# COVID-19 ve İnfluenza

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Koç Üniversitesi İş Bankası Enfeksiyon Hastalıkları Araştırma Merkezi (KUISCID)





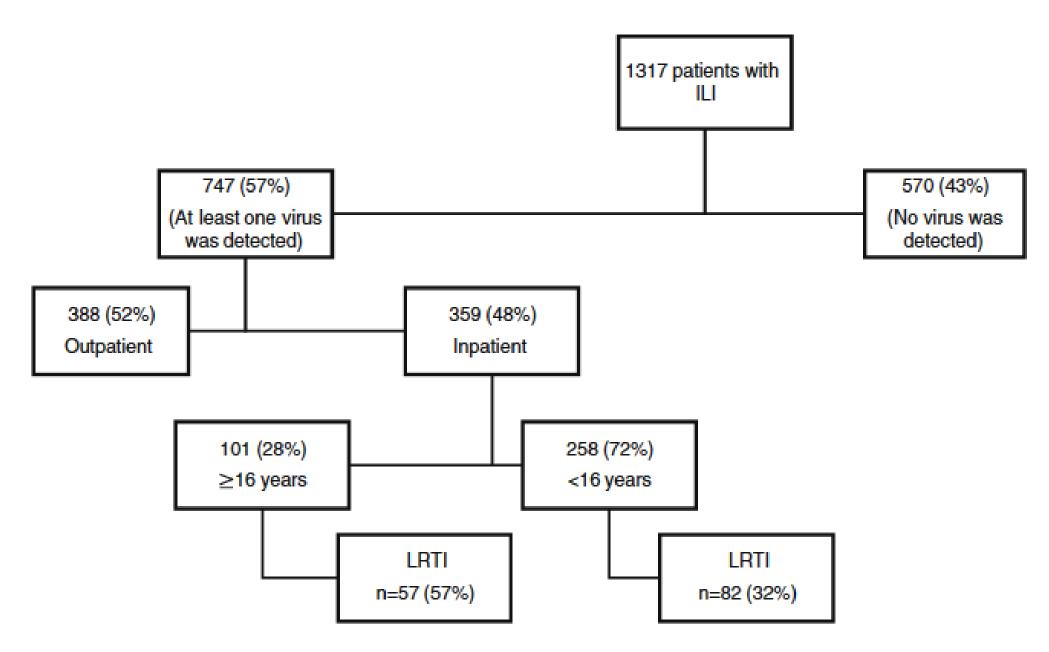
# Solunum Yolu Virüsleri

European Journal of Clinical Microbiology & Infectious Diseases (2018) 37:779–783 https://doi.org/10.1007/s10096-017-3174-6

**ORIGINAL ARTICLE** 

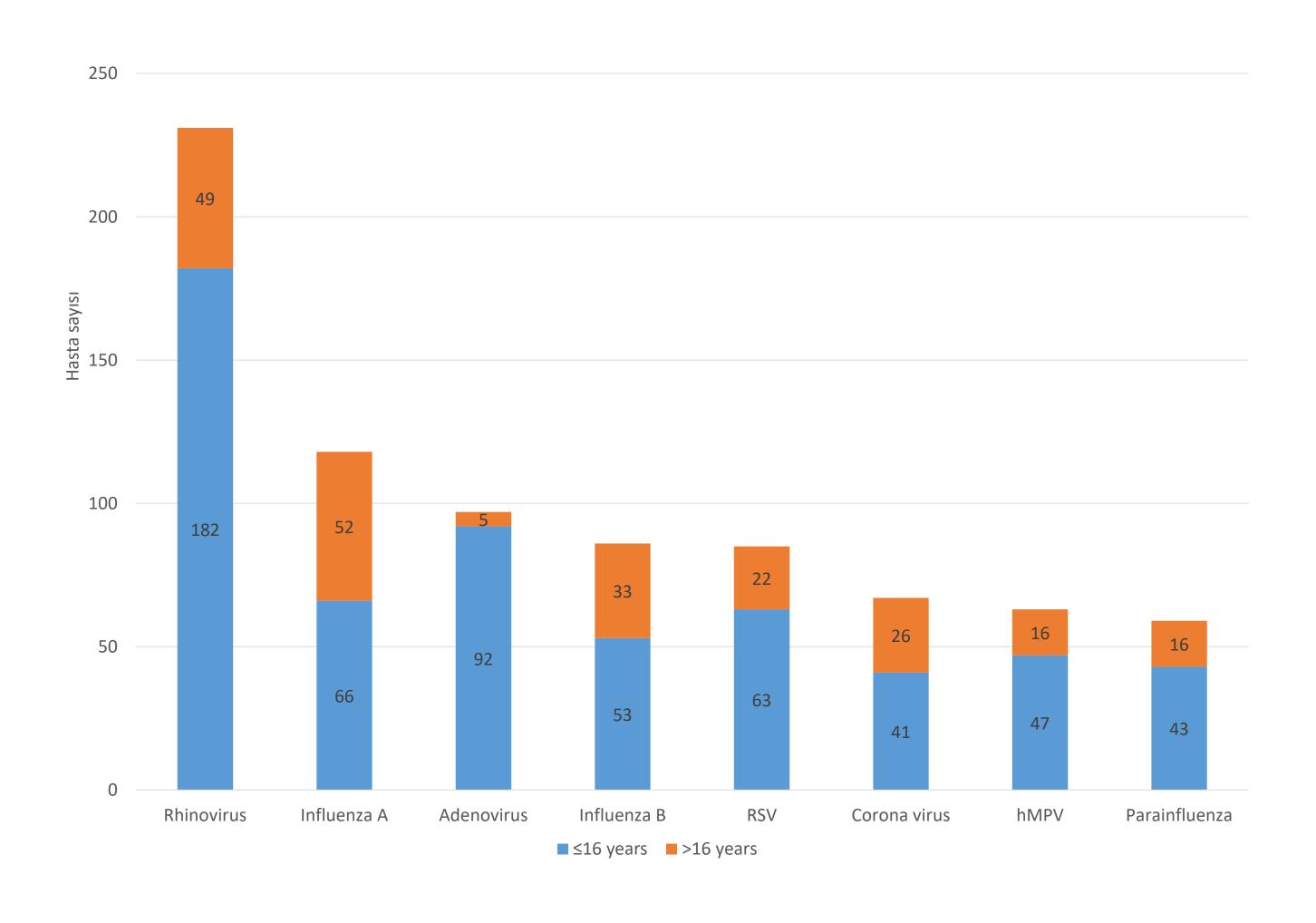
# The rapid diagnosis of viral respiratory tract infections and its impact on antimicrobial stewardship programs

Şiran Keske <sup>1</sup> • Önder Ergönül <sup>1,2</sup> • Faik Tutucu <sup>2</sup> • Doruk Karaaslan <sup>2</sup> • Erhan Palaoğlu <sup>3</sup> • Füsun Can <sup>4</sup>





# Solunum Yolu Virüsleri



|                | Koronaviruslar |      | influenza |           |
|----------------|----------------|------|-----------|-----------|
|                | SARS           | MERS | COVID-19  | pH1N1     |
| Olgu sayıları  | 8000           | 2500 | >50M      | Milyonlar |
| Ölüm Oranı (%) | 8.5            | 35   | 3         | 0.02-0.4  |
| Ro             | 1.8            | 0.5  | 3         | 1.2       |

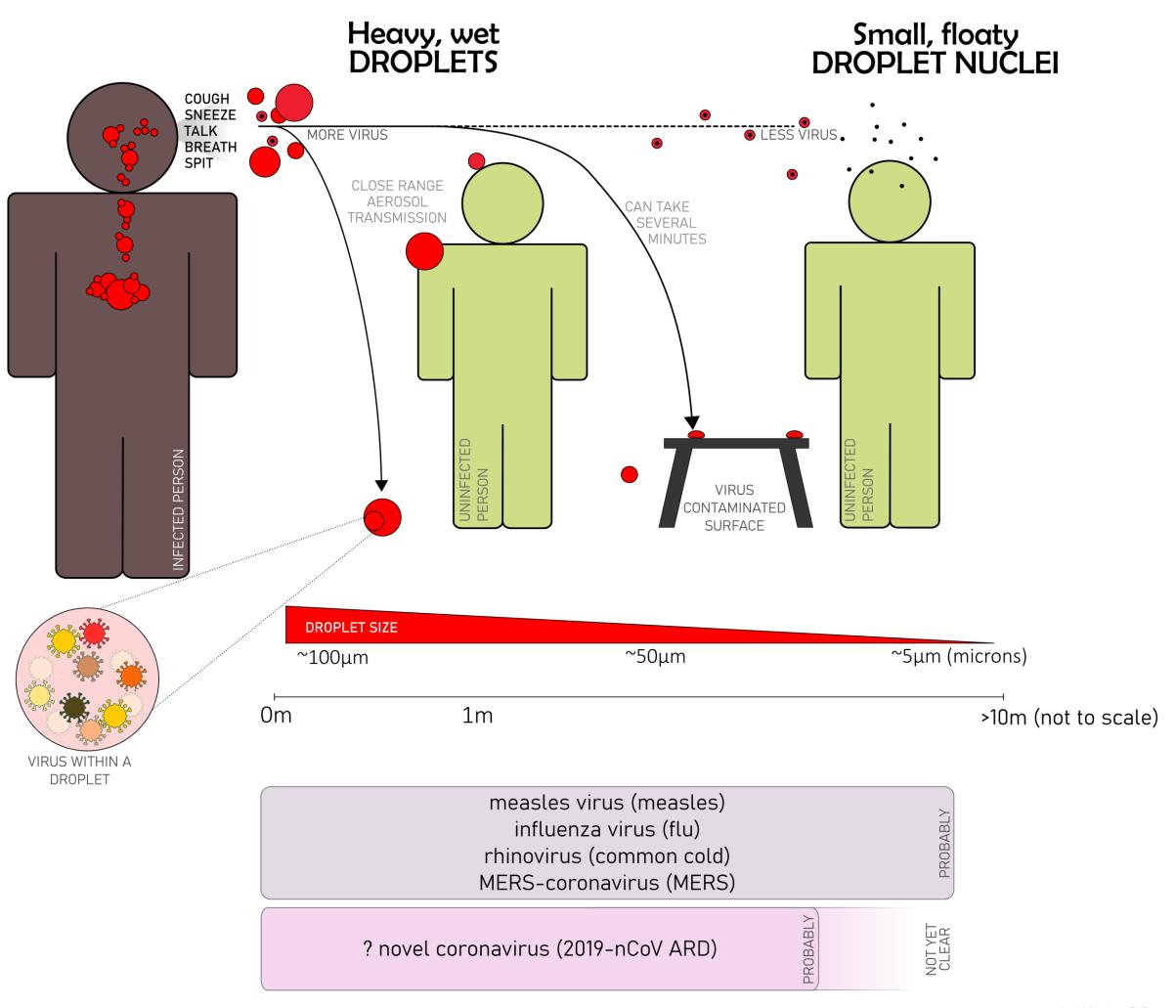
Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Peterson E. COVID-19, SARS and MERS: Are they closely related? Clinical Microbiology and Infection 2020



# COVID-19 ve Influenza

|                    | Influenza           | Covid-19               | comment                             |
|--------------------|---------------------|------------------------|-------------------------------------|
| Kuluçka süresü     | 2 (1-3)             | 5 (2-14)               |                                     |
| Semptomlar         |                     | Anosmi, ishal daha sık |                                     |
| Damlacık (Droplet) | Evet                | Evet                   |                                     |
| Aerosol            | Hayır               | Evet                   |                                     |
| Tanı               |                     |                        |                                     |
| Tam kan sayım      |                     |                        |                                     |
| Lökopeni           | Evet                | Evet                   |                                     |
| Lenfopeni          | Evet                | Evet                   |                                     |
| Thrombocytopenia   | Evet                | Evet                   |                                     |
| PCR                |                     |                        |                                     |
| Antikor testi      | Yok                 | Var                    |                                     |
| Tedavi             |                     |                        |                                     |
| Oseltamivir        | Etkili              | Değil                  | Hidroksiklorokin ile<br>verilmemeli |
| Favipiravir        | <b>,</b>            |                        | Bir taşla 2 kuş?                    |
| Aşı                | 60-70%<br>effective | 90%                    |                                     |

# Droplet ve Aerosol



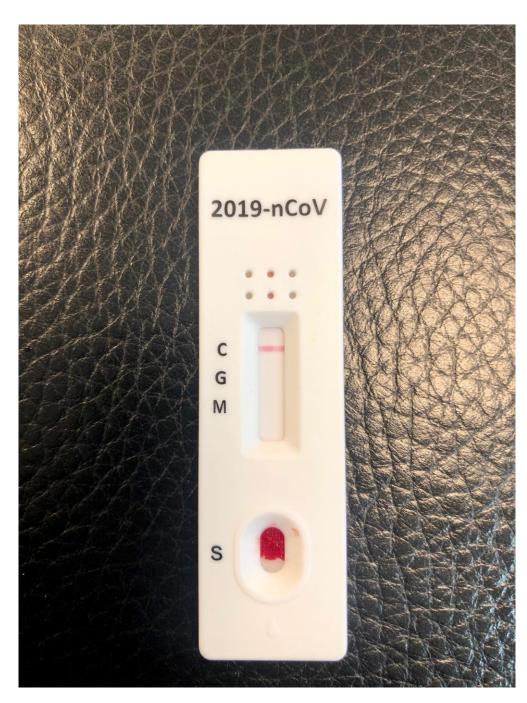
lan M Mackay, PhD ver12 17MAR2020 AEST virologydownunder.com

# Tanı Yöntemleri Çalışmıyor

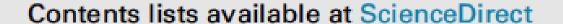
Test Duyarlılığı %55 – 60 PCR tarama için kullanılmamalı Tarama için antikor testleri

**Etkin Tedavi Yok** 

Bulaşma Yolu Tartışmalı









## Clinical Microbiology and Infection

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journal homepage: www.clinicalmicrobiologyandinfection.com

#### Original article

## National case fatality rates of the COVID-19 pandemic

Önder Ergönül <sup>1, 2, 3, \*</sup>, Merve Akyol <sup>4</sup>, Cem Tanrıöver <sup>4</sup>, Henning Tiemeier <sup>5</sup>, Eskild Petersen <sup>3, 6</sup>, Nicola Petrosillo <sup>3, 7</sup>, Mehmet Gönen <sup>2, 4, 8</sup>

Table 2
Multivariable analysis for the prediction of national case fatality rates (CFRs) (as of 18th August 2020)

| Standardized coefficient                  |       | 95% confidence interval | p value |  |
|---|-------|-------------------------|---------|--|
| Number of tests (per 1000)                | -3.54 | [-5.60, -1.47]          | 0.002   |  |
| Obesity in ages 18+ (%)                   | 3.26  | [1.20, 5.33]            | 0.003   |  |
| Tuberculosis incidence (per 1000 people)  | 3.15  | [1.09, 5.22]            | 0.004   |  |
| Duration since first death (days)         | 2.89  | [0.83, 4.96]            | 0.008   |  |
| Median age (years)                        | 2.83  | [0.76, 4.89]            | 0.009   |  |
| Number of hospital beds (per 1000 people) | -2.47 | [-4.54, -0.41]          | 0.021   |  |
| Rural population (%)                      | -2.19 | [-4.25, -0.13]          | 0.039   |  |
| Raised blood pressure in ages 18+ (%)     | 1.50  | [-0.57, 3.56]           | 0.148   |  |
| Male population (%)                       | 1.35  | [-0.71, 3.42]           | 0.189   |  |

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<sup>5)</sup> Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, USA

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<sup>7)</sup> National Institute for Infectious Diseases L. Spallanzani', IRCCS, Rome, Italy

<sup>&</sup>lt;sup>8)</sup> Koç University, College of Engineering, Department of Industrial Engineering, Istanbul, Turkey

# Yeniden Enfeksiyon Mümkün mü?

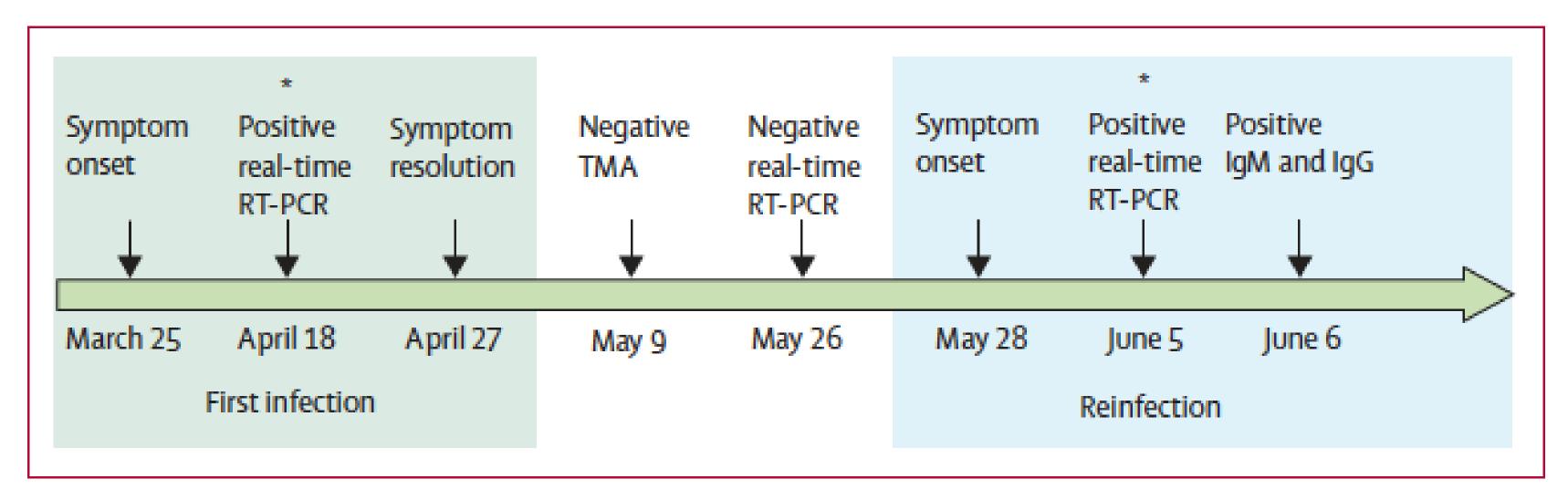


Figure 1: Timeline of symptom onset, molecular diagnosis, and sequencing of specimens TMA=transcription-mediated amplification. \*Sequenced specimens.

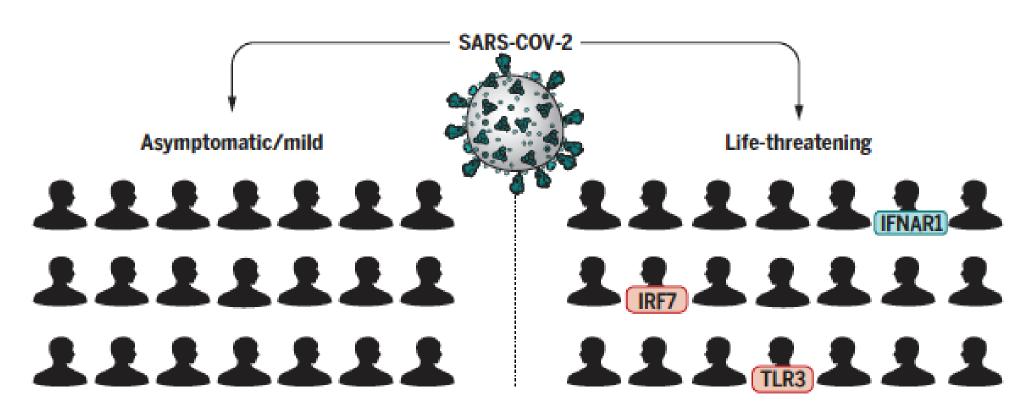
## Sorular:

- 1. Sıklığı nedir?
- 2. Daha mı ağır, daha mı hafif?
- 3. Aşılar işe yaracak mı?

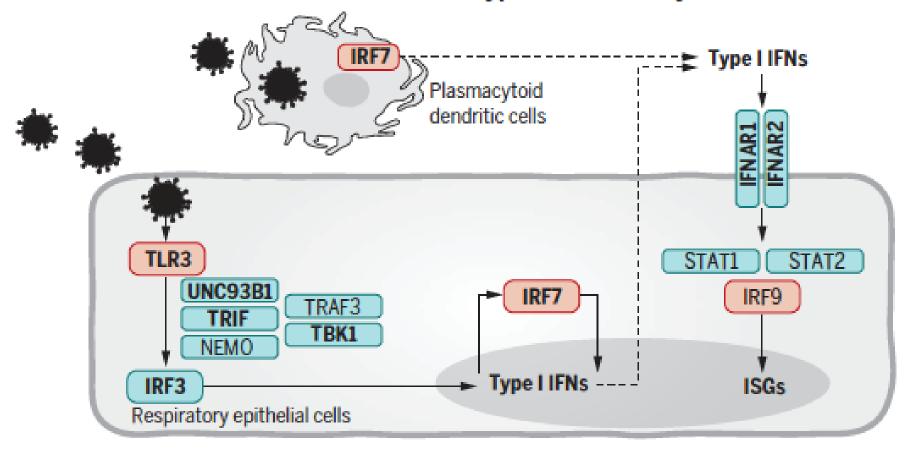
## RESEARCH ARTICLE

#### CORONAVIRUS

# Inborn errors of type I IFN immunity in patients with life-threatening COVID-19



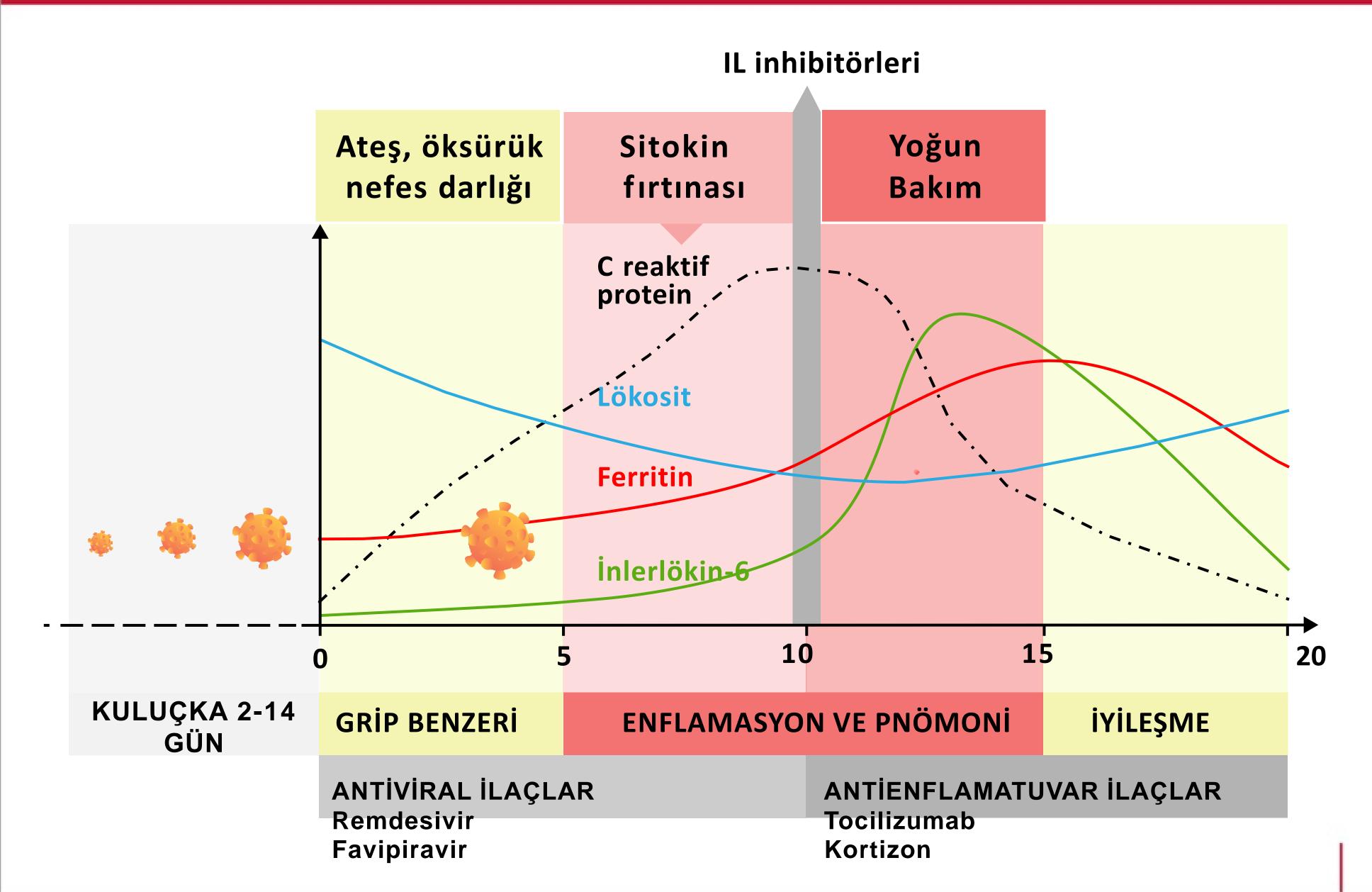
#### Inborn errors of type I IFN immunity



Inborn errors of TLR3- and IRF7-dependent type I IFN production and amplification underlie lifethreatening COVID-19 pneumonia. Molecules in red are encoded by core genes, deleterious variants of which underlie critical influenza pneumonia with incomplete penetrance, and deleterious variants of genes encoding biochemically related molecules in blue underlie other viral illnesses. Molecules represented in bold are encoded by genes with variants that also underlie critical COVID-19 pneumonia.



# The Course of The Infection





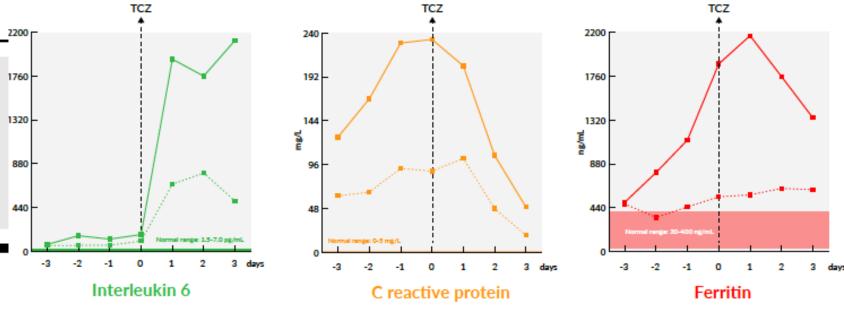


#### International Journal of Infectious Diseases 99 (2020) 338-343

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## International Journal of Infectious Diseases

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



## Appropriate use of tocilizumab in COVID-19 infection

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

# Figure 1. Laboratory parameters 3 days before and after tocilizumab among severe and critical cases. Severe cases — Critical cases D-Dimer TCZ Figure 1. Laboratory parameters 3 days before and after tocilizumab among severe and critical cases. Lymphocyte

## Toclilizumab alan toplam 43 hasta

Ciddi seyirli hastalarda yoğun bakımdan önce alanlarda ölüm yok

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<sup>&</sup>lt;sup>b</sup>Koc University, School of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey

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<sup>&</sup>lt;sup>e</sup>Koç University, College of Engineering, Department of Industrial Engineering, Istanbul, Turkey

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g Koç University, School of Medicine, Department of Chest Diseases, Istanbul, Turkey

<sup>&</sup>lt;sup>h</sup>American Hospital, Department of Radiology and Beykent University School of Medicine, Turkey



| Treatment                  | n=36 (%)    | Countries   |
|----------------------------|-------------|---|
| Primarily Antiviral effect |             |   |
| Lopinavir/ritonavir        | n=13 (36.1) | Hungary, Turkey, Italy, Poland, Thailand, Croatia, Korea, Ukraine, Albania, Cyprus, Slovenia, China, Serbia |
| HCQ                        | n=12 (33.3) | Hungary, Turkey, Thailand, Croatia, Korea, Ukraine, Albania, Peru, Cyprus, Mexico, Slovenia, Serbia         |
| Azithromycin               | n=12 (33.3) | Hungary, Turkey, Italy, Croatia, Korea, Macedonia, Albania, Peru, Cyprus, Slovenia, Bulgaria, Serbia        |
| Remdesivir                 | n=11 (30.5) | Poland, Denmark, France, Belgium, Israel, Germany, Netherlands, Sweden, Cyprus, UK, Serbia                  |
| Oseltamivir                | n=8 (22.2)  | Hungary, Turkey, Croatia, Korea, Ukraine, Cyprus, Bulgaria, Serbia  |
| Favipiravir                | n=7 (19.4)  | Hungary, Turkey, Poland, Thailand, Korea, Serbia, Portugal  |
| Ribavirin                  | n=3 (8.3)   | Korea, China, Serbia  |
| Doxycycline                | n=4 (11.1)  | Hungary, Croatia, Korea, Bulgaria   |



| Treatment                         | n=36 (%)    | Countries   |
|-----------------------------------|-------------|---|
| Primarily antiinflammatory effect |             |   |
| Corticosteroids                   | n=26 (72.2) | Hungary, Turkey, Italy, Poland, Thailand, Denmark, France, Belgium, Israel, Germany, Canada, Netherlands, Sweden, Croatia, Korea, Albania, Peru, Cyprus, Mexico, Finland, UK, Slovenia, China, Bulgaria, Serbia, Portugal |
| IL-6 blocker<br>(tocilizumab)     | n=10 (27.7) | Turkey, Italy, Poland, Thailand, Croatia, Korea, Albania, Peru, Serbia, Portugal  |
| IL-6 blocker (sarilumab)          | n=3 (8.3)   | Italy, Israel, Korea  |
| IL-1 blocker (anakinra)           | n=2 (5.5)   | Turkey, Korea   |
| Eculizumab                        | n=2 (5.5)   | Italy, Korea  |
| Bevacizumab                       | n=1 (2.7)   | Korea   |
| JAK-inhibitor (baricitinib)       | n=1 (2.7)   | Korea   |
| Convalescent plasma               | n=9 (25)    | Hungary, Turkey, Italy, Israel, Croatia, Macedonia, China, Bulgaria, Serbia   |
| Mesenchymal stem cell             | n=0         | 4   |

#### **DISEASE SEVERITY**

#### PANEL'S RECOMMENDATIONS

(Recommendations are listed in order of preference in each category below; however, all options are considered acceptable.)

Not Hospitalized or

Hospitalized but Does Not Require Supplemental Oxygen No specific antiviral or immunomodulatory therapy recommended

The Panel recommends against the use of dexamethasone (AI)

See the Remdesivir section for a discussion of the data on using this drug in hospitalized patients with moderate COVID-19.<sup>a</sup>

Hospitalized and Requires Supplemental Oxygen

(but Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO) **Remdesivir** 200 mg IV for one day, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge, whichever comes first **(AI)**<sup>b,c,d</sup>

or

Remdesivir (dose and duration as above) plus dexamethasone<sup>®</sup> 6 mg IV or PO for up to 10 days or until hospital discharge, whichever comes first (BIII)<sup>f</sup>

If **remdesivir** cannot be used, **dexamethasone** may be used instead **(BIII)** 

Hospitalized and Requires Oxygen
Delivery Through a High-Flow Device
or Noninvasive Ventilation

**Dexamethasone**<sup>d</sup> plus **remdesivir** at the doses and durations discussed above (AIII)<sup>f</sup>

or

Dexamethasoned,e at the dose and duration discussed above (AI)

Hospitalized and Requires Invasive Mechanical Ventilation or ECMO Dexamethasonede at the dose and duration discussed above (AI)

or

**Dexamethasone**° plus **remdesivir** for patients who have recently been intubated at the doses and durations discussed above **(CIII)**<sup>f</sup>

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies; III = Expert opinion

## **Summary Recommendations**

Remdesivir is the only Food and Drug Administration-approved drug for the treatment of COVID-19. In this section, the COVID-19 Treatment Guidelines Panel (the Panel) provides recommendations for using antiviral drugs to treat COVID-19 based on the available data. As in the management of any disease, treatment decisions ultimately reside with the patient and their health care provider. For more information on these antiviral agents, see <u>Table 2</u>.

#### Remdesivir

 See <u>Therapeutic Management of Patients with COVID-19</u> for recommendations on using remdesivir with or without dexamethasone.

#### Chloroquine or Hydroxychloroquine With or Without Azithromycin

- The Panel recommends against the use of chloroquine or hydroxychloroquine with or without azithromycin for the treatment of COVID-19 in hospitalized patients (AI).
- In nonhospitalized patients, the Panel recommends against the use of chloroquine or hydroxychloroquine with or without azithromycin for the treatment of COVID-19, except in a clinical trial (AI).
- The Panel recommends against the use of high-dose chloroquine (600 mg twice daily for 10 days) for the treatment of COVID-19 (AI).

#### Lopinavir/Ritonavir and Other HIV Protease Inhibitors

 The Panel recommends against using lopinavir/ritonavir (AI) or other HIV protease inhibitors (AIII) to treat COVID-19, except in a clinical trial.

#### **Ivermectin**

The Panel recommends against the use of ivermectin for the treatment of COVID-19, except in a clinical trial (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies; III = Expert opinion

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Antiviral Agents

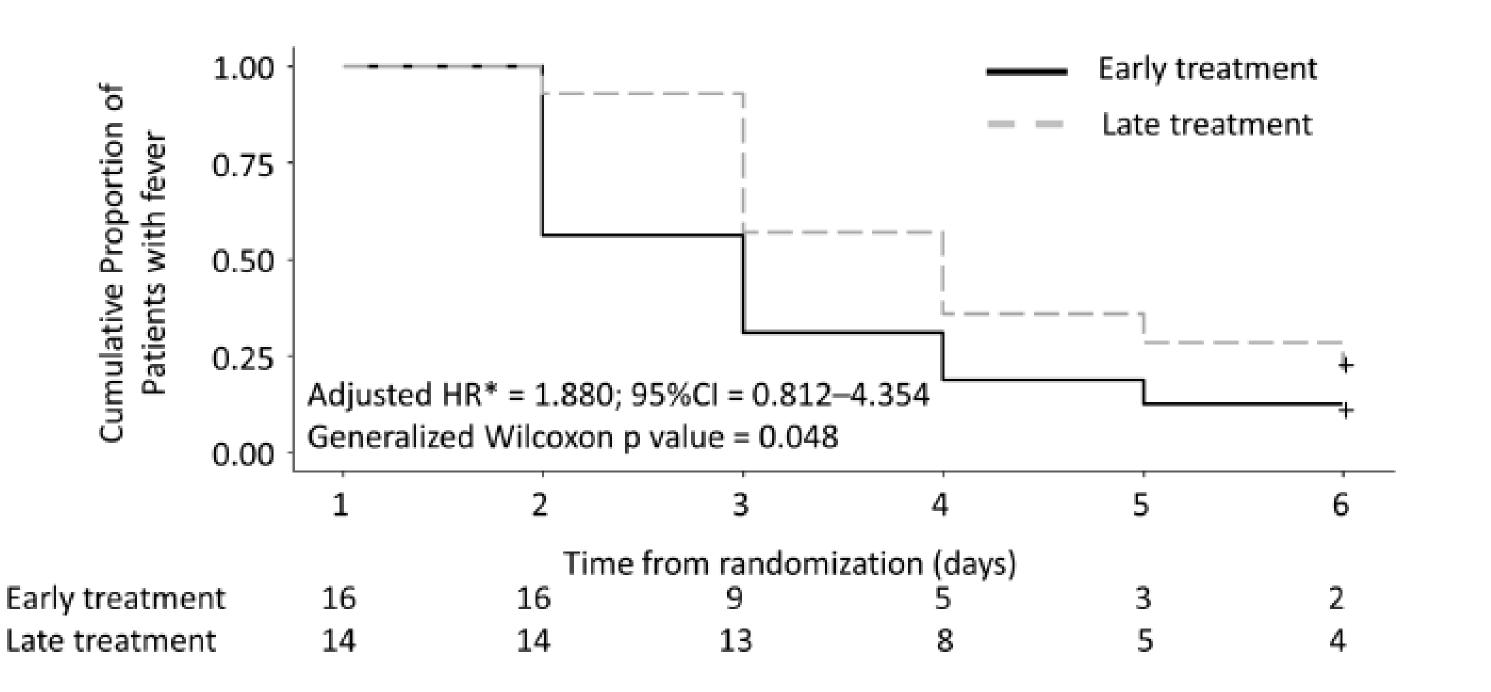
A prospective, randomized, open-label

Institutions

List late favipiravir in

# A prospective, randomized, open-label hospitalized patients with COVID-19

Yohei Doi, Masaya Hibino, Ryota Hase, Michiko Yamamoto, Yu Kasamatsu, Masahiro Hirose, Yoshikazu Mutoh, Yoshito Homma, Masaki Terada, Taku Ogawa, Fumihiro Kashizaki, Toshihiko Yokoyama, Hayato Koba, Hideki Kasahara, Kazuhisa Yokota, Hideaki Kato, Junichi Yoshida, Toshiyuki Kita, Yasuyuki Kato, Tadashi Kamio, Nobuhiro Kodama, Yujiro Uchida, Nobuhiro Ikeda, Masahiro Shinoda, Atsushi Nakagawa, Hiroki Nakatsumi, Tomoya Horiguchi, Mitsunaga Iwata, Akifumi Matsuyama, Sumi Banno, Takenao Koseki, Mayumi Teramachi, Masami Miyata, Shigeru Tajima, Takahiro Maeki, Eri Nakayama, Satoshi Taniguchi, Chang Kweng Lim, Masayuki Saijo, Takumi Imai, Hisako Yoshida, Daijiro Kabata, Ayumi Shintani, Yukio Yuzawa, Masashi Kondo



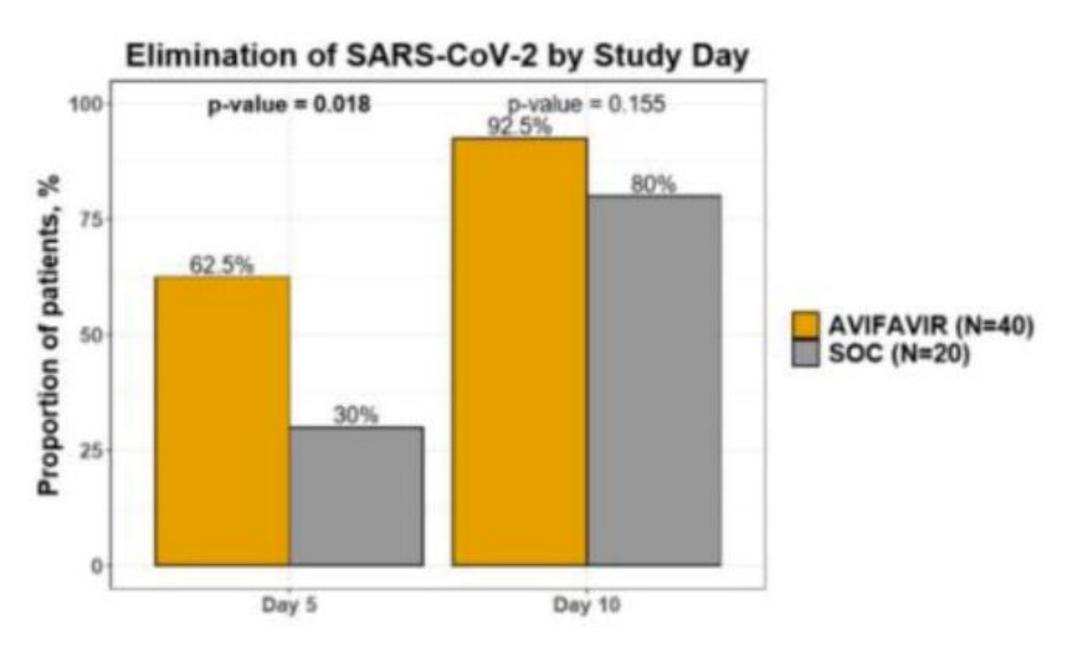


# Favipiravir, Rusya, n=60 (3 grup: 3x20)

#### **AVIFAVIR for Treatment of Patients with Moderate COVID-19:**

#### Interim Results of a Phase II/III Multicenter Randomized Clinical Trial

Andrey A. Ivashchenko<sup>1</sup>, Kirill A. Dmitriev<sup>2</sup>, Natalia V. Vostokova<sup>3</sup>, Valeria N. Azarova<sup>3</sup>, Andrew A. Blinow<sup>4</sup>, Alina N. Egorova<sup>3</sup>, Ivan G. Gordeev<sup>5</sup>, Alexey P. Ilin<sup>6</sup>, Ruben N. Karapetian<sup>7</sup>, Dmitry V. Kravchenko<sup>6</sup>, Nikita V. Lomakin<sup>8</sup>, Elena A. Merkulova<sup>3</sup>, Natalia A. Papazova<sup>9</sup>, Elena P. Pavlikova<sup>10</sup>, Nikolay P. Savchuk<sup>11</sup>, Elena N. Simakina<sup>12</sup>, Tagir A. Sitdekov<sup>2</sup>, Elena A. Smolyarchuk<sup>13</sup>, Elena G. Tikhomolova<sup>14</sup>, Elena V. Yakubova<sup>4</sup>, Alexandre V. Ivachtchenko<sup>11</sup>





# Tedavi Seçenekleri

## Yararsız antiviraller:

- 1. Hidroxychloroquine (HCQ)
  - HCQ + azitromycin
- 2. Lopinavir/ritonavir

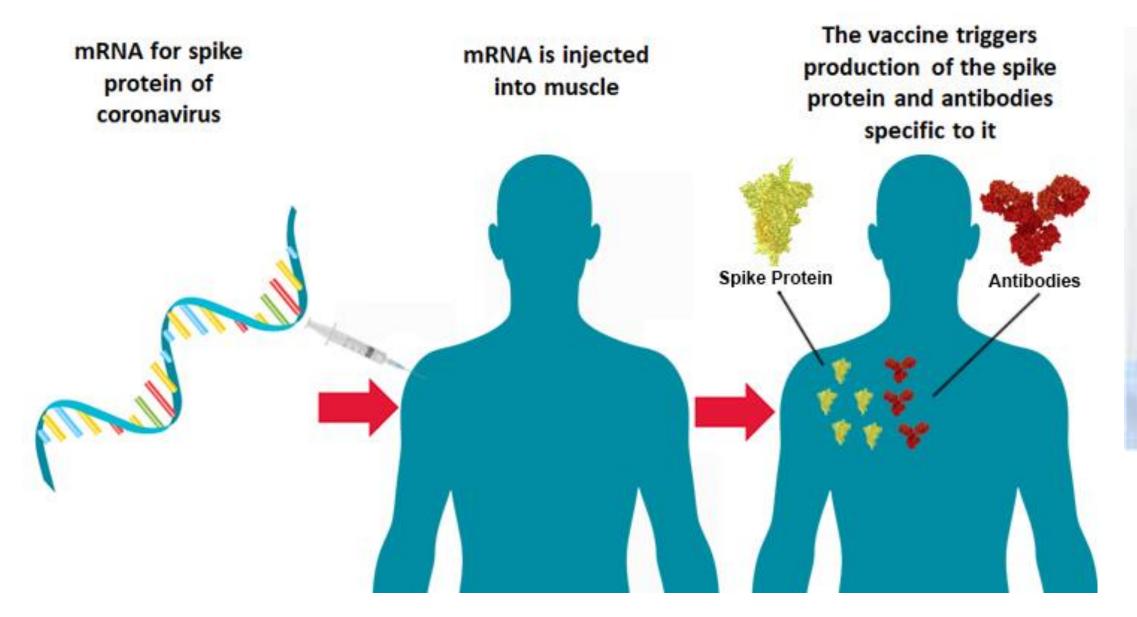
# Kısmen yararlı antiviraller:

- 1. Remdesivir
- 2. Favipiravir

# Anti-enflamatuvar:

- 1. Tocilizumab (IL-6 inhibitor)
- 2. Kortikosteroidler

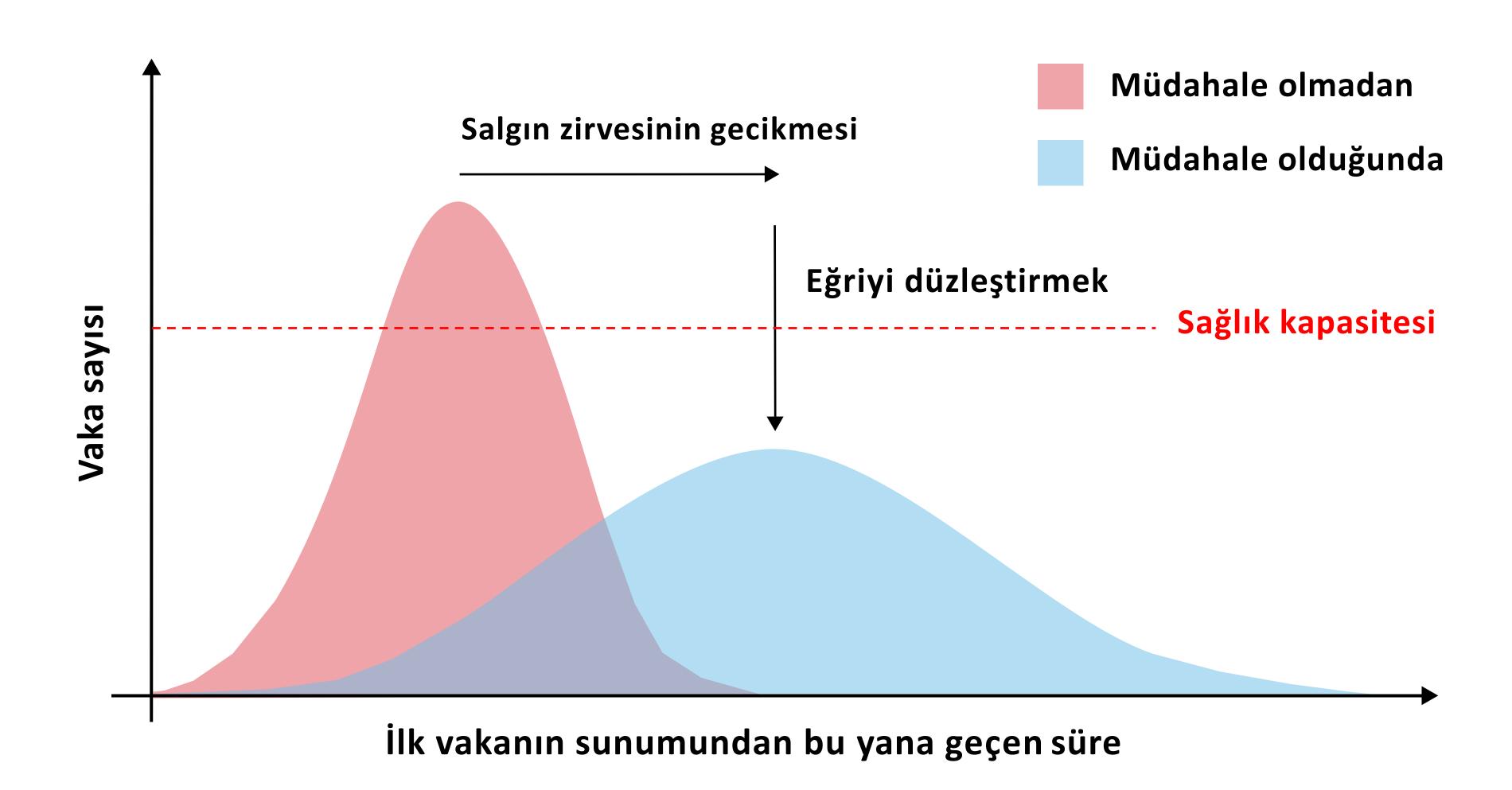








# Pandeminin Seyri



# Sonuçlar

- Maske
- Sosyal mesafe
- Temizlik
- Evde kalma

## Avoid 3 C:

- Closed : kapalı ortamlar
- Contact: temas
- Crowd: gereksiz sosyalleşmeler