SITA
Società Italiana di Terapia Antinfettiva Antibatterica Antivirale Antifungina

14° CONGRESSO NAZIONALE
GENOVA | 21-22 novembre 2024

Focus su Sars-CoV-2

Come gestire il paziente immunodepresso

Chiara Dentone
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DISCLOSURES

Advisor/speaker (past 5 years)

Angelini, Gilead,
Novartis, MSD, Astrazeneca

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Impact of COVID-19 on immunocompromised populations during the Omicron era: insights from the observational population-based INFORM study

Retrospective cohort design UK
IC vs general population
(01/01/2022-31/12/ 2022)

IC accounted for 3.9% of the study population,

- **21.9 % (4585/ 20,910) of COVID-19 hospitalisations**
- **28% (125/440) of COVID-19 ICU admissions**
- **23.8% (1145/4810) of COVID-19 deaths**

Vaccinated with ≥3 doses
(~84% IC vs 51%):
all IC groups increased risk
adjusted incidence rate ratios (aIRR) for hospitalisation 1.3 to 13.1.

At highest risk for COVID-19 hospitalisation:

- **solid organ transplant (aIRR 13.1, 95% [95% CI] 11.2–15.3),**
- **stem cell transplant (aIRR 11.0, [95% CI] 6.8–17.6)**
- **recent treatment for HM (aIRR 10.6, [95% CI] 9.5–11.9)**

Results similar for COVID-19 ICU and deaths.

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Evans RA et al. The Lancet Regional Health - Europe 2023

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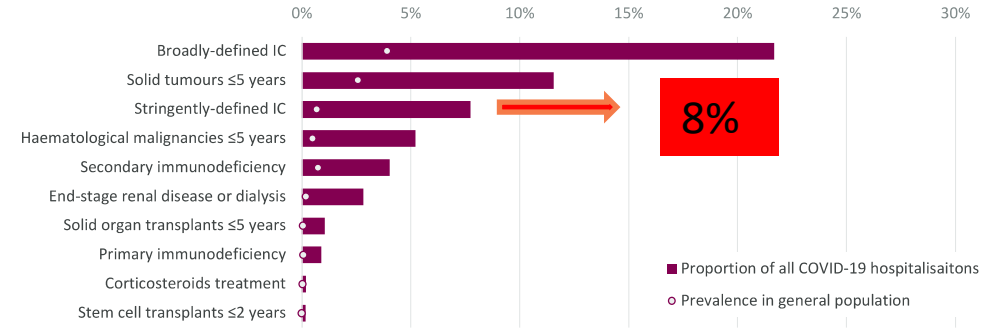
Impact of COVID-19 on immunocompromised populations during the Omicron era: insights from the observational population-based INFORM study

"Broadly-defined immunocompromised" 3.9%

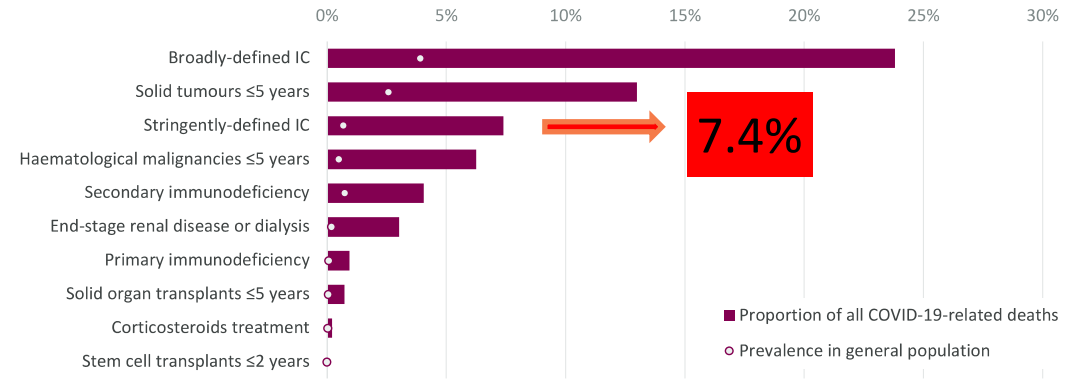
"Stringently-defined immunocompromised" 0.7%

Hospitalisation for Severe COVID-19

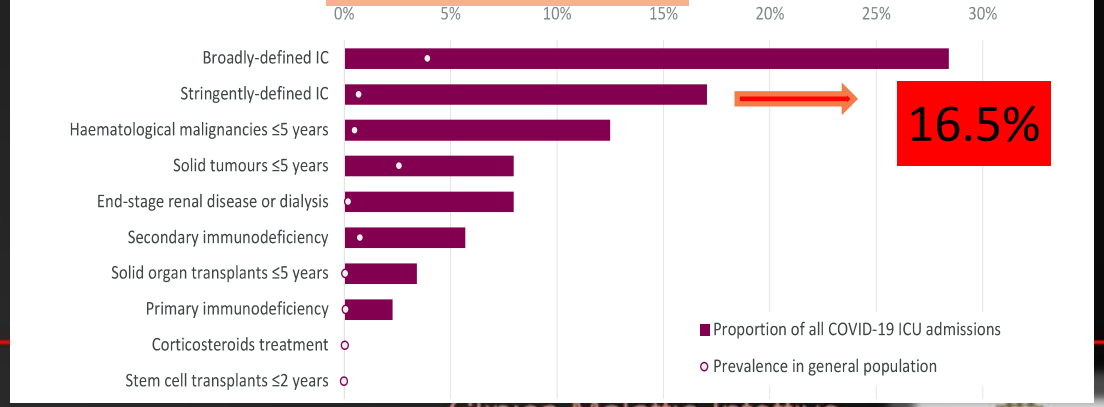


- Moderate/severe primary immunodeficiency
- Active treatment with immunosuppressive or immunomodulatory therapy
- treatment with high-dose corticosteroids
- Solid organ transplant ≤2 years
- Haematopoietic stem cell transplant ≤2 years
- solid tumour [s] or haematologic malignancies on treatment ≤6 months
- LLC, LNH, MM, LMA ≤2 years
- AIDS

COVID-19 deaths



ICU admission



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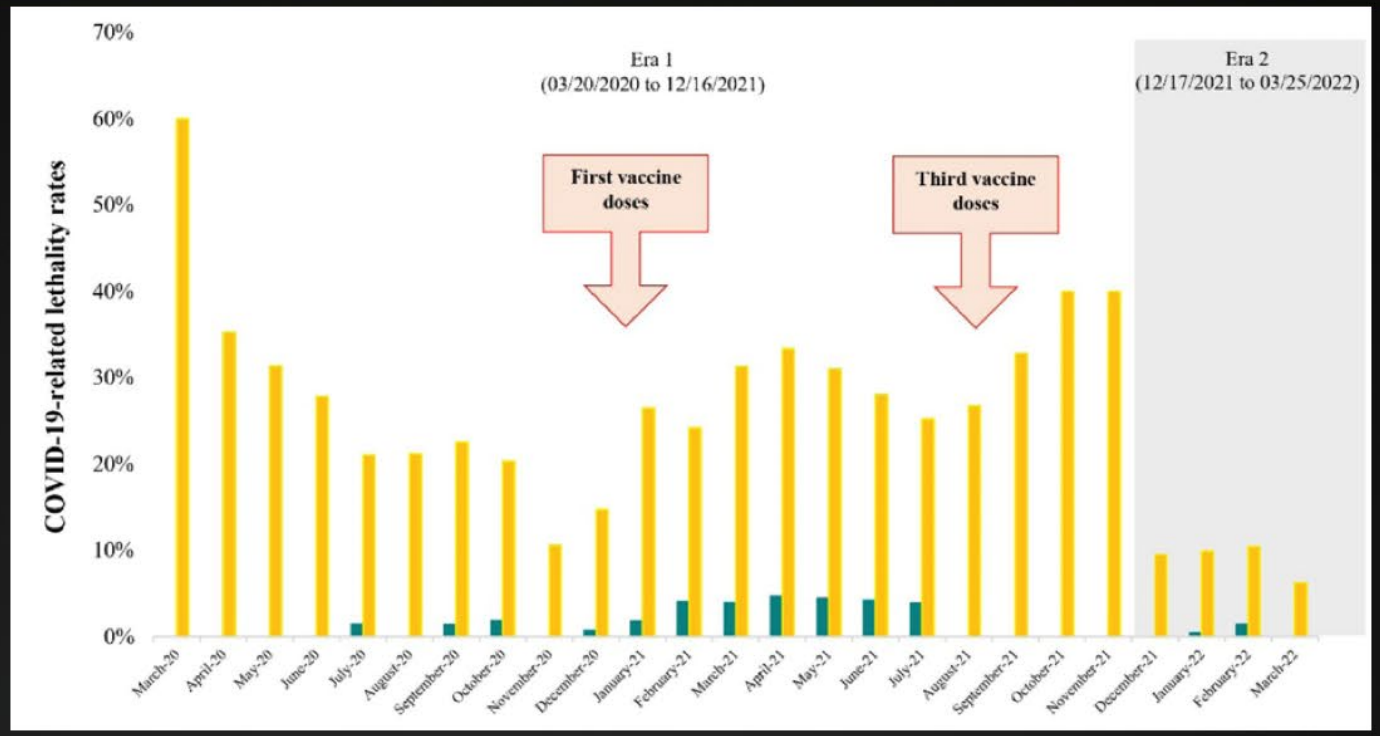
Evans RA et al. The Lancet Regional Health - Europe 2023

How Did the Omicron Surge Affect Kidney Transplant Recipients vs Cohort From the General Population

10 497 kidney transplant
vs 14506 inhabitants (Brazil).

Equivalent surveillance, diagnostic and monitoring strategies, accurate electronic database, similar sample size, and **high vaccination coverage**



	Kidney transplant recipients			General population from Ipaussu		
	Era 1	Era 2	% Change	Era 1	Era 2	% Change
Need for hospitalization, *n* (%)	1305 (57)	309 (29)	- 50%	105 (4·4)	24 (1·4)	- 68%
Need for mechanical ventilation, *n* (%)	678 (30)	172 (16)	- 46%	50 (2·1)	8 (0·5)	- 77%
Lethality, *n* (%)	610 (27)	120 (11)	- 60%	48 (2·0)	8 (0·5)	- 75%
Patients >60 years among the deads, *n* (%)	293 (48)	76 (63)	+31%	34 (71)	7 (88)	+ 24%

11% vs 0.5%

degli Studi di Genova
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Cristelli MP et al. Transplantation 2022

The interaction between the SARS-CoV-2 and the immune system of patient makes the difference

The host makes the difference, not only the treatment

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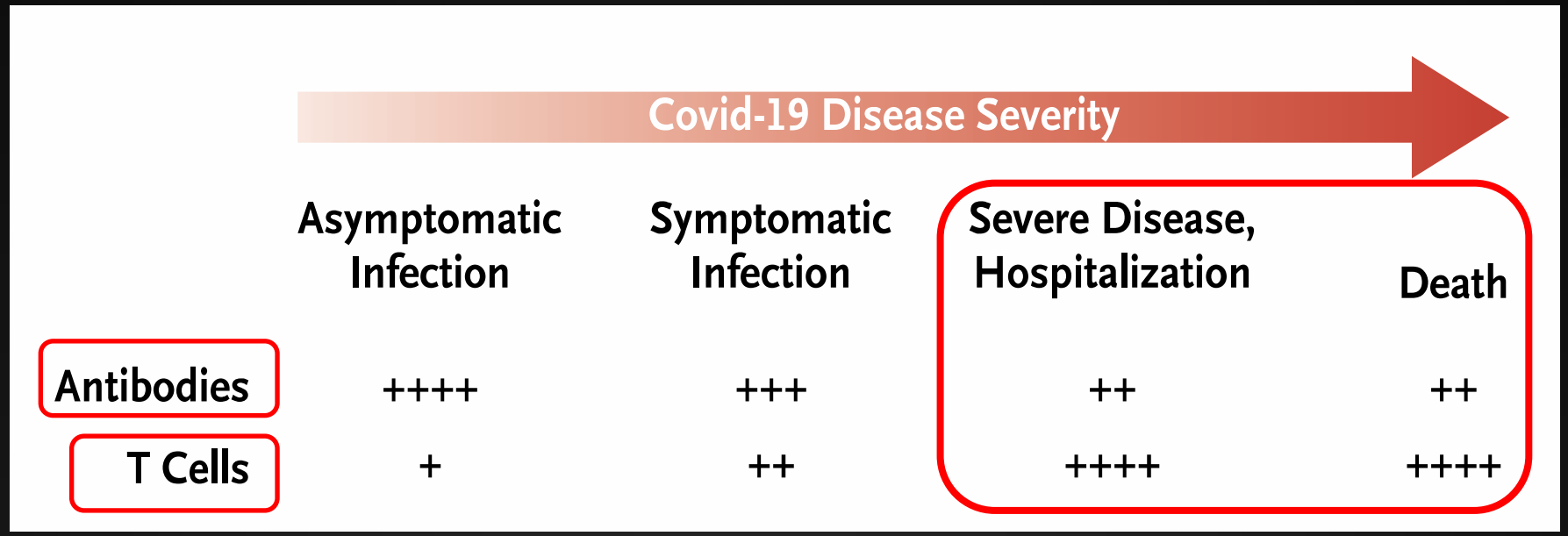
Immune Responses for Protection against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)



Combination of humoral and cellular immune responses controls viral replication after infection and prevents progression to severe disease, hospitalization, and death

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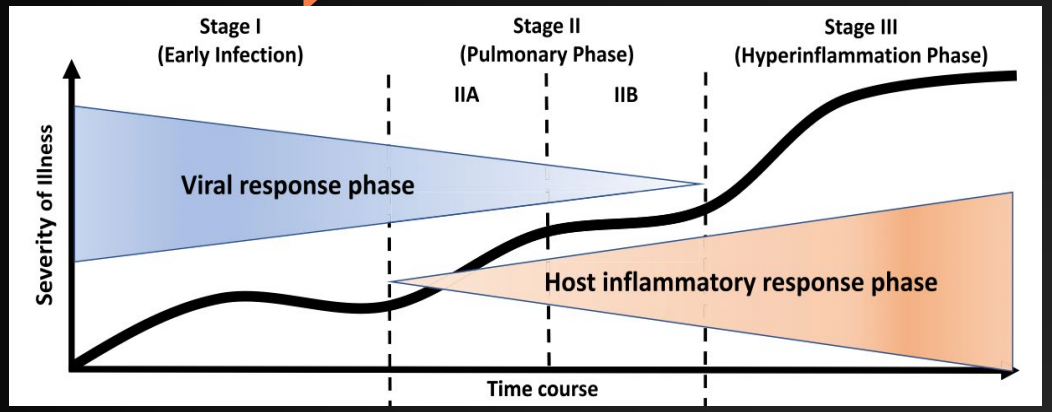
Barouch DH NEJM, 2022

Diversi Stadi di malattia e Terapie

Maggio 2020 …

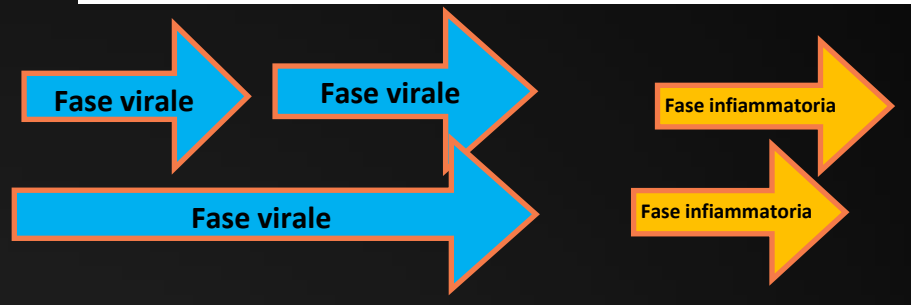
Novembre 2024 …

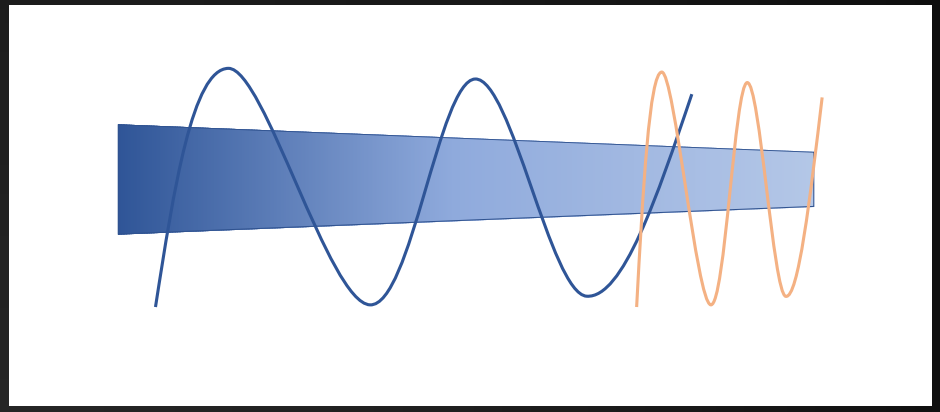
Fase virale → **Fase infiammatoria**



Siddiqi HK et al. The Journal of Heart and Lung Transplantation 2020

"Broadly-defined immunocompromised"*





Cesaro S et al. ECIL 9. Leukemia 2022

Clinical relapses or intermittend flares of symptoms and virological persistance

*Lymphopenia, recent anti-CD20 therapy, CART therapy, hypogammaglobulinaemia and haematopoietic stem cell transplantation

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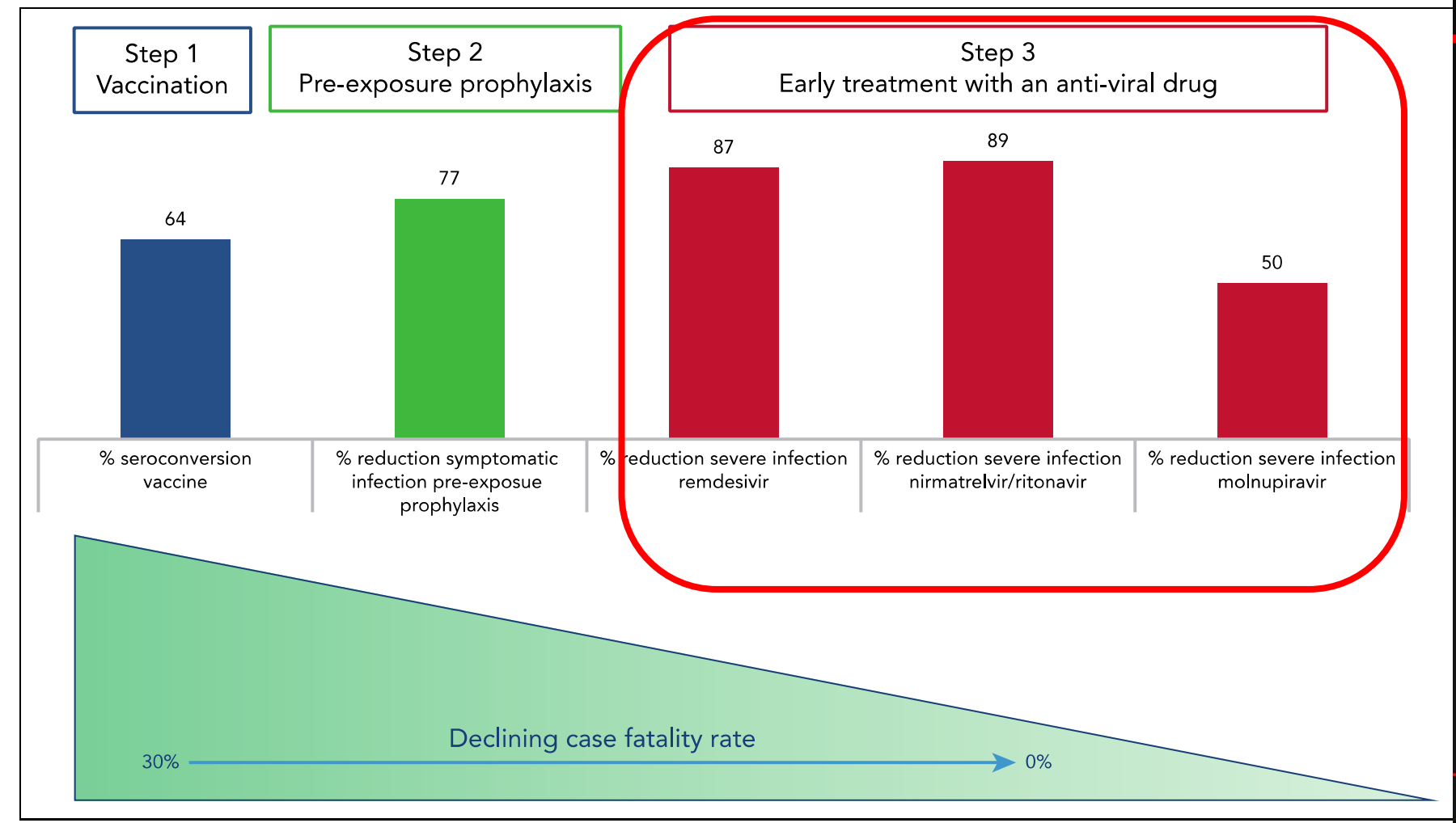
Risk Category	Example Health Condition	Example Therapeutics
Higher risk immunocompromised patients	• Stem cell transplant <2 y • Graft versus host disease, grade 3 or 4 • Hematological malignancy on therapy • Lung transplant • Fewer than 1% peripheral B-cells assessed in past 6 months	• B-cell depleting agents in past 12 months (eg, rituximab, ofatumumab, ocrelizumab, others) • CAR-T therapy in past 12 months • Abatacept
Moderate risk immunocompromised patients	• Solid organ transplant other than lung • Solid tumor on treatment • Congenital agammaglobulinemia • Graft versus host disease, grade 1 or 2 • HIV infection with CD4 <200 cells/mm^3 • Other severe primary immunodeficiency	• Tyrosine kinase inhibitor (eg, ibrutinib, acalabrutinib, others) • High-dose corticosteroids (>20 mg prednisone or equivalent for >4 wks) • Anthracycline derivates
Lower risk immunocompromised patients	• HIV infection with CD4 >200 cells/mm^3 • Inflammatory bowel disease • Cirrhosis • ESRD • Solid tumor (treatment >12 months prior)	• Anti-TNF • Anti–IL-6 • Anti–IL-12 and -23 • Corticosteroids ≤10 mg long-term, or <20 mg for <4 wks • Intra-articular steroids

Abbreviations: CAR-T, chimeric antigen receptor T-cell; ESRD, end-stage renal disease; HIV, human immunodeficiency virus; IL-, interleukin; TNF, tumor necrosis factor.

COVID-19 management in IC: half-full or half-empty glass?



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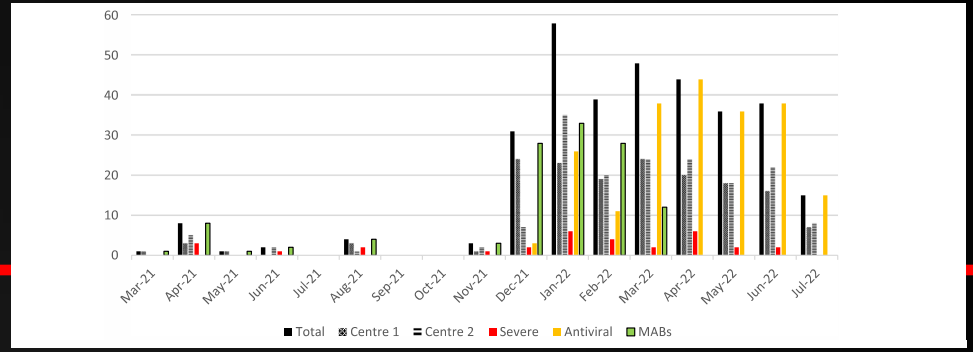
Personal modification
Scarfò L and Cuneo A. Blood 2023

Outcome of early treatment of SARS-CoV-2 infection in patients with haematological disorders

Mikulska M, Testi D, Russo C et al. B J Haem 2023



Studio retrospettivo: HM 328 paziente da marzo 21-luglio2022

120 mABs, 208 antivirals, **mediana 2 gg dai sintomi**

End point composito: treatment failure (COVID-19 grave o decesso COVID-19 relato)

Rate of failure Omicron **7.8%** e 36.8 % pre Omicron, ma >> vs pop generale **1.2-1.4%**

AML/MDS (oltre età e < vaccino) associato a treatment failure e mortalità

NHL/CLL associato a shedding prolungato

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

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C’è un beneficio clinico nell’early combination therapy?

SPAIN
Single-centre, prospective, cohort study (2022)

304 **immunocompromised (> HM, HCT, SOT)**
43 (14.1%) sotrovimab plus antiviral
261 (85.9%) monotherapy

Primary endpoint:
COVID-19 progression at 90 days
(hospital admission or death due to COVID-19)

Lower risk of progression C vs M

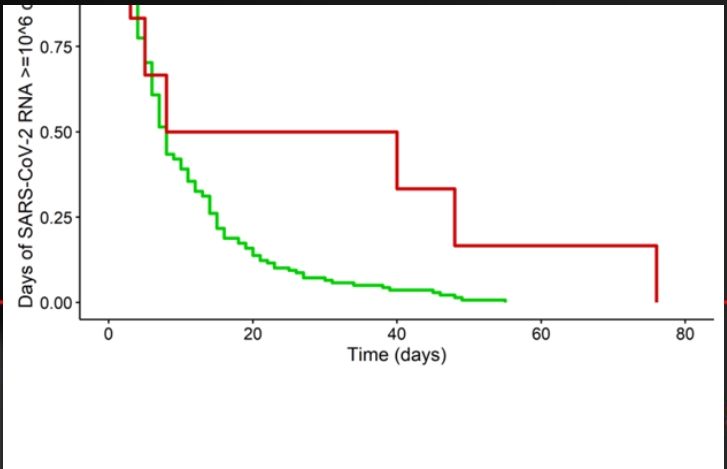
Multivariate regression of factors associated with COVID-19 progression among immunosuppressed patients who received specific treatment for early mild-moderate COVID-19.

Variable	Odds Ratio	95% CI	*P*
Combination therapy (vs. monotherapy as reference)	0.08	0.01-0.64	0.017
Anti-Spike IgG titre <750 BAU/mL	13.70	2.77-67.68	0.001
Previous anti-CD20 treatment	3.05	1.20-10.94	0.018

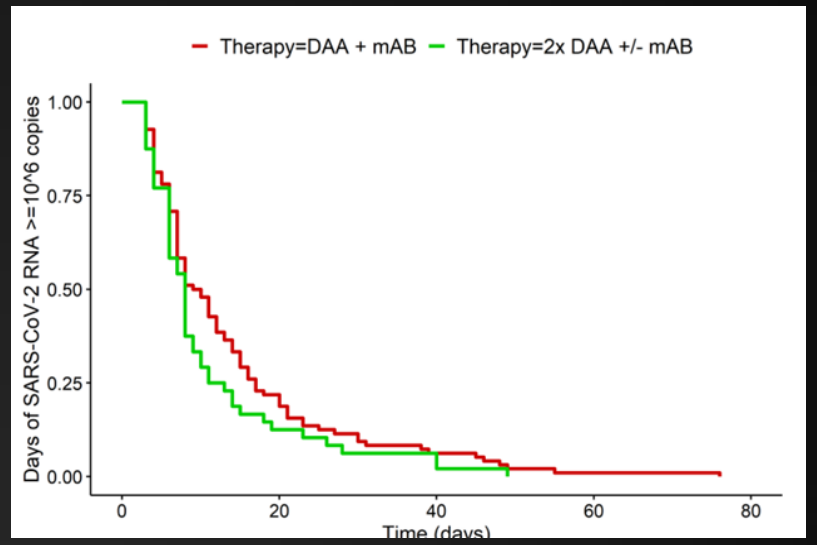
C’è un beneficio virologico nell’early combination therapy?

GERMANY
Retrospective multicentre study (2022-2023)
144 **IC**, 96 1 antiviral + mAbs,
29 with 2 antiviral
19 with 2 antiviral + mAbs

Highest risk for prolonged viral shedding:
- **Pts with a late treatment initiation (> 5 days : 30·7 days vs.≤5 days after diagnosis: 12·3 days; *p*<0·01)**



Highest risk for prolonged viral shedding:
HM (28.5%) (OR 3.5; 95% CI 1.2–9.9; *p* = 0.02)



ECT: ha evitato prolonged viral shedding in 85.6%

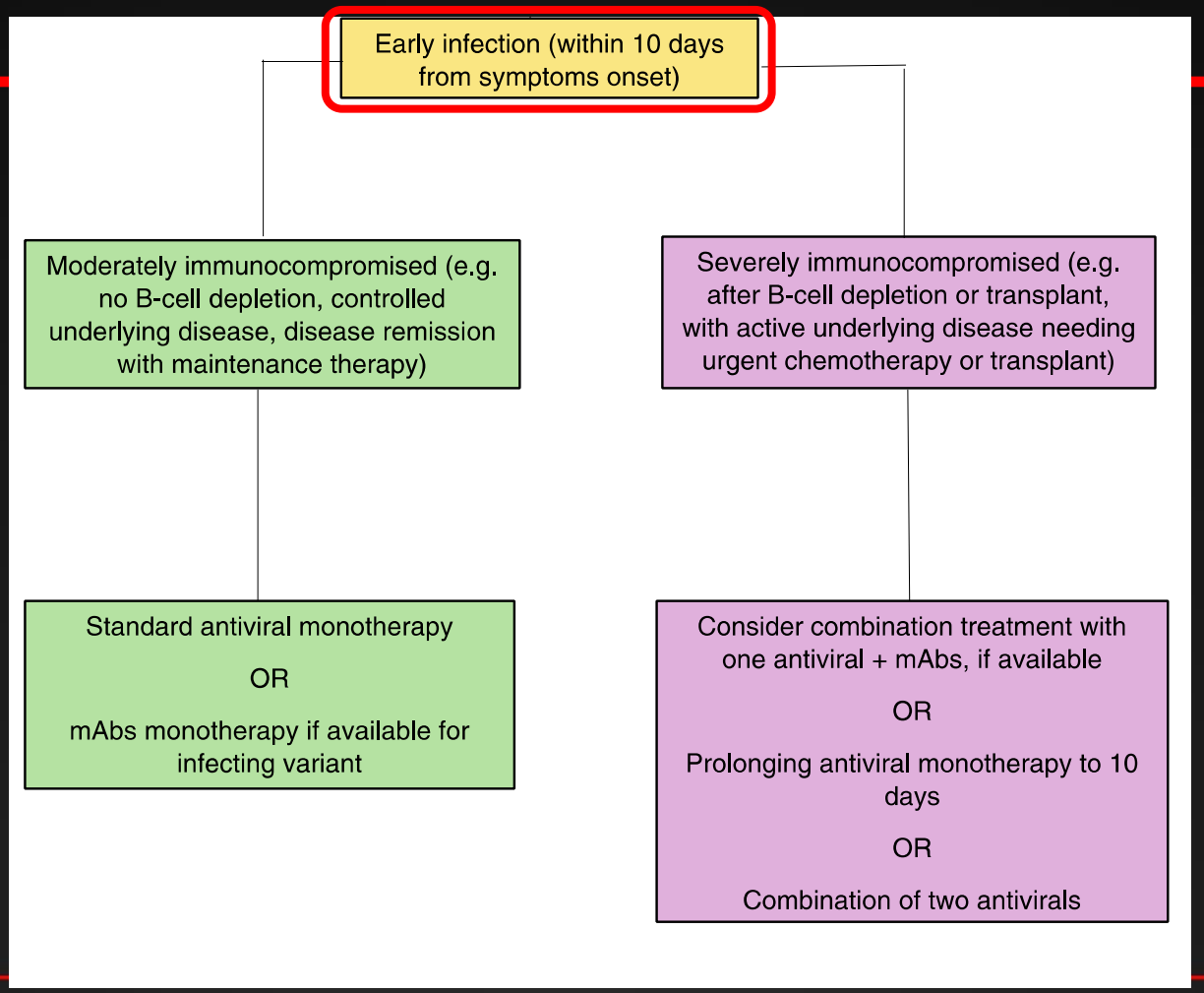
Orth H, et al. Infection 2024

Combination treatment for early SARS-CoV-2 infection (HM, SOT, B cell depletion)

Study	Country; period; (variant[a], % if reported)	Patients	COVID-19 severity	positive swab[b]/ Symptoms[c] (median) to treatment	Treatment	Length of combination treatment	Results: disease progression/ death, viral clearance	Mortality	Overall success rate of combination treatment % (n/N)	Severe adverse events	Follow up (median/last[d])
Gentile *et al.* [28▪]	Italy; April–June 2023; (Omicron[a])	7 IC 6 HM (3 LPD 0 B-cell depletion)	moderate 14% O_2 need	5 days[c]	1 RDV+N/R 6 RDV+N/R+STV	RDV: 10 days N/R: 5 days	7/7 viral clearance at 14 and 30 days	0	100% (7/7)	1 bradycardia (RDV)	40 days
Rotundo *et al.* [29]	Italy; Jan 2022–Jan 2023 (Omicron[a])	48 IC (31 LPD, 3 HCT, 8 SOT, 7 autoimmune of which 24 B-cell depleted)	asymptomatic 8.3% mild 91.7%	2 days[b] 3 days[c]	All one mAb (T/C, C/I, STV) + one antiviral (RDV, MPV, N/R)	RDV 3 days MPV and N/R for 5 days	4.2% disease progression 72.3% viral clearance within 11 days 27.7% within 18 days	COVID-19 related 1/48 (2.1%) 5 deaths during follow-up after episode, one COVID-19 related after re-infection, 4 underlying disease	46/48 (95.8%)	0	Up to 401 days[d]
Bavaro *et al.* [30▪]	Italy; July 2021–March 2022 (Delta July–December 2021, Omicron from Dec 2021[a])	331 at-risk patients (114 IC): 23 HM, 15 SOT, 62 solid cancer, 14 autoimmune diseases	mild-moderate 18% O_2 need	within 10 days[c]	IC: 11 combination RDV+mAbs 42 monotherapy 63 no therapy	RDV: 5 days	11% progression to severe COVID-19 vs. 38% with monotherapy group and 59% of no therapy group (aHR = 0.06, 95% CI = 0.02–0.77)	Overall in disease progression 36 vs. 7% in non-disease progression ($P < 0.001$)	89% (NR)	0	NR
Scotto *et al.* [32]	Italy; January–Mar 2022; (Omicron[a])	62 at-risk patients (18 IC)	mild-moderate	2 days[b] 4 days[c]	32 combination 13 RDV+C/I 19 RDV+STV 30 RDV monotherapy	RDV:3 days	Three disease progression in combination therapy; higher hospitalization rate/increased oxygen need in monotherapy (8 vs. 3.2%)	1/32 (3.1%)	90.6% (29/32)	0	21 days

Sepulcri C, et al. Current Opinion 2024

Proposed algorithm for management of HM patients with SARS-COV-2 infection



Early treatment

Early combination treatment

Sepulcri C, et al. Current Opinion 2024

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Immunocompromised Patients with Protracted COVID-19: a Review of "Long Persisters"

Veronica Dioverti[1] · Sonsoles Salto-Alejandre[1,2] · Ghady Haidar[3]

« As ID specialist, I'll give you my personal view on this topic, focusing specifically on Persistent SARS-CoV-2 infection, which is a major clinical and public health problem that should be prioritized »

A. Fauci

Proposed diagnostic criteria for protracted COVID- 19 in immunocompromised hosts (long persisters)

Criteria	
Virologic	Persistently positive SARS-CoV-2 PCR ≥ 21 days
Clinical	Persistent/relapsing symptoms (fever, dyspnea, hypoxemia) after extensive negative infectious work up
Imaging	Persistent/relapsing changes on chest-X ray or CT scan after extensive negative infectious work up
Host	Underlying immunocompromise: HCT, CAR T-cell recipient CLL, DLBCL, other lymphoma, or B-cell malignancy SOT Anti-CD19/20 therapy or other B/T cell targeted therapies Primary and acquired immunodeficiencies

Implications for Public health

- **Potential for generation of new VOC**
- **Intra-host accelerated viral evolution**
- **Resistence mutation emergence during therapy**
- **Delayed mortality**

Langerbeins P., Blood, 2022
Heldman MR., CID 2022

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Current Transplantation Reports (2022) 9:209–218

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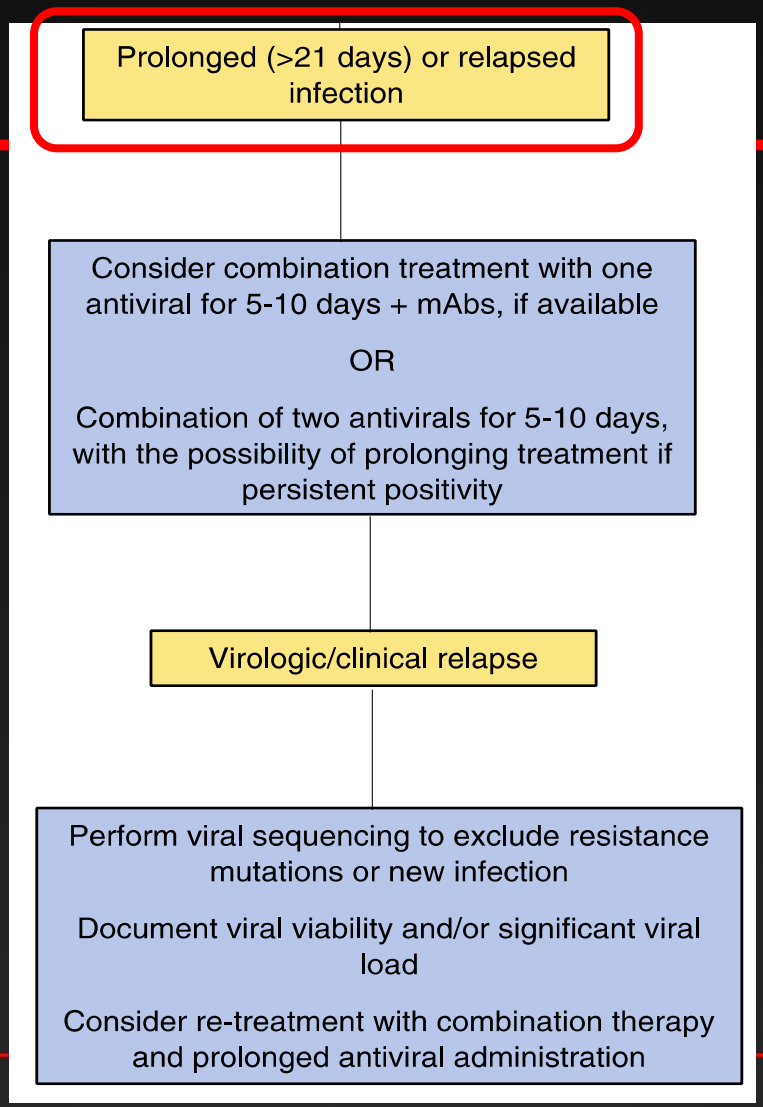
Proposed algorithm for management of HM patients with SARS-COV-2 infection



Sepulcri C, et al. Current Opinion 2024

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Successful Combination Treatment for IC with Persistent SARS-CoV-2 Infection (ID, Local Protocol Karolinska University Hospital, Sweden)

Treatment criteria
1. Underlying immunosuppression (https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-who-are-immunocompromised.html)
2. Documented NPH SARS-CoV-2 PCR positivity during period 6 wk with high viral load (Ct value <25)
3. Documented inadequate response to antiviral monotherapy (assessed 10 d after end of treatment)
4. Clinical symptoms of COVID-19 alternatively planned for severe immunosuppressive treatment for underlying disease
5. No contraindications for planned treatment

Treatment
10 days of treatment with remdesivir + nirmatrelvir/ritonavir (in case of remaining low Ct value [<25] on day 9, therapy might be extended to 14 d)
Nirmatrelvir: 150 mg 2 x 2, together with ritonavir: 100 mg 1 x 2, for 10 d. Nirmatrelvir/ritonavir dose should be adjusted in case of impaired renal function: GFR 30–60 mL/min: Nirmatrelvir: 150 mg 1 x 2, with ritonavir: 100 mg 1 x 2; GFR <30 mL/min: contraindicated
Remdesivir: 200 mg on day 1, then 100 mg once daily for a total of 10 d

Blennow O, et al CID 2023

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Combination therapy in prolonged shedding or persistent infection

Successful use of combination therapy including antivirals: RDV + NTV/r +/- MPV (+/- mAbs)

Pasquini et al. 2023
Mikulska et al. 2023
Meijer et al. 2024
Brosh-Nissimov et al. 2024
Lanzafame et al 2023
Dentone et al. 2023

Response rate 73-100%

Successful use of Extended course RDV and/or NMV/r

Martinez MA, et al. OFID 2022
Brown Li An K, et al JACI 2022
Blagdon S et al Research Square 2022
Ford ES, et al CID 2023
Blennow O, et al CID 2023
Trottier CA, et al. CID 2023
Nagai H et al Jap In f Dis 2022
Zuckerman NS, CID Feb 2024

RECOVERY was the first randomized, controlled, open-label trial to demonstrate the efficacy of the monoclonal antibodies combination of casirivimab/imdevimab and remdesivir (Lancet 2022)

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Focosi D, Nicastri E et al. IJID 2023

Protocollo Clinica Malattie Infettive, IRCCS Policlinico San Martino Genova

Strategie di gestione dell'infezione da SARS-CoV-2 nel paziente immunocompromesso

1.Strategie preventive

2. Strategie di trattamento dell'infezione precoce da SARS-CoV-2
3. Strategie di trattamento dell'infezione da SARS-CoV-2 con shedding virale prolungato (> 21 giorni)
4. Strategia di trattamento della polmonite COVID-19

2. STRATEGIE DI TRATTAMENTO PRECOCE

Monoterapia in label (AIFA) pazienti paucisintomatici (entro 5-7 gg da sintomi) **NMV/r 5 gg** **RDV 3 gg**

Fallimento virologico e/o clinico (protocollo off label) **NMV/r 10-20 gg** +/- **mAbs**

Protocollo Clinica Malattie Infettive, IRCCS Policlinico San Martino Genova

3. STRATEGIA DI TRATTAMENTO DELL'INFEZIONE LONG SHEDDING (> 21 GG)

Manifestazioni cliniche lievi (protocollo off label)	**NMV/r 10-20 gg**	**+/-**	**mAbs**			
Manifestazioni cliniche moderate (SpO2 > 94% ed evidenza clinica o radiologica di polmonite) (protocollo off label) o fallimento a NMV/r prolungata	**NMV/r 10-20 gg**	**+**	**RDV 10-20 gg**	**+/-**	**mAbs**	

4. STRATEGIE DI TRATTAMENTO DELLA POLMONITE COVID-19

Monoterapia in label (AIFA)	**RDV 10 gg**					
Fallimento virologico e/o clinico (off label)	**NMV/r 10-20 gg**	**+**	**RDV 10-20 gg**	**+/-**	**mAbs**	

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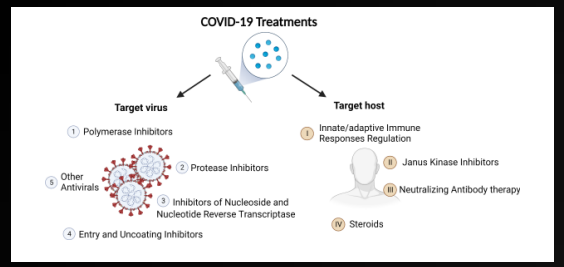


Passive immunotherapy containing neutralizing Ab:

COVID-19 convalescent plasma (High titer CCP)
Hyperimmune serum globulin preparations nAbs

Patients Who Are Immunocompromised

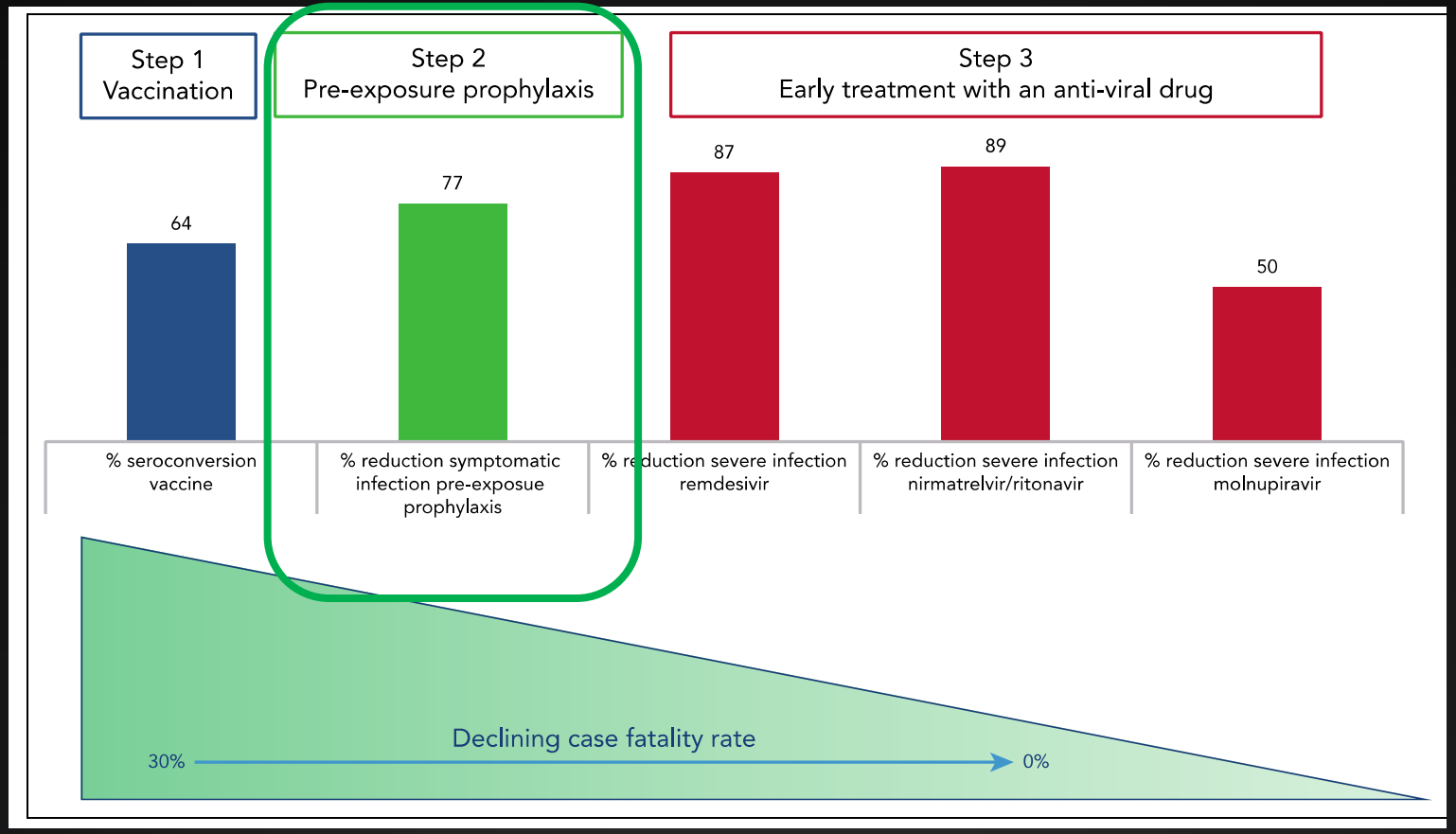
- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of high-titer CCP for the treatment of COVID-19 in hospitalized or nonhospitalized patients who are immunocompromised.
- Some people who are immunocompromised have prolonged, symptomatic COVID-19 with evidence of ongoing SARS-CoV-2 replication. The data for these approaches are not definitive, but some Panel members would use 1 or more of the following treatment options:
  - Longer and/or additional courses of ritonavir-boosted nirmatrelvir (Paxlovid)
  - Longer and/or additional courses of remdesivir
  - High-titer CCP from a vaccinated donor who recently recovered from COVID-19 likely caused by a SARS-CoV-2 variant similar to the variant causing the patient's illness

NIH COVID-19 Treatment Guidelines Update Feb 2024

No randomized, adequately powered trials that evaluated the use of CCP for the treatment of COVID-19 in IC have been published

Yuan Y, Frontiers Immunology 2023
Focosi D, Clin Microb Reviews, 2024
Kimber C, 2023
Polizzotto MN, 2022
Maor Y, 2023
Misset B, NEJM 2023

COVID-19 prophylaxis: half-full or half-empty glass?



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Scarfò L and Cuneo A. Blood 2023

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Genoa, Italy

NIH U.S. National Library of Medicine
ClinicalTrials.gov

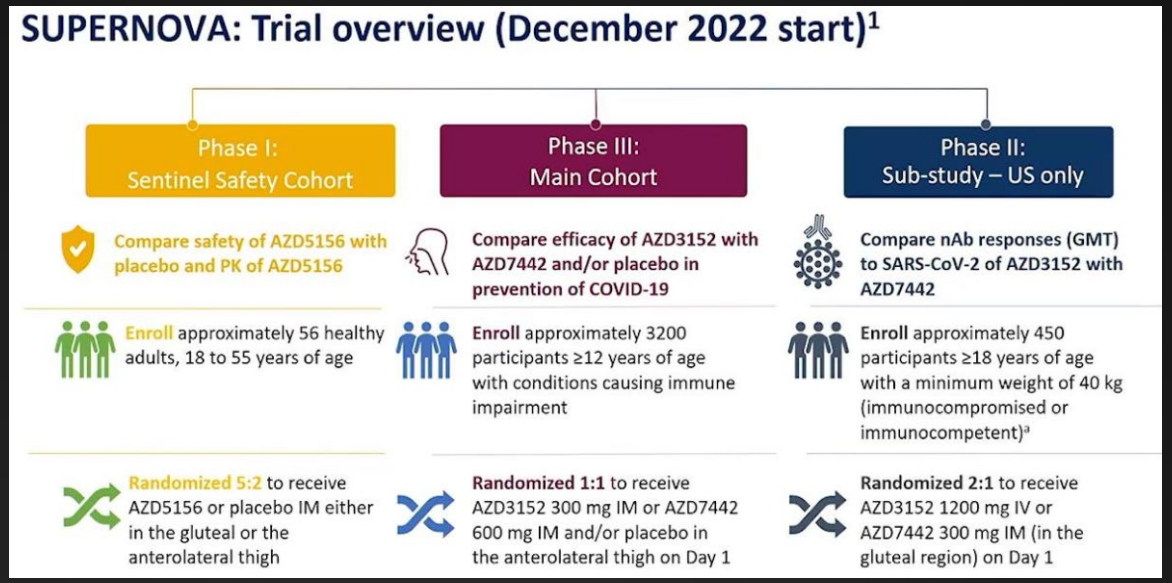
Study Understanding Pre-Exposure pRophylaxis of NOVel Antibodies (SUPERNOVA) (SUPERNOVA)

AZD5156 is an investigational, long-acting antibody combination of cilgavimab, a component of EVUSHELD (tixagevimab and cilgavimab, formerly AZD7442), and a new long-acting monoclonal antibody (mAb), AZD3152.

AZD5156 retains in vitro neutralization activity against all SARS-CoV-2 variants known to date, including BQ.1 and BQ.1.1

AZD5156
(cilga+AZD3152)

June 2024: Phase III RCT AZD3152 Sipavibart (PREP in IC)



AZD7158
(AZD3152+AZD3959)
Under evaluation
EMA

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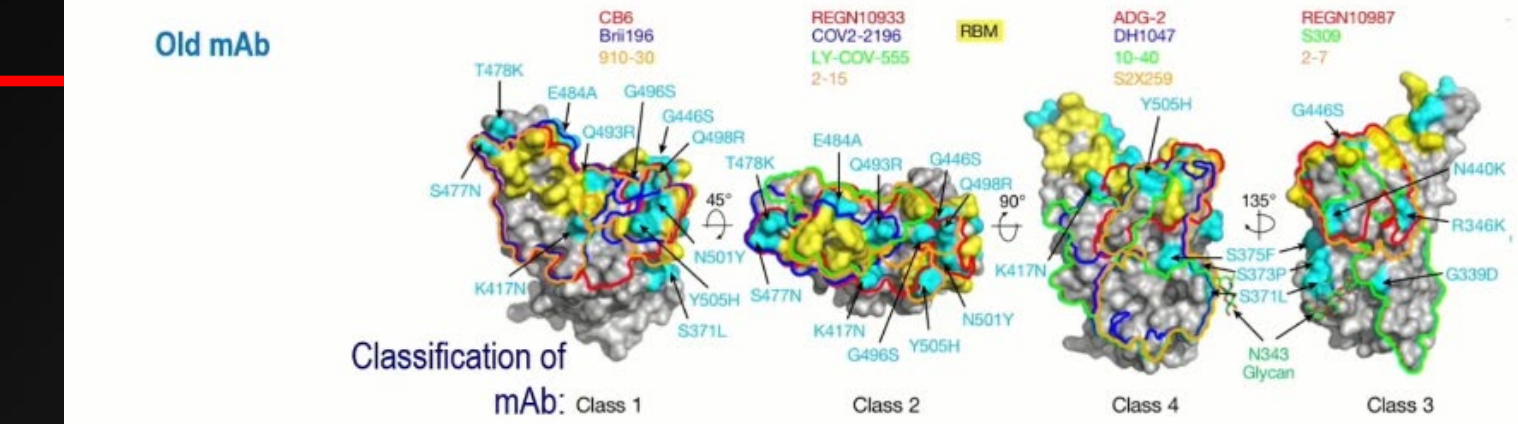
receptor binding domain (RBD)

Old mAb



New mAb	**AZD3152 (IM)** + cilgavimab (Sipavibart)
Activity against Omicron	✓ **(BA.1, BA.1.1, BA.2, BA.2.12.1, BA.5, JN.1)**
Recent VOC	X (FLiRT variants, KP.3)
Half-life (days)	80
Phase I	Safe
Phase III (SUPERNOVA-IS)	Prophylaxis in IS (EAP in France for IS)

Ordaya EE, et al. *Expert Op Biol Ther 2024*
Cai Yingun, et al. Sci Tras Med 2024

Clinical Efficacy Endpoints from the Phase 3 CANOPY Study Evaluating Pemivibart for the Prevention of COVID-19

Myra Popejoy, Anna Holmes, Chloe Katz, Anne-Marie Phelan, Kazima Tosh, Yong Li, Deepali Gupta, Pamela Hawn, Kristin Narayan, Kathryn Mahoney, Mark Wingertzahn

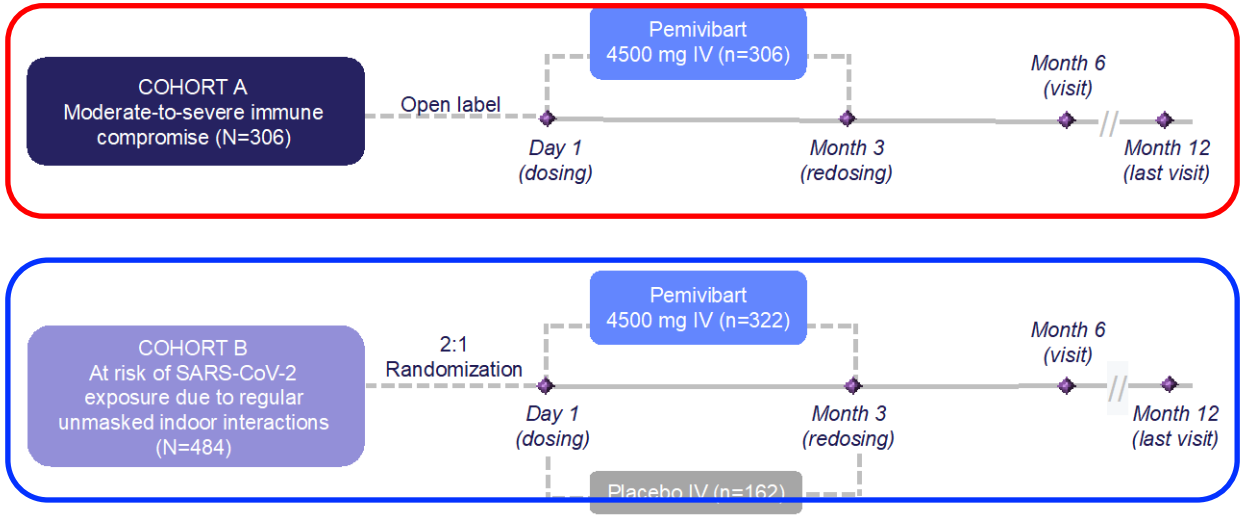
Presenting Author: Anna Holmes, PhD, Principal Clinical Scientist

Invivyd, Inc., Waltham, MA

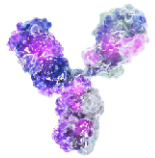
Presented at IDWeek; October 16–19, 2024; Los Angeles, CA, USA

INVIVYD

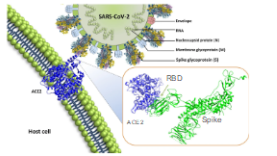
CANOPY STUDY OVERVIEW



PEMIVIBART (VYD222)



Half-life–extended mAb that has been issued an EUA by the FDA for pre-exposure prophylaxis of COVID-19 in certain adults and adolescents with moderate-to-severe immune compromise



Reproduced with permission from Saxena SK, et al. *Virusdis* 2020;31:399-407 under a Creative Commons Attribution 4.0 International licence.

Binds to the spike protein receptor binding domain (RBD) of SARS-CoV-2, interfering with the virus's ability to infect human cells[1]

EVADE — Phase 2/3 clinical trial of adintrevimab for COVID-19 prevention

STAMP — Phase 2/3 clinical trial of adintrevimab for COVID-19 treatment

Engineered from adintrevimab (ADG20), a mAb candidate that demonstrated clinical efficacy against earlier SARS-CoV-2 variants in 2 previous clinical trials[2,3]

CANOPY: Phase 3 clinical trial of Pemivibart for the pre-exposure prophylaxis of COVID-19 which enrolled adults ≥18y in two cohorts.

Cohort A is a single-arm, open-label trial in adults who have moderate-to-severe immune compromise (n=306)

Cohort B is a 2:1 randomized, placebo-controlled trial in which adults not IC received VYD222 (n=317) or placebo (n=162)

Cohort A: A low rate of RT-PCR– confirmed symptomatic COVID-19 (3.7%)

INVIVYD

May 2024 FDA granted EUA

INCIDENCE OF RT-PCR–CONFIRMED SYMPTOMATIC COVID-19, COVID-19–RELATED HOSPITALIZATIONS, AND ALL-CAUSE MORTALITY
Cohort A

- Cohort A: single-arm, open-label cohort in adults with moderate-to-severe immunocompromise

Outcome through Day 180, n (%)	Pemivibart (N=298)
Composite RT-PCR–confirmed COVID-19	11 (3.7)
Symptomatic COVID-19	9 (3.0)
COVID-19–related hospitalizations	0
All-cause mortality[a]	2 (0.7)

FDA Authorization for Emergency Use of PEMGARDA TM (Formerly VYD222) for Pre-exposure Prophylaxis (PrEP)

Cohort B: An 84% Relative RR of RT-PCR confirmed symptomatic COVID-19

INCIDENCE OF RT-PCR–CONFIRMED SYMPTOMATIC COVID-19, COVID-19–RELATED HOSPITALIZATIONS, AND ALL-CAUSE MORTALITY
Cohort B

- Cohort B: randomized, placebo-controlled cohort without moderate-to-severe immunocompromise at risk of acquiring SARS-CoV-2 due to regular indoor, unmasked face-to-face interactions

	Through Day 180, n (%)	RRR (95% CI)	Nominal *P* value
Pemivibart (n=317)	6 (1.9)	–	–
Placebo (n=160)	19 (11.9)	84.1% (61, 94)	0.000061

Table 1. Some Immunocompromising Conditions[1]

- Moderate or severe primary immunodeficiency
- Advanced or untreated HIV infection
- Active treatment for a solid-tumor or hematologic malignancy
- Hematologic malignancy associated with poor vaccine response (e.g., acute leukemia, chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma)
- Use of immunosuppressive therapy after a solid-organ or islet transplant
- Receipt of CAR T-cell therapy or hematopoietic stem cell transplant within previous 2 years
- Active treatment with other immunosuppressive or immunomodulatory drugs, such as high-dose corticosteroids (≥20 mg/day of prednisone or equivalent for ≥2 weeks) and tumor necrosis factor (TNF) inhibitors

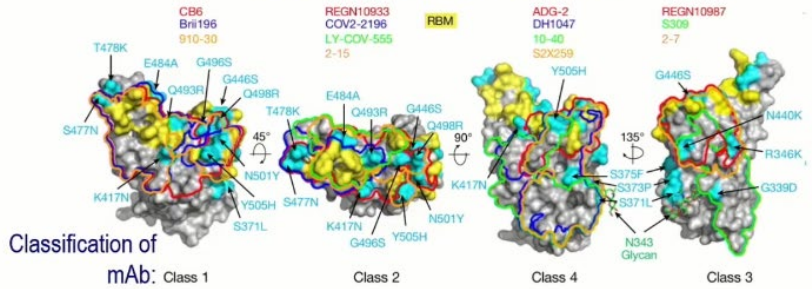
1. FDA. Fact sheet for healthcare providers: Emergency Use Authorization for Pemgarda (pemivibart). March 2024. Available at: https://bit.ly/3Q3K5AL. Accessed April 25, 2024.

A hypersensitivity or infusion-related reaction in 9% and **anaphylaxis was observed in 4/623 (0.6%) participants in CANOPY, all in Cohort A.**

Genoa, Italy

receptor binding domain (RBD)

Old mAb

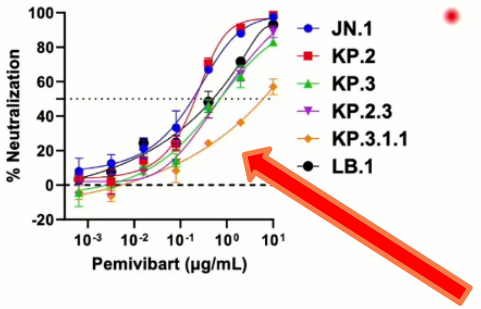


New mAb	**VYD222 (IV)** (pemivibart)
Activity against Omicron	✓ (BA.1, BA.2, BA.4/5, BQ.1.1, XBB.1, XBB.1.5, EG.5.1)
Recent VOC	✓ **JN.1 and F456L variants**
Half-life (days)	20
Phase I	Safe
Phase III (CANOPY)	Pre-exposure prophylaxis in IS and non IS patients (FDA open the Emergency use authorization)

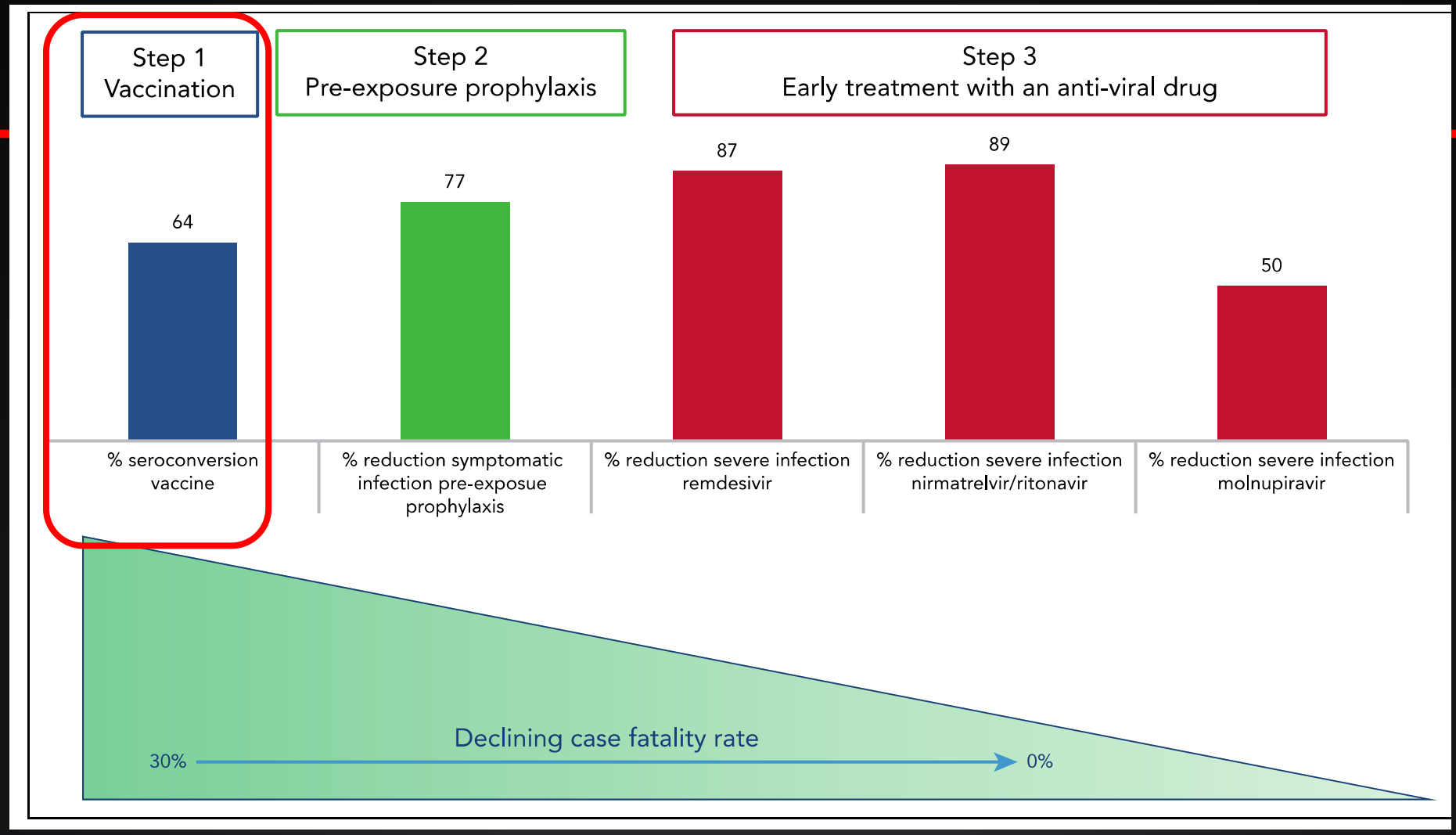
* Press release Dec 23 with positive preliminar results

Wenwei Li, et al. *Cell Rep 2022*

Quian Wang et al. Pemivibart is less active against recent SARS-CoV-2 JN.1 sublineages. ***https://doi.org/10.1101/2024.08.12.607496doi***



JN.1 sublineages	S1 mutations						IC_{50} of Pemivibart (μg/mL)	Fold increase in IC_{50} relative to JN.1
	S31	H146	Q183	R346	F456	Q493		
JN.1							0.185	-
KP.2				T	L		0.210	1.1
KP.3					L	E	0.709	3.8
KP.2.3	Δ	Q		T	L		0.708	3.8
KP.3.1.1	Δ				L	E	6.047	32.7
LB.1	Δ		H	T	L		0.501	2.7



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Scarfò L and Cuneo A. Blood 2023

Clinica Malattie Infettive
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Genoa, Italy

Impact of JN.1 booster vaccination on neutralisation of SARS-CoV-2 variants KP.3.1.1 and XEC

Prerna Arora, Christine Happle, Amy Kempf, Inga Nehlmeier, Metodi V. Stankov, Alexandra Dopfer-Jablonka, Georg M. N. Behrens, Stefan Pöhlmann, Markus Hoffmann

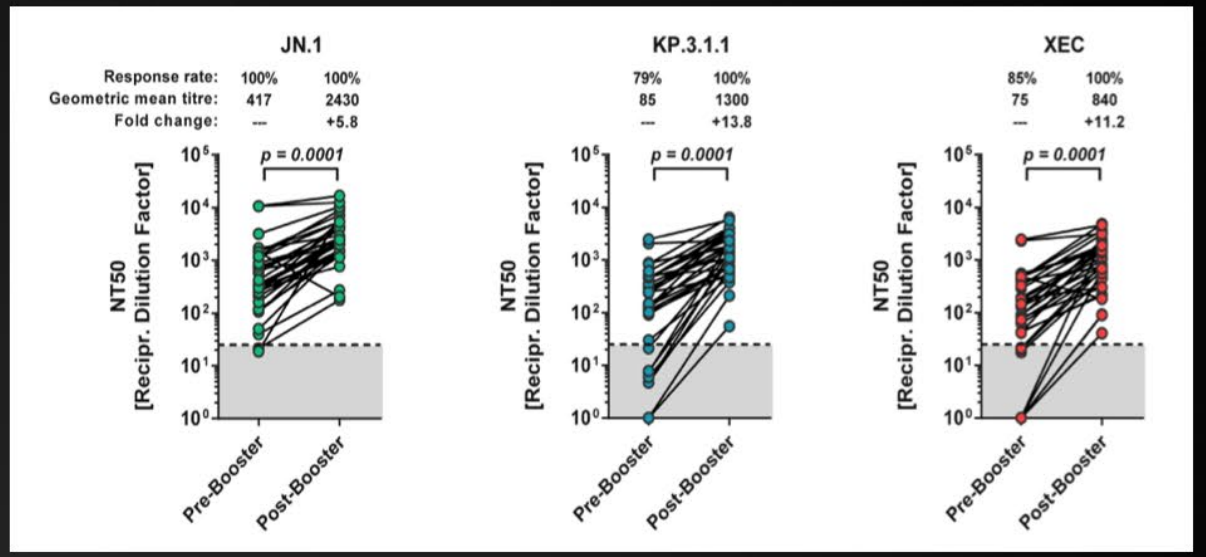
doi: https://doi.org/10.1101/2024.10.04.616448

Correspondence

www.thelancet.com/infection

Both KP.3.1.1$_{pp}$ and XEC$_{pp}$ were generally less well neutralised compared to JN.1$_{pp}$, indicating elevated immune evasion.

Importantly, JN.1-booster vaccination significantly improved neutralisation of all lineages tested and therefore will likely increase protection against hospitalisation and post-COVID sequelae from infection caused by KP.3.1.1 and XEC.



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Published online November 7, 2024 https://doi.org/10.1016/S1473-3099(24)00688-1

Step 1: Vaccination

Campagna vaccinale Autunno-Inverno 2024/2025

I dati sono aggiornati su base settimanale e sono disponibili in formato aperto con il dettaglio giornaliero.

Ultimo aggiornamento dati

14-11-2024

281.964

Totale somministrazioni dal 17/09/2024

Protocollo Clinica Malattie Infettive, IRCCS Policlinico San Martino, Genova

Strategie di gestione dell'infezione da SARS-CoV-2 nel paziente immunocompromesso

1.Strategie preventive

2. Strategie di trattamento dell'infezione precoce da SARS-CoV-2
3. Strategie di trattamento dell'infezione da SARS-CoV-2 con shedding virale prolungato (> 21 giorni)
4. Strategia di trattamento della polmonite COVID-19

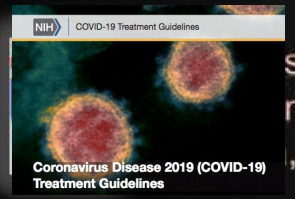
Special Considerations in People Who Are Immunocompromised

Last Updated: February 29, 2024

Summary Recommendations
Prevention of COVID-19
• The COVID-19 Treatment Guidelines Panel (the Panel) recommends COVID-19 vaccination for everyone who is eligible, including those who are immunocompromised, according to the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices **(AI)**.
• Vaccine response rates may be lower in patients who are moderately or severely immunocompromised. Specific guidance on administering vaccines to these individuals is provided by the Centers for Disease Control and Prevention.
• Clinicians should strongly encourage all household members and close contacts of patients who are immunocompromised to be vaccinated against COVID-19 **(AI)**.
• Currently, antibody tests are not recommended for assessing SARS-CoV-2 immunity following COVID-19 vaccination or for assessing the need for vaccination in a person who is unvaccinated.

Si può pensare a un modello di vaccinazione che non sia soltanto territoriale e intra-ospedaliero, ma anche intra-reparto?

Ospedale rappresenta un elemento importante di prevenzione



NIH COVID-19 Treatment Guidelines Update Feb 2024

Clinica Malattie Infettive
Ospedale Policlinico San Martino IRCCS
Genoa, Italy

Come gestire il paziente immunodepresso?

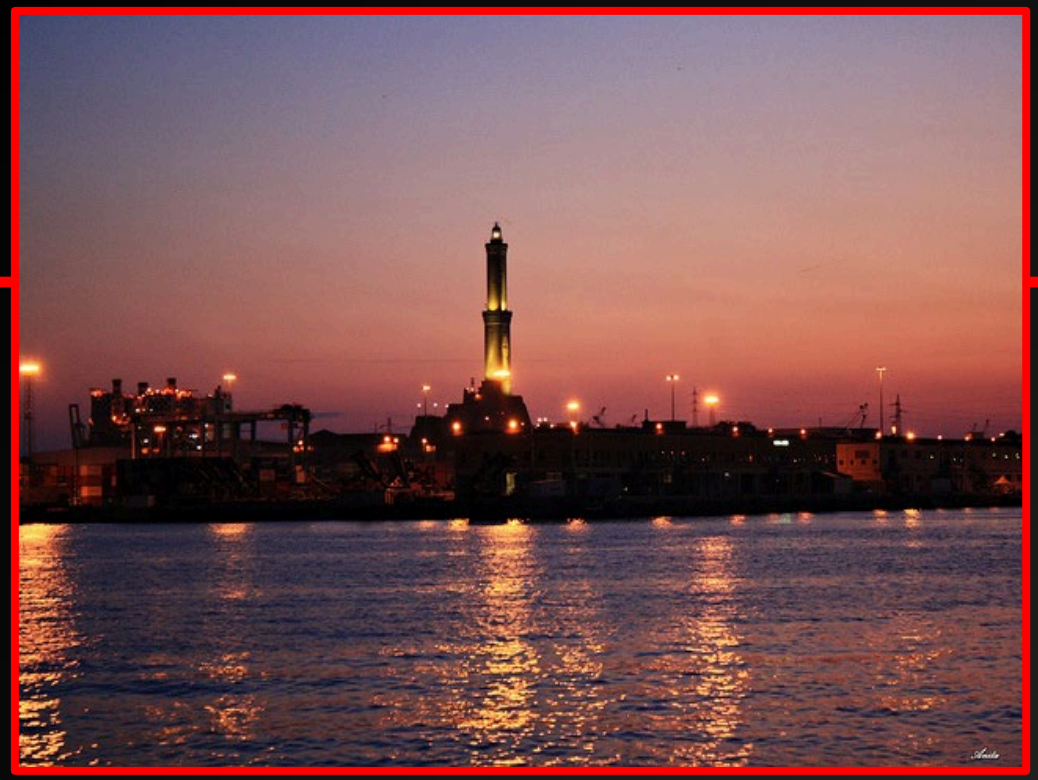
1. Informare ed educare i pazienti sui rischi che comporta l'infezione

2. Implementare la vaccinazione del paziente a rischio (territoriale, ospedaliera e/o intrareparto)

3. Profilassi pre-esposizione (se e non appena disponibile)

4. Trattare precocemente

5. Considerare sempre i fattori di rischio dell'ospite per una tailored therapy (quale, quando e per quanto tempo)



Grazie per l'attenzione

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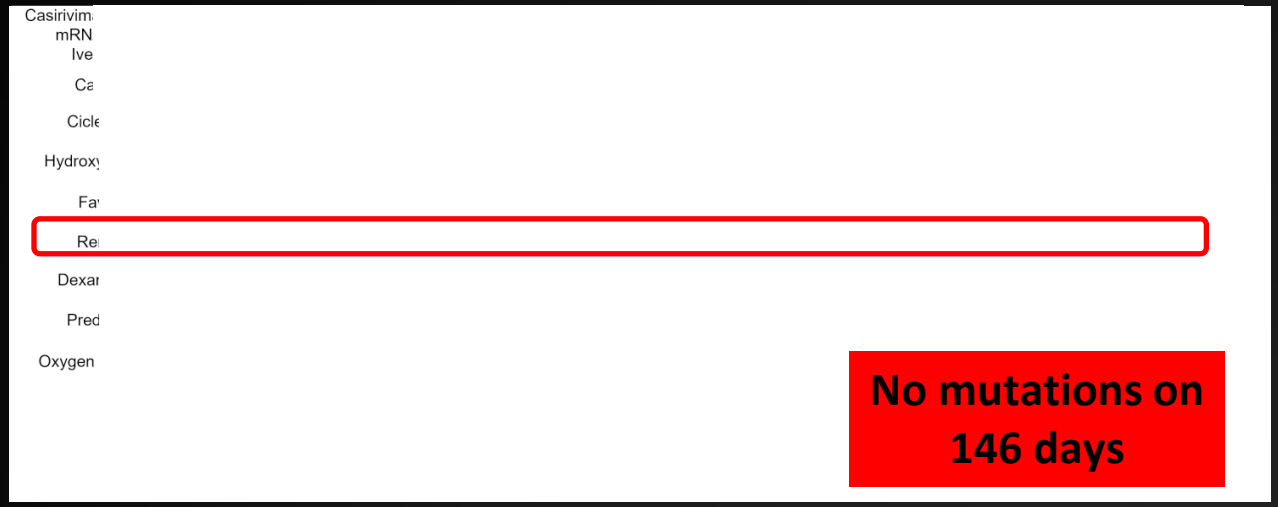
Genoa, Italy

Remdesivir: Rare emergence mutations

ACTT1 trial, Gandhi S et al Nat Comm 2022
Garcia-Vidal C, Front Microb 2022



No mutations on 146 days

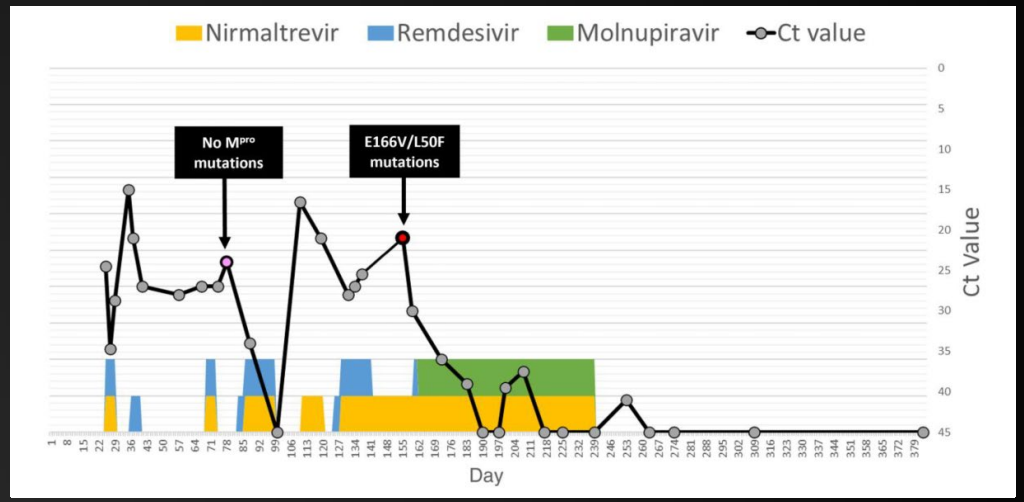
Japanese pt with follicular lymphoma (obinotuzumab) treated with 7 cycles of RDV (14 or 28 days), for 146 days of RDV

Nagai H et al Jap In f Dis 2022

NMV/r: fisrt case of resistance

JOURNAL ARTICLE

Nirmatrelvir Resistance—de Novo E166V/L50V Mutations in an Immunocompromised Patient Treated With Prolonged Nirmatrelvir/Ritonavir Monotherapy Leading to Clinical and Virological Treatment Failure—a Case Report



Zuckerman NS, CID Feb 2024

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And ……

- **Mpro:**

  Rupintrivir (selective for Rhinoviruses, but its derivative $M^{pro\ -1}$ is also effective vs SARS-COV-2)

  SY110, overcome the E166N

  In China: Simnotrelvir (RCT vs placebo 750 mg/100 mg BID)

- **RdRp:**

  Obeldesivir (GS-5245) oral nucleosid prodrug :RCT inpatient BIRCH trial (halted), RCT outpatients OAKTREE)

Focosi D, Clin Microb Reviews, 2024
Sha A, Front Cell and Dev Biol, 2023
Huang C, Nature comm 2023
Martinez DR, bioRxiv 2023
Yuan Y, Front Immunology 2023

And ……

New perspectives mAb

mAb

- Regeneron: early clinical trial of REGN17092
- Aerium therapeutics: advanced clinical trials of the AER-800 cocktail
- Brii Biosciences: amubarvimab plus romlusevimab

ARTICLE - Cell Therapy & Immunotherapy

Allogeneic, off-the-shelf, SARS-CoV-2-specific T cells (ALVR109) for the treatment of COVID-19 in high-risk patients

virus-specific T cells :
administering partially HLA-matched, third-party, cryopreserved SARS-CoV-2-specific T cells (ALVR109) in combination with other antiviral agents to four individuals who were hospitalized with COVID-19.

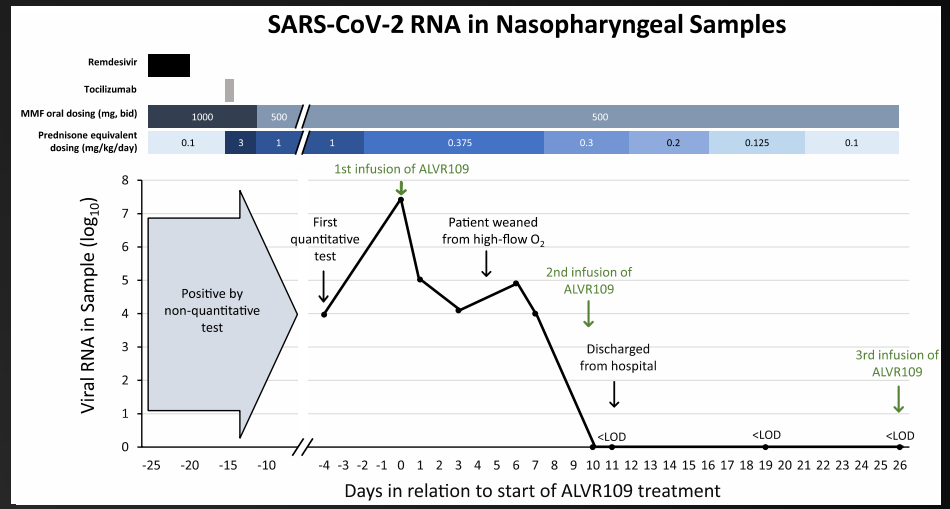
This study establishes the feasibility of preparing and delivering off-the-shelf, SARS-CoV-2-directed, virus-specific T cells to patients with COVID-19 and supports the clinical use of these products outside of the profoundly immune compromised setting (ClinicalTrials.gov number, NCT04401410).

Vasileiou S. et al, 2022

Uni… Dip… alute (DISSAL)
Genoa, Italy

ALVR109, an off-the-shelf partially HLA matched SARS-CoV-2–specific T cell therapy, to treat refractory severe COVID-19 pneumonia in a heart transplant patient: Case report

IC pt with persistent SARS-CoV-2 delta variant infection who was treated with ALVR109, an off-the-shelf SARS-CoV-2– specific T cell therapy.



Martits-Chalangari K…Gottlieb R , Am J Transpl 2021

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