İmmunkompromize Konakta

Uzamış Viral Saçılım

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[2]VKV Amerikan Hastanesi
İHKM Bölümü

[3]Koç üniversitesi-İşbankası Enfeksiyon Hastalıkları Merkezi (KUISCID)

41 yaş, kadın

Foliküler lenfoma

Nisan-Haziran 2021
Biontech

R^2 tedavisi
375mg/m^2 rituximab
20mg/day lenalidomide

12/01/2022

19/01/2022

Ateş

Kas-eklem ağrısı

SARS CoV-2 PCR (+)
Eşi de pozitif

Metil-Prednizolon
250 mg IV

02/02/2022

Metil-Prednizolon

Ateş

Kas-eklem ağrısı

SARS CoV-2 PCR (+)

17/02/2022

Metil-Prednizolon

Ateş

Kas-eklem ağrısı

01/03/2022

Metil-Prednizolon

Molnupiravir

SARS CoV-2 PCR (+)

Ateş

Kas-eklem ağrısı

15/03/2022

SARS CoV-2 PCR (+)
Ct: 13

Metil-Prednizolon
4 mg

Molnupiravir

Ateş düştü

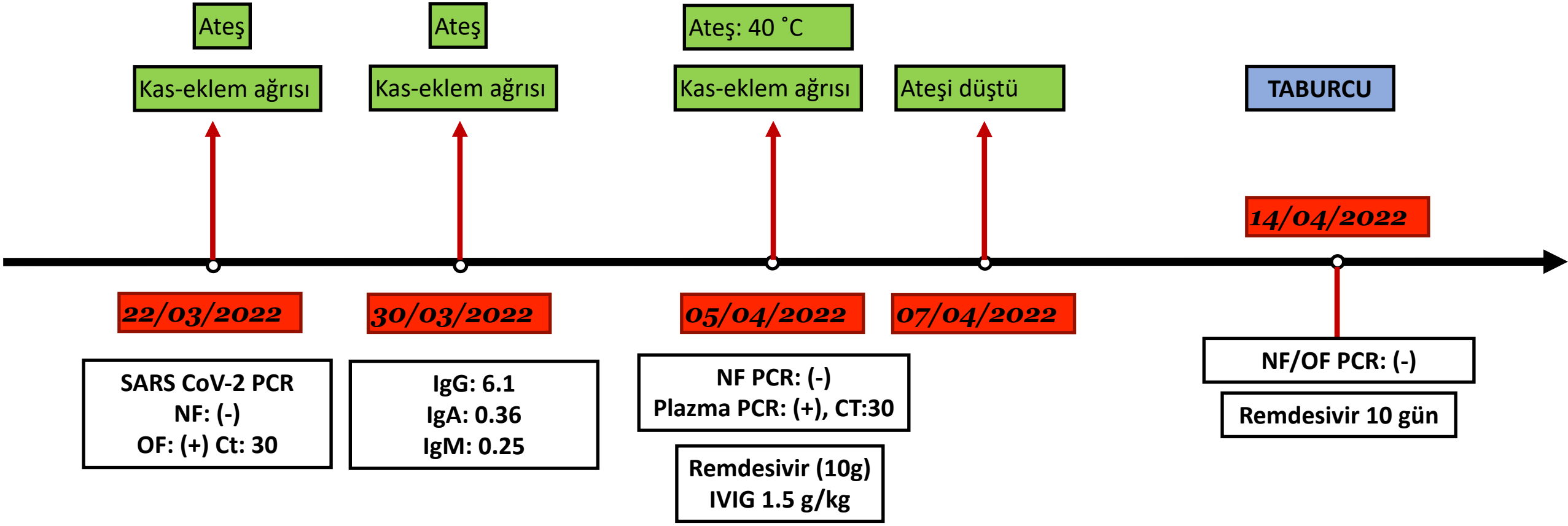
20/03/2022

SARS CoV-2 PCR (-)

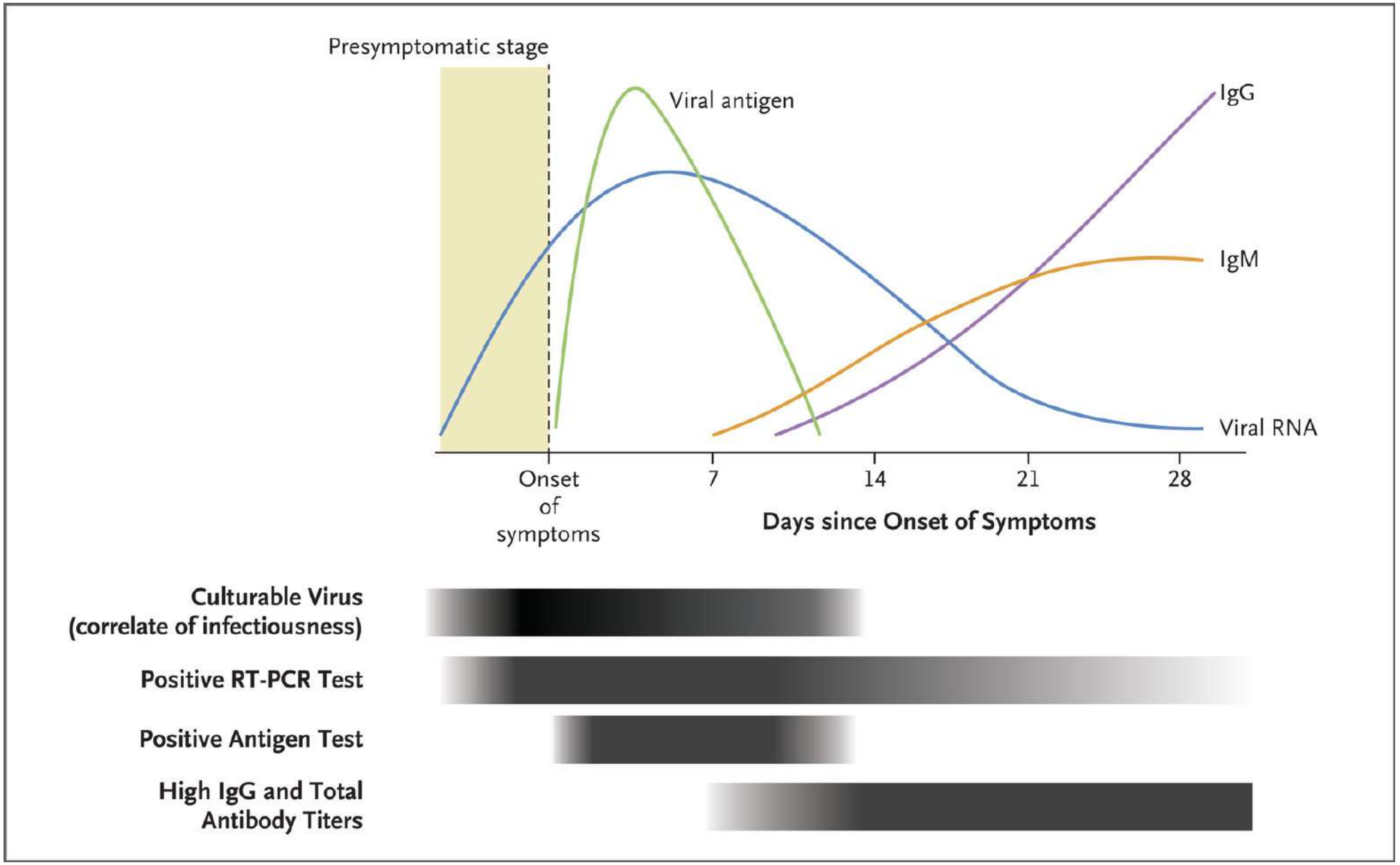
Molnupiravir
Kesildi

41 yaş, kadın

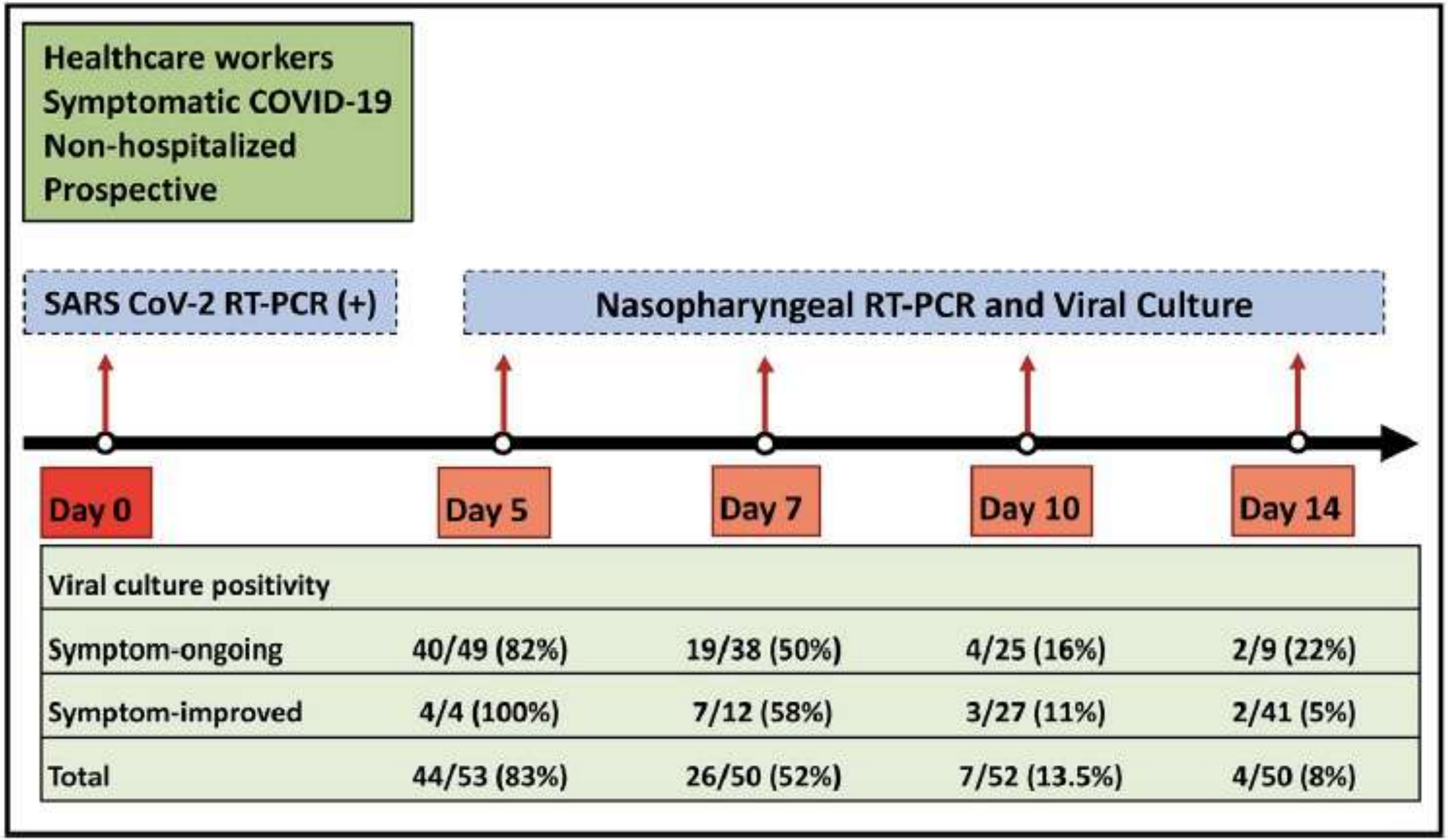
Foliküler lenfoma



COVID19'da Tanı Testleri



Drain PK. N Engl J Med 2022; 386:264-272



Viral culture positivity				
Symptom-ongoing	40/49 (82%)	19/38 (50%)	4/25 (16%)	2/9 (22%)
Symptom-improved	4/4 (100%)	7/12 (58%)	3/27 (11%)	2/41 (5%)
Total	44/53 (83%)	26/50 (52%)	7/52 (13.5%)	4/50 (8%)

Fig. 2. SARS-CoV-2 culture positivity and its relationship with the presence of the symptom.

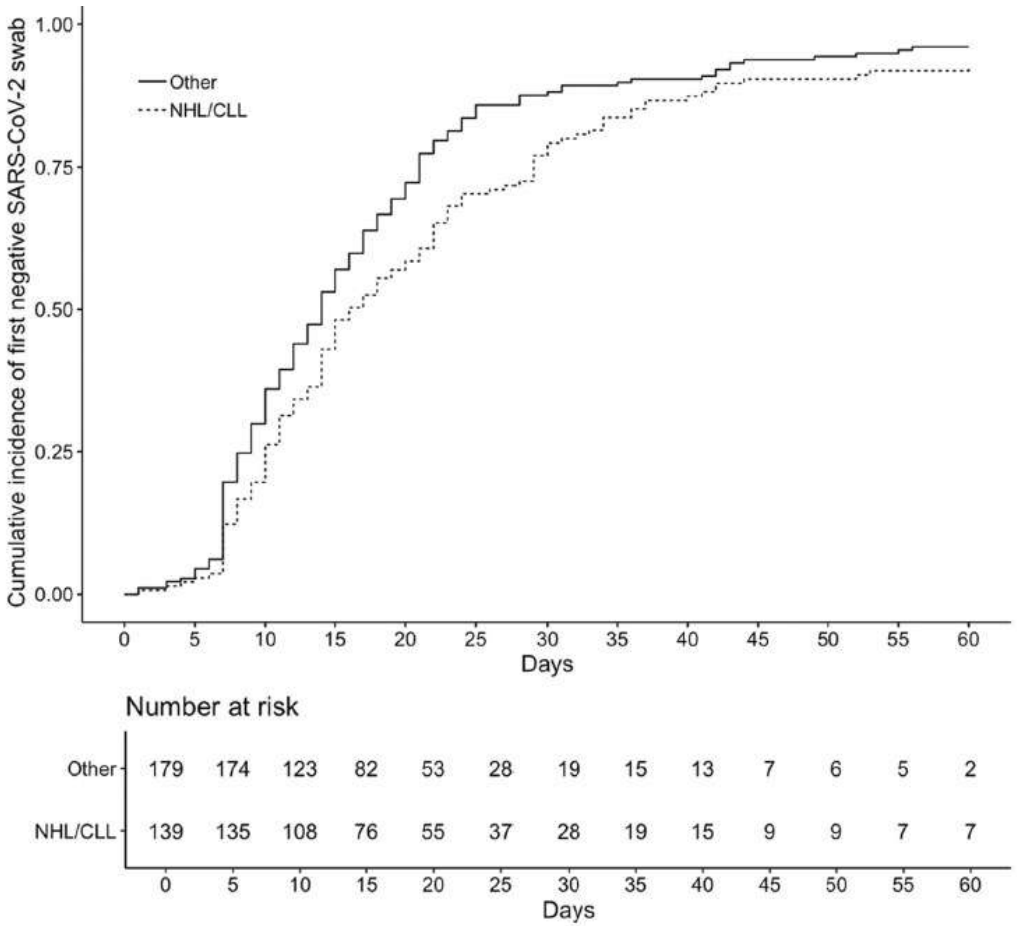


FIGURE 3 Cumulative incidence of first negative SARS-CoV-2 swab from diagnosis of non-Hodgkin lymphoma/chronic lymphocytic le (NHL/CLL) versus other diseases. *cumulative incidence was estimated considering death as a competing risk and loss to follow-up as a right

TABLE 5 Multivariable analysis of predictors of COVID-19-associated mortality and overall 90-day mortality (all variables included in multivariate models are shown).

	Adjusted cause specific HR	95% CI	*p*
COVID-19 associated mortality			
Age, years	1.068	1.011–1.129	0.012
AML/MDS versus other diseases	3.564	1.055–12.039	0.041
Early treatment with antivirals versus MABs	0.434	0.124–1.518	0.191
Omicron period versus pre-Omicron	0.121	0.034–0.437	0.001
Overall 90-day mortality			
Age, years	1.056	1.015–1.099	0.007
AML/MDS versus other diseases	5.172	1.991–13.437	0.001
Omicron period versus pre-Omicron	0.237	0.076–0.742	0.013

Abbreviations: AML/MDS, acute myeloid leukaemia and myelodysplastic syndrome; CI, confidence interval; HR, hazard ratio; MABs, anti-spike protein monoclonal antibodies.

BJHaem. 2023

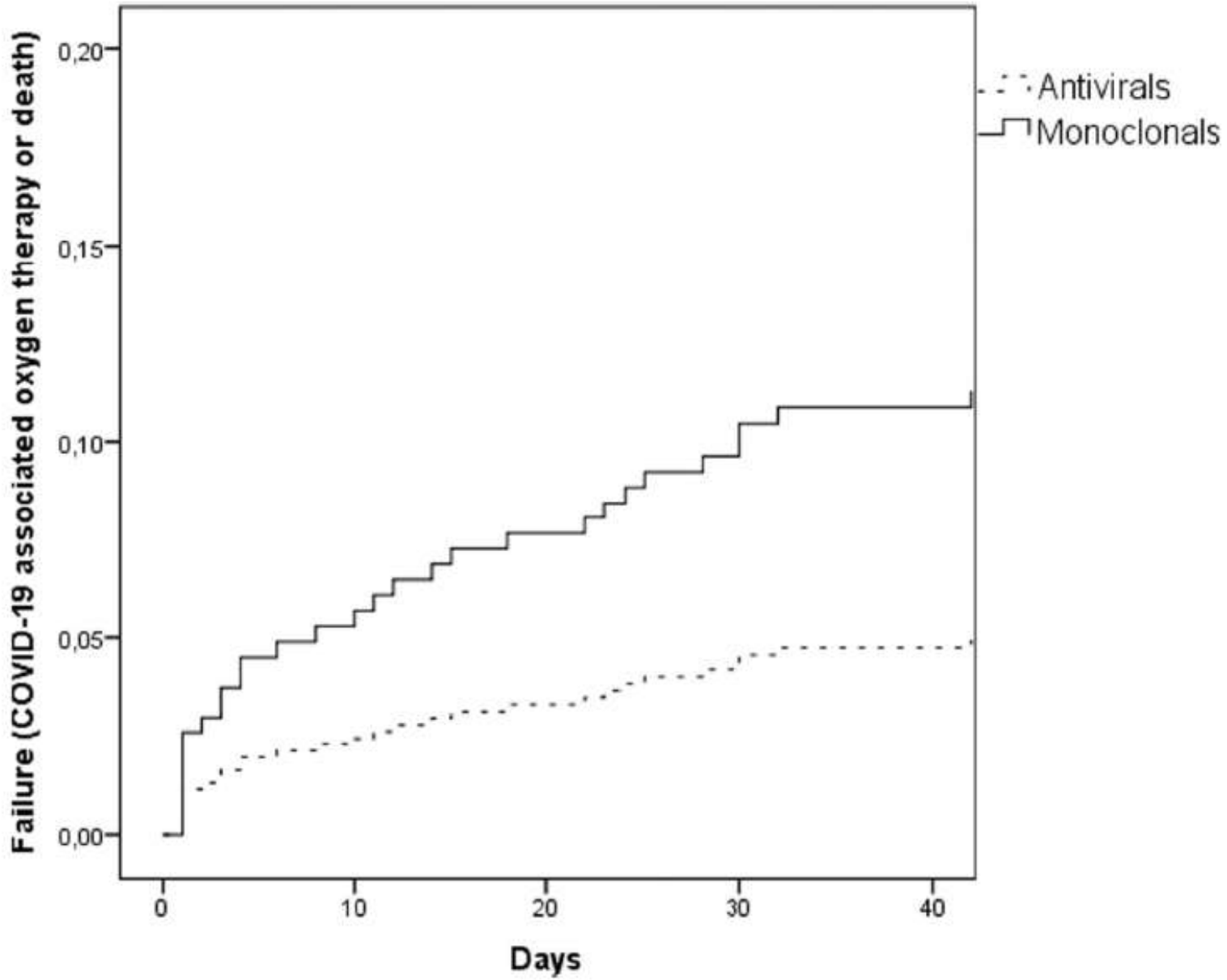
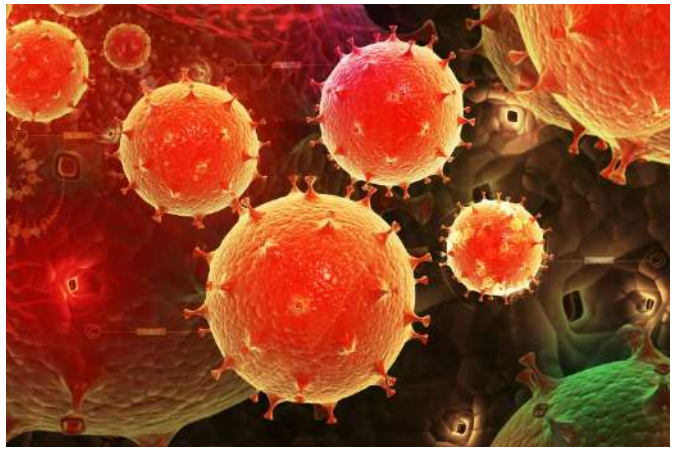


FIGURE 2 Adjusted Kaplan–Meier curve showing the risk of failure in patients receiving two different types of early treatment.

BJHaem. 2023

>20 gün



İmmunkompromize konak

Uzamış Saçılım

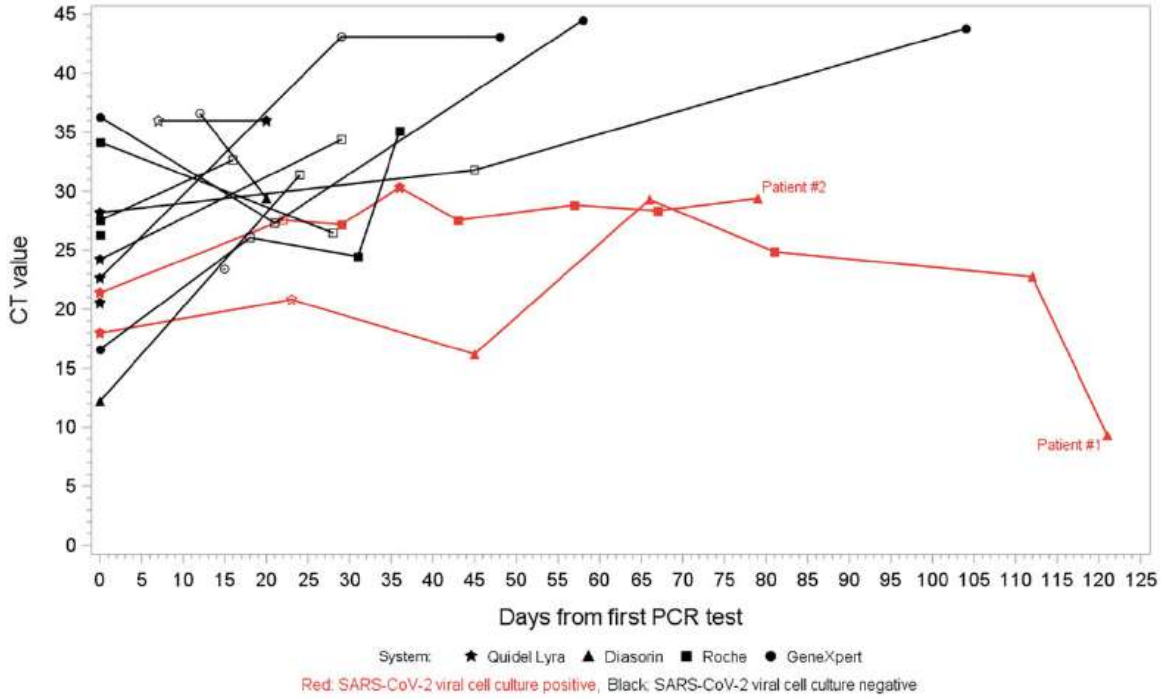
CDC

Semptom ve hastalık ciddiyetinden bağımsız olarak

Immunkompromize konakta

En az 20 gün izolasyon olmalı

İzolasyondan çıkış için ardışık 2 negatif test (antijen veya PCR) olmalı



Özellik	Hasta 1	Hasta 2
	60 y, E	75 y, E
Kronik hastalık	KLL	Marjinal zone lenfoma
SARS CoV-2 Pozitifliği (gün)	120	79
Primer hastalık tedavisi	Obinutuzumab + venetodax	Bendamustine + rituksimab
Son durum	COVID19 ilişkili ölüm	16. Haftada yaşıyor

TABLE 1 | Patient demographics.

Variable	All patients (N=20) N (%) or Median (range)
Sex	
Male	11 (55)
Race[a]	
White	14 (70)
Black	6 (30)
BMI	27.2 (20.1 – 52.0)
Age at date of first positive PCR	64 (20 – 79)
Time between first and second positive PCRs (days)	21 (7 – 62)
Number of positive PCR tests after the initial positive test	2 (1-7)
Immunosuppressive condition[b]	
Solid organ transplant	10 (50)
Hematologic malignancy	5 (25)
Bone marrow transplant 6 months beforefirst positive PCR	1 (5)
Other	3 (15)
Solid organ malignancy[b]	1 (5)
Immunosuppressive medication[c]	
Receiving high dose steroids at time of positive PCR test	5 (25)
Receiving biologic medication in prior 30 days	2 (10)
Receiving other immunosuppressive medication in prior 30 days	11 (55)

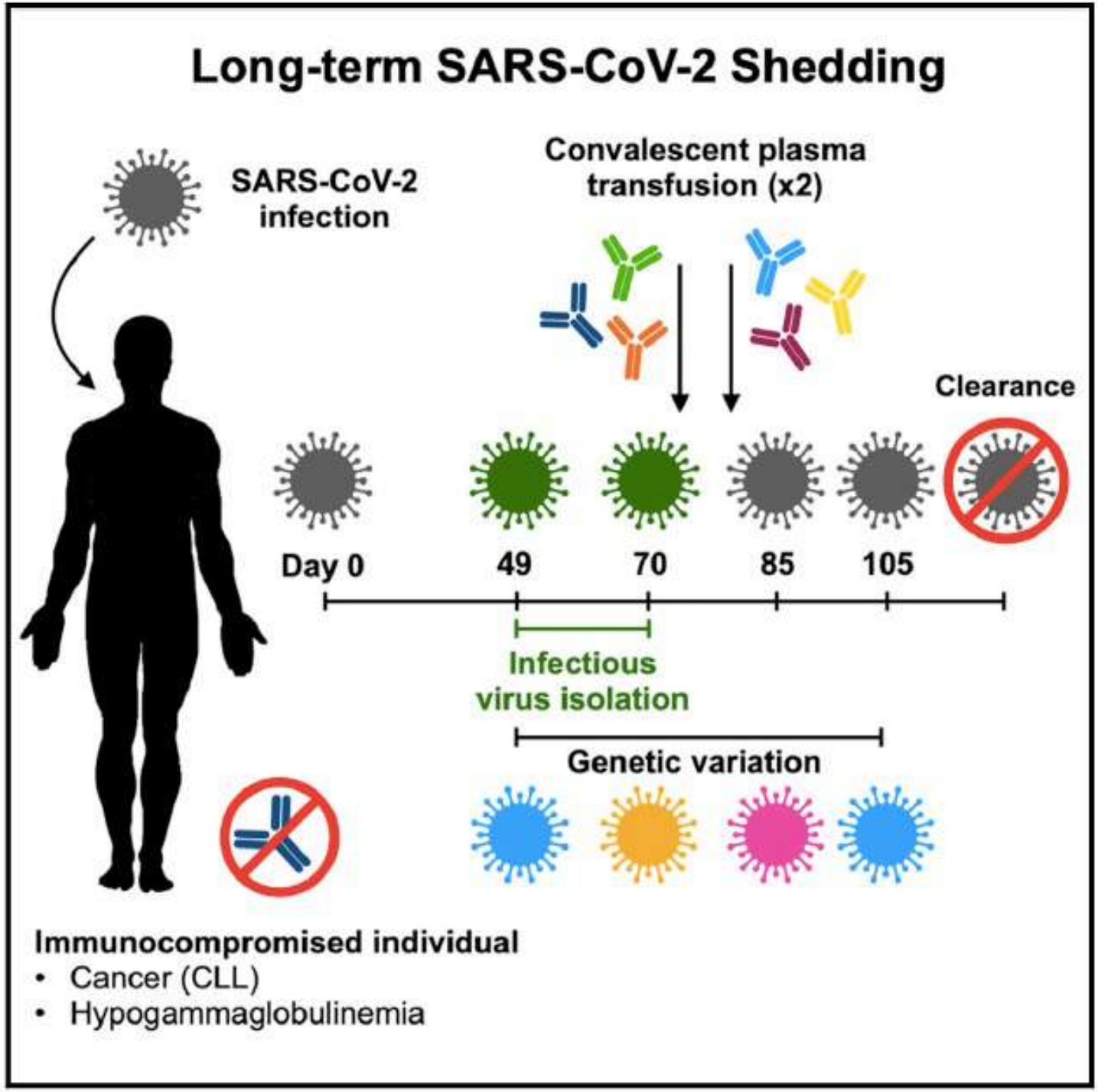
Sung ve ark. Front. Cell. Infect. Microbiol. 12:804175

Article

Cell

Case Study: Prolonged Infectious SARS-CoV-2 Shedding from an Asymptomatic Immunocompromised Individual with Cancer

70 yaş, K
KLL
Hipogamaglobulinemi



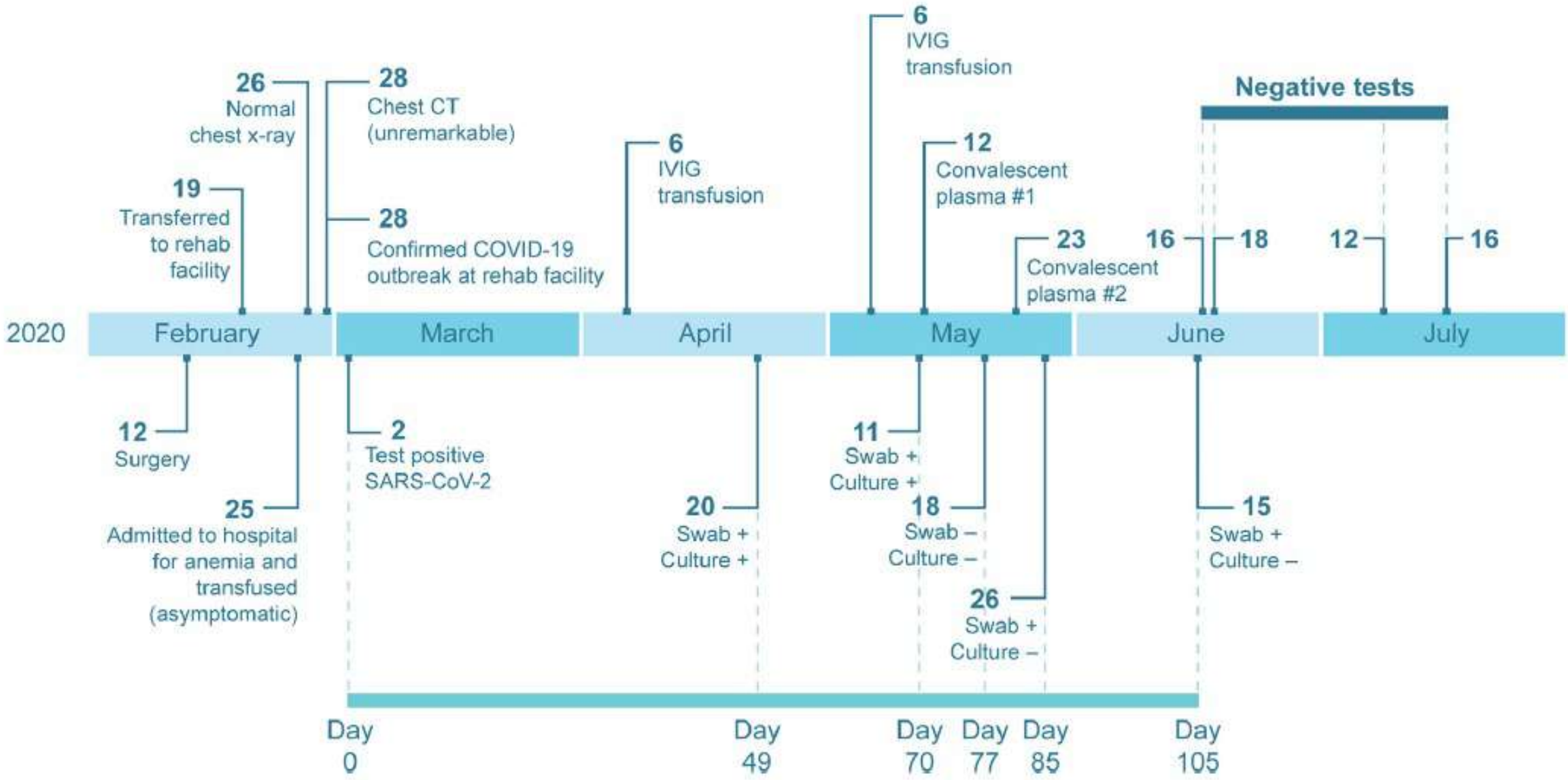
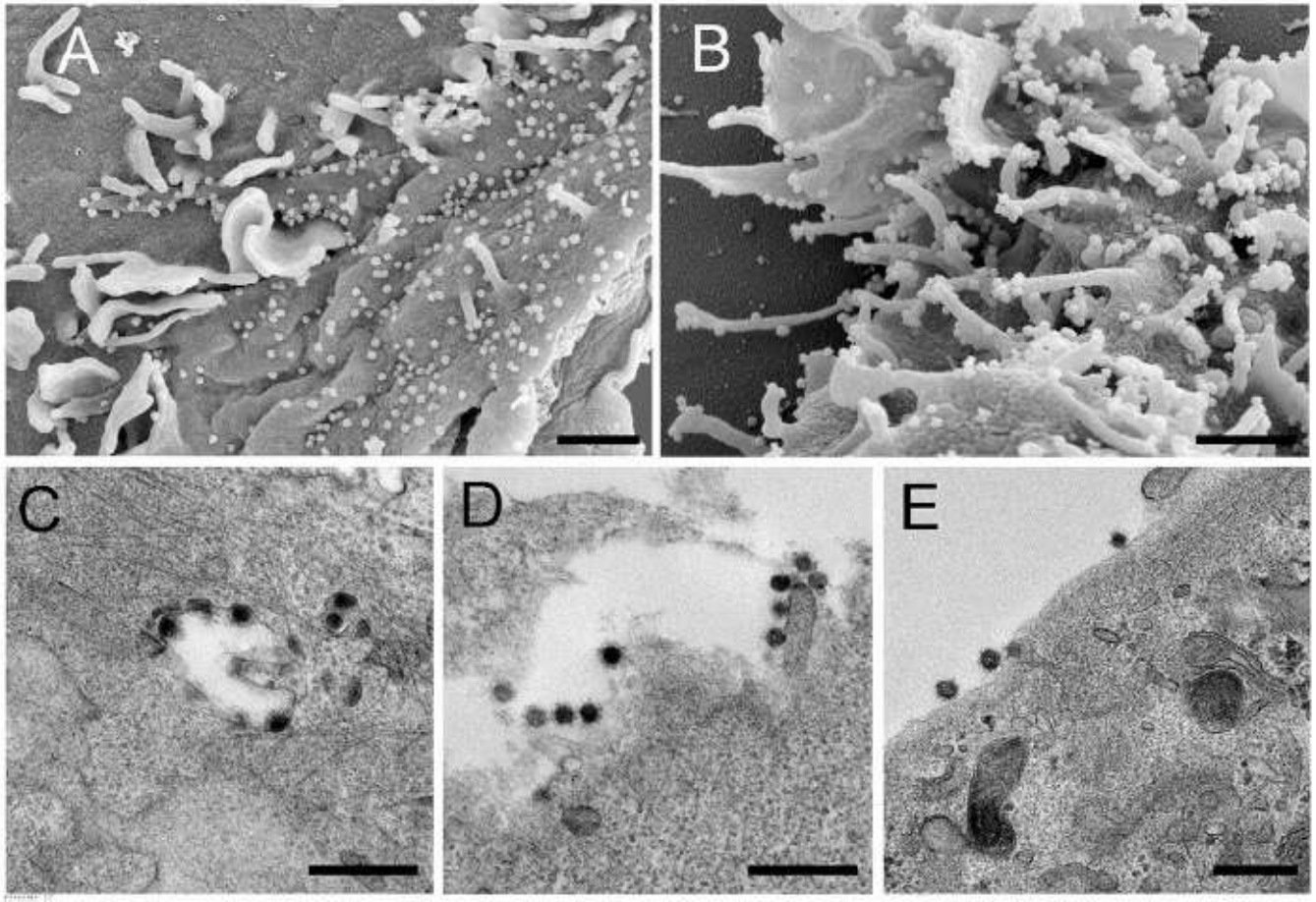


Figure 1. Timeline of Clinical Presentation, Diagnostic Tests, and Treatments of an Immunocompromised Individual with Long-Term Shedding of SARS-CoV-2



Electron Microscopy Confirms Isolation of Coronavirus from the Individual's Nasopharyngeal Swabs

SARS-CoV-2 cultured from the individual's nasopharyngeal swabs was used to inoculate Vero E6 cells for imaging by scanning and transmission electron microscopy (SEM and TEM, respectively).
(A and B) SEM images of the day 49 (A) and day 70 (B) isolates.
(C–E) TEM images of the day 49 (C) and day 70 (D and E) isolates.
SEM scale bars, 1 mM; TEM scale bars, 0.5 mM

Table 1. Virus Neutralization Titers in Pre- and Post-transfusion Sera from the Individual and Convalescent Plasma Used for Transfusion

Serum	USA/WA1/2020	Day 49 Isolate	Day 70 Isolate
Day 49	<10	<10	<10
Day 71	<10	<10	<10
Day 71 after transfusion	<10	<10	<10
Day 77	<10	<10	<10
Day 82	< 10	10	<10
Day 82 after transfusion	10	10	15
Day 105	10	<10	<10
Convalescent plasma 1	60	40	40
Convalescent plasma 2	160	160	60

Virus neutralization assays were performed for all serum and plasma samples with SARS-CoV-2 strains USA/WA1/2020 and the day 49 and day 70 isolates from the individual. Each serum/plasma sample was tested in duplicate.

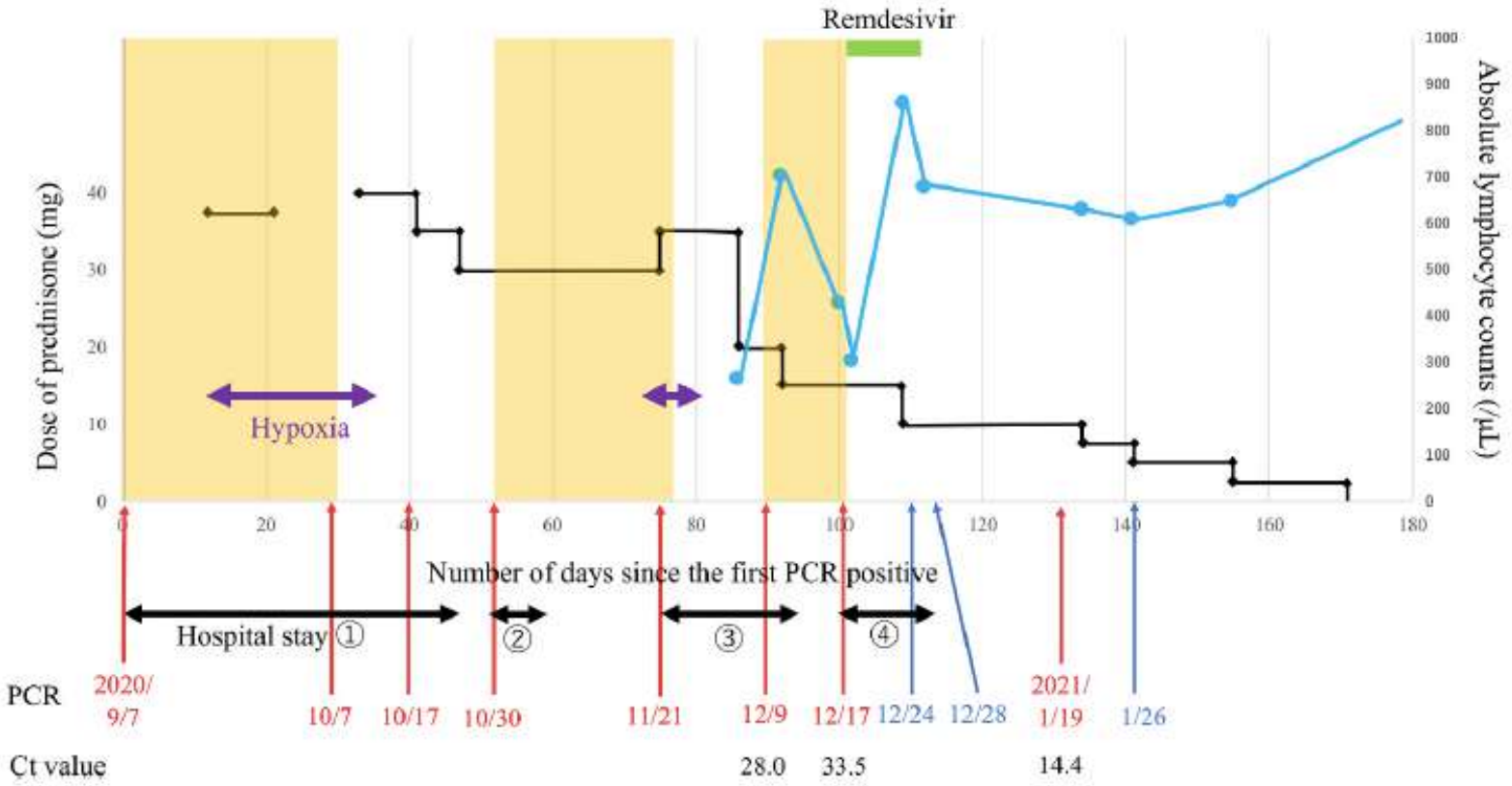
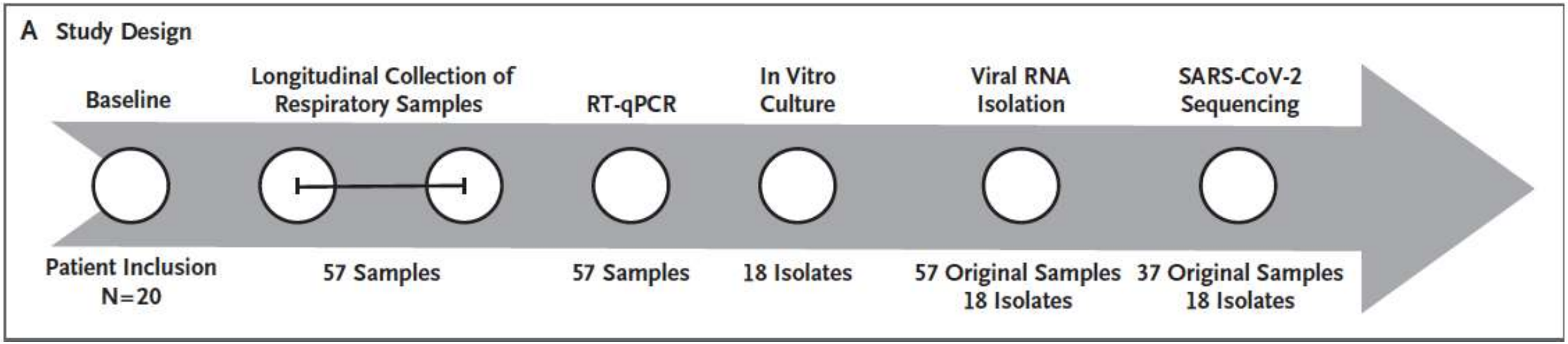


Fig. 1. Timeline of the patient. The dose of prednisone is shown in black and lymphocyte count is shown in light blue on the graph. A dexamethasone dose of 4 mg is counted as equivalent to prednisone 25 mg. The SARS-CoV-2 PCR results shown in red were positive, and those shown in blue were negative. Ct value shows cycle threshold value in PCR tests. The four hospital admissions are shown as thick black lines. The orange area represents the period of fever of 38 °C or higher.

J Infect Chemother. 2022 Jul;28(7):971-974

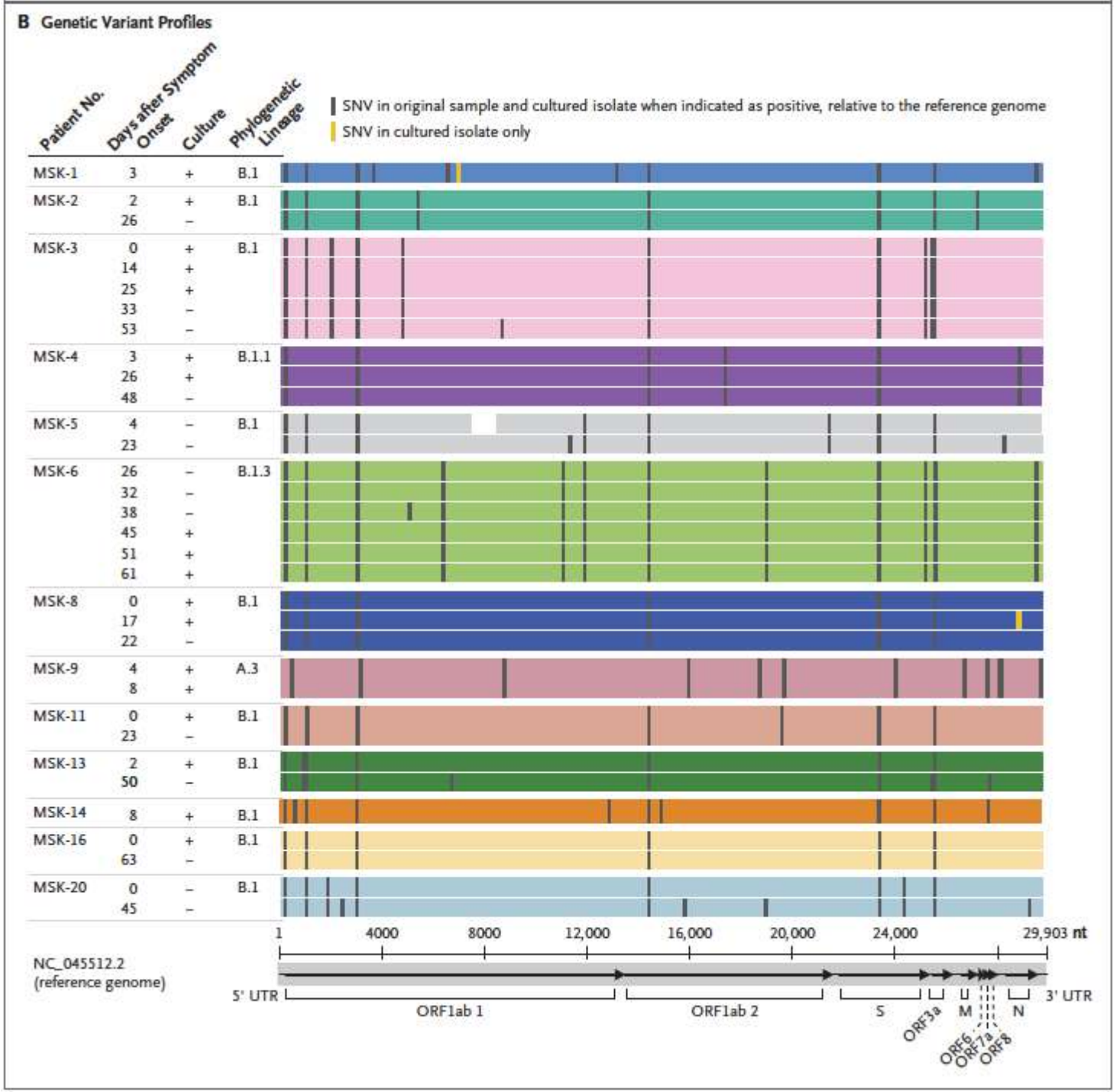


18 KİT alıcısı
2 Lenfoma

15'i aktif tedavi ya da KT alıyor.
11'i ciddi COVID19

10 Mart-20 Nisan 2020

N Engl J Med. 2020 Dec 24;383(26):2586-2588



Immunkompromize konaklar için izolasyon süresi gözden geçirilmelidir.

N Engl J Med. 2020 Dec 24;383(26):2586-2588

bjh short report

Persisting SARS-CoV-2 viraemia after rituximab therapy: two cas

Persistent COVID-19 Pneumonia and Failure to Develop Anti-SARS-CoV-2 Antibodies During lar

Persistence of SARS-CoV-2 Infection in Severely Immunocompromised Patients With Complete Remission B-Cell Lymphoma and Anti-CD20 Mo Ca

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

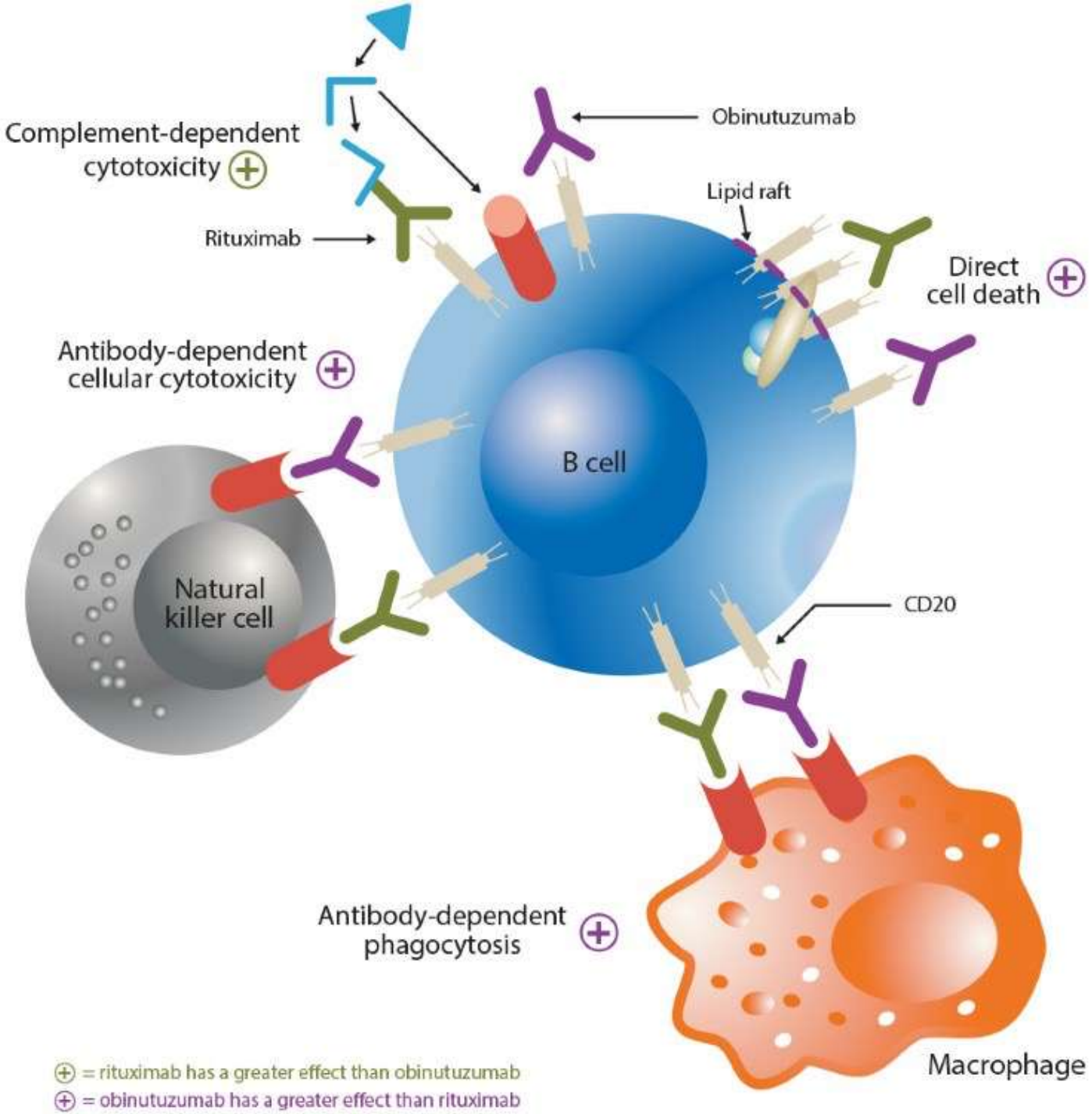
journal homepage: www.elsevier.com/locate/jic

Case Report

Persistent viral shedding of severe acute respiratory syndrome coronavirus 2 after treatment with bendamustine and rituximab: A case report☆

Rituksimab Nerede Kullanılır?

- **CD20 pozitif B hücreli NHL**
- **Kronik lenfosittik lösemi**
- **Romatoid Artrit**
- **Mikroskobik PAN**
- **Pemfigus vulgaris**



Differences in the proposed mechanisms of action of rituximab and obinutuzumab.

Rituximab is a type I antibody that functions by the stabilisation of CD20 on lipid rafts, resulting in strong complement-dependent cytotoxicity. Obinutuzumab is a glycoengineered type II antibody that leaves CD20 distributed across the surface of the B cell and has much lower complement-dependent cytotoxicity, but greater antibody-dependent cellular cytotoxicity, antibody-dependent phagocytosis and direct cell death.

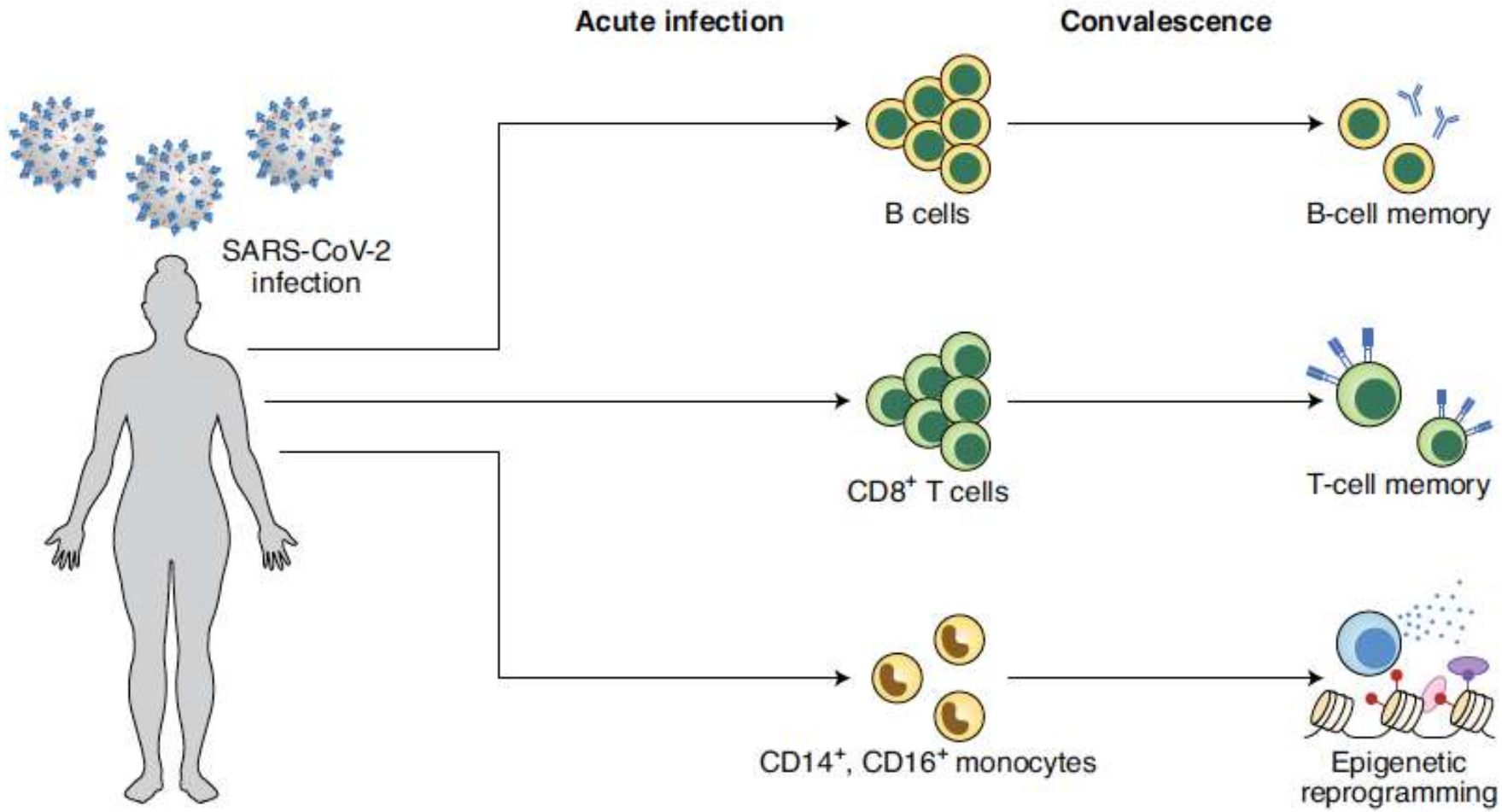


Fig. 1 | Memory responses after COVID-19 infection. COVID-19 infection leads to proliferation of B cells and T cells, which is followed by the survival of a few memory B and T cells that insure long-term protection after elimination of the virus. COVID-19 infection also leads to potent activation of myeloid cells such as monocytes and macrophages. Interestingly, recovery from the infection is accompanied by long-term transcriptional, epigenetic and functional rewiring of monocytes (also called trained immunity), inducing changes in the innate immune responses after COVID-19.

Nature Cell Biology: 23; June 2021. 580–586

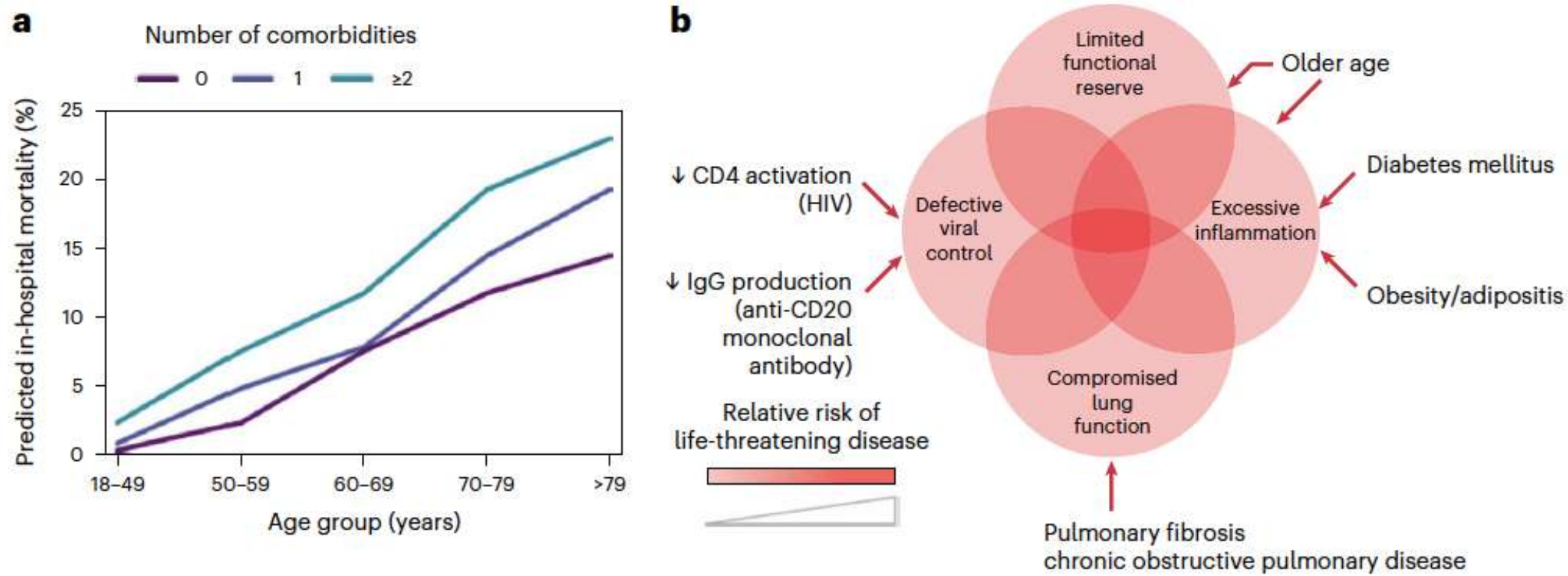
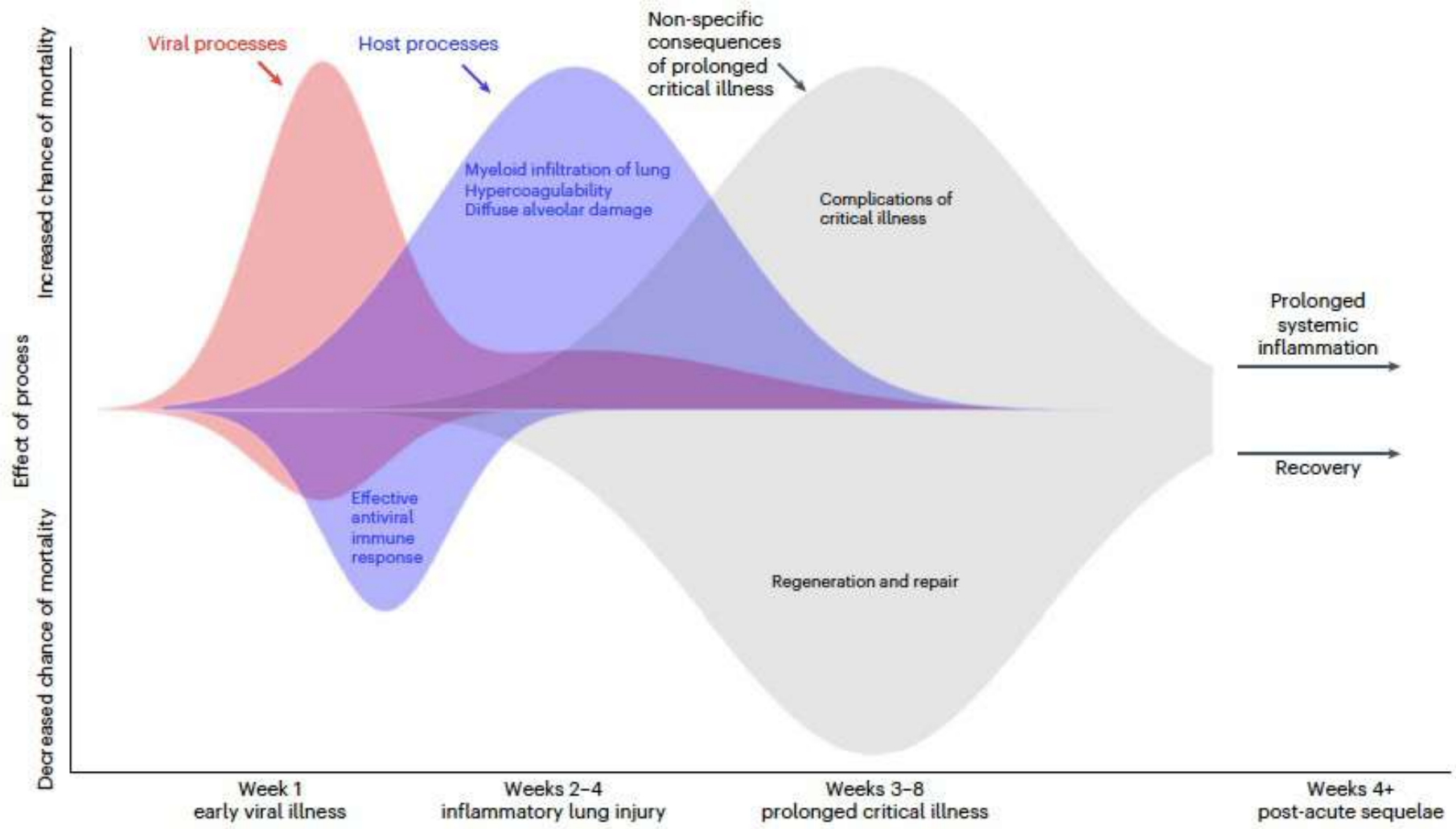


Fig. 1 | Effect of multimorbidity and comorbidity on risk of life-threatening disease. a, To illustrate the impact of multimorbidity, the ISARIC4C mortality score was used to predict in-hospital mortality for hypothetical male patients in different age groups and with different numbers of comorbidities, assuming other variables used in the score remained the same (respiratory rate < 20 breaths min^{-1}; peripheral oxygen saturation > 91%; Glasgow Coma Scale score 15; urea < 7 mmol l^{-1}; C-reactive protein < 50 mg l^{-1}). The graph illustrates the increasing risk of mortality with increasing age and increasing number of comorbidities, and that comorbidity count has an additive effect to age. **b**, Additive effects (indicated by color shading) exerted by comorbidities (multimorbidity), contributing to disease severity through different potential mechanisms.

Nat Med. 2023 Feb;29(2):334-343



Accelerated drivers of disease	B cell/antibody suppression (rituximab), impaired T cell response (HIV), failure of interferon response (host genetics)			
		Obesity (adipositis), advanced age, influenza co-infection		
Impaired tolerance of injury	Dementia, cardiac disease, chronic kidney disease, liver disease, cancer			
		Chronic respiratory disease Neuromuscular disease		
			Frailty, deconditioning, malnutrition, chronic disease, multimorbidity	

Nat Med. 2023 Feb;29(2):334-343

21 cases of persistent SARS-CoV-2 infection in immunocompromised individuals.

	Age	Sex	Baseline	Baseline-Treatment	Treatment for COVID19
Taramasso et al.	70	M	Mantle cell lymphoma	Rituximab, Bendamustine, Cytarabine	NA
	50	F	Neuromyelitis Optica	Rituximab	NA
	47	F	MM	Dexamethasone, Cisplatin, Doxorubicin, Cyclophosphamide	NA
Baang et al.	70	M	Mantle cell lymphoma	Mosunetuzumab	Remdesivir, convalescent plasma
Aydillo et al.	NA	NA	haematopoietic stem cell transplantation	NA	NA
	NA	NA	haematopoietic stem cell transplantation	NA	NA
	NA	NA	haematopoietic stem cell transplantation	NA	NA
	NA	NA	Haematological malignany	NA	NA
Nakajima et al.	47	M	Follicular lymphoma	Obinutuzumab	Favipiravir
Avanzato et al.	71	F	CLL, hypogammaglobulinaemia	IVIG	convalescent plasma
Decker et al.	62	M	Heart transplantation	MMF, steroid, Cyclophosphamide	NA
Guetl et al.	NA	NA	X-linked agammaglobulinaemia	NA	lopinavir, ritonavir and hydroxychloroquine sulfate, convalescent plasma
Choi et al.	45	M	Antiphospholipid syndrome	Rituximab, steroid	Remdesivir
Daniel et al.	37	F	Follicular Lymphoma	Rituximab, Etoposide, Cisplatin, steroid, Cytarabine	Remdesivir, convalescent plasma
Phillip et al.	56	F	Follicular Lymphoma	Rituximab	Remdesivir, convalescent plasma
Marie et al.	50s	M	CLL	Cyclophosphamide, Rituximab, Fludarabine Phosphate	Remdesivir, convalescent plasma
Jennifer et al.	70s	M	B cell Lymphoma	NA	NA
Matthew et al.	73	M	MM	CAR-T cell therapy	Remdesivir
Hassan et al.	66	M	HIV	NA	NA
	71	M	Cardiac transplantation	steroid, Mycophenolic acid, Belatacept	NA
	35	M	RA	Rituximab	NA

Abbreviations: NA; Not; Available, MM; Multiple Myeloma, CLL; Chronic Lymphocytic Leukemia, HIV; Human Immunodeficiency Virus, RA; rheumatoid arthritis, IVIG; intravenous immunoglobulin, MMF; mycophenolate mofetil, CAR; chimeric antigen receptor, COVID-19; coronavirus disease 2019.

J Infect Chemother. 2022 Jul;28(7):971-974

Özetle

- Lenfoma
- HIV (CD4 düşük)
- Romatolojik hastalıkları

- Korunma
  - Aşılama

- Monoklonal nötralizan antikorlar

- Antiviraller
  - Remdesivir (5-10 gün)
  - Molnupiravir
  - Nirmatrelvir/r

- Konvalesan plazma

- IVIG
  - doz? 1.5 g/kg