COVID-19 Vaccine: Between Myth and Reality

Paul G. Thomas

ASPET virtual seminar
Outline of talk

• Background on SARS-CoV-2/coronaviruses
• Immune mechanisms of viral control
• Vaccine platforms
• Results from vaccination efforts
• Emergence of viral variants
SARS-CoV-2 vs. Influenza virus

The Coronavirus Virion

- (S) Spike
- (M) Membrane
- Ribonucleoprotein (RNP) Core
- (N) Nucleocapsid + gRNA
- (E) Envelope

~100 nm

(+): ssRNA genome ~28-32 Kb
29 proteins

The Influenza Virus Virion

- (HA) Hemagglutinin
- NA (Neuraminidase)

~100 nm

(-): segmented ssRNA genome ~28-32 Kb
~14 Kb, 10-14 proteins
Coronavirus and influenza virus replication cycles

**Coronavirus**
- **Entry and Uncoating**
  - Entry Receptor
  - Host Protease
- **Viral RNA Translation**
  - (+) genomic RNA
  - Ribosomes
  - L-TRX-L
- **Replicase-Transcriptase Complex**
  - nsp1-16
  - DMV
- **Transcription and Replication**
  - Subgenomic mRNAs
  - 5'-3'
- **Nucleocapsid (N)**
- **Envelope (E)**
  - Spor (S)
  - Membrane (M)
- **Virion Assembly**
  - RNP Core
  - ER-Golgi Intermediate Compartment
- **Release**

**Influenza virus**
- **Binding to the target cell**
- **Endocytosis**
- **Budding**
- **Release**
- **Protein synthesis**
- **Replication**
- **Formation of RNP**
  - (M2, haemagglutinin)
  - Nucleocapsid (N)
  - RNA polymerase (NS1, NS2, NP, M1)
Distinct receptor binding features of SARS vs. influenza viruses

**Coronavirus**

- **Binding**
  - Full length ACE2
  - Truncated ACE2

- **Entry and uncoating**
  - Spike
  - TMPRSSs
  - S2/S2

**Influenza virus**

- **Binding**
  - Sialic acid
  - Cell-surface membrane
  - Fusion peptide
  - Disulfide bond

- **pH 7**
  - ACE2
  - Spike
  - Fusion peptide

- **pH 5**
  - Endosomal membrane
  - Viral membrane

Influenza HA binds to sialic acid residues on diverse surface proteins

https://doi.org/10.1101/2020.02.08.926006
How does the immune response protect from or eliminate viruses?
Two main mechanisms of viral clearance

- **Antibodies** can bind to the virus and prevent it from getting in cells to begin with.

- **CD8 T cells** can kill a cell once it is infected.

- Many other immune components can help limit infection but these do not typically have “memory”.

Antibodies are made by B cells in response to specific antigens

Virus-specific B cells “see” antigen in the lymph node, expand, and make antibody that spreads throughout the body

Virus specific B cells need “help” from CD4 T cells

Antibodies are always circulating and can block the virus from entering cells—providing “neutralizing” protection
CD8 T cells target small pieces of the virus

After learning what the virus looks like in the lymph node, CD8 T cells go to the site of infection and kill infected cells.

Figure 8-13 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)
Antibody responses target the spike protein including the receptor binding domain as well as the nucleoprotein and other targets
  • Anti-spike (and RBD) antibodies are neutralizing and correlate with protection
  • NP antibodies are not neutralizing (we do not know if they are helpful)

T-cell responses target several proteins, including the spike protein
  • Strong CD4+ response—helps antibodies
  • Relatively weak CD8+ response (in many patients)—kills infected cells

Special thanks to Florian Krammer
One more element—adjuvants are “danger signals”

• Adjuvants prime the innate immune response—little or no memory, but necessary for activating the adaptive (B and T cell) immune response

• Adjuvants mimic danger signals, patterns from pathogens that promote non-specific inflammation

• Patterns can be elements of a virus—like viral RNA or DNA
What are the goals of a vaccine?

To introduce viral antigens to the immune system, to promote expansion of antigen-specific B cells, CD8 T cells, and CD4 T cells
a. Inactivated vaccines
Inactivated vaccines contain SARS-CoV-2 viruses that are chemically inactivated

b. Recombinant proteins vaccines
Vaccines composed of recombinant spikes
Vaccines composed of receptor binding domain

Virus-like particles are devoid of genetic material but display spikes, M and E proteins on their surface

NovaVax

SARS-CoV-2

c. Viral vector vaccines
Viral vector vaccines contain another virus modified to express S protein

JNJ
AstraZeneca

Pfizer/BioNTech
Moderna

d. RNA vaccines
RNA vaccines consist of RNA packed in lipid nanoparticles

Spike gene

Spike (protein S)

Membrane protein (M)

Evelope protein (E)

Receptor binding domain

Nucleoproteins and viral RNA

e. DNA vaccines
DNA vaccines contain a circular DNA encoding the spike protein

Spike gene
What does the Spike do?

• Spike mediates fusion inside the infected cell, so it has two forms—a binding form and a postfusion form.

• Several vaccines have introduced mutations to freeze Spike in the prefusion form—the form the immune system will most likely encounter.

https://cen.acs.org/pharmaceuticals/vaccines/tiny-tweak-behind-COVID-19/98/38
Comparison: annual “flu shot” QIV

• The annual flu shot is generated by inactivating a whole, attenuated virus, fragmenting it with detergent, and reforming virosomes missing the viral RNA and most viral proteins

• There is NO ADJUVANT
<table>
<thead>
<tr>
<th>Company (reference)</th>
<th>Vaccine (type)</th>
<th>Dose range (route)</th>
<th>Neut. titre after prime</th>
<th>Neut. titre after boost</th>
<th>T cell response</th>
<th>Trial registration number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinovac*5</td>
<td>CoronaVac (inactivated SARS-CoV-2 + aluminium hydroxide)</td>
<td>3–6 μg (i.m.)</td>
<td>2x</td>
<td>ND</td>
<td>1:30–1:60 range&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ND</td>
</tr>
<tr>
<td>Sinopharm</td>
<td>Inactivated whole virus COVID-19 vaccine (inactivated SARS-CoV-2 + aluminium hydroxide)</td>
<td>2.5, 5 or 10 μg (i.m.)</td>
<td>3x (0/28/56 or 0/28)</td>
<td>5ug (i.m.) 2x (0/14 or 0/21)</td>
<td>Not reported in detail</td>
<td>1:316 (2.5 μg, 0/28/56)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CanSino*66</td>
<td>Ad5 nCoV (non-replicating AdV5 expressing spike protein)</td>
<td>5 x 10&lt;sup&gt;10&lt;/sup&gt; to 10&lt;sup&gt;11&lt;/sup&gt; VP (i.m.)</td>
<td>1:18.3–1:19.5 range&lt;sup&gt;b&lt;/sup&gt;</td>
<td>—</td>
<td>Yes</td>
<td>NCT04341389</td>
</tr>
<tr>
<td>AstraZeneca*47</td>
<td>ChAdOx1nCOV-19 (non-replicating chimpanzee AdV expressing spike protein)</td>
<td>5 x 10&lt;sup&gt;10&lt;/sup&gt; VP 1 x or 2‘ (i.m.)</td>
<td>Median 1:218&lt;sup&gt;c&lt;/sup&gt; Median 1:51&lt;sup&gt;d&lt;/sup&gt; Median 1:4–1:16&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Median 1:136&lt;sup&gt;d&lt;/sup&gt; Median 1:29&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Yes</td>
<td>NCT04324606</td>
</tr>
<tr>
<td>Moderna*59</td>
<td>mRNA-1273 (mRNA)</td>
<td>2x 25, <strong>100</strong>, 250 μg (i.m.)</td>
<td>Low</td>
<td>1:112.3 (25 μg)&lt;sup&gt;f&lt;/sup&gt; 1:343.8 (100 μg)&lt;sup&gt;f&lt;/sup&gt; 1:332.2 (250 μg)&lt;sup&gt;f&lt;/sup&gt; 1:339.7 (25 μg)&lt;sup&gt;f&lt;/sup&gt; 1:654.3 (100 μg)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Good CD4&lt;sup&gt;+&lt;/sup&gt; and low CD8&lt;sup&gt;+&lt;/sup&gt; response</td>
<td>NCT04283461</td>
</tr>
<tr>
<td>Pfizer*60</td>
<td>BNT162b1 (mRNA)</td>
<td>2x 10, 30, 100 μg (i.m.)</td>
<td>Low</td>
<td>1:180 (10 μg)&lt;sup&gt;h&lt;/sup&gt; 1:437 (30 μg)&lt;sup&gt;h&lt;/sup&gt;</td>
<td>ND</td>
<td>NCT04368728</td>
</tr>
<tr>
<td>Pfizer*84</td>
<td>BNT162b1 (mRNA) and BNT162b2 (mRNA)</td>
<td>2x 10, 20, <strong>30</strong> μg</td>
<td>Low</td>
<td>Day 28&lt;sup&gt;h&lt;/sup&gt; BNT126b1 (18–55 years): 1:168 (10 μg) 1:267 (30 μg) BNT126b1 (65–85 years): 1:37 (10 μg) 1:179 (20 μg) 1:101 (30 μg) BNT126b2 (18–55 years): 1:157 (10 μg) 1:363 (20 μg) 1:361 (30 μg) BNT126b2 (65–85 years): 1:84 (20 μg) 1:147 (30 μg)</td>
<td>ND</td>
<td>NCT04368728</td>
</tr>
<tr>
<td>Novavax*90</td>
<td>NVX CoV2373 (Matrix-M) Spike protein ‘rosettes’</td>
<td>2 x 2.5–25 μg (i.m. ± Matrix-M) 1x 25 μg (i.m. + Matrix-M)</td>
<td>1:128 (25 μg + Matrix-M)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>1:3,906 (5 μg + Matrix-M)&lt;sup&gt;i&lt;/sup&gt; 1:3,305 (25 μg + Matrix-M)&lt;sup&gt;i&lt;/sup&gt; 1:41 (25 μg unadjuvanted)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>CD4&lt;sup&gt;+&lt;/sup&gt;</td>
<td>NCT04368988</td>
</tr>
</tbody>
</table>
Vaccines in Phase III

- Moderna (94%)
- Pfizer (95%)
- AstraZeneca (62-90%)
- Janssen (72%)
- Novavax (89-96%)
- Gamaleya (91.6%)
- Sinovac/Sinopharm (3x) (50-90%)
- Cansino

For most of these vaccines two injections are required.

Special thanks to Florian Krammer
How does a Phase III study work?

Vaccine group

Conducted by independent medical centers (usually geographically distributed)

An independent committee watches the data

Analysis timepoints and success are pre-defined

Placebo control group

Special thanks to Florian Krammer
How does a Phase III study work?

Vaccine group

Placebo control group

Time

COVID-19!!!

Special thanks to Florian Krammer
What do the Pfizer results mean?

• 43,538 individuals are in the study
• 170 COVID-19 cases were recorded
  • 162 in the placebo group (9 severe)
  • 8 in the vaccine group (1 severe)
• 95% efficacy against symptomatic disease (one symptom plus PCR+, they start measuring this 7 days post dose 2)
• 94% efficacy in the 65-85 year old group
• No significant safety concerns

• The vaccine received different degrees of approval in Bahrain, the UK, Mexico, Canada, Saudi Arabia, the EU, the US etc.

Moderna data look almost identical
Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1, Dose 1 All-Available Efficacy Population

No. with events/No. at risk
A: 605158 2050170 9282974 7525696 7039199 6783209 6270218 14180750 18443702 16271258 31313398 23551394 2489482 2078942 1874084 27641480 2754990 3950
B: 605158 2050170 9282974 7525696 7039199 6783209 6270218 14180750 18443702 16271258 31313398 23551394 2489482 2078942 1874084 27641480 2754990 3950

Note: “E” indicates subjects with severe COVID-19 or COVID-19 leading to hospitalisation.

Pfizer CONFIDENTIAL. SDTM Creation: 17NOV2020 (14:45) Source Data: srcRef Table Generation: 17NOV2020 (14:45)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./pdf/uncleaned/CFA_104/srcRef_Efficacy_FA_104/Treef_E01_km_dilasi

https://www.fda.gov/media/144245/download accessed 8Dec20

Special thanks to Florian Krammer
RNA vaccines are a relatively new development

RNA vaccine trials in humans
(not including a large number of cancer vaccines and therapeutic approaches based on mRNA)

<table>
<thead>
<tr>
<th>Target</th>
<th>Started in</th>
<th>Individuals enrolled(^2)</th>
<th>Company</th>
<th>Status</th>
<th>Phase</th>
<th>Registration number</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV</td>
<td>2017</td>
<td>181</td>
<td>Moderna</td>
<td>Fully enrolled</td>
<td>Phase 1</td>
<td>NCT03382405</td>
</tr>
<tr>
<td>hMPV/PIV3</td>
<td>2019</td>
<td>114</td>
<td>Moderna</td>
<td>Recruiting</td>
<td>Phase 1</td>
<td>NCT04144348</td>
</tr>
<tr>
<td>Zika</td>
<td>2019</td>
<td>120</td>
<td>Moderna</td>
<td>Fully enrolled</td>
<td>Phase 1</td>
<td>NCT04064905</td>
</tr>
<tr>
<td>Influenza</td>
<td>2017</td>
<td>156</td>
<td>Moderna</td>
<td>Fully enrolled</td>
<td>Phase 1</td>
<td>NCT03345043</td>
</tr>
<tr>
<td>Rabies</td>
<td>2018</td>
<td>53</td>
<td>Curevac</td>
<td>Fully enrolled</td>
<td>Phase 1</td>
<td>NCT03713086</td>
</tr>
<tr>
<td>Rabies</td>
<td>2013</td>
<td>101</td>
<td>Curevac</td>
<td>Completed</td>
<td>Phase 1</td>
<td>NCT02241135</td>
</tr>
<tr>
<td>Rabies</td>
<td>2014</td>
<td>72</td>
<td>Curevac</td>
<td>Completed</td>
<td>Phase 1</td>
<td>NCT02238756</td>
</tr>
<tr>
<td>CMV</td>
<td>2020</td>
<td>452</td>
<td>Moderna</td>
<td>Recruiting</td>
<td>Phase 2</td>
<td>NCT04232280</td>
</tr>
<tr>
<td>Chikungunya(^1)</td>
<td>2019</td>
<td>39</td>
<td>Moderna</td>
<td>Fully enrolled</td>
<td>Phase 1</td>
<td>NCT03829384</td>
</tr>
</tbody>
</table>

\(^1\)Passive immunity based on *in vivo* mAb expression

\(^2\)Includes individuals who received placebo, some trials are still recruiting

Special thanks to Florian Krammer
What do the J&J results mean?

• One dose!
• 43,783 individuals are in the study
• USA, South Africa and Latin America
• US efficacy 72% against moderate to severe COVID-19 (2 symptoms plus PCR+ was counted as moderate)
• 85% efficacy across all studies against severe disease
• 100% protection against hospitalization and death
• No significant safety concerns
• Some indication of reduction of asymptomatic infections

• Now authorized for use in the US, will likely be licensed in EU in March

Special thanks to Florian Krammer
Are vectored vaccines a relatively new development?

- Ad26-based Ebola vaccine licensed in the EU
- Ad4 and Ad7 vaccines in use in the US military since 1971
Reactogenicity

- Injection site pain
- Headache
- Fatigue
- Elevated temperature
- Myalgia
- Mild flu-like symptoms

→ unpleasant, but not dangerous

AdV=mRNA>recombinant protein>inactivated vaccine

Strength of adjuvant!

Moderna/VRC mRNA 1273 via LNPs

Special thanks to Florian Krammer
# What is in each vaccine?

## Table 1. SARS-CoV-2 Vaccines under Emergency Use Authorization (EUA) or in Late-Phase Studies.

<table>
<thead>
<tr>
<th>Vaccine Platform</th>
<th>Type of Vaccine and Immunogen</th>
<th>Developer (Name of Vaccine)</th>
<th>Dose Schedule and Administration</th>
<th>Phase†</th>
<th>Excipient†</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA-based vaccine</td>
<td>mRNA encoding spike protein (30 μg)</td>
<td>BioNTech–Pfizer (BNT162b2)</td>
<td>Two doses (day 0, day 21) Intramuscular</td>
<td>Post-EUA</td>
<td>0.43 mg (14 hydroxyatracortesone, 0.6 mg sodium L-sorbate), 0.03 mg zanamivir, 0.01 mg sodium chloride, 0.001 mg monobasic potassium phosphate, 0.16 mg sodium chloride, 0.07 mg disodium phosphate, sodium chloride, and 6 mg sucrose. The diluent (0.9% sodium chloride injection) contributes an additional 2.16 mg sodium chloride per dose</td>
</tr>
<tr>
<td>RNA-based vaccine</td>
<td>mRNA encoding spike protein (180 μg)</td>
<td>Moderna (mRNA-1273)</td>
<td>Two doses (day 0, day 28) Intramuscular</td>
<td>Post-EUA</td>
<td>Lipids (SM–102, 1,2-dimyristoyl–sn–glycero–3-phosphoethanolamine N–stearylamine (DSE–SA), cholesterol, and 1,2-dioleoyl–sn–glycero–3–phosphocholine (DOPE)), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose</td>
</tr>
<tr>
<td>Adenovirus vector (nonreplicating)</td>
<td>ChAdOx1 nCoV-19</td>
<td>AstraZeneca and University of Oxford (AZD1222)</td>
<td>One (day 0) or two (day 0, day 28) doses Intramuscular</td>
<td>Phase 3</td>
<td>10 mM histidine, 3.5% (w/v) sucrose, 35.5 mM sodium chloride, 1 mM magnesium chloride, 0.1% (w/v) polybrene 80, 0.3 mM edetate disodium, 0.5% (w/v) ethanol, and at pH 6.6</td>
</tr>
<tr>
<td>Adenovirus vector (nonreplicating)</td>
<td>Ad5-nCoV2.S</td>
<td>Janssen</td>
<td>One (day 0) or two (day 0, day 56) doses Intramuscular</td>
<td>Phase 3</td>
<td>Sodium chloride, citric acid monohydrate, polybrene 80, 2 hydroxypropyl–β–cyclodextrin (HPβCD), ethanol (absolute), sodium hydroxide</td>
</tr>
<tr>
<td>Protein subunit</td>
<td>Full-length recombinant SARS-CoV-2 glycoprotein nanoparticle with Matrix M adjacent Spike protein</td>
<td>Novavax</td>
<td>Two doses (day 0, day 21) Intramuscular</td>
<td>Phase 3</td>
<td>Matrix M1 antigen, Full-length spike protein formulated in polybrene 80 detergent and Matrix M1 antigen</td>
</tr>
<tr>
<td>Protein subunit</td>
<td>SARS-CoV-2 vaccine formulation with adjuvant (5 proteins) (Baculovirus production) Spike protein</td>
<td>Sanofi Pasteur and GSK</td>
<td>Two doses (day 0, day 21) Intramuscular</td>
<td>Phase 1–2</td>
<td>Sodium phosphate monobasic monohydrate, sodium phosphate dibasic, sodium chloride, polybrene 20, disodium hydrogen phosphate, potassium dihydrogen phosphate, potassium chloride</td>
</tr>
</tbody>
</table>

† Phase information was current as of December 21, 2020. In all cases, the placebo was normal saline.
†† Bold entries are excipients potentially related to vaccine reactions that may be cross-reactive to other excipients (e.g., PEG 2000 and polybrene 80). SM-102, a component of the Moderna vaccine, is a proprietary ionizable lipid.
How long does protection last?

- Likely for years, based on what we know about immune responses in general and immune responses to SARS-CoV-2

- It might be that booster doses are needed at some point, but that is similar to other vaccines (e.g. tetanus)

Special thanks to Florian Krammer
Vaccines work in older individuals and boost memory in infected individuals

- Vaccines work faster in younger individuals and with lower doses
- With recommended dose, older individuals still generate high levels of protective immunity

- Post-infection, a single dose of the Pfizer/BioNTech vaccine was equivalent to two doses of the vaccine in naïve individuals
  - Still a significant boost!
RNA vaccines are inducing robust T cell responses

- Robust primary CD4 and CD8 T cell responses are detectable after RNA vaccines
- Similarly, AdV vaccines (like JNJ) also induced strong T cell responses
- Many T cell antigens are not prone to easy immune escape
Variants of Concern (VoC)

- **B.1.1.7 – The ‘British-origin’ variant**
  - RBD changes: N501Y
  - A little bit more infectious (approximately 35%)
  - No strong evidence that it causes more severe disease

- **B.1.351 – The ‘South African-origin’ variant**
  - RBD changes: K417N, E484K, N501Y
  - More infectious
  - No strong evidence that it causes more severe disease

- **P.1 – The ‘Brazilian-origin’ variant**
  - RBD changes: K417T, E484K, N501Y
  - See B.1.351

Special thanks to Florian Krammer

Adapted from Goran Bajic
Mutations outside of the RBD are also important, especially deletions in the NTD.

<table>
<thead>
<tr>
<th>B.1.1.7</th>
<th>B.1.351</th>
<th>P.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>69-70 del</td>
<td>L18F</td>
<td>L18F</td>
</tr>
<tr>
<td>Y144 del</td>
<td>D80A</td>
<td>T20N</td>
</tr>
<tr>
<td><strong>N501Y</strong></td>
<td>D215G</td>
<td>P26S</td>
</tr>
<tr>
<td>A570D</td>
<td><strong>K417N</strong></td>
<td>D138Y</td>
</tr>
<tr>
<td>P681H</td>
<td><strong>E484K (ERIK)</strong></td>
<td>R190S</td>
</tr>
<tr>
<td>T716I</td>
<td><strong>N501Y (NELLY)</strong></td>
<td><strong>K417T</strong></td>
</tr>
<tr>
<td>S982A</td>
<td>A701V</td>
<td><strong>E484K</strong></td>
</tr>
<tr>
<td>D1118H</td>
<td>242-244 del</td>
<td><strong>N501Y</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H655Y</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1027I</td>
</tr>
</tbody>
</table>

Adapted from Goran Bajic

Special thanks to Florian Krammer
# Monoclonal antibody therapeutics

<table>
<thead>
<tr>
<th>Variant</th>
<th>Eli Lilly’s therapeutic mAb (LY-CoV555)</th>
<th>Regeneron’s therapeutic mAb cocktail (REGN10933 and REGN10987)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1.1.7</td>
<td>Still works</td>
<td>Still works</td>
</tr>
<tr>
<td>B.1.351</td>
<td>Impaired</td>
<td>REGN10933 is impaired, REGN10987 still works</td>
</tr>
<tr>
<td>P.1</td>
<td>Is unlikely to work</td>
<td>REGN10933 is unlikely to work, if REGN10987 still works is unclear</td>
</tr>
</tbody>
</table>

Many mAbs are not impaired by the mutations and development of several of these mAbs as therapeutics is in progress.

Special thanks to Florian Krammer
AZ vaccine showed no evidence of efficacy against the SA (B.1.351) variant

Likely similar against Brazil strains and some other emerging strains in the US
### Efficacy in Vaccine Trials

<table>
<thead>
<tr>
<th>Variant</th>
<th>J&amp;J (Ad26 vector)</th>
<th>Novavax (recombinant spike)</th>
<th>AstraZeneca</th>
<th>Pfizer/BioNTech</th>
<th>Moderna</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wild type (garden variety) SARS-CoV-2</strong></td>
<td>72%</td>
<td>95.6%</td>
<td>84% (60-90%)</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>B.1.1.7</td>
<td>ND</td>
<td>85.6%</td>
<td>74.6%</td>
<td><em>In vitro</em> data only, but likely no impact on efficacy</td>
<td><em>In vitro</em> data only, but likely no impact on efficacy</td>
</tr>
<tr>
<td>B.1.351</td>
<td>57% (95% B.1.351 lineage in South African part of trial) (100% against hospitalization)</td>
<td>60% (in HIV-individuals, &gt;90% B.1.351 lineage in South African part of trial)</td>
<td>10%?</td>
<td><em>In vitro</em> data only, but likely only moderate impact on efficacy</td>
<td><em>In vitro</em> data only, but likely only moderate impact on efficacy</td>
</tr>
<tr>
<td>P.1</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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**Important Point:**
Even if vaccine efficacy against symptomatic disease is reduced, efficacy against severe disease is likely to remain high.

Special thanks to Florian Krammer.
Conclusions

• Multiple, highly effective vaccines with low levels of side effects available against SARS-CoV-2
• Difficult to estimate the extent to which asymptomatic infection is reduced—more studies are needed, but some effect is likely
• More vaccines are likely to be approved in US soon (Novavax? AZ?)
• Variants can reduce vaccine efficacy—variant emergence will be limited by rapid vaccine uptake