
COVID19
Keeping Up with a Moving Target
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COVID-19: KEEPING UP WITH A MOVING TARGET
February 3, 2021 UPDATE

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CME Information

Jointly provided by Postgraduate Institute for Medicine, DKBmed, and the Institute for Johns Hopkins Nursing.

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Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials, including a remdesivir, baricitinib, and several vaccine platforms.

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CME Information

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Learning Objectives

- Discuss changes in SARS-CoV-2 since the Wuhan strain was identified
- Discuss implications of newer variants on vaccine development

Thank You

This educational activity is supported by independent medical educational grants from Gilead Sciences, Inc., Regeneron Pharmaceuticals, Inc., and Eli Lilly and Company as well as in-kind support by DKBmed, LLC.

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Vaccine Overview

Vaccine	Type	Doses	Efficacy	Efficacy age > 65 yrs	Serious safety issues	Comments ($USD)
BioNTech162b2/Pfizer	mRNA (30µg)	2	95% [first dose 52%]	94.7%	Anaphylaxis (rare)	-70°C/-94ºF Storage $19.50/dose
Moderna	mRNA (100µg)	2	94.5% [no severe infections]	86.4%	Anaphylaxis (rare)	-20° C/-4ºF $25.00-$37.00/dose
Gamaleya	Ad5/Ad26	2	91.6%	> 60 yrs = 91.8%	None	–18°C storage 2-8°C for distribution Russia, Argentina, Belarus, Hungry, Serbia using
Oxford/AstraZeneca	ChAdOx1	2	90% [½ dose + 1] 62% [2 full doses]		None	2-8°C/36-46ºF $2.50-3.00/dose
JNJ/Janssen	Ad26	1	66% Overall 72% US 66% Latin America 57% South Africa 85% Severe COVID	Yes, similar age > 60	None reported	2-8°C/35-46ºF $10.00

Chasing Virus Variants

Girding for Impact on Vaccines and Monoclonal Antibodies

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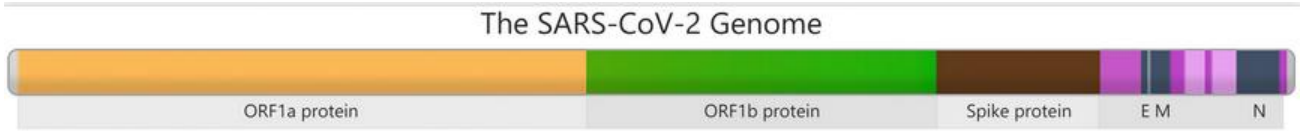
Genomic Surveillance for SARS-CoV-2 Variants



- Viruses, especially RNA, will develop genetic variations
- Routine sequencing can help track and anticipate problems
- Prominent strains (B.1.1.7 and B.1.351) more easily transmissible and possibly more virulent (B.1.1.7)

Strains to Watch

Name **(Pangolin)**	Name **(Nextstrain)**	First detected	US cases	Countries reporting cases	Key mutations	Transmissibility rate	Virulence
B.1.1.7	201/501Y.V1	UK	Yes	70	69/70 del 144Y N501Y 570d D614G P681H	~50% increase E484K now described, ?reduce vaccine impact	↑ UK Deaths
P.1	20J/501Y.V3	Japan/Brazil	Yes	>4	E484K K417N/T N501Y D614G	Not known	N/A
B.1.351	20H/501.V2	S. Africa	Yes	>30	K417N/T N501Y D614G	Not known	N/A

Adapted from CDC data (1/27/21)

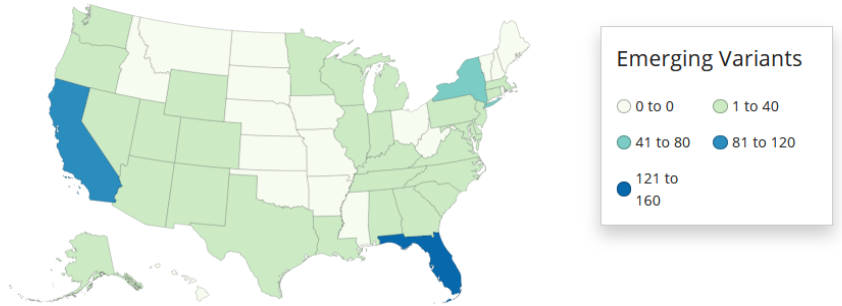
US COVID-19 Cases by Variant

US COVID-19 Cases Caused by Variants

Updated Jan. 31, 2021 Languages Print

Variant	Reported Cases in US	Number of States Reporting
B.1.1.7	467	32
B.1.351	3	2
P.1	1	1

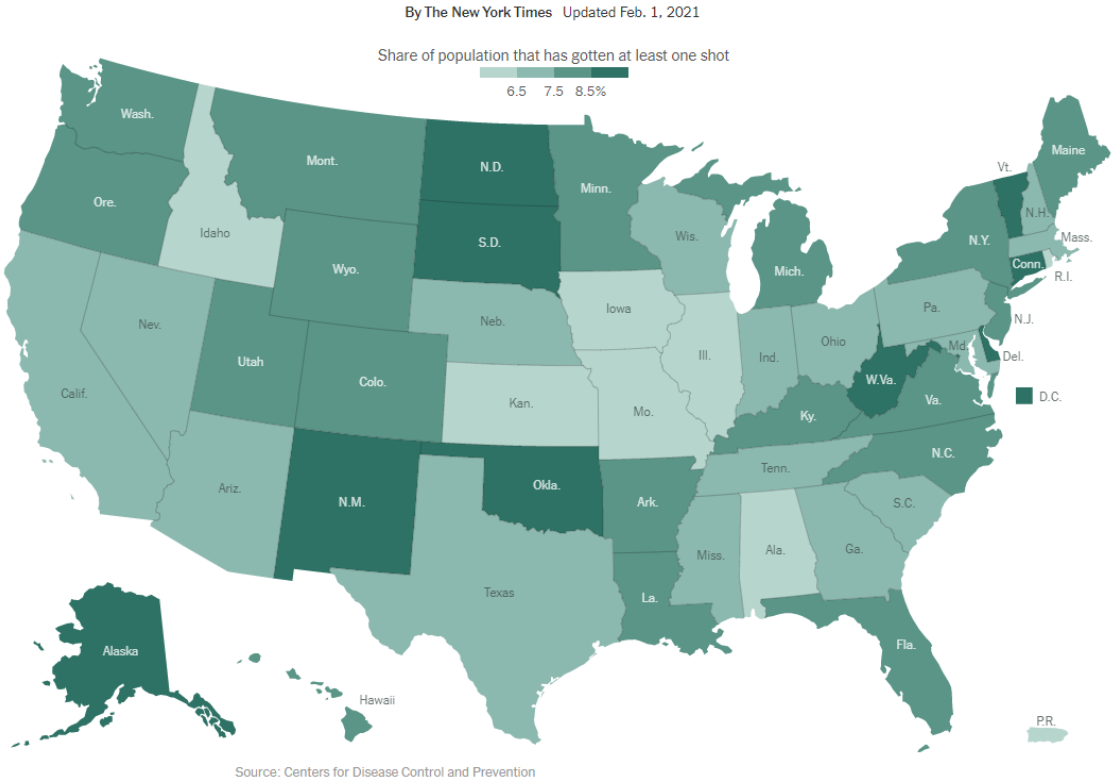
Emerging Variant Cases in the United States*†



Territories AS GU MH FM MP PW PR VI

- Worry about importing strains
- Trigger for international travel restrictions and testing
- However, US has its own strains!
- Impact of pressure from antivirals, monoclonal antibodies, convalescent plasma?

Vaccination Status in the United States



- 26M w/ 1 dose
- 5.9M w/ 2 doses
- ~1.4M doses per day
- 11.8% of US adult population received at least 1 dose
- 22.9% of prioritized population

Israel: The Opportunity for Real World Efficacy Mostly Pfizer Vaccine

Country with greatest percentage immunized

- > 30% immunized since Dec 20
- >70% over 60 yrs.
- 0.04% COVID (+) post dose #2
  - Real world efficacy ~ 92%
- 0.002% needed hospitalization

Success due to small size, national health service, electronic vaccine registry from childhood

Diagnosis, Treatment, and Prevention Impacts

Diagnosis: some platforms may have false negative (if one target)

Treatment:

- Antivirals: no known impact for remdesivir
- Monoclonal antibodies: bamlanivimab, casirivimab/imdevimab
  - 501Y.V2 complete escape
  - Retain activity against D614G and B.1.1.7 strains
  - Eli Lily starting BLAZE-4 trial (bamlanivimab + VIR-7831 g: 2 neutralizing antibodies bind different epitopes spike protein)
- Convalescent plasma: less risk, since polyclonal (if high titer)
  - 501Y.V2 with immune escape

Wiber BioRxiv 1/19/21;
Peng BioRxiv 1/22/21

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Vaccines

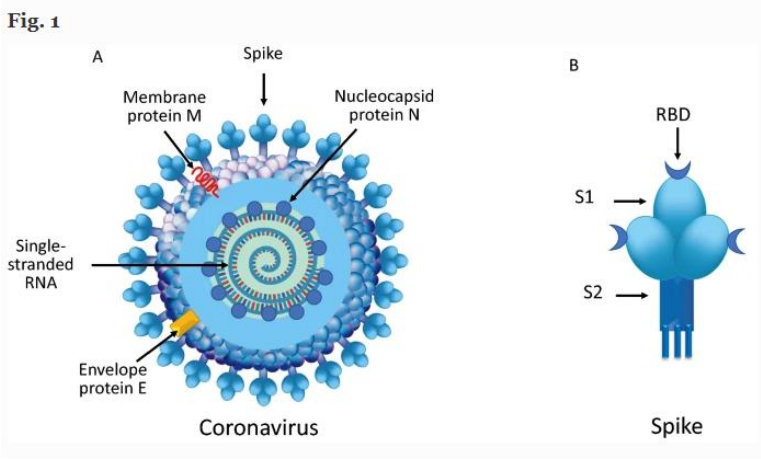
Current study focuses on neutralizing antibodies to spike protein (likely not complete story)

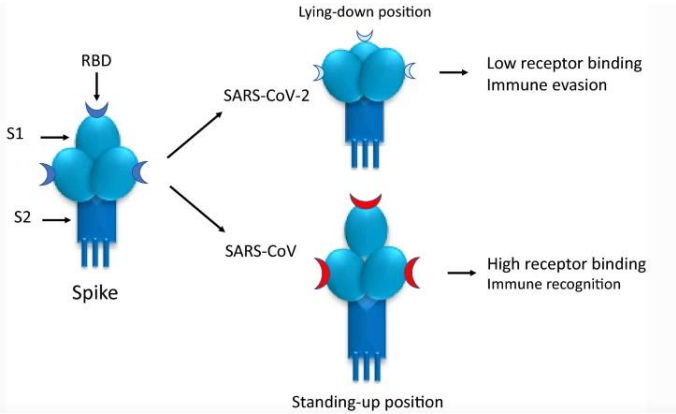
Janssen Ad26 S-protein

- Reduced activity in South African Patients

Current mRNA vaccines

- Retain sufficient activity





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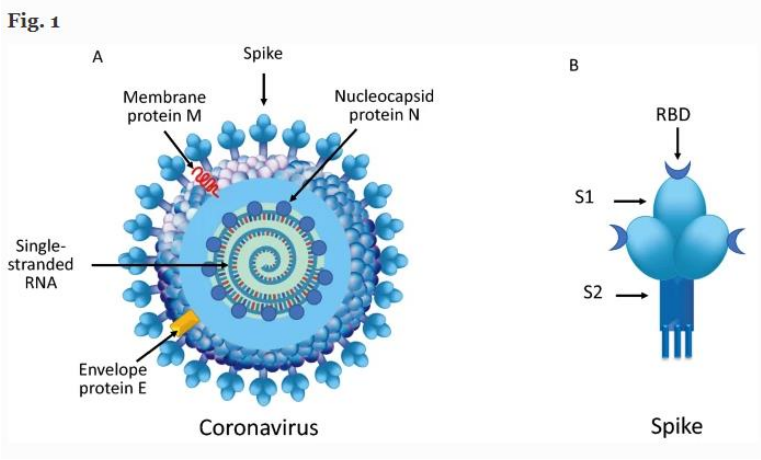
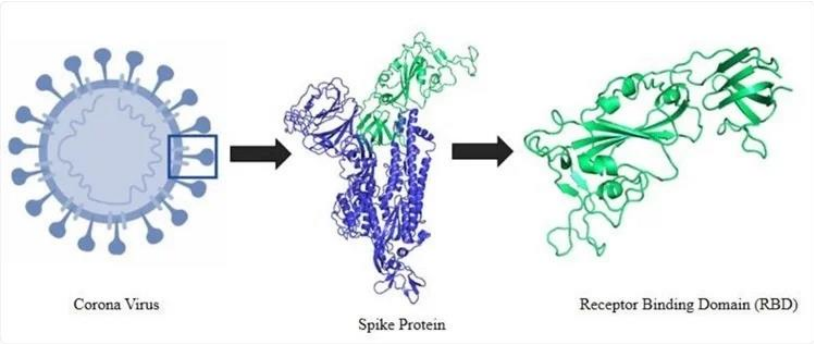




Thomas, Med Life Sci 2020

Moderna Vaccine Response

mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants 1/25/2021

Kai Wu, Anne P. Werner, Juan I. Moliva, Matthew Koch, Angela Choi, Guillaume B. E. Stewart-Jones, Hamilton Bennett, Seyhan Boyoglu-Barnum, Wei Shi, Barney S. Graham, Andrea Carfi, Kizzmekia S. Corbett, Robert A. Seder, Darin K. Edwards

doi: https://doi.org/10.1101/2021.01.25.427948

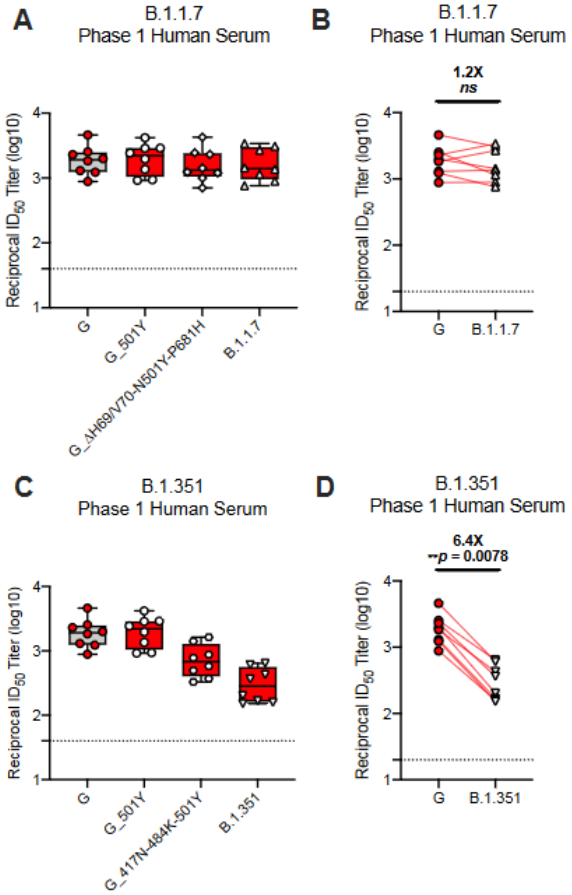
NIH/Moderna Study
Sera from 8 Phase 1 vaccine recipients (30ug or 100ug mRNA)

Similar responses to D614 S and G614S

No impact on B.1.1.7

B.1.351 = 2.7-6.4x reduction depending on extent of mutations (similar to other studies, e.g., Wang 2021)

- Still offers sufficient neutralization



Considerations

If variants predominate, current mAb therapy will be ineffective

mRNA provides sufficient antibody responses

- Other immune responses may also impact (T-cell)

Changes to mRNA vaccine?

- Change S protein mRNA
- Develop booster with variant changes included (dose #3)

To submit your own question, please email QA@dkbmed.com

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