Web Toplantılarından Kongreye COVID-19 Pandemisinin Neresindeyiz? Tedavi

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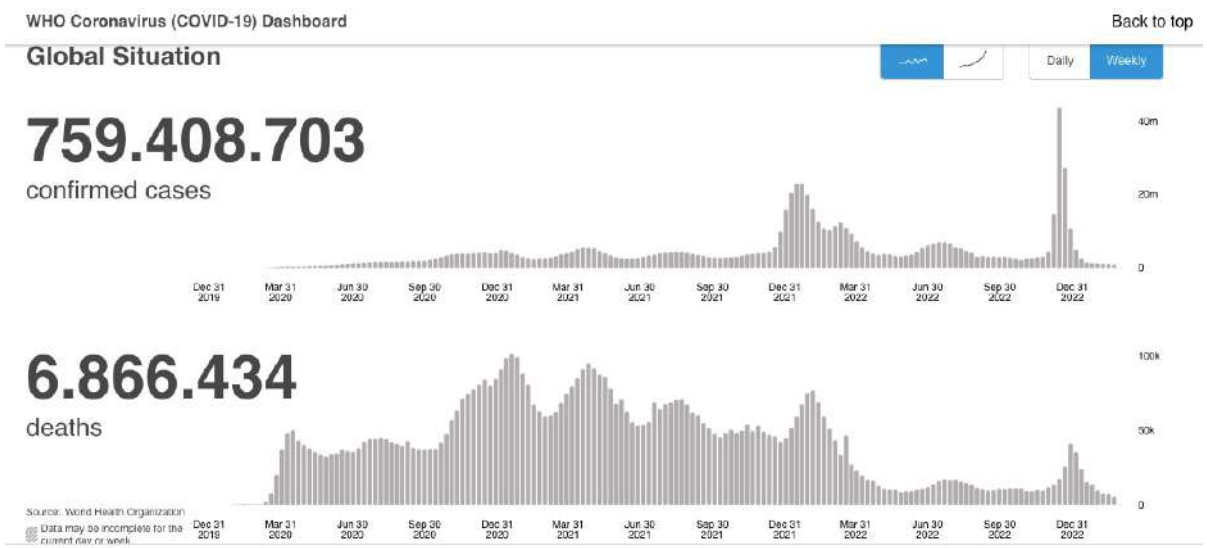
Anabilim Dalı

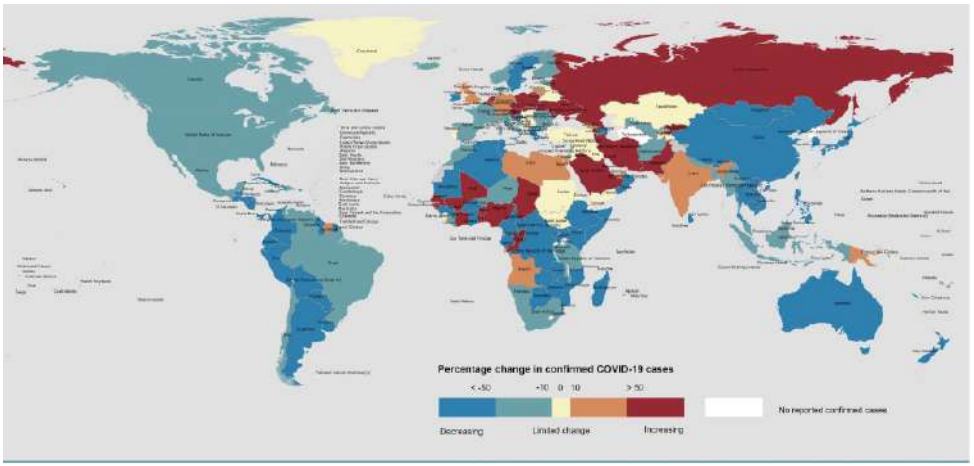
Prof. Dr. Kenan Midilli

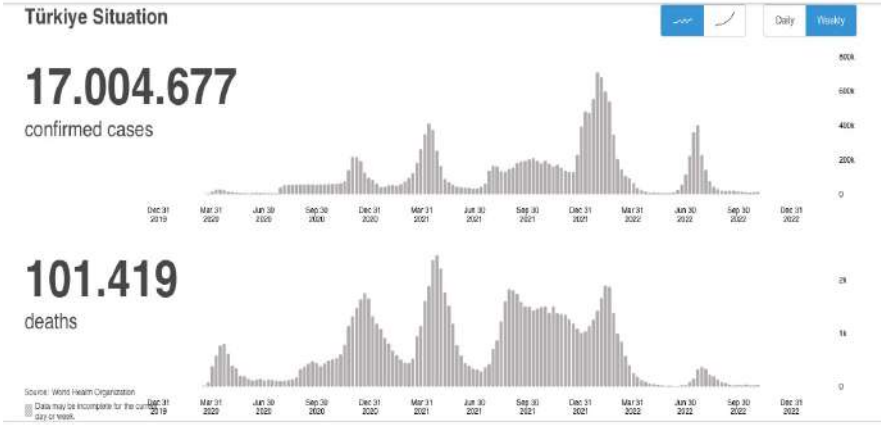
Saygı ve sevgiyle……

COVID-19 Güncel Durum



Günlük 1 milyon olgu, 5-10 bin ölüm





https://covid19.who.int/

COVID-19'da Tedavi

- Hastalığın mortalitesi aşılar ve geçirilmiş inf.lar nedeniyle düştü
  - Tüm gruplarda %0.6-1'den %0.06-0.1'e
  - Hastaneye yatırılmışlarda %15.1'den (Delta) %4.9'a
  - Ölenler >65 yaş ve ≥3 kmd olanlar , immunokompromize olanlar
- Hastaneye yatış oranları düştü
- Antiviral etkinlik çalışmaları ölüm/hastane yatış sonlanımlarıyla yapılmıştı
- Yeni sonlanımlar mı belirlenmeli?
  - Semptomların süresini azaltması?
  - Viral klirensi hızlandırması?

MMWR 2022 ; 71(37);1182–1189

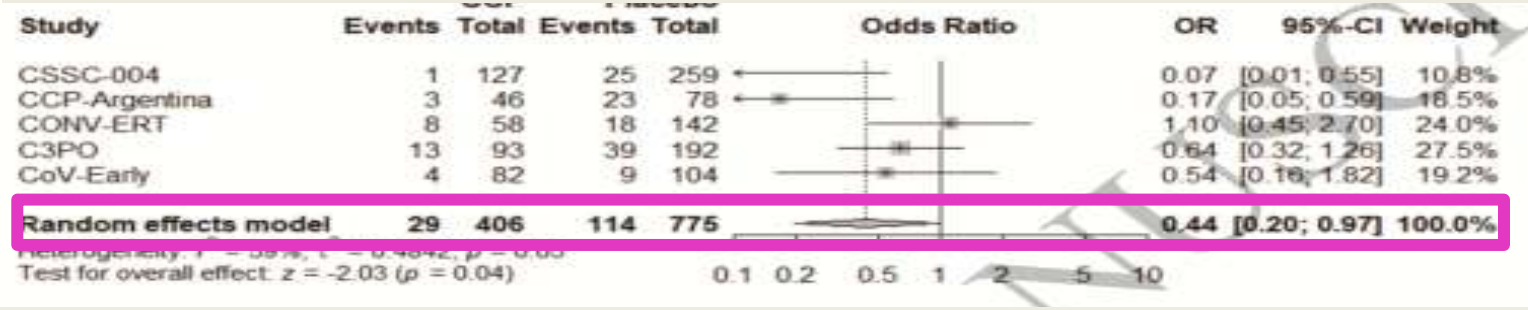
Clinical Infectious Diseases

MAJOR ARTICLE

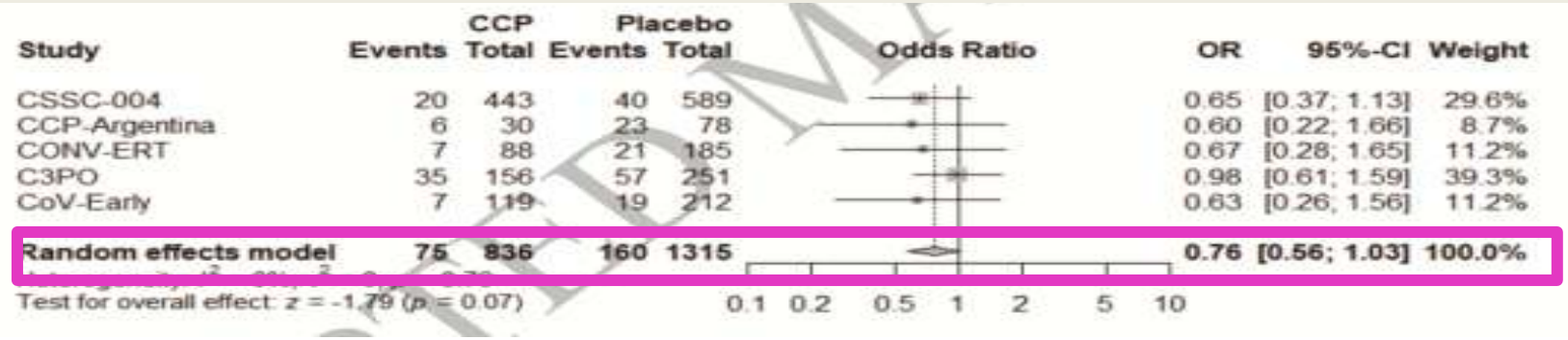
COVID-19 Convalescent Plasma Outpatient Therapy to Prevent Outpatient Hospitalization: A Meta-analysis of Individual Participant Data From Five Randomized Trials

- **Ayaktan COVID-19'da konvalesan plazma hastane yatış oranını azaltıyor , (ilk 5 günde, yüksek titreli antikor içerenlerin verilmesi halinde)**

A) Yüksek titreli KP ile 5 günde tedavi



A) Herhangi bir titredeki KP ile, herhangi bir zamanda tedavi



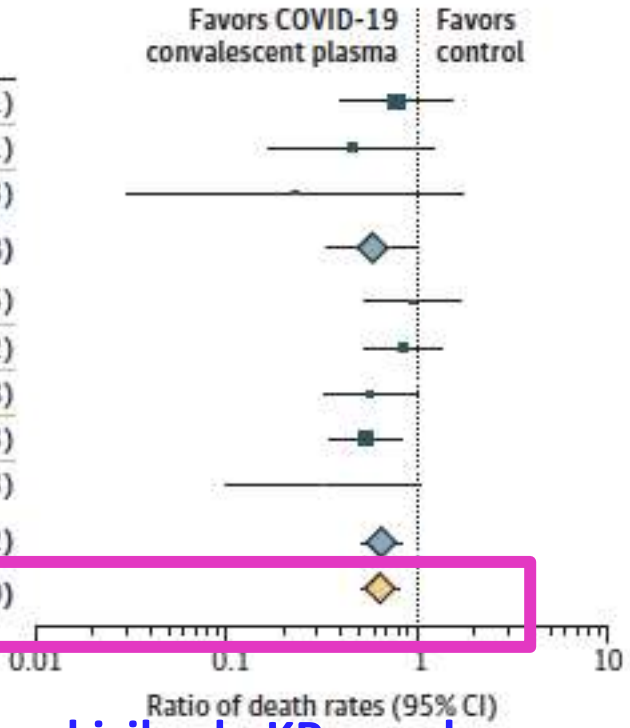
Levine AC. CID 2023;ciad088. DOI: 10.1093/cid/ciad088

JAMA Network | Open

Original Investigation | Infectious Diseases

COVID-19 Convalescent Plasma for the Treatment of Immunocompromised Patients: A Systematic Review and Meta-analysis

Source	Deaths/patients (%) CCP group	Usual care group	RR (95% CI)
Denkinger et al,[30] 2022	12/68 (18)	15/65 (23)	0.77 (0.39-1.51)
Lacombe et al,[31] 2022	4/22 (18)	11/27 (41)	0.45 (0.17-1.21)
Bar et al,[29] 2021	1/15 (7)	5/17 (29)	0.23 (0.03-1.73)
RCT total	17/105 (16)	31/109 (28)	0.58 (0.34-0.98)
Cristell et al,[33] 2021	13/58 (22)	28/116 (24)	0.93 (0.52-1.65)
Lanza et al,[36] 2022	19/79 (24)	46/159 (29)	0.83 (0.52-1.32)
Hueso et al,[35] 2022	13/61 (21)	29/76 (38)	0.56 (0.32-0.98)
Thompson et al,[34] 2021	19/143 (13)	204/823 (25)	0.54 (0.35-0.83)
Biernat et al,[32] 2021	3/23 (13)	9/22 (41)	0.32 (0.10-1.03)
MCT total	67/364 (18)	316/1196 (26)	0.64 (0.50-0.82)
Overall	84/469 (18)	347/1305 (27)	0.63 (0.50-0.79)



Refrakter infeksiyon riski olan immunosuprese kişilerde KP uygulamasının mortalite avantajı var

Senefeld JW. JAMA Network Open. 2023;6(1):e2250647. doi:10.1001/jamanetworkopen.2022.50647

COVID-19 Tedavisinde Monoklonal Antikorlar

- **Tedavide ve profilakside mevcut omikron alt tiplerine karşı etkili Mab yok**

Test\mAb	BAM	ETE	BAM/ETE	CAS	IMD	CAS/IMD	CIL	TIX	CIL/TIX	SOT	BEB	ADI
Omicron/BA.2	>1000$_{22}$	504$_{22}$	744$_{15}$	>1000$_{30}$	220$_{29}$	387$_{21}$	2.1$_{34}$	962$_{33}$	8$_{32}$	22$_{47}$	1$_{29}$	>1000$_{14}$
Omicron/BA.2.12.1	>1000$_{10}$	468$_{10}$	794$_{8}$	>1000$_{11}$	88$_{11}$	250$_{9}$	3$_{12}$	382$_{12}$	9.5$_{9}$	19$_{15}$	1$_{11}$	>1000$_{5}$
Omicron/BA.2.75	705$_{7}$	383$_{7}$	554$_{5}$	233$_{9}$	>1000$_{9}$	>1000$_{7}$	19$_{11}$	30$_{11}$	24$_{9}$	9.1$_{11}$	4.1$_{12}$	673$_{6}$
Omicron/BA.2.75.2	556$_{2}$	489$_{2}$	>1000$_{1}$	589$_{4}$	588$_{4}$	>1000$_{3}$	>1000$_{6}$	>1000$_{6}$	>1000$_{6}$	7.5$_{7}$	3.0$_{6}$	509$_{2}$
Omicron/XBB	-	-	-	177$_{1}$	175$_{1}$	200$_{1}$	700$_{2}$	819$_{2}$	738$_{2}$	14$_{2}$	>1000$_{3}$	-
Omicron/XBB.1	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{4}$	>1000$_{4}$	>1000$_{4}$	12$_{5}$	900$_{4}$	-
Omicron/XBB.1.5	-	-	-	-	-	-	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	19$_{2}$	462$_{2}$	-
Omicron/BA.4/5	>1000$_{17}$	432$_{17}$	588$_{11}$	>1000$_{23}$	143$_{23}$	379$_{16}$	8.6$_{28}$	>1000$_{28}$	24$_{24}$	23$_{34}$	1$_{25}$	968$_{12}$
Omicron/BA.4.6	556$_{2}$	489$_{2}$	>1000$_{1}$	589$_{4}$	173$_{4}$	738$_{3}$	527$_{6}$	819$_{6}$	738$_{6}$	44$_{5}$	1$_{7}$	509$_{2}$
Omicron/BQ.1	-	-	-	177$_{1}$	175$_{1}$	200$_{1}$	>1000$_{3}$	>1000$_{3}$	>1000$_{3}$	25$_{4}$	900$_{4}$	-
Omicron/BQ.1.1	>1000$_{1}$	943$_{1}$	>1000$_{1}$	>1000$_{3}$	>1000$_{3}$	>1000$_{3}$	>1000$_{6}$	>1000$_{6}$	>1000$_{6}$	118$_{7}$	>1000$_{6}$	>1000$_{1}$
Omicron/BF.7	-	-	-	>1000$_{1}$	383$_{1}$	878$_{1}$	>1000$_{3}$	>1000$_{3}$	>1000$_{3}$	49$_{4}$	1.3$_{4}$	-
Omicron/CH.1.1	-	-	-	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	>1000$_{1}$	13$_{1}$	>1000$_{1}$	-

https://covdb.stanford.edu/susceptibility-data/table-mab-susc/

COVID-19 Tedavisinde Monoklonal Antikorlar/ İstenmeyen Etkiler

- **PROVENT çalışmasının post-hoc analizinde kardiyak ciddi istenmeyen etkiler Tiksageviman/Silgavimab grubunda daha fazla belirlenmiş**

	EVUSHELD N= 3,461	Placebo N= 1,736
Subjects with any cardiac SAE*	22 (0.6%)	3 (0.2%)
SAEs related to coronary artery disease or myocardial ischemia†	10 (0.3%)	2 (0.1%)
Myocardial infarctions‡	8 (0.2%)	1 (0.1%)
SAEs related to cardiac failure§	6 (0.2%)	1 (0.1%)
SAEs related to an arrhythmia¶	4 (0.1%)	1 (0.1%)
Other (cardiomegaly, cardiomyopathy, and cardio-respiratory arrest)	3 (0.1%)	0

- **FDA, T/S alacaklara bu kardiyak istenmeyen etkiden ve omikronda kullanılan daha yüksek dozla artıp artmayacağının bilinmediğinden bahsedilmesini önerdi**

https://www.fda.gov/media/154701/download

Cardiovascular Outcomes After Tixagevimab and Cilgavimab use for Pre-exposure Prophylaxis Against COVID-19: A Population-based Propensity-matched Cohort Study

Morgan Birabaharan,[1] Eddie Hill,[1] Maedha Begur,[1] David C. Kaelber,[2,3] Thomas C. S. Martin,[1,4] and Sanjay R. Mehta[1,4]

- **Retrospektif, eğilim skoruna göre eşleştirilmiş kohort analizi**
- **T/S uygulamasından sonraki 90 gün içinde, öncesinde KVH olanlar dahil artmış kardiyovasküler olay görülmemiş**

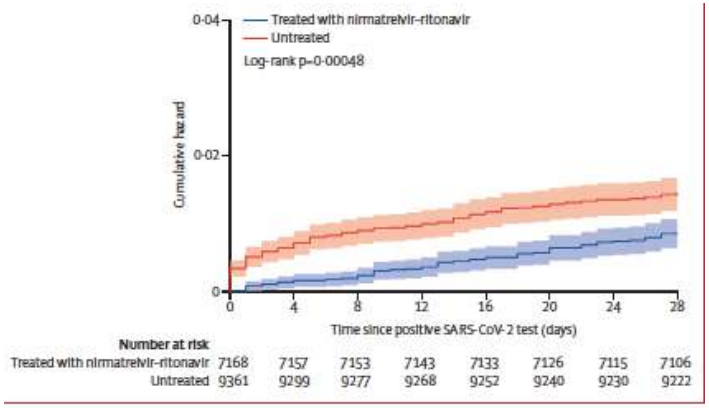
	Before Matching			After Matching		
Characteristics	T&C	Controls	P value	T&C	Controls	P value
Total no.	8627	295 347		8048	8048	
Age, mean, y	61.5 ± 13.8	53.7 ± 20.2	.46	61.5 ± 13.9	63.1 ± 16.0	.12
Sex, %						
Male	53.4	37.8	<.001	52.1	51.2	.29
Female	46.6	62.2	<.001	47.9	48.8	.28
Unknown	0.12	0.02	<.001	0.12	0.12	1.00
Ethnicity, %						
Hispanic/Latino	3.64	3.49	.44	3.60	3.70	.71
Not Hispanic/Latino	73.4	75.6	<.001	73.4	72.6	.29
Unknown	23.0	20.9	<.001	23.0	23.7	.34
Race, %						
Black	8.94	4.69	<.001	8.74	8.47	.56
Asian	1.58	1.86	<.001	1.62	1.42	.30
White	[illegible]	[illegible]	[illegible]	83.8	84.2	.52
American Indian or Alaska Native	[illegible]	[illegible]	[illegible]	0.24	0.36	.15
Native Hawaiian or other Pacific Islander	0.12	0.06	.03	0.12	0.12	1.00
Unknown	[illegible]	[illegible]	[illegible]	5.52	5.48	.92
Adverse socioeconomic determinants of health, %	[illegible]	[illegible]	[illegible]	8.20	8.97	.08
BMI, %[a]						
0–25 kg/m²	26.8	20.3	<.001	26.3	26.8	.49
25–30 kg/m²	[illegible]	[illegible]	[illegible]	[illegible]	31.9	.056
30–35 kg/m²	[illegible]	[illegible]	[illegible]	[illegible]	23.5	.14
≥35 kg/m²	13.6	8.08	<.001	13.3	13.9	.30
Comorbidities, %						
Hypertension	64.3	35.3	<.001	63.2	64.7	.05
Hyperlipidemia	55.5	38.9	<.001	55.3	57.6	.004
Type 2 diabetes mellitus	32.7	13.4	<.001	31.9	32.5	.39
Tobacco use	8.71	6.95	<.001	8.75	9.06	.49
Ischemic heart disease	32.3	12.9	<.001	31.7	32.3	.47
HIV	2.43	1.54	<.001	2.42	2.49	.80
Organ transplant	46.1	1.69	<.001	42.3	41.3	.19
Medications, %						
Anticoagulants	74.8	19.5	<.001	73.1	74.7	.02
Diuretics	59.5	24.9	<.001	57.7	55.9	.04
Beta blockers	57.4	23.7	<.001	55.9	56.4	.50
Platelet aggregation inhibitors	53.8	24.6	<.001	52.6	52.6	.99
Antilipemic	50.4	29.0	<.001	49.8	51.7	.02
Calcium channel blocker	43.6	15.6	<.001	42.1	42.8	.43
Insulin	39.5	7.03	<.001	37.3	36.7	.49
ACE inhibitor	26.2	15.9	<.001	26.2	28.6	<.001
Angiotensin II inhibitors	21.3	11.6	<.001	21.1	21.9	.20
Oral hypoglycemics	17.3	8.94	<.001	17.2	17.8	.28

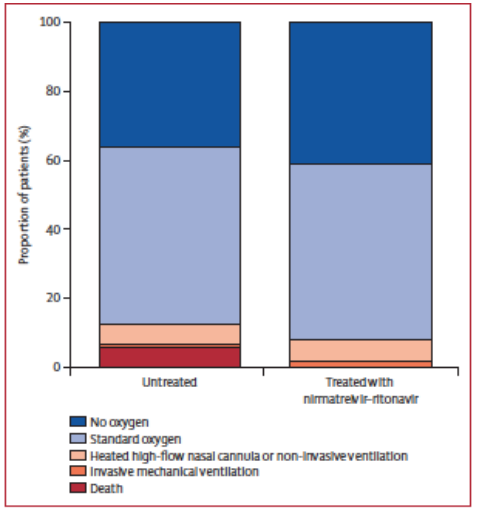
90.Gün MI riski (RR 0.81, %95 CI: .73–.90)
Aritmi riski (RR 0.92, %95 CI: .84–1.01)
Klap yetmezliği riski (RR 0.94, %95 CI: 0.70–1.27).

Morgan Birabaharan. CID 2023; https://doi.org/10.1093/cid/ciac894

Nirmatrelvir/r Gerçek Yaşam Verileri/ABD

- ABD, retrospektif kohort, ayaktan, riskli, ilk 5 gündeki COVID-19
- BA.2, BA2.12.1, BA.4 ve BA.5
- 9881N/r vs eğilime göre eşleştirilmiş tedavi almayan 11 612 hasta
- 28 gün içinde hastane yatışı: %0·9 *vs* %1·4 (OR) 0·45 [%95 CI 0·33–0·62]; p<0·0001)
- 28 günlük mortalite <%0·1 vs %0·2; aOR 0.15 [%95 CI 0·03–0·50]; p=0·0010)
- Acil başvurusu %3·9 vs %4·7; aOR 0·74 [%95 CI 0·63–0·87]; p=0·0002)
- Aşılılarda ve Omikron BA-4-5'de dahil ETKİLİ

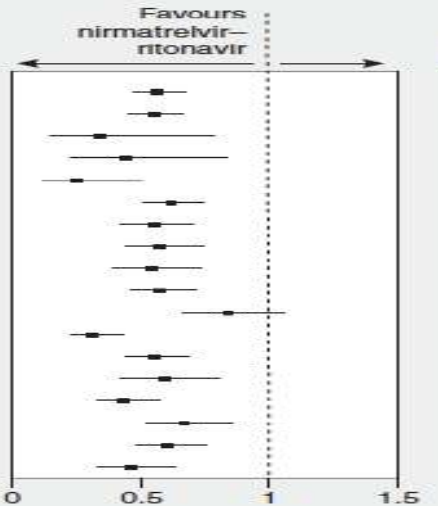




Aggarwal NR. Lancet Infect Dis 2023. https://doi.org/10.1016/ S1473-3099(23)00011-7

Nirmatrelvir/r Gerçek Yaşam Verileri-Kanada

Subgroup	Nirmatrelvir–ritonavir weighted, %	Unexposed weighted, %	OR (95% CI)
Primary analysis	2.1	3.7	0.56 (0.47–0.67)
Age ≥ 70 yr	2.8	5.0	0.55 (0.45–0.66)
Age < 70 yr	0.3	0.8	0.34 (0.15–0.79)
No vaccine	3.0	6.6	0.44 (0.23–0.84)
Vaccine doses: 1–2	1.1	4.4	0.25 (0.12–0.50)
Vaccine doses: 3 or more	2.2	3.5	0.62 (0.51–0.75)
Last vaccine dose: 14–179 d	1.8	3.2	0.55 (0.42–0.70)
Last vaccine dose: 180 or more d	2.6	4.5	0.57 (0.44–0.74)
Comorbidities: 3 or more	1.2	2.3	0.54 (0.39–0.73)
Comorbidities: < 3	3.3	5.7	0.57 (0.46–0.71)
Long-term care resident	4.7	5.6	0.84 (0.66–1.06)
Not in long-term care	0.9	2.9	0.31 (0.23–0.43)
OST risk group: high	3.5	6.2	0.55 (0.44–0.68)
OST risk group: standard	1.1	1.9	0.59 (0.42–0.81)
April to June 2022	1.6	3.7	0.43 (0.33–0.57)
July to August 2022	2.6	3.8	0.67 (0.52–0.86)
DDI level 2	2.9	4.8	0.60 (0.48–0.76)
No DDI	2.6	5.5	0.46 (0.33–0.63)



Schwartz KL. CMAJ 2023;195:E220-6. doi: 10.1503/cmaj.221608

Hastaneye Yatırılan Ciddi Komorbiditeli COVID-19 Hastalarında Nirmatrelvir/r

- Çin'de, Omikron BA2.2 döneminde, açık etiketli, RCT
- Ciddi komorbiditeli, semptomlarının ilk 5 gününde, yarısı hafif, yarısı orta seyirli, %75'i aşısız hastalar
- 132 N/r vs 132 standard bakım
- 28 günlük mortalite %3.79 vs 6.82 (ARD, 2.27; %95 CI −2.94-7.49, P = 0.39)
- SARS-CoV-2 RNA klirensi süresi 10 gün vs 10.50 ARD, −0.62; 95% CI −2.29 to 1.05, P = 0.42
- 7. günde viral klirens oranı %27.27 vs %25.76
- 14.günde viral klirens oranı %78.03 vs %74.24
- ETKİSİZ???

Liu J. The Lancet Regional Health -Western Pacific 2023; 100694. https://doi.org/10.1016/j.lanwpc.2023.100694

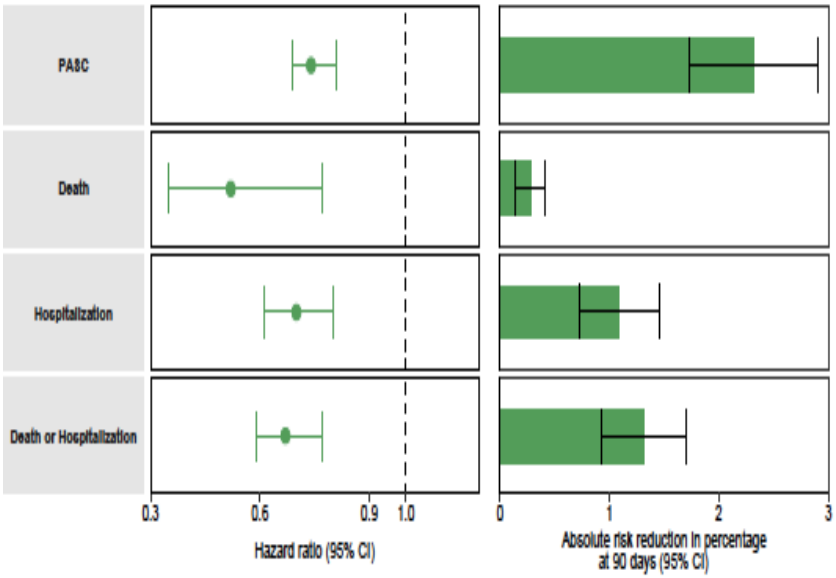
Gebede Nirmatrelvir/r*

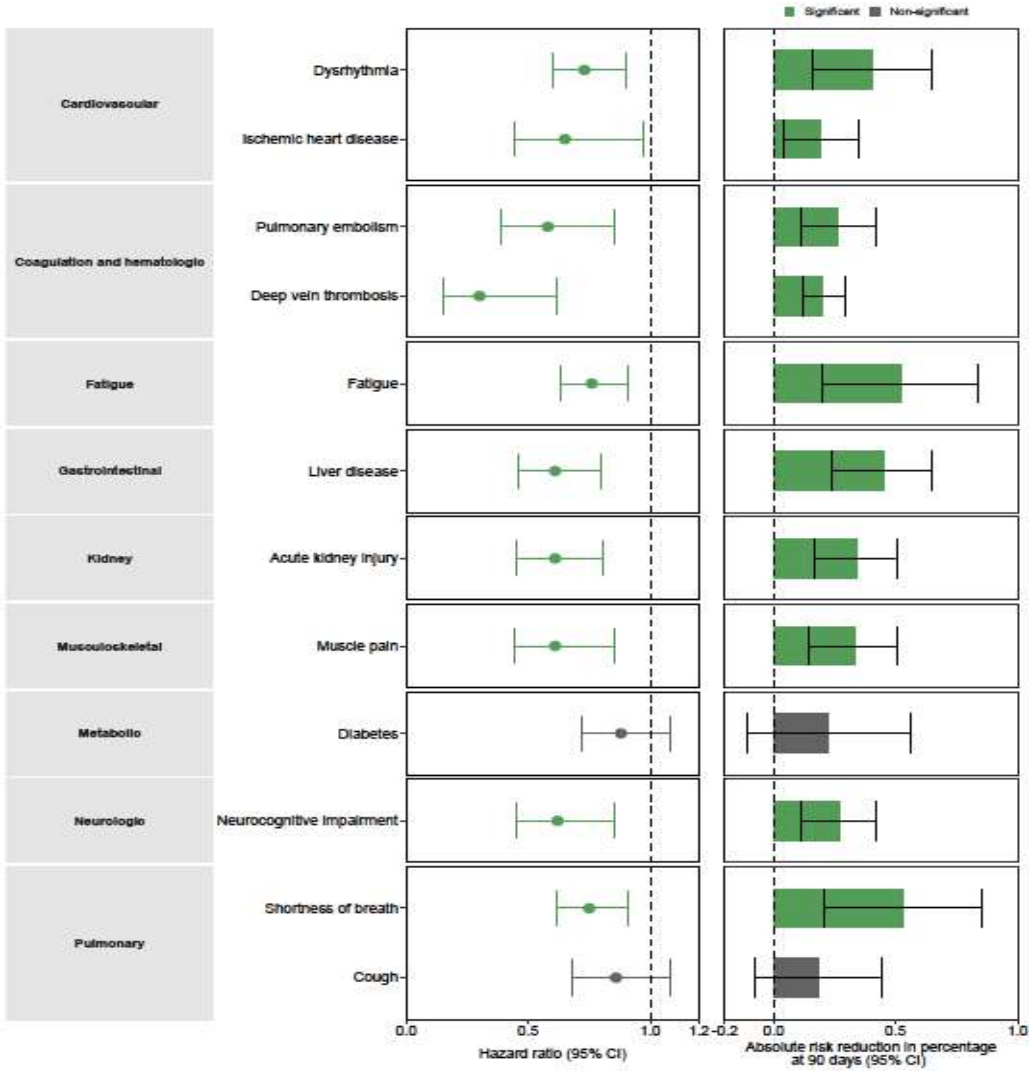
- COVID-19 nedeniyle N/r almış 47 gebe
  - ort yaş 34, ort gebelik haftası 28.4 (4.3-39.6)
- %63.8'inde gebelik+ek komorbidite
- Sadece 2 hasta yan etki nedeniyle tedaviyi bırakmış
- N/r gebede iyi tolere edilmiş, sezaryen doğum oranı fazla olmuş
- Anne ve bebeklerde ciddi istenmeyen etki görülmemiş
- Gebelerin SARSCoV-2 infeksiyonlarında düşünülebilir

Garneau WM. JAMA Network Open. 2022;5(11):e2244141. doi:10.1001/jamanetworkopen.2022.44141

COVID-19'un Post-Akut Sekellerinde Nirmatrelvir/r

- ABD'de, riskli, ilk 30 gün yaşayan, 9217N/r alan vs 47.123 tedavi almayan hasta
- ETKİLİ





Xie Y. medRxiv preprint doi: https://doi.org/10.1101/2022.11.03.22281783

Nirmatrelvir/r Direnci

- **Hücre kültüründe N/r etkisinde SARS-CoV-2 Mpro'da mutasyonlarla direnç gelişmiş**
  - **E166V ve L50F + E166V, kültürde, replikonda ve Mpro sisteminde yüksek direnç**
  - **L50F, E166V ve L50F + E166V replikasyon ve Mpro aktivitesini azaltmış, L50F ve L50F + E166V varyantları infeksiyöz sistemde yüksek fitness göstermiş**
  - **L50F, E166V'in fitness cost'unu giderip viral kaçışı kolaylaştırmış**
  - **E166V ve L50F + E166V nirmatrelvir-Mpro bağlanmasını zayıflatmış**

Zhou et al., Sci. Adv 2022; 8, eadd7197

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

SARS-CoV-2 3CL^{pro} mutations selected in a VSV-based system confer resistance to nirmatrelvir, ensitrelvir, and GC376

Emmanuel Heilmann[1†*], Francesco Costacurta[1†], Seyed Arad Moghadasi[2], Chengjin Ye[3], Matteo Pavan[4], Davide Bassani[4], Andre Volland[1], Claudia Ascher[5], Alexander Kurt Hermann Weiss[5], David Bante[1], Reuben S. Harris[2,6,7], Stefano Moro[4], Bernhard Rupp[8,9], Luis Martinez-Sobrido[3], Dorothee von Laer[1*]

Protease inhibitors are among the most powerful antiviral drugs. Nirmatrelvir is the first protease inhibitor specifically developed against the SARS-CoV-2 protease 3CL^{pro} that has been licensed for clinical use. To identify mutations that confer resistance to this protease inhibitor, we engineered a chimeric vesicular stomatitis virus (VSV) that expressed a polyprotein composed of the VSV glycoprotein (G), the SARS-CoV-2 3CL^{pro}, and the VSV polymerase (L). Viral replication was thus dependent on the autocatalytic processing of this precursor protein by 3CL^{pro} and release of the functional viral proteins G and L, and replication of this chimeric VSV was effectively inhibited by nirmatrelvir. Using this system, we applied nirmatrelvir to select for resistance mutations. Resistance was confirmed by retesting nirmatrelvir against the selected mutations in additional VSV-based systems, in an independently developed cellular system, in a biochemical assay, and in a recombinant SARS-CoV-2 system. We demonstrate that some mutants are cross-resistant to ensitrelvir and GC376, whereas others are less resistant to these compounds. Furthermore, we found that most of these resistance mutations already existed in SARS-CoV-2 sequences that have been deposited in the NCBI and GISAID databases, indicating that these mutations were present in circulating SARS-CoV-2 strains.

Nirmatrelvir/r Alan Almayanlarda Yineleme

- **Prospektif kohort çalışması: Nr kabul eden etmeyenlerde viral ve semptom yinelemesi sıklığı**

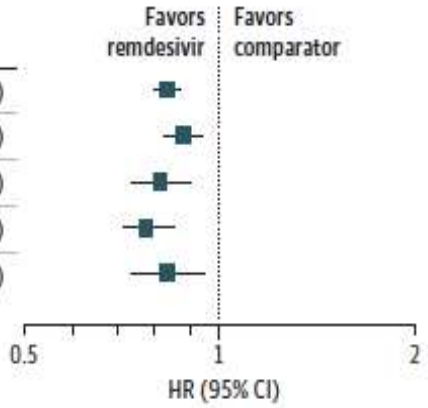
	NPR Treatment (n=127)	Control (n=43)	p-value
COVID-19 Recovery			
Viral (Testing) Rebound	18 (14.2)	4 (9.3)	0.41
Symptom Rebound	24 (18.9)	3 (7.0)	0.06
Consistently Positive	5 (3.9)	0 (0.0)	0.20
First Positive Test to First Negative Test, Days (SD)	7.1 (3.4)	7.0 (3.9)	0.85
Symptom Start to First Day of No Symptoms, Days (SD)	10.5 (4.9)	10.7 (4.7)	0.80
Symptom Start to Test Negative, Days (SD)	6.8 (3.4)	6.1 (2.9)	0.25

Pandit JA. CID 2023 Feb 22;ciad102. doi: 10.1093/cid/ciad102.

Yatan Hastada Remdesivir

- **ABD'de retrospektif kohort çalışma**
- **COVID-19 nedeniyle hastanede yatıp remdesivir alan 24856 ve eğilim skoruna göre eşleştirilmiş remdesivir almayan 24856 hastada mortalite karşılaştırması**

	Control group				Remdesivir group				
Subgroups	Patients, No.	Events, No.	Person-months	Rate per person-month	Patients, No.	Events, No.	Person-months	Rate per person-month	HR (95% CI)
Overall	24856	3775	6072	0.6	24856	3557	6912	0.5	0.83 (0.79-0.87)
Room air	15709	1553	3492	0.4	15709	1510	3948	0.4	0.88 (0.82-0.94)
Low-flow oxygen	5523	725	1296	0.6	5523	677	1452	0.5	0.81 (0.73-0.90)
High-flow oxygen or NIV	2646	1007	912	1.1	2646	884	1032	0.9	0.77 (0.71-0.85)
ECMO/IMV	728	450	312	1.4	728	423	360	1.2	0.83 (0.73-0.95)



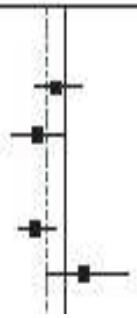
Chokkalingam AP. JAMA Network Open. 2022;5(12):e2244505. doi:10.1001/jamanetworkopen.2022.44505

Effects of remdesivir in patients hospitalised with COVID-19: a systematic review and individual patient data meta-analysis of randomised controlled trials

Alain Amstutz*, Benjamin Speich*, France Mentré, Corina Silvia Rueegg, Drifa Belhadi, Lambert Assoumou, Charles Burdet, Srinivas Murthy, Lori Elizabeth Dodd, Yeming Wang, Kari A O Tikkinen, Florence Ader, Maya Hites, Maude Bouscambert, Mary Anne Trabaud, Mike Fralick, Todd C Lee, Ruxandra Pinto, Andreas Barratt-Due, Fridtjof Lund-Johansen, Fredrik Müller, Olli P O Nevalainen, Bin Cao, Tyler Bonnett, Alexandra Griessbach, Ala Taji Heravi, Christof Schönenberger, Perrine Janiaud, Laura Werlen, Soheila Aghlmandi, Stefan Schandelmaier, Yazdan Yazdanpanah, Dominique Costagliola, Inge Christoffer Olsen, Matthias Briel

- **8 RCT'dan 10854 hasta verisi**
- **28 .günde mortalite R 662/5317 (%12.5) vs P 706/5005 (%14.1) [aOR] 0·88, %95 CI 0·78–1·00, p=0·045**

	Participants	Remdesivir	No remdesivir	aOR (95% CI)	P interaction
Age					
<70 years	7989	393/4111	401/3878	0·93 (0·80–1·08)	0·118*
≥70 years	2318	269/1199	305/1119	0·81 (0·67–1·00)	
Ventilation at baseline					
None or low-flow oxygen	8632	409/4473	465/4159	0·80 (0·70–0·93)	0·019
High-flow or non-invasive, mechanical, or ECMO	1690	253/844	241/846	1·10 (0·88–1·38)	



Amstutz A. Lancet Respir Med 2023; https://doi.org/10.1016/ S2213-2600(22)00528-8

The NEW ENGLAND JOURNAL of MEDICINE

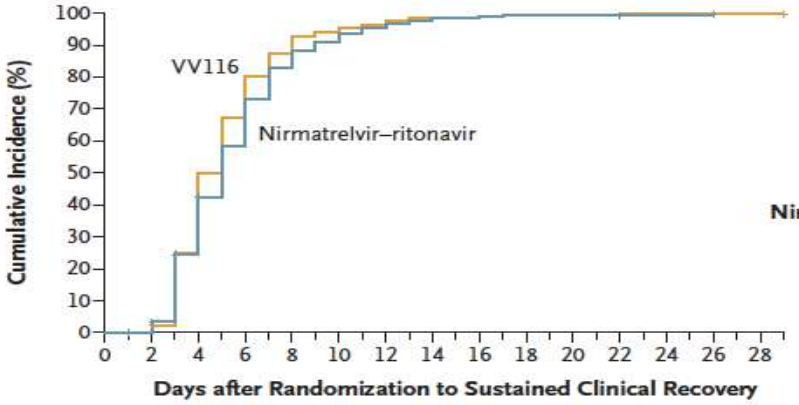
ORIGINAL ARTICLE

VV116 versus Nirmatrelvir–Ritonavir for Oral Treatment of Covid-19

Z. Cao, W. Gao, H. Bao, H. Feng, S. Mei, P. Chen, Yueqiu Gao, Z. Cui, Q. Zhang, X. Meng, H. Gui, W. Wang, Y. Jiang, Z. Song, Y. Shi, J. Sun, Y. Zhang, Q. Xie, Y. Xu, G. Ning, Yuan Gao, and R. Zhao

- **Çin'de omikron sırasında yapılmış Faz-3, RKÇ**
- **VV116 (Remdesivirin Oral Analoğu) vs Nirmatrelvir/r**

A Sustained Clinical Recovery, Full Analysis Population



	No. of Participants	No. of Events (%)	25th Percentile (95% CI)	Median
			days	*days*
VV116	384	378 (98.4)	4.0 (3.0–4.0)	4.0
Nirmatrelvir–Ritonavir	387	378 (97.7)	4.0 (3.0–4.0)	5.0

Hazard ratio, 1.17 (95% CI, 1.02–1.36)

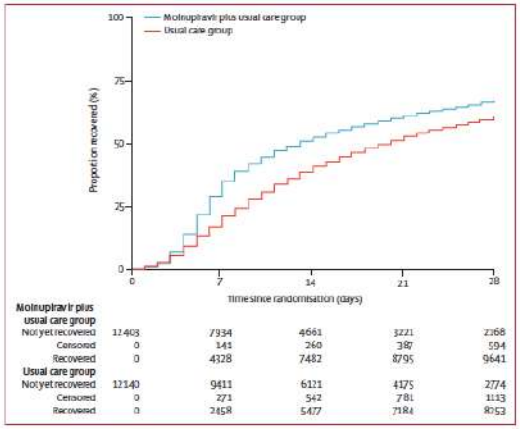
No. at Risk

VV116	384	384	285	124	48	22	14	6	5	3	2	2	1	1	1 1
Nirmatrelvir–ritonavir	387	386	287	157	64	34	17	9	6	3	3	3	1	1	0 0

Cao Z. NEJM 2022; DOI: 10.1056/NEJMoa2208822Cao Z.

Molnupiravir PANAROMIC Çalışması

- İngiltere'de, açık etiketli, çok kollu, platform, RCT ≥50veya ≥18+komorbidite, ≤5 gündür hastada, doğrulanmış, %99'u aşılı ayaktan COVID-19'da molnupiravir vs standard bakım
- 28 günde hastane yatışı/ölüm farksız (%0·8)
- İyileşme süresi
  - Molnupiravir 9 gün vs 15 gün
- 7. günde belirlenemez SARS-CoV-2
  - Molnupiravir (%21) vs (%3) (p=0.039)
- İstenmeyen etkiler benzer
- İyileşme süresi mlnpr grubunda belirgin olarak daha kısa



Butler C. Lancet 2022; https://doi.org/10.1016/S0140-6736(22)02597-1

communications biology

ARTICLE

https://doi.org/10.1038/s42003-022-04322-8 OPEN

A proof-of-concept study on the genomic evolution of Sars-Cov-2 in molnupiravir-treated, paxlovid-treated and drug-naïve patients

Claudia Alteri[1,2], Valeria Fox[1,2,6], Rossana Scutari[1,2,6], Giulia Jole Burastero[3], Sara Volpi[3], Matteo Faltoni[3], Vanessa Fini[1], Annarita Granaglia[1], Sara Esperti[3], Altea Gallerani[3], Valentino Costabile[1], Beatrice Fontana[3], Erica Franceschini[4], Marianna Meschiari[4], Andrea Campana[5], Stefania Bernardi[5], Alberto Villani[5], Paola Bernaschi[1], Cristina Russo[1], Giovanni Guaraldi[3], Cristina Mussini[3] & Carlo Federico Perno[1]✉

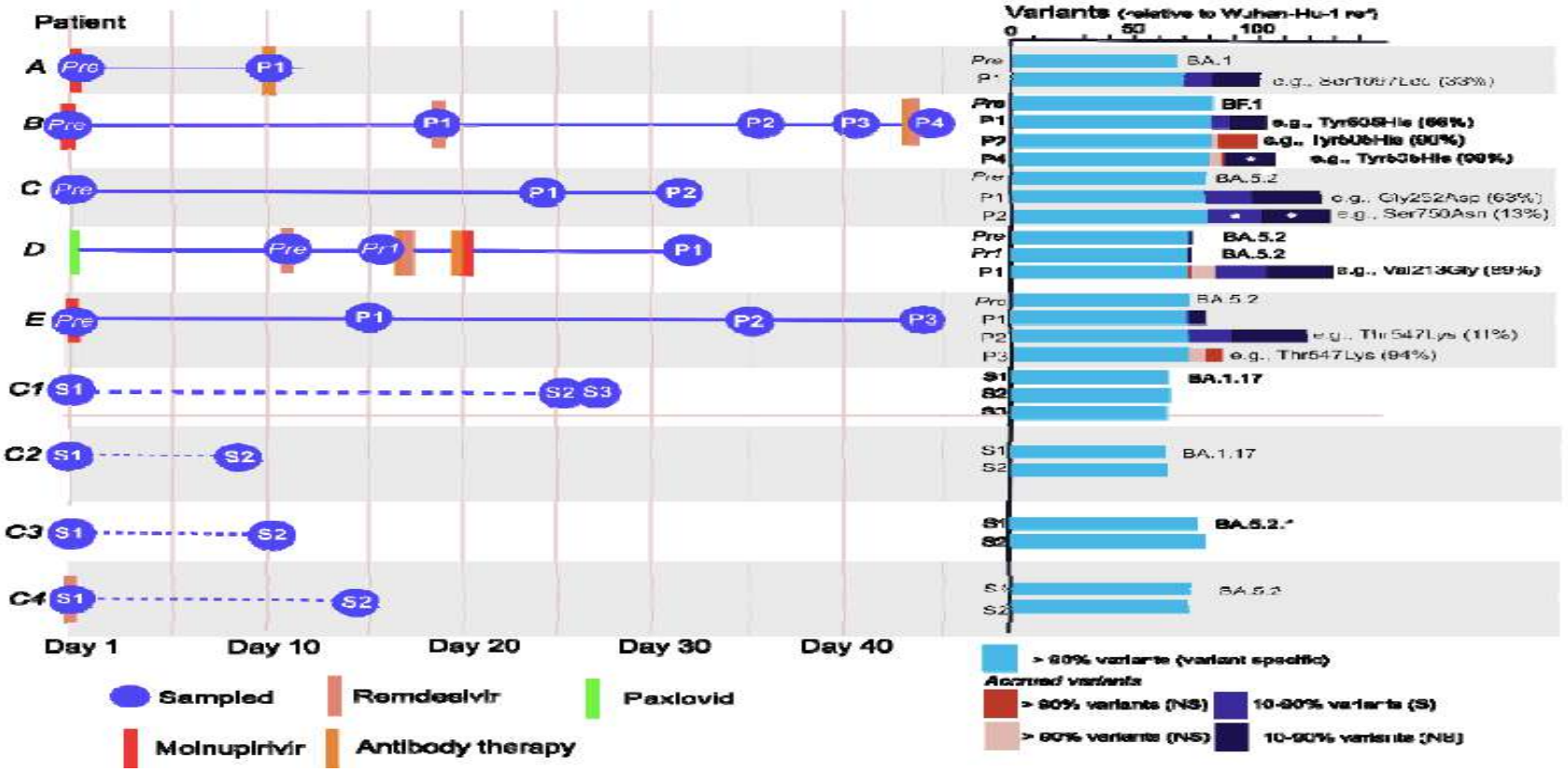
Little is known about SARS-CoV-2 evolution under Molnupiravir and Paxlovid, the only antivirals approved for COVID-19 treatment. By investigating SARS-CoV-2 variability in 8 Molnupiravir-treated, 7 Paxlovid-treated and 5 drug-naïve individuals at 4 time-points (Days 0-2-5-7), a higher genetic distance is found under Molnupiravir pressure compared to Paxlovid and no-drug pressure (nucleotide-substitutions/site mean±Standard error: $18.7 \times 10^{-4} \pm 2.1 \times 10^{-4}$ vs. $3.3 \times 10^{-4} \pm 0.8 \times 10^{-4}$ vs. $3.1 \times 10^{-4} \pm 0.8 \times 10^{-4}$, $P = 0.0003$), peaking between Day 2 and 5. Molnupiravir drives the emergence of more G-A and C-T transitions than other mutations ($P = 0.031$). SARS-CoV-2 selective evolution under Molnupiravir pressure does not differ from that under Paxlovid or no-drug pressure, except for orf8 ($dN > dS$, $P = 0.001$); few amino acid mutations are enriched at specific sites. No RNA-dependent RNA polymerase (RdRp) or main proteases (Mpro) mutations conferring resistance to Molnupiravir or Paxlovid are found. This proof-of-concept study defines the SARS-CoV-2 within-host evolution during antiviral treatment, confirming higher in vivo variability induced by Molnupiravir compared to Paxlovid and drug-naive, albeit not resulting in apparent mutation selection.

Molnupiravir SNP indüklüyor , bunlar çok nadiren birikebiliyor, tedavi altında mutant varyantların gelişim riski düşük

https://doi.org/10.1038/s42003-022-04322-8

Antiviral treatments lead to the rapid accrual of hundreds of SARS-CoV-2 mutations in immunocompromised patients

Authors: Nicholas M. Fountain-Jones[1,2*], Robert Vanhaeften[1], Jan Williamson[1], Janelle Maskell[1], I-Ly J Chua[1], Michael Charleston[2] & Louise Cooley[1,3]



Bağışıklığı baskılanmışlarda mlnprv tedavisi sonrası aminoasit değişikliğine yol açan ve virusun ölmediğ çok sayıda mutasyonlar gözlenmiş

Fountain-Jones NM. medRxiv preprint doi: https://doi.org/10.1101/2022.12.21.22283811

Top Story

EU panel recommends against approval of Merck & Co.'s COVID drug Lagevrio

Ref: Business Wire, EMA, FinanzNachrichten, Interactive Investor, Morningstar, San Francisco Chronicle

Matthew Dennis

PUBLISHED: FEBRUARY 24, 2023

https://firstwordpharma.com/story/5709379

CONFIDENTIAL UNTIL PUBLISHED

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final draft guidance

Therapeutics for people with COVID-19

Mild COVID-19

***Nirmatrelvir plus ritonavir is recommended** because the likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources.

*The cost-effectiveness estimates for sotrovimab are also within what NICE considers an acceptable use of NHS resources, but only for people for whom nirmatrelvir plus ritonavir is contraindicated or unsuitable. **So, sotrovimab is recommended in this group.**

***Remdesivir is not recommended** because the likely cost-effectiveness estimates are higher than what NICE usually considers an acceptable use of NHS resources.

***Casirivimab plus imdevimab, molnupiravir and tixagevimab plus cilgavimab are not recommended** because they are unlikely to be effective at treating COVID-19 and it is not possible to reliably estimate their cost effectiveness.

Severe COVID-19

***Tocilizumab is recommended** because the likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources

Febr 21, 2023; https://www.nice.org.uk/guidance/gid-ta10936/documents/final-appraisal-determination-document

IDSA Molnupiravir Önerisi

Recommendation 1(UPDATED 02/23/2023): In ambulatory patients (≥18 years) with mild-to-moderate COVID-19 at high risk for progression to severe disease who have no other treatment options*, the IDSA guideline panel suggests molnupiravir initiated within five days of symptom onset rather than no molnupiravir. (Conditional recommendation†, Low certainty of evidence)

Last reviewed and updated 2/8/2023

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	molnupiravir	no molnupiravir	Relative (95% CI)	Absolute (95% CI)		
Mortality (follow-up: range 28 days to 29 days)												
3 [1-3]	randomized trials	not serious	not serious	serious [a,b]	serious [c]	none	4/13328 (0.0%)	14/13314 (0.1%)	RR 0.28 (0.09 to 0.86)	1 fewer per 1,000 (from 1 fewer to 0 fewer)	⨁⨁◯◯ LOW	CRITICAL

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

Effectiveness of Favipiravir monotherapy in the treatment of COVID-19: real world data analysis from Thailand

Attasit Srisubat,[a] Somchai Thanasitthichai,[a] Subsai Kongsaengdao,[b,c,*] Narong Maneeton,[d] Benchalak Maneeton,[d] and Somsak Akksilp[a]

[a]Department of Medical Services, Ministry of Public Health of Thailand, Nonthaburi, 11000, Thailand
[b]Division of Neurology, Department of Medicine, Rajavithi Hospital, Department of Medical Services, Ministry of Public Health of Thailand, Bangkok, Thailand
[c]Department of Medicine, College of Medicine, Rangsit University, Bangkok, Thailand
[d]Department of Psychiatry, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

The Lancet Regional Health - Southeast Asia 2023;■: 100166

Published Online XXX
https://doi.org/10.1016/j.lansea.2023.100166

Summary

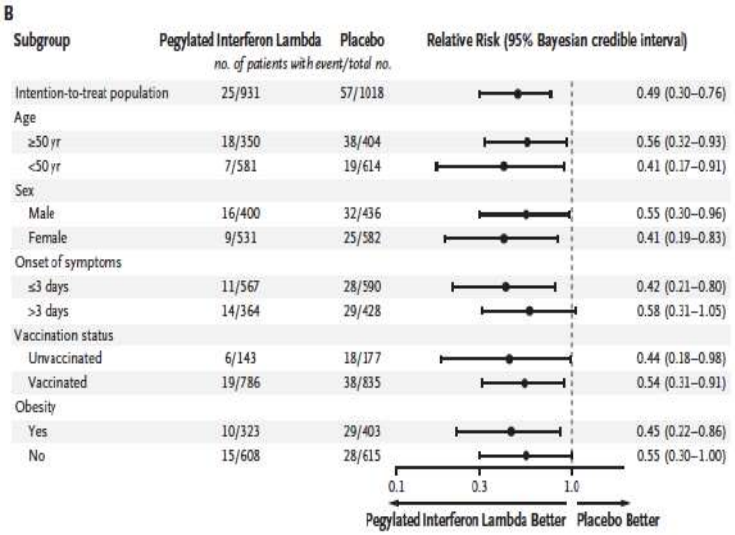
Background Previous studies showed that Favipiravir, a selective viral ribonucleic acid dependent-ribonucleic acid polymerase inhibitor, exhibited a trend of clinical improvement within 14 days and promoted viral clearance by day 7, without reduction of mortality rate in COVID-19.

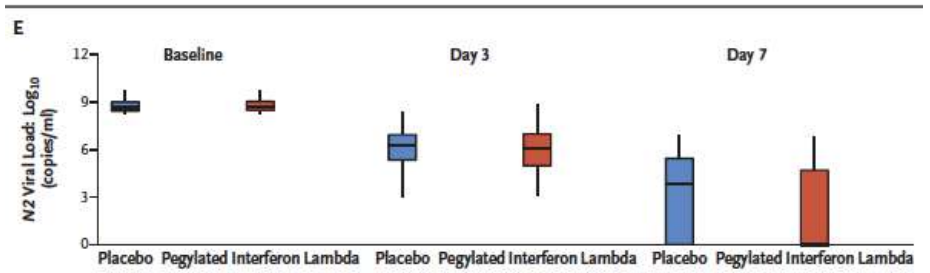
Methods During the COVID-19 pandemic, Department of Medical Services (Thailand) formulated National Clinical Treatment Guidelines for COVID-19 and approved Favipiravir to eight medical centres. After treatment with Favipiravir monotherapy, we compared real-world data analysis to supportive treatment without antiviral agents.

Findings We analysed 12,888 COVID-19 patients between June 1, 2021, and July 31, 2021. This group study excluded 66 asymptomatic and 4634 COVID-19 patients treated with other antiviral agents. The 4896 mild, 2357 moderate, and 935 severe COVID-19 patients were analysed. All patients neither had previous SARS-CoV-2 infection nor received an mRNA vaccine during study period. Favipiravir monotherapy reduced the 28-day mortality risk in severe COVID-19 by relative risk (RR) = 0.72 (95% CI 0.58–0.91 P = 0.006) after adjustment for aging and hypertension. However, in mild and moderate COVID-19, Favipiravir monotherapy did not significantly reduce 28-day mortality risk by RR = 0.59 (95% CI 0.06–5.43 P = 0.65) after adjustment for aging, and RR = 0.60 (95% CI 0.32–1.13 P = 0.11) after adjustment for aging and obesity, respectively. In the patient with recovery, Favipiravir monotherapy exhibited a shortening time to recovery when compared to supportive treatment without antiviral agents (mean ± SD by 9.6 ± 7.1 vs. 12.9 ± 7.6 days: P < 0.0001, 10.0 ± 5.9 vs. 12.4 ± 5.3 days: P < 0.0001, and 11.2 ± 7.8 vs. 13.1 ± 8.0 days: P < 0.0001 in mild, moderate, and severe COVID-19 respectively).

COVID-19'da Pegile İnterferon Lambda

- İlk 7 günde, riskli, %83'ü aşılı, hastada RKÇ
- 933hasta 180 µg PİL vs 1018hasta plasebo
- Hastane yatışı veya acilde >6st izlenme %2.7 vs %5.6, fark %51 (RR, 0.49; %95 ByCI, 0.30 - 0.76; plasebodan üstün olma olasılığı >%99.9
- Hastane yatışı : HR 0.57; %95 ByCI, 0.33-0.95
- Hastane yatışı ve ölüm: HR 0.59; %95 ByCI, 0.35 -0.97
- Başlangıçta viral yükü yüksek olanlarda 7.gün viral yük PİL grubunda daha düşük





Reis G. N Engl J Med 2023;388:518-28.
DOI: 10.1056/NEJMoa2209760

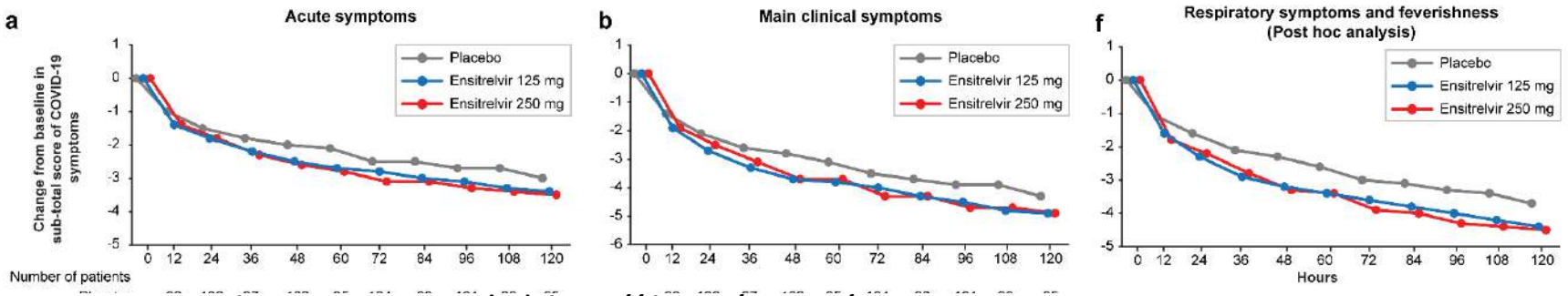
COVID-19'da Ensitrelvir Fumarat

- **Faz 2a, 42 hastada RCT, viral klirens**

	Time to infectious viral clearance (hours), median [95% CI]	Difference from placebo (hours), median [95% CI]	P Value
Placebo (n=14)	111.1 [23.2, 158.5]	-	-
Ensitrelvir 125 mg (n = 15)	61.3 [38.0, 68.4]	-49.8 [-96.7, 30.9]	0.0159
Ensitrelvir 250 mg (n = 13)	62.7 [39.2, 72.3]	-48.4 [-95.9, 28.5]	0.0205

- **Faz 2b, 341 hasta, viral klirens ve iyileşme**

	Ensitrelvir 125 mg n = 111	Ensitrelvir 250 mg n = 113	Placebo n = 108
Median (hours) [95% CI]	51.3 [44.1, 61.8]	62.1 [43.7, 66.5]	91.9 [84.0, 109.9]
Difference from placebo (hours) [95% CI]	-40.6 [-58.5, -26.5]	-29.8 [-52.0, -23.6]	–
P Value	<.0001	<.0001	–



Mukae H. AAC 2022; 66 (10); https://doi.org/10.1128/aac.00697-22

Mukae H. CID 2023; https://doi.org/10.1093/cid/ciac933

Yotsuyanagi H. Medicine 2023;102:8(e33024).http://dx.doi.org/10.1097/MD.0000000000003302

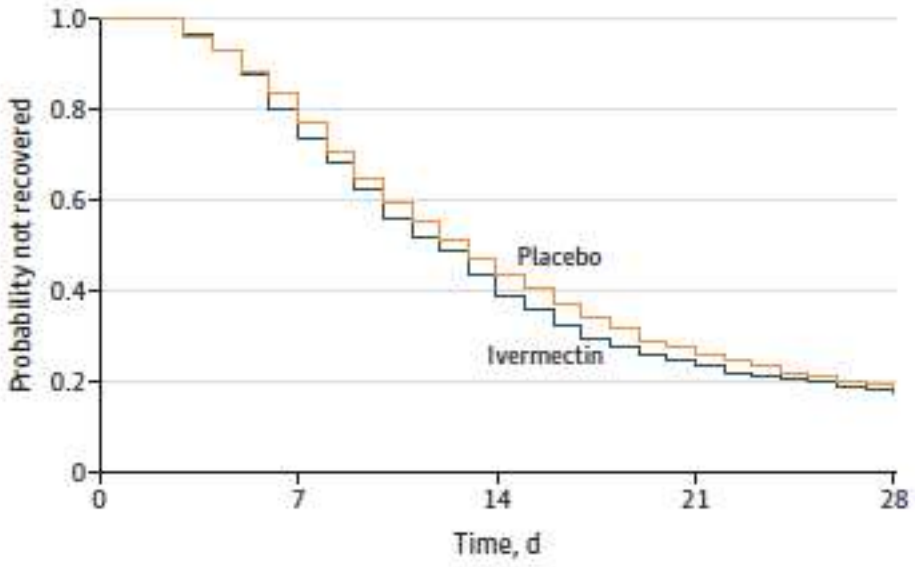
JAMA | Original Investigation

Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19

A Randomized Clinical Trial

- **İvermektin 400 µg/kg/gün, 3 gün vs plasebo**
- **Klinik iyileşme süresi**

Kaplan-Meier Curve for Primary Outcome of Time to Recovery



No. at risk					
Ivermectin	817	641	339	192	138
Placebo	774	637	348	201	138

Naggie S. JAMA. 2022;328(16):1595-1603. doi:10.1001/jama.2022.18590

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Metformin, Ivermectin, and Fluvoxamine for Covid-19

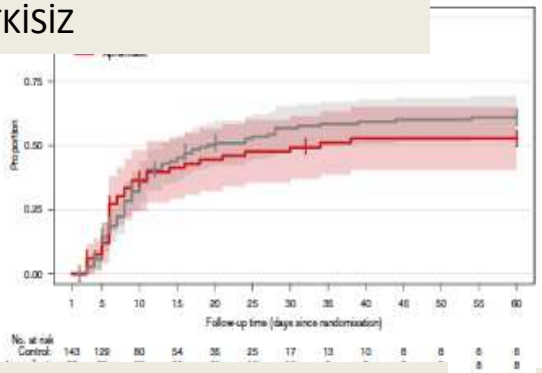
- **1431 hastalık çift-kör RCT, obez veya fazla kilolu, %52 aşılı**
- **Primer sonlanım: Sat ≤%93, acil başvurusu, hastane yatışı, ölüm**
- **Metformin aOR 0.84 (% 95 CI 0.66 -1.09; P = 0.19)**
- **İvermektin aOR 1.05 (%95 CI, 0.76 - 1.45; P = 0.78)**
- **Fluvoksamin 0.94 (%95 CI, 0.66 -1.36; P = 0.75)**
- **Üçü de ETKİSİZ**

Bramante CT. N Engl J Med 2022; 387:599-610; DOI: 10.1056/NEJMoa2201662

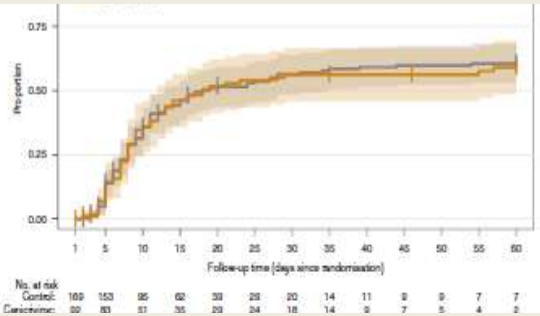
ISY COVID-19 Çalışmas-ABD-RKÇ

- **Ağır COVID-19'da deksametazon+rmdsvr + 6 ajandan biri vs deksametazon+ rmdsvr**
- **İyileşme (2 gün oksijen ihtiyacı olmaması), Ölüm**

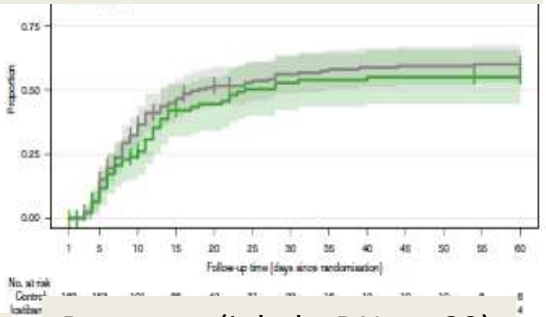
Apremilast (PDE4 inhibitör,67)
ETKİSİZ



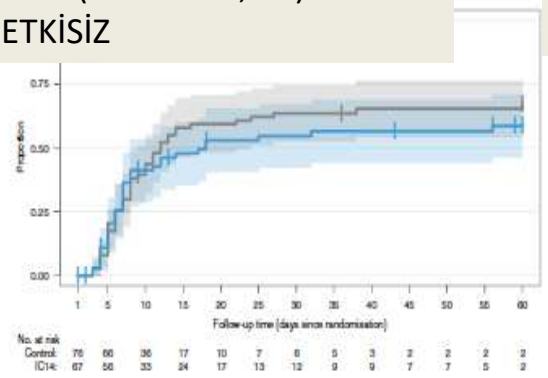
Senikrivirok(CCR2/5 antgnst,92)
ETKİSİZ



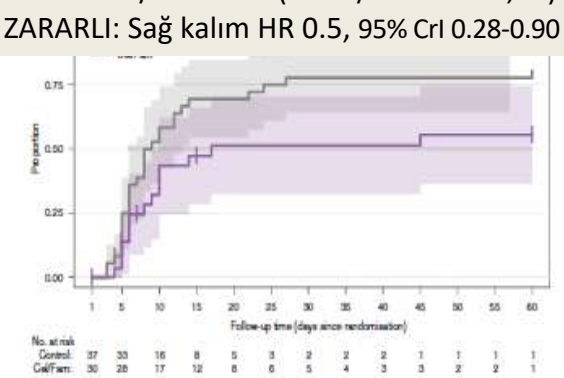
Satibant (bradikinin antgnst,96)
ETKİSİZ



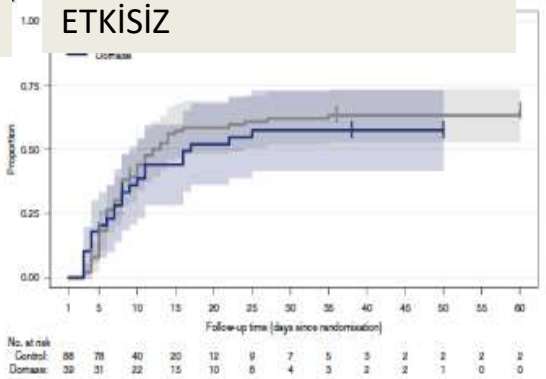
IC14 (anti-CD14, 67)
ETKİSİZ



Selekoksib/famotidin(COX2/histmn inh,30):
ZARARLI: Sağ kalım HR 0.5, 95% CrI 0.28-0.90



Dornase α(inhalerDNase,39)
ETKİSİZ



The I-SPY COVID ConsortiumeClinicalMedicine 2023;58: 101889; https://doi.org/10.1016/j.eclinm.2023.101889

Ağır COVID-19 Tedavilerinin 180.Gün Sonuçlara Etkisi

REMAPCAP çalışmasında randomize edilmiş 4869 hasta

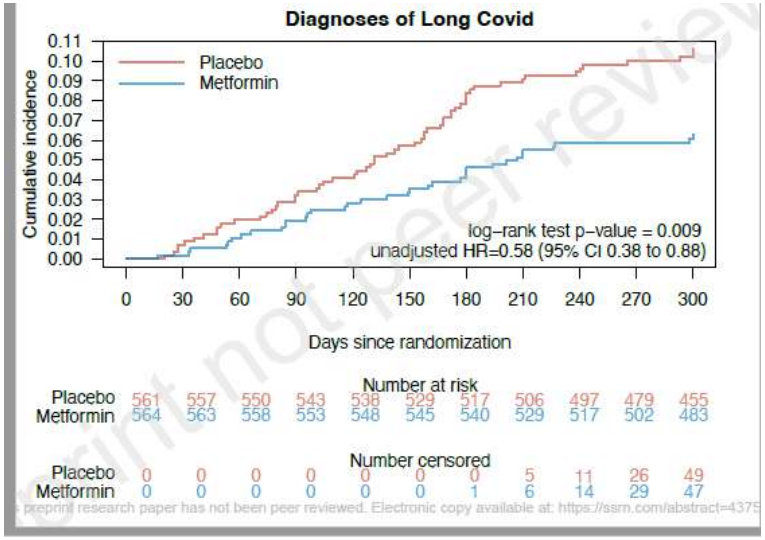
- **Kontrollere göre 6 aylık sürviyi uzatanlar**
  - **IL-6 receptor antagonistleri %99.9 olasıkla, HR, 0.74 [%95 CrI, 0.61-0.90]**
  - **Antitrombosit ajanlar %95 olasılıkla aHR, 0.85 [%95CrI, 0.71-1.03])**
- **Faydasız olanlar**
  - **Terapötik antikoagülasyon (HR, 1.13 [%95CrI, 0.93-1.42]),**
  - **Konvalesan plazma: HR, 0.99 [%95CrI, 0.86-1.14]),**
  - **Lopinavir-ritonavir (HR, 1.06 [95%CrI, 0.82-1.38])**
- **Zarar verenler**
  - **Hidroksiklorokin (HR, 1.51 [%95CrI,0.98-2.29])**
  - **Lopinavir-ritonavir + Hidroksiklorokin (HR, 1.61 [95%CrI, 0.97-2.67])**
- **Kortikosteroid kolu erken durdurulmuştu 6 aylık sürviyi %57-%611 olasıkla uzatıyor**

Remapcap Investigators. JAMA 2022; doi:10.1001/jama.2022.23257

Long COVID-19'da Tedavi

Ayaktan COVID-19'da metformin, ivermektin, fluvoksamin'i test eden ABD-COVID-OUT RKÇ'na alınmış hastalarda 9 ayda COVID-19 Long COVID-19 sıklığı

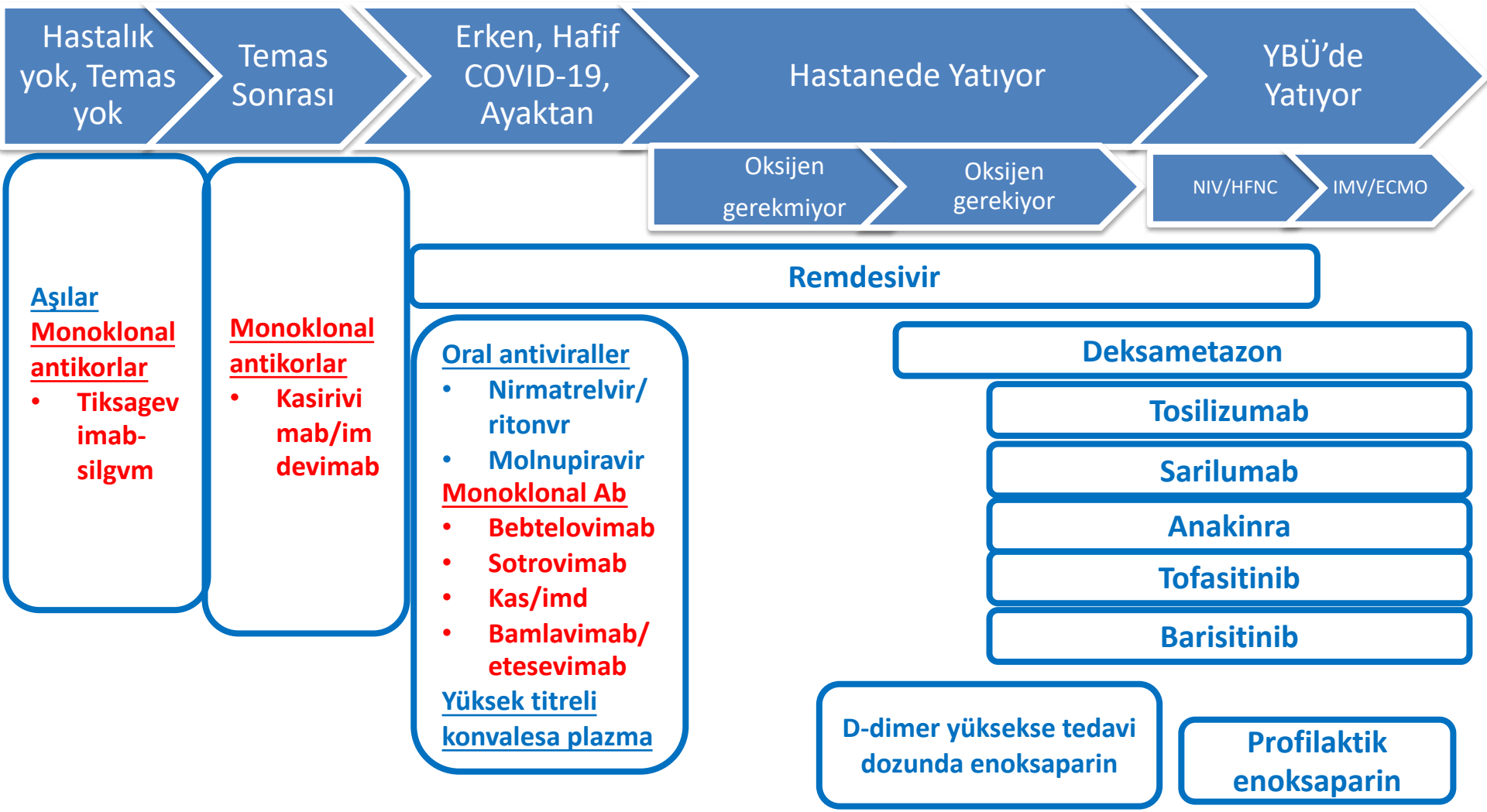
- **İvermektin ve fluvoksaminde plasebodan farksız, metforminde plasebodan belirgin olarak daha düşük**



Subgroup	Metformin	Placebo	Hazard Ratio (95% CI)
All Participants	35/564 (6.2%)	59/561 (10.5%)	0.58 (0.38 to 0.88)
Assessment of treatment effect across a priori subgroups of pre-randomization baseline risk factors:			
Biologic sex			
Female	24/305 (7.9%)	46/326 (14.1%)	0.54 (0.33 to 0.89)
Male	11/259 (4.2%)	13/235 (5.5%)	0.76 (0.34 to 1.70)
BMI			
<30 kg/m2	20/298 (6.7%)	23/279 (8.2%)	0.80 (0.44 to 1.46)
>=30 kg/m2	15/266 (5.6%)	36/282 (12.8%)	0.43 (0.23 to 0.78)
Days since symptom onset			
< 4 days	6/130 (4.6%)	17/143 (11.9%)	0.37 (0.15 to 0.95)
>=4 days	29/427 (6.8%)	42/407 (10.3%)	0.64 (0.40 to 1.03)
Age			
<45 years	13/265 (4.9%)	33/272 (12.1%)	0.39 (0.20 to 0.73)
>=45 years	22/299 (7.4%)	26/289 (9.0%)	0.82 (0.46 to 1.44)
Dominant variant			
Alpha	1/34 (2.9%)	4/29 (13.8%)	0.21 (0.02 to 1.87)
Delta	27/399 (6.8%)	40/401 (10.0%)	0.67 (0.41 to 1.08)
Omicron	7/131 (5.3%)	15/131 (11.5%)	0.45 (0.18 to 1.11)
Vaccination status			
Not Vaccinated	15/238 (6.3%)	38/269 (14.1%)	0.43 (0.23 to 0.78)
Vaccinated	20/326 (6.1%)	21/292 (7.2%)	0.85 (0.46 to 1.56)
Additional study drug			
Nothing/Placebo	11/221 (5.0%)	23/229 (10.0%)	0.48 (0.23 to 0.98)
Ivermectin	11/189 (5.8%)	19/188 (10.1%)	0.56 (0.27 to 1.18)
Fluvoxamine	13/154 (8.4%)	17/144 (11.8%)	0.72 (0.35 to 1.48)

Bramante CT. MedRxiv 2022 Dec 23;2022.12.21.22283753. doi: 10.1101/2022.12.21.22283753

Hastalığın Evrelerine Göre COVID-19 Tedavisi



ABD NIH COVID-19 Tedavi Önerisi (28 Aralık 2022)

Hastane veya oksijen ihtiyacı olmayan, ayaktan veya başka nedenle hastanede yatan

Tüm hastalara semptomatik tedavi önerilmeli (AIII)

Ağır hastalık riski olanlara şunlardan biri önerilir (tercih sırasına göre)

- **Nirmatrelvir/r (pakslovid)** (AIIa)
- **Remdesivir** (BIIa)

Alternatif Tedaviler (sadece, yukarıdakilerin verilemediği hastalarda)

- **Molnupiravir** (CIIa)

Başka indikasyon olmadıkça deksametazon veya diğer kortikosteroidlerin kullanımı önerilmez (AIII).

ABD NIH COVID-19 Tedavi Önerisi (28 Aralık 2022)

Hastanede yatan ama oksijen ihtiyacı olmayan	Deksametazon (AIIa) ve Kortikosteroidler (AIII) **ÖNERİLMEZ**. Riskli Hastalarda: Remdesivir (BIII)	Profilaktik dozda heparin önerilir (kontrindikasyan ve VTE yoksa).
Hastanede yatan, oksijen ihtiyacı olan	**Remdesivir:** minimal oksijen desteği gerekene (BIIa) **Remdesivir+Deksametazon:** Hemen her hastaya (BIIa) **Deksametazon:** Remdesivir yoksa (BI) Deksametazon altında oksijen ihtiyacı hızla artana **barisitinib** veya **tosilizumab** eklenir	Gebe olmayan ve D-Dimer>ULN olanlara tedavi dozunda heparin. Diğerlerine profilaktik dozda heparin
Hastanede yatan ve HFNC veya NIV'le oksijen ihtiyacı olan	**Deksametazon+ barisitinib** () (AI) veya **Deksametazon+ tosiluzumab** (BIIa) **Barisitinib, tofasitinib, tosilizumab veya sarilumab** bulunamazsa **Deksametazon (AI)** **Bazı hastalarda +Remdesivir** (CIIa)	Profilaktik dozda heparin önerilir (kontrindikasyan ve VTE yoksa).
Hastanede yatan ve İMV veya ECMO ihtiyacı olan	**Deksametazon+ barisitinib** () (AI) veya **Deksametazon+ tosiluzumab** (BIIa) **Barisitinib, tofasitinib, tosilizumab veya sarilumab** bulunamasa **Deksametazon (AI)**	Profilaktik dozda heparin önerilir (kontrindikasyan ve VTE yoksa).*

***Servisteyken terapötik dozda heparin başlananlarda YBÜ'de profilaktik doza geçilir.**

COVID-19 Tedavisi-IDSA

Ajan	Temas öncesi sonrası profilaksi	Ayaktan, hafif-orta	Yatan, oksijen gerekmeyen hafif -orta	Yatan, ağır, kritik değil	Yatan, kritik hasta (MV, ECMO vb)
HCQ	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙
HCQ+azitromisin			ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙
Lopinavir/r	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙
Remdesivir		ÖNERİLİR ⊕⊕⊙⊙	ÖNERİLİR ⊕⊕⊙⊙	ÖNERİLİR ⊕⊕⊙⊙	RUTİN ÖNERİLMEZ ⊕⊙⊙⊙
Nirmatrelvir/r		ÖNERİLİR ⊕⊕⊙⊙			
Molnupiravir		ÖNERİLİR ⊕⊕⊙⊙			
İvermektin		ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊙⊙⊙	ÖNERİLMEZ ⊕⊙⊙⊙	ÖNERİLMEZ ⊕⊙⊙⊙
Fluvoksamin		Klinik çalışmalarda			
Konvalesan Plazma		ÖNERİLİR ⊕⊕⊙⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙

COVID-19 Tedavisi-IDSA

Ajan	Temas öncesi sonrası profilaksi	Ayaktan, hafif-orta	Yatan, oksijen gerekmeyen hafif - orta	Yatan, ağır, kritik değil	Yatan, kritik hasta (MV, ECMO vb)
Kortikosteroid			ÖNERİLMEZ ⊕⊕⊙⊙	ÖNERİLİR ⊕⊕⊕⊙	ÖNERİLİR ⊕⊕⊕⊙
İnhaler kortikosteroid		ÖNERİLMEZ ⊕⊕⊙⊙			
Tosilizumab				ÖNERİLİR ⊕⊕⊙⊙	ÖNERİLİR ⊕⊕⊙⊙
Sarilumab				ÖNERİLİR ⊕⊙⊙⊙	ÖNERİLİR ⊕⊙⊙⊙
Tofasitinib				ÖNERİLİR ⊕⊙⊙⊙	
Kolşisin		ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙	ÖNERİLMEZ ⊕⊕⊕⊙
Famotidin		ÖNERİLMEZ ⊕⊕⊙⊙		ÖNERİLMEZ ⊕⊕⊙⊙	

Aklımızda Kalsın

- COVID-19 tedv de ölüm/hst yatışı azaltma amacı yaşlı, çok kmd olan, bağışıklığı baskılanmışlarda geçerli
- Konvalesan plazma başka seçenek olmayan, bağışıklığı baskılanmış, erken dönem hastalarda, yüksek antikor titreli ve uygun varyantla inf geçirmiş donör varsa düşünülebilir
- Mab'lar son omikron alt varyantlarında az etkili, sotrovimab yüksek doz?
- Nirmatrelvir/ritonavir halen en etkili oral tedavi, long COVID için de etkili, gebede de kullanılabilir
- Molnupiravir, başka seçenek yoksa verilebilir, bağışıklığı baskılanmışlarda mutant varyantlara dikkat
- Remdesivir oral analogları umut verici, remdesivir yatan hastalarda da etkili
- İvermektin, fluvoksamin etkisiz
- Ensitrelvir klinik çalışma sonuçları umut verici
- İnterferon lambda tek doz etkili görünüyor
- Long COVID için metformin umut verici