Diagnostické a terapeutické stratégie zamerané na COVID – 19

Pavol Jarčuška

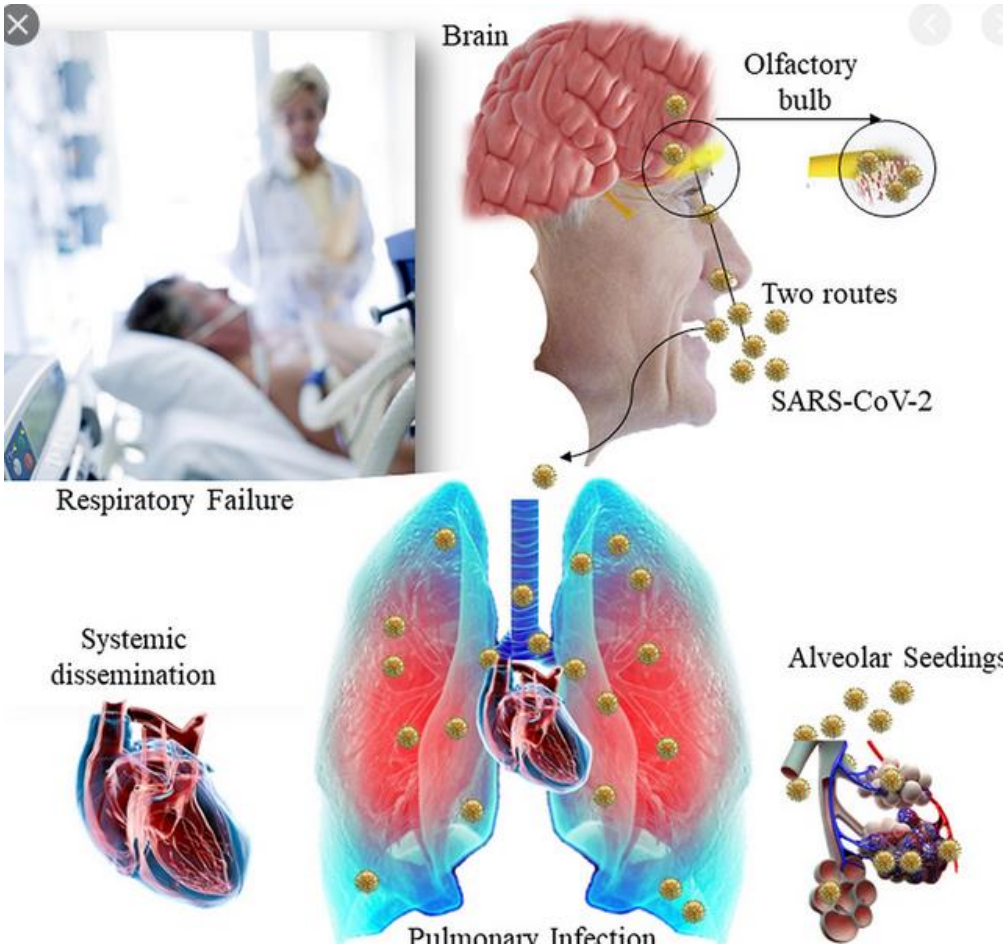
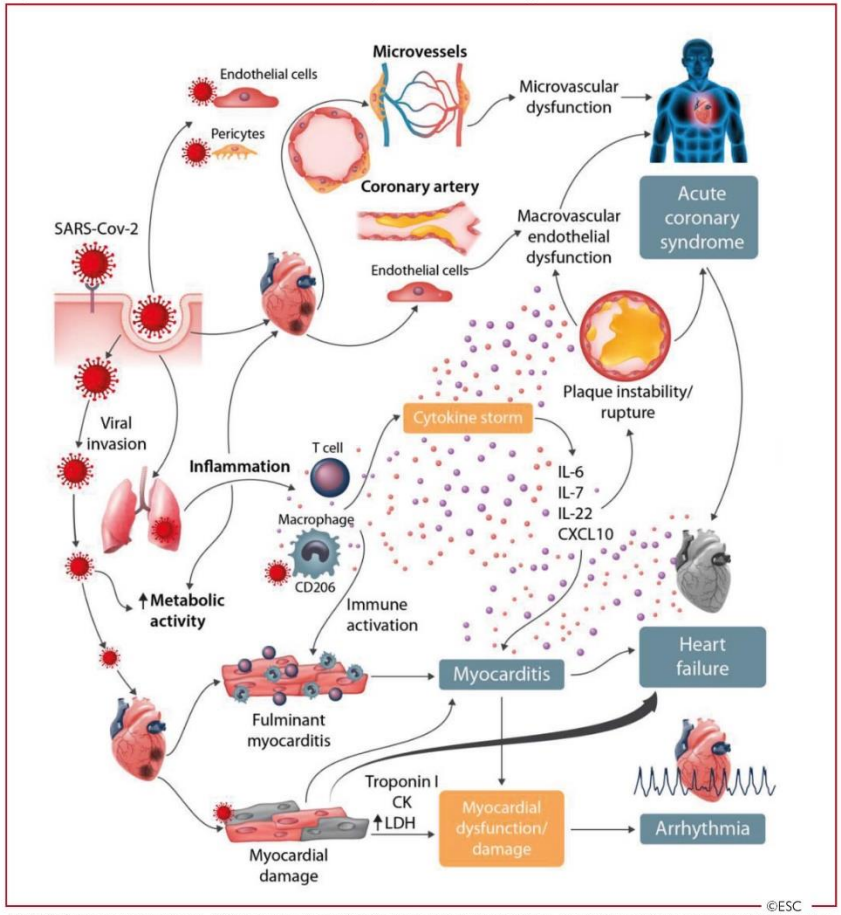

Brain
Olfactory bulb
Two routes
SARS-CoV-2
Respiratory Failure
Systemic dissemination
Alveolar Seedings
Pulmonary Infection

Figure 3 Cardiovascular involvement in COVID-19 – key manifestations and hypothetical mechanisms



SARS-CoV-2 anchors on trans-membrane ACE2 to enter the host cells including type-2 pneumocytes, macrophages, endothelial cells, pericytes and cardiac myocytes leading to inflammation and multi-organ failure. Infection of endothelial cells or pericytes is of particular importance because this could lead to severe microvascular and macrovascular dysfunction. In addition, immune over-reactivity can potentially destabilize atherosclerotic plaques and explain the development of acute coronary syndromes. Infection of the respiratory tract, particularly type-2 pneumocytes, by SARS-CoV-2 is manifested by the progression of systemic inflammation and immune cell over-activation leading to "cytokine storm", resulting in increased levels of cytokines such as IL-6, IL-7, IL-22 and CXCL10. Subsequently, it is possible that activated T cell and macrophages may infiltrate infected myocardium resulting in the development of fulminant myocarditis and severe cardiac damage. This process may be further intensified by a cytokine storm. Similarly, the viral invasion may cause cardiac myocyte damage directly leading to myocardial dysfunction and contribute to the development of arrhythmias. From Guzik et al., COVID-19 and the cardiovascular system - implications for risk assessment, diagnosis and treatment options. Cardiovasc Res., 2020, doi: 10.1093/cvr/cvaa106.[42]

Indikácie ku hospitalizácii

- Ťažký celkový stav
- Pneumónia
- Závažná komorbidita, imunosupresia
- Nemožnosť izolácie doma zo sociálnych dôvodov

- Saturácia O2< 93% bez oxygenoterapie
- Dychová frekvencia > 24/min
- Srdcová frekvencia >120/min

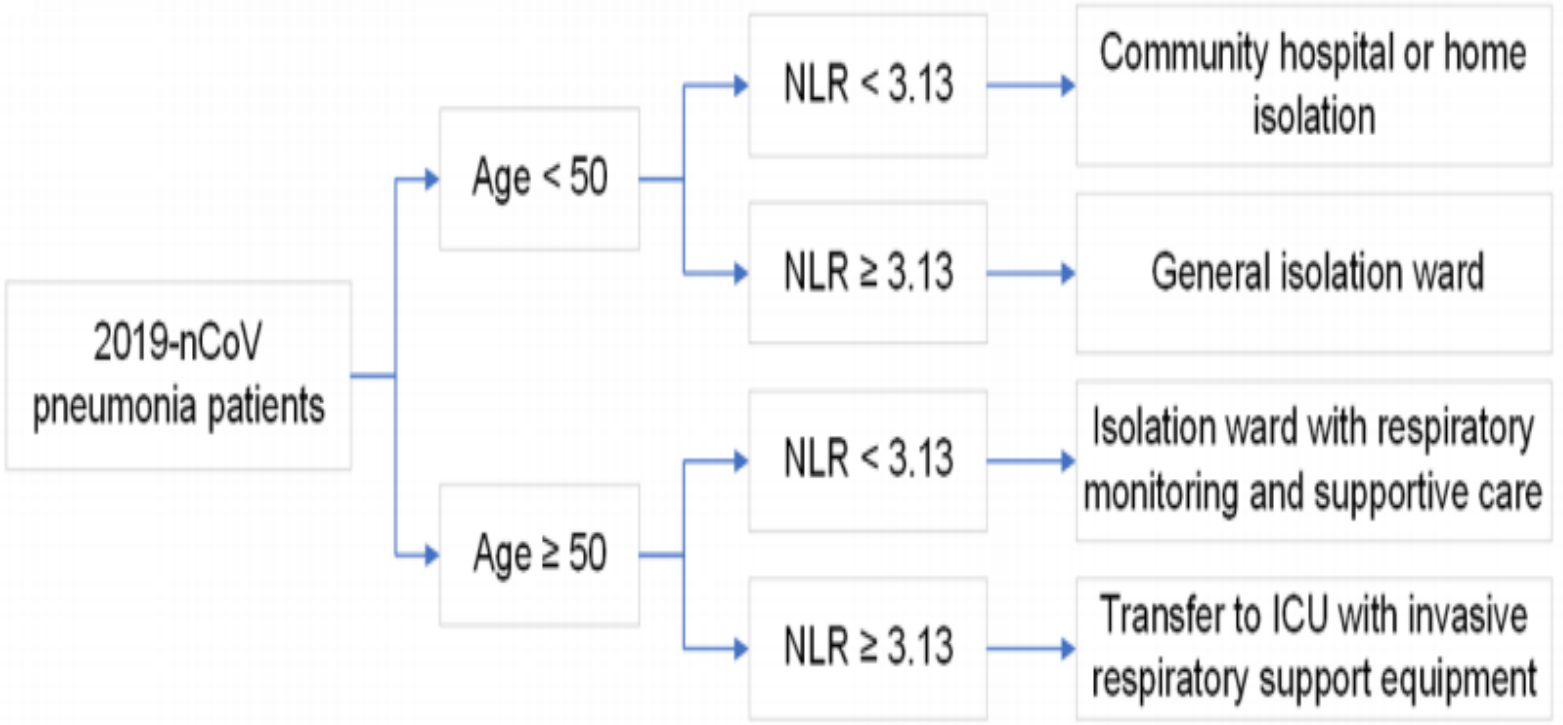
Vyšetrenia pri príjme

- Pulzná oxymetria
- Vyšetriť základné biochemické a hematologické parametra, index neutrofily/lymfocyty
- Vyšetriť panel biomarkerov ku stratifikácii rizika pacientov – IL – 6, CRP, prokalcitonín, , kardiálny troponín I, D- diméry, fibrinogén, ďalšie podľa dostupnosti.
- Prietoková cytometria, hladina vitamínu D3
- Vyšetriť USG pľúc, event RTG pľúc – v prípade pozitívneho nálezu vyšetrenie HRCT pľúc
- V prípade nálezu pneumónie stratifikácia rizika podľa CURB 65
- Iné vyšetrenia podľa potreby

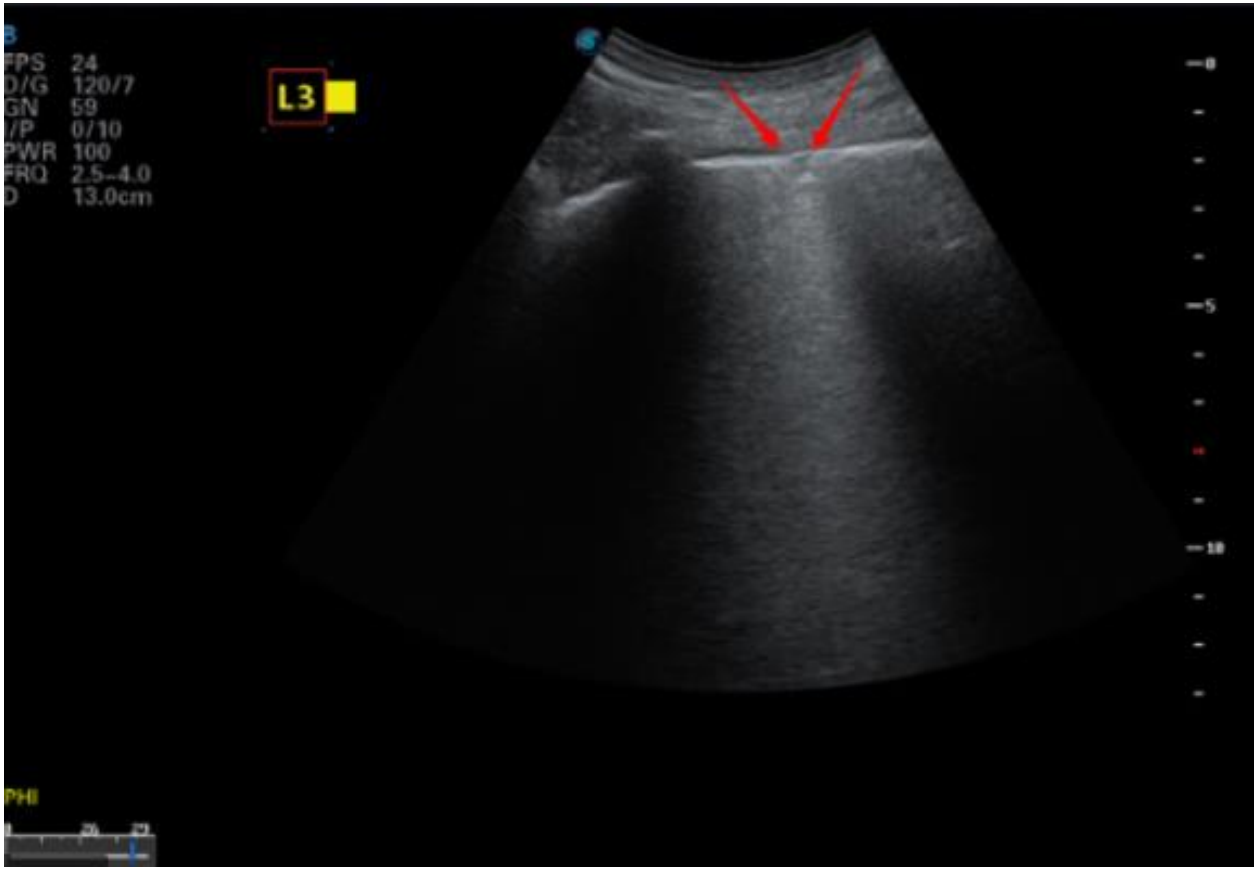
Biomarkery

- **CRP** pri zvýšení nad 20 – 30 mg/l je podozrenie na baktériovú/mykotickú supreinfekciu, hranica priaznivá/nepriaznivá prognóza je 60 mg/l.
- **Prokalcitonín** nad 0,4 – 0,5 ng/ml, možná bakteriálna superinfekcia, orgánová dysfunkcia
- **Interleukín 6** - stredne ťažké formy zvýšený na 10- 20 pg/ml, ťažké formy 20 – 40 pg/ml. Vyššie hodnoty znamenajú sekundárnu infekciu.
- **D-diméry**, pri hodnote ≥ 1,0 mg/l mortalita prudko stúpa, najsilnejší nezávislý prediktor mortality
- **Kardiálny troponín I** - TnI ≥ 10 pg/ml = kardiálna dysfunkcia, u ťažkých foriem TnI ≥ 30 pg/ml
- **Feritín** stredne ťažké formy >300 µg/L, závažné formy s vysokou mortalitou vzostup >1000 µg/L

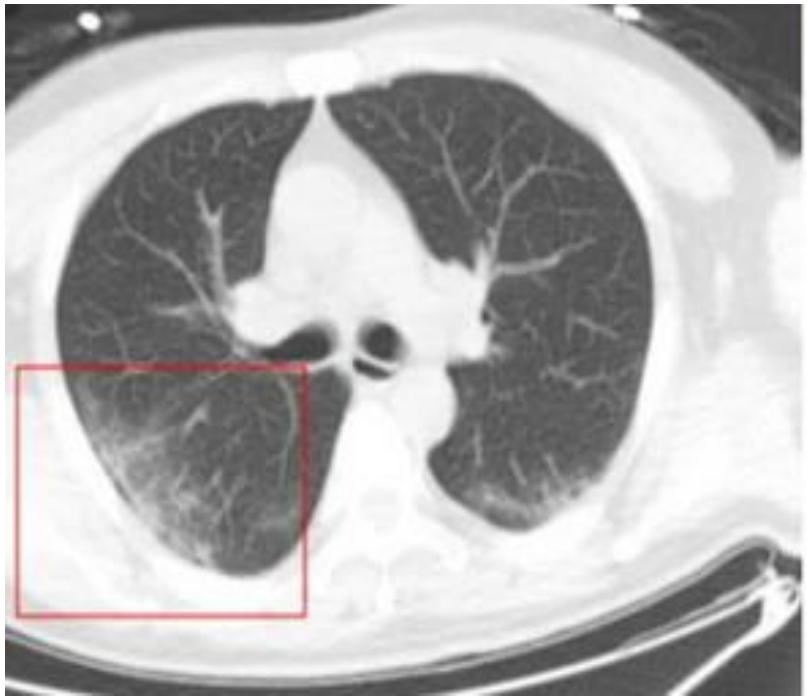
Pomer neutrofily/lmyfocyty

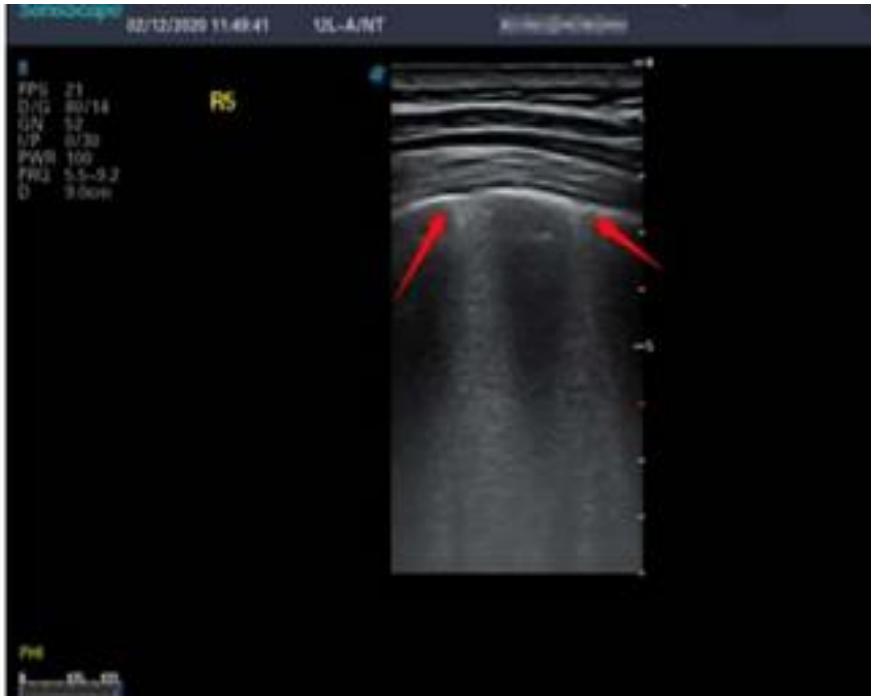


Ultrazvuk pľúc – B línie



Korelácia CT a USG





Original Research

Free Access

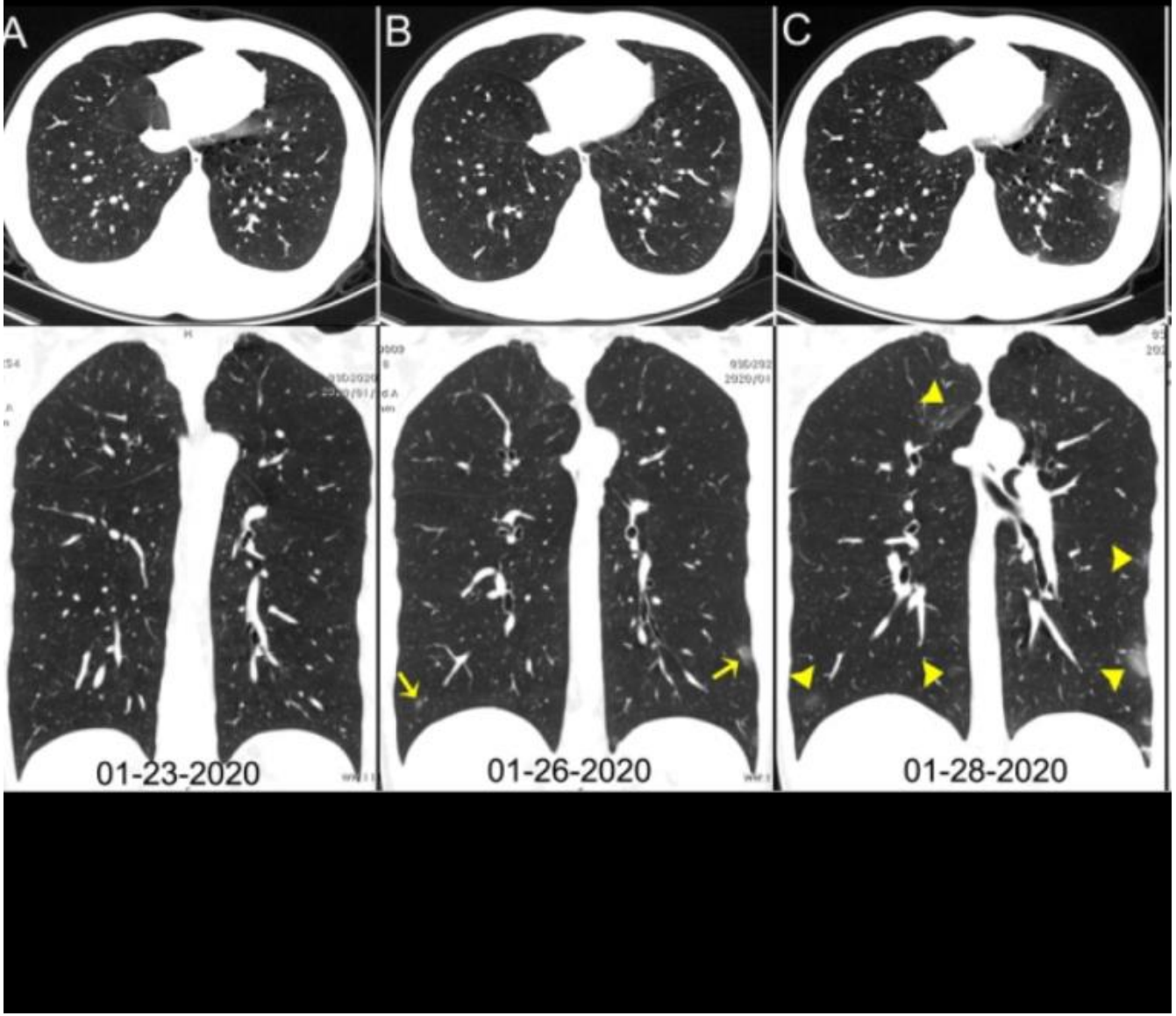
Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases

Tao Ai*, Zhenlu Yang*, Hongyan Hou, Chenao Zhan, Chong Chen, Wenzhi Lv, Qian Tao, Ziyong Sun, Liming Xia

* Tao Ai and Zhenlu Yang contributed equally to this work.

Author Affiliations

Published Online: Feb 26 2020 | https://doi.org/10.1148/radiol.2020200642


A
B
C
01-23-2020
01-26-2020
01-28-2020

Liečba COVID 19

- Rozhodujúci je kyslík – suplementácia, High flow, UPV
- liek s overenou autorizáciou v SPC – remdesivir
- Klinické dáta pre zlepšenie prežívania – dexametazón
- Klinické dáta pre profylaxiu - polyoxidonium
- Hydroxichlorochín, chlorochín – zlyhanie režimov
- Lopinavir ritonavir nejednoznačné údaje
- Parciálne údaje viacero liečiv – favipiravir, arbidol, polyoxidonium
- Prebieha veľké množstvo klinických štúdií
- Existujú retrospektívne dáta SARS a MERS

EUnetHTA Joint Action 3 WP4

Rapid Collaborative Review

REMDESIVIR FOR THE TREATMENT OF COVID-19
PICO AND EVIDENCE GAPS

Project ID: PTRCR15

Version 1.0, 29 September 2020
Template version 1.0, September 2020

Table 2.1. Assessment scope: relevant PICO(s) identified for the planned assessment.

Description	Assessment scope		
PICO			
Population	Adults (aged > 18 years) and adolescents (aged 12 years and older with body weight at least 40 kg) hospitalized with confirmed COVID-19 pneumonia		
Intervention	Remdesivir plus standard of care/supportive treatment[a] (may include other drugs that potentially also change the course of the disease, such as dexamethasone)		
Comparison	Standard of care/supportive treatment* (may include other drugs that potentially also change the course of the disease, such as dexamethasone)		
Outcomes	**Clinical effectiveness**	**Rate**	**Relative importance**
	All-cause mortality	9	critical
	Time to recovery (using an Ordinal Scale for Clinical Improvement, e.g. WHO)	6	important
	Clinical improvement; using difference of stage on Ordinal Scale for Clinical Improvement, e.g. WHO)	6	important
	Additional need for non-invasive ventilation or high-flow oxygen	8	critical
	Duration of non-invasive ventilation or high-flow oxygen, in patients requiring it	7	critical
	Additional need for invasive mechanical ventilation or ECMO	8	critical
	Duration of invasive mechanical ventilation or ECMO, in patients requiring it	7	critical
	Length of stay (hospital and critical care unit)	5	important
	Safety		
	Adverse events	6	important
	Serious adverse events	8	critical
	Adverse events leading to treatment discontinuation	7	critical
	Treatment-related mortality	9	critical

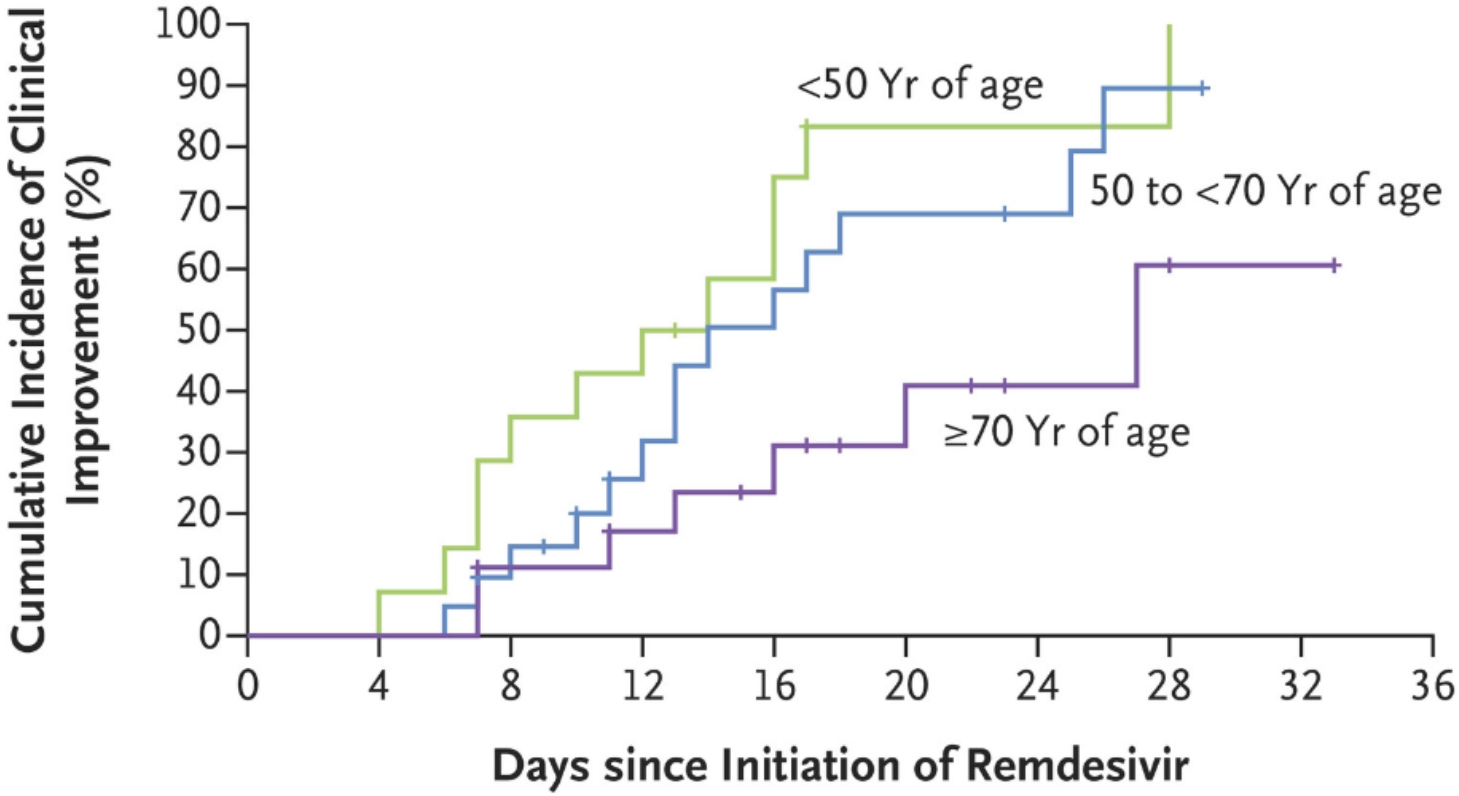
[a] Standard of care may include, but is not limited to, supplemental oxygen or ventilatory support, dexamethasone, pharmacological thromboprophylaxis, empiric/targeted antimicrobial therapy, hemodynamic support, renal replacement therapy, investigational agents, other supportive measures.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

J. Grein, N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M.L. Green, F.-X. Lescure, E. Nicastri, R. Oda, K. Yo, E. Quiros-Roldan, A. Studemeister, J. Redinski, S. Ahmed, J. Bernett, D. Chelliah, D. Chen, S. Chihara, S.H. Cohen, J. Cunningham, A. D'Arminio Monforte, S. Ismail, H. Kato, G. Lapadula, E. L'Her, T. Maeno, S. Majumder, M. Massari, M. Mora-Rillo, Y. Mutoh, D. Nguyen, E. Verweij, A. Zoufaly, A.O. Osinusi, A. DeZure, Y. Zhao, L. Zhong, A. Chokkalingam, E. Elboudwarej, L. Telep, L. Timbs, I. Henne, S. Sellers, H. Cao, S.K. Tan, L. Winterbourne, P. Desai, R. Mera, A. Gaggar, R.P. Myers, D.M. Brainard, R. Childs, and T. Flanigan


Cumulative Incidence of Clinical Improvement (%)
100
90
80
70
60
50
40
30
20
10
0
0
4
8
12
16
20
24
28
32
36
Days since Initiation of Remdesivir
<50 Yr of age
50 to <70 Yr of age
≥70 Yr of age

Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial

Yeming Wang*, Dingyu Zhang*, Guanhua Du*, Ronghui Du*, Jianping Zhao*, Yang Jin*, Shouzhi Fu*, Ling Gao*, Zhenshun Cheng*, Qiaofa Lu*, Yi Hu*, Guangwei Luo*, Ke Wang, Yang Lu, Huadong Li, Shuzhen Wang, Shunan Ruan, Chengqing Yang, Chunlin Mei, Yi Wang, Dan Ding, Feng Wu, Xin Tang, Xianzhi Ye, Yingchun Ye, Bing Liu, Jie Yang, Wen Yin, Aili Wang, Guohui Fan, Fei Zhou, Zhibo Liu, Xiaoying Gu, Jiuyang Xu, Lianhan Shang, Yi Zhang, Lianjun Cao, Tingting Guo, Yan Wan, Hong Qin, Yushen Jiang, Thomas Jaki, Frederick G Hayden, Peter W Horby, Bin Cao, Chen Wang

Lancet 2020; 395: 1569–78

Published Online
April 29, 2020
https://doi.org/10.1016/S0140-6736(20)31022-9

Summary

Background No specific antiviral drug has been proven effective for treatment of patients with severe coronavirus disease 2019 (COVID-19). Remdesivir (GS-5734), a nucleoside analogue prodrug, has inhibitory effects on pathogenic animal and human coronaviruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in vitro, and inhibits Middle East respiratory syndrome coronavirus, SARS-CoV-1, and SARS-CoV-2 replication in animal models.

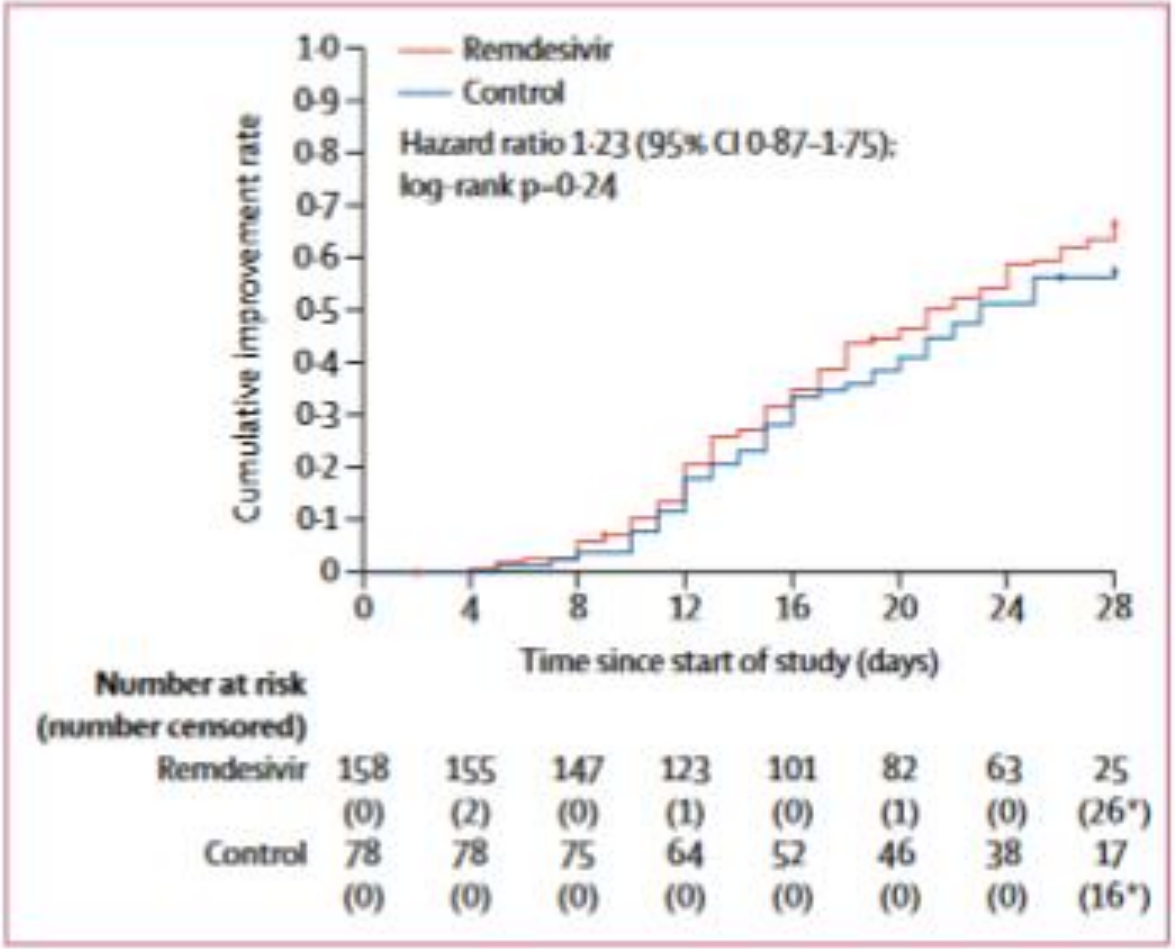


Figure 2: **Time to clinical improvement in the intention-to-treat population**
Adjusted hazard ratio for randomisation stratification was 1·25 (95% CI 0·88–1·78). *Including deaths before day 28 as right censored at day 28, the number of patients without clinical improvement was still included in the number at risk.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

ABSTRACT

BACKGROUND

Although several therapeutic agents have been evaluated for the treatment of coronavirus disease 2019 (Covid-19), no antiviral agents have yet been shown to be efficacious.

METHODS

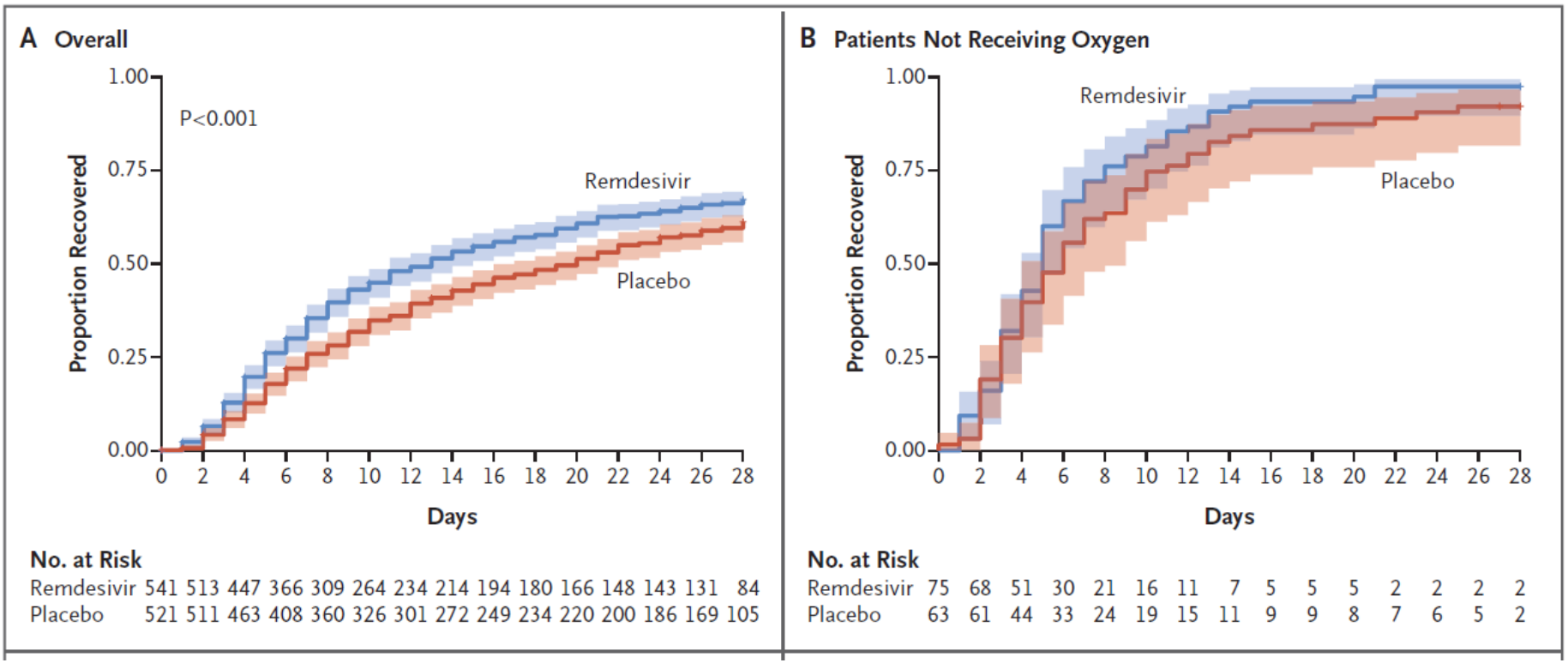
We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only.

RESULTS

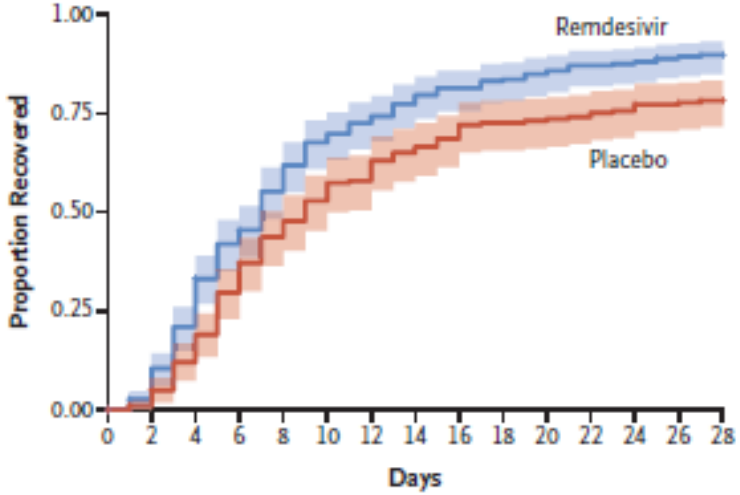
The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Beigel at the National Institute of Allergy and Infectious Diseases, National Institutes of Health, 5601 Fishers Ln., Rm. 7E60, MSC 9826, Rockville, MD 20892-9826, or at jbeigel@niaid.nih.gov.

*A complete list of members of the ACTT-1 Study Group is provided in the Supplementary Appendix, available at NEJM.org.

A preliminary version of this article was published on May 22, 2020, at NEJM.org. This article was published on October 8, 2020, at NEJM.org.

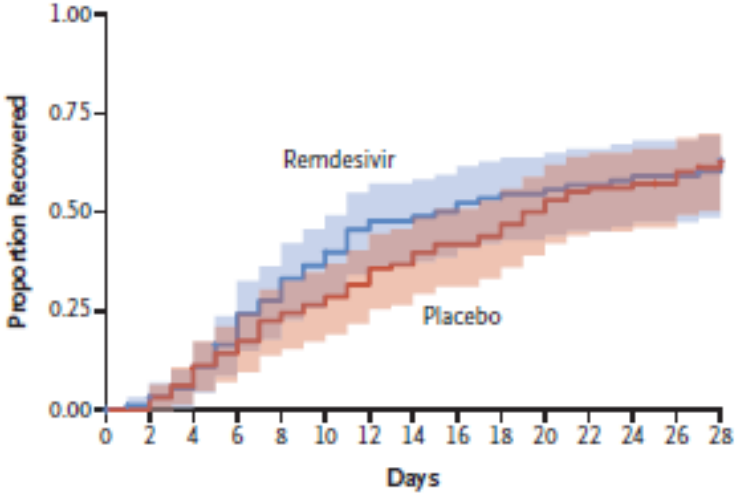

A Overall
1.00
0.75
0.50
0.25
0.00
Proportion Recovered
P<0.001
Remdesivir
Placebo
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days
No. at Risk
Remdesivir 541 513 447 366 309 264 234 214 194 180 166 148 143 131 84
Placebo 521 511 463 408 360 326 301 272 249 234 220 200 186 169 105
B Patients Not Receiving Oxygen
1.00
0.75
0.50
0.25
0.00
Proportion Recovered
Remdesivir
Placebo
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days
No. at Risk
Remdesivir 75 68 51 30 21 16 11 7 5 5 5 2 2 2 2
Placebo 63 61 44 33 24 19 15 11 9 9 8 7 6 5 2

C Patients Receiving Oxygen



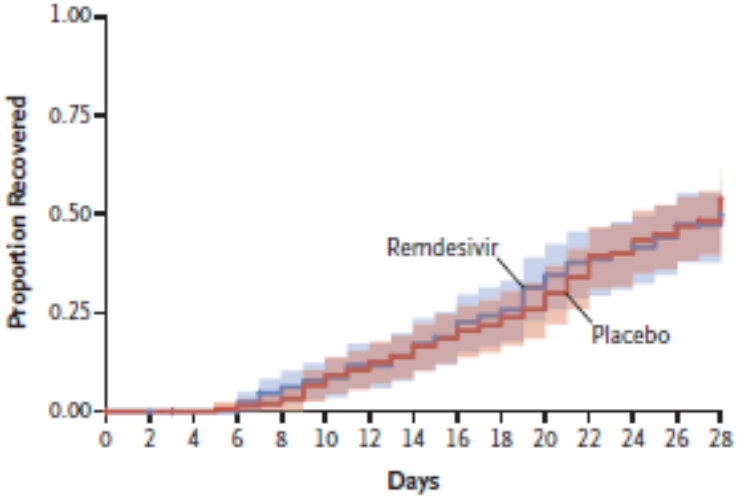
No. at Risk															
Remdesivir	232	223	181	132	101	73	62	51	42	38	34	29	28	24	13
Placebo	203	199	175	140	111	93	83	69	62	54	53	51	48	44	28

D Patients Receiving High-Flow Oxygen or Noninvasive Mechanical Ventilation



No. at Risk															
Remdesivir	95	91	86	75	65	57	48	46	44	41	40	38	37	36	27
Placebo	98	98	92	84	76	72	67	62	57	55	49	44	43	41	27

E Patients Receiving Mechanical Ventilation or ECMO



No. at Risk															
Remdesivir	131	131	129	129	122	118	113	110	103	96	87	79	76	69	42
Placebo	154	153	152	151	149	142	136	130	121	116	110	98	89	79	48

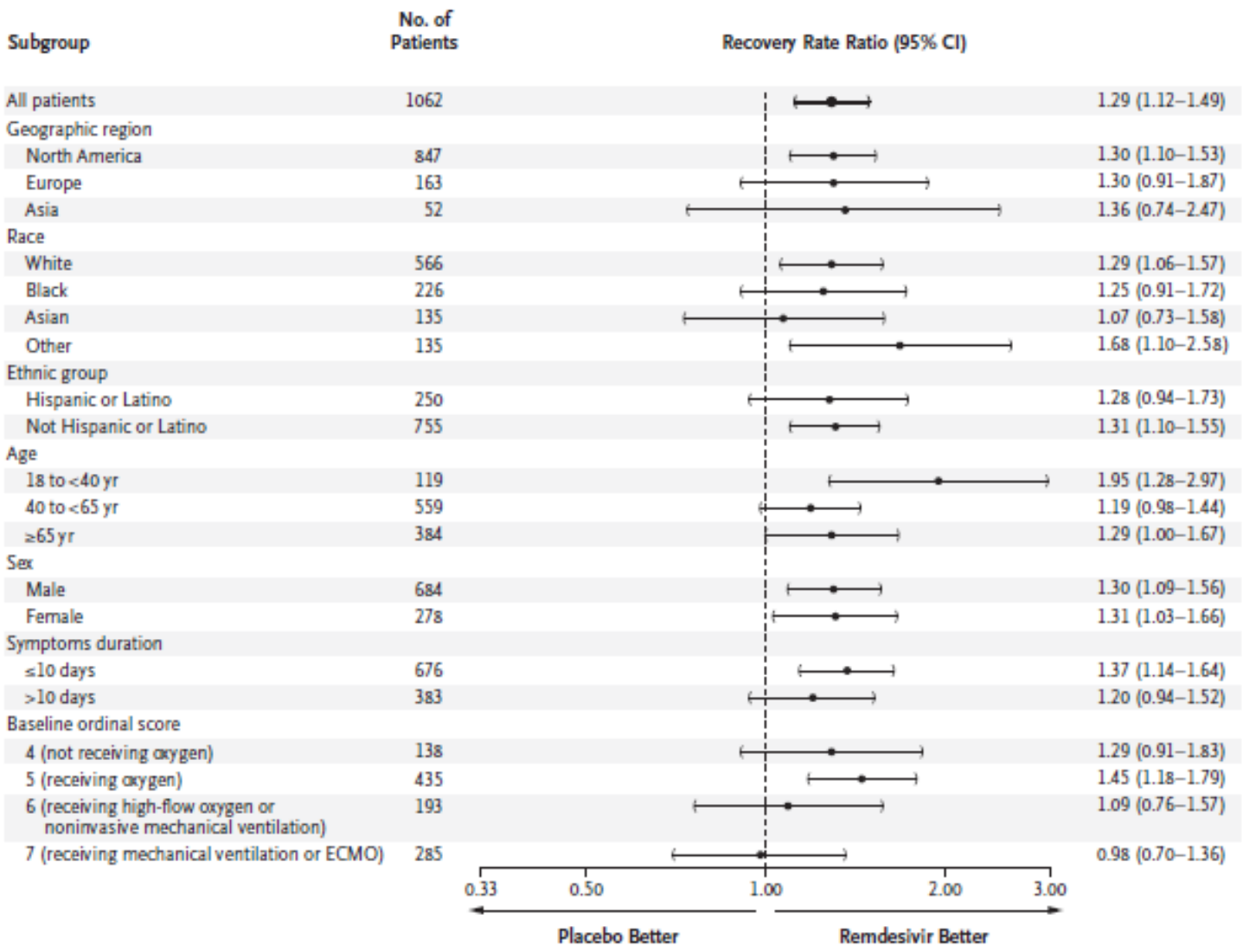


Figure 3. Time to Recovery According to Subgroup.

The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients.

Table 3. Additional Secondary Outcomes.

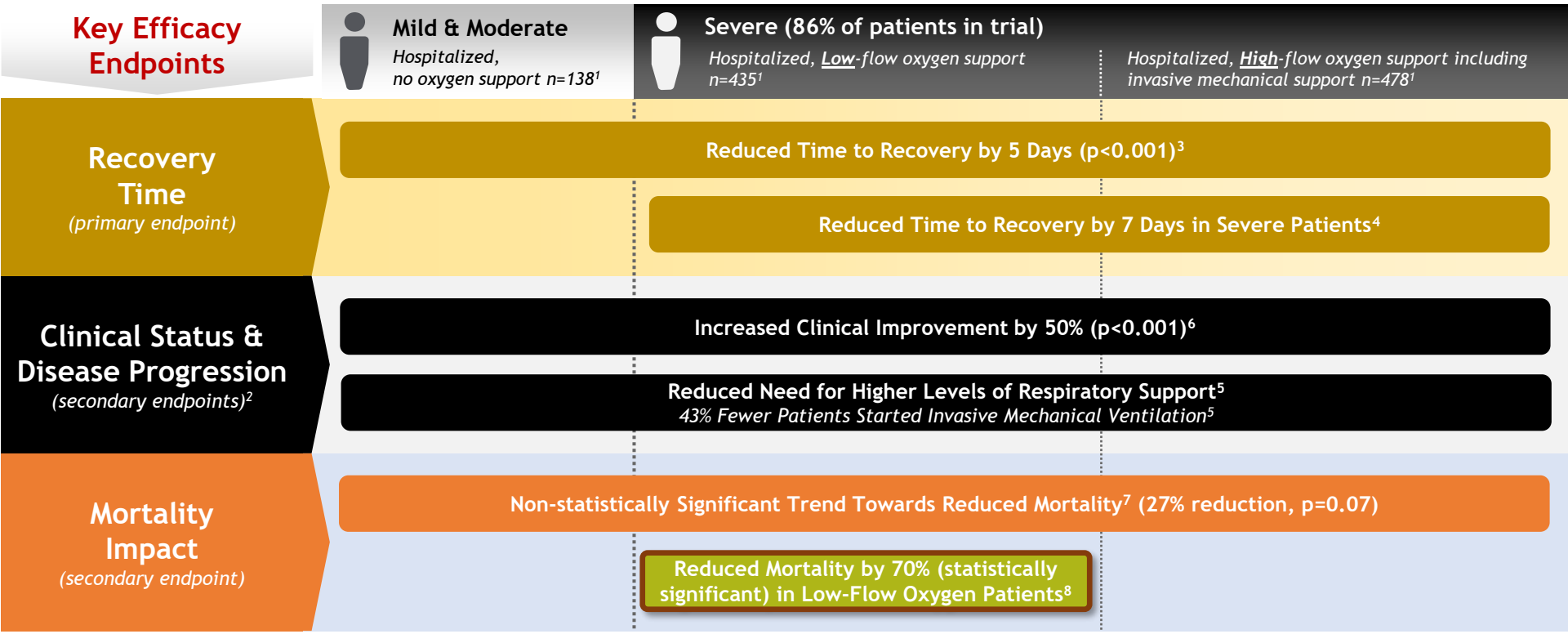
	Remdesivir (N=541)	Placebo (N=521)	Rate Ratio (95% CI)
Median time to clinical improvement (95% CI) — days			
Improvement of one category on ordinal scale	7.0 (6.0 to 8.0)	9.0 (8.0 to 11.0)	1.23 (1.08 to 1.41)
Improvement of two categories on ordinal scale	11.0 (10.0 to 13.0)	14.0 (13.0 to 15.0)	1.29 (1.12 to 1.48)
Discharge or National Early Warning Score ≤2 for 24 hr*	8.0 (7.0 to 9.0)	12.0 (10.0 to 15.0)	1.27 (1.10 to 1.46)
			Difference (95% CI)
Hospitalization			
Median duration of initial hospitalization (IQR) — days†	12 (6 to 28)	17 (8 to 28)	−5.0 (−7.7 to −2.3)
Median duration of initial hospitalization among those who did not die (IQR) — days	10 (5 to 21)	14 (7 to 27)	−4.0 (−6.0 to −2.0)
Patients rehospitalized — % (95% CI)	5 (3 to 7)	3 (2 to 5)	2 percentage points (0 to 4)
Oxygen			
Median days receiving oxygen if receiving oxygen at baseline (IQR)	13 (5 to 28)	21 (8 to 28)	−8.0 (−11.8 to −4.2)
New use of oxygen			
No. of patients/total no.	27/75	28/63	
Percent of patients (95% CI)	36 (26 to 47)	44 (33 to 57)	−8 (−24 to 8)
Median days receiving oxygen (IQR)	4 (2 to 12)	5.5 (1 to 15)	−1.0 (−7.6 to 5.6)
Noninvasive ventilation or high-flow oxygen			
Median days of noninvasive ventilation or high-flow oxygen use during study if receiving these interventions at baseline (IQR)	6 (3 to 18)	6 (3 to 16)	0 (−2.6 to 2.6)
New use of new noninvasive ventilation or high-flow oxygen use during the study			
No. of patients/total no.	52/307	64/266	
Percent of patients (95% CI)	17 (13 to 22)	24 (19 to 30)	−7 (−14 to −1)
Median days of use during the study (IQR)	3 (1 to 10.5)	4 (2 to 23.5)	−1.0 (−4.0 to 2.0)
Mechanical ventilation or ECMO			
Median days of mechanical ventilation or ECMO during study if receiving these interventions at baseline (IQR)	17 (9 to 28)	20 (8 to 28)	−3.0 (−9.3 to 3.3)
New use of mechanical ventilation or ECMO during study			
No. of patients/total no.	52/402	82/364	
Percent of patients (95% CI)	13 (10 to 17)	23 (19 to 27)	−10 (−15 to −4)
Median days of use during the study (IQR)	21.5 (9 to 28)	23 (12 to 28)	1.0 (−6.0 to 8.0)

* The National Early Warning Score includes six physiological measures; total scores range from 0 to 20, with higher scores indicating greater clinical risk.

† The duration of initial hospitalization for patients who died was imputed as 28 days.

Remdesivir ACTT-1 Clinical Trial Results Published in NEJM

A Randomized, Double-blind, Placebo-controlled Phase 3 Study (1,062 patients)



Remdesivir - indikácie

- Pacient starší ako 12 rokov s infekciou COVID 19 a pneumóniou vyžadujúcou oxygenoterapiu

Používanie remdesiviru na infekčných klinikách/oddeleniacha reprofilizovaných oddeleniach pre liečbu pacientov s COVID 19.

Remdesivir je podľa SPC indikovaný pre liečbu pacientov s dokumentovanou infekciou SARS COV-2, ktorí majú dokumentovanú pneumóniu a ktorí vyžadujú oxygenoterapiu, čo je spojené s poklesom p02 pri použití pulznej oxymetrie pod 92%. Liečbu je potrebné indikovať v súlade s SPC preparátu Veklury, ktorý obsahuje účinnú látku remdesivir

Remdesivir je v súčasnosti dostupný na 3 pracoviskách – v UNB Bratislava – KIGM Nemocnica Kramáre, FN FDR Banská Bystrica, infekčné oddelenie, UNLP Košice – KICM.

Indikácia pre použitie remdesiviru je posudzovaná

1. prim. MUDr. Alena Koščalová, KICM UNB Bratislava – e- mail alena.koscalova@gmail.com tel. 0903 214 821
2. prim. MUDr. Diana Vološinová, PhD., MBA – infekčné oddelenie FDR Banská Bystrica – e mail volosinovad@gmail.com, tel. 0908 236 672
3. prof. MUDr. Pavol Jarčuška, PhD. – KICM UNLP Košice - e mail jarcuska@gmail.com, tel. 0903 738 133, 055 615 2202.

Ku schváleniu žiadosti je potrebné telefonicky konzultovať jedného z vyššie uvedených lekárov, odoslať e- mail so základnými údajmi o pacientovi vrátane prístupu do PACS, event. Scan CT snímky pacienta.

V prípade indikácie dôjde ku schváleniu žiadosti s podaním remdesiviru. Súčasne sa určí dĺžka liečby v trvaní 5 alebo 10 dní, pričom sa logistika zabezpečenia remdesiviru pre pracovisko, ktoré ho požaduje.

Od budúceho týždňa bude remdesivir dostupný na infektologických klinikách a oddelniac nasledujúcich nemocníc:

UNB Bratislava, FN Nitra, FN Trnava, FN Trenčín, UN Martin, FN Ružomebrok, FN FDR Banská Bystrica, Všeobecná nemonica Lučenec n.o., FN prešov, UNLP Košice, Nemocnica Svet zdravia Michalovce.

Effect of Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report

Running title: Dexamethasone for COVID-19 – Preliminary Report

RECOVERY Collaborative Group*

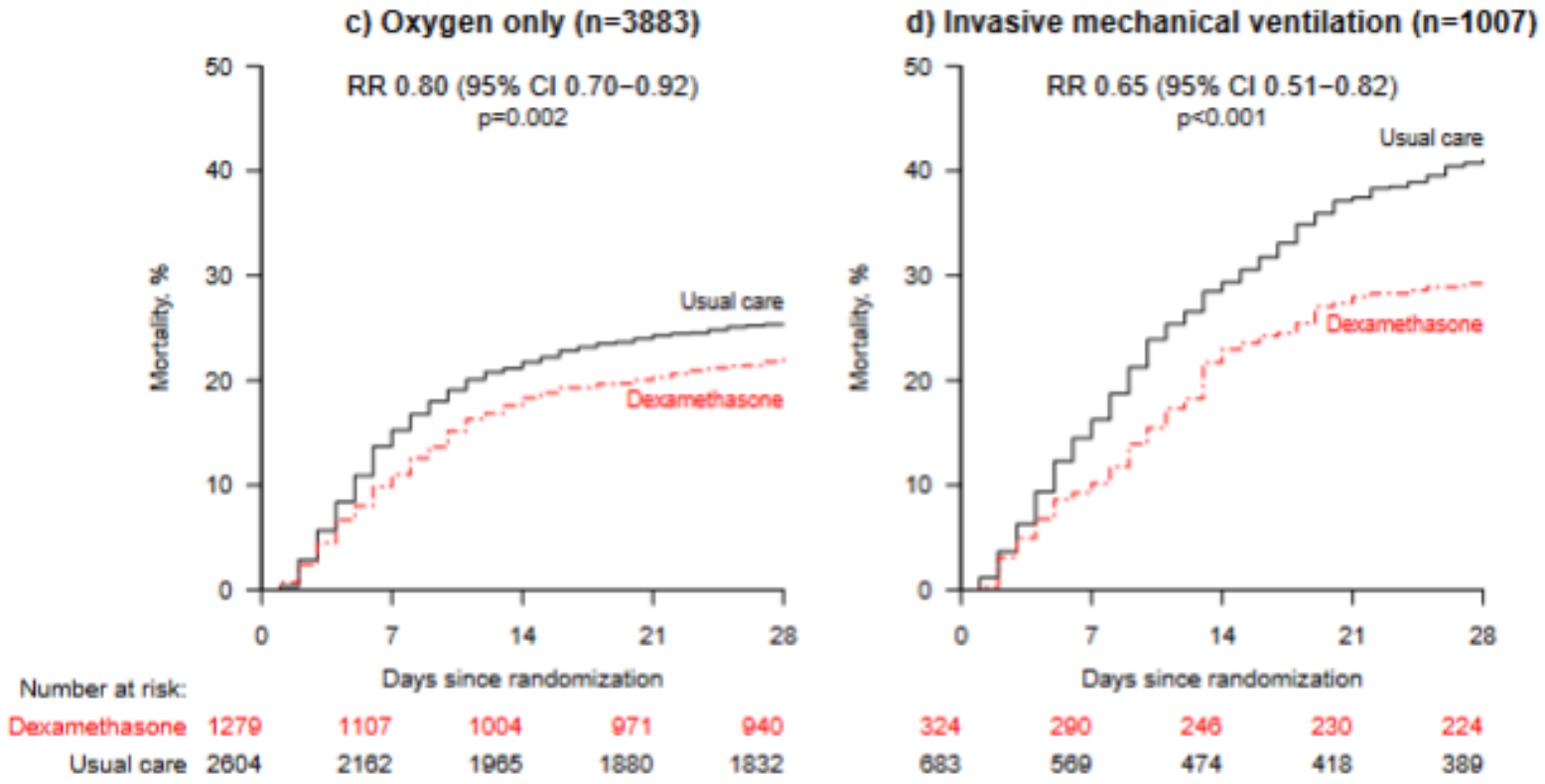
*The writing committee and trial steering committee are listed at the end of this manuscript and a complete list of collaborators in the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial is provided in the Supplementary Appendix.

Correspondence to: Dr Peter W Horby and Dr Martin J Landray, RECOVERY Central

Table 2: Effect of allocation to dexamethasone on main study outcomes

	Treatment allocation			
	Dexamethasone (n=2104)	Usual care (n=4321)	RR (95% CI)	p-value
Primary outcome:				
28-day mortality	454 (21.6%)	1065 (24.6%)	0.83 (0.74-0.92)	<0.001
Secondary outcomes:				
Discharged from hospital within 28 days	1360 (64.6%)	2639 (61.1%)	1.11 (1.04-1.19)	0.002
Receipt of invasive mechanical ventilation or death*	425/1780 (23.9%)	939/3638 (25.8%)	0.91 (0.82-1.00)	0.049
Invasive mechanical ventilation	92/1780 (5.2%)	258/3638 (7.1%)	0.76 (0.61-0.96)	0.021
Death	360/1780 (20.2%)	787/3638 (21.6%)	0.91 (0.82-1.01)	0.07

RR=Rate Ratio for the outcomes of 28-day mortality and hospital discharge, and risk ratio for the outcome of receipt of invasive mechanical ventilation or death (and its subcomponents). Estimates of the RR and its 95% confidence interval are adjusted for age in three categories (<70 years , 70-79 years, and 80 years or older). * Analyses exclude those on invasive mechanical ventilation at randomization.


c) Oxygen only (n=3883)
RR 0.80 (95% CI 0.70–0.92)
p=0.002
Mortality, %
50
40
30
20
10
0
Usual care
Dexamethasone
0
7
14
21
28
Days since randomization
Number at risk:
Dexamethasone 1279 1107 1004 971 940
Usual care 2604 2162 1965 1880 1832
d) Invasive mechanical ventilation (n=1007)
RR 0.65 (95% CI 0.51–0.82)
p<0.001
Mortality, %
50
40
30
20
10
0
Usual care
Dexamethasone
0
7
14
21
28
Days since randomization
324 290 246 230 224
683 569 474 418 389

› medRxiv. 2020 May 13;2020.05.08.20095893. doi: 10.1101/2020.05.08.20095893. Preprint

Association of Vitamin D Deficiency and Treatment with COVID-19 Incidence

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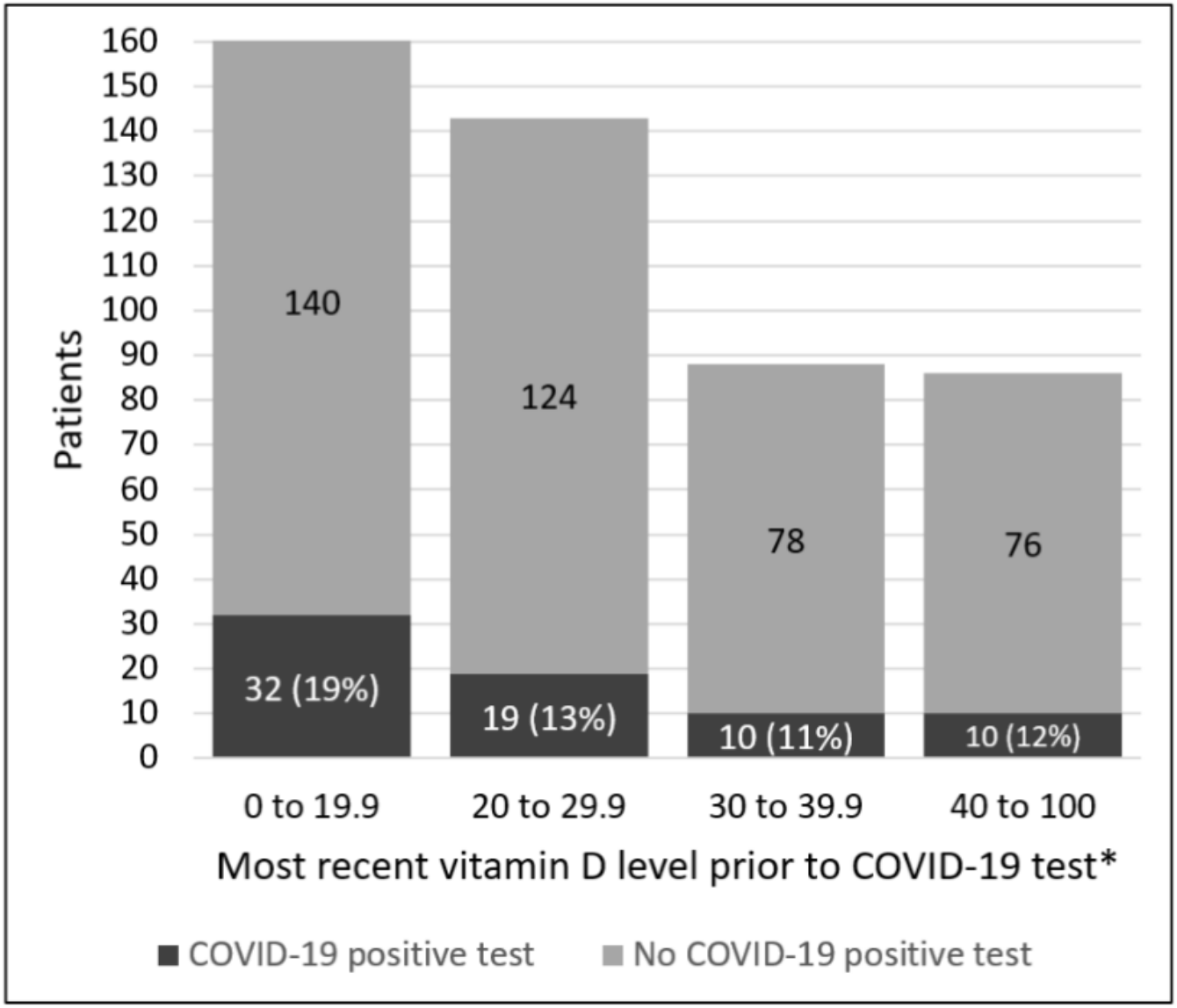
PMID: 32511549 PMCID: PMC7274230 DOI: 10.1101/2020.05.08.20095893

Free PMC article

Abstract

Importance: Vitamin D treatment has been found to decrease incidence of viral respiratory tract infection, especially in vitamin D deficiency. It is unknown whether COVID-19 incidence is associated with vitamin D deficiency and treatment.

Objective: To examine whether vitamin D deficiency and treatment are associated with testing positive for COVID-19.



*Shown are the last vitamin D levels between 1 year before and 14 days before COVID-19 test orders (N=489 distinct patients). Seven levels are in pg/ml from a test of $1,25(OH)_2$-vitamin D and the remainder are in ng/ml from a test of 25(OH)-vitamin D.

Table 4. Bivariate analysis of most recent active vitamin D treatment before most recent vitamin D level at least 14 days before COVID-19 test order and whether that level was <20 ng/ml, among patients with a diagnosis of vitamin D deficiency within 2 years or a level <20 ng/ml.

Most recent active vitamin D treatment before most recent vitamin D level	Total patients	Vitamin D Deficient (Most recent vitamin D in past year <20 ng/ml)	
	N	N	%
No Vitamin D	139	87	63
1-1000 IU D3/Multivitamin	92	50	54
2000 IU D3	38	13	34
3000+ IU D3	25	15	21
D2	107	73	68
Calcitriol	5	3	60
Total	406	241	59
		Fisher's exact test p =	0.009

Table 1. Results of vitamin D randomized controlled trials (RCTs) on risk of influenza.

Country	Population	Baseline 25(OH)D (ng/mL)	Vitamin D Dose (IU/d)	Influenza Cases in Vitamin D, Placebo Arms	Outcome	Ref
Japan	Schoolchildren aged 6–15 yrs	N/A	0, 1200	Type A: 18/167; 31/167. If not taking vitamin D before enrollment: 8/140; 22/140. Type B: 39/167; 28/167	Type A: RR = 0.58 (95% CI, 0.34 to 0.99); if not taking vitamin D before enrollment, RR = 0.36 (95% CI, 0.17 to 0.79); no effect for Type B	[52]
Japan	High school students, including many vaccinated against influenza	N/A	0, 2000	20/148; 12/99	Type A, RR = 1.11 (95% CI, 0.57 to 2.18)	[54]
China	Infants, 3–12 mos	17	400, 1200		Diff. in influenza A viral load, high vs. low vitamin D on day 4 of illness: 1.3 ± 0.5 vs. $4.5 \pm 1.4 \times 10^6$ copies/mL	[53]
Japan	223 patients with IBD, mean age 45 yrs	23–24	0, 500	8/115; 6/108	RR = 1.25 (95% CI, 0.45 to 3.49)	[55]
Vietnam	Children aged 3–17 yrs	26	0, 14,000 /wk	50/650; 43/650	HR = 1.18 (95% CI, 0.79 to 1.78)	[56]

Note: 95% confidence interval (95% CI); day (d); hazard ratio (HR); inflammatory bowel disease (IBD); months (mos); not available (N/A); relative risk (RR); upper respiratory tract infection (URTI); week (wk); years (yrs).

EXPERIENCE OF PREVENTING NEW CORONAVIRUS INFECTION (COVID-19) AMONG HEALTHCARE WORKERS

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[2]Urals State Medical University of the Ministry of Healthcare of Russia
[3]Novokuznetsk State Institute of Advanced Medical Studies - branch of Russian Medical Academy of Continuing Professional Education of the Ministry of Healthcare of Russia

The aim of the study was to assess the prophylactic efficacy of Polyoxidonium in healthcare workers working with COVID-19 patients.
Material and methods. The main group (n=100) included healthcare professionals who received Polyoxidonium 12 mg tablets (sublingually) once a day for 30 days. The control group (n=50) included healthcare professionals who did not receive drug prophylaxis. The number of ARVI and COVID-19 diseases was assessed in both groups over the treatment period. Lysozyme activity and secretory immunoglobulin A (sIgA) content in the nasal secretion were evaluated. We used several medical scales for the assessment of anxiety and depression.

Table 3. The incidence of ARVI in the groups of healthcare providers who work with patients with COVID-19 during the study (n = 150)

Parameters	Incidence of ARVI ONE MONTH BEFORE THE STUDY in the compared groups who received prophylaxis (azoximer bromide)			The treatment-emergent incidence of ARVI (azoximer bromide)		
	Control group	Group of prophylaxis with azoximer bromide	Significance of the differences, p	Control group	Group of prophylaxis with azoximer bromide	Significance of the differences, p
Incidence of ARVI (%)	6	8	0.8559	8	0	<0.0001
Incidence of COVID-19 (%)	4	4	0.6688	4	0	<0.0001
Combined incidence of ARVI and COVID-19 (%)	10	12	0.7582	12	0	<0.0001
Note: control (%) — n = 50; group of prophylaxis with azoximer bromide — n = 100.						

Efficacy from clinical trials in China further supports use of Favipiravir in COVID-19

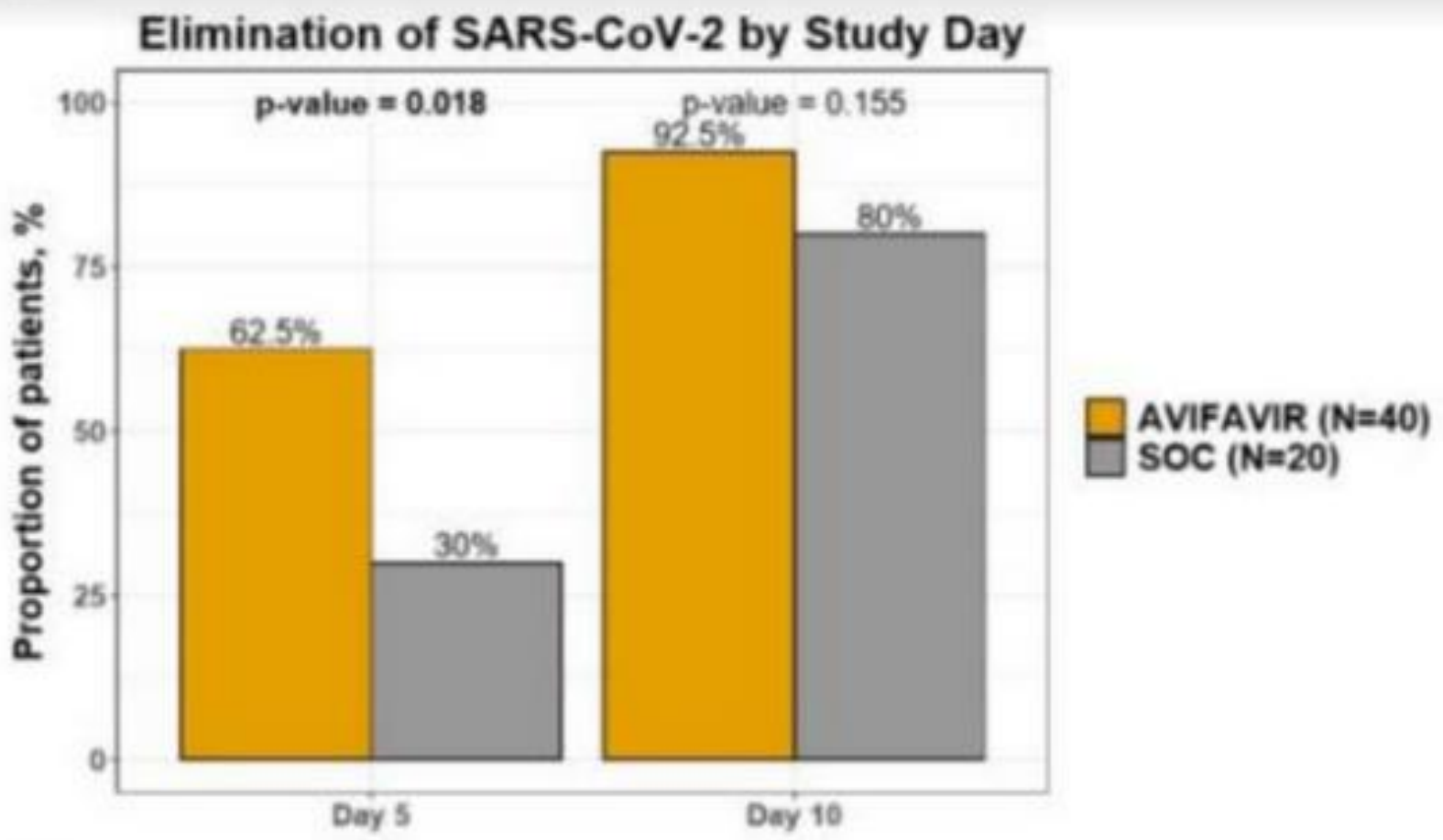
Variables	Favipiravir group	Arbidol group
Total patients	**(N = 116)**	**(N = 120)**
Recovered, n (%)	71 (61.21)	62 (51.67)
Ordinary patients	**(N = 98)**	**(N = 111)**
Recovered, n (%)	70 (71.43)	62 (55.86)
Critical patients	**(N = 18)**	**(N = 9)**
Recovered, n (%)	1 (5.56)	0 (0.00)
Patients with hypertension and/or diabetes	**(N = 42)**	**(N = 35)**
Recovered, n (%)	23 (54.76)	18 (51.43)

Effectiveness was better in the patients treated with Favipiravir (clinical recovery rate of day 7 was 71.43%) than Arbidol group (55.86%).

The same effects were observed for the average antipyretic and cough remission time

Favipiravir showed significantly better treatment effects on COVID-19 in terms of disease progression

(A)


Elimination of SARS-CoV-2 by Study Day
p-value = 0.018
p-value = 0.155
92.5%
80%
62.5%
30%
Proportion of patients, %
100
75
50
25
0
Day 5
Day 10
AVIFAVIR (N=40)
SOC (N=20)

Povolenia MZ SR na terapeutické použite liekov v neschválenej indikácii infekcie COVID-19

- Avigan, Remdesivir do 31.10.2020
- Lopinavir and Ritonavir do 30.9.2020
- Chloroquine do 30.9.2020
- RoActemra do 30.9.2020
- RoActemra do 30.9.2020
- Ribavirin 200 mg Ribavirin 400 mg do 30.9.2020
- Plaquenil do 30.9.2020
- MD Ribavirin do 30.9.2020
- MD Plaquenil do 30.9.2020
- MD Kaletra IntronA do 30.9.2020
- MD Darunavir Ritonavir do 30.9.2020
- Lopinavir/Ritonavir Mylan do 30.9.2020
- Kaletra do 30.9.2020
- Darunavir Mylan Ritonavir do 30.9.2020

Návrh na rozdelenia liekov pre jednotlivé pracoviská
Návrh na rozdelenia lieku IntronA na základe Povolenia na terapeutické použitie registrovaného lieku
Návrh na rozdelenia lieku RoActemra na základe Povolenia na terapeutické použitie registrovaného lieku