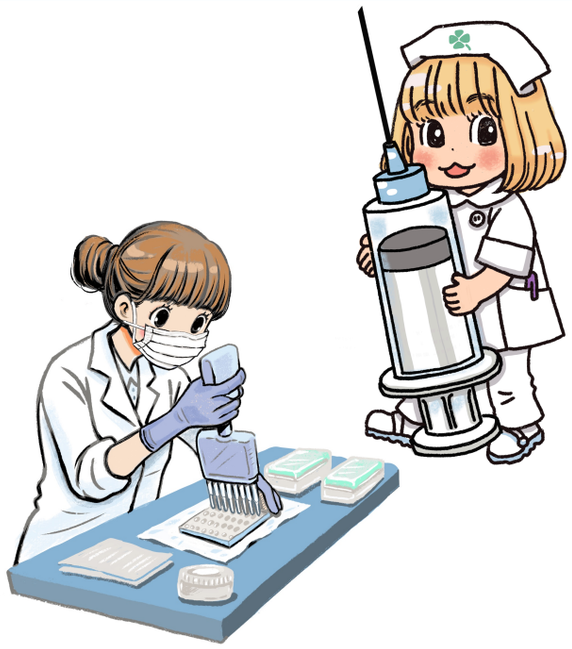
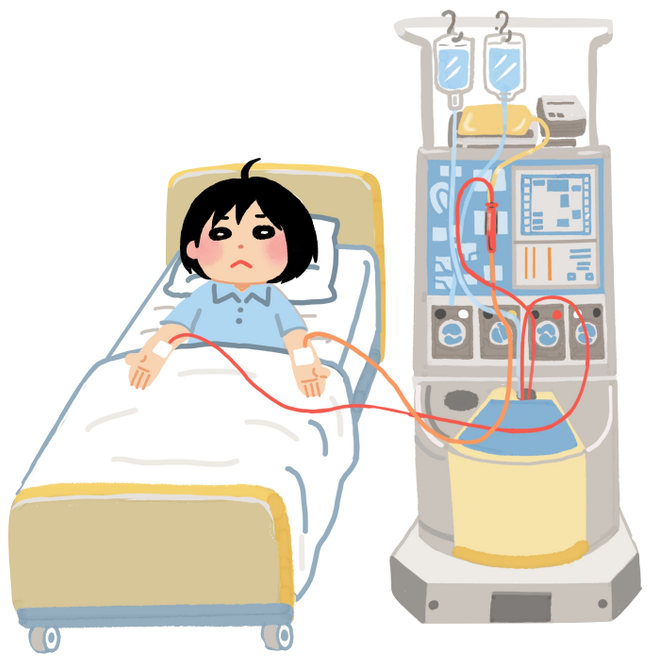
DOI: 10.1056/NEJMcp2009249

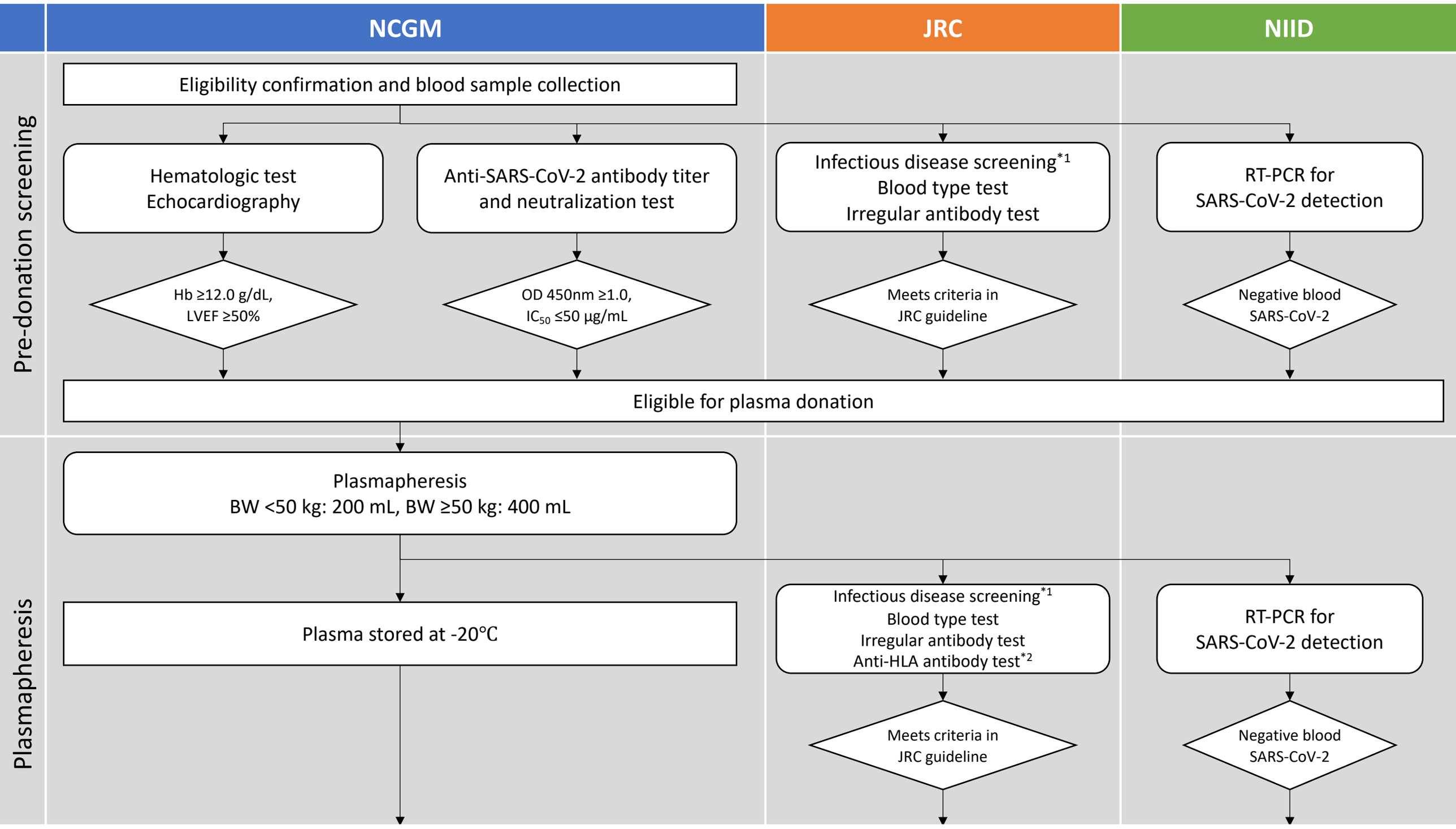
| | Advantage | Disadvantage |
|---|---|---|
| Convalescent Plasma | Simplicity<br>Rapidity<br>Available for mutant strains? | Heterogeneity of antibody titer<br>High volume<br>Side effects of blood transfusion |
| Monoclonal Antibody | Not require many convalescent Pts.<br>High titer<br>No transfusion side effects | Expensive<br>Dealing with mutant strains |
| IVIG | High potency<br>Low volume<br>Fewer transfusion side effects<br>Available for mutant strains? | Time to manufacture<br>Takes many recoverers |

# System for collection/ administration of convalescent plasma in Japan



# Status of collection, storage and administration of COVID-19 convalescent plasma at NCGM

| Screening of convalescent patients | Collection of plasma | Plasma administration |
|---|---|---|
|  |  |  |
| 680 volunteers | 200 Donors | 11 Pts |

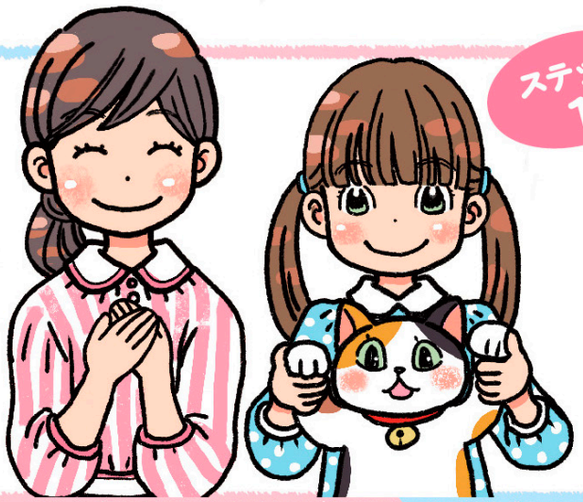



Terada M, Kutsuna S, et al. Transfusion accepted

新型コロナから回復したあなたが

# 新型コロナに苦しむだれかにできること

東京・名古屋・大阪で参加者募集中！



ステップ1

## 抗体を測るために血液検査をします！

- 新型コロナの診断書や退院サマリー、保健所発行の就業制限通知書などの書類をご準備ください。（発症日か診断日がわかるもの）
- ご予約の上で東京・名古屋・大阪の研究参加施設で採血を行い、後日、抗体検査の結果をお伝えします。※ただし抗体が持続する期間や再感染する可能性は分かりません。

ステップ2

## 抗体検査の結果に応じて、供血にご協力をお願いします！

- 総合的に抗体力価が高かった方には再度医療機関にご来院の上血漿成分の供血をお願いさせていただいております。（所要時間：約２時間）
- 新型コロナから回復した方の持つ抗体が治療に有効な可能性があり、いただいた血漿はその検証のための臨床研究に活用します。


イラスト：羽海野チカ／協力：白泉社

研究代表者：国立国際医療研究センター　忽那賢志

研究参加のご予約は右上のQRコードまたはhttps://covipla.ncgm.go.jp/からお申し込みください。

厚生労働科学研究費 新興・再興感染症及び予防接種政策推進研究事業「COVID-19 回復者血漿治療の有効性・安全性に関する基礎的、臨床的検討」

新型コロナウイルス感染症から回復した

あなたにしかできないことがあります。

©羽海野チカ・白泉社

あなたの血液が、次の感染者の治療に役立つ可能性があります。

## 次の感染者と未来を救うためにご協力ください。

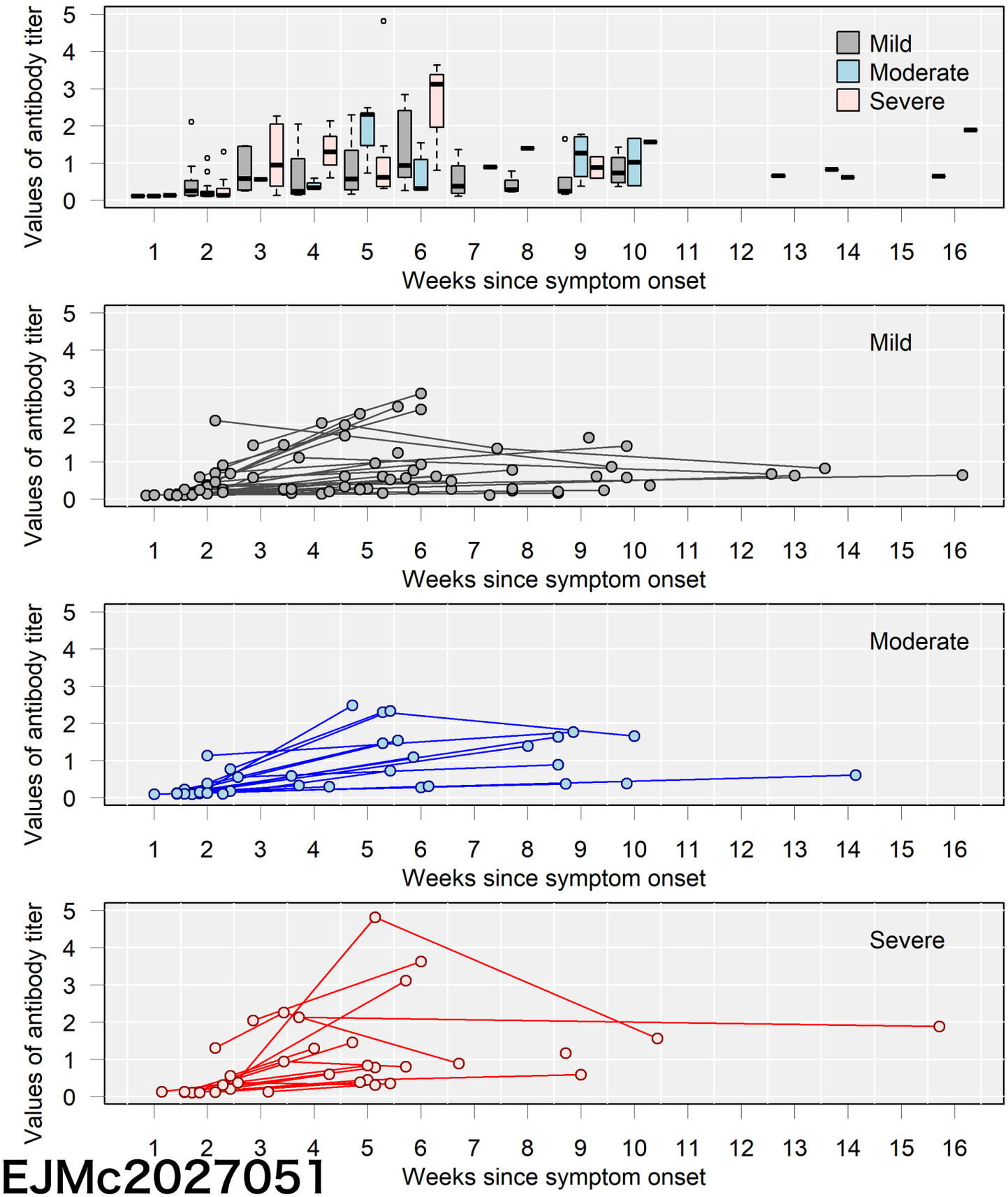
取組み内容　新型コロナウイルス感染症から回復された方はウイルスに対する抗体（抵抗力）ができます。
この研究は、抗体を多く含む回復者の血漿を提供いただき、次に新型コロナに罹った方への治療に役立てるものです。

詳しくはこちら

問合せ先　【電話】03-3202-7181　【HP】https://covipla.ncgm.go.jp/


AP-1003
COM.TEC
Fresenius Kabi

# Differences in antibody titer trends by severity of illness in convalescent patients of COVID-19




DOI: 10.1056/NEJMc2027051

CORRESPONDENCE

# Loss of Anti–SARS-CoV-2 Antibodies in Mild Covid-19

**TO THE EDITOR:** Ibarrondo et al. found that titers of anti–receptor-binding domain IgG antibodies in patients with mild cases of Covid-19 were attenuated after 90 days from the onset of symptoms. These results are consistent with the reduced antibody titers in patients with asymptomatic and mild cases, as reported by Long et al.[1]

We examined the trends in antibody titers not only in patients with mild disease but also in those with moderate disease who received oxygen inhalation therapy and in those with severe disease who underwent intubation. We measured anti–SARS-CoV-2 spike protein antibody titers using an enzyme-linked immunosorbent assay (ELISA)[2] in 81 patients with Covid-19 (46 with mild disease, 19 with moderate disease, and 16 with severe disease). Each sample was assayed in triplicate, and all measurement values were normalized against the mean value of the positive control sample.

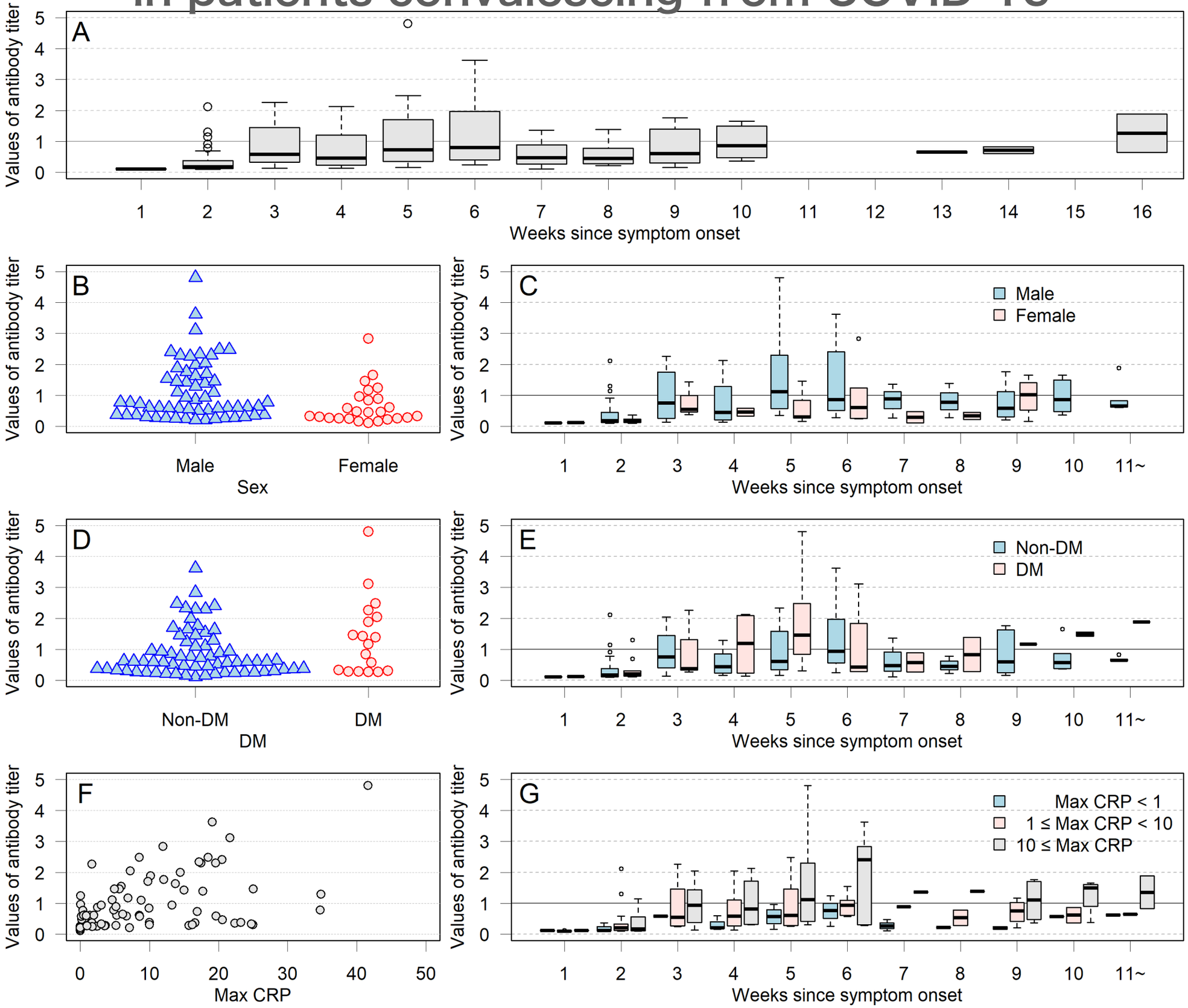
Antibody titers tended to be higher in patients with severe disease than in those with mild or moderate disease. However, patients with moderate and severe disease, as well as those with mild disease, seemed to show a decrease in antibody titers after 60 days from the onset of symptoms. These results suggest that although antibody titers are higher in patients with a greater severity of disease, they will eventually decline.

Satoshi Kutsuna, M.D., Ph.D.
Yusuke Asai, Ph.D.
Akihiko Matsunaga, Ph.D.

National Center for Global Health and Medicine
Tokyo, Japan
skutsuna@hosp.ncgm.go.jp

DOI: 10.1056/NEJMc2027051

# Factors associated with anti-SARS-CoV-2 IgG antibody production in patients convalescing from COVID-19




Kutsuna et al. DOI: https://doi.org/10.1016/j.jiac.2021.01.006

# No SARS-CoV-2 RNA detected in the convalescent plasma of COVID-19 patients with different disease severity

| Variables | Disease severity | | |
|---|---|---|---|
| | Mild (n = 77, 77.0%) | Moderate (n = 19, 19.0%) | Severe (n = 4, 4.0%) |
| Demographics | | | |
| Median age, years (range) | 45 (21–167) | 55 (31–67) | 63.5 (52–69) |
| Males | 40 (51.9%) | 16 (84.2%) | 2 (50.0%) |
| Comorbidities | | | |
| Hypertension | 11 (14.3%) | 9 (47.4%) | 0 (0%) |
| Diabetes mellitus | 5 (6.5%) | 4 (2.1%) | 1 (25.0%) |
| Dyslipidemia | 11 (14.3%) | 6 (3.2) | 0 (0%) |
| Chronic obstructive pulmonary disease | 1 (0.01%) | 0 (0%) | 0 (0%) |
| Cardiovascular disease | 0 (0%) | 0 (0%) | 0 (0%) |
| Presence of pneumonia by imaging studies | 0 (0%) | 19 (100.0%) | 4 (100.0%) |
| Supportive therapy | | | |
| Oxygen administration | 0 (0%) | 19 (100.0%) | 4 (100.0%) |
| Mechanical ventilation | 0 (0%) | 0 (0%) | 4 (100.0%) |
| ECMO | 0 (0%) | 0 (0%) | 2 (50.0%) |
| Medications | | | |
| Steroid | 0 (0%) | 8 (42.1%) | 2 (50.0%) |
| Lopinavir/ritonavir | 0 (0%) | 2 (10.5%) | 2 (50.0%) |
| Favipiravir | 0 (0%) | 3 (15.8%) | 1 (25.0%) |
| Hydroxychloroquine | 0 (0%) | 5 (26.3%) | 0 (0%) |
| Remdesivir | 0 (0%) | 4 (21.1%) | 0 (0%) |
| Tocilizumab | 0 (0%) | 1 (10.5%) | 0 (0%) |
| Days from disease onset to the test (range) | 74 (21–167) | 65 (27–102) | 98.5 (57–162) |
| RT-PCR in the plasma | UND | UND | UND |

Nomoto H, Kutsuna S, et al. DOI:https://doi.org/10.1016/j.jiac.2021.01.004

臨床研究実施計画・研究概要公開システム

Top

English

臨床研究・治験計画情報の詳細情報です。

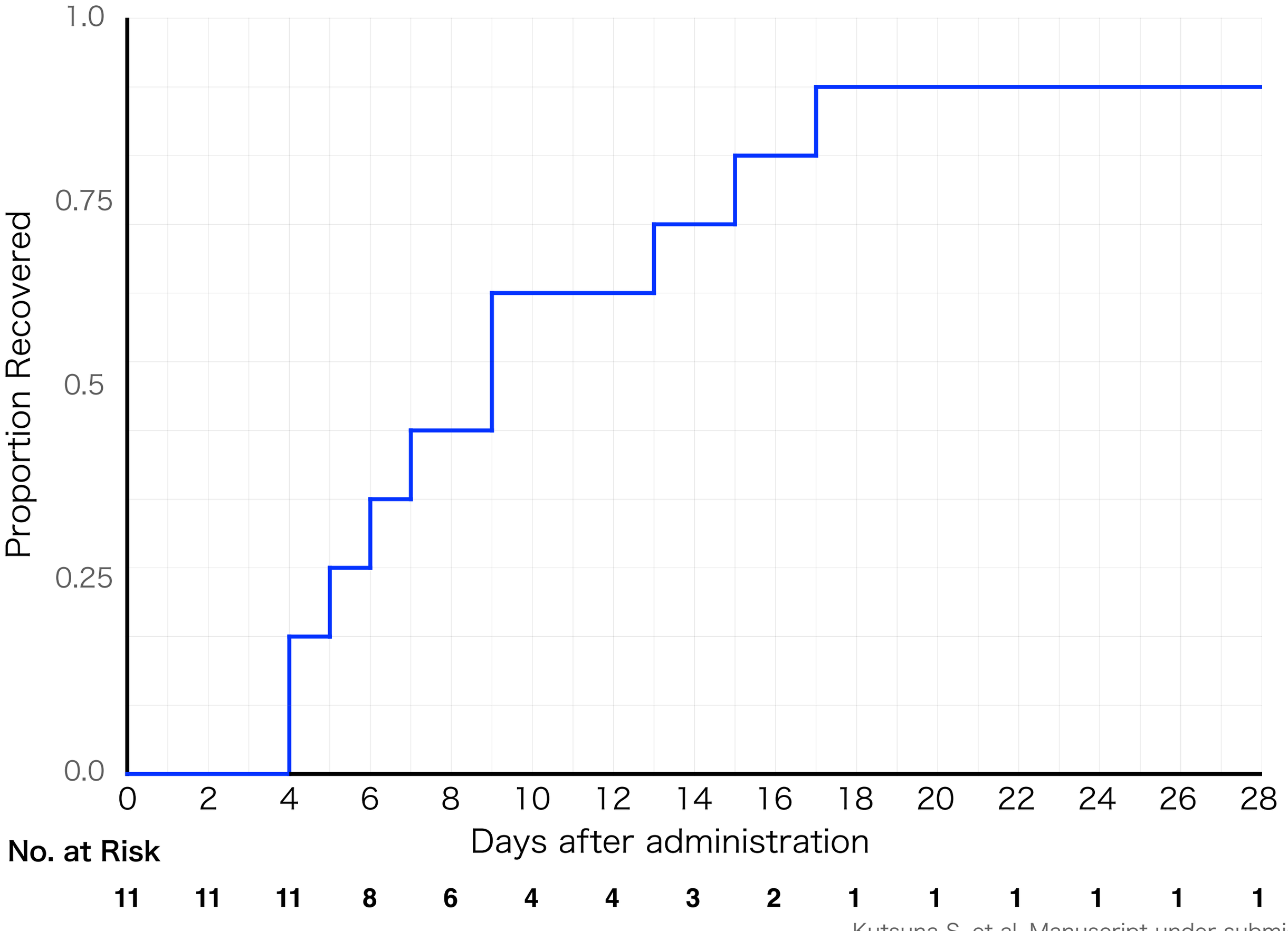
| | |
|---|---|
| **研究の種別** | 特定臨床研究 |
| **初回公表日** | 令和2年9月17日 |
| **最終公表日** | |
| **中止年月日** | |
| **観察期間終了日** | |
| **研究名称** | COVID-19回復者血漿を用いた治療の有効性・安全性の検討 |
| **平易な研究名称** | COVIPLA-R |
| **研究責任（代表）医師の氏名** | 忽那　賢志 |
| **研究責任（代表）医師の所属機関** | 国立研究開発法人国立国際医療研究センター病院 |
| **研究・治験の目的** | COVID-19回復者血漿の有効性の検討、安全性・症状短縮・臨床的改善・ウイルス量推移などを評価すること |
| **試験のフェーズ** | N/A |
| **対象疾患名** | COVID-19、新型コロナウイルス感染症 |
| **進捗状況** | 募集中 |
| **医薬品等の一般名称** | COVID-19 回復期血漿 |

# 11 patients who received convalescent plasma for safety validation.

| | Age (years) | Sex | Underlying diseases | Treatment for COVID-19 | Days from COVID-19 onset to | Oxygen dose at the time of plasma administ | Oxygen dose at the worst point of managt | Intubation or death | Adverse event | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 46 | M | HIV infection | REM /DEX | 10 | 1 L/min | 4 L/min | None | None | Recovery |
| 2 | 59 | M | Diabetes, hypertension, COPD, hyperlipidemia | REM /DEX | 8 | NHF | NHF | None | None | Recovery |
| 3 | 46 | M | Hypertension, obesity | REM /DEX | 7 | 1 L/min | 2 L/min | None | None | Recovery |
| 4 | 39 | M | Previous history of hepatitis B | DEX | 12 | 2 L/min | 5 L/min | None | None | Recovery |
| 5 | 61 | M | Membranous nephropathy, bronchial asthma, hyperuricemia, dyslipidemia | REM /DEX | 12 | 4 L/m | 5 L/min | None | None | Recovery |
| 6 | 61 | M | Interstitial pneumonia | REM /DEX | 7 | 2 L/m | 2 L/min | None | None | Recovery |
| 7 | 60 | M | Hypertension | REM /DEX | 8 | 2 L/m | 2 L/min | None | None | Recovery |
| 8 | 64 | F | Osteoporosis | REM /DEX | 10 | 4 L/min | NHF | None | Erythema at the infusion site | Recovery |
| 9 | 90 | F | Interstitial pneumonia, hypertrophic heart disease, hypertension | REM /DEX | 9 | 5 L/min | NHF | Yes | None | Death |
| 10 | 66 | M | Hypertension | REM /DEX | 7 | 3 L/min | NHF | None | None | Recovery |
| 11 | 86 | F | Hypertension, dyslipidemia | REM /DEX | 6 | 1 L/min | 1 L/min | None | None | Recovery |

Kutsuna S, et al. Manuscript under submission

# Time to recovery in 11 COVID patients who received plasma

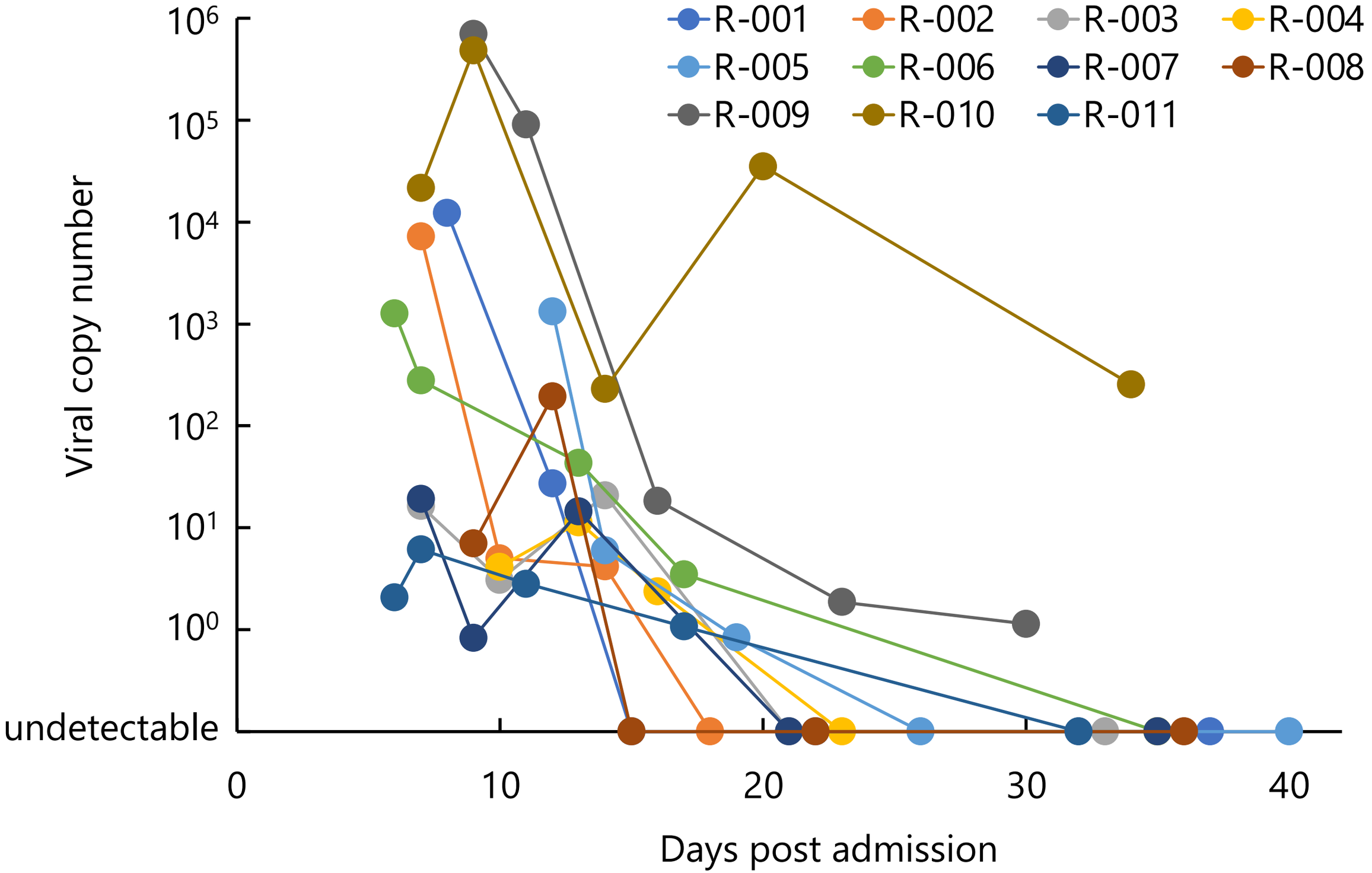



**No. at Risk**

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **11** | **11** | **11** | **8** | **6** | **4** | **4** | **3** | **2** | **1** | **1** | **1** | **1** | **1** | **1** |

Kutsuna S, et al. Manuscript under submission

# Changes in viral load in 11 COVID patients who received plasma




Kutsuna S, et al. Manuscript under submission

# Randomized controlled trial

## Validating the efficacy of convalescent plasma therapy for COVID-19

- Design: Multicenter open-label randomized controlled trial
- Patients: COVID-19 patients who met all of the following criteria: (1) within 5 days of onset, (2) SpO2 >95% by room air, and (3) age >60 years or underlying disease.
- Primary endpoint: Time-weighted mean change in SARS-CoV-2 viral load in nasopharyngeal swabs from day 0 to days 3 and 5
- Secondary endpoints: avoidance of ventilatory management or death, mortality, duration of oxygen use, symptom reduction (time to clinical improvement), and safety assessment
- Cases: 200 patients
- Started on February 24, 2021

| | |
|---|---|
| **研究の種別** | 特定臨床研究 |
| **初回公表日** | 令和3年2月24日 |
| **最終公表日** | 令和3年4月15日 |
| **中止年月日** | |
| **観察期間終了日** | |
| **研究名称** | COVID-19回復者血漿を用いた治療の有効性を検討する非盲検ランダム化比較試験 |
| **平易な研究名称** | COVID-19回復者血漿を用いた治療の有効性を検討する非盲検ランダム化比較試験 |
| **研究責任（代表）医師の氏名** | 忽那　賢志 |
| **研究責任（代表）医師の所属機関** | 国立研究開発法人 国立国際医療研究センター病院 |
| **研究・治験の目的** | COVID-19から回復した者から採取した回復者血漿の有効性を評価する |
| **試験のフェーズ** | 2-3 |
| **対象疾患名** | COVID-19 |
| **進捗状況** | 募集中 |
| **医薬品等の一般名称** | COVID-19回復期血漿 |
| **販売名** | なし |
| **認定委員会の名称** | 国立研究開発法人国立国際医療研究センター 臨床研究審査委員会 |
| **認定番号** | CRB3200011 |

# Summary


- Antibody therapy includes convalescent plasma, monoclonal antibodies, and advanced immunoglobulin preparations, which are expected to be therapeutic agents for COVID-19. Each has its advantages and disadvantages, such as simplicity and rapidity, time to manufacture, cost, and uniformity of antibody titer.

- Both antibody therapies have been shown to be effective when administered early in the course of the disease, but many studies have shown that they are not effective when administered after the disease has become severe.

- No major safety problems have been reported, including ADEs.

- A system for the implementation of plasma therapy for convalescent patients has been established in Japan, and randomized controlled trials are currently being conducted to verify efficacy.