19ª edición

POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

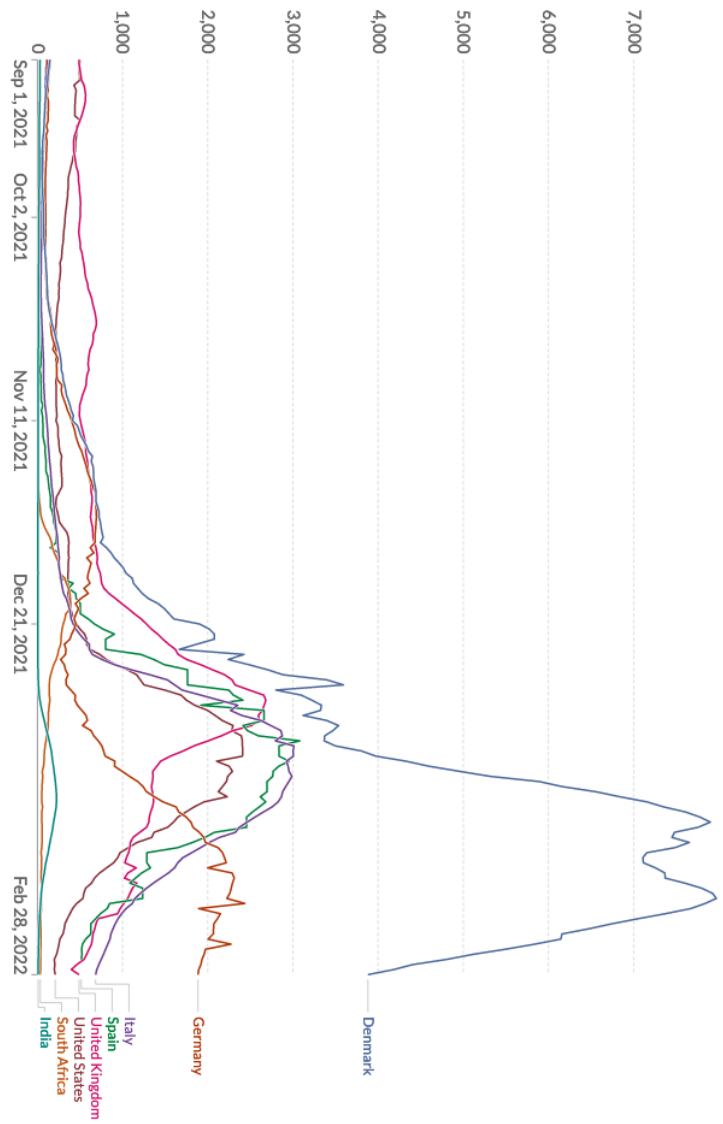
Tratamiento con ac neutralizantes y vacunas preventivas frente a las variantes de preocupación del SARS CoV 2

Julià Blanco, PhD

Senior Researcher IrsiCaixa/IGTP/UVIC-UCC

The calendar vs the virus

Date	Event
SEPTEMBER 1, 2021	General Abstract and Scholarship Submissions Opens
NOVEMBER 1, 2021	General Abstract and Scholarship Submissions Deadline at 5:00 PM Pacific Time
LATE FALL 2021	General Registration Opens
DECEMBER 10, 2021	General Abstract and Scholarship Dispositions Sent by Email
DECEMBER 13, 2021	Late-Breaking Abstract Submission Opens
JANUARY 5, 2022	Late-Breaking Abstract Submission Deadline at 5:00 PM Pacific Time
JANUARY 14, 2022	Late-Breaking Abstract Disposition Sent by Email
FEBRUARY 12 TO 16, 22, 23, 24, 2022	CROI 2022



https://www.croiconference.org/important-dates/

https://ourworldindata.org/

Anti SARS-CoV-2 antibodies at CROI

One session

Oral Abstract Session-9 SARS-CoV-2 ANTIVIRALS AND OUTCOMES
9:45 AM MT - 11:45 AM MT

Oral Abstract Moderators

Robert T. Schooley, *University of California San Diego, La Jolla, CA, USA*

Huldrych F Günthard, *University Hospital Zurich, Zurich, Switzerland*

Some posters

Poster Session-D07 SARS-CoV-2 IMMUNE THERAPY
2:00 PM MT - 3:30 PM MT

Poster Session-H01 CLINICAL TRIALS OF THERAPY FOR SARS-CoV-2: ANTIVIRALS AND IMMUNE MODIFIERS
2:00 PM MT - 3:30 PM MT

Poster Session-Q06 ALL THINGS COVID-19 IN CHILDREN
2:00 PM MT - 3:30 PM MT

One workshop

Workshop-2 FRONTIERS IN LABORATORY TECHNOLOGIES CME
11:00 AM MT - 1:00 PM MT

Target Audience: This session is directed to scientists, clinicians, funders, stakeholders, students, and members of the community at large, who are interested in understanding the impact of novel laboratory technologies.

CROI 2022

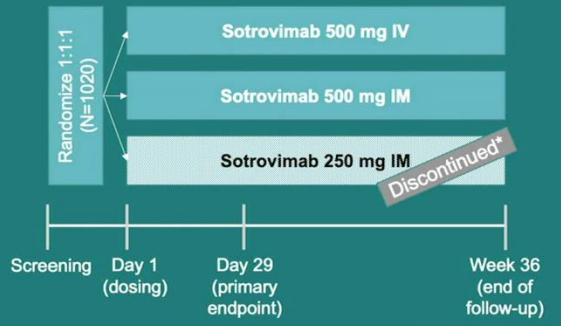
INTRAMUSCULAR SOTROVIMAB IS NONINFERIOR TO INTRAVENOUS SOTROVIMAB FOR COVID-19

Adrienne E. Shapiro , Elias Sarkis, Jude Acloque, Yaneicy Gonzalez-Rojas, Rubaba (Ruby) Hussain, Erick Juarez, Jaynier Moya, David Inman, Andrew Skingsley, Daren Austin, Amanda Peppercorn, Jennifer E. Sager, Elizabeth Alexander, Leah A. Gaffney, Anita Kohli

Study Design

Patient population:

- COVID-19+ with symptoms ≤7 days
- Age ≥12 years and at high risk of progression
  - ≥55 years old
  - Diabetes, obesity, CKD, sickle-cell disease, congenital heart disease, neurodevelopmental disorders, chronic lung disease, immunosuppression or chronic liver disease



Primary endpoint, Day 29: Hospitalization >24 hours for acute management of illness or death, **due to any cause**

Non-inferiority study with a 3.5% NI margin on absolute scale (per feedback from the FDA)

Enrollment occurred from June to August 2021, coinciding with a surge of the Delta variant

*Ongoing safety review led to early discontinuation of the 250 mg IM arm due to an increased rate of hospitalizations compared with the 500 mg arms.

Primary Efficacy Endpoint

Hospitalization >24 hours or death through Day 29, due to any cause

	Sotrovimab 500 mg IV (N=382)	Sotrovimab 500 mg IM (N=379)
Key inclusion/exclusion criteria violations,* n (%)	4 (1)	3 (<1)
Progression status, n (%)		
n	378	376
Hospitalized >24 hours and/or death	5 (1.3)	10 (2.7)
Hospitalized >24 hours	5 (1.3)	10 (2.7)
Death	0	2 (0.5)
Alive and not hospitalized >24 hours	365 (96.6)	356 (94.7)
Missing†	8 (2.1)	10 (2.7)
Sotrovimab 500 mg IM vs 500 mg IV: Hospitalization >24 hours and/or death		
Risk difference (%)‡	1.07	
95% CI	(–1.25, 3.39)	

*Fully vaccinated, immunocompetent participants who were randomized in violation of amendment 2 (IV, n=4; IM, n=1) and 2 participants in the IM arm who did not have a positive SARS-CoV-2 result.
†Missing progression status = participants who were randomized but not dosed (n=6) or withdrew prior to Day 29 (n=12) and had not had a progression event.
‡Analysis performed using binomial regression model with identity link function and with treatment (500 mg IV, 500 mg IM), age (<65, ≥65 years), and sex (male, female) as covariates.

In the 250 mg IM group, 10/183 (5.5%) of participants were hospitalized >24 hours through Day 29.

Day 29 analysis DCO: October 28, 2021.

Conclusions

- The primary endpoint was met: treatment with sotrovimab 500 mg IM was **non-inferior** to sotrovimab 500 mg IV
  - Adjusted risk difference: 1.07% (95% CI: –1.25%, 3.39%), with the upper limit of the CI lower than the pre-specified non-inferiority margin of 3.5%
- Sotrovimab 500 mg administered as 2 × 4 mL injections in bilateral dorsogluteal muscles was well tolerated
- The safety profile of sotrovimab 500 mg continues to be favorable, with a low rate of adverse events and rare infusion-related reactions
- The ability to administer sotrovimab via intramuscular administration is anticipated to allow increased access for patients in need of urgent treatment

Pre Omicron era

CROI 2022

EFFECT OF SEROSTATUS ON THE EFFICACY OF SOTROVIMAB IN PREVENTING COVID-19 PROGRESSION

Anil Gupta, Elias Sarkis, Andrea L. Cathcart, Elizabeth Alexander, Wendy W. Yeh, Megan Smithey, Nicola Scott, Andrew Skingsley, Helen A. Watson, Melissa Aldinger, Adrienne E. Shapiro

Study Design & Methods

Study Design (NCT04545060):

- Double-blind, placebo-controlled study, randomized 1:1 to 500 mg IV sotrovimab or placebo
- Blood samples were collected for anti-SARS-CoV-2 anti-nucleocapsid (N) antibody on Study Day 1 (pre-dose test)

Patient Population:

- COVID-19+ with symptoms ≤5 days
- ≥55 years old or ≥18 years old with a comorbid condition*
- Unvaccinated and no prior infection with COVID-19

Enrollment Period:

- August 2020 to March 2021
- Alpha, Epsilon, and Gamma were predominant circulating variants in countries where COMET-ICE recruited[1]

Primary Endpoint:

- All-cause hospitalization >24 hours or death due to any cause by Day 29
  - A post-hoc review was conducted to evaluate potential relatedness to COVID-19

Serology Assay:

- Qualitative measurement of IgG to anti-SARS-CoV-2 nucleocapsid (N) protein (Abbott SARS-CoV-2 IgG assay, Architect i2000SR immunoassay analyzer)
  - Positive anti-SARS-CoV-2 N protein result indicates an endogenous immune response to infection

*Diabetes requiring medication, obesity, chronic kidney disease, congestive heart failure, COPD, or moderate to severe asthma.

1. https://covariants.org/per-country

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Results

Primary Endpoint by Baseline Serostatus

Proportion of Participants Who Have Progression of COVID-19 Through Day 29 by Seropositivity at Baseline

	Seropositive		Seronegative	
	Placebo	Sotrovimab	Placebo	Sotrovimab
Number of participants in subgroup	97	105	375	365
Progression status, n (%)				
Hospitalization >24 hours and/or death	4 (4%)	2 (2%)	25 (7%)	4 (1%)
Hospitalized >24 hours	4 (4%)	2 (2%)	25 (7%)	4 (1%)
Death	0	0	2 (<1%)	0
Relative risk ratio; 95% CI	0.49 (0.09, 2.64)		0.16 (0.06, 0.45)	

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Implications

- Limited data exist on the natural history of COVID-19 disease by serostatus
  - Lower baseline nasopharyngeal viral loads among seropositive participants
  - Lower rates of hospitalization among seropositive participants (4% vs 7%), no deaths
  - Unclear relevance in setting of newer variants, re-infections, and vaccine-elicited seropositivity
- Treatment with sotrovimab reduced progression to severe COVID-19 regardless of serostatus
  - Treatment benefit observed for progression to COVID-19–related hospitalization
  - Safety profile by serostatus is consistent with that reported in the overall study population
  - Small numbers limit strength of inference
- In the pandemic setting where drug supply may be limited, selection of patients who will benefit the most from monoclonal antibody therapy based on serostatus remains challenging

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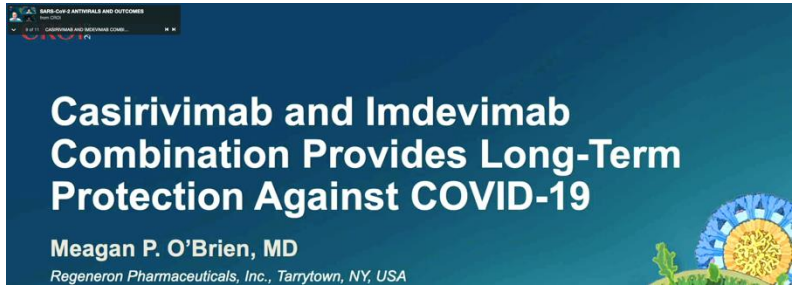
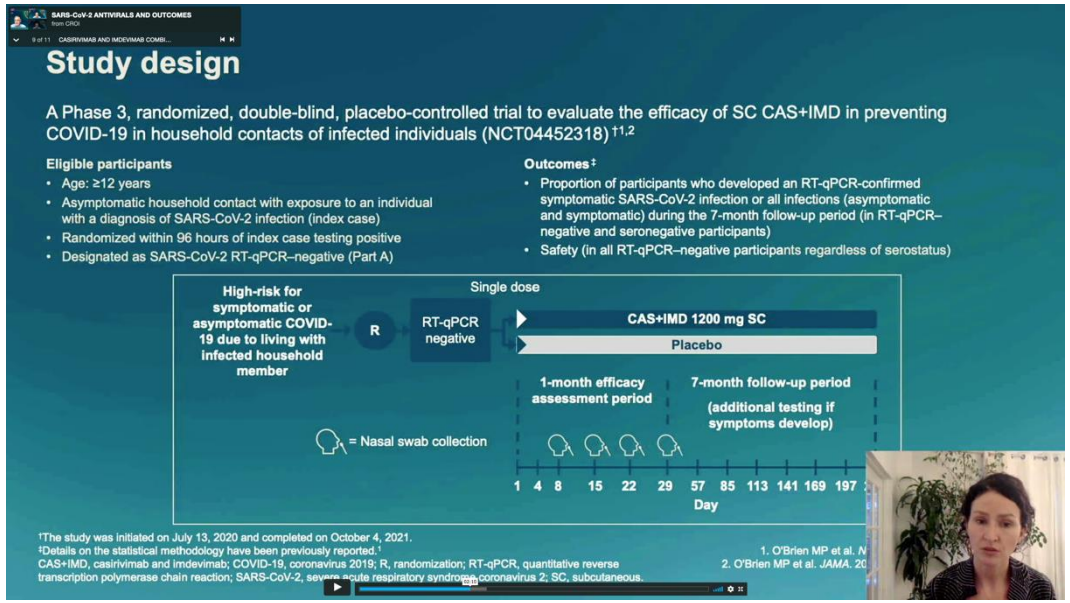
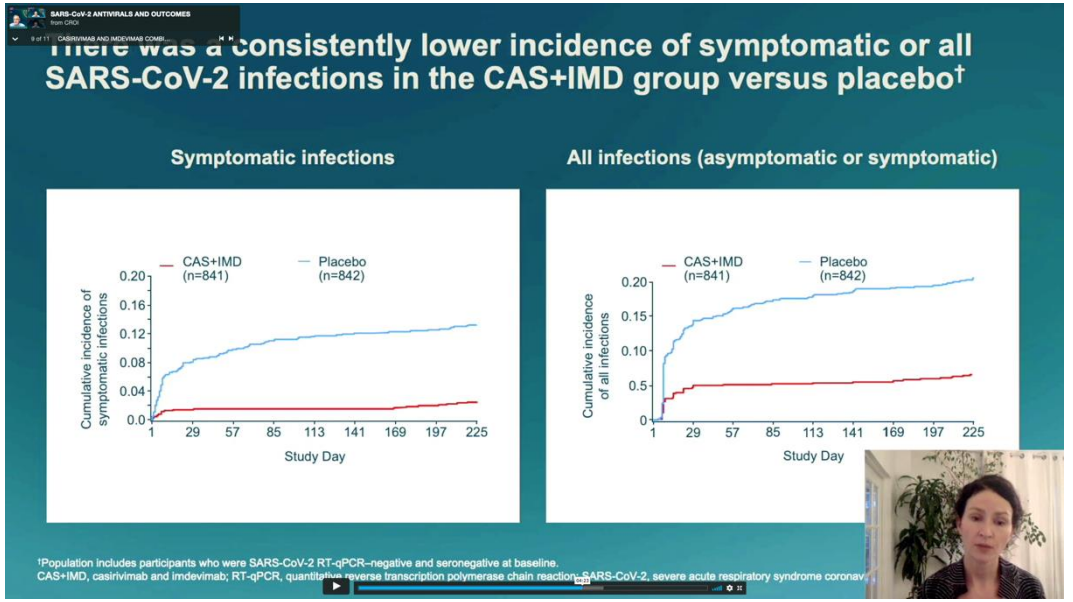
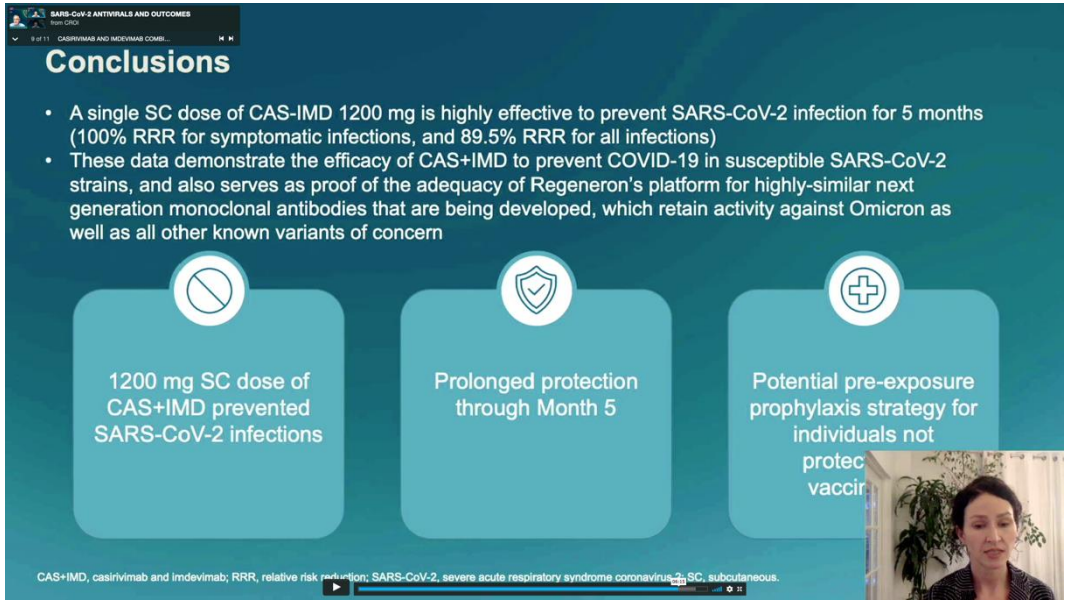
Pre Omicron era

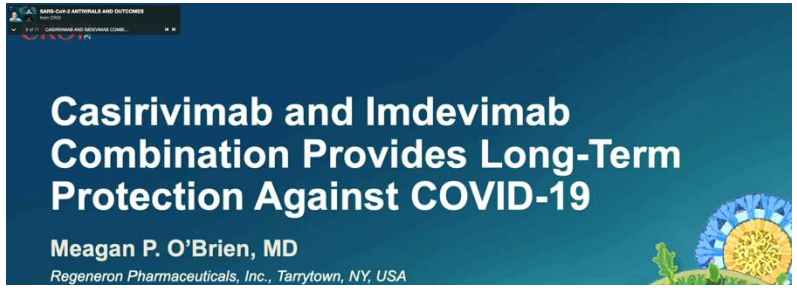


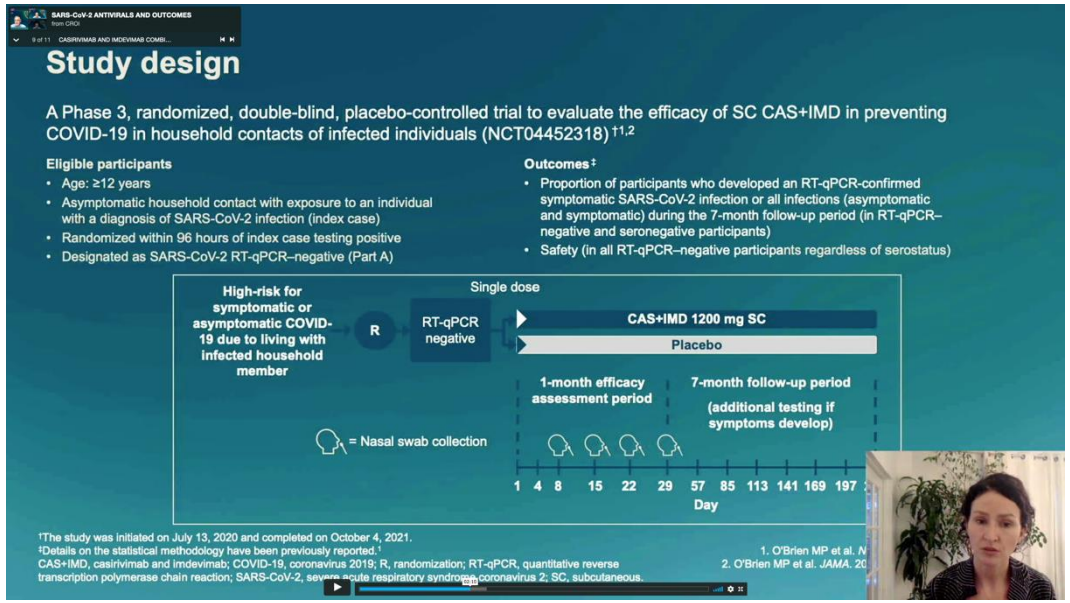


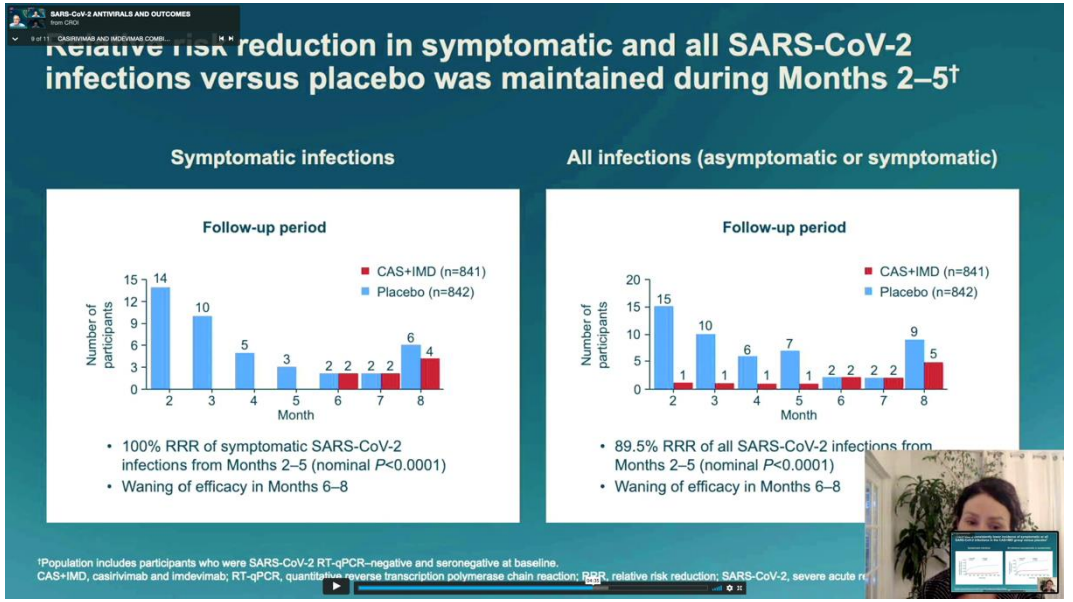


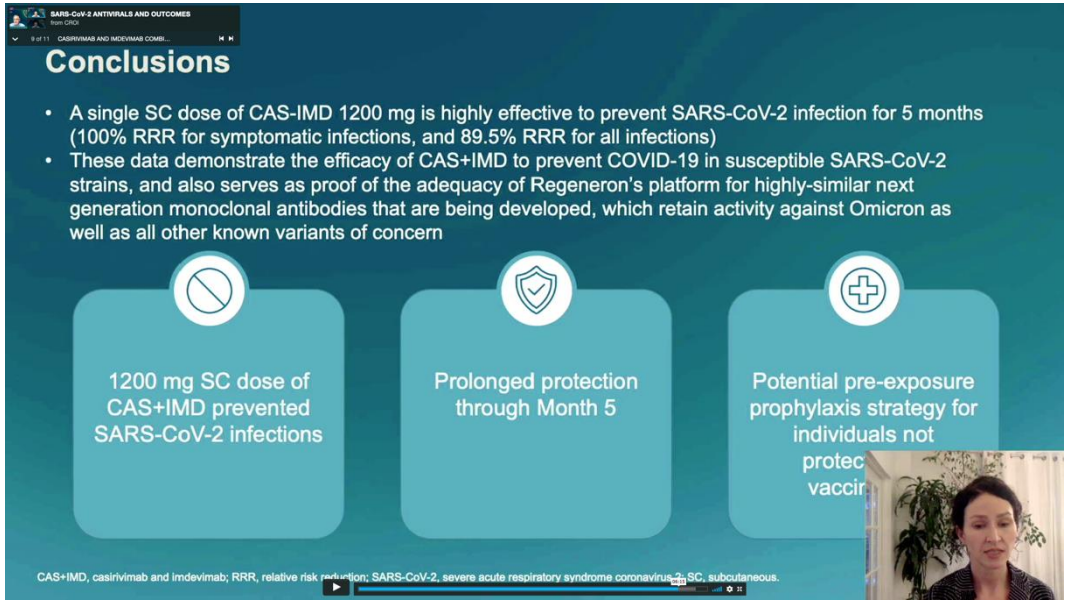


Pre Omicron era









Pre Omicron era

Poster sessions: antibodies and adults

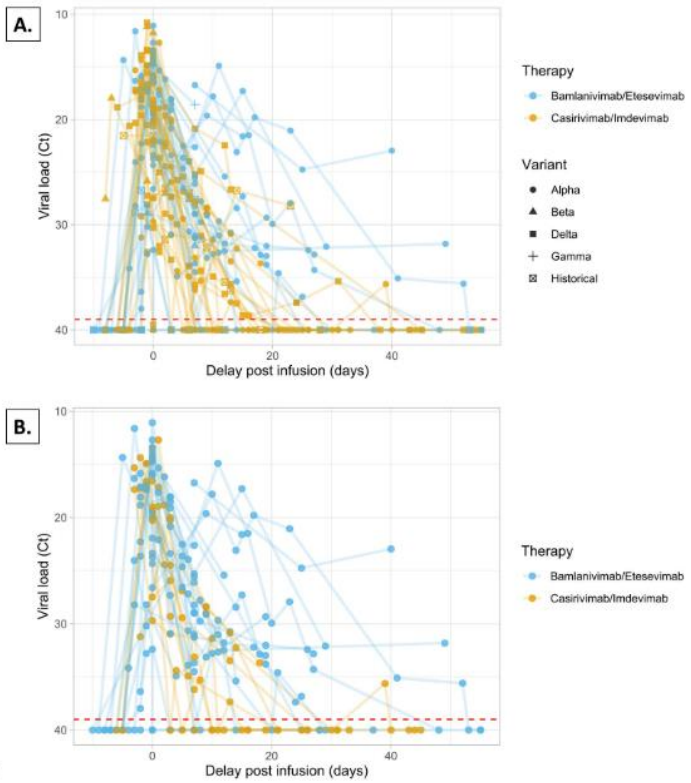
CROI

POSTER #299

Clinical and virological evolution of patients at high risk of severe COVID-19 treated with early administration of dual monoclonal antibodies

Valentine M. Ferré[1*], Nathan Peiffer-Smadja[2], Laura Kramer[3], Alicha Kanté[4], Margaux Debarge[3], Christophe Choquet[5], Romain Coppée[6], Donia Bouzid[7], Jonathan Messika[8], Jennifer Le Grand[3], Michael Thy[9], Solen Kerneis[10], Diane Descamps[1], Benoit Visseaux[1], Jade Ghosn[2]

Poster 299



Relevance??

Pre Omicron era

Presentation number: 00943

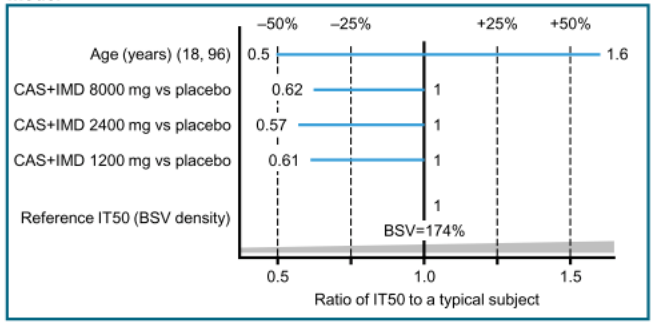
Effects of Casirivimab and Imdevimab on Symptom Outcomes in Outpatients with COVID-19

Yuhuan Wang[1], Mohamed Hussein[1], Diana Rofail[1], Kuan-Ju Lin[1], Daniela J. Conrado[1], Kenneth C. Turner[1], Samit Ganguly[1], Hazem E. Hassan[1], Qian Huang[1], Zhichao Lyu[1], Hong Yan[1], Thomas Norton[1], Shazia Ali[1], John D. Davis[1], Nidal Al-Huniti[1]

[1]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

Poster 457

Figure 2. Effect of dose of CAS+IMD and age on IT50 based on the final model



Note: X axis is the ratio of IT50 to a typical subject in analysis dataset: an asymptomatic female on placebo, whose baseline BMI is 30.6 kg/m^2, albumin 43 g/L, age 49 years, and viral load 6.9 $\log_{10}$ copies/mL. Continuous covariate range represents the extreme values from analysis dataset. To model the trajectory of latent score, an immediate response model with nominal time as driver was used:
Score (t)=S0×(1- (Imax×t)/(IT50+t)), where Score (t) is latent score at nominal time t. S0 is baseline latent score, Imax is the maximal magnitude of reduction in latent score, and IT50 the time taken to achieve half of the maximal response.
BSV, between-subject variability; IT50, time taken to achieve half of the maximal response.

Presentation number: 00461

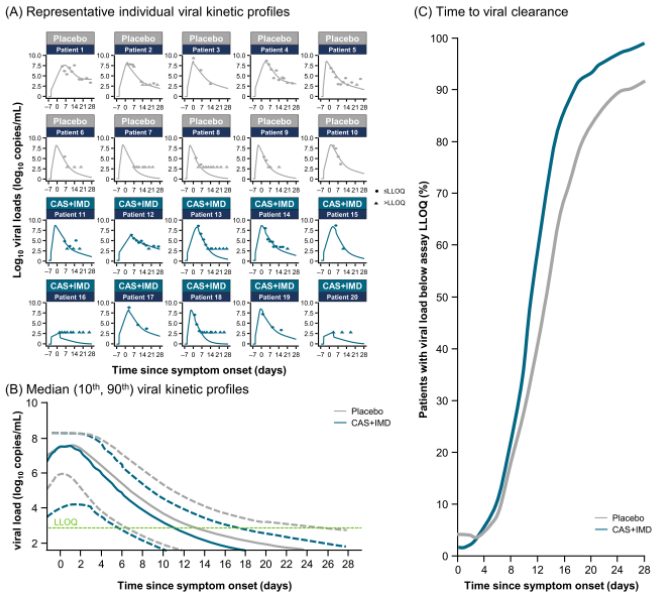
Viral Kinetics in COVID-19 Outpatients Treated with Casirivimab+Imdevimab Combination

Daniela J. Conrado[1], Kashyap Patel[2], Kuan-Ju Lin[1], Yuhuan Wang[1], Jiraganya (JJ) Bhongsatiern[1], Mohamed A. Kamal[1], Kenneth C. Turner[1], Samit Ganguly[1], Hazem E. Hassan[1], Hong Yan[1], Cynthia Portal-Celhay[1], John D. Davis[1], Patrick F. Smith[2], Jeremie Guedj[3], Nidal Al-Huniti[1]

[1]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [2]Certara, Princeton, NJ, USA; [3]Université de Paris, IAME, INSERM, Paris, France

Poster 461

Figure 2. Model predictions



Poster sessions: antibodies and children

Poster 743

- The PK analysis confirms that the weight-based doses selected for pediatric patients (0 to <12 years) provide comparable exposures to those observed in adults (≥18 years) and pediatric patients ages 12 to <18 years, weighing at least 40 kg. Thereby, the PK analysis results supported extrapolation of efficacy from adults based on exposure-matching for authorization.
- Pre-specified parameters support efficacy extrapolation from adults to pediatric patients.
- The safety profile of BAM + ETE in pediatric patients ages 0 to <12 years old identified no new safety risks compared to the established safety profile.
- In contrast to adults, no COVID-19 hospitalizations or deaths were reported in pediatric populations.

Similar PK

Faster VL decay

Similar safety profile

No severe cases

Pre Omicron era

Poster sessions: antibodies and mice

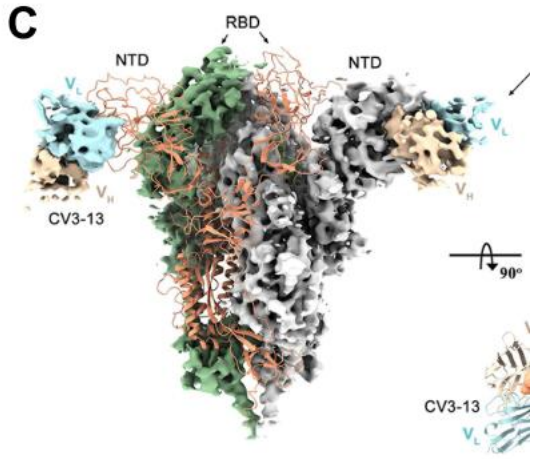
00301

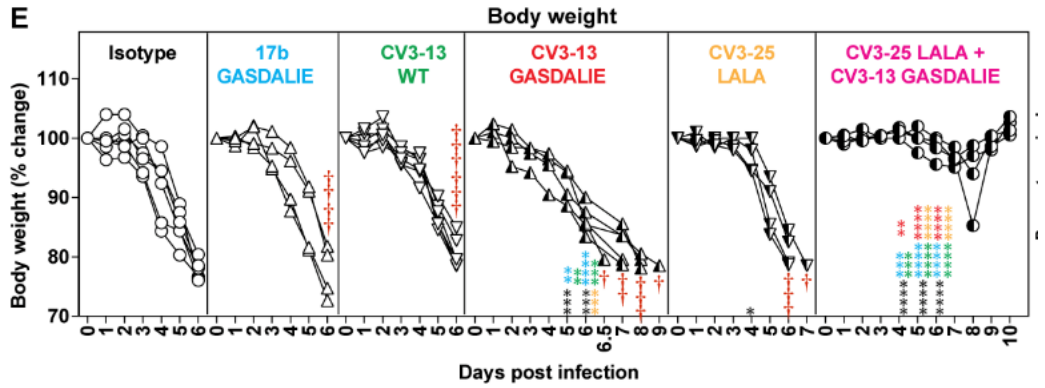
A Fc-enhanced non-neutralizing antibody delays SARS-CoV-2 induced death in mice

Guillaume Beaudoin-Bussières[1,2,*], Yaozong Chen[3,*], Irfan Ullah[4,*], Jérémie Prévost[1,2], William D. Tolbert[3], Kelly Symmes[4], Shilei Ding[1], Mehdi Benlarbi[1], Fei Zhou[5], Edwin Pozharski[6,7], Priti Kumar[4], Walther Mothes[8], Pradeep D. Uchil[8,**], Marzena Pazgier[3,**] and Andrés Finzi[1,2,9,10,**]

[1]Centre de recherche du CHUM, Montréal, Canada, [2]Département de Microbiologie, Infectiologie et Immunologie, Université de Montréal, Montréal, Canada, [3]Infectious Disease Division, Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, [4]Department of Internal Medicine, Section of Infectious Diseases, Yale University School of Medicine, New Haven, USA, [5]Division of Basic and Translational Biophysics, Unit on Structural Biology, NICHD, NIH, Bethesda, MD, USA, [6]University of Maryland Institute for Bioscience and Biotechnology Research, Rockville, MD, USA, [7]Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, MD, USA, [8]Department of Microbial Pathogenesis, Yale University School of Medicine, New Haven, CT, USA, [9]Department of Microbiology and Immunology, McGill University, Montreal, Canada, *These authors contributed equally, **Corresponding authors, [10] Lead contact

Poster 301





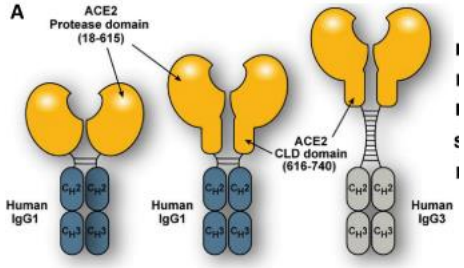
D07

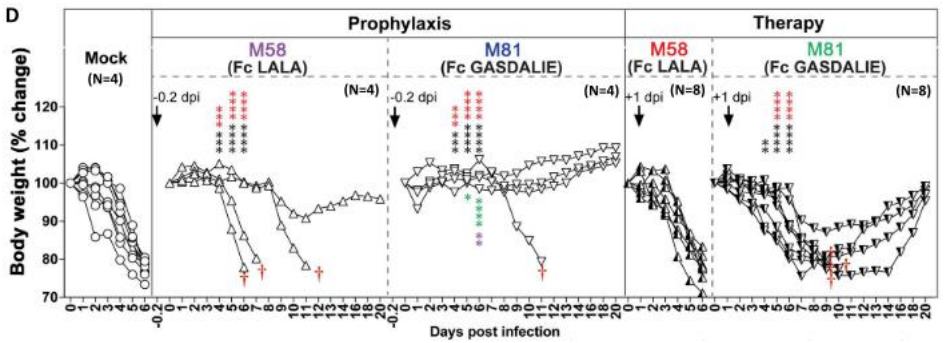
IN VIVO EFFICACY OF ENGINEERED ACE2-FC IN PREVENTING LETHAL SARS-COV-2 INFECTION

Yaozong Chen[1,§], Lulu Sun[2,§], Irfan Ullah[3,§], Guillaume Beaudoin-Bussières[4,5], Andrew P. Hederman[6], William D. Tolbert[1], Rebekah Sherburn[1], Dung N. Nguyen[1], Priti Kumar[6], Margaret E. Ackerman[6], Walther Mothes[7], Andrés Finzi[4,5], Pradeep D. Uchil[7], Frank J. Gonzalez[2], Marzena Pazgier[1#]

[1]Infectious Disease Division, Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD 20814-4712, USA. [2]Laboratory of Metabolism, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, Maryland, USA. [3]Department of Internal Medicine, Section of Infectious Diseases, Yale University School of Medicine, New Haven, CT 06520, USA. [4]Centre de recherche du CHUM, Montreal, QC H2X 0A9, Canada. [5]Département de Microbiologie, Infectiologie et Immunologie, Université de Montréal, Montreal, QC H2X 0A9, Canada. [6]Thayer School of Engineering, Dartmouth College, Hanover, NH 03755, USA. [7]Department of Microbial Pathogenesis, Yale University School of Medicine, New Haven, CT 06510, USA. §equal contribution. #corresponding author (marzena.pazgier@usuhs.edu)

Poster 300





Workshop-2 FRONTIERS IN LABORATORY TECHNOLOGIES

CME

11:00 AM MT - 1:00 PM MT

Target Audience: This session is directed to scientists, clinicians, funders, stakeholders, students, and members of the community at large, who are interested in understanding the impact of novel laboratory technologies.

Conveners

Galit Alter, *Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, USA*

Frank Kirchhoff, *Ulm University Medical Center, Ulm, Germany*

5 **POPULATION-LEVEL VIRAL SEQUENCING**

11:00 **Tulio de Oliveira**, *University of KwaZulu-Natal, Durban, South Africa*

Viral evolution

6 **DEEP MUTATIONAL SCANNING TO INTERPRET VIRAL EVOLUTION**

11:30 **Jesse Bloom**, *Fred Hutchinson Cancer Research Center, Seattle, WA, USA*

Viral evolution and impact on antibody resistance
(Excellent presentation)

https://jbloomlab.github.io/SARS2_RBD_Ab_escape_maps/escape-calc/

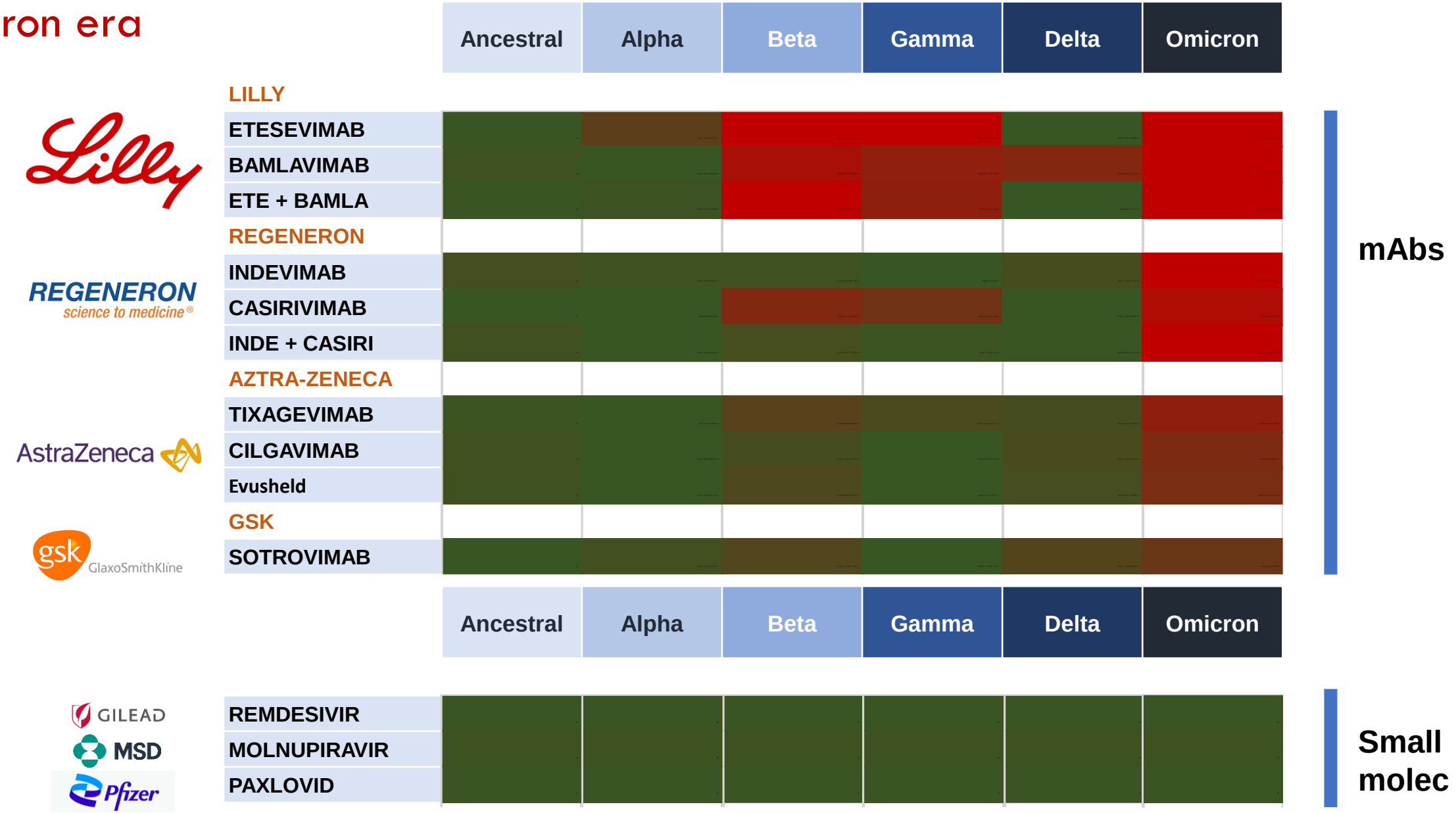
11:50 **LIVE QUESTIONS AND ANSWERS**

7 **AI-INSPIRED MONOCLONAL THERAPEUTIC ANTIBODY DESIGN**

12:00 **Regina Barzilay**, *Massachusetts Institute of Technology, Cambridge, MA, USA*

In silico antibody design

Omicron era



Adapted from : D0I: 10.1056/NEJMc2119407

Omicron era

Updated follow-up of effectiveness for

- Vaccines
- Antibodies
- Antivirals
- Convalescent plasma

https://opendata.ncats.nih.gov/variant/activity

19ª edición

POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

GRÀCIES

Julià Blanco, PhD

Senior Researcher IrsiCaixa/IGTP/UVIC-UCC