George D. Yancopoulos, MD, PhD
Co-Founder, President & Chief Scientist

REGENERON

REGENERON... *the only large-cap biopharma company in America that was founded by, and still run by, scientists*

- **Only major biopharma company that invents all its own foundational technologies, and then uses them to create its novel new medicines – all "in-house"**
  - ***VelociGene:*** Leading mouse genetics technology – from simple knockouts to "mega-base" humanizations
  - ***VelocImmune:*** "Human Antibody Mouse" in which >6 mega-bases of immune genes were "humanized"
  - ***Veloci-Bi:*** Leading platform for "Bispecific Antibodies" – derived from 2nd generation *VelocImmune* mouse
  - **Regeneron Genetics Center:** Leading human sequencing effort – over 1M individuals sequenced...
    - Sequencing the entire UK BioBank, Geisinger Health System, etc
- **10 FDA-approved Antibodies (Or "Ab-like") Over Last ~10 Yrs (& Dozens In The Pipeline)**
  - ***EYLEA®:*** Leading biologic to fight blindness due to macular degeneration and diabetes
  - ***DUPIXENT®:*** Leading biologic to simultaneously fight allergic diseases such as asthma and atopic dermatitis
  - ***PRALUENT®:*** 1st in class treatment blocking PCSK9 (based on genetics) to fight heart disease
  - ***Immunotherapies & BiSpecifics to fight cancer:*** 1st in class for squamous cell carcinoma, lymphoma etc
  - ***REGN-EB3®:*** Antibody Cocktail (3 Abs): 1st FDA-approved treatment of any kind versus Ebola
    - Dozens more Antibodies and 'Bi-Specifics' in pipeline and clinical trials

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VelociGene: *Nature Biotechnology 21:652–659 (2003)*

World's fastest mouse genome engineering technology – point mutations to megabase-scale "genetic humanizations" – using highly automated robotic platforms

VelocImmune & Veloci-T: *PNAS 111:5153 (2014), PNAS 111:5147 (2014)*

Mice with genetically humanized immune systems... standard for rapid generation of fully-human antibodies & TCRs

Regeneron Genetics Center: *e.g., Nature 586:749-756 (2020)*

Over 1,000,000 people sequenced... All linked to detailed electronic health records (EHRs)... "Big Data" linking human genetic variation to biologic variation

- Still focused on mouse & human genetics, and still innovating…

REGENERON... *the only large-cap biopharma company in America that was founded by, and still run by, scientists*

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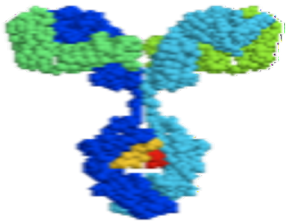


VELOCIMMUNE™

Only by virtue of VelociGene…

Mouse with Genetically Humanized Immune system…

Challenge *VelocImmune* mouse with almost any disease or disease target

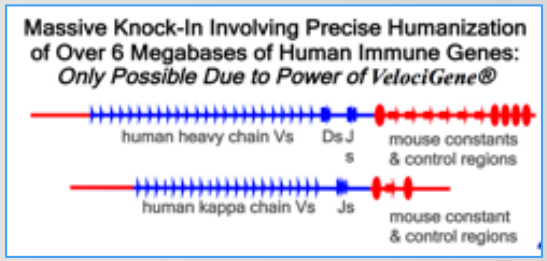
>>> get a human therapeutic Antibody (Asthma to Cancer)!!!

❖ *featured in Forbes as "Drug Factory of the Future"*

In 1985, while at Columbia, Alt & Yancopoulos were the first to propose making a mouse with a genetically humanized immune system so as to make fully human antibodies…

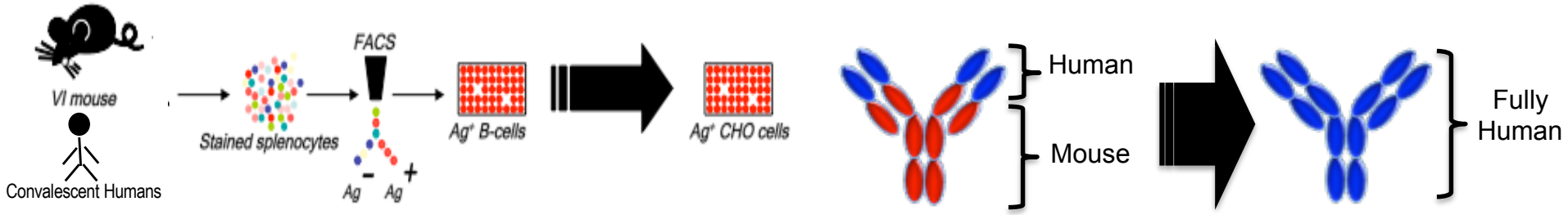
Trends in Genetics (1985; 1:231-236): *"One could imagine, for example, engineering a mouse to make specific human antibodies. Such a mouse might even be used to optimize such an antibody…*

…in the most easily conceived version germline VH & VL segments could be introduced... Although conceptually outlandish, such genetic programming experiments may actually be realized in the not too distant future."



VELOCIMAB®

B cell isolation method to identify Abs from VelocImmune "genetically-humanized" mice and Convalescent Humans & rapidly generate manufacturing-quality high-yield (>5g/L) CHO cell lines



- B-cell Sorting Technology (BST)
  - Allows high-throughput rapid screening for antibodies directly from immunized "*VelocImmune* mice" as well as from convalescent humans
  - Platform Cell Line and Process Developed for Speed and Consistency
    - Ab variable regions cloned with human constants into ESSYR® C1 CHO cell lines
    - Manufacturing-quality high-yield (>5g/L) C1 CHO cell lines generated ~2wks
  - Combine with robust and predictable platform manufacturing process
    - ZERO experimentation or optimization occurs for speed to clinic production
  - Industry's shortest timeline for large-scale (10,000L) bioreactor production of >5 g/L manufacturing quality cell lines capable of supporting commercial scale

Clinical Cell Line Available the Day Lead Antibody is Selected

VELOCIMAB®

J. Hansen *et al.*, *Science*, (2020).

"NATURAL IMMUNITY" & VACCINES…. compared to "antibody cocktails"

- ***Regeneron*** pioneered making fully-human antibodies (& "antibody-like" proteins such as Traps & BiSpecifics) outside the human body – e.g., from both VelocImmune mice and "convalescent humans" – growing them in large bioreactors – highly purifying them – and giving them back as a new class of medicines – to treat diseases ranging from Blindness to Asthma and Cancer
  - ***EYLEA***® : World's leading medicine to fight blindness due to macular degeneration or diabetes
  - ***Dupixent***® : World's leading medicine that can simultaneously treat asthma and atopic dermatitis/eczema etc.
  - ***Libtayo***® : First antibody medicine treating most common forms of skin cancer (& also lung and other cancers)
  - ***Praluent***® : First antibody medicine targeting PCSK9 to treat high cholesterol and heart disease
- ***Regeneron*** *has also applied its pioneering approaches to treat viral infections, starting with Ebola*
  - ***Our efforts in this area headed by Dr. Christos Kyratsous***
    - ***Integrated rapid automated harvesting from convalescent humans, as well as VelocImmune mice***
  - Unlike vaccines, directly making and providing these "anti-viral antibodies" provides immediate protection
    - Its like having been already vaccinated, but with the most effective possible vaccine…
  - And it can not only prevent infection - like a vaccine - it can also be used to treat already infected individuals
    - ***EBOLA as first example using REGN "antibody cocktail" approach for infectious disease…***

"Regeneron Rapid Response" for Global Good

Using VelociSuite technologies, discovery and preclinical validation has been compressed to **3-6 MONTHS** vs. years with a standard process

OUTBREAK → Isolation of fully human antibodies (no need for human survivor samples) → Creation of and preclinical testing in genetically-humanized mice → Creation of manufacturing-ready cell lines (18 days vs. 6-9 months) → Manufacture of clinical-grade antibodies for human use → **CLINICAL TRIALS**

Simplification of handoff reduces clinical manufacturing to **LESS THAN 3-6 MONTHS**

APPLICATIONS TO DATE FOR EPIDEMICS:

In WHO-run clinical trial, REGN-EB3 was dramatically superior at preventing Ebola deaths vs. ZMapp control

Approved by FDA in October 2020

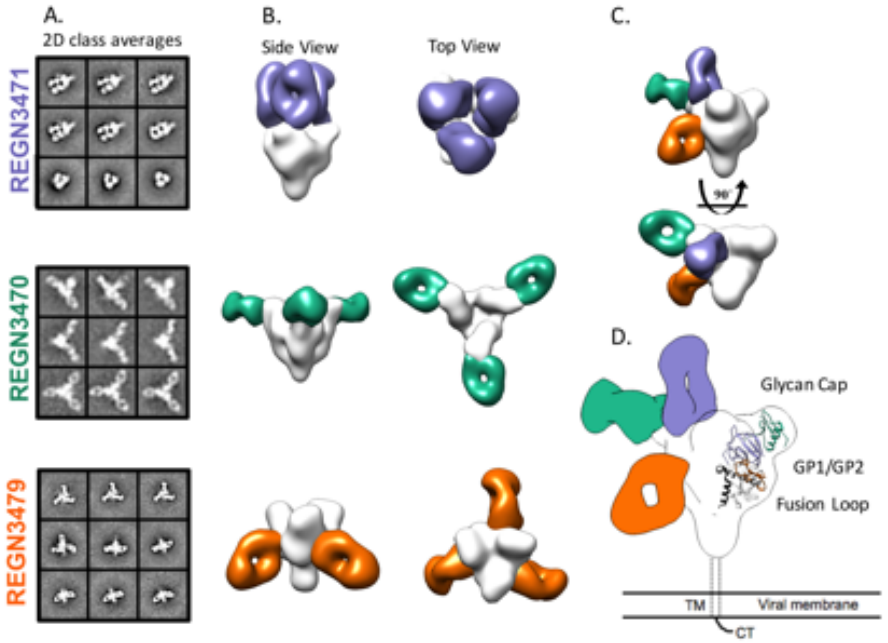
ID and validation of REGN3048-3051 spike-protein blocking antibodies against MERS coronavirus

Phase 1 clinical testing completed

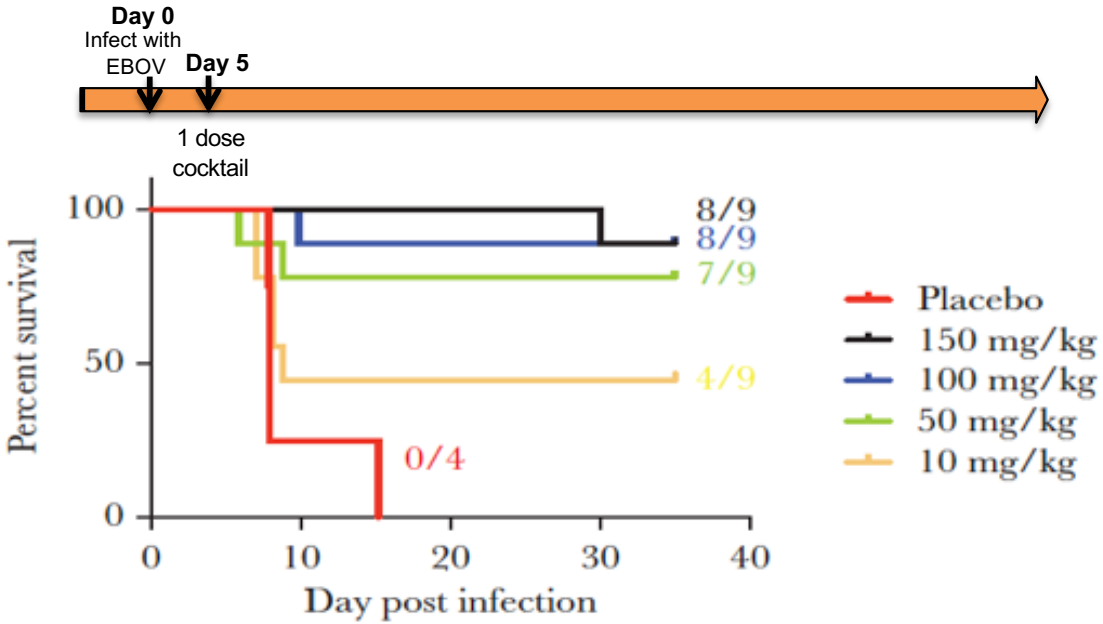
Discover and develop antibody therapies for various infectious diseases, including influenza and novel coronavirus, SARS-CoV-2

Binding of Regeneron Cocktail to Ebola Virus Glycoprotein

REGN-EB3 Cocktail has marked survival benefit in non-human primates already infected with Ebola



Survival Study in Already Infected NHPs
(initiate treatment 5 days after infection)



Pascal et al,.
J Infect Dis 218:S612–S626 (2018)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 12, 2019 VOL. 381 NO. 24

A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics

Sabue Mulangu, M.D., Lori E. Dodd, Ph.D., Richard T. Davey, Jr., M.D., Olivier Tshiani Mbaya, M.D., Michael Proschan, Ph.D., Daniel Mukadi, M.D., Mariano Lusakibanza Manzo, Ph.D., Didier Nzolo, M.D., Antoine Tshomba Oloma, M.D., Augustin Ibanda, B.S., Rosine Ali, M.S., Sinaré Coulibaly, M.D., Adam C. Levine, M.D., Rebecca Grais, Ph.D., Janet Diaz, M.D., H. Clifford Lane, M.D., Jean-Jacques Muyembe-Tamfum, M.D., and the PALM Writing Group, for the PALM Consortium Study Team*

REGN-EB3 Reduces Ebola Mortality compared to Zmapp (& Remdesivir)

In October 2020, REGN-EB3 became first FDA-approved treatment of any kind for Ebola

Survival in late-stage patients with high viral load:

REGN-EB3:	***36.4%***
Zmapp:	***13.8%***
Remdesivir:	***14.6%***

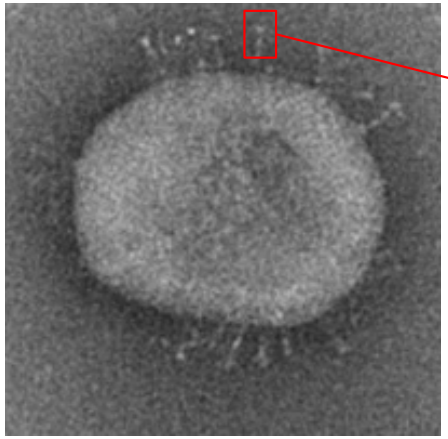
Table 2. Comparison of Death at 28 Days According to Treatment Group.

Population	ZMapp	Remdesivir	Difference, Remdesivir vs. ZMapp	MAb114	Difference, MAb114 vs. ZMapp	REGN-EB3	ZMapp Subgroup	Difference, REGN-EB3 vs. ZMapp Subgroup
	no. of deaths/ total no. (%)	*no. of deaths/ total no. (%)*	*percentage points (95% CI)*	*no. of deaths/ total no. (%)*	*percentage points (95% CI)*	*no. of deaths/ total no. (%)*	*no. of deaths/ total no. (%)*	*percentage points (95% CI)*
Overall	84/169 (49.7)	93/175 (53.1)	3.4 (−7.2 to 14.0)	61/174 (35.1)	−14.6 (−25.2 to −1.7)*	52/155 (33.5)	79/154 (51.3)	−17.8 (−28.9 to −2.9)*
Patients with high viral load†	60/71 (84.5)	64/75 (85.3) **14.6%**	0.8 (−15.3 to 17.2)	51/73 (69.9)	−14.6 (−33.0 to −0.5)	42/66 (63.6) **36.4%**	56/65 (86.2) **13.8%**	−22.5 (−41.8 to −5.1) **+ 22.6%**
Patients with low viral load†	24/98 (24.5)	29/100 (29.0)	4.5 (−9.1 to 19.1)	10/101 (9.9)	−14.6 (−32.4 to −2.6)	10/89 (11.2)	23/89 (25.8)	−14.6 (−32.6 to −2.3)

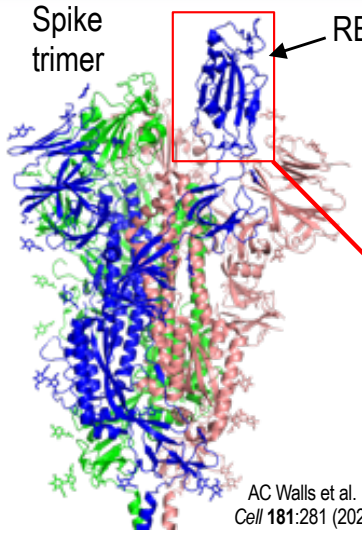
REGN-EB3 dose 150 mg/kg in combination of 3 mAbs at 50 mg/kg each

SARS-COV-2: RECEPTOR-BINDING DOMAIN (RBD) OF THE SPIKE PROTEIN IS CRITICAL FOR VIRAL INFECTION

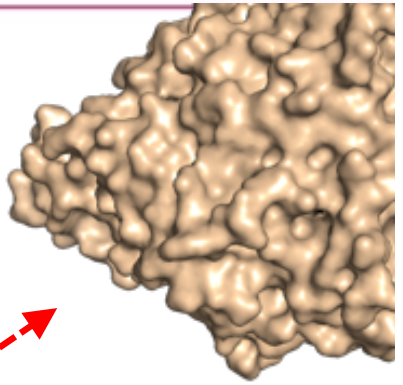
EM image of SARS-CoV-2 virus



C Liu et al. bioRxiv preprint. https://doi.org/10.1101/2020.03.02.972927.

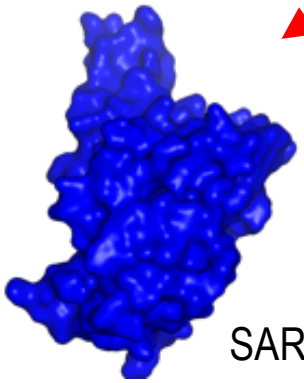


AC Walls et al.
Cell **181**:281 (2020)



ACE2

targeting interaction



SARS-CoV-2 RBD

- The surface of SARS-CoV-2 virus is decorated with a number of "spikes", trimeric proteins critical for viral infectivity. The head of each spike contains a region called the receptor-binding domain, or RBD.
- The RBD (in its "up" conformation) can engage with a protein on the surface of the target cell: angiotensin-converting enzyme 2, or ACE2. ACE2's normal function is in maturation of angiotensin, a peptide hormone regulating blood pressure.

SARS2 SPIKE 'RBD' BINDING TO ACE2 RECEPTORS INITIATES INFECTION OF HUMAN LUNG CELLS: CAN REGN TECHNOLOGIES BLOCK THIS INTERACTION?

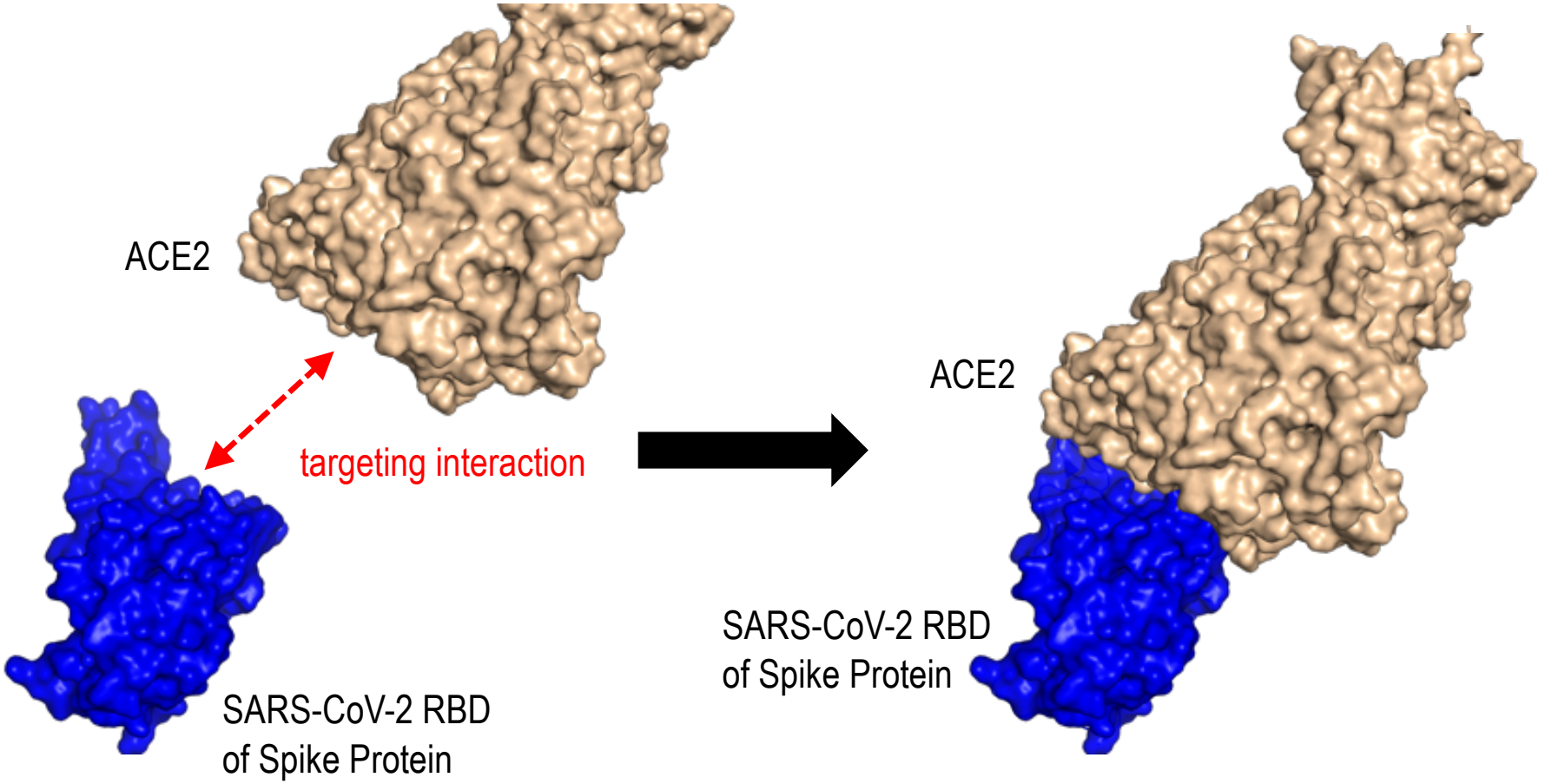
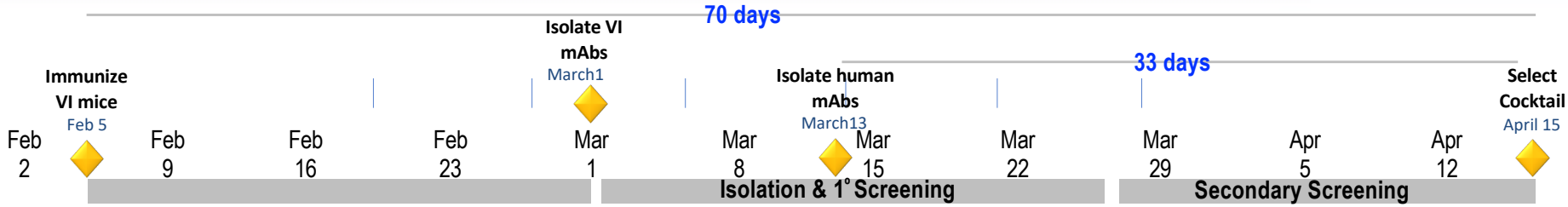


Figure is derived from a published structure of SARS-CoV-2 RBD bound to the extracellular portion of ACE2: R Yan et al, *Science* **367**:1444 (2020)..

SARS-CoV-2 Rapid Response: Timeline And Summary



Prospective Goal: Lead Antibody Success Criteria

- **Potent SARS-CoV-2 neutralizers with neutralization breadth against known spike RBD SNP variants**.
  - Preferably "cocktail" of two non-competing antibodies to allow for high neutralization potency while protecting against new variants and "mutant escape".
  - Combination to be used for prophylaxis and/or treatment of COVID-19.

Lead Antibody selection cascade:

- Isolated and screened ~3,300 Ab pairs (~2800 "VI-mice", ~500 "convalescent human") for neutralization of SARs-CoV-2 pseudoparticles (VSV-SARS-2-spike), MSD binding to pseudoparticles, ELISA binding to soluble protein, biacore affinity to soluble protein, luminex feature binning and sequence diversity, blocking ELISA, FCγRIIIa signaling assay
  - 46 mAbs advanced for further characterization as purified mAbs
  - 9 broad and potent neutralizing SARS-CoV-2 (chosen based on activity against all known human circulating variants) mAbs resulting in 17 combinations were evaluated for neutralization potency and escape under selective pressure
    - Paired into "antibody cocktails" of two antibodies that can simultaneously bind conserved epitopes of the Spike RBD
  - More antibodies are currently being evaluated

J. Hansen *et al.*, *Science*, 369:1010-1014 (2020); A. Baum *et al.*, *Science*, 369:1014-1018 (2020);

REGN TECHNOLOGIES DELIVER MAB1 & MAB2 'ANTIBODY COCKTAIL' THAT NOT ONLY POTENTLY BLOCKS INFECTION, BUT AVOIDS "MUTANT ESCAPE"

- REGN VG & VI technologies created Ebola "antibody cocktail" in just 9 months from initiation to clinical trials, and was proven highly effective in World Health Organization's PALM trial in the Congo
- Now we used our technologies to create COVID19 antibody cocktail ready for trials in ~5 months:
  - Largest collection (1000's) of highly-potent Abs from both VI mice and convalescent humans
  - Selected highly-potent (picomolar) Abs that are resistant to all naturally-occurring viral mutants described to date
  - But individual Abs are not enough – we demonstrate 'rapid viral escape mutants" to all single Abs tested
  - However – using a 'selected antibody cocktail' consisting of two Abs that bind and block at same time – we can prevent 'viral escape'

J. Hansen et al., Science, 369:1010-1014 (2020); A. Baum et al., Science, 369:1014-1018 (2020);

Our prospectively-designed approach was based on the fundamental realization that – as previously demonstrated for HIV and other viruses – "combination drug therapies" could prevent viral drug-resistance by requiring simultaneous mutation at multiple genetic positions. We reasoned that the same approach might be required to prevent escape to "anti-viral antibodies".

Thus while others have focused on the potential of single antibody treatments, we have pioneered and demonstrated the value of "antibody cocktails", and how they are necessary to avoid rapid viral escape.

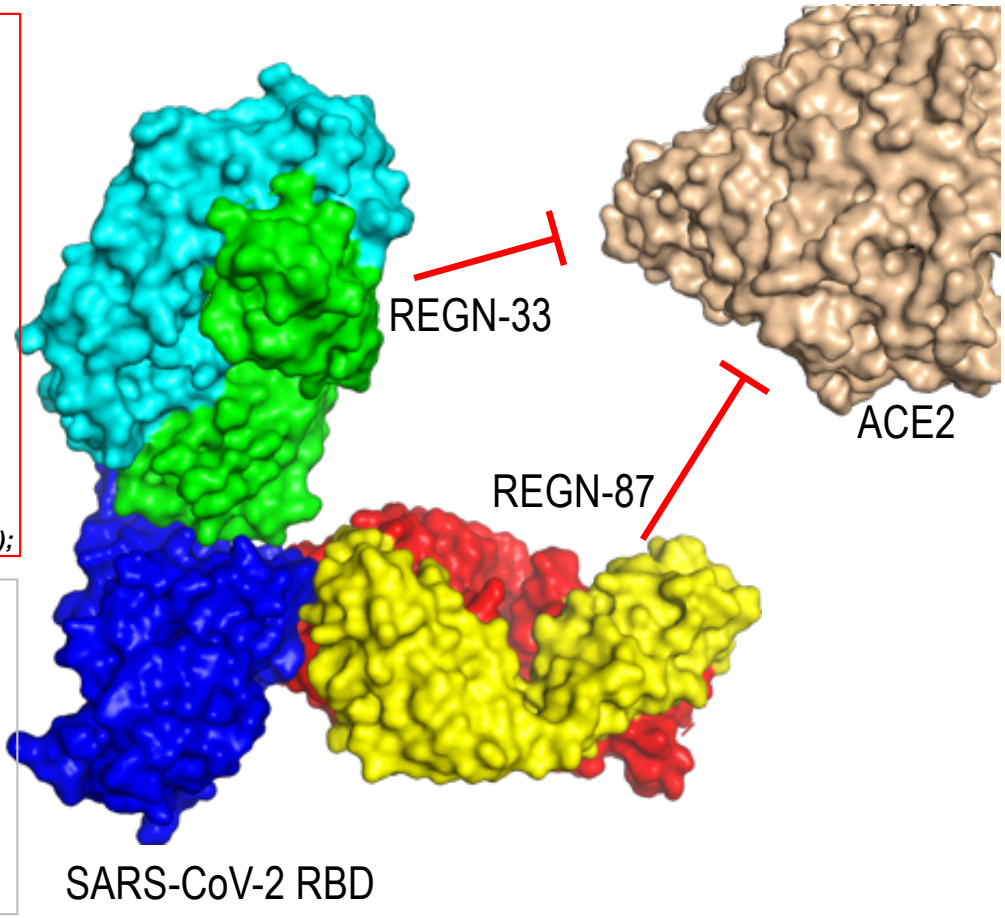
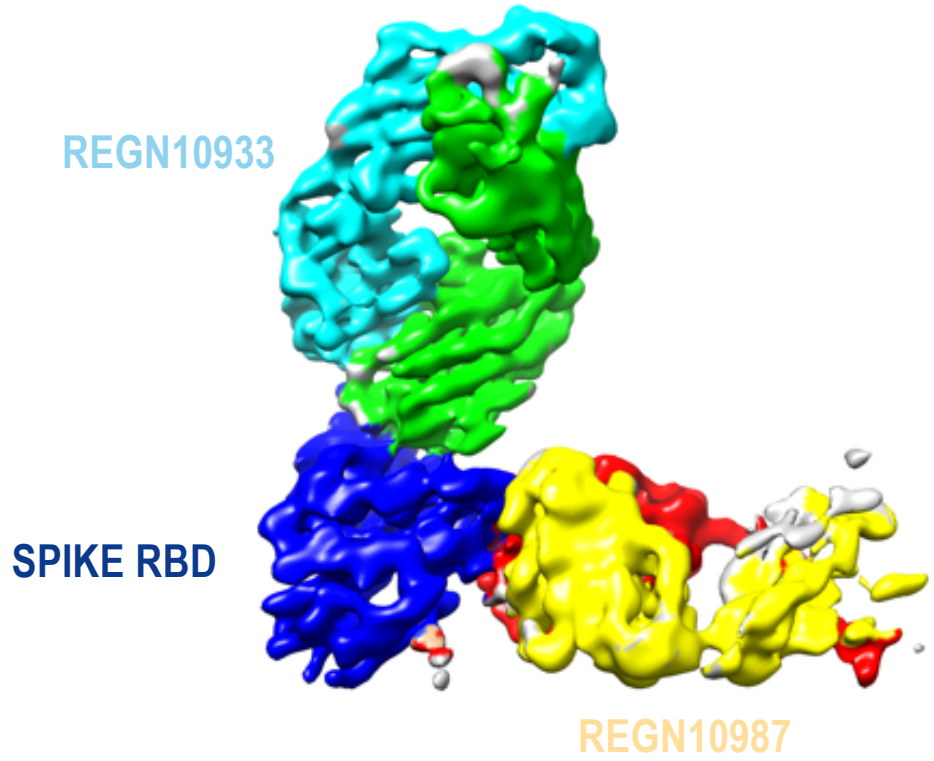


Figure is derived from a 3.9 Å cryo-electron microscopy structure of recombinant SARS-CoV-2 RBD bound to the Fab (fragment antigen-binding) portions of mAb1 and mAb2. Hansen et al., Science 2020.

CRYO-EM STUDIES CONFIRM "ANTIBODY COCKTAIL" OF TWO ANTIBODIES THAT CAN SIMULTANEOUSLY BIND TO RBD



J. Hansen et al., Science, 369:1010-1014 (2020); A. Baum et al., Science, 369:1014-1018 (2020);

SUMMARY PRECLINICAL DATA ON REGN-COV2 COCKTAIL

- REGN-COV2 is a cocktail of two potent, neutralizing antibodies targeting distinct (i.e., "noncompeting") epitopes on the "receptor binding domain" (RBD) of the SARS-CoV-2 Spike (S) protein.
  - Regeneron utilized an analogous approach to develop a similar cocktail to target the Ebola virus ***(J Infect Dis 218:S612)***
  - REGN-EB3 cocktail was recently approved by the FDA based on providing a significant mortality benefit ***(NEJM 381:2293)***
- The use of multiple antibodies in the REGN-COV2 cocktail has been shown to prevent mutational escape in preclinical experiments (as compared to single antibody treatments) ***(Science 369:1010–1014, Science 369:1014–1018)***
  - (1) This strategy mitigates against the loss of efficacy in the clinic, and perhaps more importantly,
  - (2) Prevents seeding of viral escape mutants into the broader population (that might be more resistant to other antibody treatments, or even to vaccines)
- The anti-viral activity of REGN-COV2 has been validated in nonclinical studies ***(Science eabe2402, in press)***
  - Protection against clinical findings in hamsters
  - Viral load reductions in both the prophylactic and therapeutic settings in non-human primates

ADVANTAGES OF FULLY HUMAN MONOCLONAL "ANTIBODY COCKTAILS" AS A RAPID RESPONSE CAPABILITY FOR INFECTIOUS DISEASES LIKE COVID19

We need vaccines ("herd immunity"), but there are separate advantages and roles for "antibody cocktails"

- Unlike vaccines, mAbs can provide immediate protection that may last for an extended duration (i.e., several months from a single treatment)
- Unlike vaccines, mAbs may also be used to treat existing infection
- Based on Ebola (and primate) experience, the earlier the better…

Multiple clinical trials ongoing with REGN "antibody cocktail" for both Prophylaxis and Treatment

REGN-COV2 HAS A BROAD ONGOING CLINICAL DEVELOPMENT PROGRAM

STUDY 2093 Normal volunteer multidose PK/Safety (SQ)

STUDY 2069 Household contacts prophylaxis (SQ) P3

STUDY 2067 Outpatient (IV): Seamless P1/2/3

- **Symptomatic**
- Asymptomatic

Hospitalized:

STUDY 2066 - Hospitalized (IV): Seamless P1/2/3

Four Cohorts

- No O2 requirement
- Low flow O2
- High flow O2
- Mechanical ventilation

UK/NHS RECOVERY Phase 3 Hospitalized Study

Approximately 4500 patients enrolled as of 30Oct2020

Independent Data Review Committees are watching the trials to evaluate safety and have recommended to continue the trials as designed, except for last two cohorts of Hospitalized study which have been put on "hold" with no further dosing until ongoing patients can be evaluated (see note below***)

No safety concerns have been noted with treatment of COVID 19 in outpatients and prophylaxis treatment in both household exposed subjects and healthy volunteers.

Few patients experienced infusion reactions; mainly mild to moderate

***Specifically, based on a potential safety signal and an unfavorable risk/benefit profile at this time, the IDMC recommends further enrollment of patients requiring high-flow oxygen or mechanical ventilation be placed on hold pending collection and analysis of further data on patients already enrolled. The IDMC also recommends continuing enrollment of hospitalized patients requiring either no or low-flow oxygen as the risk/benefit remains acceptable in these cohorts. Finally, the IDMC recommends continuation of the outpatient trial without modification

PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS WAS CONFIRMED

As with most viruses, we proposed that the majority COVI19 patients would rapidly mount their own immune response (i.e., antibodies) and rapidly lower their viral load, and have favorable outcomes

However, some might mount slower immune responses, and thus more slowly clear the virus, and thus be at higher risk for poor outcomes

Thus, we prospectively proposed to use serology - before treatment - to divide patients into those who were "SeroAb-Positive" (had measurable endogenous Abs to COVID19) vs those "SeroAb-Negative" (no measurable Abs)

- **We hypothesized that we would the see greatest benefit in "slow responders", and hopefully convert them into the equivalent of "fast responders"**

PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS WAS CONFIRMED

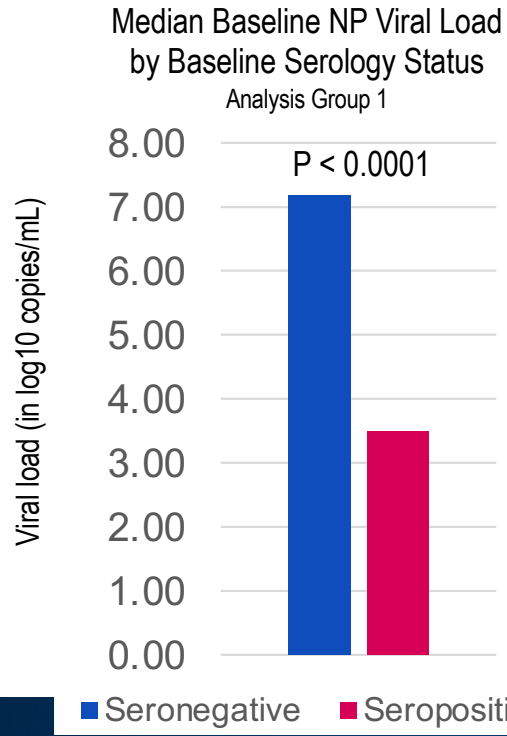
Natural History: By studying all patients at baseline, and Placebo patients over time

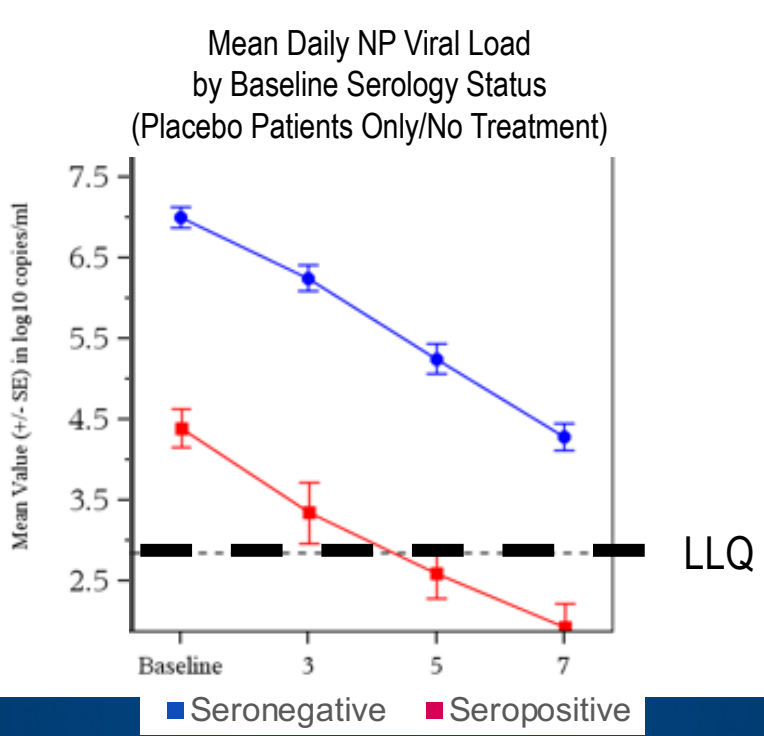
As expected, "SeroAb-Positive" patients had much lower viral levels at baseline compared to "SeroAb-Negative" patients (p<0.0001), and rapidly achieved viral loads below "LLQ" even without treatment

Seronegative: 113/275 (41%)
Seropositive*: 123/275 (45%)
Other**: 39/275 (14%)

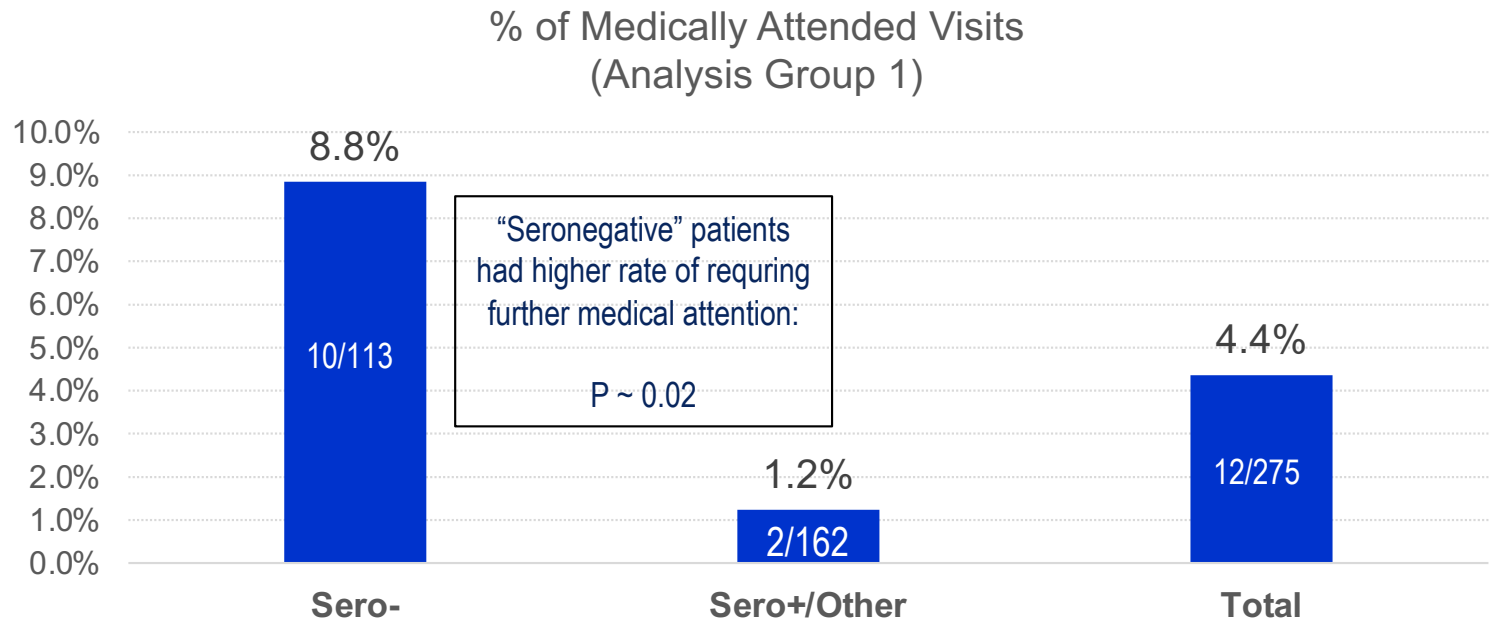
Viral load (median) in NP swab
Seroneg: 7.18 log10 copies/mL
Seropos: 3.49 log10 copies/mL

Mean days of COVID-19 symptoms before randomization: 3.5 days





PATIENTS WHO HAD MOUNTED AN IMMUNE RESPONSE AT BASELINE (SERO-POSTIVE) HAD MUCH LOWER RATE OF MEDICALLY ATTENDED VISITS (ANALYSIS GROUP 1: *PBO NATURAL HISTORY*)



CONCLUSION: *Among outpatients, those who have already mounted their own immune response more effectively lower their viral levels, and avoid the need for further medical attention*

Prospective Hypothesis: *In outpatients who have not yet mounted their own immune response (i.e., are seronegative at baseline), providing the exogenous REGN-COV2 cocktail will more rapidly lower viral levels, and decrease need for further medical attention*

PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS WAS CONFIRMED

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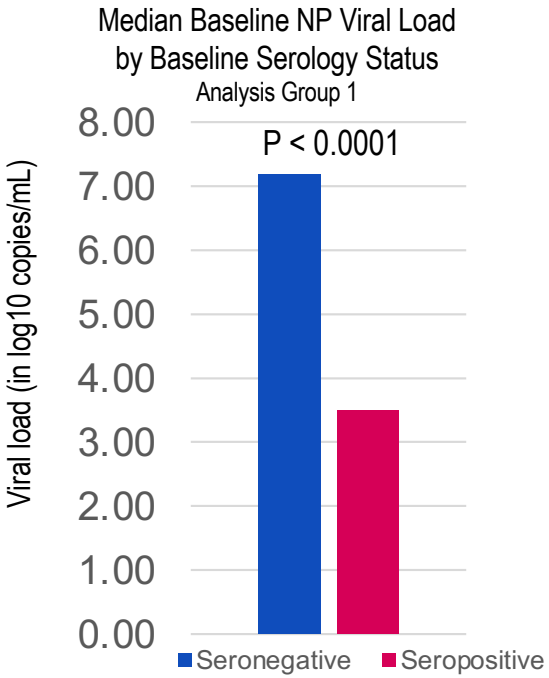

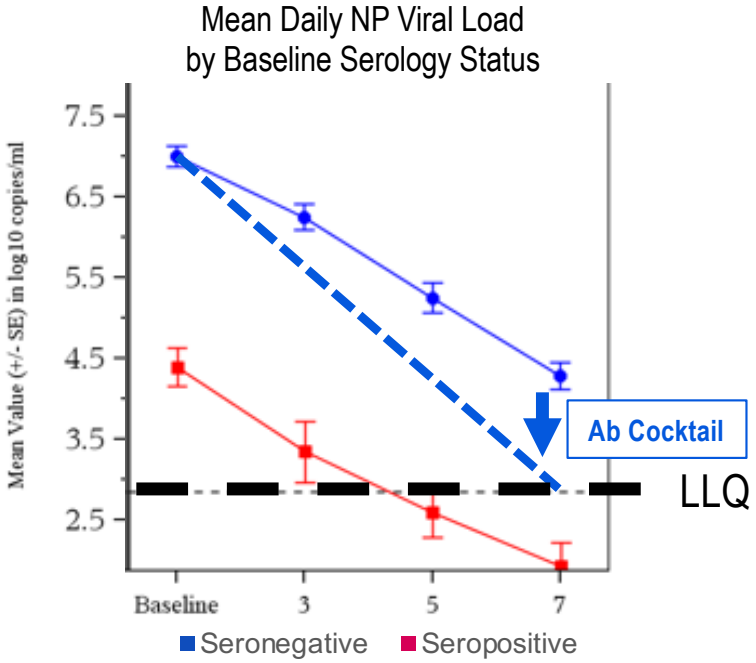

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Outpatient Seamless Ph1/2/3 Study Design for 2 Analysis Sets:

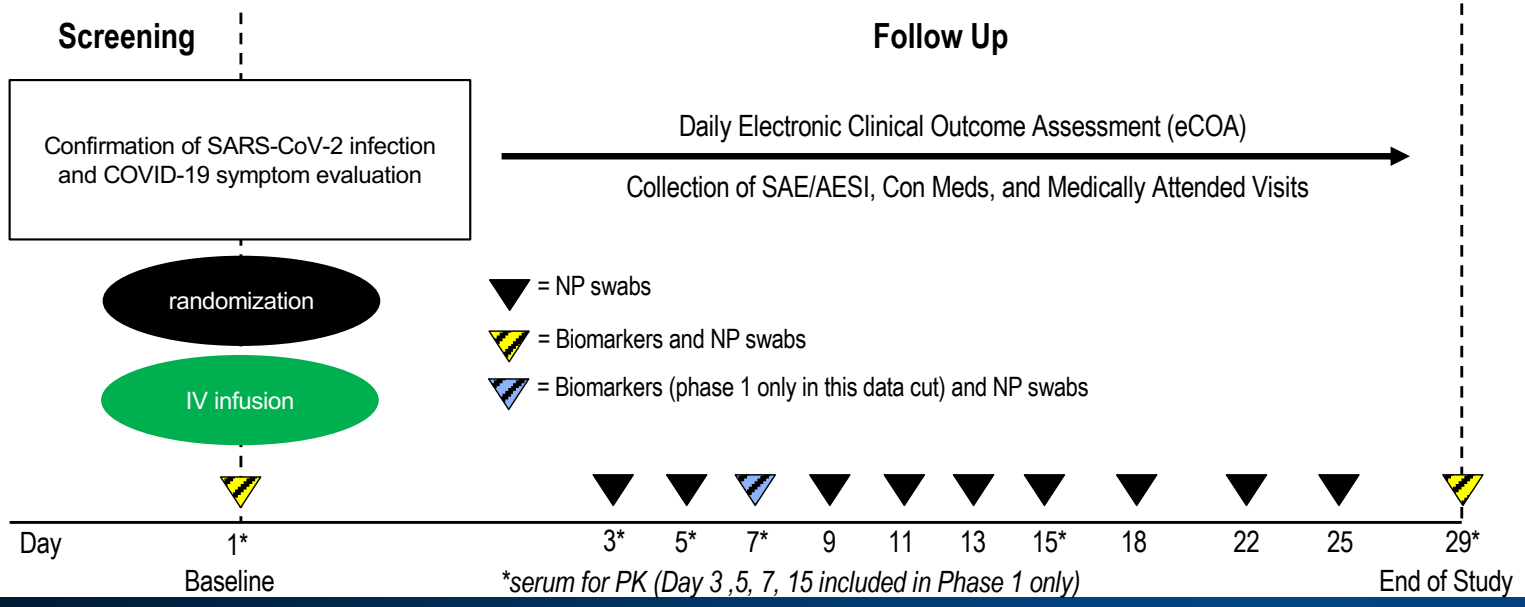
Analysis Group 1 (Descriptive & Hypothesis Generating): 1st 275 Patients; Analysis Group 2 (Prospective Confirmation): Next 524 Patients (Total A1/2: 799)

Patient Population:

- Adult, *non-hospitalized* COVID-19 patients
- Symptom onset ≤7 days from randomization
- SARS-CoV-2 confirmed by molecular testing ≤72 hours from randomization
- Not on any putative COVID-19 therapies

R 1:1:1

- REGN10933 + REGN10987 2.4 g IV - lower dose
- REGN10933 + REGN10987 8 g IV - higher dose
- Placebo IV



ANALYSIS GROUP 2 PROSPECTIVELY CONFIRMS ALL VIRAL ENDPOINTS

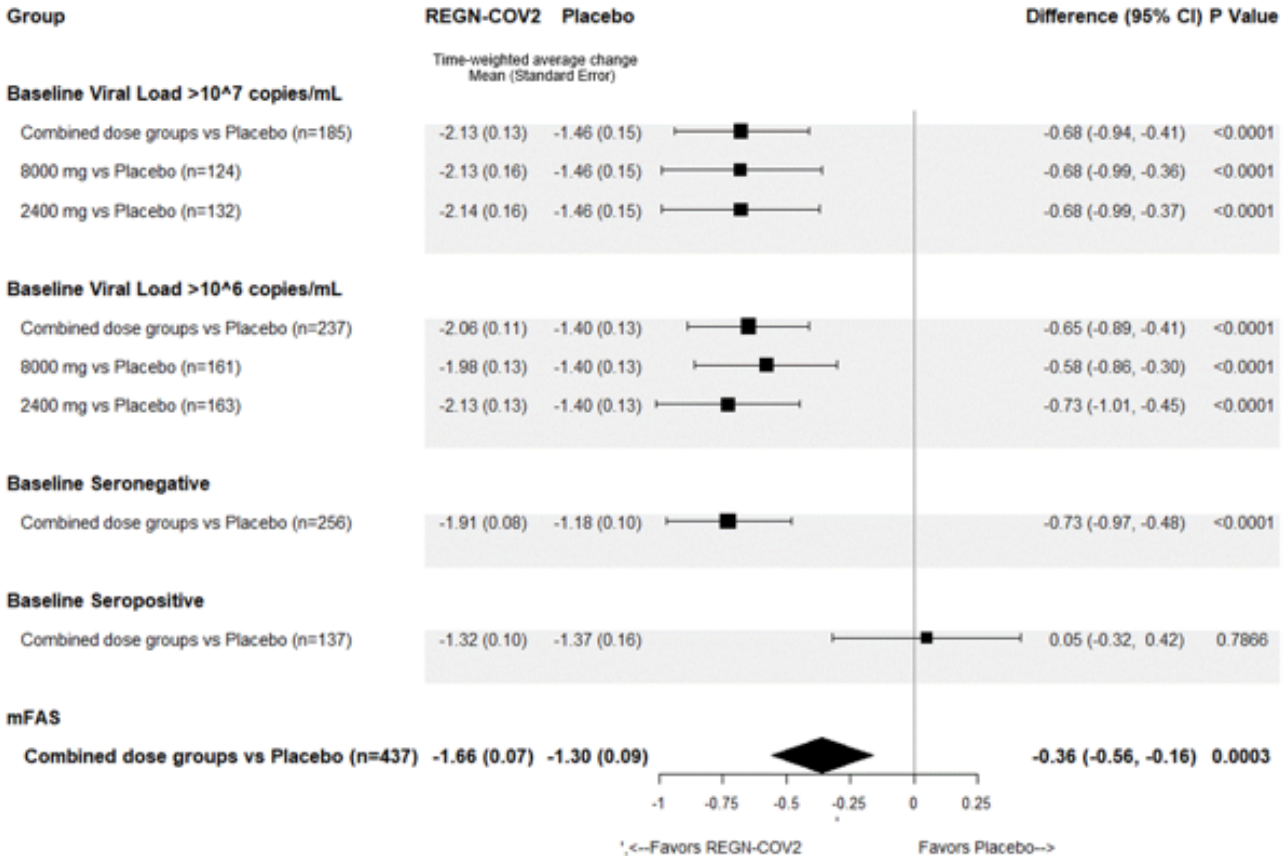
(AND IN BOTH DOSE GROUPS)

Prospective combined analysis for "medically attended visits" (MAVs) also significant

Hypothesis Testing Hierarchy	Analysis 1 (N=275)	Analysis 2 (N=524)
1. **TWA change from baseline viral load thru D7 in the mFAS population with baseline viral load>10^7 copies/mL for the *combined* dose group vs placebo**	Diff from Placebo: -1.21 (0.0001)	Diff from Placebo: -0.68 (<**0.0001**)
2. TWA change from baseline viral load thru D7 in the mFAS population with baseline viral load>10^6 copies/mL for the *combined* dose group vs placebo	-0.95 (0.0003)	-0.65 (<**0.0001**)
3. TWA change from baseline viral load thru D7 in seronegative mFAS for the *combined* dose group vs placebo	-0.56 (0.0165)	-0.73 (<**0.0001**)
4. TWA change from baseline viral load thru D7 in mFAS for the *combined* dose group vs placebo	-0.41 (0.0089)	-0.36 (**0.0003**)
5. TWA change from baseline viral load thru D7 in the mFAS population with baseline viral load>10^7 copies/mL for the *high dose* group vs placebo	-1.32 (0.0002)	-0.68 (<**0.0001**)
6. TWA change from baseline viral load thru D7 in the mFAS population with baseline viral load>10^7 copies/mL for the *low dose* group vs placebo	-1.03 (0.0061)	-0.68 (<**0.0001**)
7. TWA change from baseline viral load thru D7 in the mFAS population with baseline viral load>10^6 copies/mL for the *high dose* group vs placebo	-1.14 (0.0002)	-0.58 (<**0.0001**)
8. TWA change from baseline viral load thru D7 in the mFAS population with baseline viral load>10^6 copies/mL for the *low dose* group vs placebo	-0.81 (0.0063)	-0.73 (<**0.0001**)
	Analysis 1/2 (N=799)	
9. Proportion of patients with MAVs through D29 in the mFAS for the *combined* dose group vs placebo (patients 1-799)	Placebo: 15/231 (6.5%) Combined Treatment: 12/434 (2.8%) **P=0.0240**	
10. Proportion of patients with a subset of MAVs (hospitalization, ER visit, or urgent care visit) through D29 in the mFAS for the *combined* dose group vs placebo (patients 1-799)	Placebo: 10/231 (4.3%) Combined Treatment: 10/434 (2.3%) **P=0.1575**	

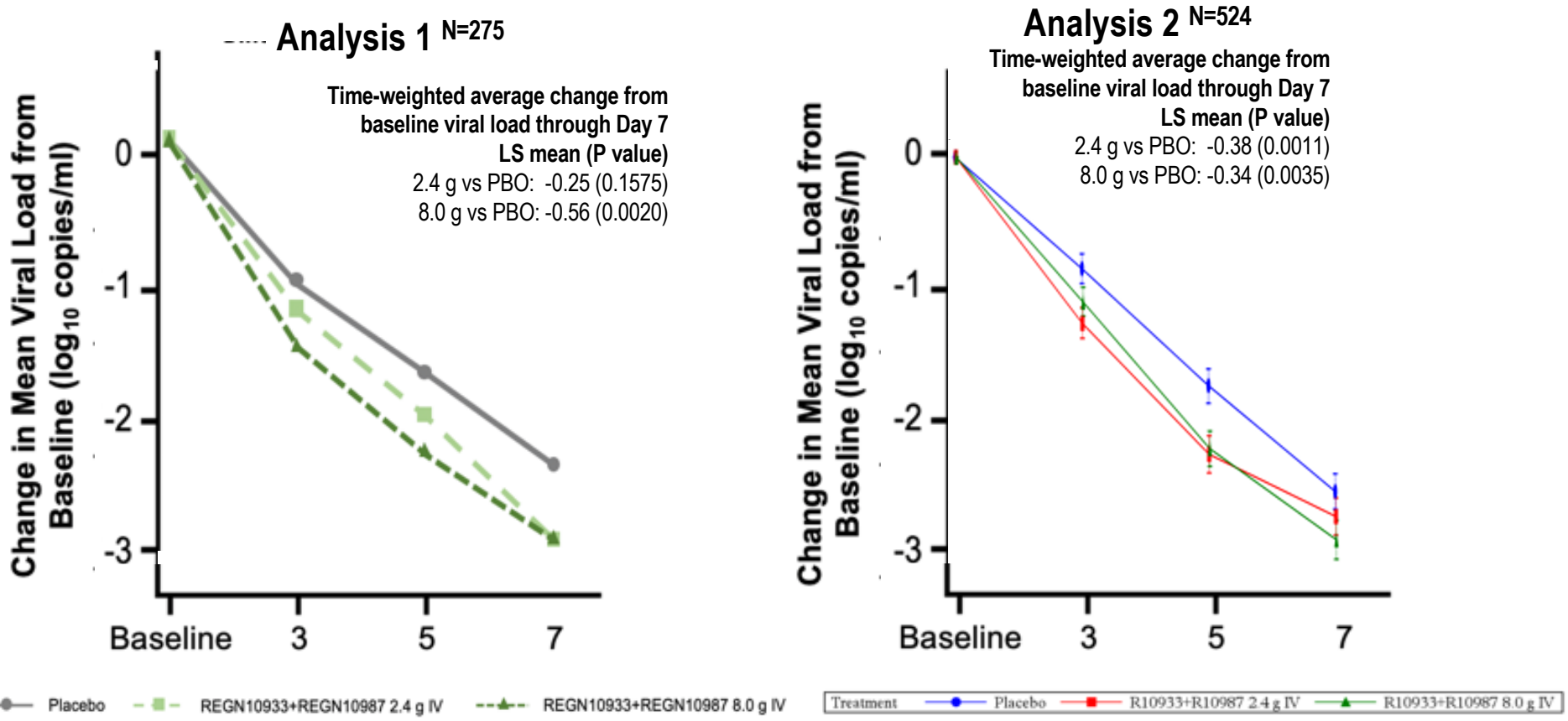
SIMILAR EFFECTS OF BOTH DOSE GROUPS: LOW DOSE SUFFICIENT FOR MAXIMAL EFFECT

FOREST PLOTS: VIROLOGY ENDPOINTS DRIVEN BY "SERONEGATIVE" GROUP



SIMILAR EFFECTS OF BOTH DOSE GROUPS: LOW DOSE SUFFICIENT FOR MAXIMAL EFFECT

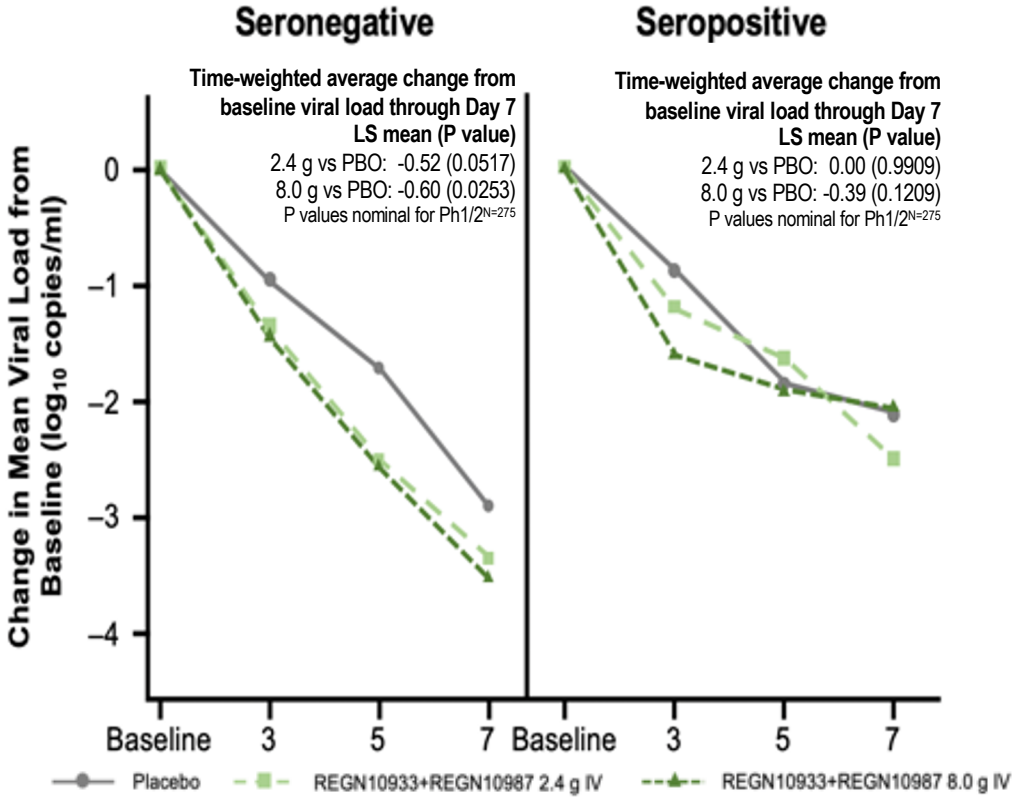
SIMILAR ANTIVIRAL EFFECTS IN OVERALL POPULATIONS OF ANALYSIS GROUP 1 (N=275) AND ANALYSIS GROUP 2 (N=524)



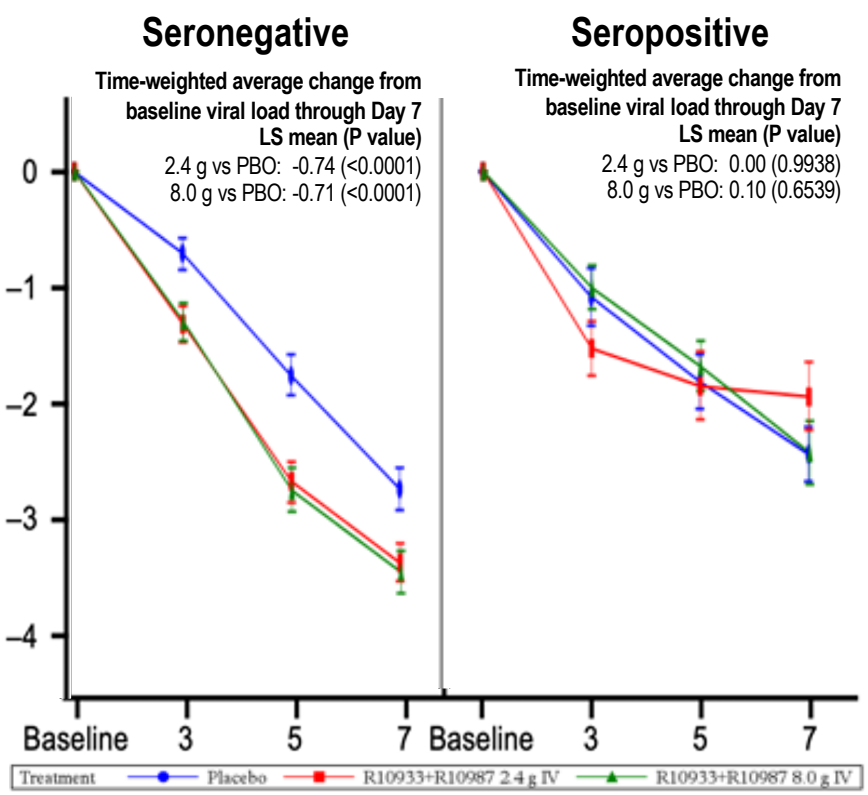
SIMILAR EFFECTS OF BOTH DOSE GROUPS: LOW DOSE SUFFICIENT FOR MAXIMAL EFFECT

ANALYSIS GROUP 2 PROSPECTIVELY CONFIRMS THAT VIRAL LOAD REDUCTION IS DRIVEN BY SERONEGATIVES (PATIENTS WHO DID NOT MOUNT THEIR OWN IMMUNE RESPONSE)

Analysis Group 1 (N=275)

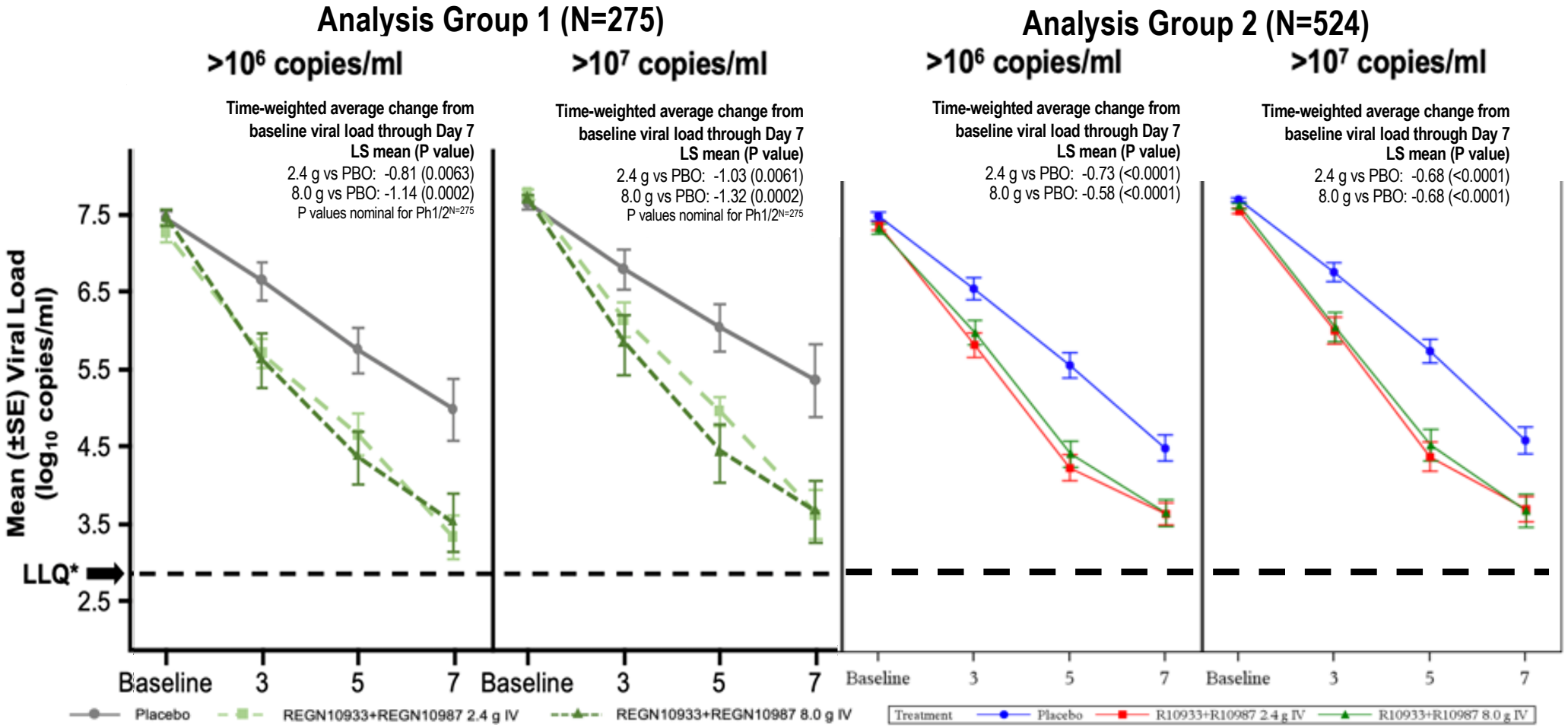


Analysis Group 2 (N=524)



SIMILAR EFFECTS OF BOTH DOSE GROUPS:
LOW DOSE SUFFICIENT FOR MAXIMAL EFFECT

ANALYSIS GROUP 2 CONFIRMS LARGEST VIRAL REDUCTIONS IN PATIENTS WITH HIGHEST VIRAL LOADS AT BASELINE (SIMILAR IN BOTH DOSE GROUPS)



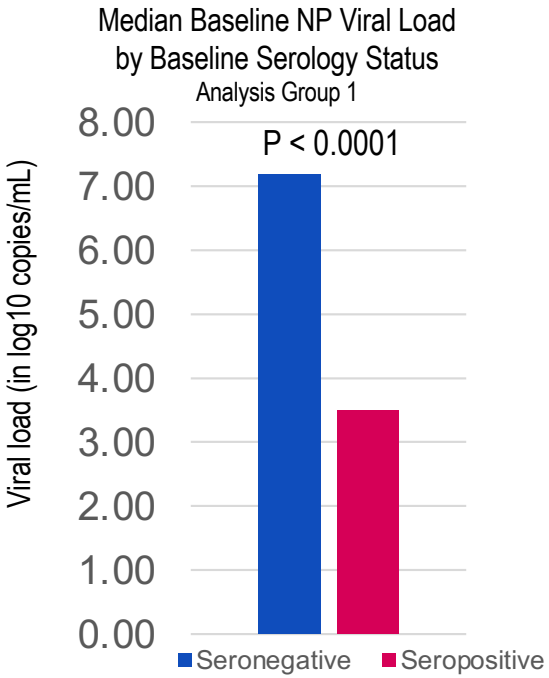
PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS WAS CONFIRMED

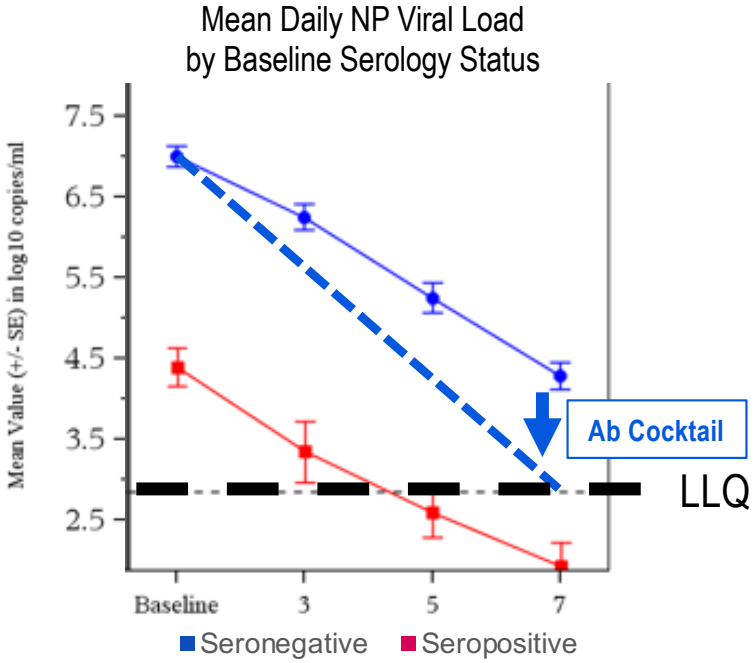
As expected, "SeroAb-Positive" patients had much lower viral levels at baseline compared to "SeroAb-Negative" patients (p<0.0001), and rapidly achieved viral loads below "LLQ" even without treatment

Seronegative: 113/275 (41%)
Seropositive*: 123/275 (45%)
Other**: 39/275 (14%)

Viral load (median) in NP swab
Seroneg: 7.18 log10 copies/mL
Seropos: 3.49 log10 copies/mL

Mean days of COVID-19 symptoms before randomization: 3.5 days





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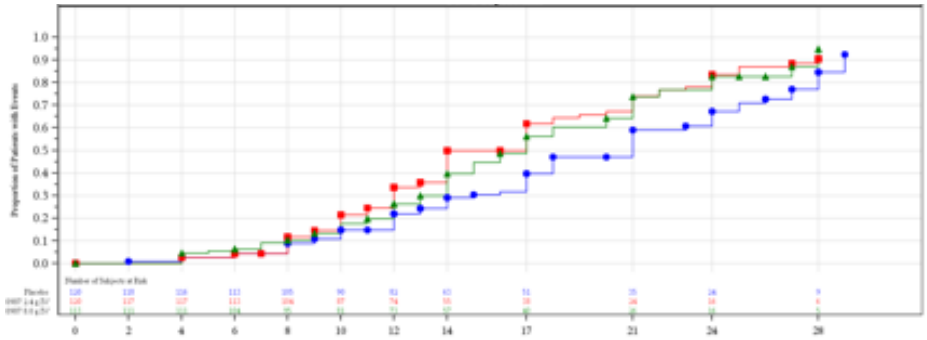
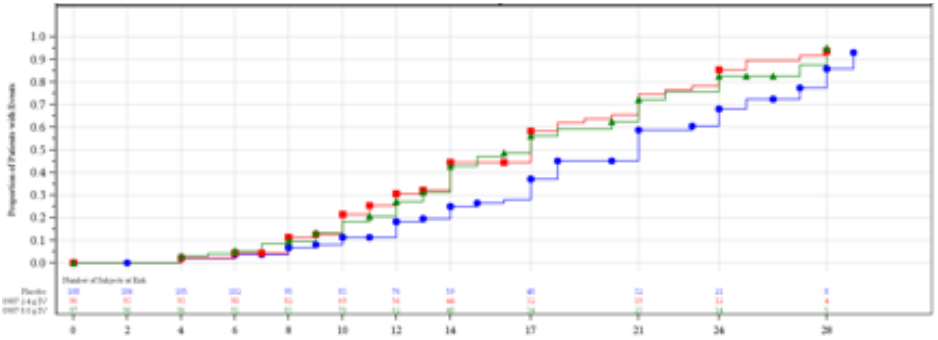
REGN-COV2 SHORTENS TIME TO SUSTAINED NEGATIVE RT-qPCR IN THE >10^4, >10^5, >10^6, AND >10^7 GROUPS (SIMILAR IN BOTH DOSE GROUPS)

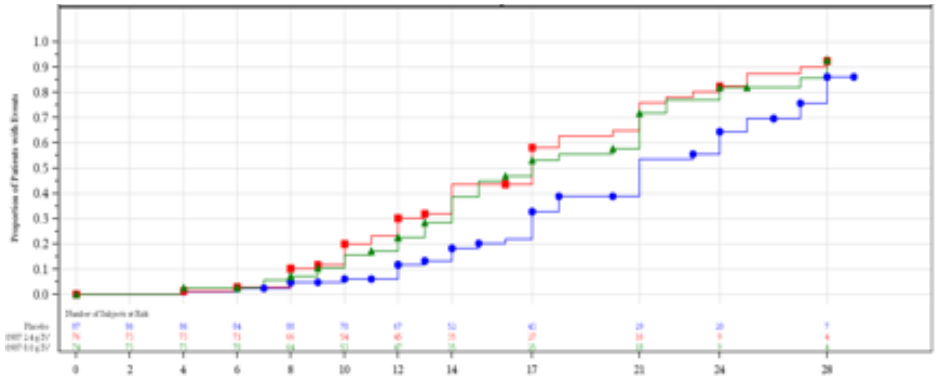
>10^4 copies/mL



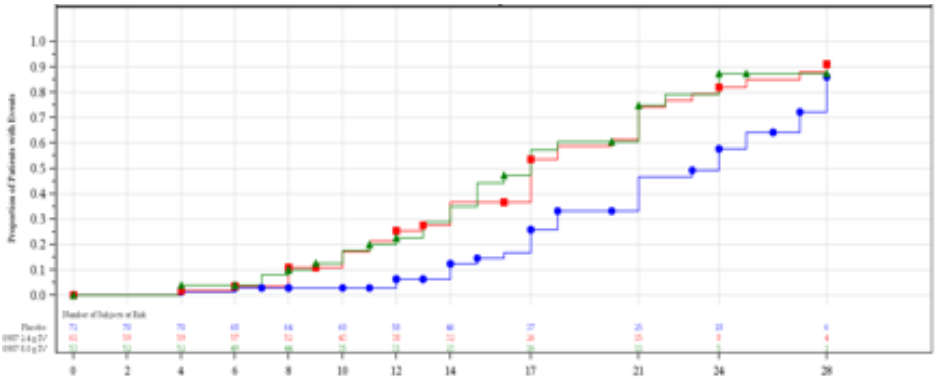
>10^5 copies/mL



>10^6 copies/mL



>10^7 copies/mL



Treatment

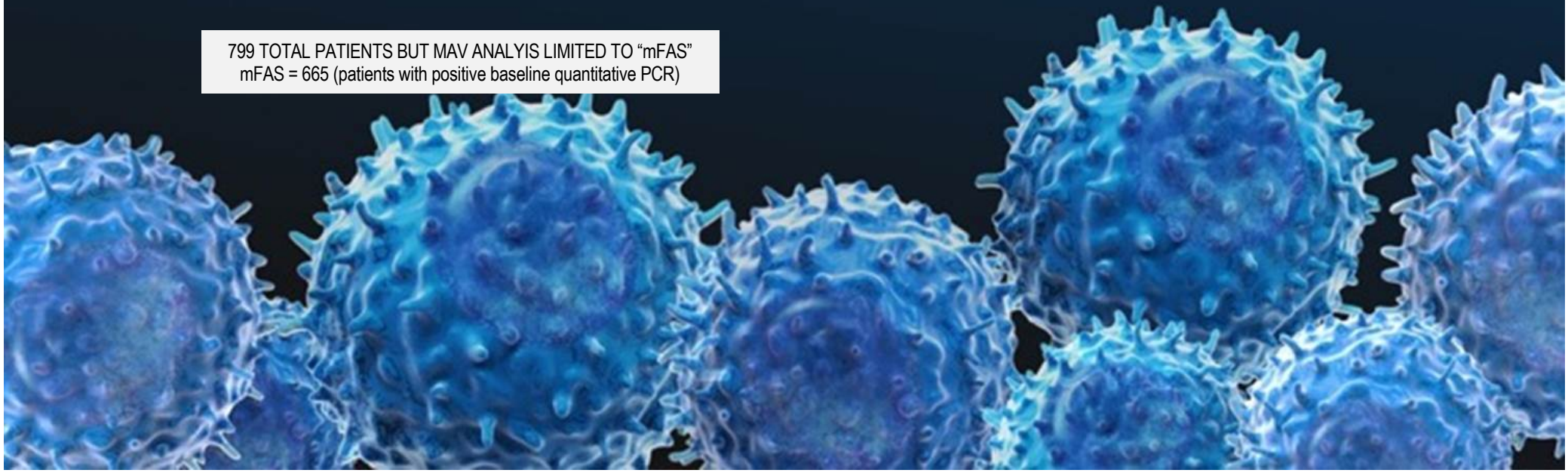
Placebo
Placebo
R10933+R10987 2.4 g IV
R10933+R10987 2.4 g IV
R10933+R10987 8.0 g IV
R10933+R10987 8.0 g IV

MEDICALLY ATTENDED VISITS (MAVs)

REGENERON

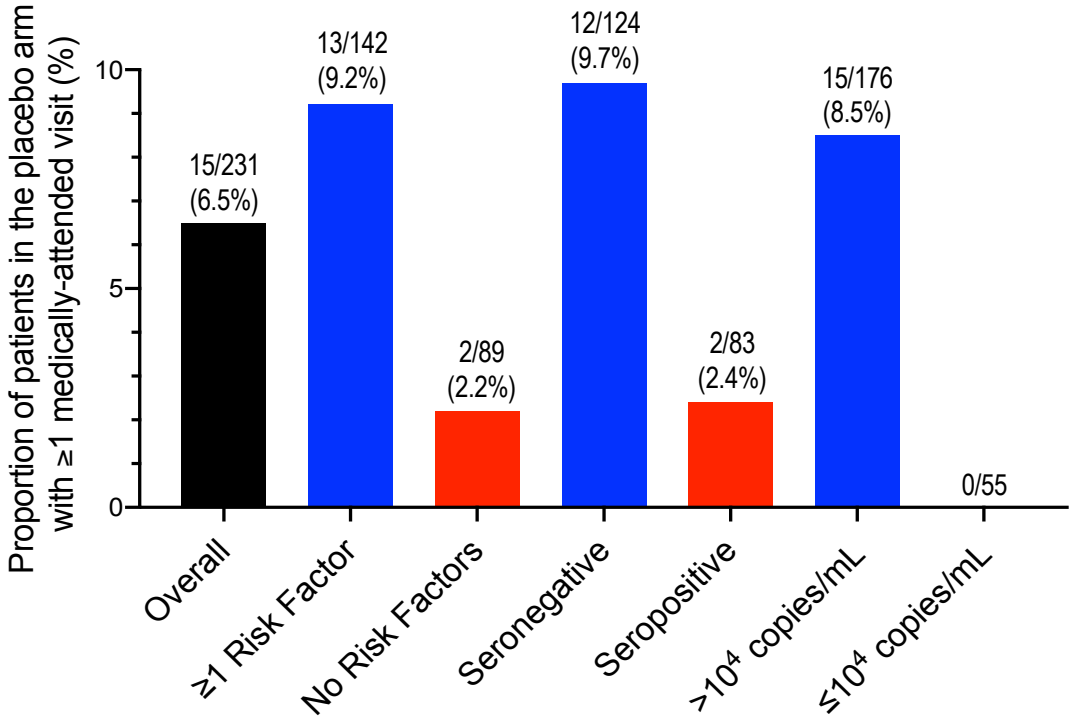
PROSPECTIVE COMBINED ANALYSIS

799 TOTAL PATIENTS BUT MAV ANALYIS LIMITED TO “mFAS”
mFAS = 665 (patients with positive baseline quantitative PCR)



PLACEBO GROUP IN ANALYSIS GROUPS 1/2 CONFIRMS NATURAL HISTORY OF OUTPATIENT DISEASE

MEDICALLY-ATTENDED VISITS WERE MARKEDLY ENRICHED IN SARS-COV-2 PCR POSITIVE PATIENTS WHO AT BASELINE WERE SERONEGATIVE, OR HAD VIRAL LOAD >10^4 COPIES/ML, OR HAD ≥1 RISK FACTOR* FOR SEVERE COVID-19



- Approximately 75% of MAVs were Hospitalizations or ER visits.
  - Most of remaining 25% were physician visits
- PBO group overall event rate of 6.5% (15/231):
  - Hospitalizations: 2.2% (5/231)
  - Hospitalizations, ER visits or UCC visits: 4.3% (10/231)
  - Physician office/telemedicine visits: 2.2% (5/231)
- Median viral load 10x higher in patients with MAVs (6.42 log10 copies/mL) compared to overall population (5.42 log10 copies/mL)

* Risk Factors:
- Age>50 years
- BMI>30
- Cardiovascular disease, eg, hypertension
- Metabolic disease, eg, diabetes
- Lung disease, eg, asthma
- Chronic liver disease
- Chronic kidney disease
- Immunosuppressed

REGN-COV2 REDUCED MAVS IN PATIENTS WHO WERE SARS-COV-2 PCR POSITIVE AT BASELINE BY 57% COMPARED TO PLACEBO IN OVERALL POPULATION, mFAS (& BY 65% IN SERONEGATIVES)

Overall Population (mFAS, n=665):

- 57% reduction (6.5% vs 2.8%)

(P=0.0240)

Consistent reduction with initial Analysis Group 1 (N=275): 6 (PBO), 1(low dose), 2 (high dose)

Overall (n=27)	PBO (n=231)	Low Dose (n=215)	High Dose (n=219)
Hospitalization	5 (2.2%)	2 (0.9%)	1 (0.5%)
ER visit	5 (2.2%)	2 (0.9%)	3 (1.4%)
UCC Visit	0	1 (0.5%)	1 (0.5%)
Phys Off/Tele	5 (2.2%)	1 (0.5%)	1 (0.5%)
Totals:	15 (6.5%)	6 (2.8%)	6 (2.7%)

Seronegative (mFAS):

- 65% reduction (9.7% vs 2.4%)

Seronegative (n=20)	PBO (n=124)	Low Dose (n=121)	High Dose (n=115)
Hospitalization	3 (2.4%)	1 (0.8%)	0
ER visit	4 (3.2%)	2 (1.7%)	3 (2.6%)
UCC Visit	0	1 (0.8%)	0
Phys Off/Tele	5 (4%)	0	1 (0.9%)
Totals:	12 (9.7%)	4 (3.3%)	4 (3.5%)

No Benefit in Seropositives:

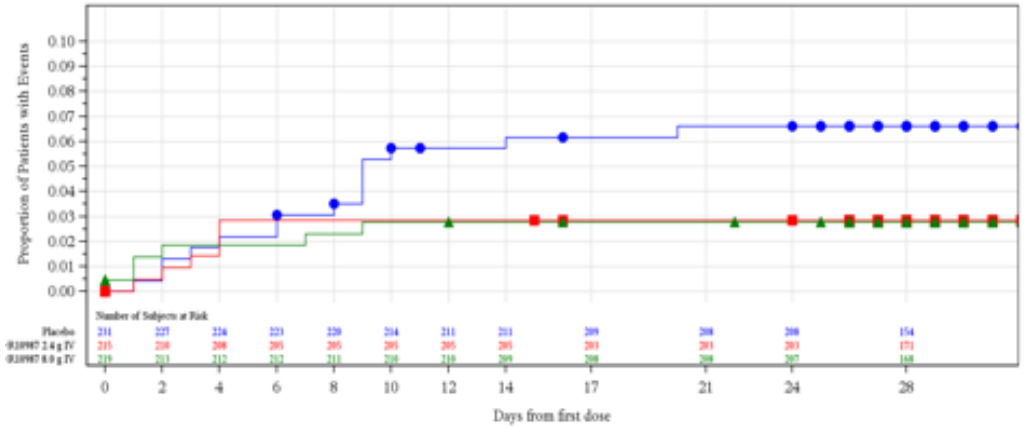
- Few events, not modifiable…

Seropositive (n=5)	PBO (n=83)	Low Dose (n=73)	High Dose (n=80)
Hospitalization	1 (1.2%)	1 (1.4%)	0
ER visit	1 (1.2%)	0	0
UCC Visit	0	0	1 (1.3%)
Phys Off/Tele	0	1 (1.4%)	0
Totals:	2 (2.4%)	2 (2.7%)	1 (1.3%)

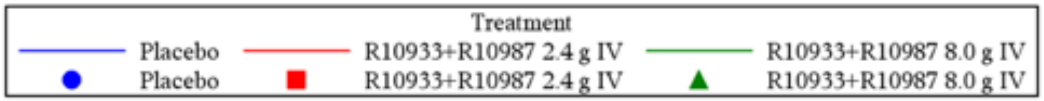
RISK FOR MEDICALLY-ATTENDED VISIT REDUCED 60% WITH REGN-COV2 (mFAS)

TREATMENT BEGIN TO SEPARATE ABOUT A WEEK AFTER TREATMENT INITIATION (EARLY MAVs MAY NOT BE MODIFIABLE)

Overall Population (mFAS, N=665)



HR vs. placebo (95% CI)
Low dose: 0.4 (0.2, 1.1); p = 0.04
High dose: 0.4 (0.2, 1.1); p = 0.04



Symbols represent censoring due to ongoing, early termination, or study completion

SELECTING FOR SERONEGATIVE PATIENTS WITH VIRAL LOAD >10^4 and ≥1 RISK FACTOR:

>>>THIS DEFINES 25% OF POPULATION WITH MOST OF THE EVENTS (& GREATEST RISK)

>>> 84% TREATMENT REDUCTION IN THIS HIGH-RISK POPULATION

Baseline Viral Load	PBO (n=266)	Low Dose (n=266)	High Dose (n=267)
Missing Baseline Viral Load	0/7	0/23	1/17 (5.8%)
≤ 10^4 (including undetectable)	1/83 (1.2%)	3/63 (4.8%)	0/83
> 10^4	15/176 (8.5%)	5/180 (2.8%)	6/167 (3.6%)
> 10^5	12/149 (8.1%)	3/148 (2%)	5/142 (3.5%)
> 10^6	11/114 (9.6%)	3/110 (2.7%)	3/108 (2.8%)
> 10^7	8/93 (8.6%)	1/82 (1.2%)	3/81 (3.7%)

Patients with ≥1 risk factor

- 72% reduction vs PBO (nominal p=0.0065)

mFAS	PBO (n=231)	Low Dose (n=215)	High Dose (n=219)
No Risk Factor	2/89 (2.2%)	3/81 (3.7%)	2/87 (2.3%)
≥1 Risk Factor	13/142 (9.2%)	3/134 (2.2%)	4/132 (3%)

Seronegative & VL>10^4 & High-Risk

- 84% reduction (12.8% vs 1.2%) (nominal p=0.0017)

mFAS	PBO (n=231)	Low Dose (n=215)	High Dose (n=219)
≥1 Risk Factor, seronegative and viral load >10^4	10/78 (12.8%)	1/81 (1.2%)	2/66 (3.0%)

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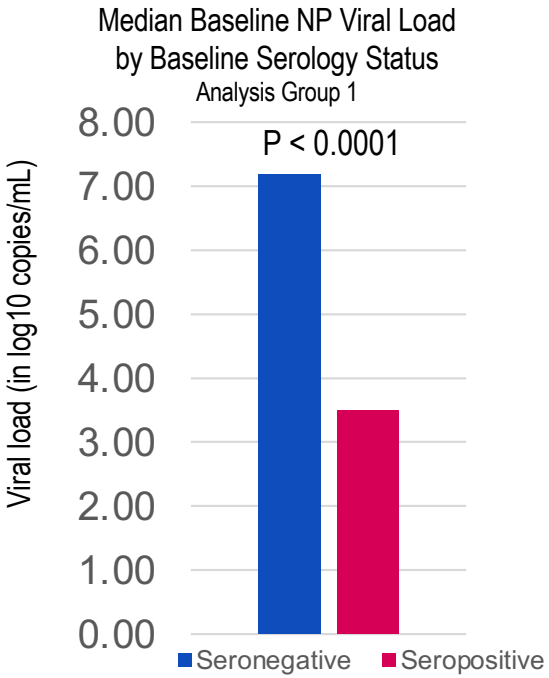

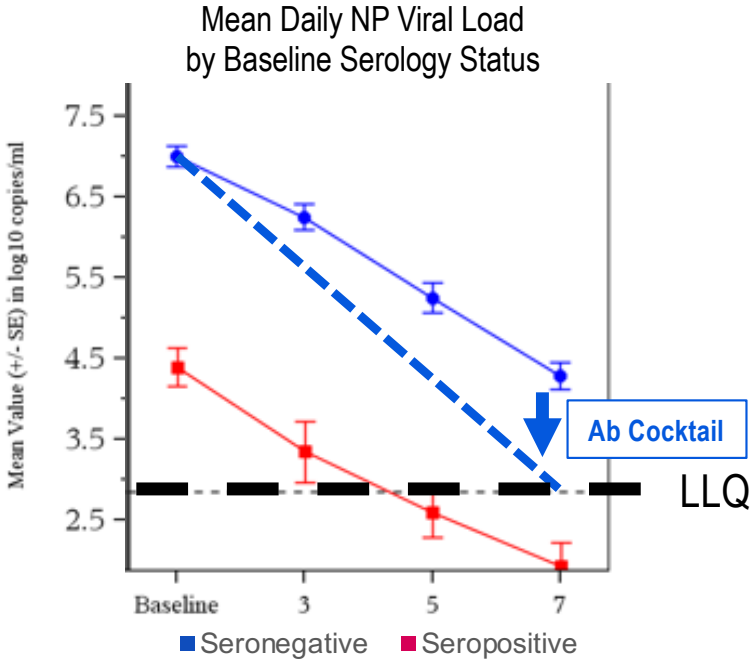

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REGN-COV2 HAS A BROAD ONGOING CLINICAL DEVELOPMENT PROGRAM

STUDY 2093 Normal volunteer multidose PK/Safety (SQ)

STUDY 2069 Household contacts prophylaxis (SQ) P3

STUDY 2067 Outpatient (IV): Seamless P1/2/3

- **Symptomatic**
- Asymptomatic

Hospitalized:

STUDY 2066 - Hospitalized (IV): Seamless P1/2/3

Four Cohorts

- No O2 requirement
- Low flow O2
- High flow O2
- Mechanical ventilation

UK/NHS RECOVERY Phase 3 Hospitalized Study

Approximately 4500 patients enrolled as of 30Oct2020

Independent Data Review Committees are watching the trials to evaluate safety and have recommended to continue the trials as designed, except for last two cohorts of Hospitalized study which have been put on "hold" with no further dosing until ongoing patients can be evaluated (see note below***)

No safety concerns have been noted with treatment of COVID 19 in outpatients and prophylaxis treatment in both household exposed subjects and healthy volunteers.

Few patients experienced infusion reactions; mainly mild to moderate

***Specifically, based on a potential safety signal and an unfavorable risk/benefit profile at this time, the IDMC recommends further enrollment of patients requiring high-flow oxygen or mechanical ventilation be placed on hold pending collection and analysis of further data on patients already enrolled. The IDMC also recommends continuing enrollment of hospitalized patients requiring either no or low-flow oxygen as the risk/benefit remains acceptable in these cohorts. Finally, the IDMC recommends continuation of the outpatient trial without modification

FUNDING SUPPORT AND COLLABORATIONS

- REGN-COV2's development and manufacturing has been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services under OT number: HHSO100201700020C.
- Inmazeb (REGN-EB3) was developed in collaboration and with federal funds from BARDA, part of the Office of the Assistant Secretary for Preparedness and Response at the HHS under ongoing USG Contract Nos. HHSO100201700016C and HHSO100201500013C.
- Regeneron has partnered with Roche to increase the global supply of REGN-COV2 beginning in 2021. If REGN-COV2 proves safe and effective in clinical trials and regulatory approvals are granted, Regeneron will manufacture and distribute it in the U.S. and Roche will develop, manufacture and distribute it outside the U.S.