Webinar
ECM

Aspetti epidemiologici e clinici del virus Sars-CoV-2 ed effetti della pandemia sulla circolazione delle altre malattie infettive

GIOVEDÌ 24 NOVEMBRE 2022
ORE 9.30-14.00

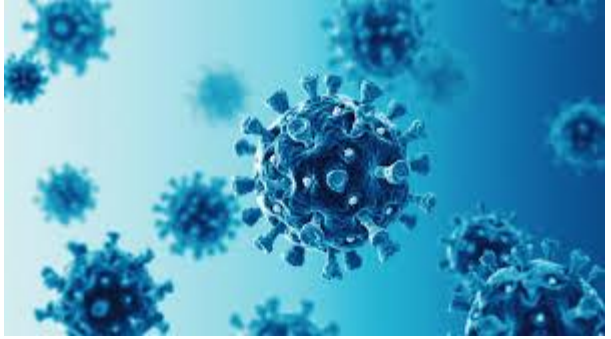
Quali terapie per i pazienti Covid-19

Mario Tumbarello

Azienda ospedaliero-universitaria Senese

UNIVERSITÀ DI SIENA 1240

Farmaci utilizzabili per il trattamento della malattia COVID-19



ANTIVIRALI **REMDESIVIR** 200 mg LD poi 100 mg qd ev per 3/5 giorni

MOLNUPIRAVIR 800 mg bid x 5 giorni

NIRMATRELVIR/RITONAVIR 300/100 mg bid x 5 giorni

ANTICORPI MONOCLONALI **SOTROVIMAB** (500 mg)

TIXAGEVIMAB-CILGAVIMAB (150+150 mg)

(300+300 mg)

Single shot

2022

ANTIVIRALS

Molnupiravir

RNA-polymerase inhibitor (cytidine nucleoside analogue)

Remdesivir

RNA-polymerase inhibitor (adenosine nucloside analogue)

Nirmatrelvir-Ritonavir

Nirmatrelvir is a SARS-CoV-2 main protease inhibitor (Mpro), and ritonavir is an HIV1 protease inhibitor and CYP3A inhibitor

2022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients

A. Jayk Bernal, M.M. Gomes da Silva, D.B. Musungaie, E. Kovalchuk, A. Gonzalez, V. Delos Reyes, A. Martín-Quirós, Y. Caraco, A. Williams-Diaz, M.L. Brown, J. Du, A. Pedley, C. Assaid, J. Strizki, J.A. Grobler, H.H. Shamsuddin, R. Tipping, H. Wan, A. Paschke, J.R. Butterton, M.G. Johnson, and C. De Anda, for the MOVe-OUT Study Group*

This article was published on December 16, 2021, at NEJM.org.

A phase 3, double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of treatment with molnupiravir started within 5 days after the onset of signs or symptoms in nonhospitalized, unvaccinated adults with mild-to-moderate, laboratory-confirmed Covid-19 and at least one risk factor for severe Covid-19 illness. Participants in the trial were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for 5 days. The primary efficacy end point was the incidence hospitalization or death at day 29.

total of 1433 participants underwent randomization; 716 were assigned to receive molnupiravir and 717 to receive placebo. With the exception of an imbalance in sex, baseline characteristics were similar in the two groups. A planned interim analysis was performed when 50% of 1550 participants had been followed through day 29.A

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The risk of hospitalization for any cause or death through day 29 was lower with molnupiravir (28 of 385 participants [7.3%]) than with placebo (53 of 377 [14.1%]) (difference, −6.8 percentage points; 95% confidence interval, −11.3 to −2.4; P = 0.001).

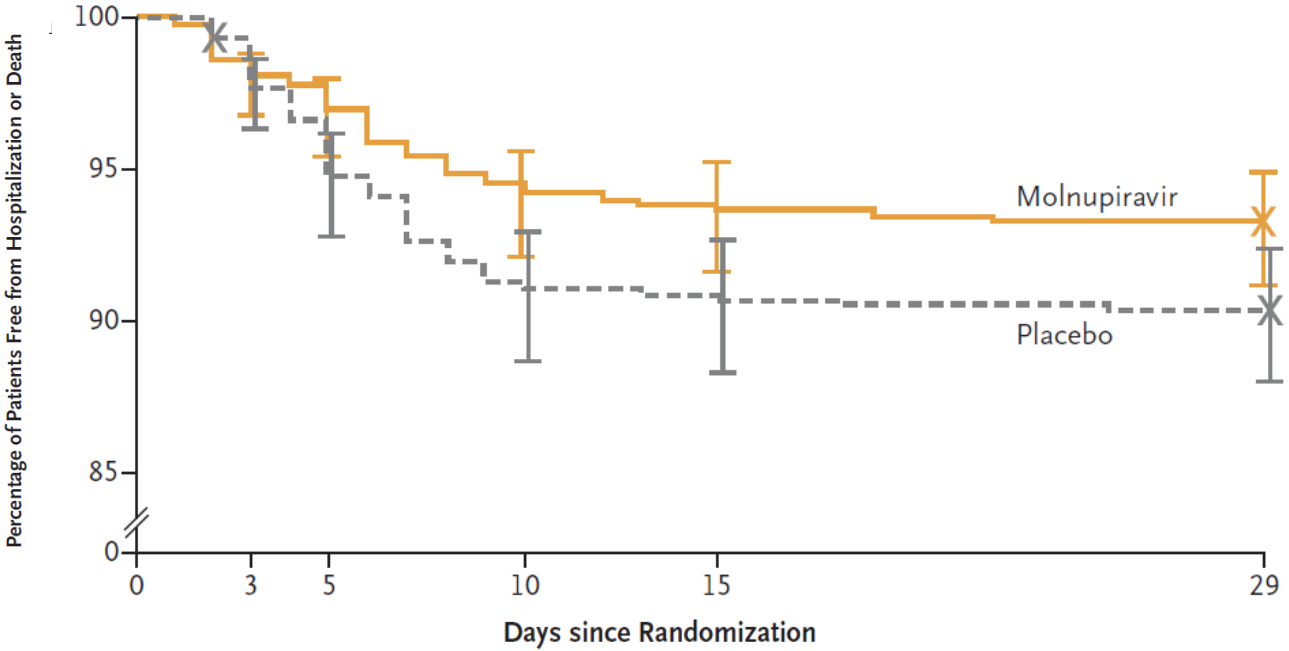

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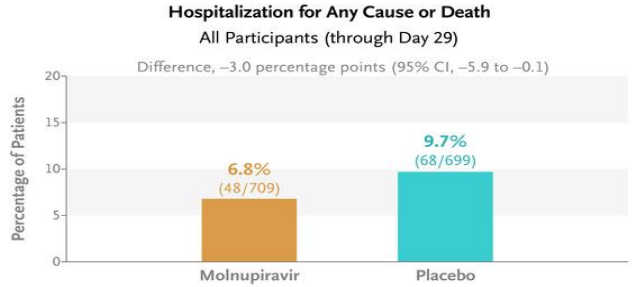
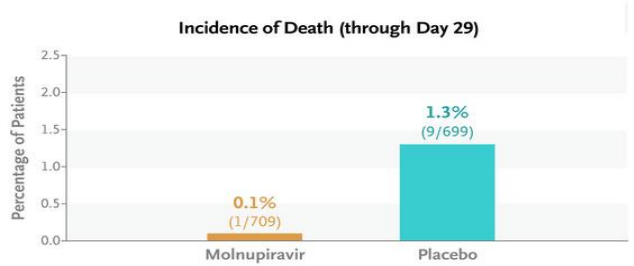
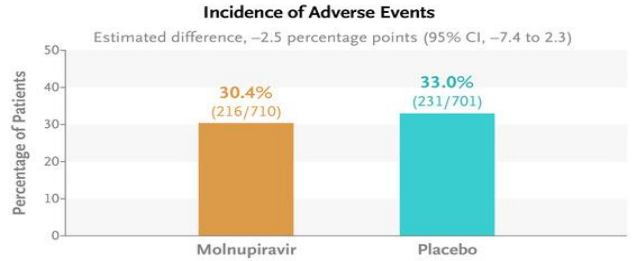
Table 2. Incidence of Adverse Events in the Safety Population.

Adverse Events and Discontinuation	Molnupiravir (N=710)	Placebo (N=701)	Estimated Difference (95% CI)*
	number (percent)		*percentage points*
Participants with adverse events			
≥1 Adverse event	216 (30.4)	231 (33.0)	−2.5 (−7.4 to 2.3)
≥1 Adverse event related to the assigned regimen†	57 (8.0)	59 (8.4)	−0.4 (−3.3 to 2.5)
≥1 Serious adverse event	49 (6.9)	67 (9.6)	−2.7 (−5.6 to 0.2)
≥1 Serious adverse event related to the assigned regimen†	0	1 (0.1)	−0.1 (−0.8 to 0.4)
Death	2 (0.3)	12 (1.7)	−1.4 (−2.7 to −0.5)
Participants who discontinued the assigned regimen because of an adverse event			
Adverse event	10 (1.4)	20 (2.9)	−1.4 (−3.1 to 0.1)
Adverse event related to the assigned regimen†	4 (0.6)	3 (0.4)	0.1 (−0.8 to 1.1)
Serious adverse event	5 (0.7)	13 (1.9)	−1.2 (−2.5 to 0.0)
Serious adverse event related to the assigned regimen†	0	0	0.0 (−0.5 to 0.5)

Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients







Jayk Bernal et al. N Engl J Med 2022;386:509-520

Active cancer 2%

Average efficacy 30%

MOLNUPIRAVIR

Pros:
-Oral administration
- No drug-drug interaction

Cons:
-Clinical data from RCT

2022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients

R.L. Gottlieb, C.E. Vaca, R. Paredes, J. Mera, B.J. Webb, G. Perez, G. Oguchi, P. Ryan, B.U. Nielsen, M. Brown, A. Hidalgo, Y. Sachdeva, S. Mittal, O. Osiyemi, J. Skarbinski, K. Juneja, R.H. Hyland, A. Osinusi, S. Chen, G. Camus, M. Abdelghany, S. Davies, N. Behenna-Renton, F. Duff, F.M. Marty,* M.J. Katz, A.A. Ginde, S.M. Brown, J.T. Schiffer, and J.A. Hill, for the GS-US-540-9012 (PINETREE) Investigators†

This article was published on December 22, 2021, at NEJM.org.

A randomized, double-blind, placebo-controlled trial involving non hospitalized patients with Covid-19 who had symptom onset within the previous 7 days and who had at least one risk factor for disease progression (age ≥60 years, obesity, or certain coexisting medical conditions). Patients were randomly assigned to receive intravenous remdesivir (200 mg on day 1 and 100 mg on days 2 and 3) or placebo. The primary efficacy end point was a composite of Covid-19–related hospitalization or death from any cause by day 28.

A total of 562 patients who underwent randomization and received at least one dose of remdesivir or placebo were included in the analyses: 279 pts in the remdesivir arm and 283 in the placebo arm.

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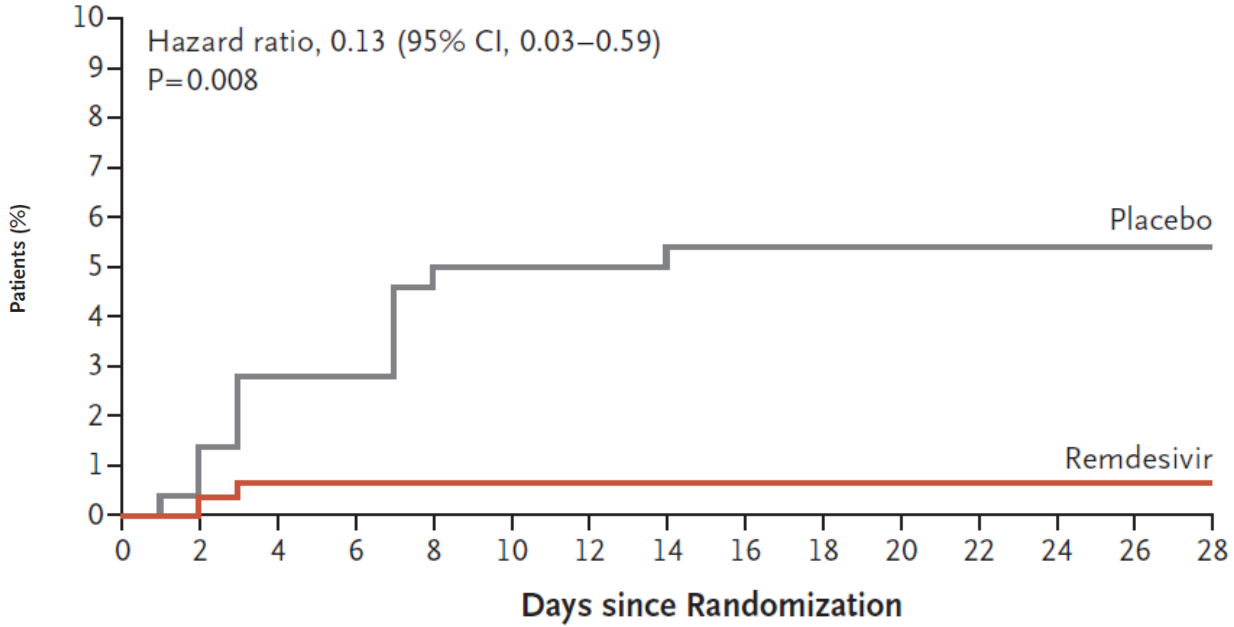
Covid-19–related hospitalization or death from any cause occurred in 2 patients (0.7%) in the remdesivir group and in 15 (5.3%) in the placebo group (hazard ratio, 0.13; 95% confidence interval [CI], 0.03 to 0.59; P = 0.008).

Covid-19–Related Hospitalization or Death from Any Cause



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Covid-19–Related Hospitalization or Death from Any Cause at Day 28, According to Demographic and Clinical Characteristics at Baseline.

Subgroup	Remdesivir	Placebo	Hazard Ratio (95% CI)
	no./total no. of patients (%)		
Residence in the United States	2/264 (0.8)	12/267 (4.5)	0.17 (0.04–0.76)
Age ≥60 yr	1/83 (1.2)	9/87 (10.3)	0.11 (0.01–0.86)
Male sex	1/148 (0.7)	9/145 (6.2)	0.11 (0.01–0.84)
Diabetes mellitus	2/173 (1.2)	14/173 (8.1)	0.14 (0.03–0.63)
Obesity	1/154 (0.6)	9/156 (5.8)	0.11 (0.01–0.88)
Hypertension	2/138 (1.4)	10/130 (7.7)	0.17 (0.04–0.76)
Ethnic group			
Not Hispanic or Latinx	2/146 (1.4)	8/158 (5.1)	0.26 (0.06–1.22)
Hispanic or Latinx	0/123	6/112 (5.4)	—
Chronic lung disease	0/67	4/68 (5.9)	—
Cardiovascular or cerebrovascular disease	0/20	2/24 (8.3)	—
Current cancer	0/12	2/18 (11.1)	—

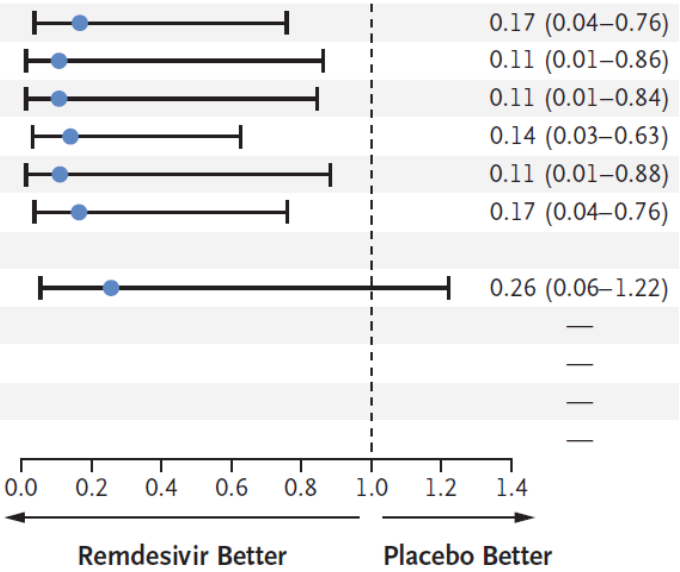

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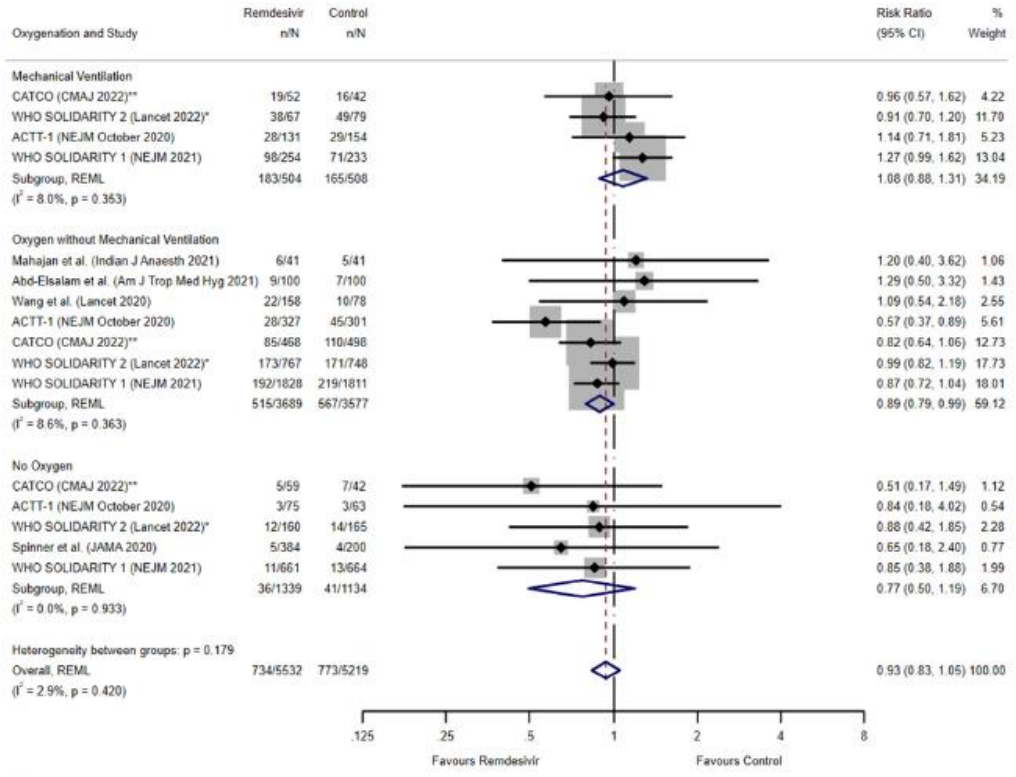
Table 3. Adverse Events.*

Event	Remdesivir (N=279)	Placebo (N=283)
	no. of patients (%)	
Primary safety end point: any adverse event	118 (42.3)	131 (46.3)
Adverse events		
Nausea	30 (10.8)	21 (7.4)
Headache	16 (5.7)	17 (6.0)
Cough	10 (3.6)	18 (6.4)
Diarrhea	11 (3.9)	11 (3.9)
Dyspnea	7 (2.5)	15 (5.3)
Fatigue	10 (3.6)	11 (3.9)
Ageusia	8 (2.9)	7 (2.5)
Anosmia	9 (3.2)	6 (2.1)
Dizziness	5 (1.8)	10 (3.5)
Chills	6 (2.2)	8 (2.8)
Pyrexia	1 (0.4)	11 (3.9)
Covid-19 pneumonia	2 (0.7)	8 (2.8)
Adverse event related to trial regimen	34 (12.2)	25 (8.8)
Serious adverse event†	5 (1.8)	19 (6.7)
Adverse event leading to discontinuation of trial regimen	2 (0.7)	5 (1.8)
Death	0	0

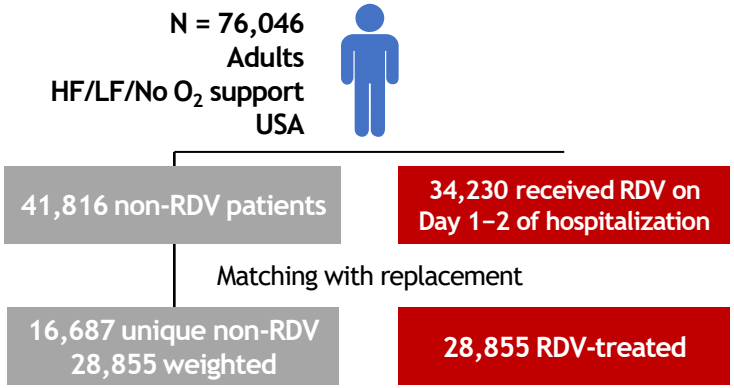
Remdesivir for the treatment of COVID-19: a systematic review and meta-analysis

Lee T Clinical Microbiology and Infection 28 (2022) 1203e1210



Retrospective, multicenter study from US Premier inpatient database

Mozaffari E, et al. Clin Infect Dis 2021 Oct 1;ciab875

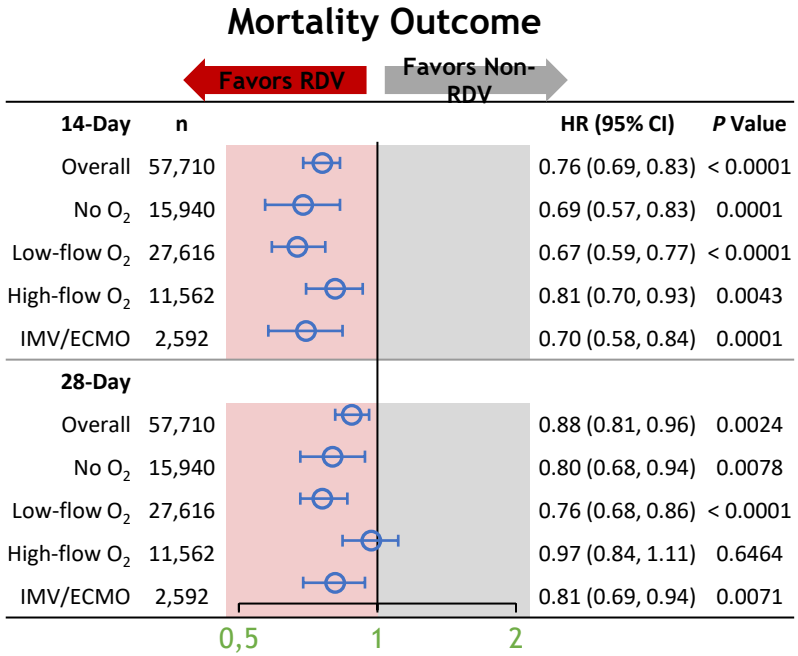


- **Key inclusion criteria**
  - Adults with a primary or secondary discharge diagnosis of COVID-19 (ICD-10-CM: U07.1), AND
  - Requiring NIV/HF, LF, or on oxygen upon admission
- **Key exclusion criteria**
  - Pregnant
  - Length of hospitalization > 100 days
  - Received RDV as part of a clinical trial
  - Received 1st RDV administration after the first 2 days of hospitalization

2022

Retrospective, multicenter study from US Premier inpatient database

Mozaffari E, et al. Clin Infect Dis 2021 Oct 1;ciab875



RDV associated with a statistically significant reduction in mortality by day 14 and day 28 in the overall population, and in most baseline oxygen subgroups

2022

REMDESIVIR

Pros:
- Efficacy (80% reduction of hospitalization or death)

Cons:
-IV administration

The NEW ENGLAND JOURNAL of MEDICINE

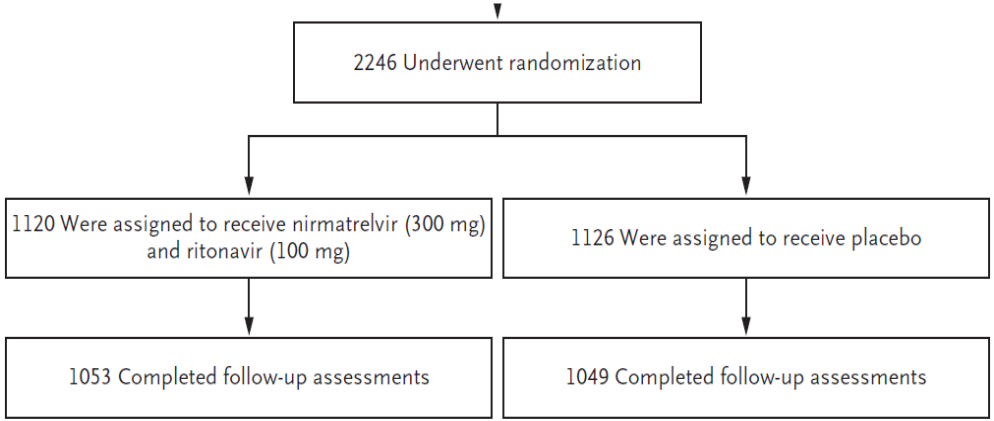
ORIGINAL ARTICLE

Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Jennifer Hammond, Ph.D., Heidi Leister-Tebbe, B.S.N., Annie Gardner, M.P.H., M.S.P.T., Paula Abreu, Ph.D., Weihang Bao, Ph.D., Wayne Wisemandle, M.A., MaryLynn Baniecki, Ph.D., Victoria M. Hendrick, B.Sc., Bharat Damle, Ph.D., Abraham Simón-Campos, M.D., Rienk Pypstra, M.D., and James M. Rusnak, M.D., Ph.D., for the EPIC-HR Investigators*

This article was published on February 16, 2022, at NEJM.org.

A phase 2–3 double-blind, randomized, controlled trial in which symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe coronavirus disease 2019 were assigned in a 1:1 ratio to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir (or placebo every 12 hours for 5 days. Covid-19–related hospitalization or death from any cause through day 28, viral load, and safety were evaluated

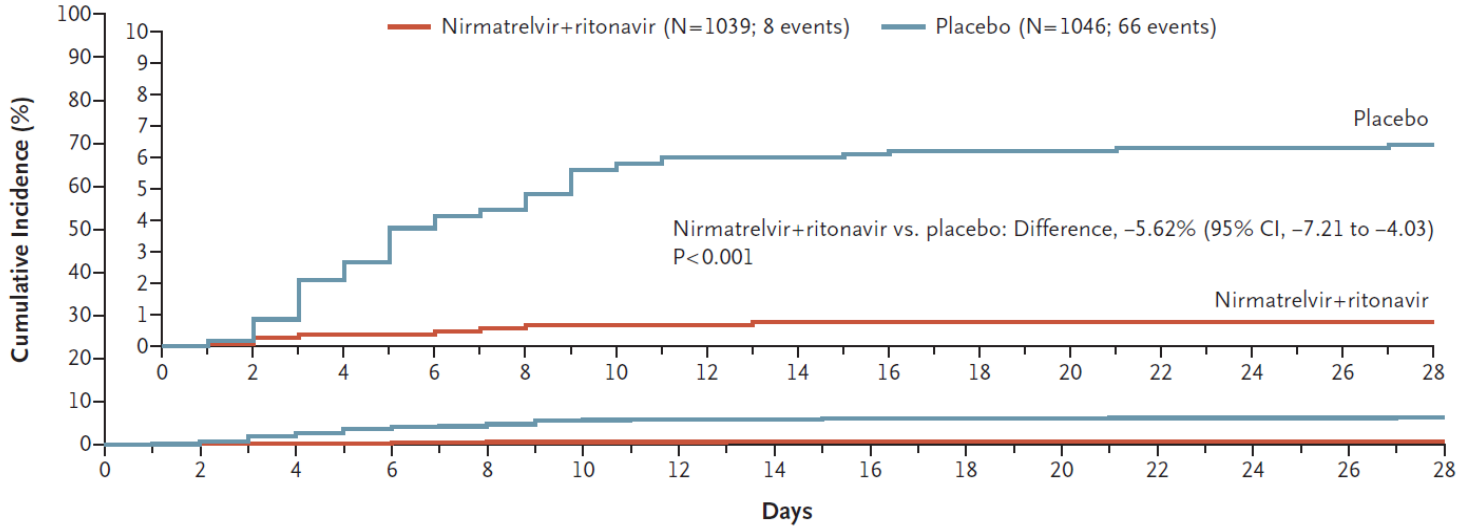


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Covid-19–Related Hospitalization or Death from Any Cause through Day 28 among Patients Treated ≤5 Days after Symptom Onset



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Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Outcomes According to Time Since Onset of Covid-19 Symptoms

	Treated ≤3 Days after Onset of Symptoms (modified intention-to-treat population)		Treated ≤5 Days after Onset of Symptoms	
	Nirmatrelvir+ritonavir (N=697)	Placebo (N=682)	Nirmatrelvir+ritonavir (N=1039)	Placebo (N=1046)
Patients with event — no. (%)	5 (0.72)	44 (6.45)	8 (0.77)	66 (6.31)
Hospitalization for Covid-19	5 (0.72)	44 (6.45)	8 (0.77)	65 (6.21)
Death from any cause	0	9 (1.32)	0	12 (1.15)
Average time at risk for event — days	27.29	26.19	27.05	25.97
Average follow-up — days	27.45	27.25	27.20	27.05
Estimated percentage with event (95% CI) — %	0.72 (0.30 to 1.73)	6.53 (4.90 to 8.68)	0.78 (0.39 to 1.56)	6.40 (5.06 to 8.08)
Difference (±SE) from placebo — percentage points	−5.81±1.01		−5.62±0.81	
95% CI of difference	−7.78 to −3.84		−7.21 to −4.03	
P value	<0.001		<0.001	

NIRMATRELVIR

Pros:

- Efficacy (87% reduction of hospitalization or death)

-Oral

- Reduction of viral load

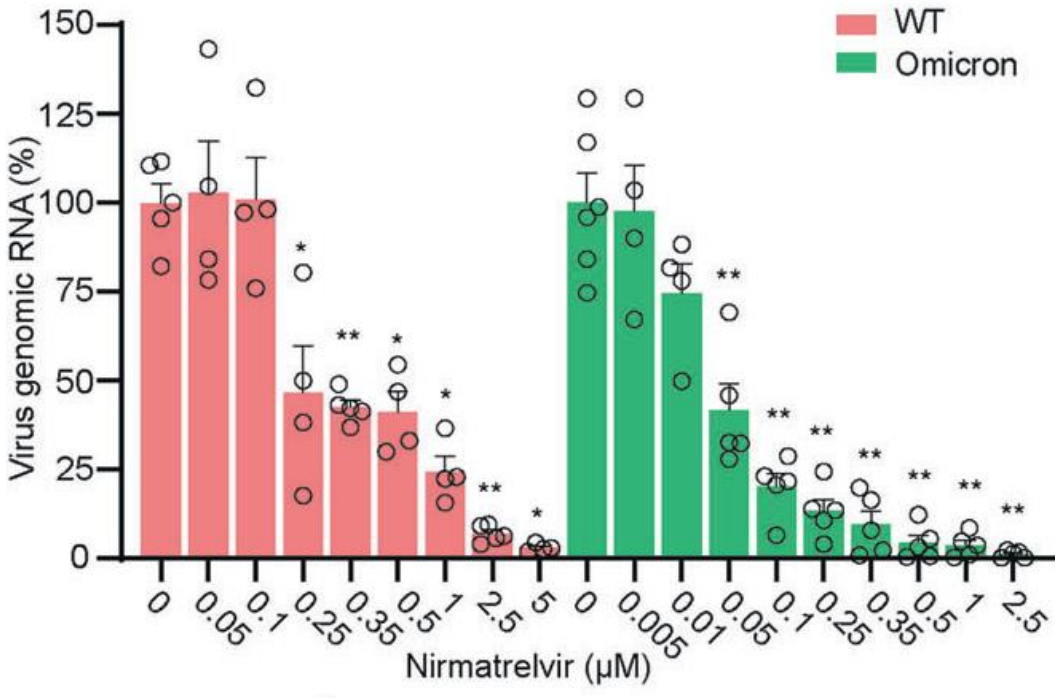
Cons:

-Drug interactions

(Nirmatrelvir is a substrate and potential inhibitor for P-gp and CYP3A4 enzymes.
Ritonavir is a substrate and inhibitor primarily for CYP3A4 but also CYP2D6. Ritonavir induces CYP3A, CYP1A2, CYP2C9, CYP2C19, CYP2B6)

SARS-CoV-2 Omicron variant is highly sensitive to molnupiravir, nirmatrelvir, and the combination

Pi L et al Cell Research 2022 0:1–3; https://doi.org/10.1038/s41422-022-00618-w

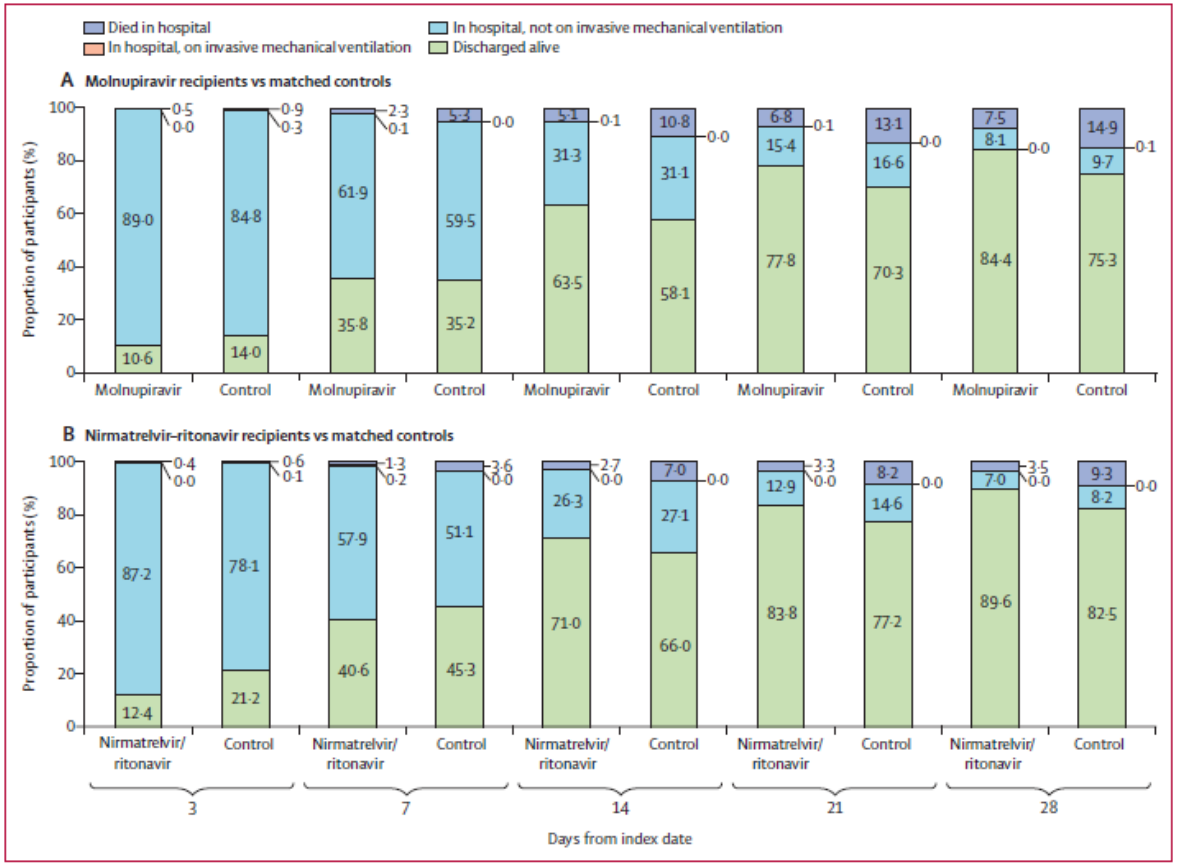


Real-world effectiveness of early molnupiravir or nirmatrelvir– ritonavir in hospitalised patients with COVID-19 without supplemental oxygen requirement on admission during Hong Kong's omicron BA.2 wave: a retrospective cohort study

Wong C Lancet Infect Dis 2022

Patients included

- 1856 molnupiravir recipients
- 1856 matched controls
- 890 nirmatrelvir-ritonavir recipients
- 890 matched-controls



2022

Rebound of SARS-CoV-2 Infection after Nirmatrelvir–Ritonavir Treatment

Charness N Engl J Med. 2022 Sep 15;387(11):1045-1047

- 3 cases of virological documented (WGS, viral culture) cases of clinical and virological rebound
- 10 additioanl presumptive cases reported
- 2 possible transmission of SARS-Cov-2

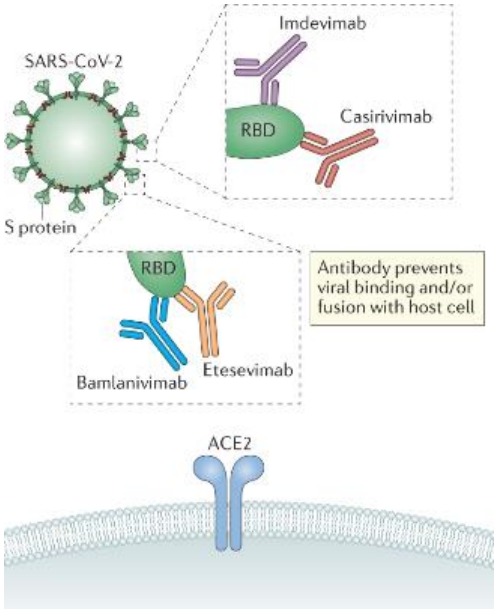
2022

MONOCLONAL ANTIBODIES

Anti-SARS-CoV-2 monoclonal antibodies (mAbs) that target the spike protein

Proposed for treatment and prophylaxis

Available in Italy
- Bamlanivimab/Etesemivab
- Casirivimab/Imdevimab
- Sotrovimab
- Cilgavimab/Tixagevimab



bamlanivimab-etesevimab

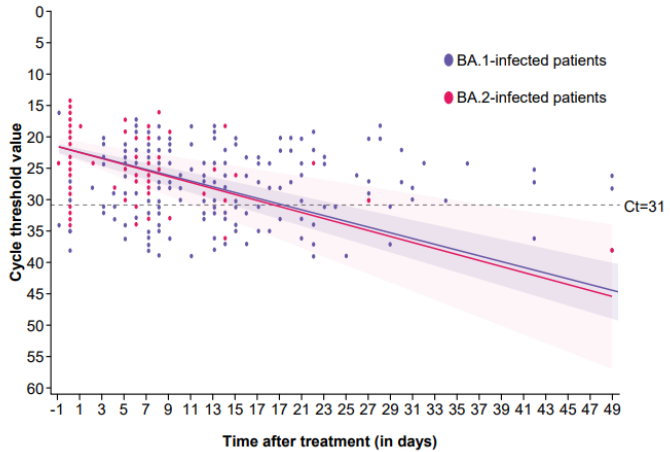
casirivimab-imdevimab

AGENZIA ITALIANA DEL FARMACO

Sotrovimab to prevent severe COVID-19 in high-risk patients infected with Omicron BA.2

Martin-Blondel G. Et al.- J Infect. 2022 Jul 5:S0163-4453(22)00406-6

Treatment with sotrovimab in individuals infected with Omicron BA.2 was associated with a similarly low rate of COVID-19–related hospitalisation and decline in viral load as in those infected with Omicron BA.1



	BA.1-infected patients (n=143)	BA.2-infected patients (n=47)
Day 28 outcome (% of patients with available data)	125 (87)	42 (89)
COVID-19–related hospitalisation	3 (2)	1 (2)
COVID-19–related death	0	0

Figure and table adapted with permission from Martin-Blondel G, et al. *J Infect.* 2022;doi:10.1016/j.jinf.2022.06.033.
Cycle threshold describes the amount of virus in an infected individual or the number of PCR cycles needed to detect the virus.[2] *Including patients with available data at Day 28.[1]

Sotrovimab in vitro neutralization activity against Omicron sublineages in a pseudotyped viral assay

Cathcart AL, et al al.. doi:10.1101/2021.03.09.434607v9
Park Y-J, Pinto D, Walls AC, et al. bioRxiv (preprint). 2022; 10.1101/2022.05.08.491108v3

SARS-CoV-2 lineage	Key mutations	Fold-change in IC_{50} vs wild-type
Omicron BA.1	A67V, H69-, V70-, T95I, G142D, V143-, Y144-, Y145-, N211-, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F	2.7
Omicron BA.1.1	A67V, H69-, V70-, T95I, G142D, V143-, Y144-, Y145-, N211-, L212I, ins214EPE, G339D, R346K, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F	3.3
Omicron BA.2	T19I, del24-26, A27S, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K	16.0
Omicron BA.2.12.1	T19I, L24-, P25-, P26-, A27S, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452Q, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, S704L, N764K, D796Y, Q954H, N969K	16.6
Omicron BA.3	A67V, H69-, V70-, T95I, G142D, V143-, Y144-, Y145-, N211-, L212I, G339D, S371F, S373P, S375F, D405N, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K	7.3
Omicron BA.4	V3G, T19I, L24-, P25-, P26-, A27S, del69-70, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K	21.3
Omicron BA.5	T19I, L24-, P25-, P26-, A27S, del69-70, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K	22.6

Efficacy of Antiviral Agents against the Omicron Subvariant BA.2.75

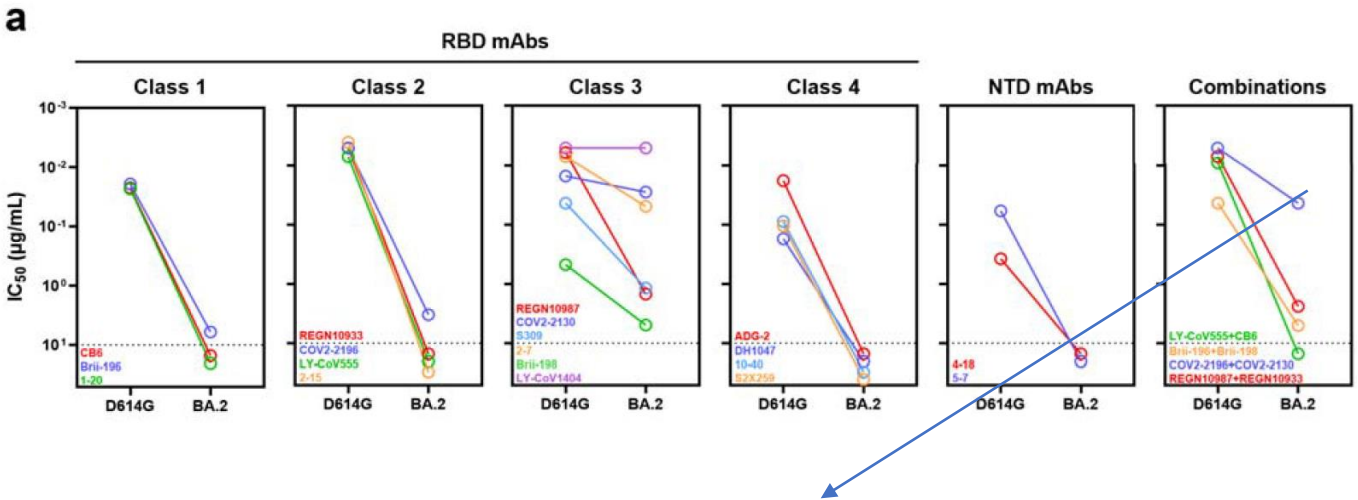
Takashita E et al, N Engl J Med. 2022 Sep 29;387:1236-1238

WHO Label (Pango Lineage): Virus Strain	Neutralization Activity of Monoclonal Antibody†							
	REGN10987, Imdevimab	REGN10933, Casirivimab	COV2-2196, Tixagevimab	COV2-130, Cilgavimab	S309, Sotrovimab Precursor	LY-CoV1404, Bebtelovimab	REGN10987 plus REGN10933	COV2-2196 plus COV2-2130
	nanograms per milliliter							
Ancestral strain (A): SARS-CoV-2/ UT-NC002-1T/ Human/2020/Tokyo	4.36 ±0.96	2.42 ±0.93	1.91 ±0.95	5.36 ±1.21	32.80 ±11.22	1.40 ±0.79	2.23 ±0.42	6.47 ±2.31
Omicron (BA.2): hCoV-19/Japan/UT-NCD1288-2N/2022	958.28 ±363.87	>50,000	4374.21 ±1483.72	21.59 ±8.57	>50,000	6.09 ±0.67	968.50 ±58.35	43.22 ±8.16
Omicron (BA.5): hCoV-19/Japan/TY41-702/2022	174.37 ±52.55	>50,000	>50,000	54.02 ±20.29	6240.39 ±1883.65	2.43 ±1.26	192.91 ±82.50	123.65 ±55.81
Omicron (BA.2.75): hCoV-19/Japan/ TY41-716/2022	>50,000	1153.19 ±104.61	122.31 ±67.08	101.71 ±53.24	28,536.48 ±6444.42	6.21 ±2.80	1811.78 ±600.23	34.19 ±7.60

The individual monoclonal antibodies were tested at a starting concentration of 50,000 ng per milliliter as a 50% focus reduction neutralization test titer. The monoclonal antibody combinations were tested at a starting concentration of 10,000 ng per milliliter for each antibody.

Antibody Evasion Properties of SARS-CoV-2 Omicron Sublineages

Iketani et al bioRxiv preprint doi: https://doi.org/10.1101/2022.02.07.479306;

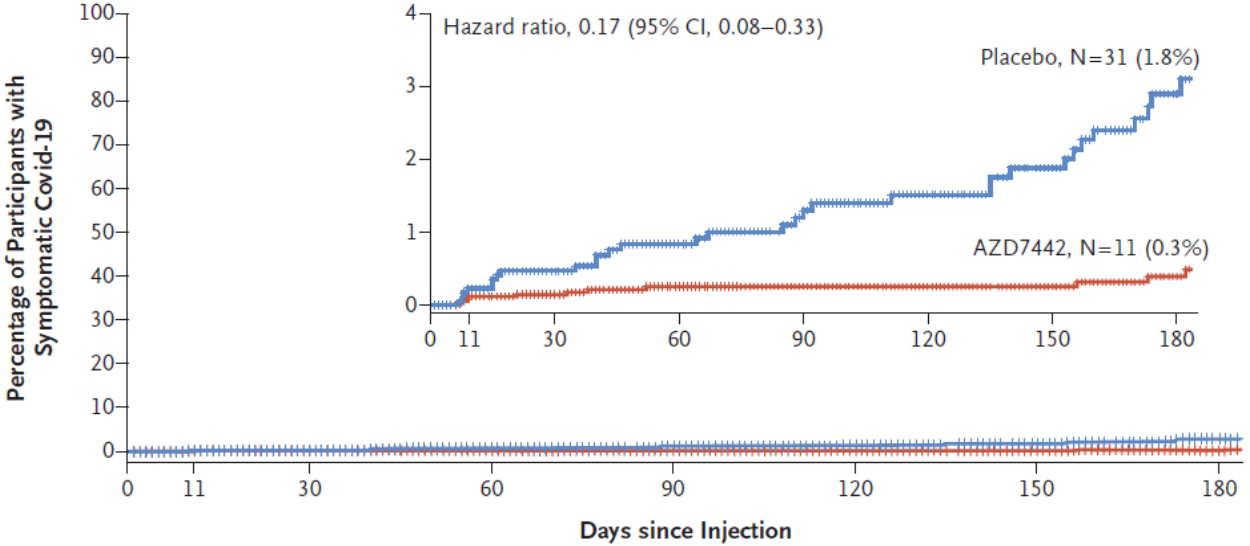


cilgavimab combined tixagevimab retained activity against BA.2

Intramuscular AZD7442 (Tixagevimab– Cilgavimab) for Prevention of Covid-19

Levin MJ et al, N Engl J Med 2022;386:2188-200.

Time to First SARS-CoV-2 RT-PCR–Positive Symptomatic Illness



No. at Risk								
Placebo	1731	1680	1483	1177	991	856	774	472
AZD7442	3441	3323	2957	2393	2054	1815	1667	1044

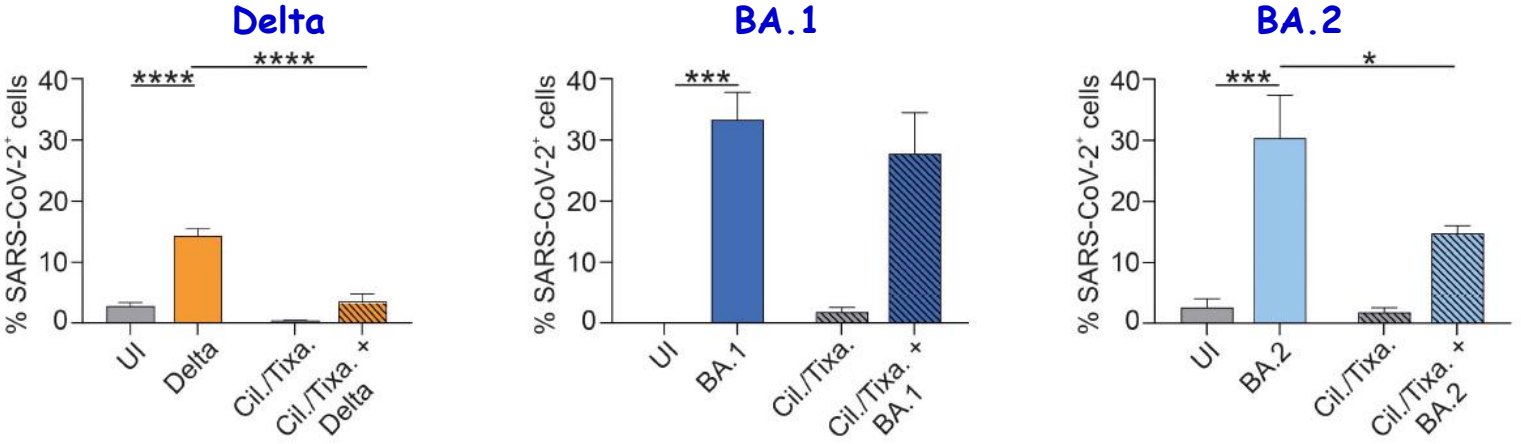
Cilgavimab/Tixagevimab as alternative therapeutic approach for BA.2 infections

Dichtl S et al. Front. Med., 2022 Sep 29

Primary human airway epithelia (HAE) cells in a 3D tissue model were infected with clinical isolates of SARS-CoV-2 Delta, BA.1 or BA.2. To mimic the therapeutic use of mAbs, Regdanvimab, Sotrovimab or Cilgavimab/Tixagevimab were added 6 h after infection. In order to mirror the prophylactic use of Cilgavimab/Tixagevimab, this compound was added 6 h prior to infection to the fully differentiated, pseudostratified epithelia cultured in air-liquid interphase.

Efficacy of the prophylactic and therapeutic use of mAb cocktail C/T against SARS-CoV-2 Delta, BA.1 or BA.2

After 72 h of infection, NHBE cells grown on transwell filters were analyzed by IF



Efficacy and safety of intramuscular administration of tixagevimab–cilgavimab for early outpatient treatment of COVID-19 (TACKLE): a phase 3, randomised, double-blind, placebo-controlled trial

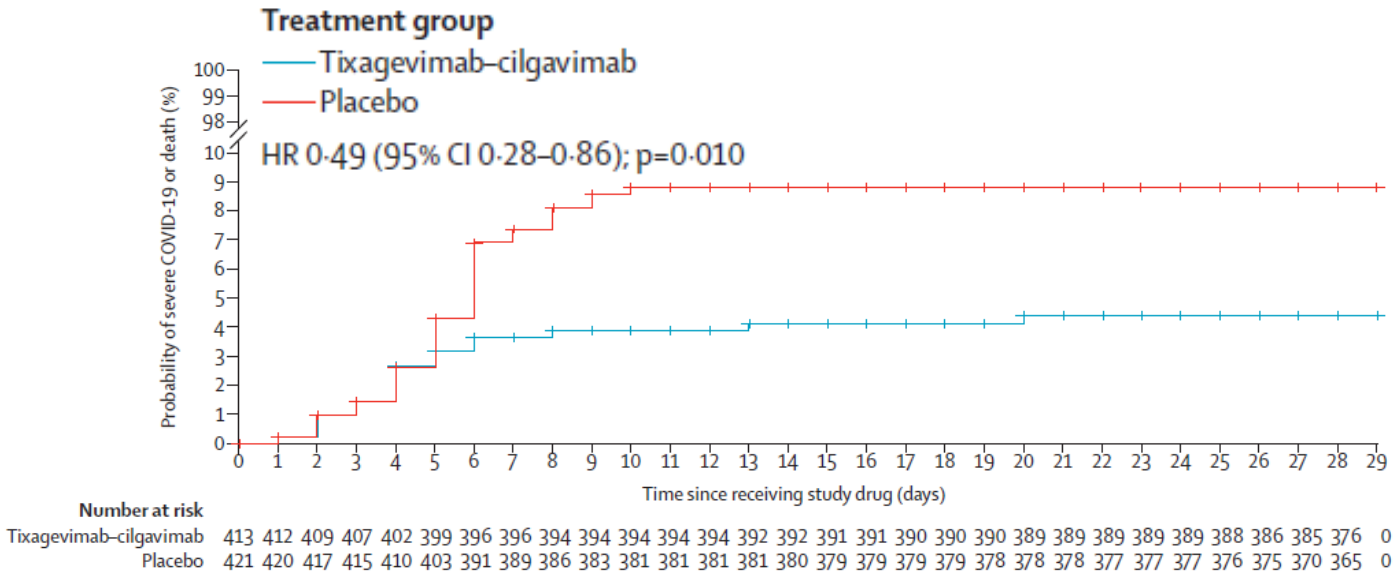
Montgomery H et al, Lancet Respir Med 2022; 10: 985–96

Between Jan 28, 2021, and July 22, 2021, 1014 participants were enrolled, of whom 910 were randomly assigned to a treatment group (456 to receive tixagevimab–cilgavimab and 454 to receive placebo).

The mean age of participants was 46·1 years (SD 15·2).

Efficacy and safety of intramuscular administration of tixagevimab–cilgavimab for early outpatient treatment of COVID-19 (TACKLE): a phase 3, randomised, double-blind, placebo-controlled trial *Montgomery H et al, Lancet Respir Med 2022; 10: 985–96*

Analysis of the composite primary endpoint of severe COVID-19 or death from any cause up to day 29 after receiving study drug



KEY MESSAGES for mAbs use

1. Conceptually MoABs work and could have a role for prevention of SARS-CoV-2 related disease in selected patients, mainly those with an absence or low expectancy of antibody rising after viral exposure or vaccination.

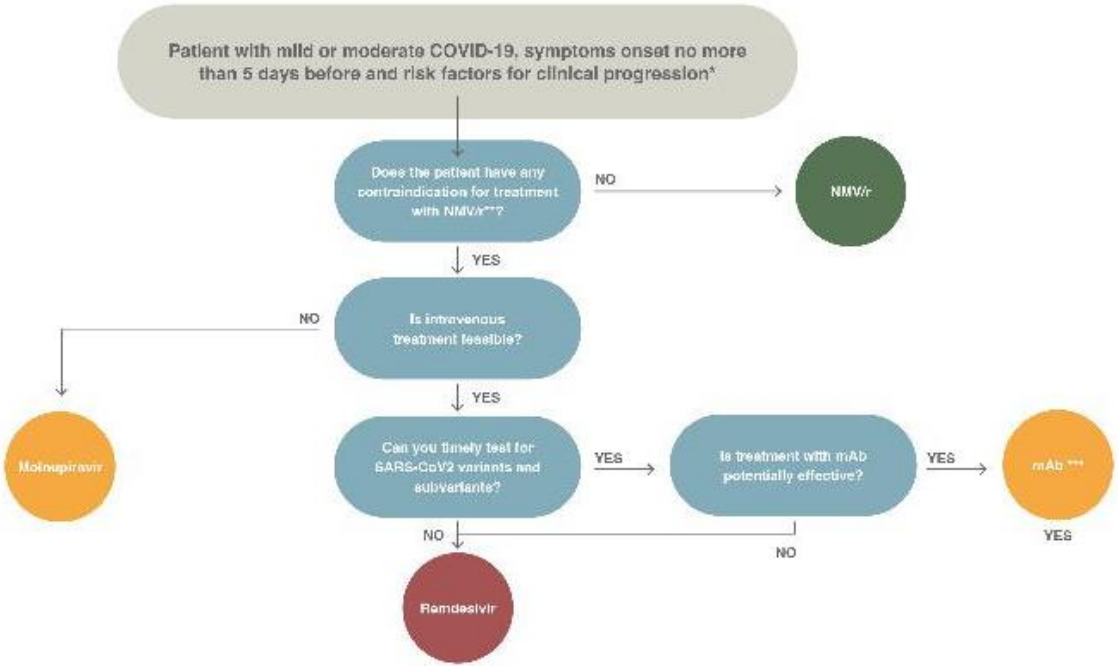
2. The role in treatments protocols must be well defined and should be reserved for patients with demonstrated absence of antibody response and/or non-vaccinated people.

3. A putative role of combination therapy with antivirals should be considered and evaluated.

4. Indications for use of any specific MoAB must not be "written in stone" but should evolve and change when needed on the basis of viral epidemiology.

ESCMID COVID-19 guidelines: update on treatment for patients with mild/moderate disease

Bartoletti M et al Clin Microbiol Infect . 2022 Aug 23;S1198-743X(22)00429-3



Clinical Infectious Diseases

BRIEF REPORT

REAL LIFE

Successful treatment of prolonged, severe COVID-19 lower respiratory tract disease in a B-cell ALL patient with an extended course of remdesivir and nirmatrelvir/ritonavir.

A patient with B-cell acute lymphoblastic leukemia (ALL) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had persistent, progressive pneumonia with viremia after 5 months of infection despite monoclonal antibodies, IV remdesivir and prolonged oral steroids.

Twenty days of nirmatrelvir/ritonavir and 10 days of IV remdesivir led to full recovery

Conclusion

- The managment of COVID-19 is changing dramatically with the availability of antivirals and mAb and after the immunization campaign
- The current unmet need is represented by immunocompromised patients