

# Izazovi u procesu prikupljanja COVID- 19 konvalescentne plazme u Hrvatskom zavodu za transfuzijsku medicinu

Ana Hećimović, HZTM

26. svibanj 2022., Matica Hrvatska, Zagreb

„BORBA PROTIV BOLESTI COVID-19 ISTRAŽIVANJIMA“



# Povijest

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- Pasivna imunoterapija stoljetna je praksa primjene protutijela, od izložene i oporavljene ili cijepljene osobe, pacijentu osjetljivom na dotičnu bolest.
- 1890 - E. von Behring – serumsko terapija; difterija i tetanus
- *Spasitelj djece i vojnika*
- Prva Nobelova nagrada za medicinu



## Naši počeci

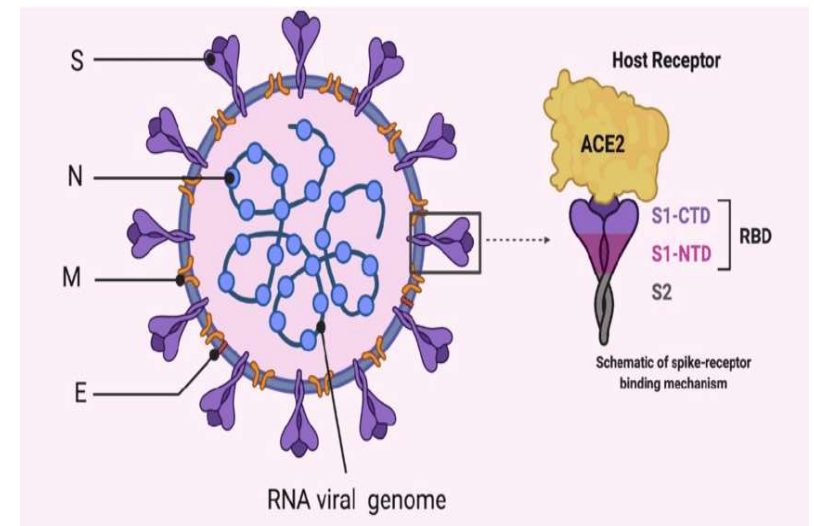
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1. Povoljna iskustva primjene KP od prije 15-ak godina kada imamo izbijanje korona virusa u južnoj Aziji i na Bliskom Istoku (SARS i MERS).
2. Covid-19 – na početku nije postojala efektivna etiološka terapija
3. Ideja o **COVID-19 konvalescentnoj plazmi**, kao obliku specifične terapije, nametnula se sama po sebi

# Mehanizmi djelovanja

## 1. Antivirusni mehanizam - vrlo vjerojatan

- Djelovanje neutralizirajućih protutijela (anti –Spike protein) na prodor virusa u stanice
- Aktivacija komplementa
- ADCC
- Fagocitoza



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

Denise J Wooding <sup>1</sup>, Horacio Bach <sup>2</sup>

Affiliations + expand

PMID: 32791241 PMCID: PMC7417293 DOI: 10.1016/j.cmi.2020.08.005

[Free PMC article](#)

**JCI** The Journal of Clinical Investigation

## The convalescent sera option for containing COVID-19

Arturo Casadevall, Liise-anne Pirofski

*J Clin Invest.* 2020;130(4):1545-1548. <https://doi.org/10.1172/JCI138003>.

**Viewpoint** COVID-19

As of early 2020, humanity is confronting a pandemic in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 causes coronavirus disease, abbreviated as COVID-19. At the time of this writing, SARS-CoV-2 is spreading in multiple countries, threatening a pandemic that will affect billions of people. This virus appears to be a new human pathogen. Currently there are no vaccines, monoclonal antibodies (mAbs), or drugs available for SARS-CoV-2, although many are in rapid development and some may be available in a short time. This Viewpoint argues that human convalescent serum is an option for prevention and treatment of COVID-19 disease that could be rapidly available when there are sufficient numbers of people who have recovered and can donate immunoglobulin-containing serum. Passive antibody therapy Passive antibody therapy involves the administration of antibodies against a given agent to a susceptible individual for the purpose of preventing or treating an infectious disease due to that agent. In contrast, active vaccination requires the induction of an immune response that takes time to develop and varies depending on the vaccine recipient. Thus, passive antibody administration is the only means of providing immediate immunity to susceptible persons. Passive antibody therapy has a storied history going back to the 1890s and was the only means of treating certain infectious diseases prior to the development of antimicrobial therapy in [...]

# Važni datumi!

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- 30. siječanj, 2020. – WHO - međunarodni hitni događaj
- 28. veljače, 2020. – WHO - vrlo visoki rizik
- 11. ožujak, 2020. – WHO proglašava pandemiju



Odluka o proglašenju pandemije na cijelom teritoriju RH

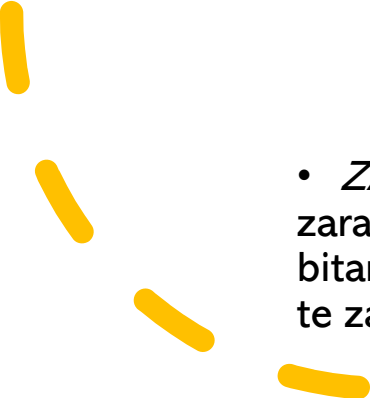


## Što to znači?

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1. Da se radi o izvanrednoj situaciji u javnom zdravstvu koja značajno može utjecati na nacionalnu sigurnost ili zdravlje i sigurnost građana u RH.

2. Da postoje okolnosti koje opravdavaju odobrenje hitne uporabe lijekova i bioloških proizvoda tijekom pandemije.

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- *ZAKON O ZAŠTITI PUČANSTVA OD ZARAZNIH BOLESTI:* u slučaju proglašenja epidemije zarazne bolesti..... Vlada Republike Hrvatske je ovlaštena na prijedlog Ministra utvrditi bitan interes Republike Hrvatske za nabavu roba, usluga i radova u cilju sprečavanja i suzbijanja te zarazne bolesti.

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Uključuje organizaciju etičkih pitanja i uključuje odobrenja institucionalnih tijela

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Uključuje organizaciju infrastrukturnih pitanja

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Uključuje usklađivanje s regulatornim zahtjevima



REPUBLIKA HRVATSKA  
MINISTARSTVO ZDRAVSTVA

KLASA: 023-03/20-01/235  
URBROJ: 534-04-3-2/2-20-11  
Zagreb, 8. lipnja 2020. godine

REPUBLIKA HRVATSKA 251-541 HRVATSKI ZAVOD ZA TRANSFUZIJSKU MEDICINU			
Primljeno:	16-06-2020		
Klasifikacijski oznaka:		I strojstvena jedinica	
023-03/20-01/15	8/11		
Uredbeni broj:		Pribori	Vrijednost
534-20-20			

Hrvatski zavod za transfuzijsku medicinu  
Petrova 3  
10 000 Zagreb  
n/p doc.dr.sc. Irena Jukić, dr.med.

**PREDMET: Proizvodnja svježe zamrznute COVID-19 konvalescentne plazme dobivene aferezom za potrebe transfuzijskog liječenja oboljelih od COVID-19 - suglasnost, dostavlja se**

Poštovani,

Ministarstvo zdravstva zaprimilo je Vaš zahtjev za odobrenjem pripravljanja svježe zamrznute COVID-19 konvalescentne plazme dobivene postupkom afereze (KLASA: 023-03/20-01/15, URBROJ: 251-541-01/1-20/16), od 24. travnja 2020. godine, te smo na isti zatražili i mišljenje Službe za inspekciju krvi, tkiva i stanica.

Nastavno na zaprimljeno inspeksijsko mišljenje (KLASA: 543-02/20-13/01, URBROJ: 534-09-3/1-20-2) od 7. svibnja 2020. godine i dostavljene otklonjene nesukladnosti od strane Vaše ustanove (KLASA: 023-03/20-01/235, URBROJ: 381-20-10) od 18. svibnja 2020. godine, obavještavam Vas kako je Ministarstvo zdravstva suglasno da Vaša ustanova započne sa postupcima za pripravljanje svježe zamrznute COVID-19 konvalescentne plazma osoba koje su preboljele COVID-19 za potrebe transfuzijskog liječenja oboljelih od COVID-19.

S poštovanjem,



Na znanje:

Klinika za infektivne bolesti „dr. Fran Mihaljević“



Ksaver 200a, 10 000 Zagreb, Republika Hrvatska, T +385 1 46 07 555, F +385 1 46 77 076



**Odobrenje Ministarstva RH**

HRVATSKI ZAVOD ZA  
TRANSFUZIJSKU MEDICINU  
ZAGREB, Petrova 3  
Etičko povjerenstvo  
KLASA: 003-06/20-04/02  
URBROJ: 251-541-06/6-20-2  
U Zagrebu, 07. svibnja 2020.

Raspravljajući o zahtjevu doc.prim.dr.sc. Irene Jukić, dr.med., Etičko povjerenstvo Hrvatskog zavoda za transfuzijsku medicinu na sastanku održanom elektroničkim putem donijelo je sljedeće:

### MIŠLJENJE

Udovoljava se pisanom zahtjevu doc.prim.dr.sc. Irene Jukić, dr. med. te odobrava prikupljanje konvalescentne plazme COVID-19 postupkom afereze od osoba koje su preboljele infekciju uzrokovanu SARS-Cov-2 virusom. Konvalescentna COVID-19 plazma izdavalna bi se na zahtjev kliničara u strogoj indikaciji za liječenje COVID-19 te na zahtjev Centra za istraživanje i prijenos znanja u biotehnologiji Sveučilišta u Zagrebu u svrhu proizvodnje specifičnih imunoglobulina.

Svi prikupljeni podaci o osobama koje su se oporavile od COVID-19 i pristupile darivanju konvalescentne plazme bili bi trajno pohranjeni i zaštićeni od neovlaštenog uvida.

Davatelji konvalescentne plazme će biti upoznati s cjelokupnim postupkom i svrhom prikupljanja konvalescentne COVID-19 plazme, što bi potvrdili potpisanim informativnim pristankom.

Etičko povjerenstvo:

*Jagić* Sandra Jagrić, dr.med., spec.transfuziolog.  
*Tomislav Vuk* Prim.dr.sc. Tomislav Vuk, dr.med., spec.transfuziolog.  
*Patricija Topić Šestan* Patricija Topić Šestan, dr.med., spec.transfuziolog.  
*Mušlin* Tatjana Mušlin, dr.med.,  
*Marko Jadro* Marko Jadro, mag.oec.

**Odobrenje Etičkog povjerenstva**

**HZTM**

**1. „Upravljanje zaraznim bolestima uzrokovanim  
koronavirusima te društvenim i obrazovnim aspektima  
pandemije”  
(IP-CORONA-2020-04)**

*„Development of premises for implementation of SARSCoV-  
2 serotherapy in Croatia“ (IP CORONA-2020-04-2053)*

**- Lipanj 2020.**

**2. Increasing EU capacity for Covid-19 Convalescent  
Plasma Collection**

**- Lipanj 2020.**



Agreement number PPPA-ECI-CCP-2020

Mono beneficiary model  Ref. Ares(2020)7333419 - 04/  
grant agreement: August 2019



EUROPEAN COMMISSION  
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY  
Health Systems, medical products and innovation

GRANT AGREEMENT FOR AN ACTION  
UNDER EMERGENCY SUPPORT INSTRUMENT (ESI)  
AGREEMENT NUMBER — PPPA-ECI-CCP-2020 – SI2.839205



EUROPEAN COMMISSION  
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation  
B4 - Medical products: quality, safety, innovation

Brussels,  
SANTÉ B4/DF/

## An EU programme of COVID-19 convalescent plasma collection and transfusion

### Guidance on collection, testing, processing, storage, distribution and monitored use

*This document has been endorsed by the Competent Authorities for Substance of Human Origin Expert Group (CASoHO E01718) following consultation of the competent authorities for blood and blood components and by the European Centre for Disease Prevention and Control. While this document is not legally binding, it aims to facilitate a common approach across EU Member States to the donation, collection, testing, processing, storage, distribution and monitoring of convalescent plasma for the treatment of Covid-19. This document is without prejudice to the requirements of the Union blood legislation, any more stringent national measures in place at Member State level and national requirements on the use of this treatment, all of which continue to apply. This guidance will be updated as needed, in line with scientific developments.*

Version 1.0 April 4 2020

#### Background

Plasma collected from patients that have recovered from an infectious disease has been used over many decades for a variety of different infectious agents<sup>1</sup>, although evidence of its effectiveness and safety is mostly limited to empirical reports. Referred to as convalescent plasma, it can be transfused to patients fighting an infection or can be used to manufacture immune globulin concentrates (plasma derived medicinal products). During a rapidly expanding outbreak of a viral infection, large populations of susceptible persons may become ill early in the event, prior to availability of effective vaccines and antiviral therapies. As highlighted by the WHO Blood Regulators Network<sup>1</sup>, an organised programme to collect convalescent plasma or serum from disease survivors could provide a potentially valuable empirical intervention while data on effectiveness and safety of its use are being gathered through structured clinical trials.

The COVID-19 pandemic is a clear situation where plasma from recovered patients might be a valuable resource to support the disease treatment within randomised or case-control clinical trials or observational studies of plasma transfusion and in the development of a plasma-derived

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HRVATSKI LIJEČNIČKIZBOR  
Hrvatsko društvo za transfuzijsku medicinu  
10 000 Zagreb  
Šubičeva 9  
MB 3271676  
OIB60192951611



## PREPORUKE HRVATSKOG DRUŠTVA ZA TRANSFUZIJSKU MEDICINU TIJEKOM PANDEMIJE VIRUSA SARS-CoV-2

### Šesto izdanje

26.11.2021.

Ovaj dokument pruža smjernice o upravljanju opskrbom krvnim pripravcima kao odgovor na pandemiju COVID-19 i smjernice o zaštiti djelatnika u transfuzijskoj djelatnosti. Namijenjen je svim transfuzijskim ustanovama koje su odgovorne za opskrbu krvnim pripravcima kao i bolničkim transfuzijskim jedinicama.

**U šestom izdanju dokument se mijenja u cijelosti, izmjene se poglavito odnose na kriterije za odabir darivatelja, postdonacijske informacije, vezano uz informacije o cijepljenju i/ili preboljenju COVID-19.**

## Izazovi/ Problemi

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Dostupnost populacije koja može darivati konvalescentnu plazmu

Senzibilizacija kako stručne tako i opće javnosti - medijska kampanja: TV, novine, žurnali, web, letak, društvene mreže

Organizacija rada u postojećim uvjetima

Vremensko razdoblje prvog vala

Dostupnost testova

Oslanjanje na vlastite snage – Centar za istraživanje i prijenos znanja u biotehnologiji, Sveučilišta u Zagrebu

Laboratorijsku podršku za provođenje testova neutralizacije, BSL3

Klinika za infektivne bolesti Dr Fran Mihaljević

15. ožujak 2020.

## Effectiveness of convalescent plasma therapy in severe COVID-19 patients

Kai Duan<sup>a,h,1</sup>, Bende Liu<sup>a,1</sup>, Cesheng Li<sup>a,1</sup>, HuaJun Zhang<sup>a,1</sup>, Ting Yu<sup>a,1</sup>, Jieming Qu<sup>a,h,1</sup>, Min Zhou<sup>a,h,1</sup>, Li Chen<sup>1,1</sup>, Shengli Meng<sup>b</sup>, Yong Hu<sup>d</sup>, Cheng Peng<sup>b</sup>, Mingchao Yuan<sup>b</sup>, Jinyan Huang<sup>b</sup>, Zejun Wang<sup>b</sup>, Jianhong Yu<sup>d</sup>, Xiaoxiao Gao<sup>e</sup>, Dan Wang<sup>b</sup>, Xiaoqi Yu<sup>a</sup>, Li Li<sup>b</sup>, Jiayou Zhang<sup>b</sup>, Xiao Wu<sup>d</sup>, Bei Li<sup>e</sup>, Yanping Xu<sup>a,h,1</sup>, Wei Chen<sup>b</sup>, Yan Peng<sup>d</sup>, Yeqin Hu<sup>b</sup>, Lianzhen Lin<sup>d</sup>, Xuefei Liu<sup>a,h,1</sup>, Shihe Huang<sup>g</sup>, Zhijun Zhou<sup>g</sup>, Lianghao Zhang<sup>g</sup>, Yue Wang<sup>g</sup>, Zhi Zhang<sup>h</sup>, Kun Deng<sup>d</sup>, Zhiwu Xia<sup>b</sup>, Qin Gong<sup>g</sup>, Wei Zhang<sup>g</sup>, Xiaobei Zheng<sup>g</sup>, Ying Liu<sup>g</sup>, Huichuan Yang<sup>g</sup>, Dongbo Zhou<sup>h</sup>, Ding Yu<sup>h</sup>, Jifeng Hou<sup>h</sup>, Zhengli Shi<sup>h</sup>, Saijuan Chen<sup>h</sup>, Zhu Chen<sup>h</sup>, Xinxin Zhang<sup>h</sup>, and Xiaoming Yang<sup>a,h,2</sup>

<sup>a</sup>China National Biotec Group Company Limited, 100029 Beijing, China; <sup>b</sup>National Engineering Technology Research Center for Combined Vaccines, Wuhan Institute of Biological Products Co., Ltd., 430207 Wuhan, China; <sup>c</sup>First People's Hospital of Jiangxia District, 430200 Wuhan, China; <sup>d</sup>Sinopharm Wuhan Institute of Biological Products Co., Ltd., 430207 Wuhan, China; <sup>e</sup>Key Laboratory of Special Pathogens, Wuhan Institute of Virology, Center for Biosafety and Plasma-derived Biotherapies Co., Ltd., 430271 Wuhan, China; <sup>f</sup>Wuhan Jinyintan Hospital, 430023 Wuhan, China; <sup>g</sup>Department of Respiratory and Mega-Science, Chinese Academy of Sciences, 430075 Wuhan, China; <sup>h</sup>Department of Respiratory and Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; <sup>i</sup>Institute of Research Center for Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; <sup>j</sup>Department of Gastroenterology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; <sup>k</sup>Clinical Research Center, Department of Respiratory Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200018 Shanghai, China; <sup>l</sup>Wuhan Blood Center, 430030 Wuhan, China; <sup>m</sup>State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, National Research Center for Translational Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; <sup>n</sup>Research Laboratory of Clinical Virology, Ruijin Hospital and Ruijin Hospital North, National Research Center for Translational Medicine, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; and <sup>o</sup>National Institute for Food and Drug Control of China, 102629 Beijing, China

## Abstract

Currently, there are no approved specific antiviral agents for novel coronavirus disease 2019 (COVID-19). In this study, 10 severe patients confirmed by real-time viral RNA test were enrolled prospectively. One dose of 200 mL of convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640 was transfused to the patients as an addition to maximal supportive care and antiviral agents. The primary endpoint was the safety of CP transfusion. The second endpoints were the improvement of clinical symptoms and laboratory parameters within 3 d after CP transfusion. The median time from onset of illness to CP transfusion was 16.5 d. After CP transfusion, the level of neutralizing antibody increased rapidly up to 1:640 in five cases, while that of the other four cases maintained at a high level (1:640). The clinical symptoms were significantly improved along with increase of oxyhemoglobin saturation within 3 d. Several parameters tended to improve as compared to pretransfusion, including increased lymphocyte counts ( $0.65 \times 10^9/L$  vs.  $0.76 \times 10^9/L$ ) and decreased C-reactive protein (55.98 mg/L vs. 18.13 mg/L). Radiological examinations showed varying degrees of absorption of lung lesions within 7 d. The viral load was undetectable after transfusion in seven patients who had previous viremia. No severe adverse effects were observed. This study showed CP therapy was well tolerated and could potentially improve the clinical outcomes through neutralizing viremia in severe COVID-19 cases. The optimal dose and time point, as well as the clinical benefit of CP therapy, needs further investigation in larger well-controlled trials.

Case Reports > JAMA. 2020 Apr 28;323(16):1582-1589. doi: 10.1001/jama.2020.4783.

## Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma

Chenguang Shen<sup>1</sup>, Zhaoqin Wang<sup>1</sup>, Fang Zhao<sup>1</sup>, Yang Yang<sup>1</sup>, Jinxiu Li<sup>1</sup>, Jing Yuan<sup>1</sup>, Fuxiang Wang<sup>1</sup>, Delin Li<sup>1,2</sup>, Minghui Yang<sup>1</sup>, Li Xing<sup>1</sup>, Jinli Wei<sup>1</sup>, Haixia Xiao<sup>1,2</sup>, Yan Yang<sup>1</sup>, Jiuxin Qu<sup>1</sup>, Ling Qing<sup>1</sup>, Li Chen<sup>1</sup>, Zhixiang Xu<sup>1</sup>, Ling Peng<sup>1</sup>, Yanjie Li<sup>1</sup>, Haixia Zheng<sup>1</sup>, Feng Chen<sup>1</sup>, Kun Huang<sup>1</sup>, Yujing Jiang<sup>1</sup>, Dongjing Liu<sup>1</sup>, Zheng Zhang<sup>1</sup>, Yingxia Liu<sup>1</sup>, Lei Liu<sup>1</sup>

Affiliations + expand

PMID: 32219428 PMID: PMC7101507 DOI: 10.1001/jama.2020.4783

Epub 2020 March 27

**Conclusions and relevance:** In this preliminary uncontrolled case series of 5 critically ill patients with COVID-19 and ARDS, administration of convalescent plasma containing neutralizing antibody was followed by improvement in their clinical status. The limited sample size and study design preclude a definitive statement about the potential effectiveness of this treatment, and these observations require evaluation in clinical trials.

Case Reports > J Med Virol. 2020 Oct;92(10):1890-1901. doi: 10.1002/jmv.25882.

Epub 2020 Jun 29.

## Treatment with convalescent plasma for COVID-19 patients in Wuhan, China

Mingxiang Ye<sup>1 2</sup>, Dian Fu<sup>2 3</sup>, Yi Ren<sup>2 4</sup>, Faxiang Wang<sup>2 5</sup>, Dong Wang<sup>1 2</sup>, Fang Zhang<sup>1 2</sup>, Xinyi Xia<sup>6 7</sup>, Tangfeng Lv<sup>1 2</sup>

Affiliations + expand

PMID: 32293713 PMID: PMC7262027 DOI: 10.1002/jmv.25882

### Abstract

The discovery of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the outbreak of coronavirus disease 2019 (COVID-19) are causing public health emergencies. A handful pieces of literature have summarized its clinical and radiologic features, whereas therapies for COVID-19 are rather limited. To evaluate the efficacy of convalescent plasma therapy in COVID-19 patients, we did this timely descriptive study. Six laboratory-confirmed COVID-19 patients were enrolled and received the transfusion of ABO-compatible convalescent plasma. The efficacy of this intervention was determined by the alleviation of symptoms, changes in radiologic abnormalities and laboratory tests. No obvious adverse effect observed during the treatment. Transfusion of convalescent plasma led to a resolution of ground-glass opacities and consolidation in patients #1, #2, #3, #4, and #6. In patients #1 and #5 who presented with SARS-CoV-2 in throat swab, convalescent plasma therapy elicited an elimination of the virus. Serologic analysis indicated an immediate increase in anti-SARS-CoV-2 antibody titers in patients #2 and #3, but not in patient #1. This study indicates that convalescent plasma therapy is effective and specific for COVID-19. This intervention has a special significance for eliminating SARS-CoV-2 and is believed to be a promising state-of-the-art therapy during COVID-19 pandemic crisis.

## Ključna ograničenja

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- Mali broj ispitanika
- Nedostatak kontrolne skupine, čiji izostanak onemogućuje donošenje zaključka o istinskim kliničkim učincima terapije - bi li se bolesnici oporavili i bez transfuzije?
- Nalazi i ishodi su mogli biti i rezultat istodobne primjene drugog liječenja, uključujući antivirusne lijekove i steroide



JAMA

View Article ▶

JAMA. 2020 Aug 4; 324(5): 1–11.

Published online 2020 Jun 3. doi: [10.1001/jama.2020.10044](https://doi.org/10.1001/jama.2020.10044)

PMCID: PMC7270883

PMID: [32492084](https://pubmed.ncbi.nlm.nih.gov/32492084/)

## Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19

A Randomized Clinical Trial

[Ling Li](#), MD, PhD,<sup>1,2</sup> [Wei Zhang](#), MD,<sup>3,4</sup> [Yu Hu](#), MD, PhD,<sup>5</sup> [Xunliang Tong](#), MD, PhD,<sup>6</sup> [Shangen Zheng](#), MD,<sup>7</sup> [Juntao Yang](#), PhD,<sup>8</sup> [Yujie Kong](#), MD,<sup>1,2</sup> [Lili Ren](#), PhD,<sup>9,10</sup> [Qing Wei](#), MD,<sup>11</sup> [Heng Mei](#), MD, PhD,<sup>5</sup> [Caiying Hu](#), MD,<sup>12</sup> [Cuihua Tao](#), MD,<sup>13,14</sup> [Ru Yang](#), MD,<sup>15</sup> [Jue Wang](#), MD,<sup>1,2</sup> [Yongpei Yu](#), PhD,<sup>16</sup> [Yong Guo](#), PhD,<sup>17</sup> [Xiaoxiong Wu](#), MD,<sup>18</sup> [Zhihua Xu](#), MD,<sup>12,19</sup> [Li Zeng](#), MD,<sup>3,20</sup> [Nian Xiong](#), MD, PhD,<sup>12,21</sup> [Lifeng Chen](#), MD,<sup>22</sup> [Juan Wang](#), MD,<sup>11</sup> [Ning Man](#), MD,<sup>23</sup> [Yu Liu](#), PhD,<sup>1</sup> [Haixia Xu](#), MD,<sup>1,2</sup> [E Deng](#), MS,<sup>1</sup> [Xuejun Zhang](#), MS,<sup>1</sup> [Chenyue Li](#), MD,<sup>1,2</sup> [Conghui Wang](#), PhD,<sup>9</sup> [Shisheng Su](#), PhD,<sup>17</sup> [Linqi Zhang](#), PhD,<sup>24</sup> [Jianwei Wang](#), PhD,<sup>9,10</sup> [Yanyun Wu](#), MD, PhD,<sup>25</sup> and [Zhong Liu](#), MD, PhD<sup>1,2</sup>

In summary, the first randomized clinical trial of convalescent plasma in COVID-19, reported by Li et al in JAMA, showed no statistically significant benefit in clinical improvement at 28 days or mortality among all randomized patients, but does provide an important signal of possible benefit in the subgroup of severely ill patients and suggests that high titer antibody against SARS-CoV-2 may have antiviral efficacy. These results, while preliminary and subject to important study limitations, should stimulate more clinical trials to establish the optimal conditions for antibody therapies against COVID-19 and suggest that future studies should focus on determining efficacy in less severely ill patients. If the efficacy of convalescent plasma is established by future studies, the ratio of donor to patients is favorable because individuals who recover from COVID-19 can donate 2 or 3 units of plasma, which could be used to treat more than 1 person with COVID-19 disease. Therapeutic success against such a complex and challenging disease as COVID-19 is likely to require more than 1 modality, and the results from Li et al<sup>8</sup> provide optimism for the future of antibody therapy in this disease.

# Kriteriji za odabir davatelja

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- Davatelji konvalescentne plazme moraju zadovoljiti kriterije za odabir dobrovoljnih darivatelja krvi i krvnih sastojaka na staničnom separatoru
  - prethodna dijagnoza COVID-19, potvrđena pozitivnim RT-PCR testom, SARS-CoV-2 antigenskim testom ili testom na SARS-CoV-2 protutijela, bez obzira na prisutnost simptoma.
  - pojedinci koji su imali tipične simptome COVID-19, ali bolest nije potvrđena niti jednim od testova također mogu pristupiti darivanju, o čemu odlučuje liječnik na pregledu DDK, uzimajući u obzir anamnestičke i epidemiološke podatke.
  - 14 dana od izlaska iz izolacije.
  - ukoliko je osoba bila asimptomatska, a laboratorijski joj je potvrđena infekcija SARS-CoV-2, period odgode od 14 dana počinje teći od datuma uzimanja uzorka za testiranje na SARS-CoV-2.
  - preboljenje COVID-19 unutar posljednja 4 mjeseca ako nisu cijepljeni; ukoliko su preboljeli i cijepljeni, nema vremenskog ograničenja

# Cijepljenje



Updated 04 14 2021

Updated Information from FDA on Donation of CCP, Blood Components and HCT/Ps, Including Information on COVID-19 Vaccines, Treatment with CCP or Monoclonals



Updated 04 14 2021

- individuals who had a positive diagnostic test for SARS-CoV-2 (e.g., nasopharyngeal swab), but never developed symptoms, refrain from donating at least 14 days after the date of the positive test result,
- individuals who are tested and found positive for SARS-CoV-2 antibodies, but who did not have prior diagnostic testing and never developed symptoms, can donate without a waiting period and without performing a diagnostic test (e.g., nasopharyngeal swab),
- individuals who received a nonreplicating, inactivated, or mRNA-based COVID-19 vaccine can donate blood without a waiting period,
- individuals who received a live-attenuated viral COVID-19 vaccine, refrain from donating blood for a short waiting period (e.g., 14 days) after receipt of the vaccine,
- individuals who are uncertain about which COVID-19 vaccine was administered, refrain from donating for a short waiting period (e.g., 14 days) if it is possible that the individual received a live-attenuated viral vaccine.

FDA will continue to monitor the situation and issue updated information as it becomes available.

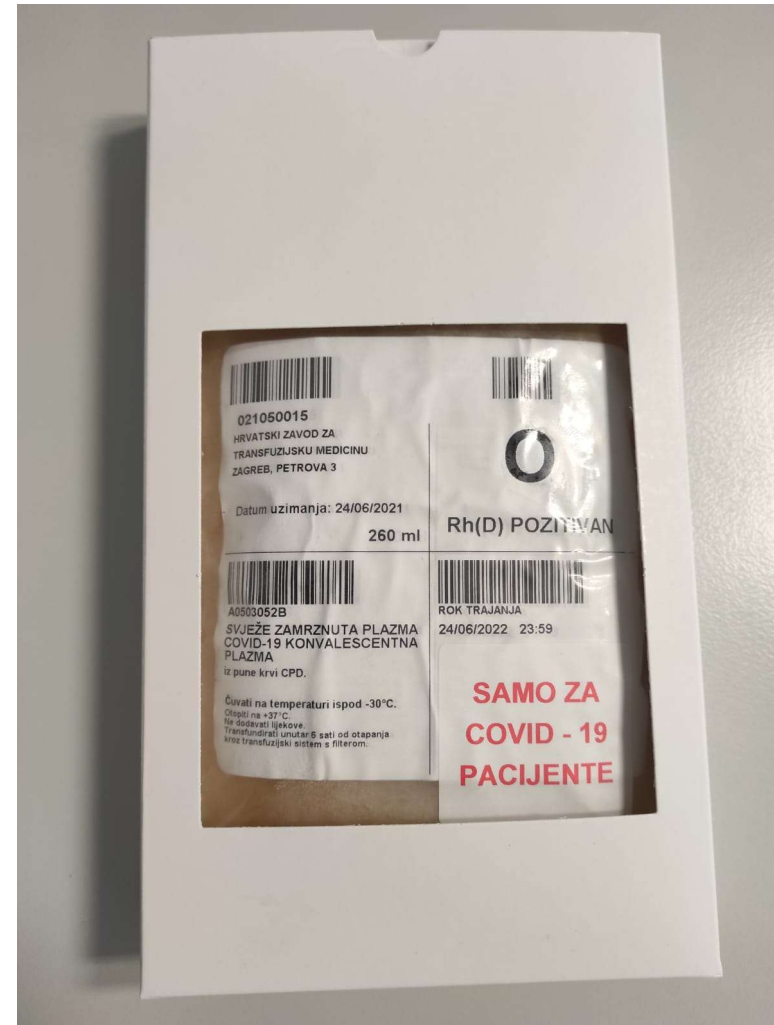
# Metode

## 1. Afereza – prva KP - 28. srpnja, 2020.

- Na početku KP su davale oporavljene osobe koje do tada nikada nisu darivale krv.

## 2. Iz Pune krvi - od 01. svibnja, 2021.

- Širenjem zaraze sve je veći broj regularnih DDK, koji su preboljeli COVID-19 – novi resurs
- Sve je veći broj i preboljelih DDK koji su cijepljeni – najkvalitetniji resurs
- Izvrsno rješenje - zbog velikih zahtjeva i potencijalnih problema sa zadovoljavanjem potreba



## Testiranje

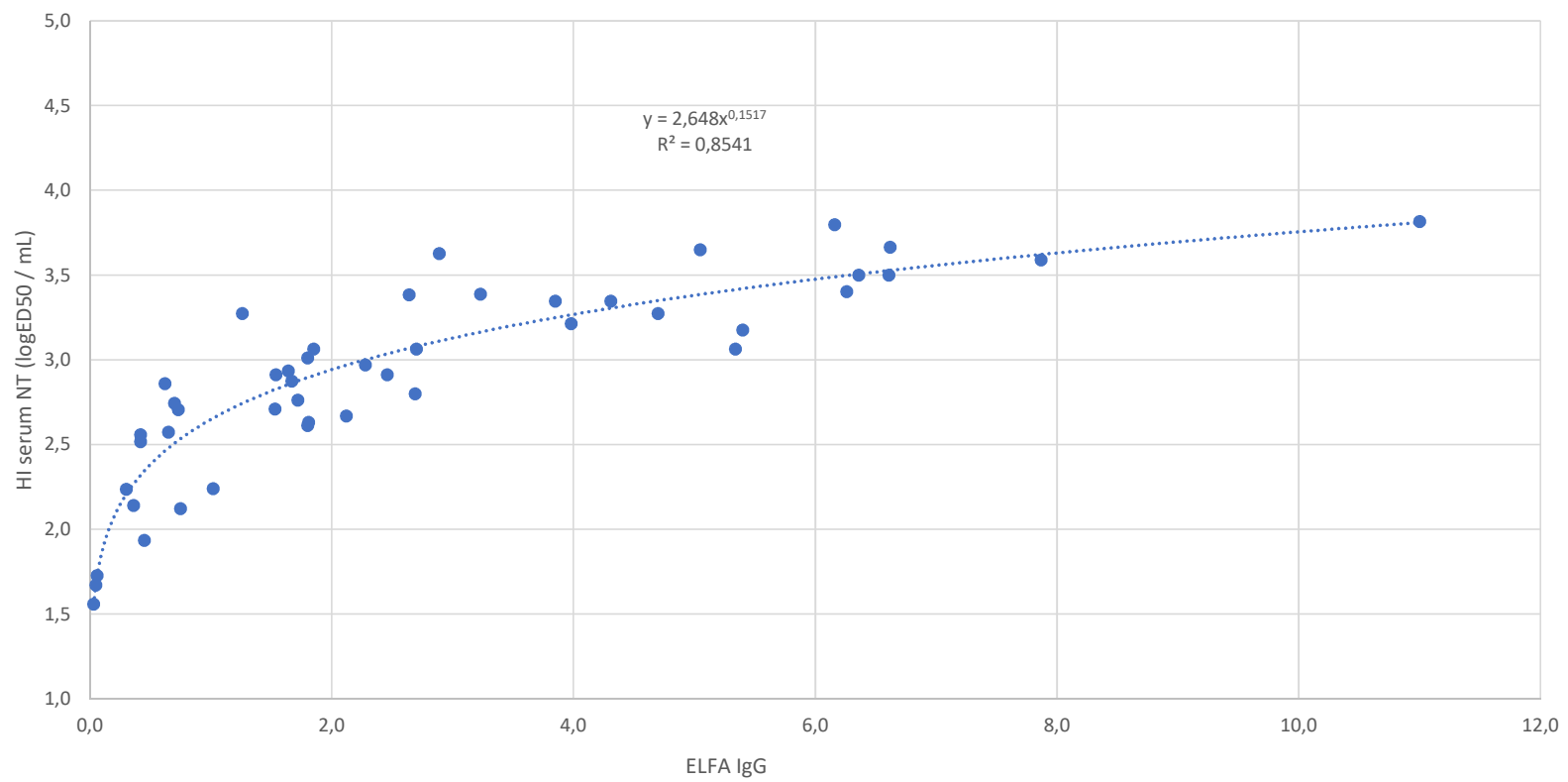
Titar NPt mjereno je sa SARS-CoV-2 neutralizacijskim testom za kvantifikaciju SARS-CoV-2 NPt u BSL3 uvjetima.

– *zlatni standard*



- Zbog kompleksnosti testa i čekanja na rezultate rađena je regresijska analiza sa serološkim testom VIDAS SARS CoV-2 IgG, postavljen cut-off za visoki titar  $\geq 10$  TV
- Postignuta bolja protočnost
- Regresijske analize rađene i za Banke krvi u RH

NT versus ELFA IgG





Medicines & Healthcare products  
Regulatory Agency

WHO International Standard  
WHO International Standard for SARS-CoV-2 antibody (human)  
NIBSC code: 20/136  
Instructions for use  
(Version 1.00, Dated)

#### 1. INTENDED USE

The WHO International Standard for anti-SARS-CoV-2 antibody is the freeze-dried equivalent of 0.25 mL of pooled plasma obtained from eleven individuals recovered from SARS-CoV-2 infection. The preparation has been evaluated in a WHO International Collaborative study (1). The intended use of the International Standard is for the calibration and harmonisation of serological assays detecting anti-SARS-CoV-2 neutralising and binding antibody. The material has the same assigned unitage for neutralising and binding antibody. Secondary reagents should be calibrated to the International Standard in the type of assay required. The preparation has been solvent-detergent treated to minimise the risk of the presence of enveloped viruses (2).

#### 2. CAUTION

**This preparation is not for administration to humans or animals in the human food chain.**

The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

#### 3. UNITAGE

The assigned potency of the WHO International Standard for SARS-CoV-2 antibody is 250 IU/ampoule for neutralising activity and 250 IU/ampoule for binding activity. After reconstitution in 0.25 mL of distilled water, the final concentration of the preparation is 1000 IU/mL for neutralising and binding antibody.



#### 8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials.

#### 9. REFERENCES

(1) Mattiuzzo et al. Establishment of the WHO International Standard and Reference Panel for anti-SARS-CoV-2 antibody. 2020, WHO Expert Committee on Biological Standardization. WHO/BS/2020.xxxx  
(2) Dichtelmüller et al. Robustness of solvent/detergent treatment of plasma derivatives: a data collection from Plasma Protein Therapeutics Association member companies. Transfusion. 2009;49:1931-43.

#### 10. ACKNOWLEDGEMENTS

We would like to wholeheartedly thank the anonymous donors of the plasma samples for their consent which has allowed this material to be prepared; we would like to express our gratitude to those groups and individuals who have coordinated the collection of the convalescent plasma: Malcolm Semple (University of Liverpool, UK), Lance Turtle (University of Liverpool, UK), Peter Openshaw (Imperial College London, UK) and Kenneth Ballie (University of Edinburgh) on behalf of the ISARIC4C Investigators; Heli Harvala Simmonds and David Roberts (National Health Service Blood and Transplant, UK). We would also like to thank NIBSC Standards Production and Development staff for the formulation and distribution of materials. The International Standard for SARS-CoV-2 antibody wouldn't have been possible without the Coalition for Epidemic Preparedness Innovations (CEPI) sponsored the sourcing and formulation of the candidate material.

#### 11. FURTHER INFORMATION

Further information can be obtained as follows;  
This material: [enquiries@nibsc.org](mailto:enquiries@nibsc.org)  
WHO Biological Standards:  
<http://www.who.int/biologicals/en/>  
JCTLM Higher order reference materials:  
<http://www.bipm.org/en/committees/cj/jctlm/>

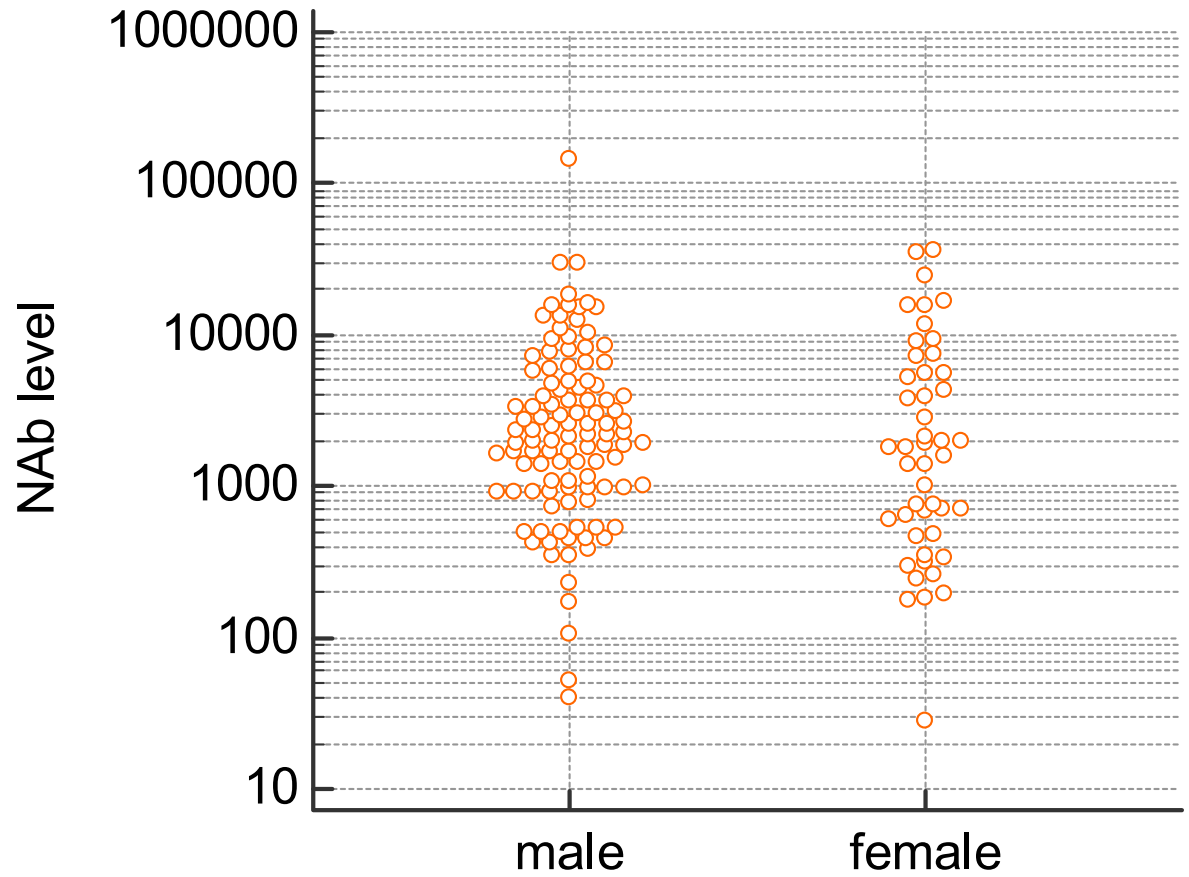
- Različnost izražavanja rezultata – nemoguća usporedba
- Prvi WHO Internacionalni standard NIBSC code 20/136 za izražavanje rezultata testiranja u IU/ml

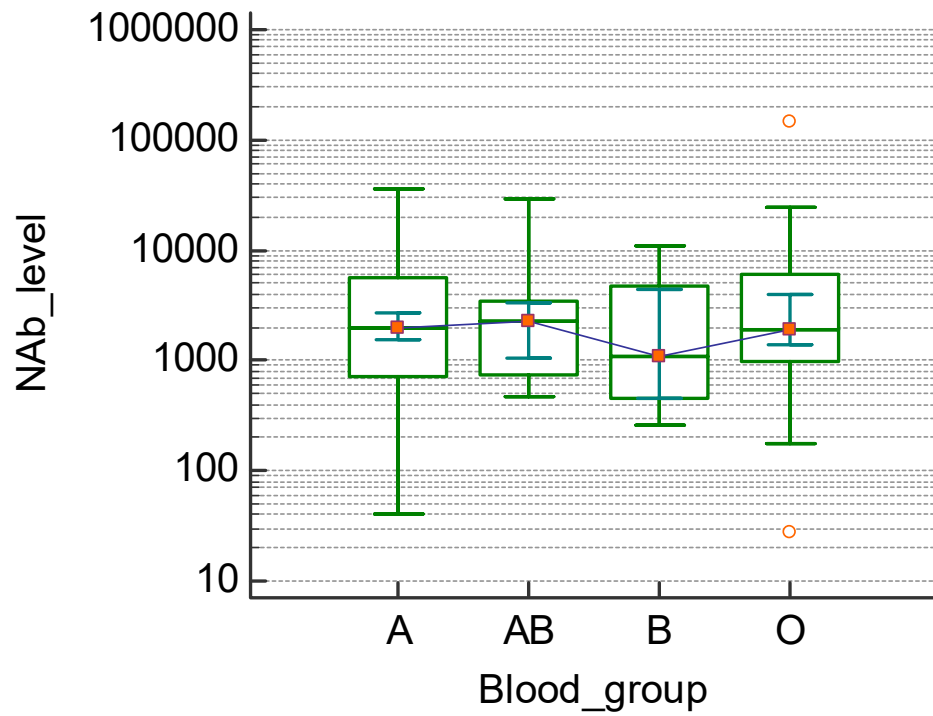
- Biomerieux Vidas SARS CoV -2 IgG  $\geq 10$  TV  
~ 170IU/ml

---

- NAb level did not statistically differ between genders.

- ( $P = 0.262, Z = 1.12$ )





---

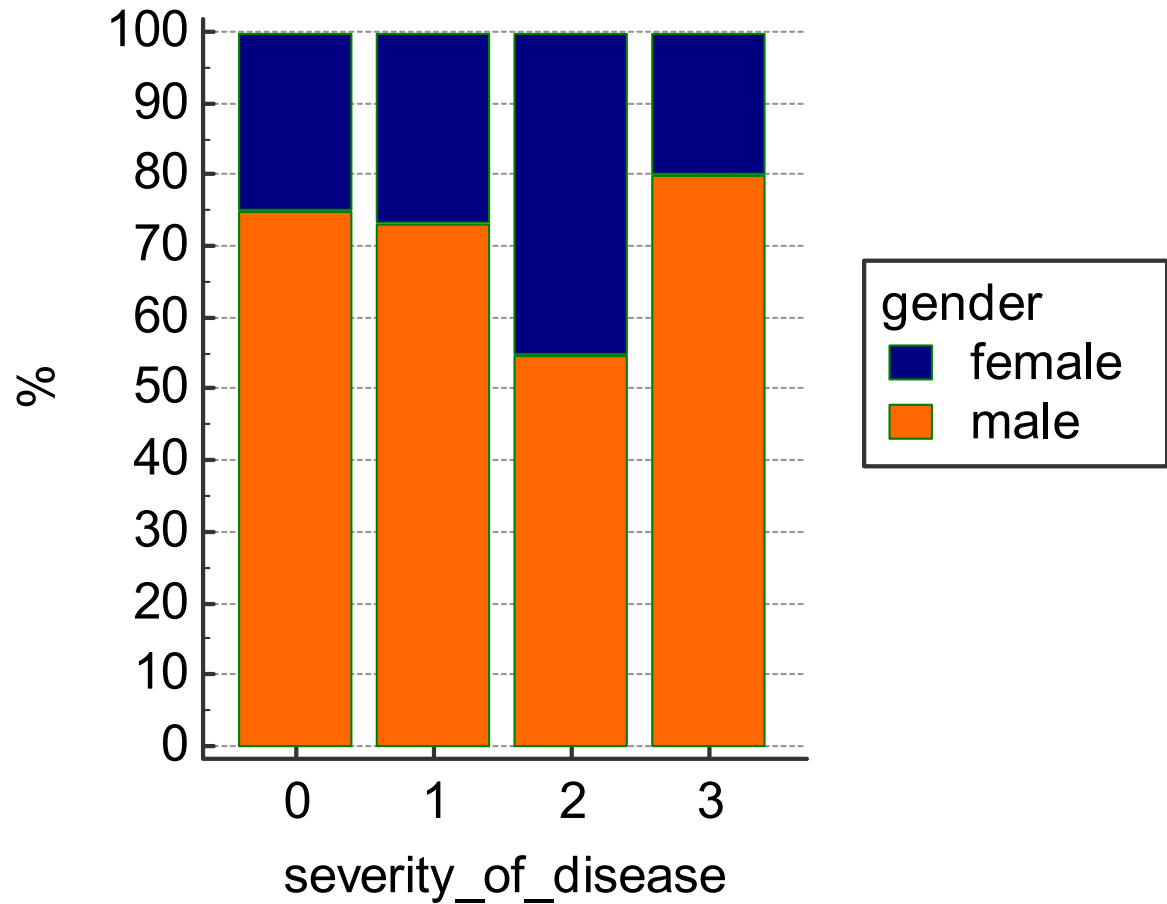
- NAb level did not statistically differ between blood groups.

- ( $P = 0.842, \chi^2 = 0.83$ )

---

- Severity of disease did not statistically differ between genders.

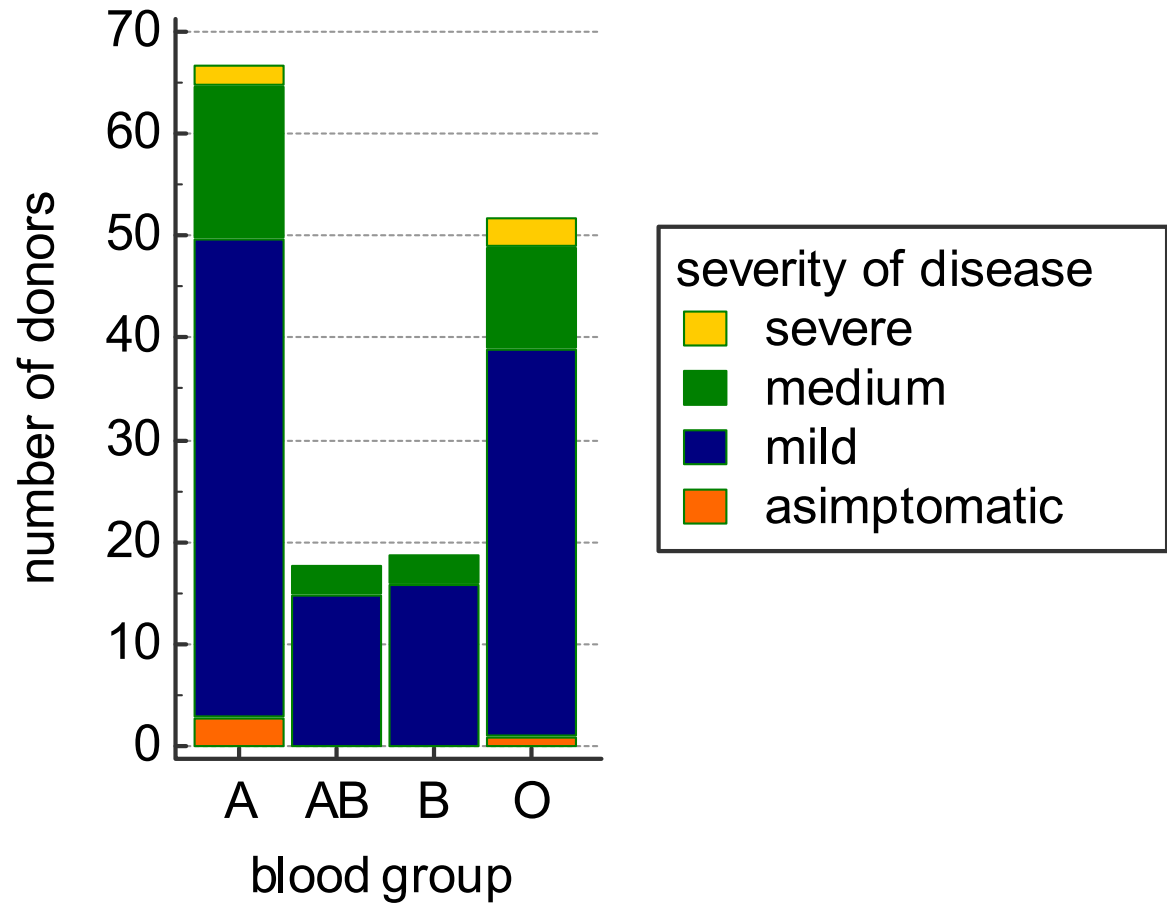
- ( $P = 0.23$ ,  $\chi^2 = 4.26$ )



---

- Severity of disease did not statistically differ between blood groups.

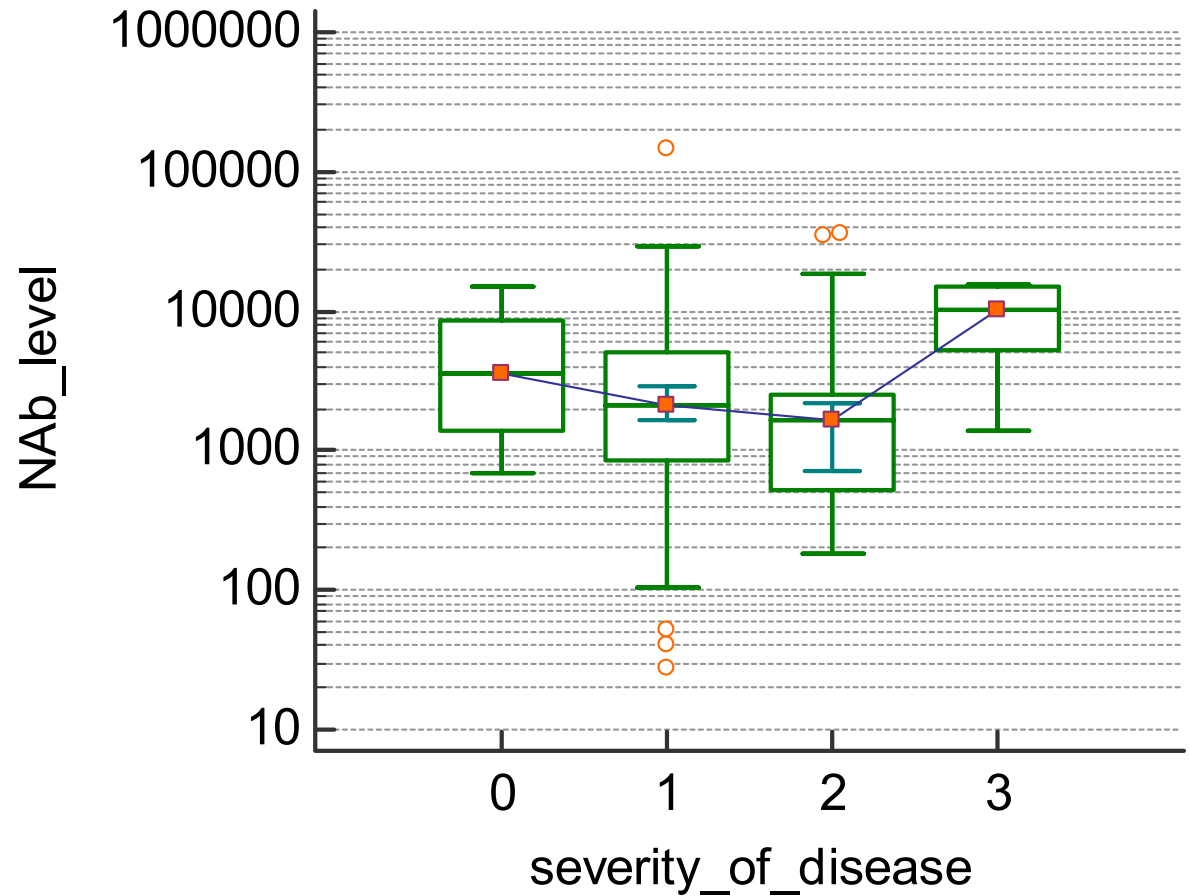
- ( $P = 0.803$ ,  $\chi^2 = 5.34$ )



---

- NAb level did not statistically differ between severity of symptoms.

- ( $P = 0.072, \chi^2 = 6.99$ )



	AFEREZA	PUN KRV	UKUPNO
PERIOD	28.srpanj 2020.- 04.svibanj 2022.	03. svibanj 2021.- 04.svibanj 2022.	
BROJ DOZA	382	2235	2722
MEDIJAN	36 (18-62)	40 (18-67)	
SPOL	60,6% M 30.4% Ž	100% M	
VISOKI TITAR	75%	91%	

---

do 04.svibanj 2022.

AFEREZA

PUNA KRV

UKUPNO

HZTM

361

1601

1962

Split

-

337

337

Rijeka

36

220

256

Osijek

90

-

90

Zadar

-

50

50

Varaždin

-

27

27

---

Registrirano je više od 140 kliničkih studija – procjena učinkovitost i sigurnost - ogroman broj dostupnih podataka.

Kako bi se uskladili rezultati primarnih kliničkih ispitivanja, posljednjih godinu dana objavljeno je nekoliko sustavnih pregleda i metaanaliza.

**Zaključci - prilično oprečni** i odražavaju široku heterogenost između različitih studija u smislu dizajna studije, proizvoda KP i primjene, karakteristika bolesti i karakteristika bolesnika.

Čini se svojstveno za izvanredne situacije

---

# Safety and Efficacy of Convalescent Plasma in COVID-19: An Overview of Systematic Reviews

Massimo Franchini <sup>1</sup>, Fabiana Corsini <sup>2</sup>, Daniele Focosi <sup>3</sup>, Mario Cruciani <sup>1</sup>

Affiliations [+](#) expand

PMID: 34574004 PMCID: [PMC8467957](#) DOI: [10.3390/diagnostics11091663](#)

[Free PMC article](#)

## Abstract

Convalescent plasma (CP) from patients recovered from COVID-19 is one of the most studied anti-viral therapies against SARS-COV-2 infection. The aim of this study is to summarize the evidence from the available systematic reviews on the efficacy and safety of CP in COVID-19 through an overview of the published systematic reviews (SRs). A systematic literature search was conducted up to August 2021 in [Embase, PubMed, Web of Science, Cochrane and Medrxiv databases](#) to identify systematic reviews focusing on CP use in COVID-19. Two review authors independently evaluated reviews for inclusion, extracted data and assessed quality of evidence using AMSTAR (A Measurement Tool to Assess Reviews) and GRADE tools. The following outcomes were analyzed: mortality, viral clearance, clinical improvement, length of hospital stay, adverse reactions. In addition, where possible, subgroup analyses were performed according to study design (e.g., RCTs vs. non-RCTs), CP neutralizing antibody titer and timing of administration, and disease severity. The methodological quality of included studies was assessed using the checklist for systematic reviews AMSTAR-2 and the GRADE assessment. Overall, [29 SRs](#) met the inclusion criteria based on [53 unique primary studies \(17 RCT and 36 non-RCT\)](#). Limitations to the methodological quality of reviews most commonly related to absence of a protocol (11/29) and funding sources of primary studies (27/29). Of the 89 analyses on which GRADE judgements were made, effect estimates were judged to be of high/moderate certainty in four analyses, moderate in 38, low in 38, very low in nine. Despite the variability in the certainty of the evidence, mostly related to the risk of bias and inconsistency, [the results of this umbrella review highlight a mortality reduction in CP over standard therapy when administered early and at high titer, without increased adverse reactions.](#)

## Štetne reakcije

---

Početni strahovi vezani za primjenu KP:

TRALI - transfusion-related acute lung injury

TACO - Transfusion-associated circulatory overload

ADE - antibody dependent enhancement

- Literaturni podaci pokazali da nije bilo bitne razlike u pojavnosti štetnih reakcija između KP i SZP
- Sustav hemovigilancije u RH – isti zaključci

Author	Country	Viral etiology		Adverse events
Zhang; et al. (2020) [111]	China	COVID-19	None	
Shen et al. (2020) [38]	China	COVID-19	None	
Duan et al. (2020) [39]	China	COVID-19		Self-limited facial erythema in 2/10 patients. No major adverse events.
Ye et al. (2020) [37]	China	COVID-19	None	
Anh et al. (2020) [34]	South Korea	COVID-19	None	
Soo et al (2004) [40]	China	SARS-CoV	None	
Cheng et al (2005) [41]	China	SARS-CoV	None	
Nie et al. (2003) [5]	China	SARS-CoV	None	
Yeh et al (2005) [42]	Taiwan	SARS-CoV	None	
Zhou et al. (2003) [43]	China	SARS-CoV	None	
Kong et al. (2003) [44]	China	SARS-CoV	None	
Wong et al (2003) [45]	China	SARS-CoV	None	
Ko et al. (2018) [35]	South Korea	MERS-CoV	None	
Van Griensven et al. (2016) [25]	Guinea	Ebola		Nausea, skin erythema, fever. No major adverse events.
Hung et al. (2011) [46]	China	Influenza A(H1N1)	None	
Chan et al. (2010) [47]	China	Influenza A(H1N1)	None	
Yu et al. (2008) [48]	China	Influenza A(H5N1)	None	
Kong et al. (2006) [49]	China	Influenza A(H5N1)	None	



March 9, 2021

Nikki Bratcher-Bowman  
Acting Assistant Secretary for Preparedness and Response  
Office of the Assistant Secretary for Preparedness and Response  
Office of the Secretary  
U.S. Department of Health and Human Services  
200 Independence Avenue, SW  
Washington, DC 20201

Dear Ms. Bratcher-Bowman:

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19 (the virus was later named SARS-CoV-2).<sup>1</sup> On March 27, 2020, on the basis of such determination, the Secretary of HHS declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act, subject to the terms of any authorization issued under that section.<sup>2</sup>

On August 23, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the emergency use of COVID-19 convalescent plasma for the treatment of hospitalized patients with Coronavirus Disease 2019 (COVID-19), pursuant to Section 564 of the Act.<sup>3</sup> Subsequently, FDA reissued the Letter of Authorization to add tests acceptable to be used in the manufacture of COVID-19 convalescent plasma, the names and dates of each test are currently listed in Appendix A.<sup>4</sup>

## II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized high titer COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19, early in the course of disease, and those hospitalized with impaired humoral immunity. The emergency use of the authorized high titer COVID-19

convalescent plasma under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below.



EUROPEAN COMMISSION  
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Ref. Ares(2021)1739358 - 10/03/2021

Directorate B - Health systems, medical products and innovation  
B4 – Medical products: quality, safety, innovation

Brussels,  
SANTÉ B4/DF/

## An EU programme of COVID-19 convalescent plasma collection and transfusion

### Guidance on collection, testing, processing, storage, distribution and monitored use

*This document has been endorsed by the Competent Authorities for Substance of Human Origin Expert Group (CASoHO E01718) following consultation of the competent authorities for blood and blood components and by the European Centre for Disease Prevention and Control. While this document is not legally binding, it aims to facilitate a common approach across EU Member States to the donation, collection, testing, processing, storage, distribution and monitoring of convalescent plasma for the treatment of COVID-19 (CCP). This document is without prejudice to the requirements of the Union blood legislation, any more stringent national measures in place at Member State level and national requirements on the use of this treatment, all of which continue to apply. This guidance is updated as needed, in line with scientific developments. 10 March 2021*  
Version 4.0

### Distribution of COVID-19 convalescent plasma

Convalescent plasma should be distributed by blood establishments on the request of a hospital in the following circumstances:

- the specific patient has laboratory confirmed COVID-19 and is in the early or moderate clinical stage of disease (WHO classification) or has impaired humoral immunity;
- CCP should be applied to these patients as early as possible, ideally within 3 days of symptom onset or as early as possible after hospital admission;
- the patient has been hospitalised, unless the plasma is supplied in the context of a clinical trial on early transfusion of non-hospitalised patients;
- the patient, or their legal representative, has given informed consent to transfusion with COVID-19 convalescent plasma.

The uncertainty about the efficacy of convalescent plasma in treating patients with COVID-19 should be communicated to potential recipients or their legal representatives, whether they are part of a clinical trial or of monitored use, to avoid fostering unfounded expectations and to ensure that prospective recipients or their legal representatives make informed decisions regarding treatment.

Blood services should aim to issue the components with the highest antibody titres available, while respecting the treatment and clinical trial protocols in place locally. An evidence-base for a minimal titre of neutralising antibodies with significant clinical efficacy of convalescent is limited. The US data described above, together with initial research [5, 6], suggests that a titre of  $\geq 1:160$  might be an appropriate threshold to apply but a definitive threshold is yet to be established in clinical trials. There is no international standardized unit for "titre" nor is there currently any calibration possible to reliably compare titres among unrelated studies. Therefore, each CCP programme should specify its threshold titre of neutralizing antibodies to allow for a correlation of antibody titre and patient outcome. Only CCP with high neutralising antibody titres should be used in the treatment of COVID-19 patients<sup>1</sup>. A suggested dose of high titre convalescent plasma is one unit; for low titre plasma, two units of convalescent plasma might be transfused. If two units are to be transfused they should be from different donors.



- 07. prosinca, WHO je ažurirao svoje smjernice za KP.
- Preporuke protiv upotrebe CCP-a za pacijente s COVID-19, dodajući da se on smije koristiti samo u kliničkim ispitivanjima za teško i kritično bolesne pacijente s COVID-19.

## Open letter to WHO for revisions to CCP recommendations

97 people have signed this petition. [Add your name now!](#) 

 Madison Walsh  26 Comments



**NATIONAL COVID-19  
CONVALESCENT  
PLASMA PROJECT**

April 27, 2022

Dr Tedros Adhanom Ghebreyesus

Director

World Health Organization

Geneva, Switzerland

Dear Dr Tedros Adhanom  
Ghebreyesus,

We write to request that the WHO update its COVID-19 convalescent plasma (CCP) recommendations, last issued on December 7, 2021, that recommended against its use in early disease stages. A prior statement by the U.S. COVID-19 Convalescent Plasma Project leadership argued that this recommendation was misguided based on the knowledge available at the time (1). WHO recommendations are based largely on the analysis of randomized controlled trials published early in the pandemic that focused on hospitalized patients with late-stage disease. As we have noted in a comprehensive analysis (2), the majority of these RCTs used CCP too late in the course of disease to affect outcome. There are now algorithms that identify patients likely to benefit from CCP (3).

- na temelju dostupnih znanja - ova preporuka je pogrešna!
- preporuke WHO-a uglavnom su temeljene na analizi randomiziranih kontroliranih ispitivanja objavljenih u ranoj fazi pandemije koja su se usredotočila na hospitalizirane pacijente s kasnom fazom bolesti.
- od prosinca 2021. objavljeni su dodatni snažni dokazi koji pokazuju da je CCP učinkovit kada se koristi u ranoj fazi bolesti s visokom koncentracijom protutijela na SARS-CoV-2, da tada smanjuje vjerojatnost hospitalizacije i smanjuje smrtnost.
- KP nalazi veliku primjenu kod imunosupresivnih pacijenata koji često ne mogu dati odgovarajući odgovor protutijela nakon cijepljenja ili nakon infekcije.
- Infectious Disease Society of America i Association for the Advancement of Blood & Biotherapies (AABB) i FDA i EK

- u tijeku je u EU veliko istraživanje o KP koje će se temeljiti na podacima prikupljenim i dijeljenim putem baze podataka SUPPORT-E EU CCP, koja sadrži podatke o >150 000 donacija KP
- analiza podataka i izvlačenje zaključaka je u tijeku, a rezultati će biti predstavljeni na kraju projekta
- preporuke o nekorištenju KP trebale bi biti službene samo u jednoj od dvije situacije: (i) kada terapija pokazuje štetu pacijentima ili (ii) kada istraženo pitanje više nije relevantno ili vrijedno istraživanja.
- **Ne mislimo da je to tako!!!**



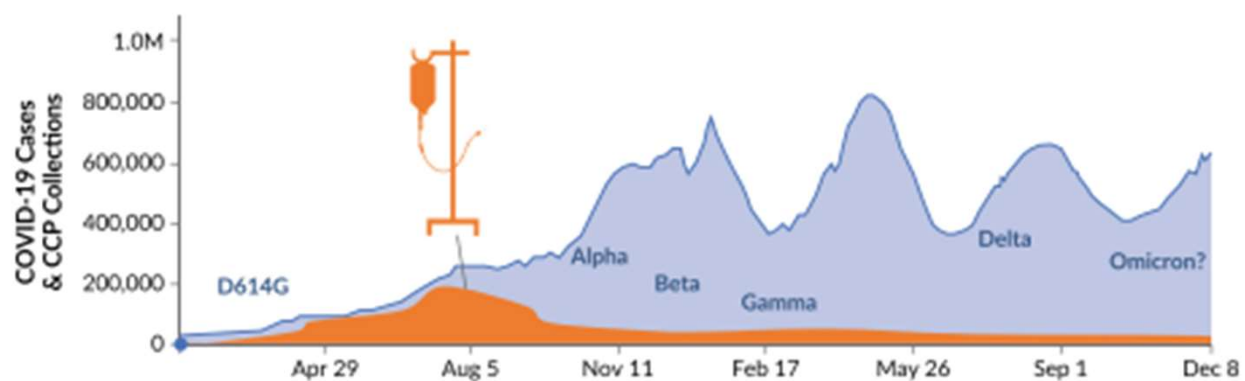
**Monitoring of ESI grants for Increasing  
Capacity for Covid-19 Convalescent  
Plasma Collection: Final Report**

### 5.5. CCP units collected: 165,444

Table 5 reports the number of CCP units collected as indicated by data available in the final reports. 165,444 CCP units were collected (min/Country 140, max/Country 97,140). As previously mentioned, it should be noted that these figures are different from those found in the periodic surveys because some countries reported them only in the final report.

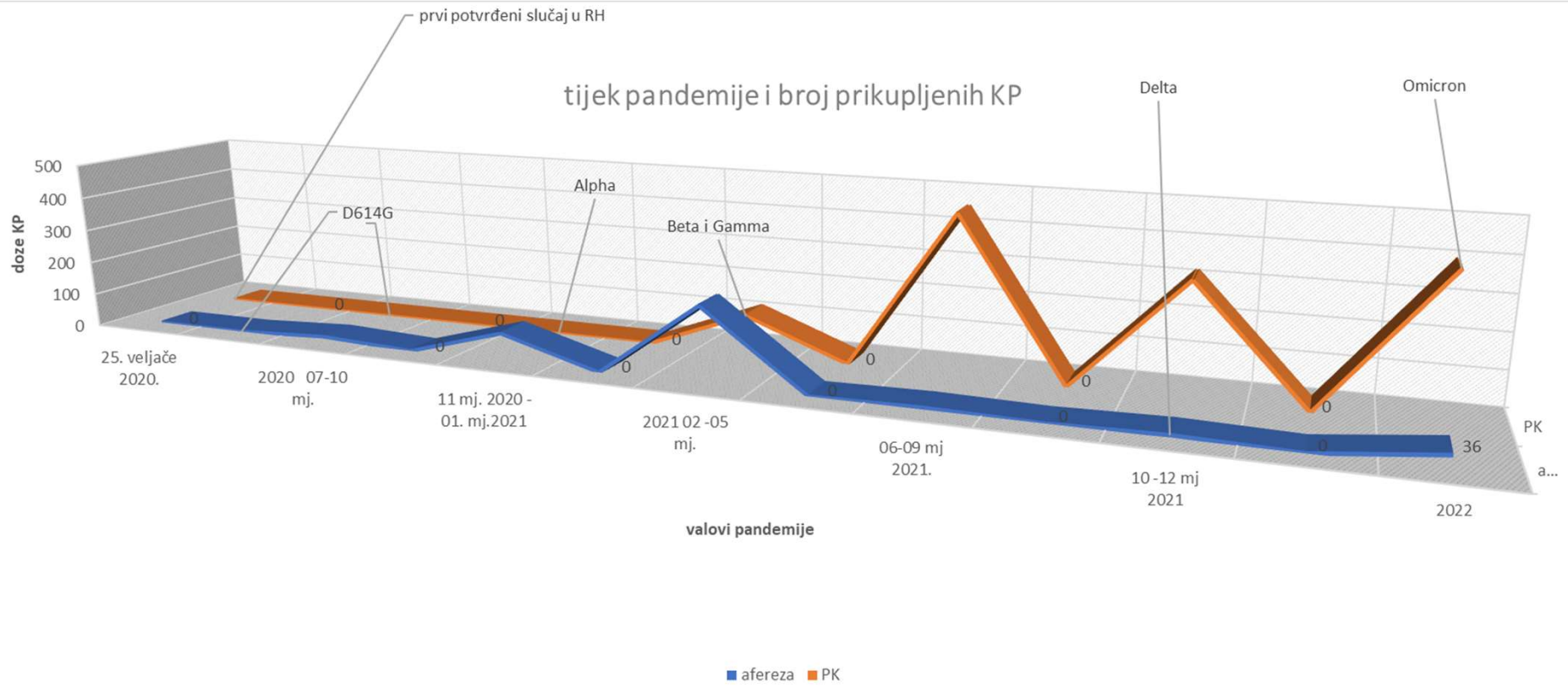
Country	First survey received	Last survey received	Final report
BE	1,390	1,442	1,442
BG	0	60	697
DE	5,806	6,434	4,692
DK	140	220	662

FR	1,476	3,985	4,697
HR	0	0	1,408
IE	4	12	0
IT	7,569	10,557	7,860
PL	857	3,841	16,185
RO	0	0	0
SI	600	1,500	3,921
UK	0	0	97,164
Total	<b>29,361</b>	<b>47,941</b>	<b>165,444</b>



**FIGURE 1** Kinetics of COVID-19 convalescent plasma (CCP) collections across the COVID-19 pandemic waves, driven by different variants of concern. Collections (and usage) declined after the first waves, making current bulks poorly useful and requiring a restart of collections from convalescent vaccines to counteract the upcoming Omicron variant

# tijek pandemije i broj prikupljenih KP



---

Od proglašenja pandemije pa do uspostave procesa prikupljanja i testiranja testom neutralizacije prošlo je **manje od četiri mjeseca**.

---

Procjena neutralizacijske sposobnosti VIDAS SARS CoV-2 testom omogućila je bolju protočnost – povećanje zaliha i brže izdavanje.

---

Iskorak u zadovoljenju zahtjeva bio je i prelazak na prikupljanje KP iz PK.

Do sada je u RH prikupljeno **>3000 doza**.

---

**Prva KP izdana je 17. prosinca 2020.** u Specijalnu bolnicu za plućne bolesti – hematološki bolesnik.

## Zaključak 1

---

---

Do sada je iz HZTM-a izdano > 1700 doza.

Tjedno izdavanje u jeku epidemije: 40-50 CCP, danas: 15-20 CCP

---

Najviše doza KP izdano je u KB Dubrava i KBC Zagreb – najčešće hematološkim bolesnicima.

---

KP s individualno provjerenim razinama NAb, kao vanjskog izvora antitijela, pokazala je obećavajuće rezultate u poboljšanju stanja ovih pacijenata tijekom infekcije SARS-CoV-2.

---

Naše iskustvo omogućilo je i prikupljanje KP i u drugim BK u RH – do tada je opskrba išla iz HZTM-a

---

Naše iskustvo doprinijet će kvalitetnom odgovoru u pripremi učinkovite intervencije u slučaju ponovnog izbijanja hCoV-a u budućnosti.

---

## Zaključak 2

# ZAHVALA

1. SVIM DARIVATELJIMA

2. Kolegama:

Tatjana Mušlin - HZTM

Patricija Topić Šestan - HZTM

Mate Vinković - HZTM

Marko Karlo Radovčić - HZTM

Tomislav Vuk - HZTM

Irena Jukić - HZTM

Nataši Lukežić - RI

Deana Bogdanić - ST

Marina Samardžija - OS

Gordana Jaklin - VŽ

Marijana Nadinić - ZD

Kolegama iz Centra za istraživanje i prijenos znanja u biotehnologiji Sveučilišta u Zagrebu

CROATIAN SCIENCE FOUNDATION PROJECT



IP-CORONA-04-2053