KUISCID
KOÇ UNIVERSITY - İŞBANK
CENTER FOR INFECTIOUS DISEASES

KLİMİK
TÜRK KLİNİK MİKROBİYOLOJİ VE
İNFEKSİYON HASTALIKLARI DERNEĞİ

COVID-19'da Anti-Inflamatuvar, Anti-Sitokin Anti-Koagülan Tedaviler

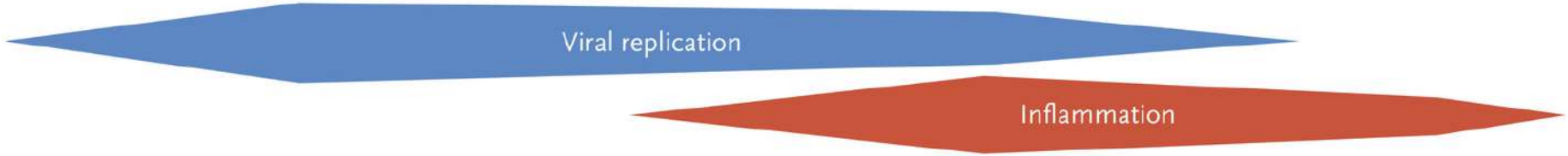
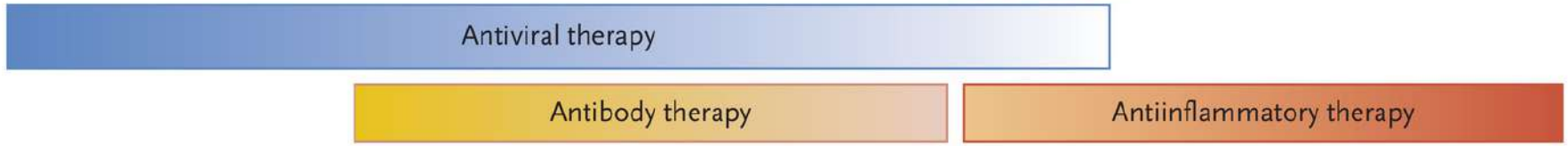
Şiran Keske

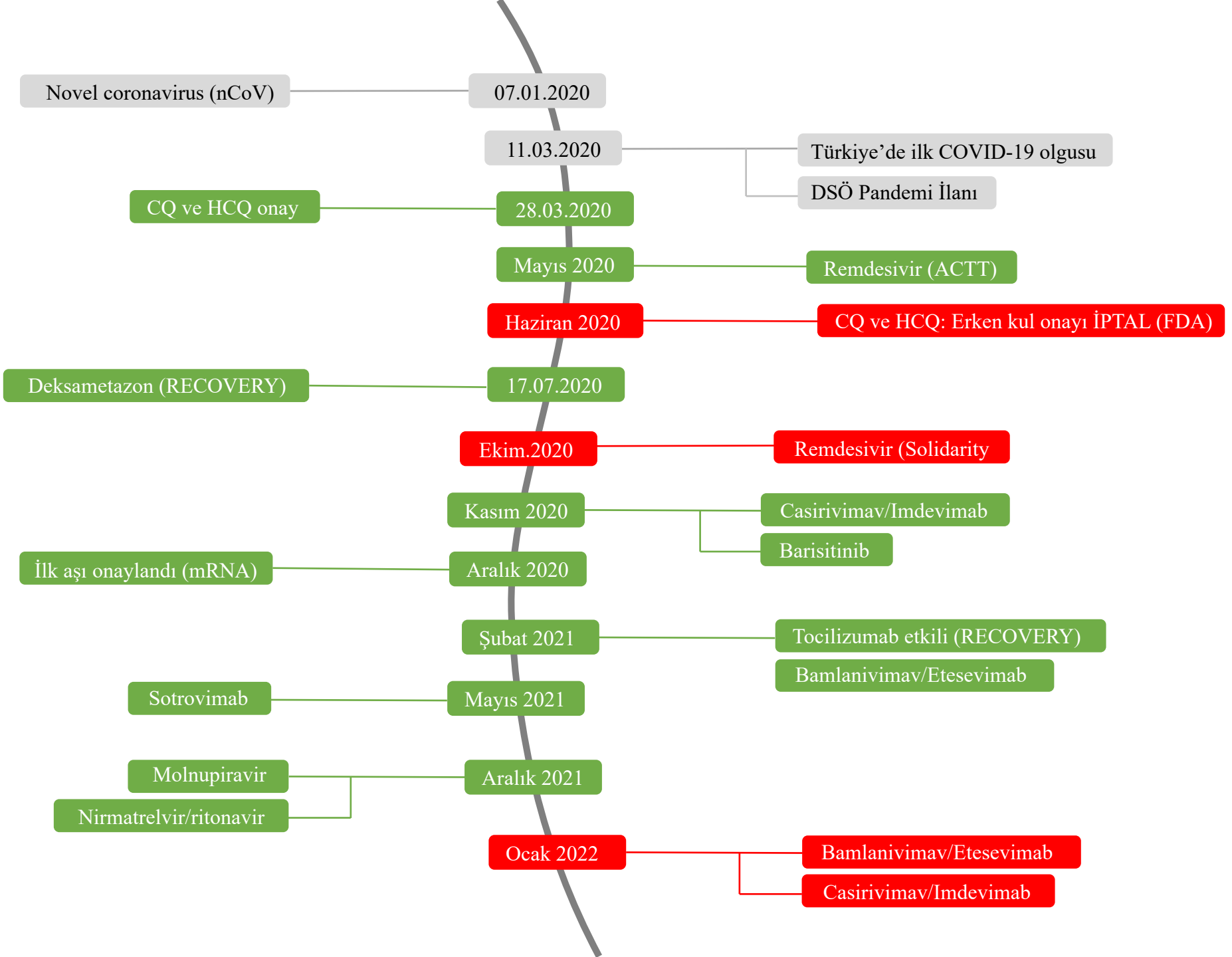
Amerikan Hastanesi, İstanbul

Koç Üniversitesi Tıp Fakültesi, İstanbul

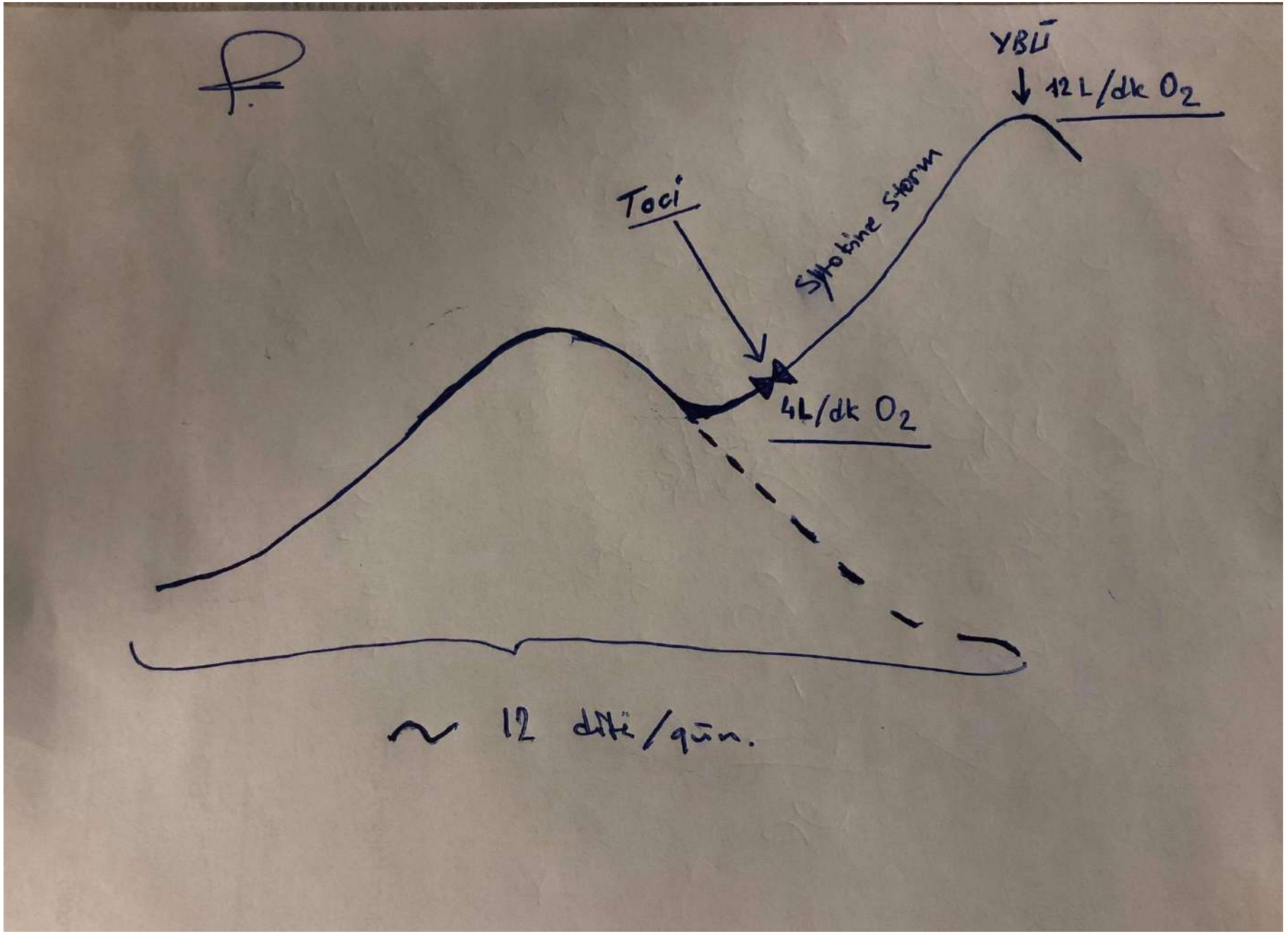
Koç University İş Bankası Enfeksiyon Hastalıkları Araştırma Merkezi (KUISCID), Istanbul

Future considerations

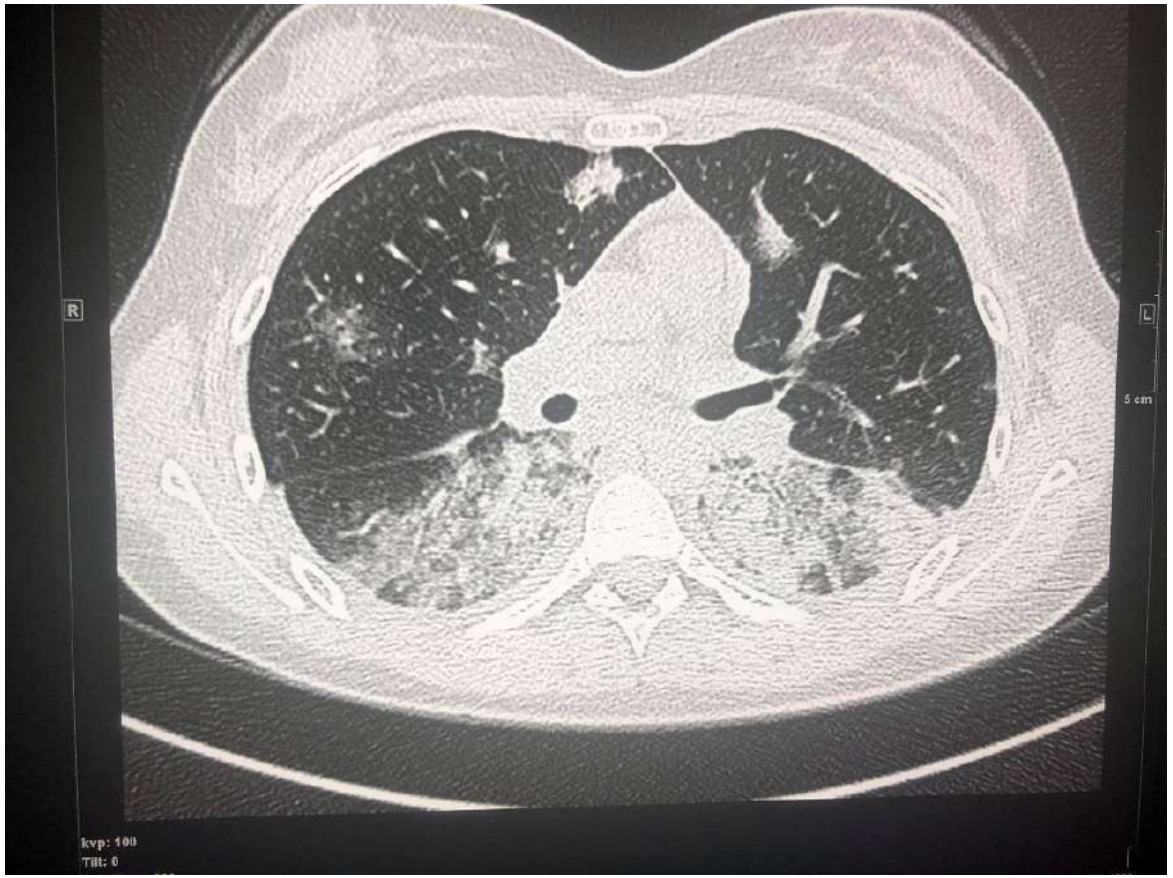
	Asymptomatic or Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical Illness
Features	Positive SARS-CoV-2 test; no symptoms	Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94%	Oxygen saturation <94%; respiratory rate ≥30 breaths/min; lung infiltrates >50%	Respiratory failure, shock, and multiorgan dysfunction or failure
Testing	Screening testing; if patient has known exposure, diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing
Isolation	Yes	Yes	Yes	Yes	Yes
Proposed Disease Pathogenesis					
Potential Treatment					
Management Considerations	Monitoring for symptoms	Clinical monitoring and supportive care	Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir	Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone)	Critical care and specific therapy (dexamethasone, possibly remdesivir)


Novel coronavirus (nCoV)
07.01.2020
11.03.2020
Türkiye'de ilk COVID-19 olgusu
DSÖ Pandemi İlanı
CQ ve HCQ onay
28.03.2020
Mayıs 2020
Remdesivir (ACTT)
Haziran 2020
CQ ve HCQ: Erken kul onayı İPTAL (FDA)
Deksametazon (RECOVERY)
17.07.2020
Ekim.2020
Remdesivir (Solidarity
Kasım 2020
Casirivimav/Imdevimab
Barisitinib
İlk aşı onaylandı (mRNA)
Aralık 2020
Şubat 2021
Tocilizumab etkili (RECOVERY)
Bamlanivimav/Etesevimab
Sotrovimab
Mayıs 2021
Molnupiravir
Nirmatrelvir/ritonavir
Aralık 2021
Ocak 2022
Bamlanivimav/Etesevimab
Casirivimav/Imdevimab

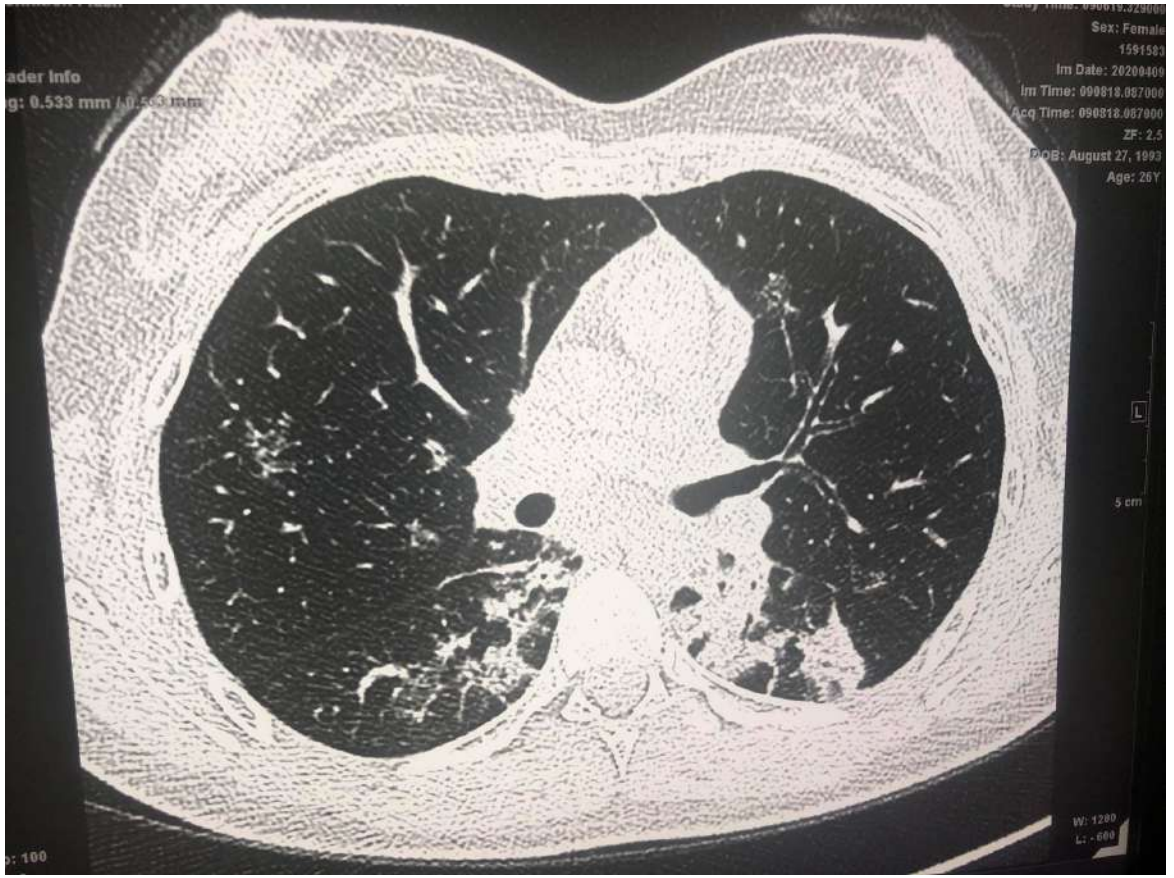
27 Mart 2020



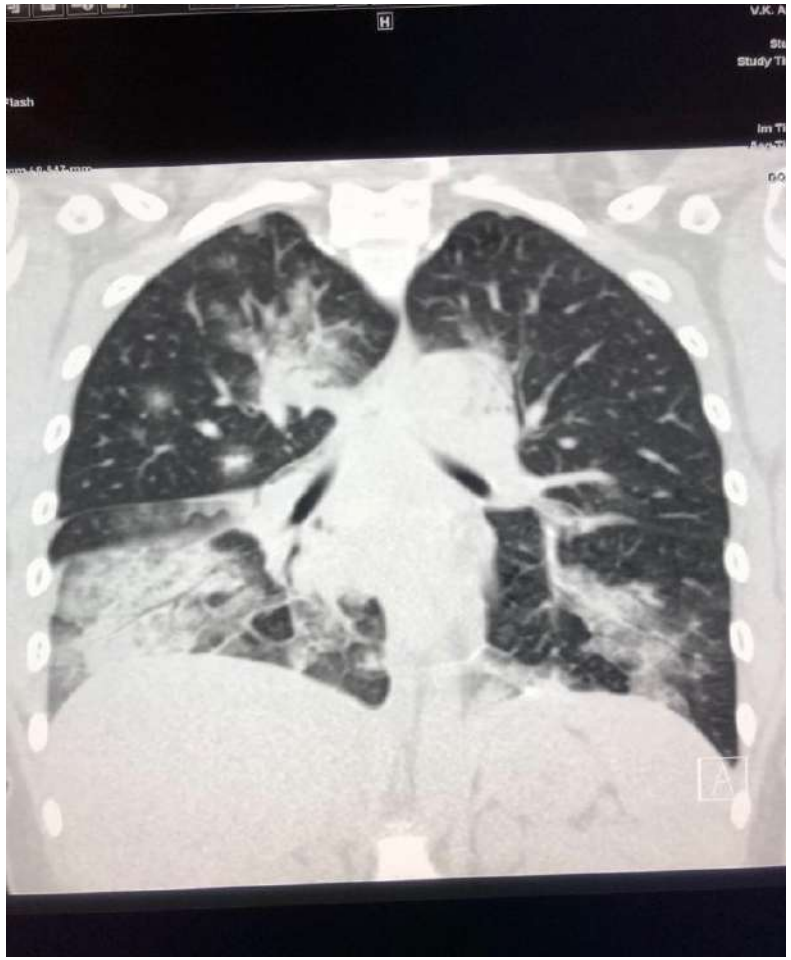
27 yaş kadın
Myastenia gravis



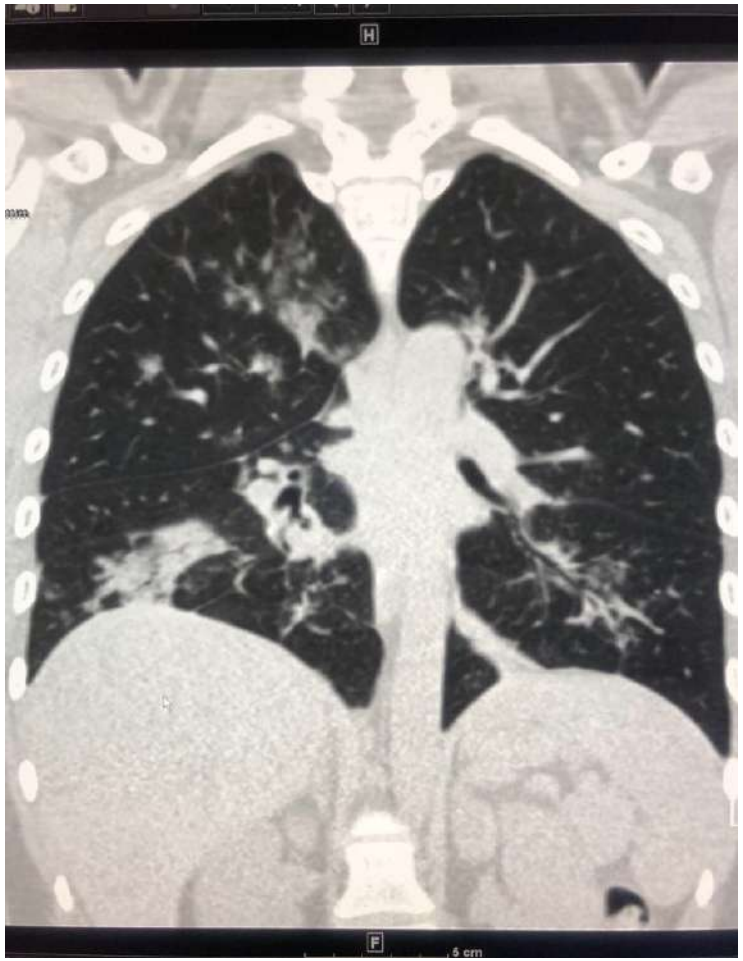
8th day of onset of symptom
Toci was started !! (31st March, 2020)



15th day of onset of symptom
7th day of Toci !!



8th day of onset of symptom
Tocilizumab was started !! (31st March, 2020)



15th day of onset of symptom
7th day of Tocilizumab !!

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Appropriate use of tocilizumab in COVID-19 infection

Şiran Keske[a], Süda Tekin[b], Bilgin Sait[c], Pelin İrkören[b], Mahir Kapmaz[b], Cansu Çimen[a], Semra Uğur[d], İrfan Çelebi[h], Veli Oğuzalp Bakır[e], Erhan Palaoğlu[f], Evren Şentürk[d], Benan Çağlayan[g], Nahit Çakar[d], Levent Tabak[g], Önder Ergönül[b,*]

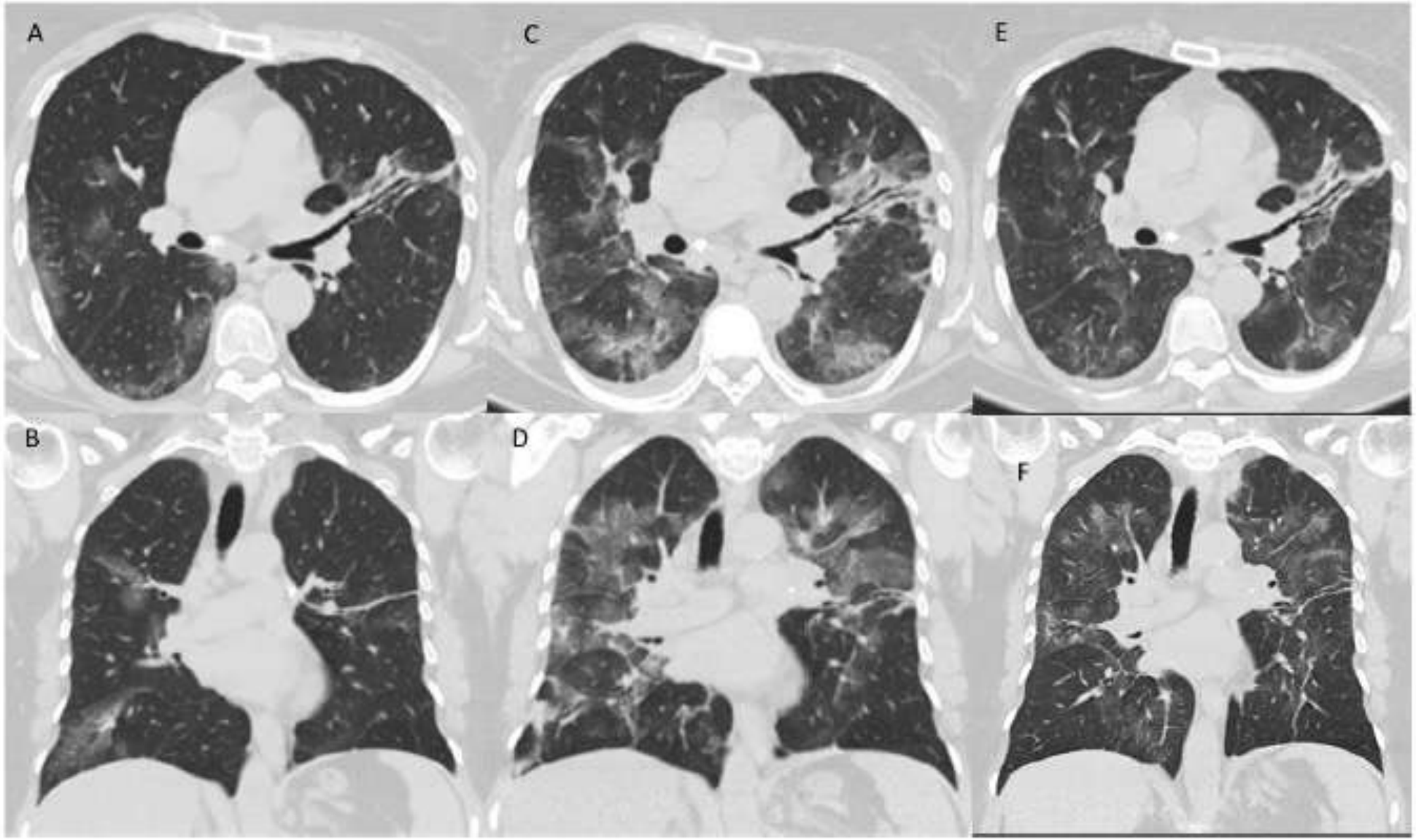


Figure 3. A 59-year-old woman with Covid-19. Same level of mid-axial (A, C and E) and mid-coronal (B, D and F) chest CT scans on admission (A–B), on the day of tocilizumab given because of requirement of oxygen support and progressive lung imaging (C–D) and 7 days after onset of tocilizumab (E–F), retrospectively.
A–B: Focal peripheral ground-glass opacities. The left upper lobe lesions were accompanied by consolidation with bronchiectasis.

Araştırma sonucu

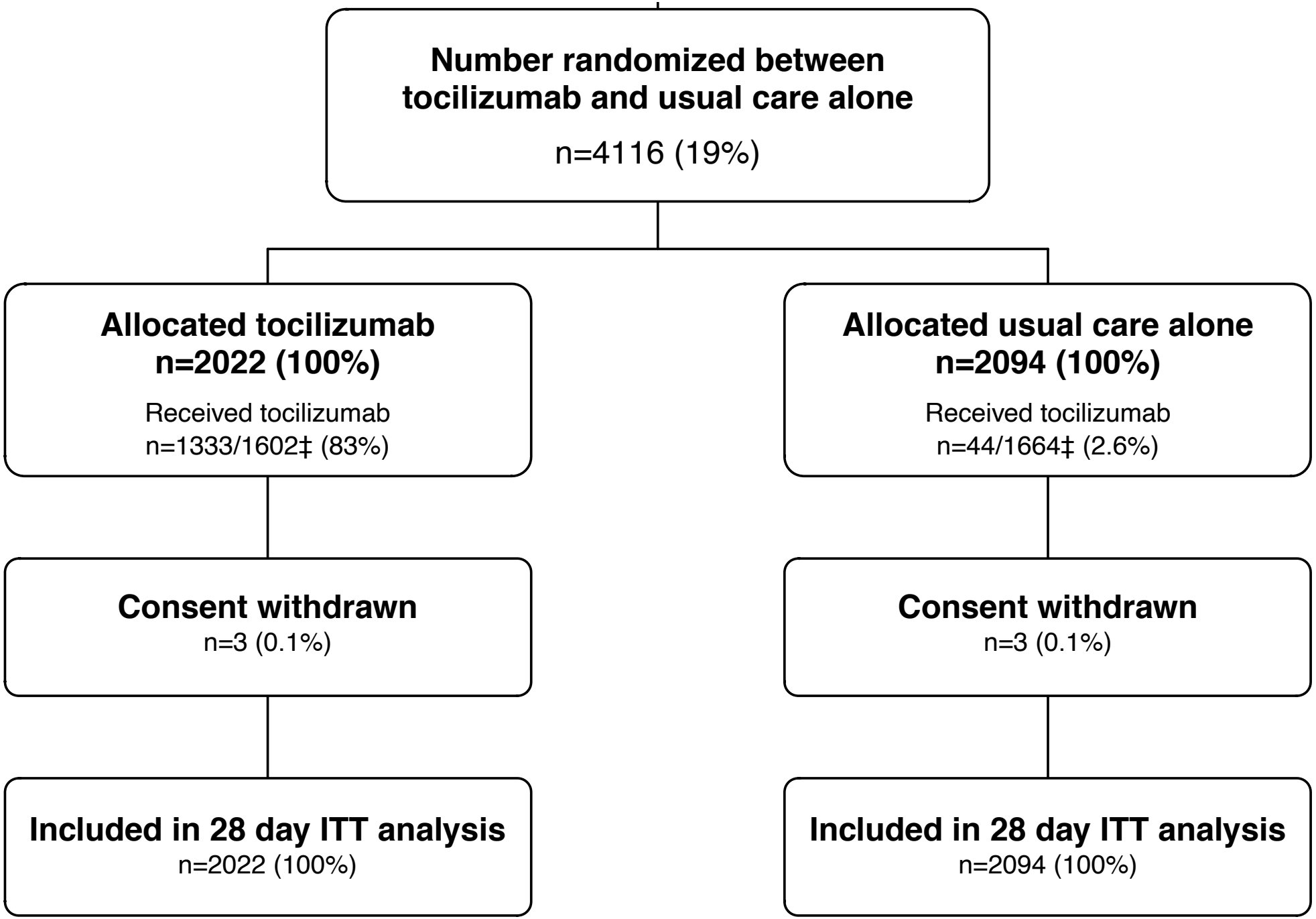
In conclusion, earlier use of TCZ in COVID-19 infection was beneficial for survival, length of hospitalization and duration of oxygen support. This recommendation for the administration of TCZ was based on the increase in requirement of oxygen support, progression of thoracic CT, and elevation of inflammation markers including IL-6, CRP, ferritin, D-dimer, and decrease in % lymphocytes. Secondary bacterial infections should be borne in mind after TCZ use.

Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial

Running title: Tocilizumab for COVID-19

RECOVERY Collaborative Group*

11 Feb 2021


Number randomized between tocilizumab and usual care alone
n=4116 (19%)
Allocated tocilizumab n=2022 (100%)
Received tocilizumab n=1333/1602‡ (83%)
Allocated usual care alone n=2094 (100%)
Received tocilizumab n=44/1664‡ (2.6%)
Consent withdrawn
n=3 (0.1%)
Consent withdrawn
n=3 (0.1%)
Included in 28 day ITT analysis
n=2022 (100%)
Included in 28 day ITT analysis
n=2094 (100%)

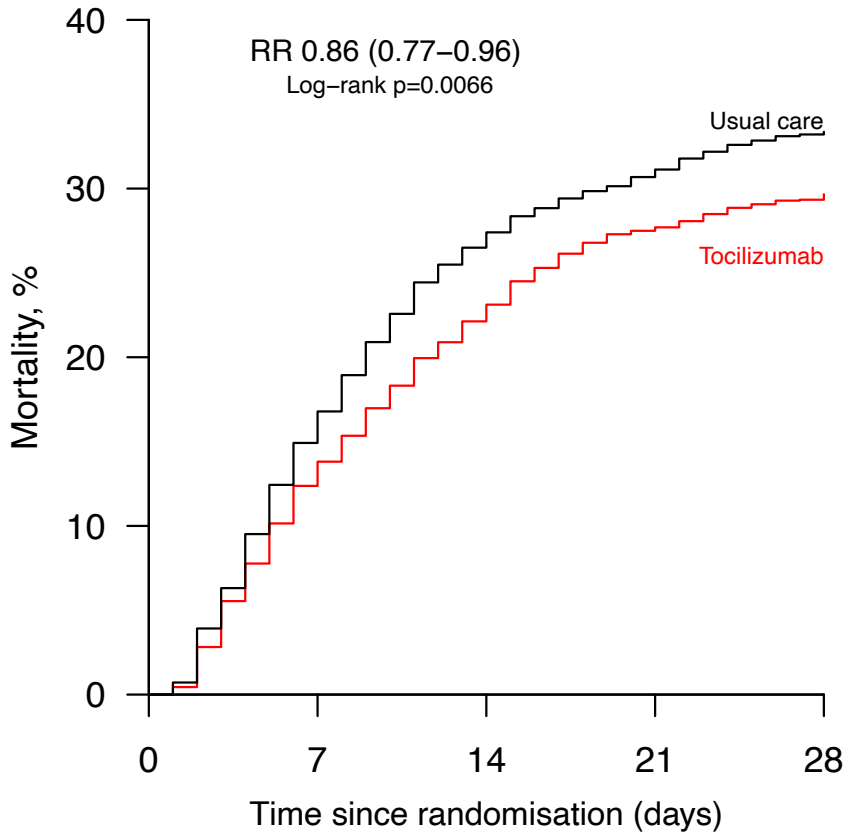
	Tocilizumab (n=2022)	Usual care (n=2094)
Part A allocation		
Usual care	839 (41%)	869 (41%)
Lopinavir/ritonavir	51 (3%)	64 (3%)
Dexamethasone	49 (2%)	45 (2%)
Hydroxychloroquine	37 (2%)	38 (2%)
Azithromycin	197 (10%)	177 (8%)
Use of systemic corticosteroids^		
Yes	1664 (82%)	1721 (82%)
No	357 (18%)	367 (18%)
Unknown	1 (<1%)	6 (<1%)

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

	Treatment allocation			
	Tocilizumab (n=2022)	Usual care (n=2094)	RR (95% CI)	p value
Primary outcome				
Total: 28-day mortality	596 (29%)	694 (33%)	0.86 (0.77-0.96)	0.0066
Secondary outcomes				
Median time to being discharged alive, days	20	>28		
Discharged alive from hospital within 28 days	1093 (54%)	990 (47%)	1.22 (1.12-1.34)	<0.0001
Receipt of invasive mechanical ventilation or death*	571/1754 (33%)	687/1800 (38%)	0.85 (0.78-0.93)	0.0005
Invasive mechanical ventilation	215/1754 (12%)	273/1800 (15%)	0.81 (0.68-0.95)	0.01
Death	471/1754 (27%)	552/1800 (31%)	0.88 (0.79-0.97)	0.01
Subsidiary clinical outcomes				
Receipt of ventilation†	233/935 (25%)	242/933 (26%)	0.96 (0.82-1.12)	0.61
Non-invasive ventilation	222/935 (24%)	223/933 (24%)	0.99 (0.84-1.17)	0.94
Invasive mechanical ventilation	45/935 (5%)	63/933 (7%)	0.71 (0.49-1.03)	0.07
Successful cessation of invasive mechanical ventilation‡	91/268 (34%)	94/294 (32%)	1.07 (0.80-1.43)	0.64
Use of haemodialysis or haemofiltration§	103/2003 (5%)	142/2075 (7%)	0.75 (0.59-0.96)	0.02

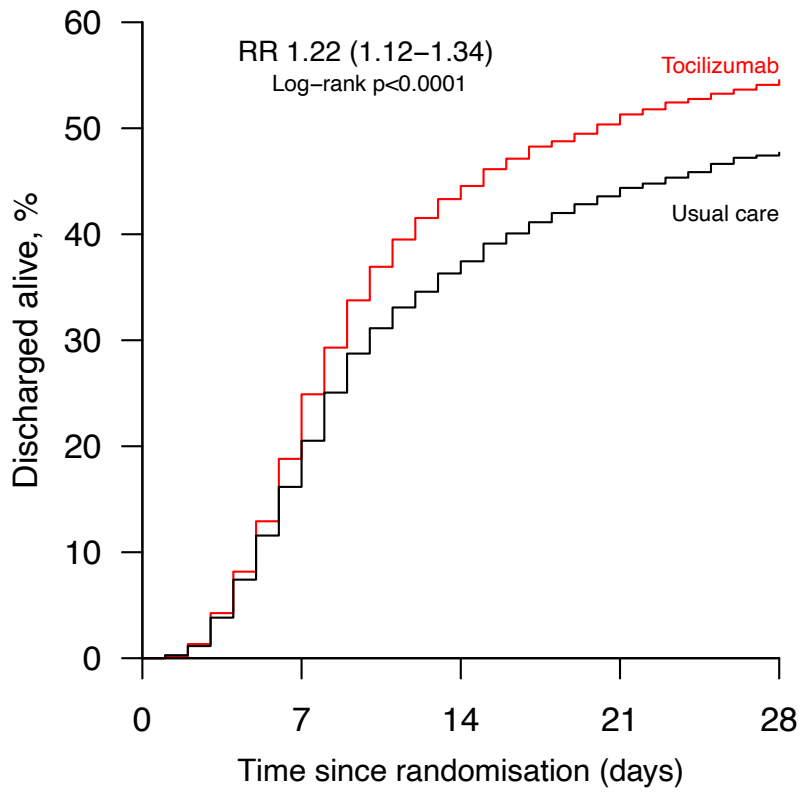
Data are n(%), n/N (%), or median (interquartile range). RR=rate ratio for the outcomes of 28-day mortality, hospital discharge and successful cessation of invasive mechanical ventilation, and risk ratio for other outcomes. * Analyses include only those on no ventilator support or non-invasive ventilation at second randomisation. † Analyses include only those on no ventilator support at second randomisation. ‡ Analyses restricted to those on invasive mechanical ventilation at second randomisation. § Analyses exclude those on haemodialysis or haemofiltration at second randomisation.

(a)



Number at risk					
Active	2022	1741	1553	1386	1284
Control	2094	1740	1518	1372	1250

(b)

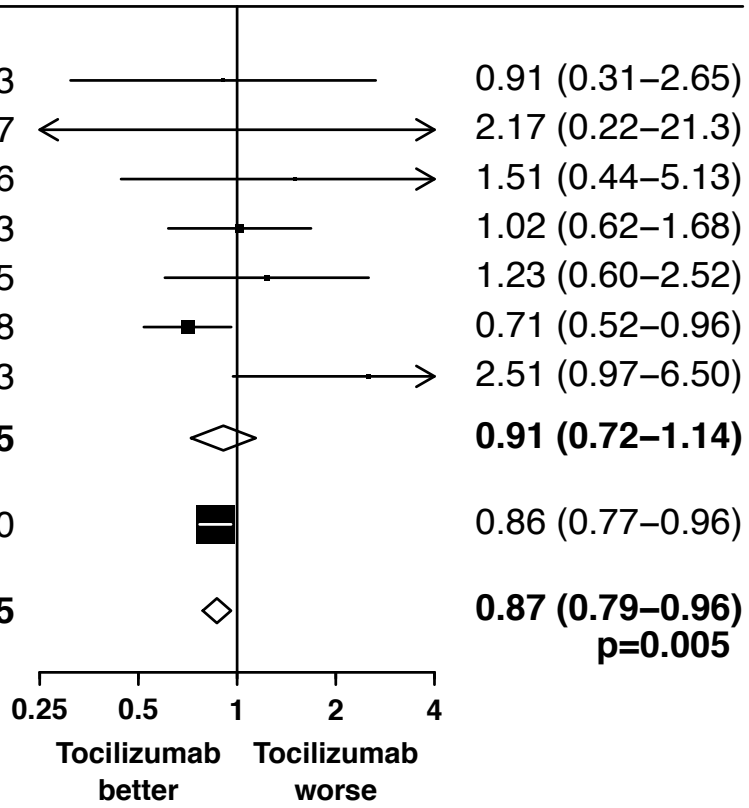


Number at risk					
Active	2022	1517	1120	911	787
Control	2094	1662	1308	1096	954

Figure 4: Tocilizumab vs usual care in patients hospitalised with COVID – Meta–analysis of mortality in RECOVERY and other trials

	Deaths / Patients randomised (%)		Observed–Expected		Ratio of death rates, RR (95% CI)
	Tocilizumab	Usual care	(O–E)*	Var(O–E)	
COR–IMUNO TOCI	7/64 (10.9)	8/67 (11.9)	–0.3	3.3	0.91 (0.31–2.65)
RCT–TCZ–COVID–19	2/60 (3.3)	1/66 (1.5)	0.6	0.7	2.17 (0.22–21.3)
BACC Bay	9/161 (5.6)	(3/82) x2† (3.7)	1.0	2.6	1.51 (0.44–5.13)
COVACTA	58/294 (19.7)	(28/144) x2† (19.4)	0.3	15.3	1.02 (0.62–1.68)
EMPACTA	26/249 (10.4)	(11/128) x2† (8.6)	1.6	7.5	1.23 (0.60–2.52)
REMAP–CAP	98/353 (27.8)	142/402 (35.3)	–14.2	40.8	0.71 (0.52–0.96)
TOCIBRAS	14/65 (21.5)	6/64 (9.4)	3.9	4.3	2.51 (0.97–6.50)
Subtotal: 7 trials	**214/1246 (17.2)**	**241/1307 (18.4)**	**–7.2**	**74.5**	**0.91 (0.72–1.14)**
RECOVERY	596/2022 (29.5)	694/2094 (33.1)	–48.2	316.0	0.86 (0.77–0.96)
All trials	**810/3268 (24.8)**	**935/3401 (27.5)**	**–55.4**	**390.5**	**0.87 (0.79–0.96) p=0.005**

Heterogeneity between RECOVERY and previous trials: χ^2_1=0.2



* Log–rank O–E for RECOVERY, O–E from 2x2 tables for the other trials. RR is calculated by taking ln RR to be (O–E)/V with Normal variance 1/V. Subtotals or totals of (O–E) and of V yield inverse–variance–weighted averages of the ln RR values.

† For balance, controls in the 2:1 studies count twice in the control totals and subtotals.

JAMA Network Open

Original Investigation | Critical Care Medicine

Mortality Rates Among Hospitalized Patients With COVID-19 Infection Treated With Tocilizumab and Corticosteroids

A Bayesian Reanalysis of a Previous Meta-analysis

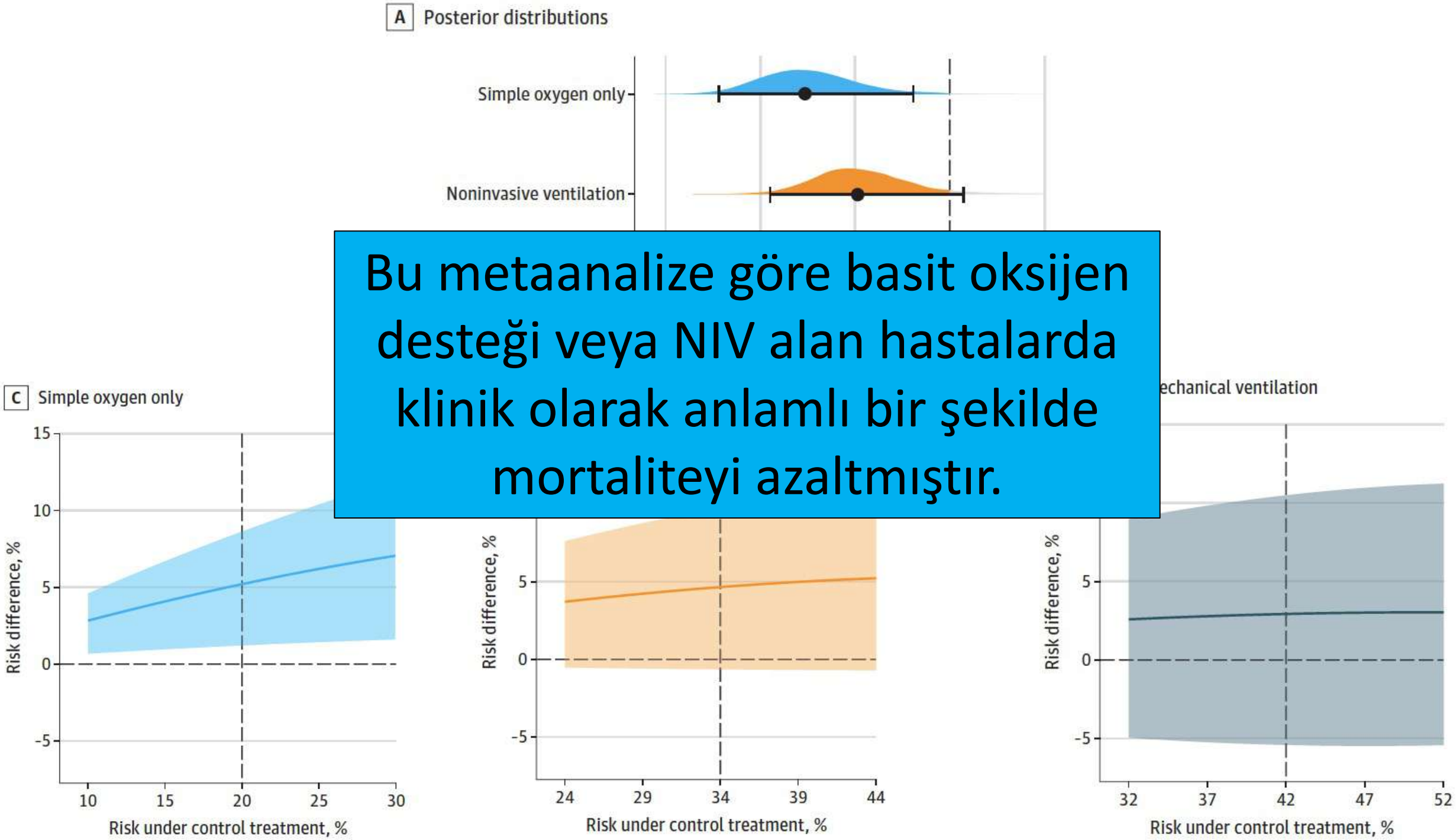
Arthur M. Albuquerque; Lucas Tramujas, MD; Lorenzo R. Sewanan, MD, PhD; Donald R. Williams, BA; James M. Brophy, MD, PhD

15 RKÇ dahil edilmiş

Sadece steroid alanlar dahil edilmiş

- 5339 hasta
  - 2117 basit oksijen desteği
  - 2505 NIV
  - 717 IMV

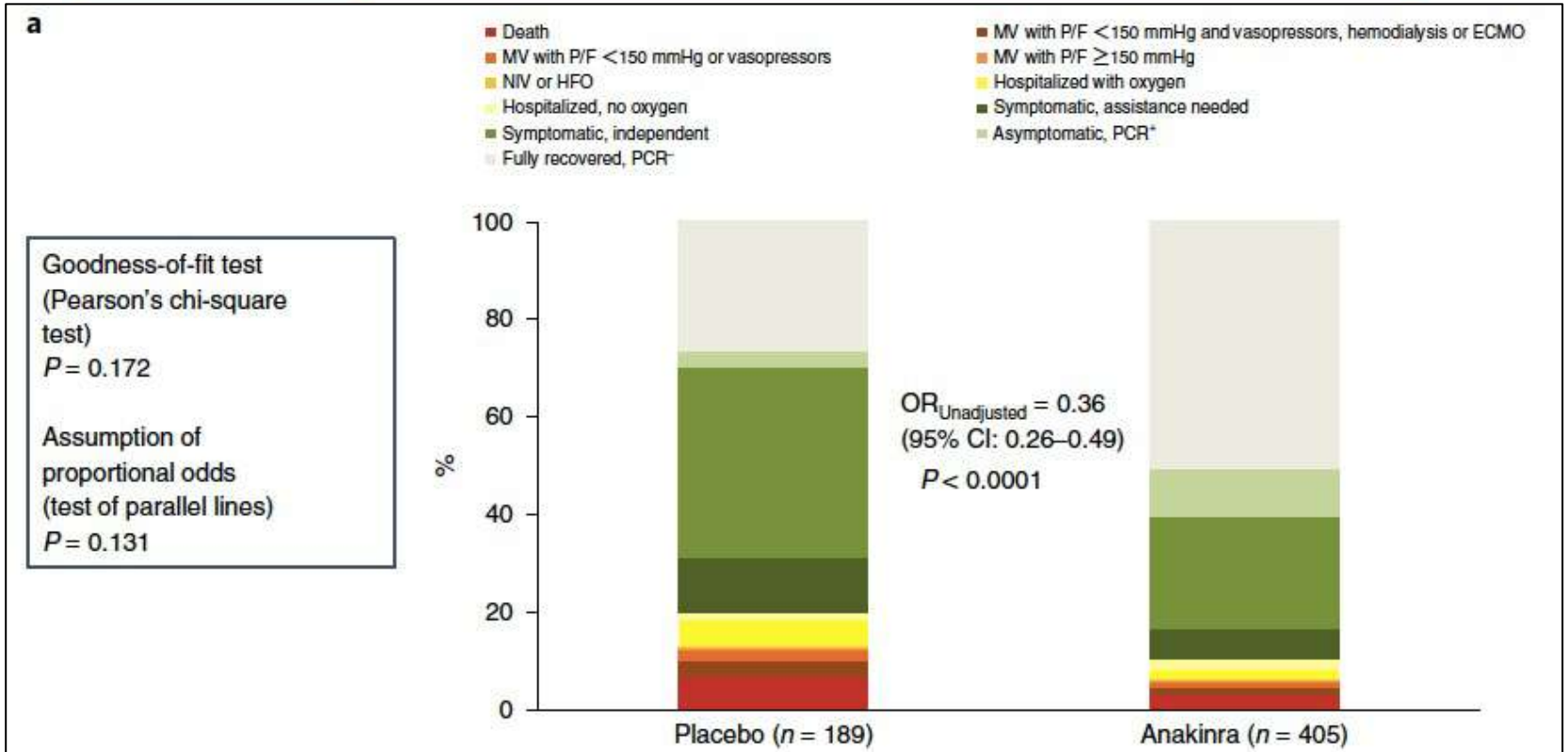
28 Şubat 2022



Bu metaanalize göre basit oksijen desteği veya NIV alan hastalarda klinik olarak anlamlı bir şekilde mortaliteyi azaltmıştır.

ANAKINRA

a



b

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Group of treatment (Anakinra vs placebo)	0.36	0.26–0.49	<0.0001	0.36	0.26–0.50	<0.0001
Intake of dexamethasone (Yes/No)	1.90	1.28–2.83	0.002	1.49	0.59–3.80	0.395
Severe COVID-19 by WHO (Yes/No)	1.95	1.31–2.90	0.001	1.29	0.51–3.27	0.582
BMI >30 kg m^{-2} (Yes/No)	1.27	0.87–1.61	0.267	1.10	0.81–1.50	0.530
Country (Italy vs Greece)	1.18	0.74–1.88	0.482	1.25	0.77–2.03	0.350

	Anakinra		Control		Weight	Odds ratio (95% CI)
	Events	Total	Events	Total		
Balkhair et al (2021)[30]	13	45	11	24	8·0%	0·48 (0·17–1·34)
Bozzi et al (2021)[25]	9	65	19	55	13·9%	0·30 (0·12–0·75)
Cauchois et al (2020)[22]	0	12	1	10	0·9%	0·07 (0·00–46·88)
Cavalli et al (2021)[26]	3	62	62	275	17·0%	0·17 (0·05–0·58)
Huet et al (2020)[23]	7	52	19	44	13·9%	0·20 (0·08–0·55)
Kooistra et al (2020)[28]	4	21	7	39	3·1%	1·08 (0·28–4·20)
Kyriazopoulou et al (2021)[29]	15	130	29	130	20·1%	0·45 (0·23–0·90)
The CORIMUNO-19 Collaborative group (2021)[24]	13	59	13	55	8·2%	0·91 (0·38–2·19)
Pontali et al (2021)[27]	9	63	19	44	15·0%	0·22 (0·09–0·55)
Total (95% CI)		**509**		**676**	**100·0%**	**0·37 (0·27– 0·51)**

Heterogeneity: τ^2= 0·2966; χ^2=11·52, df=8 (p=0·17); I^2=31%

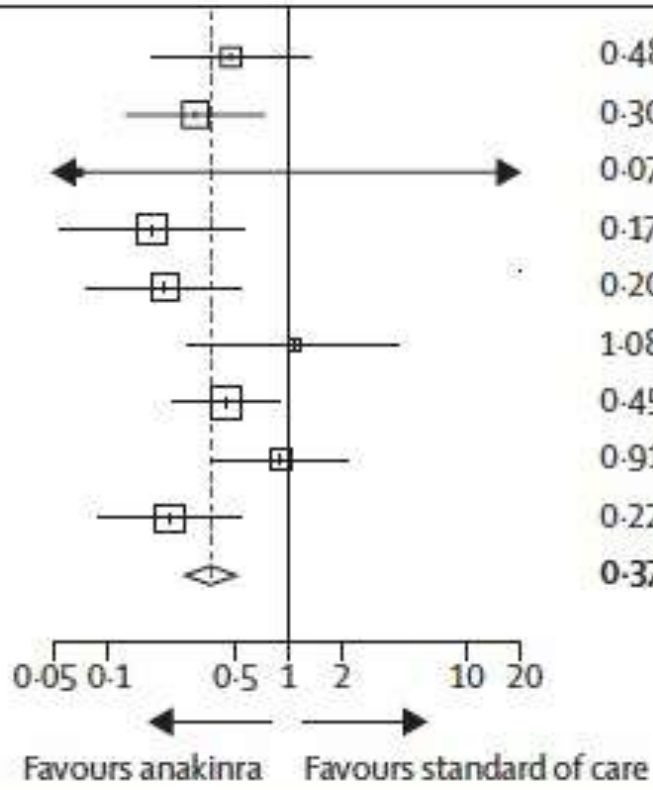


Figure 2: **Forest plot showing mortality from aggregate data meta-analysis**
Odds ratios calculated with a fixed-effects Mantel-Haenszel test.

Effect of anakinra on mortality in patients with COVID-19: a systematic review and patient-level meta-analysis
Lancet Rhemotology. August 9, 2021

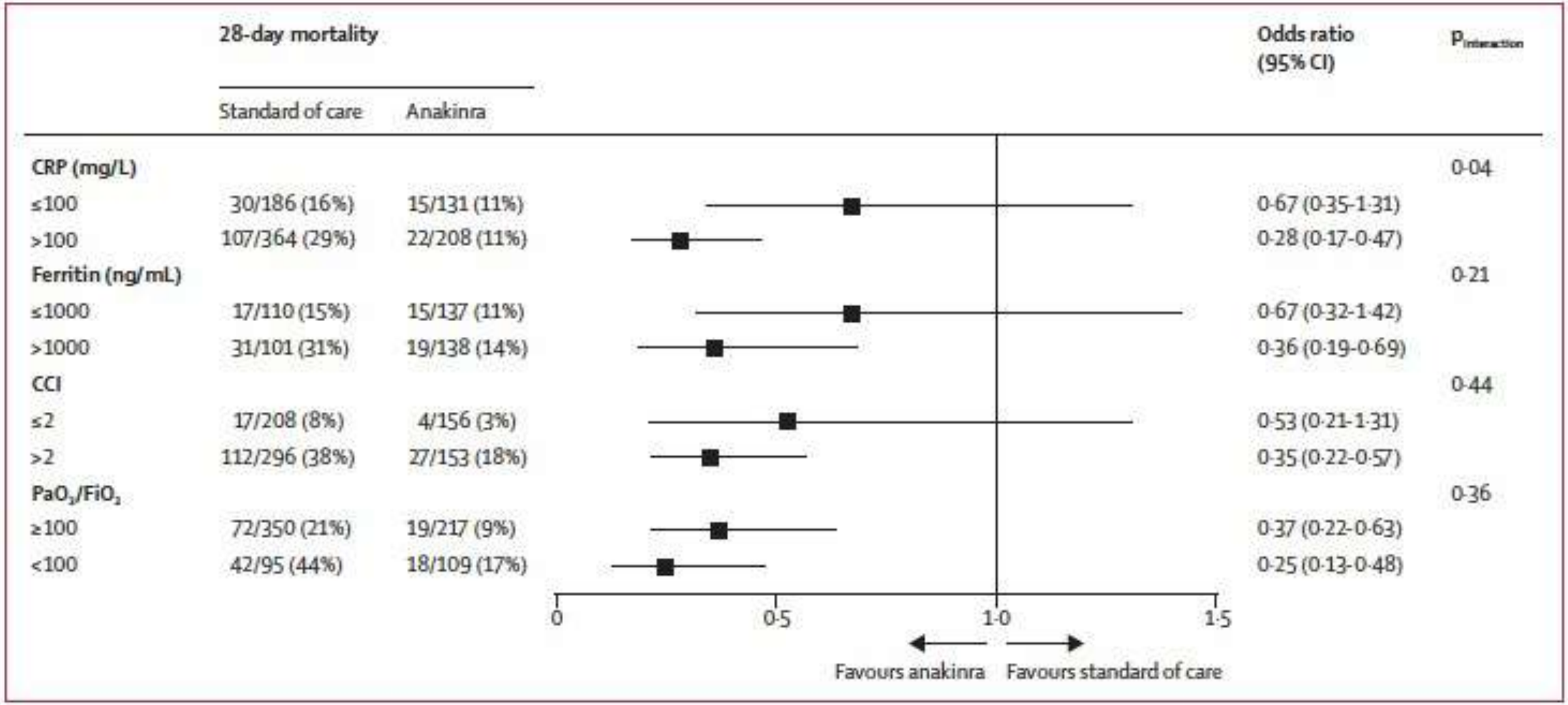


***Figure 3*: Subgroup analysis of mortality in patients treated with anakinra versus those treated with standard of care**

p values of the interaction effect of the treatment on mortality, in each subgroup and among the studies are provided. CRP=C-reactive protein. CCI=Charlson comorbidity index. PaO_2/FiO_2=ratio of the arterial partial oxygen pressure divided by the fraction of inspired oxygen.

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Anakinra treatment	0·38 (0·26–0·56)	<0·0001	0·32 (0·20–0·51)	<0·0001
Age >72 years*	4·97 (3·5–7·06)	<0·0001	1·89 (1·12–3·20)	0·018
Charlson comorbidity index >2*	6·35 (4·01–10·06)	<0·0001	3·75 (1·99–7·07)	<0·0001
PaO_2/FiO_2 <100	2·18 (1·50–3·17)	<0·0001	2·89 (1·80–4·64)	<0·0001
CRP >100 mg/L	1·76 (1·21–2·55)	0·003	1·21 (0·76–1·92)	0·42
Lymphopenia (<580 lymphocytes per mm^3)*	3·08 (2·12–4·49)	<0·0001	3·05 (1·90–4·89)	<0·0001
Study	..	0·15	..	..

CRP=C-reactive protein. PaO_2/FiO_2=ratio of the arterial partial oxygen pressure divided by the fraction of inspired oxygen. *For continuous variables, the best cutoff was estimated from the receiver operating characteristic using the Youden Index.

***Table 2:* Univariate and multivariate logistic regression analysis of variables associated with mortality in the individual patient-level data analysis of 895 patients**

Effect of anakinra on mortality in patients with COVID-19: a systematic review and patient-level meta-analysis
Lancet Rhemotology. August 9, 2021

RHEUMATOLOGY

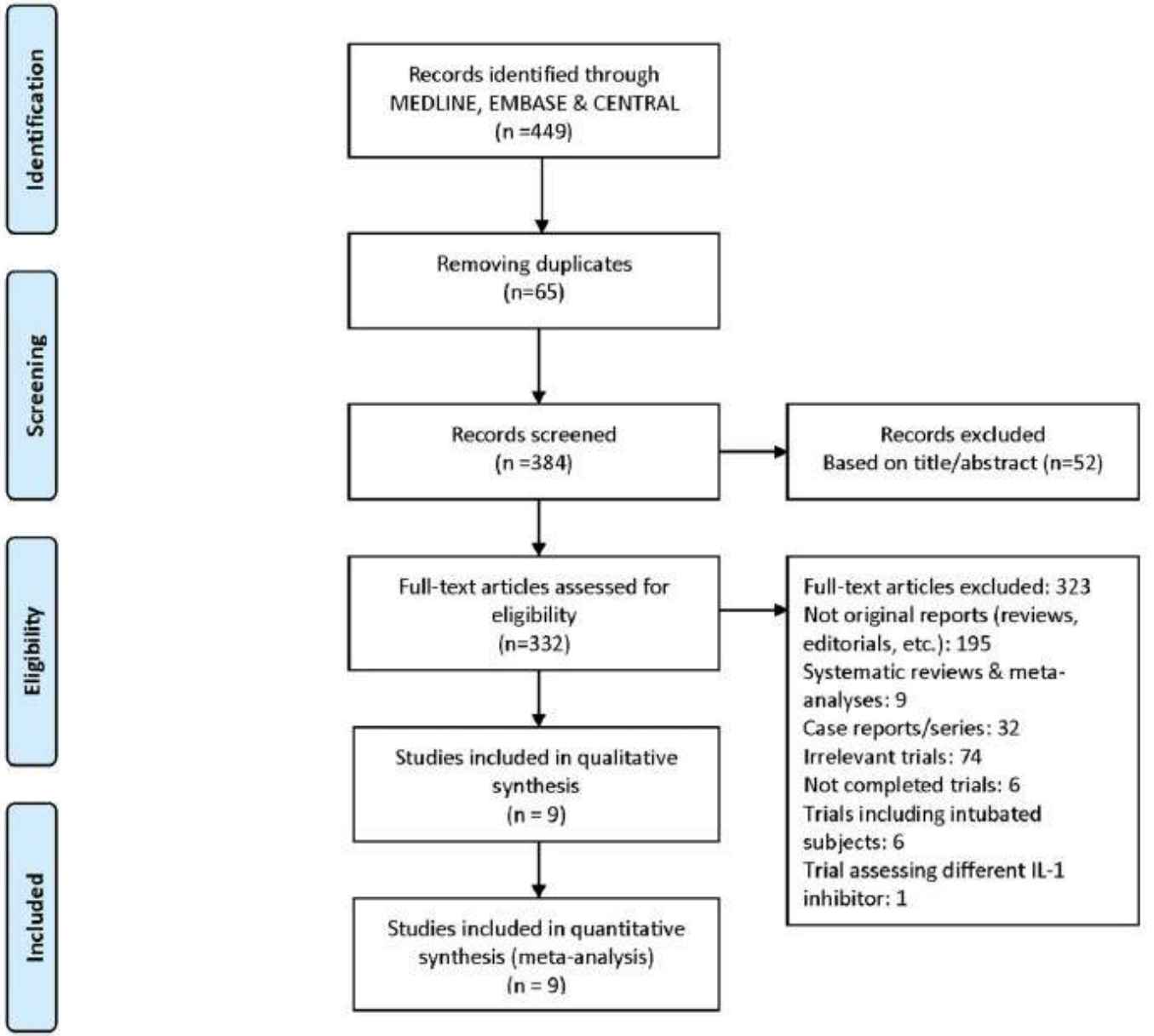
Rheumatology 2021;60:5527–5537
doi:10.1093/rheumatology/keab447
Advance Access publication 17 May 2021

Systematic review and meta analysis

Anakinra in hospitalized non-intubated patients with coronavirus disease 2019: a Systematic review and meta-analysis

Fotios Barkas[1], Sebastian Filippas-Ntekouan[1], Maria Kosmidou[1], Evangelos Liberopoulos[1], Angelos Liontos[1] and Haralampos Milionis[1]

FIG. 1 PRISMA flowchart of study selection



PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Rheumatology (Oxford). 2021 Dec 1;60(12):5527-37

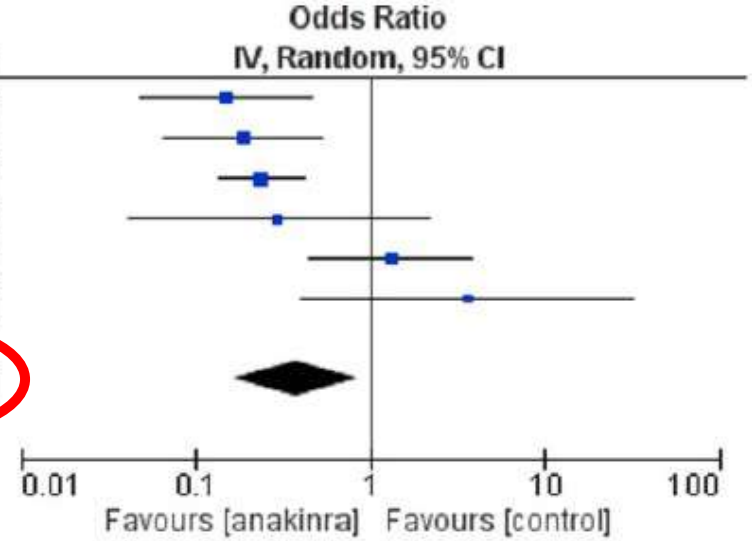
FIG. 2 Forest plot for the need for invasive mechanical ventilation (**A**) and mortality risk (**B**)

A

Study or Subgroup	Anakinra Events	Anakinra Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI
Balkhair et al.	14	45	18	24	18.1%	0.15 [0.05, 0.46]
Huet et al.	6	52	18	44	19.0%	0.19 [0.07, 0.53]
Kyriazopoulou et al.	25	130	65	130	24.5%	0.24 [0.14, 0.41]
Cauchois et al.	2	12	4	10	10.5%	0.30 [0.04, 2.16]
Franzetti et al.	9	42	8	46	18.8%	1.30 [0.45, 3.74]
Cavalli et al. 2020	7	36	1	16	9.2%	3.62 [0.41, 32.22]
Total (95% CI)		**317**		**270**	**100.0%**	**0.38 [0.17, 0.85]**
Total events	63		114			

Heterogeneity: $Tau^2 = 0.62$; $Chi^2 = 15.18$, $df = 5$ ($P = 0.010$); $I^2 = 67\%$

Test for overall effect: $Z = 2.34$ ($P = 0.02$)

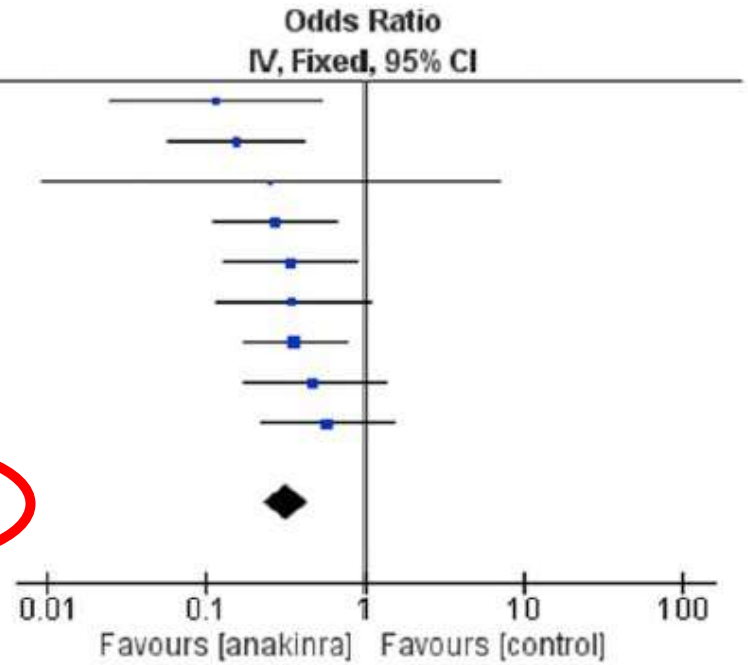


B

Study or Subgroup	Anakinra Events	Anakinra Total	Control Events	Control Total	Weight	Odds Ratio IV, Fixed, 95% CI
Cavalli et al. 2020	3	36	7	16	5.0%	0.12 [0.03, 0.55]
Huet et al.	7	52	22	44	12.0%	0.16 [0.06, 0.42]
Cauchois et al.	0	12	1	10	1.1%	0.25 [0.01, 6.94]
Franzetti et al.	11	42	26	46	14.6%	0.27 [0.11, 0.67]
Kyriazopoulou et al.	6	130	16	130	12.5%	0.34 [0.13, 0.91]
Bozzi et al.	6	47	10	34	9.3%	0.35 [0.11, 1.09]
Cavalli et al. 2021	9	62	88	275	21.0%	0.36 [0.17, 0.76]
Balkhair et al.	13	45	11	24	11.2%	0.48 [0.17, 1.34]
Tharaux et al. 2021	9	59	13	55	13.3%	0.58 [0.23, 1.49]
Total (95% CI)		**485**		**634**	**100.0%**	**0.32 [0.23, 0.45]**
Total events	64		194			

Heterogeneity: $Chi^2 = 6.10$, $df = 8$ ($P = 0.64$); $I^2 = 0\%$

Test for overall effect: $Z = 6.46$ ($P < 0.00001$)



Özetle Anakinra

COVID-19'da etkinliğini gösteren az sayıda çalışma var

- Çalışmalarda kullanılan dozlar çok farklı
  - 3x200
    - 7 & 14 gün
  - 2x100 (7 gün)

Çalışma sayısı daha az.

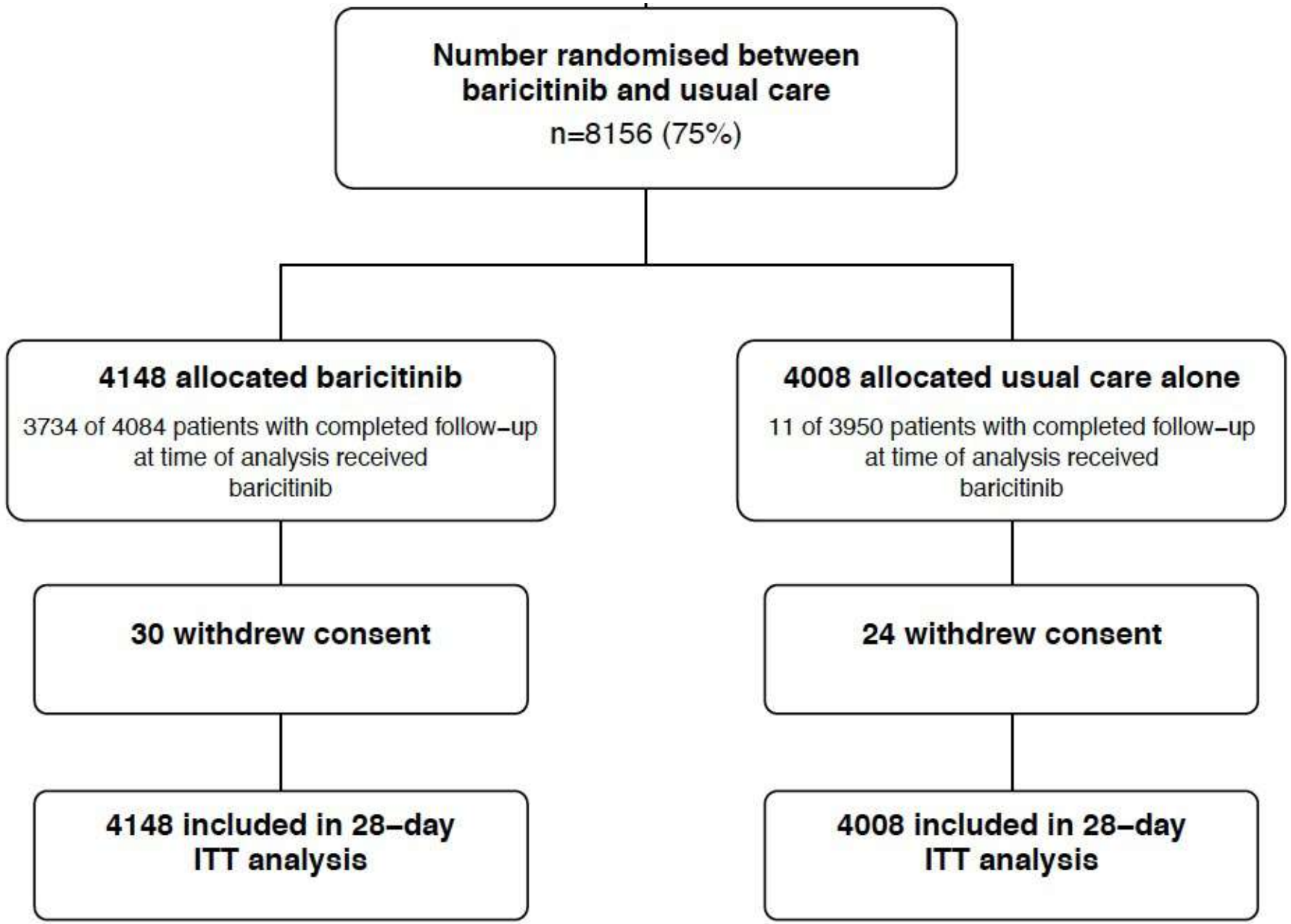
Rehberlerde yer bulamadı

JAK Inhibitörleri

Baricitinib in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial and updated meta-analysis

Running title: Baricitinib for COVID-19

RECOVERY Collaborative Group*


Number randomised between baricitinib and usual care
n=8156 (75%)
4148 allocated baricitinib
3734 of 4084 patients with completed follow–up at time of analysis received baricitinib
4008 allocated usual care alone
11 of 3950 patients with completed follow–up at time of analysis received baricitinib
30 withdrew consent
24 withdrew consent
4148 included in 28–day ITT analysis
4008 included in 28–day ITT analysis

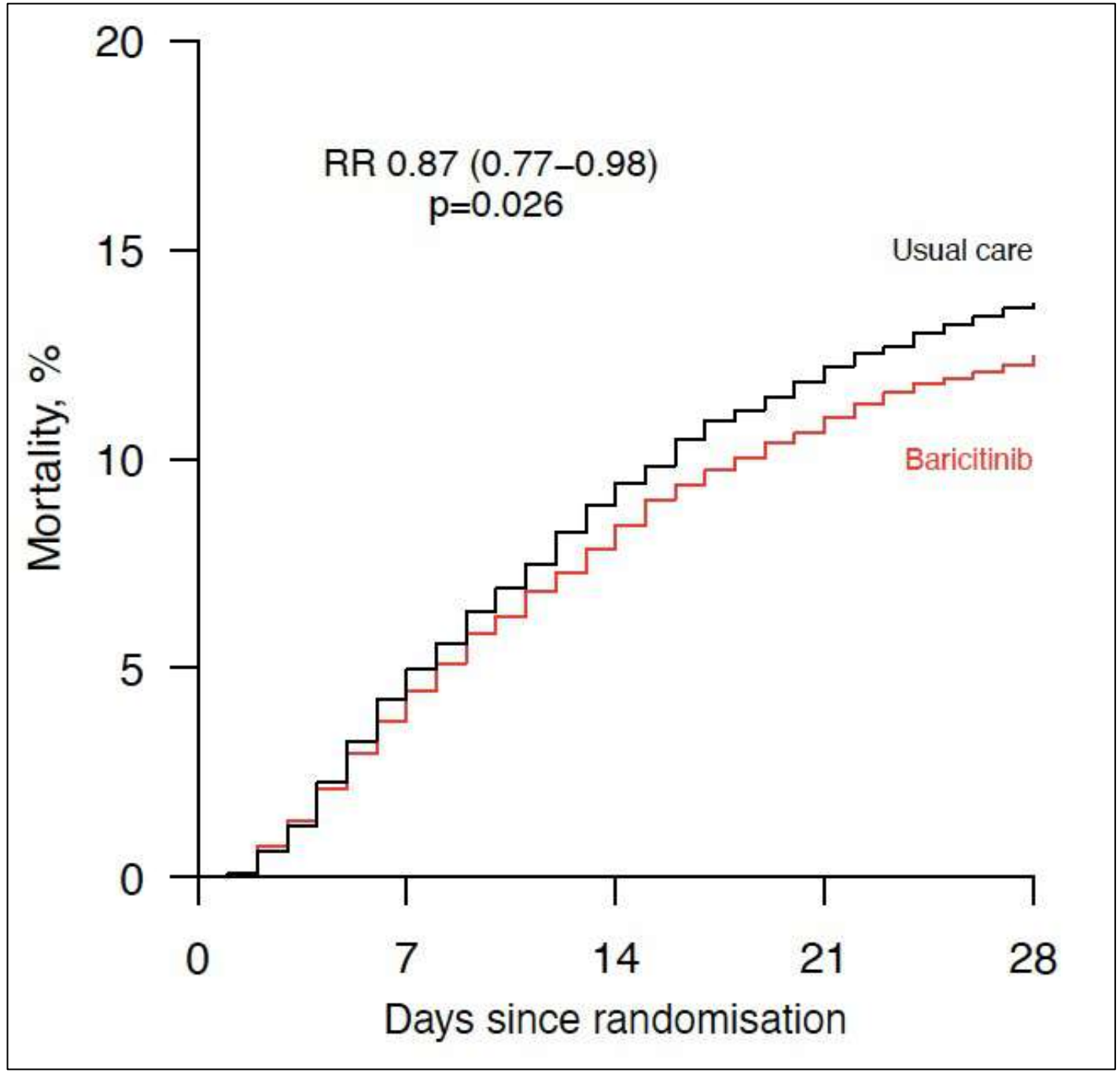
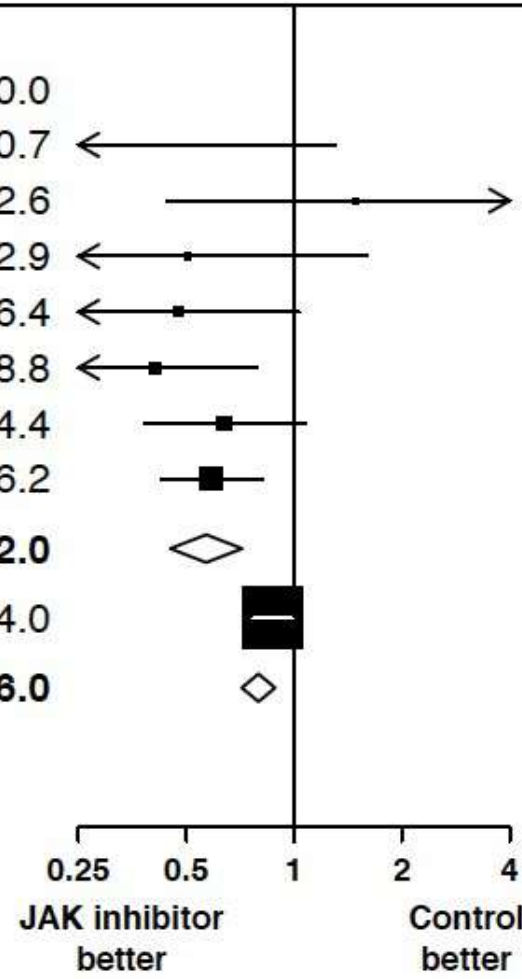

20
15
10
5
0
Mortality, %
RR 0.87 (0.77–0.98)
p=0.026
Usual care
Baricitinib
0
7
14
21
28
Days since randomisation

Figure 4: JAK inhibitor vs usual care in patients hospitalised with COVID – Meta–analysis of mortality in RECOVERY and other trials

	Deaths / Patients randomised (%)		Observed–Expected		Ratio of death rates, RR (95% CI)
	JAK inhibitor	Control	(O–E)*	Var(O–E)	
Murugesan***	0/50 (0%)	0/50 (0%)	0.0	0.0	
Cao et al.***	0/20 (0%)	3/21 (14%)	–1.5	0.7	0.13 (0.01–1.31)
RUXCOVID***	9/287 (3%)	(3/145) x2** (2%)	1.0	2.6	1.48 (0.44–4.99)
Guimarães et al.***	4/144 (3%)	8/145 (6%)	–2.0	2.9	0.50 (0.16–1.60)
COV–BARRIER (critically ill)	20/51 (39%)	29/50 (58%)	–4.7	6.4	0.47 (0.22–1.03)
RUXCOVID–DEVENT***	90/164 (55%)	(36/47) x4** (77%)	–7.9	8.8	0.41 (0.21–0.79)
ACTT2	24/515 (5%)	37/518 (7%)	–6.4	14.4	0.64 (0.38–1.07)
COV–BARRIER	62/764 (8%)	100/761 (13%)	–19.2	36.2	0.59 (0.43–0.82)
Subtotal: 8 trials	**209/1995 (10%)**	**327/2023 (16%)**	**–40.7**	**72.0**	**0.57 (0.45–0.72)**
RECOVERY	513/4148 (12%)	546/4008 (14%)	–36.2	264.0	0.87 (0.77–0.98)
All trials	**722/6143 (12%)**	**873/6031 (14%)**	**–76.9**	**336.0**	**0.80 (0.71–0.89) p<0.001**

Heterogeneity between RECOVERY and previous trials: χ^2_1=10.3 (p=0.001)



Sorular

Antisitokinler için doğru zaman ne zaman?

CRP ya da diğer belirteçler için bir eşik değer olabilir mi?

Önce antisitokinler mi steroid mi ya da aynı anda mı?

İlaçların dozları süreleri nedir?

Anti-sitokinlerin yan etkileri?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

17 Temmuz, 2020

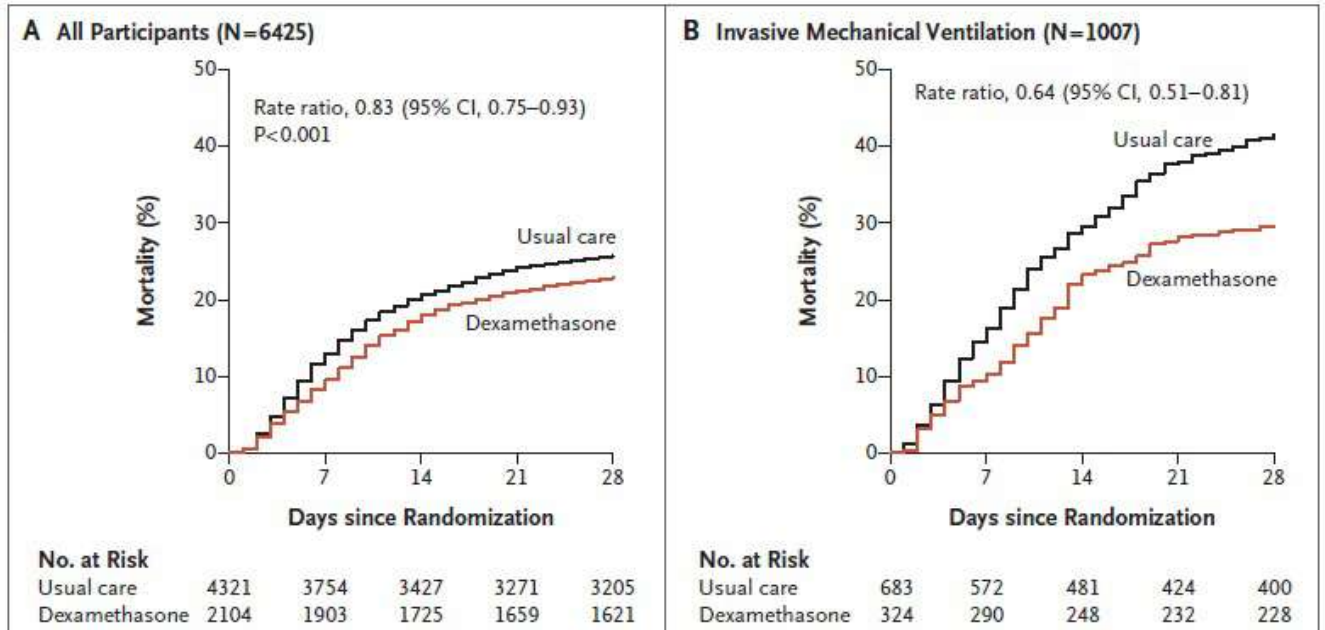


Figure 2. Mortality at 28 Days in All Patients and According to Respiratory Support at Randomization.

Respiratory Support at Randomization	Dexamethasone	Usual Care	Rate Ratio (95% CI)
	no. of events/total no. (%)		
Invasive mechanical ventilation	95/324 (29.3)	283/683 (41.4)	0.64 (0.51–0.81)
Oxygen only	298/1279 (23.3)	682/2604 (26.2)	0.82 (0.72–0.94)
No oxygen received	89/501 (17.8)	145/1034 (14.0)	1.19 (0.91–1.55)
All Patients	**482/2104 (22.9)**	**1110/4321 (25.7)**	**0.83 (0.75–0.93)**
			P<0.001

Chi-square trend across three categories: 11.5

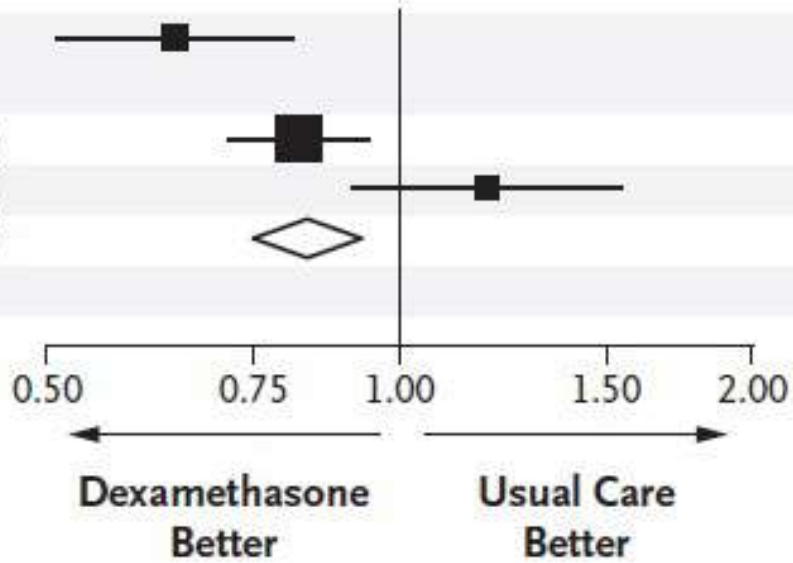


Figure 3. Effect of Dexamethasone on 28-Day Mortality, According to Respiratory Support at Randomization.

Shown are subgroup-specific rate ratios for all the patients and for those who were receiving no oxygen, receiving oxygen only, or undergoing invasive mechanical ventilation at the time of randomization. Rate ratios are plotted as squares, with the size of each square proportional to the amount of statistical information that was available; the horizontal lines represent 95% confidence intervals.

Pharmacological Reports
https://doi.org/10.1007/s43440-021-00341-0

ARTICLE

Comparing efficacy and safety of different doses of dexamethasone in the treatment of COVID-19: a three-arm randomized clinical trial

Negar Toroghi[1] · Ladan Abbasian[2] · Anahid Nourian[1] · Effat Davoudi-Monfared[1] · Hossein Khalili[1] · Malihe Hasannezhad[2] · Fereshteh Ghiasvand[2] · Sirous Jafari[2] · Hamid Emadi-Kouchak[2] · Mir Saeed Yekaninejad[3]

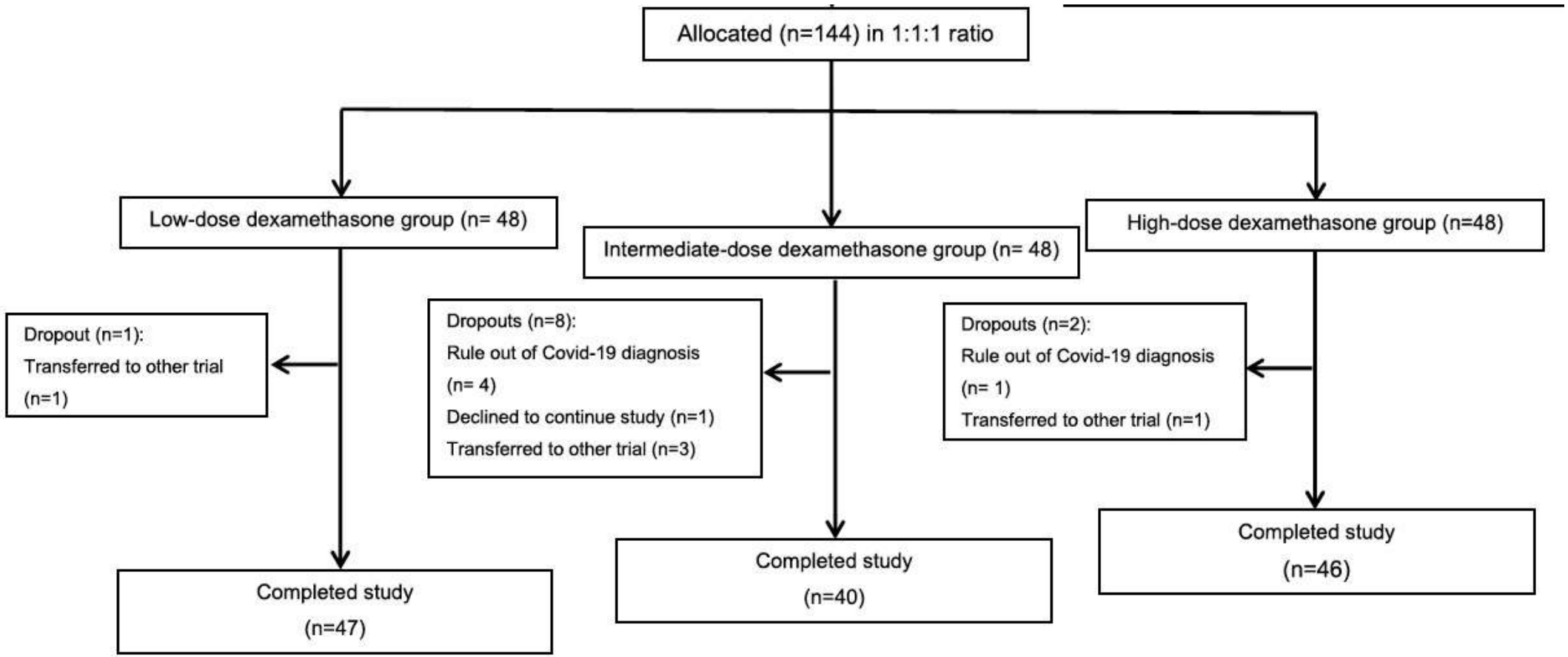
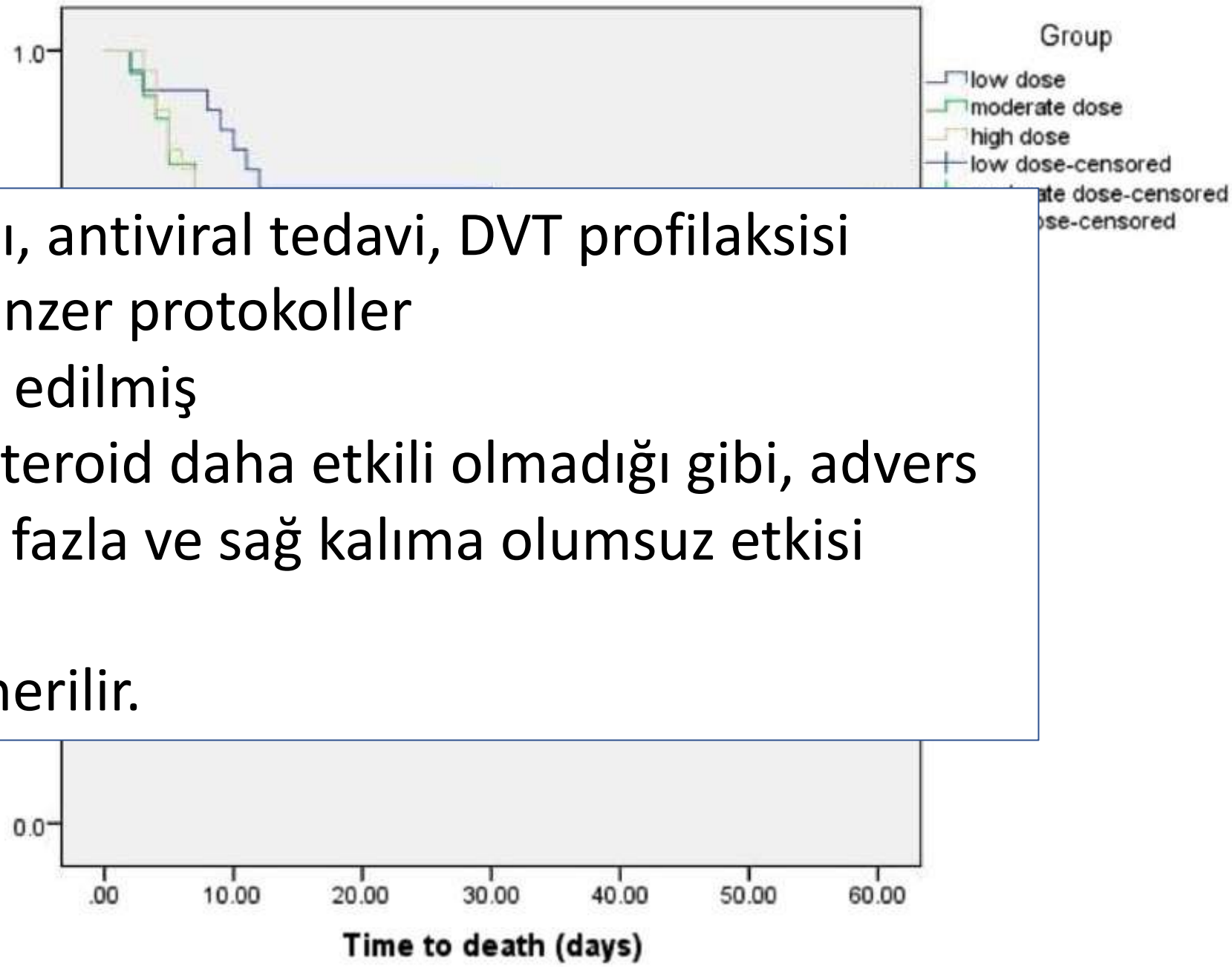


Fig. 2 Kaplan–Meier plot for survival time. In Kaplan–Meier plot, survival was significantly longer in the low-dose than the high-dose group $p=0.02$). However, this was
cally different betv
intermediate-dose
dose groups ($p=0$



- Sağlık bakımı, antiviral tedavi, DVT profilaksisi açısından benzer protokoller
- 60 gün takip edilmiş
- Yüksek doz steroid daha etkili olmadığı gibi, advers olaylar daha fazla ve sağ kalıma olumsuz etkisi olmuştur.
- 8 mg/gün önerilir.

EUROPEAN RESPIRATORY JOURNAL
RESEARCH LETTER
S. DHOORIA ET AL.

High-dose *versus* low-dose prednisolone in symptomatic patients with post-COVID-19 diffuse parenchymal lung abnormalities: an open-label, randomised trial (the COLDSTER trial)

We allocated subjects 1:1 by computer-generated simple randomisation (allocation concealment in consecutively numbered sealed opaque envelopes) to receive either high-dose prednisolone (40 $mg \cdot day^{-1}$ for 1 week, followed by 30 $mg \cdot day^{-1}$ for 1 week, 20 $mg \cdot day^{-1}$ for 2 weeks and 10 $mg \cdot day^{-1}$ for 2 weeks) or low-dose prednisolone (10 $mg \cdot day^{-1}$ for 6 weeks). We assessed the resting oxygen saturation, dyspnoea

In conclusion, we did not find high-dose prednisolone better than low-dose prednisolone in improving the clinical, radiological, physiological and HRQoL outcomes in PC-DPLAS. A placebo-controlled trial of glucocorticoids is required to better inform clinical practice for treating PC-DPLAS.

COVID-19'da Antikoagülan Kullanımı

Hasta özellikleri	Ayaktan	Yatan Servis (Hipoksik)	Süre	Yatan Yoğun Bakım Ünitesi
Gebe		Profilaktik DMAH		
Gebe olmayan	Önerilmez[1]	Tedavi Dozu[2] DMAH	14 gün veya taburcu edilene kadar	Profilaktik[3] DMAH

[1] -Taburculuk sonrası profilaktik AKA önerilmez.
-MICHELLE çalışması: Düşük doz rivaroksaban VTE riski olanlara verilsin.

[2] -D-dimer normalden yüksek
-Kanama riski yoksa *(PLT<50, Hb<8, son 30 günde kanama öyküsü, kanama diyatezi sorunu)*

[3] -Servisten yoğun bakım ünitesine geçenlerde profilaktik doza geçilmeli
-Orta doz ya da tam tedavi dozu ÖNERİLMEZ

NIH. 22 Şubat 2022

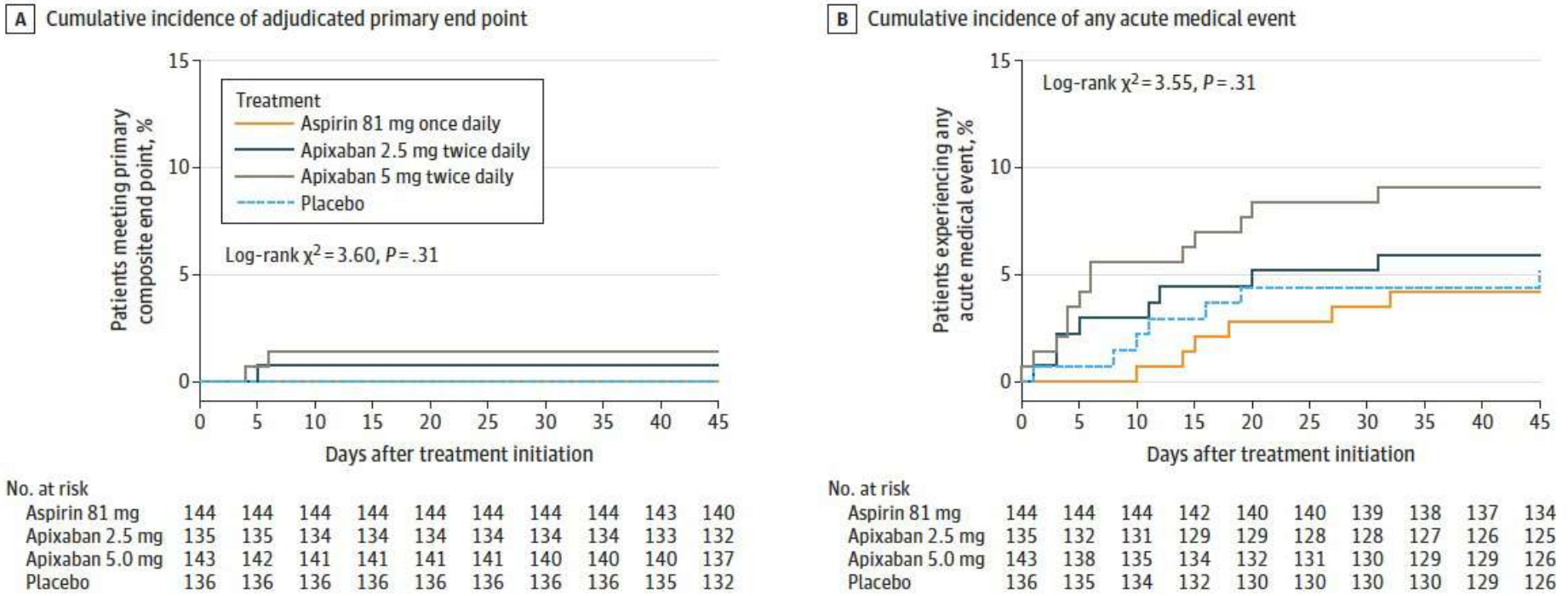
COVID-19'da Aspirin Kullanımı

JAMA | Original Investigation

Effect of Antithrombotic Therapy on Clinical Outcomes in Outpatients With Clinically Stable Symptomatic COVID-19

The ACTIV-4B Randomized Clinical Trial

Figure 2. Cumulative Incidence of the Adjudicated Primary Trial End Point and the Cumulative Incidence for Any Acute Medical Event Among Randomized Trial Participants Who Initiated Trial Therapy, Stratified by Assigned Treatment



No. at risk

Aspirin 81 mg	144	144	144	144	144	144	144	144	143	140
Apixaban 2.5 mg	135	135	134	134	134	134	134	134	133	132
Apixaban 5.0 mg	143	142	141	141	141	141	140	140	140	137
Placebo	136	136	136	136	136	136	136	136	135	132

No. at risk

Aspirin 81 mg	144	144	144	142	140	140	139	138	137	134
Apixaban 2.5 mg	135	132	131	129	129	128	128	127	126	125
Apixaban 5.0 mg	143	138	135	134	132	131	130	129	129	126
Placebo	136	135	134	132	130	130	130	130	129	126

JAMA. October 11, 2021

COVID-19’da Aspirin Kullanımı

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

RECOVERY Collaborative Group*

Summary

Background Aspirin has been proposed as a treatment for COVID-19 on the basis of its anti-thrombotic properties. *Lancet* 2022; 399: 143–51

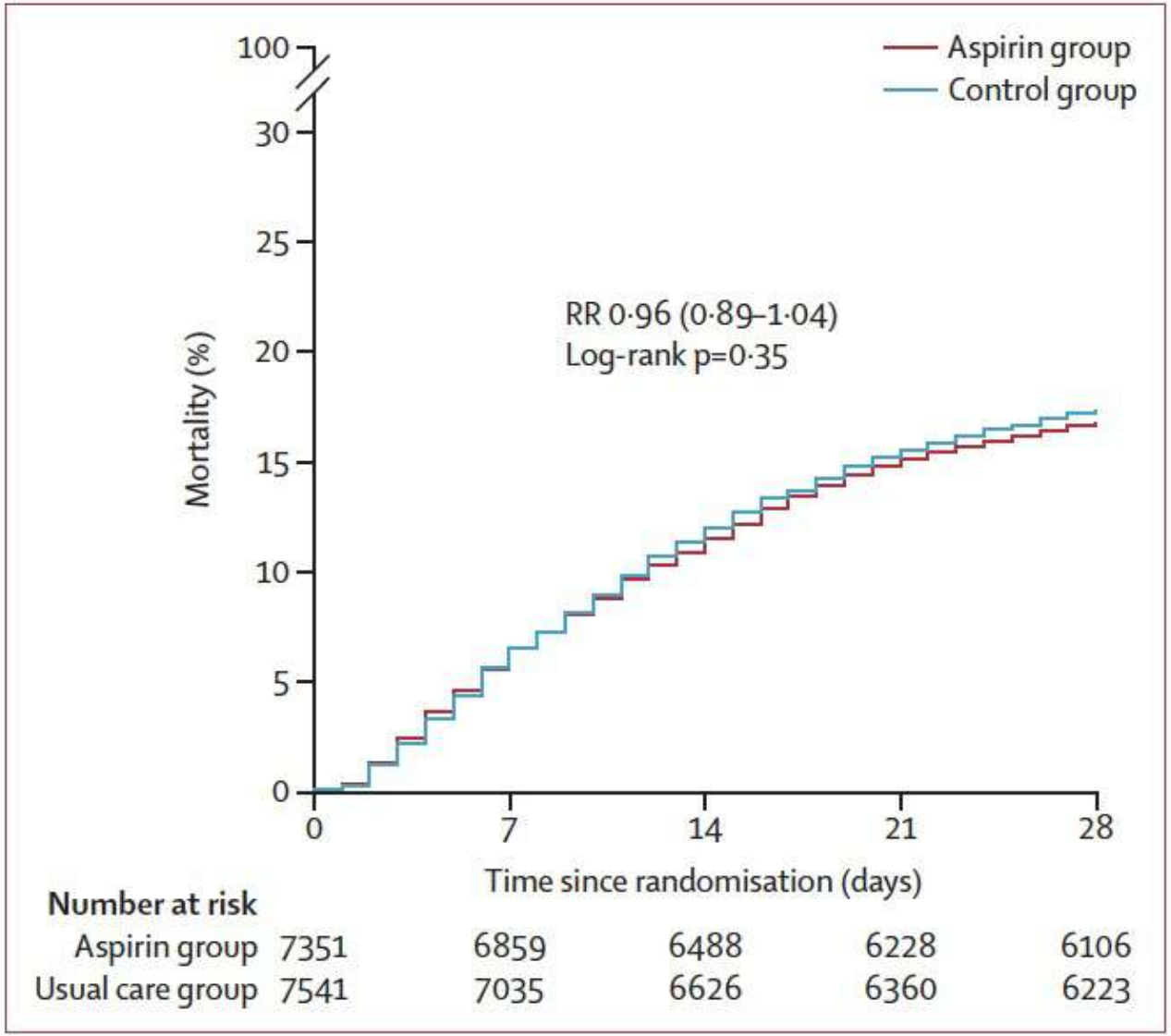
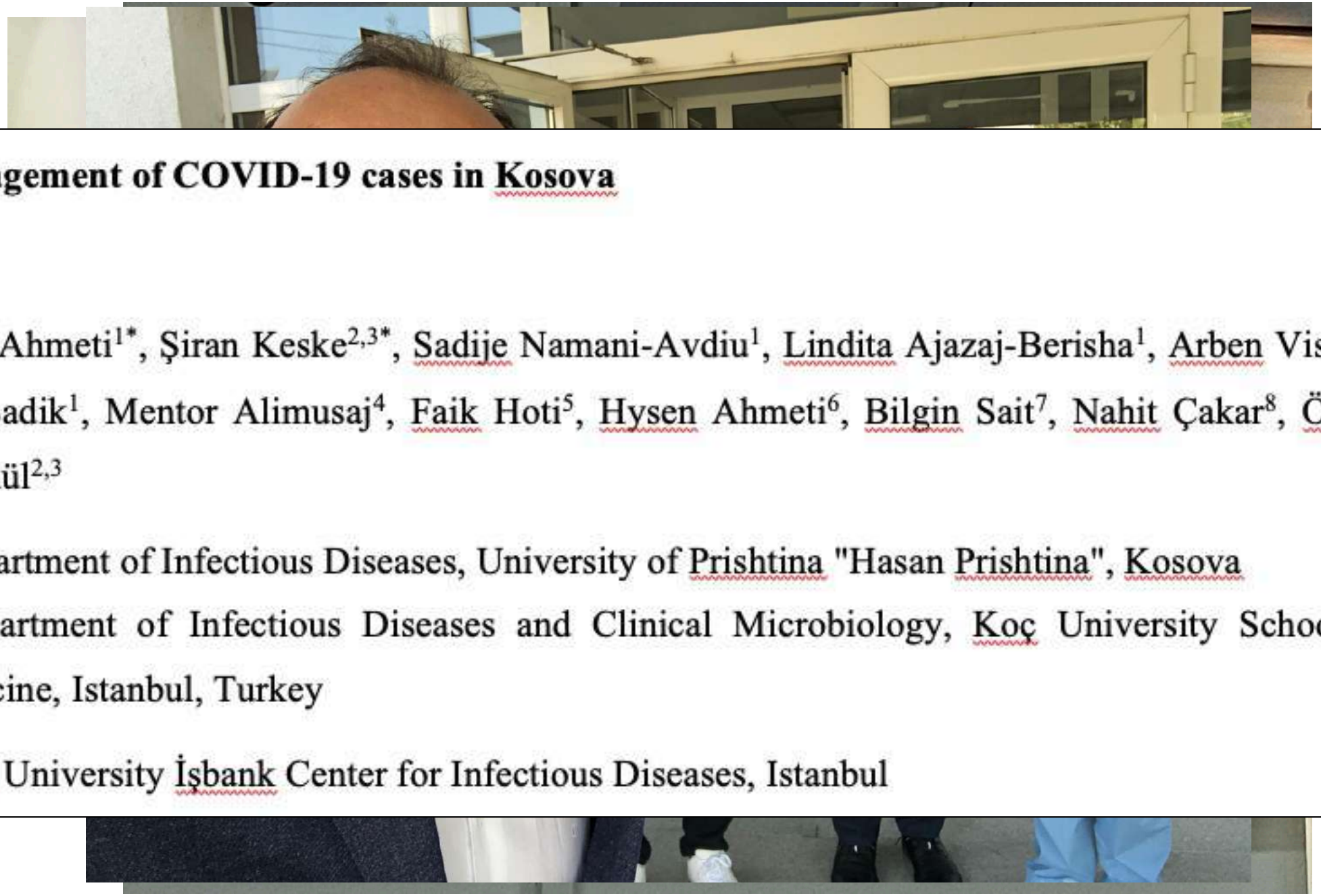


Figure 2: Effect of allocation to aspirin on 28 day mortality
RR=rate ratio.



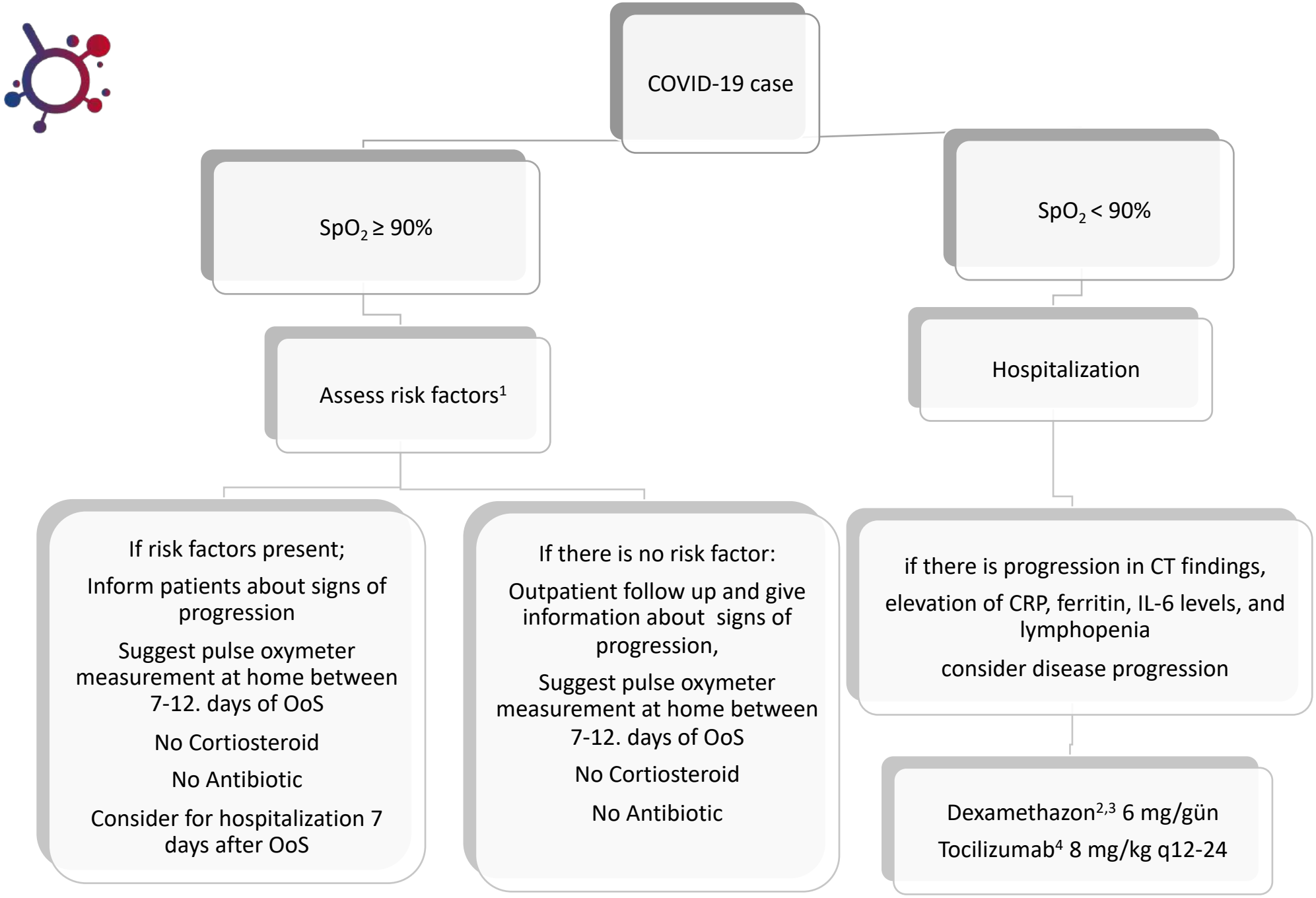
Management of COVID-19 cases in Kosova

Salih Ahmeti[1*], Şiran Keske[2,3*], Sadije Namani-Avdiu[1], Lindita Ajazaj-Berisha[1], Arben Vishaj[1], Izet Sadik[1], Mentor Alimusaj[4], Faik Hoti[5], Hysen Ahmeti[6], Bilgin Sait[7], Nahit Çakar[8], Önder Ergönül[2,3]

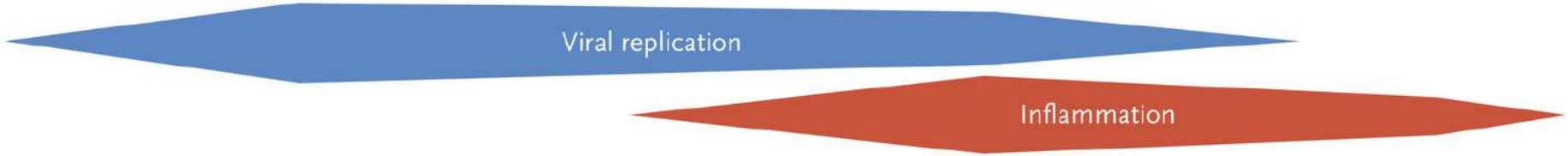
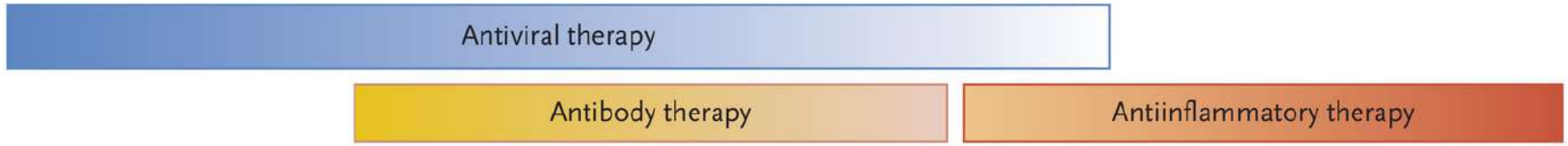
[1] Department of Infectious Diseases, University of Prishtina "Hasan Prishtina", Kosova

[2] Department of Infectious Diseases and Clinical Microbiology, Koç University School of Medicine, Istanbul, Turkey

[3] Koç University İşbank Center for Infectious Diseases, Istanbul


COVID-19 case
$SpO_2 \geq 90\%$
$SpO_2 < 90\%$
Assess risk factors[1]
Hospitalization
If risk factors present;
Inform patients about signs of progression
Suggest pulse oxymeter measurement at home between 7-12. days of OoS
No Cortiosteroid
No Antibiotic
Consider for hospitalization 7 days after OoS
If there is no risk factor:
Outpatient follow up and give information about signs of progression,
Suggest pulse oxymeter measurement at home between 7-12. days of OoS
No Cortiosteroid
No Antibiotic
if there is progression in CT findings,
elevation of CRP, ferritin, IL-6 levels, and lymphopenia
consider disease progression
Dexamethazon[2,3] 6 mg/gün
Tocilizumab[4] 8 mg/kg q12-24

Future considerations

	Asymptomatic or Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical Illness
Features	Positive SARS-CoV-2 test; no symptoms	Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94%	Oxygen saturation <94%; respiratory rate ≥30 breaths/min; lung infiltrates >50%	Respiratory failure, shock, and multiorgan dysfunction or failure
Testing	Screening testing; if patient has known exposure, diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing
Isolation	Yes	Yes	Yes	Yes	Yes
Proposed Disease Pathogenesis					
Potential Treatment					
Management Considerations	Monitoring for symptoms	Clinical monitoring and supportive care	Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir	Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone)	Critical care and specific therapy (dexamethasone, possibly remdesivir)

Teşekkürler

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