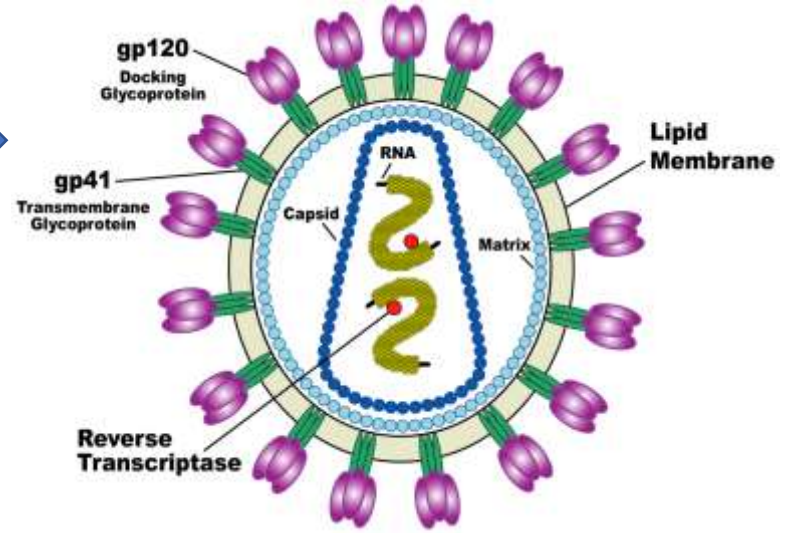
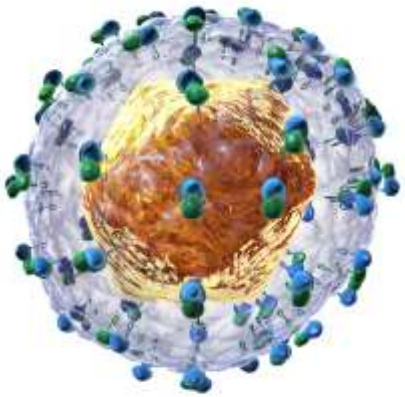
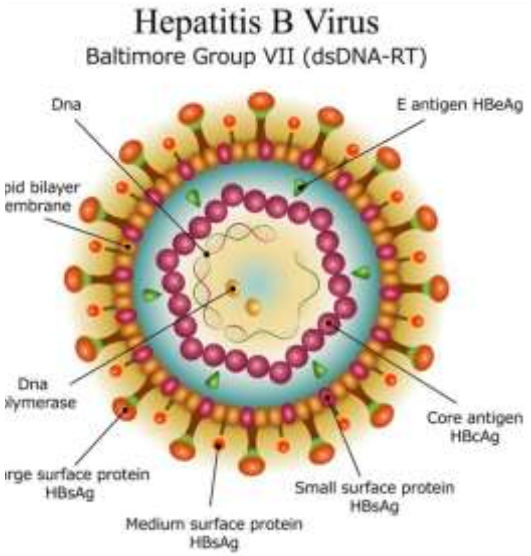
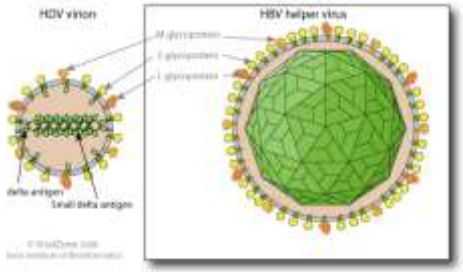
Clinical Pharmacology of Antiretrovirals

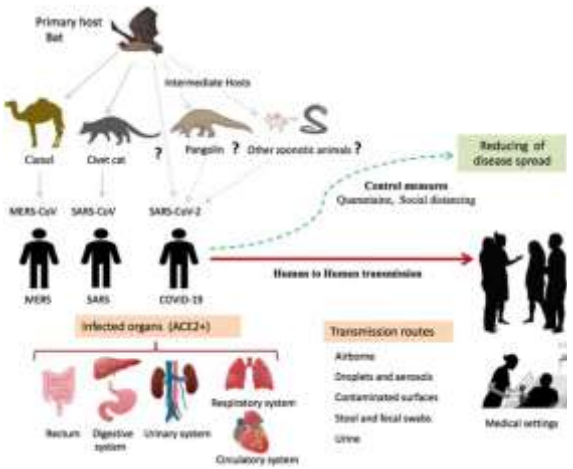


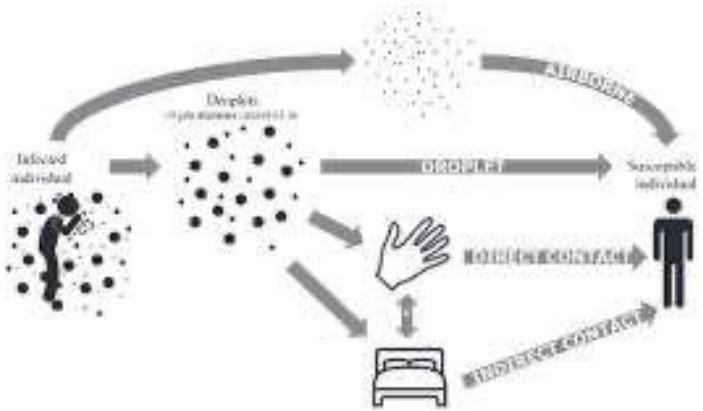


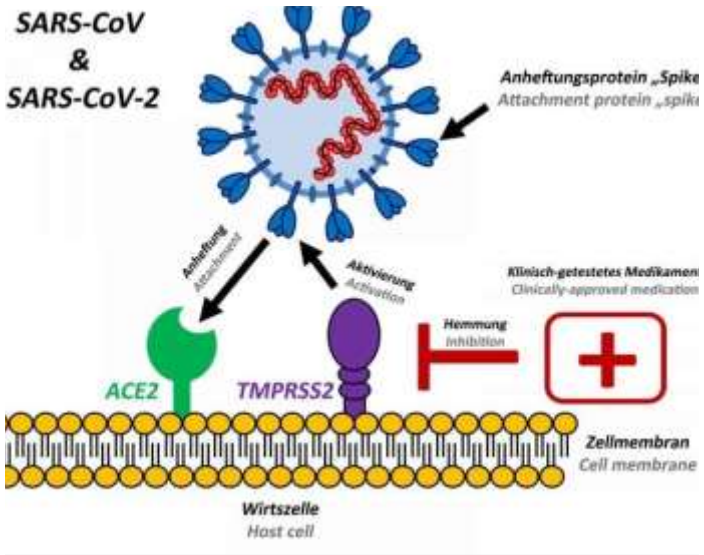
Hepatis C Virus (HCV)











Antivirals:

Hydroxychloroquine

Remdesivir

Lopinavir/Ritonavir

Darunavir/Ritonavir

Umifenovir

Favipiravir

Antiinflammatory

Tocilizumab

Sarilumab

Siltuximab

Anakinra

Baricitinib

Low-Molecular Weight Heparin (LMWH)

Plasma from COVID-19 convalescents

Remdesivir for the Treatment of Covid-19 — Preliminary Report

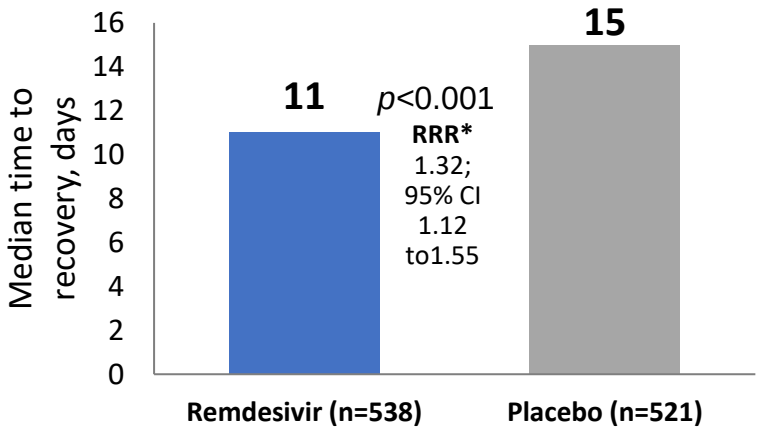
Beigel JH, et al. NEJM 2020; May 28: DOI: 10.1056/NEJMoa2007764

METHODS

We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults hospitalized with Covid-19 with evidence of lower respiratory tract involvement. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the **time to recovery**, defined by either discharge from the hospital or hospitalization for infection-control purposes only.

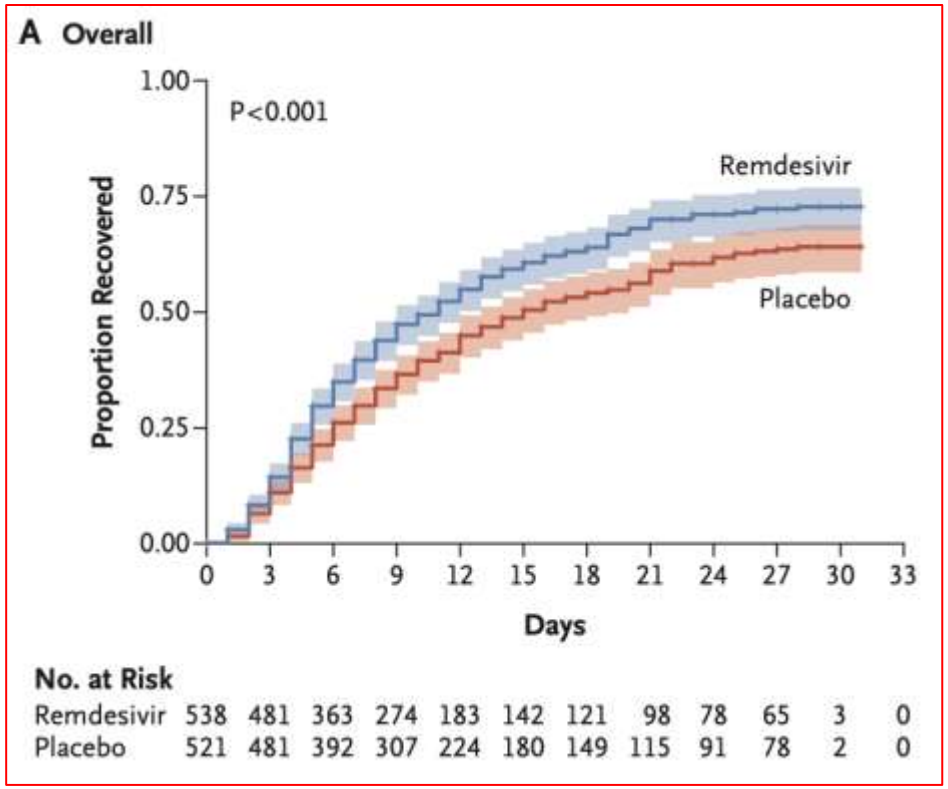
538 assigned to remdesivir and 521 to placebo

CONCLUSIONS Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection.



RRR, recovery rate ratio

*RRR and hazard ratios were calculated from the stratified Cox model; P values for these ratios were calculated with the stratified log-rank test.



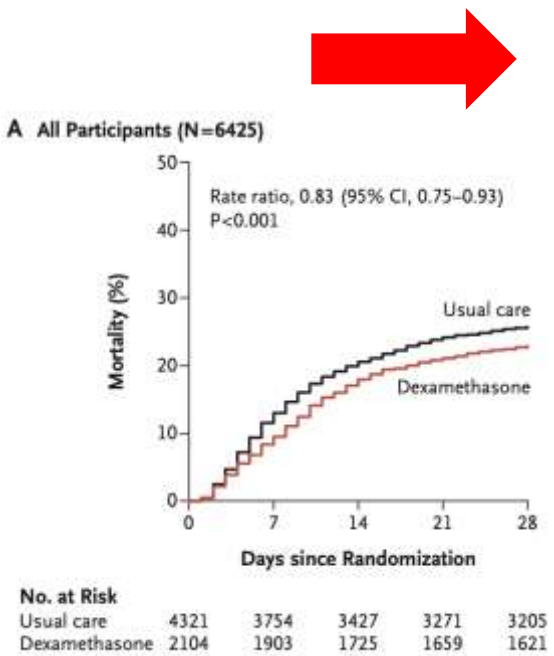
Dexamethasone in Hospitalized Patient with Covid-19 — Preliminary Report

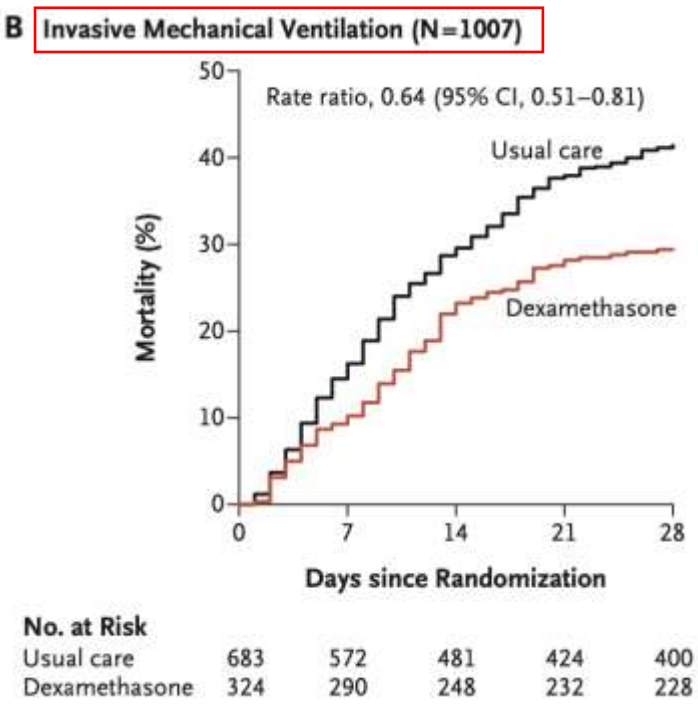
The RECOVERY Collaborative Group*

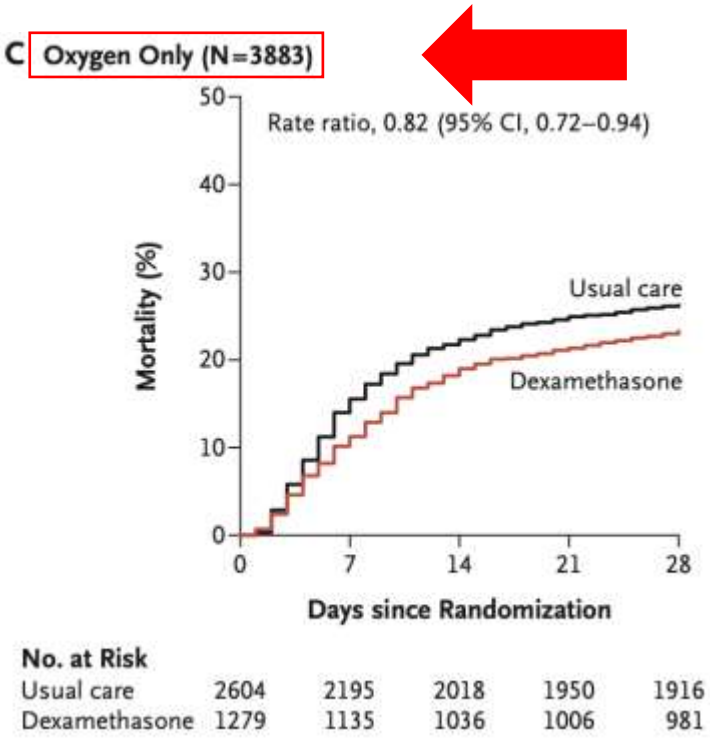
The NEW ENGLAND JOURNAL of MEDICINE

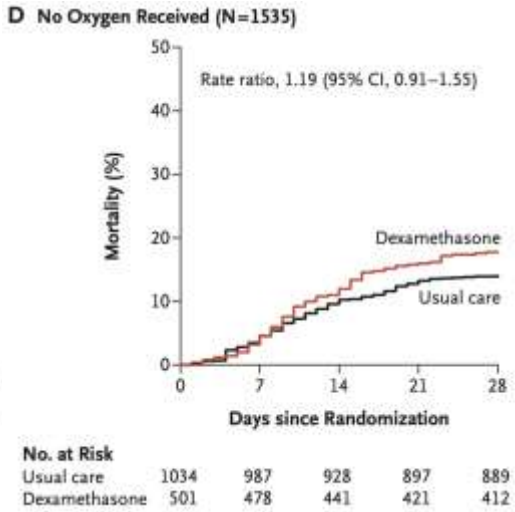
July 17, 2020 DOI: 10.1056/NEJMoa2021436

We randomly assigned patients to receive oral or intravenous dexamethasone (at a dose of 6 mg once daily) for up to 10 days or to receive usual care alone. The primary outcome was 28-day mortality.







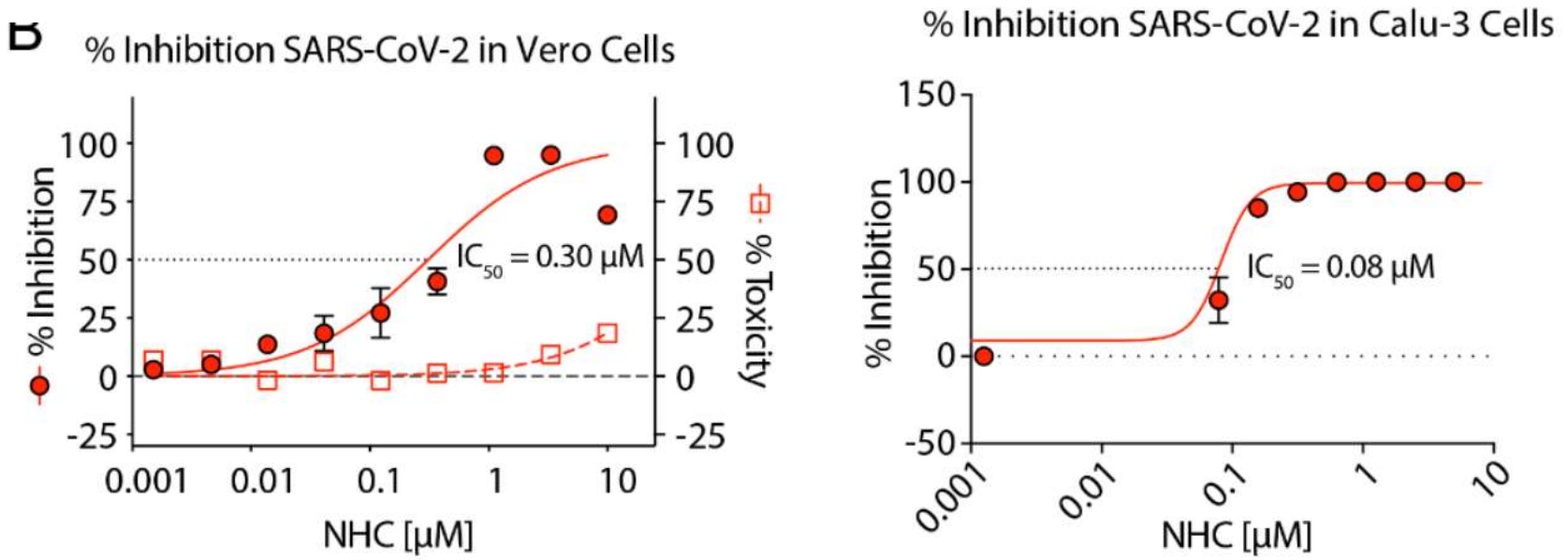


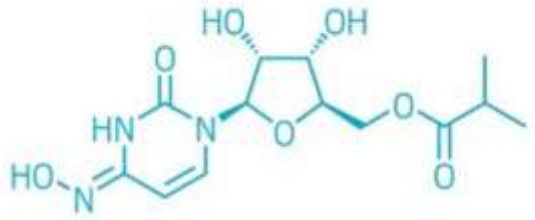
Science Translational Medicine

An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice

T. P. Sheahan *et al*., *Sci. Transl. Med.* 10.1126/scitranslmed.abb5883 (2020)

The drug has broad spectrum antiviral activity against SARS-CoV-2, MERS-CoV, SARS-CoV, and related zoonotic group 2b or 2c Bat-CoVs.





EIDD-2801

ORIGINAL ARTICLE

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

Peter Chen, M.D., Ajay Nirula, M.D., Ph.D., Barry Heller, M.D., Robert L. Gottlieb, M.D., Ph.D., Joseph Boscia, M.D., Jason Morris, M.D., Gregory Huhn, M.D., M.P.H.T.M., Jose Cardona, M.D., Bharat Mocherla, M.D., Valentina Stosor, M.D., Imad Shawa, M.D., Andrew C. Adams, Ph.D., et al., for the BLAZE-1 Investigators*

ORIGINAL ARTICLE

A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

ACTIV-3/TICO LY-CoV555 Study Group*

nature biotechnology

Explore our content ⌄ Journal information ⌄ Publish with us ⌄

nature › nature biotechnology › q&as › article

Q&A | Published: 21 October 2020

COVID-19 antibodies on trial

Laura DeFrancesco ✉

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19

FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF CASIRIVIMAB AND IMDEVIMAB

AUTHORIZED USE

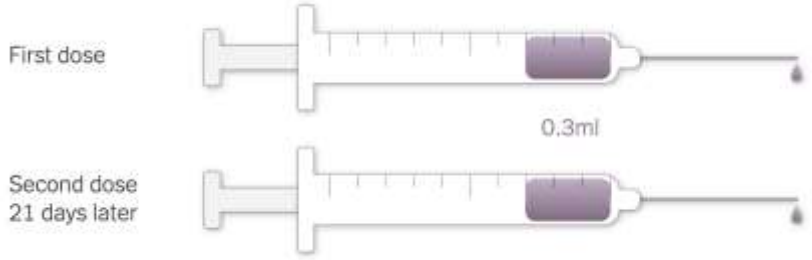
The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products casirivimab and imdevimab to be administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Casirivimab and imdevimab are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

Casirivimab and imdevimab have been authorized by FDA for the emergency uses described above.

Casirivimab and imdevimab are not FDA-approved for these uses.



Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

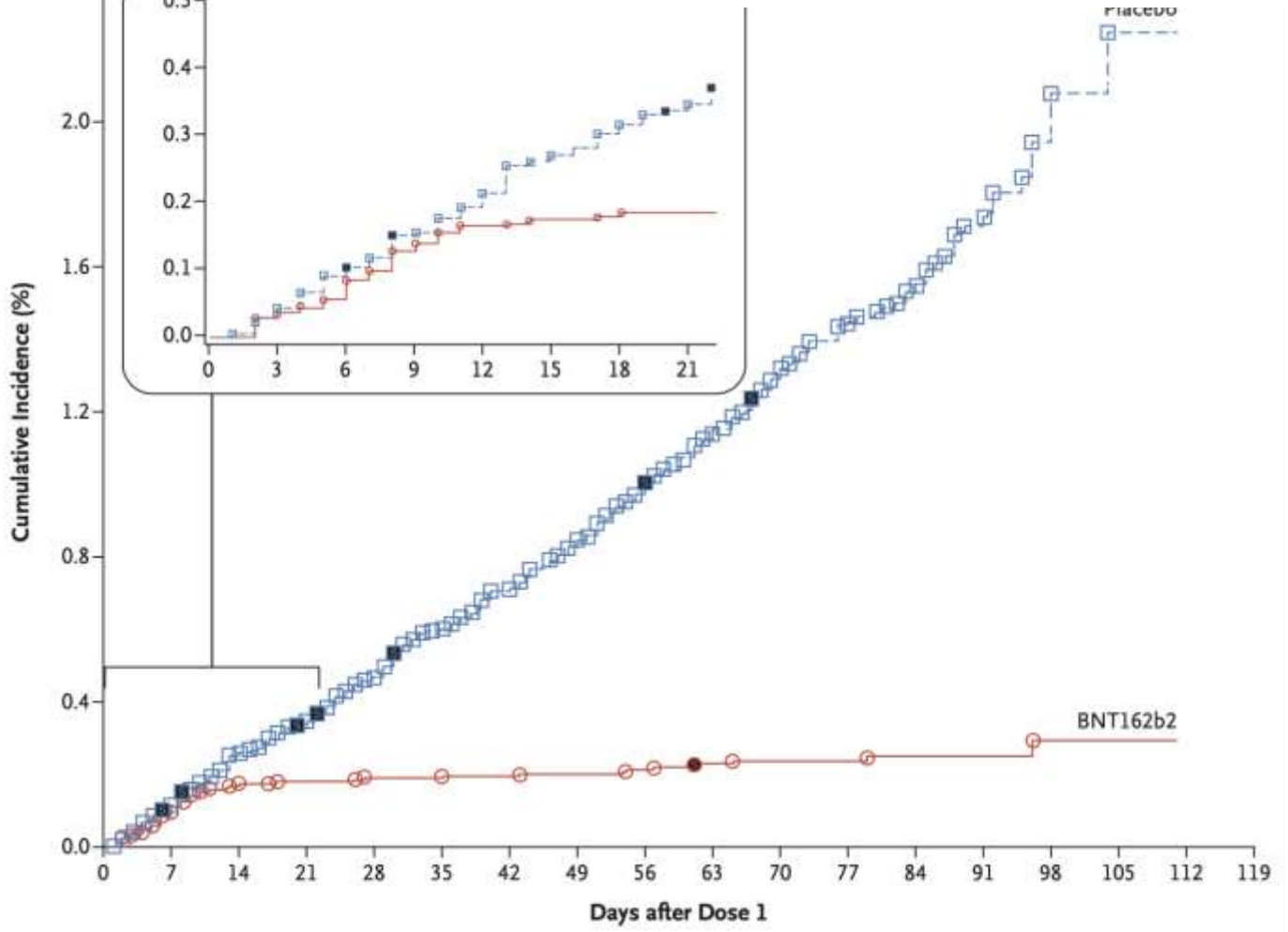
Fernando P. Polack, et al.

This article was published on December 10, 2020, at NEJM.org.

Quanto ci protegge il nostro vaccino?

La maggior parte dei casi di infezione da SARS-CoV-2 nelle persone che hanno ricevuto il vaccino si è sviluppata **nei primissimi giorni** dello studio; se consideriamo il tempo necessario affinchè il vaccino metta in atto il suo effetto protettivo, si può vedere che **già dopo 10 giorni** dalla prima delle due iniezioni il gruppo dei vaccinati (**rosso**) si discosta definitivamente da Chi ha invece ricevuto il placebo (**blu**). L'incidenza di infezione rimane costante nel tempo nel **gruppo placebo**, mentre si abbassa ai minimi termini nei **vaccinati**.

The NEW ENGLAND JOURNAL of MEDICINE



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669) No. of participants	BNT162b2, 30 μg (N=21,669) Surveillance time *person-yr (no. at risk)*	Placebo (N=21,686) No. of participants	Placebo (N=21,686) Surveillance time *person-yr (no. at risk)*	VE (95% CI) *percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

J Antimicrob Chemother 2020; **75**: 2381–2383
doi:10.1093/jac/dkaa272 Advance Access publication 26 June 2020

Journal of Antimicrobial Chemotherapy

The challenging pathway towards the identification of SARS-CoV-2/COVID-19 therapeutics

Marco Siccardi[1]*, Jonathan Schapiro[2], Giovanni Di Perri[3] and David J Back[1]

[1]Department of Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, UK; [2]National Hemophilia Center, Tel Aviv, Israel; [3]Department of Clinical Infectious Diseases, Amedeo Hospital, University of Turin, Turin, Italy

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The development of therapeutic agents against SARS-CoV-2/COVID-19 faces numerous barriers and a multidisciplinary approach to evaluating drug efficacy and toxicity is essential. Experimental and preclinical data should be integrated into a comprehensive analysis, where drug potency, the timing of therapy initiation, drug combinations, variability in systemic and local drug exposure and short- and long-term toxicities represent fundamental factors for the rational identification of candidates and prioritization of clinical investigations. Although the identification of SARS-CoV-2 therapeutics is a priority, rigorous and transparent methodologies are crucial to ensure that accelerated research programmes result in high-quality and reproducible findings.

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE 2020

Illustrations: Niklas Elmehed

Harvey J. Alter

Michael Houghton

Charles M. Rice

"for the discovery of Hepatitis C virus"

And my personal gratitude to all my Friends, Coworkers and all Attendees