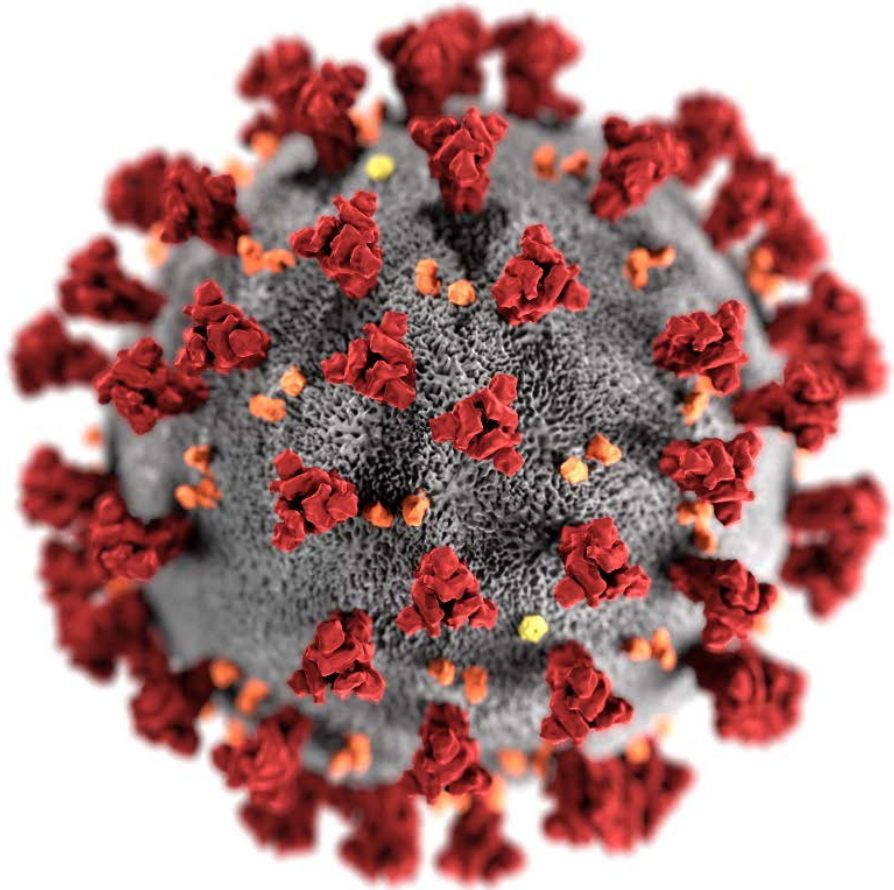
ACIP COVID-19 Vaccines



Work Group interpretations of data

Sara Oliver MD, MSPH

ACIP Meeting

January 27, 2021

Clinical Trial Data: AstraZeneca

Immunogenicity Information Reviewed by Work Group

AZD1222 (AstraZeneca)

- Neutralizing antibodies and binding antibodies measured in participants after 1 dose and 2-dose series
- Responses similar to convalescent sera comparison
- Th1 biased T-cell response
- **$5x10^{10}$** dose (2 doses, 28 days apart) selected for US Phase III clinical trials

Safety Information Reviewed by Work Group

AZD1222 (AstraZeneca)

- **Phase I/II studies**
  - Local and systemic symptoms mild to moderate in severity
  - Injection site pain, feeling feverish, muscle ache and headache most common symptoms reported
  - Reactogenicity symptoms lower after second dose (small numbers) and in older adults
  - No vaccine-related serious adverse events (SAEs) reported
- **Global Phase III studies**
  - Similar to results from Phase I/II studies
  - Reactogenicity symptoms milder and reported less frequently after second dose and in adults ≥65 years of age
- **Clinical Hold/Safety Pause**
  - Study paused due to report of transverse myelitis in the UK
  - FDA reviewed neurologic events in all trials
  - Study allowed to be resumed with changes, including independent expert neurology panel

Efficacy Information Reviewed by Work Group

AZD1222 (AstraZeneca)

- Preliminary data from interim global efficacy analysis reviewed
  - ~11,000 participants in UK/Brazil interim analysis
  - Several dose regimens and inter-dose intervals included in interim analysis

- VE estimate for SD/SD regimen: **62.1**% (41.0-75.7%)
  - Estimate for dose/schedule that is currently being studied in US Phase III trials (SD/SD)

- Pooled VE estimate: **70.4**% (54.8-80.6%)
  - Estimate includes individuals with a lower dose (LD) as the first dose, and standard dose (SD) as the second dose

Plans for U.S. Phase III Trials

- Phase III trial in the US is ongoing and will be the primary basis for EUA application
- Over 32,000 people enrolled in Phase III efficacy trials
- Primary endpoint: symptomatic, virologically confirmed COVID-19 disease
- Targets to enroll diverse populations:
  - Race and ethnicity
  - Age (<65 years and ≥65 years of age)
  - Underlying medical conditions

Work Group Interpretation

AZD1222 (AstraZeneca)

- Phase I/II data from the vaccines show induction of binding and neutralizing antibodies as well as T-cell responses, favorable safety/reactogenicity profile, supporting advance to Phase III trials

- Safety pauses are expected with large clinical trials, indicate the process is working appropriately
  - Transparency around safety pause and resolution is critical

- Await results of US Phase III data for EUA application
  - 2 doses of $5x10^{10}$ dose, 28 days apart

COVID-19 and children

Work Group interpretation
COVID-19 and children

- While overall burden of COVID-19 may be lower among children, preventable infections, hospitalizations, long-term sequelae and deaths are an important public health problem
- Clinical trials to evaluate safety and immunogenicity of COVID-19 vaccines in children are essential
- Given the disparities noted among COVID-19 cases among children and MIS-C, will be crucial for pediatric clinical trials to enroll a **diverse** population

Vaccine Effectiveness Studies

Work Group interpretation

COVID-19 vaccine effectiveness studies

- “Real-world” vaccine effectiveness studies are needed for a variety of populations, ages, and conditions
- Diverse trial designs will be important to address variety of questions
- Isolates obtained through VE platforms can help address concerns around SARS-CoV-2 variants

SARS-CoV-2 variants

SARS-CoV-2 Variants

- In fall of 2020, several SARS-CoV-2 variants emerged, with changes in receptor-binding domain of spike protein – confer increased transmissibility

Amino acid change in spike protein	**United Kingdom** (B.1.1.7)	**South Africa** (20H/501Y.V2 or B.1.351)	**Brazil** (P.1)
No. of spike changes	8	10	12
N501Y	✓	✓	✓
E484K		✓	✓
K417T/N		✓	✓

Emerging SARS-CoV-2 Variants | CDC

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Does the variant have the ability to evade vaccine -induced immunity?

Emerging SARS-CoV-2 Variants | CDC

SARS-CoV-2 Variants: Implications for vaccination

Following vaccination, study participant sera (n=8–20) tested in neutralization assays:

- Pfizer BioNTech COVID-19 vaccine:
  - Several studies have demonstrated equivalent neutralizing titers against a panel of 19 individual SARS-CoV-2 spike variants[1] and N501Y (variant)[2] compared to wildtype virus
  - Reductions to neutralizing titers have been noted against the B.1.1.7 (UK) variant (all mutations):
    - 1.3-fold average reduction[3]
    - 3.9-fold median reduction[4]
  - One study with modest reduction (<3-fold) for some with neutralization against certain SARS-CoV-2 spike mutations from B.1.351 (South African) and P.1 (Brazil) variants: E484K and K417N:E484K:N501Y[5]
- Moderna COVID-19 Vaccine:
  - One study with modest reduction (<3-fold) for some with neutralization against certain SARS-CoV-2 spike mutations from B.1.351 (South African) and P.1 (Brazil) variants: E484K and K417N:E484K:N501Y[5]
  - Another study with no significant impact on neutralizing titers against B.1.1.7 (UK) variant, but 6-fold reduction for B.1.351 (South African) variant[6]

1. Sahin et al. medRxiv preprint (Dec 11, 2020a); doi: https://doi.org/10.1101/2020.12.09.20245175
2. Xie et al. bioRxiv preprint (Jan 07, 2021) ; doi: https://doi.org/10.1101/2021.01.07.425740
3. Muik et al. bioRxiv preprint (Jan 19, 2021); doi: https://doi.org/10.1101/2021.01.18.426984
4. Collier et al. medRxiv preprint (Jan 20, 2021); doi: https://doi.org/10.1101/2021.01.19.21249840
5. Wang et al. bioRxiv preprint (Jan 15, 2021) ; doi: https://doi.org/10.1101/2021.01.15.426911
6. Wu et al. BioRxiv preprint ((Jan 25, 2021); doi: https://doi.org/10.1101/2021.01.25.427948

SARS-CoV-2 Variants: Strain Surveillance in the U.S.

- **National SARS-CoV-2 Strain Surveillance ("NS3")**
  - Being scaled to process ~750 samples nationally per week
  - Allows for characterization of viruses beyond sequencing
- **Surveillance in partnership with national reference laboratories**
  - ~1,750 samples per week +
- **Universities**
  - CDC has contracts with seven universities to conduct genomic surveillance in collaboration with PH agencies
- **Sequencing within state and local health departments**
  - Epidemiology and Laboratory Capacity Program supports integrating next-generation sequencing and bioinformatics into the U.S. public health system
- **The SPHERES consortium**
  - CDC leads a national consortium of ~160 laboratories sequencing SARS-CoV-2 (SPHERES)
- **Sequencing of vaccine breakthrough cases**

Emerging SARS-CoV-2 Variants | CDC

Implications and discussion

- In most of the studies reviewed, minimal to moderate reduction (1.3–6-fold) in neutralization activity for vaccine-immune sera in some persons
  - Implications for ‘real world’ effectiveness unclear- sera from mRNA vaccine recipients had higher neutralization activity than COVID-19 convalescent human sera in early phase clinical trials
  - Limited studies, small numbers
- Evidence quickly evolving, so continued review of data critical
  - Studies evaluating the full sets of mutation from variants likely more informative than studies of single mutations
  - Studies of vaccine breakthrough cases are planned and may serve as an early waring
- Moderna has announced they are developing a vaccine against B.1.351 (South African) variant

COVID-19 vaccine dosing and schedules

Dosing and administration

- mRNA vaccines are recommended for a two-dose series administered intramuscularly
  - Pfizer-BioNTech: **Three weeks** apart
  - Moderna: **Four weeks** apart
- Persons should not be scheduled to receive the second dose earlier than the recommended intervals
  - However, doses administered earlier should not be repeated
- The second dose should be administered as close to the recommended interval as possible. However, if it is not feasible to adhere to the recommended interval, the second dose of Pfizer-BioNTech and Moderna COVID-19 vaccines may be scheduled for administration up to **6 weeks** (**42 days**) after the first dose.

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Alternative Dosing/Schedules:

- Currently, recommended schedule and doses from Phase III trials where safety and high efficacy were demonstrated
- If data become available for alternative schedules or doses, ACIP can review data and consider new recommendations
- However, in the absence of additional data to support alternative schedules or doses, the current recommendations will remain

Dosing and administration

- mRNA vaccines are not **interchangeable** with each other or other COVID-19 vaccines
  - Either vaccine series may be used; ACIP does not state a product preference
  - Every effort should be made to determine which vaccine product was received as the first dose
  - In **exceptional** situations in which the first-dose vaccine product cannot be determined or is no longer available, any available mRNA COVID-19 vaccine may be administered at a minimum interval of 28 days between doses

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Dosing and administration

- mRNA vaccines should be **administered alone**, with a minimum interval of 14 days before or after administration with any other vaccines
  - However, mRNA COVID-19 vaccines and other vaccines may be administered within a shorter period in situations where benefits of vaccination are deemed to outweigh the potential unknown risks of vaccine coadministration
  - If mRNA COVID-19 vaccines are administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Next Steps

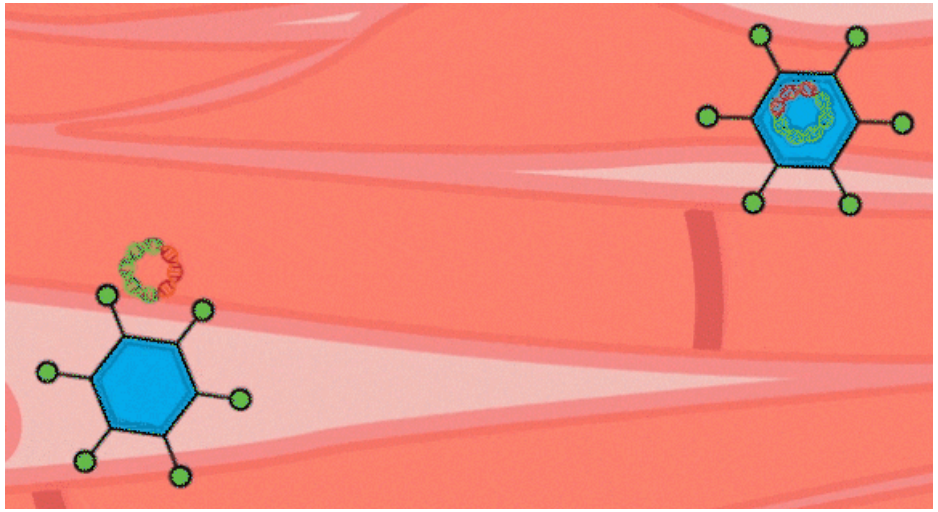
Next Steps

- Any vote on the use of additional COVID-19 vaccines will take place at an Emergency ACIP meeting once FDA has authorized the vaccine and data are reviewed by ACIP, including safety and efficacy results from Phase III trials

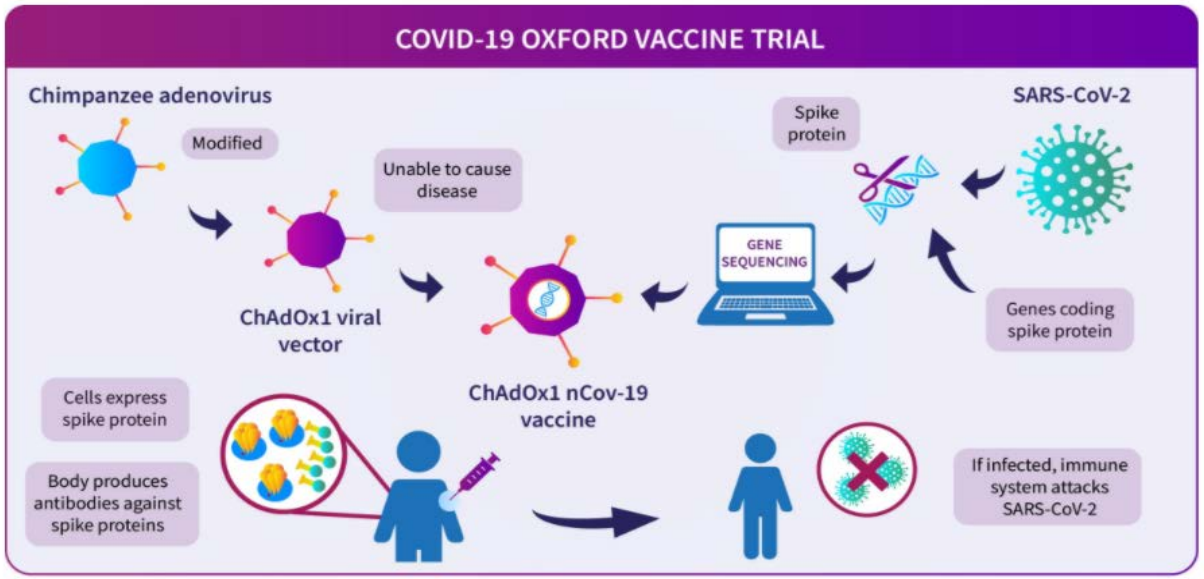
- Janssen vaccine may have results from Phase III trial within next several weeks
  - Adenovirus 26 (Ad.26) vector vaccine
  - Current U.S. Phase III trials evaluating a single dose

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Adenovirus vector vaccines



Graphic source: https://www.janssen.com/infectious-diseases-and-vaccines/vaccine-technology



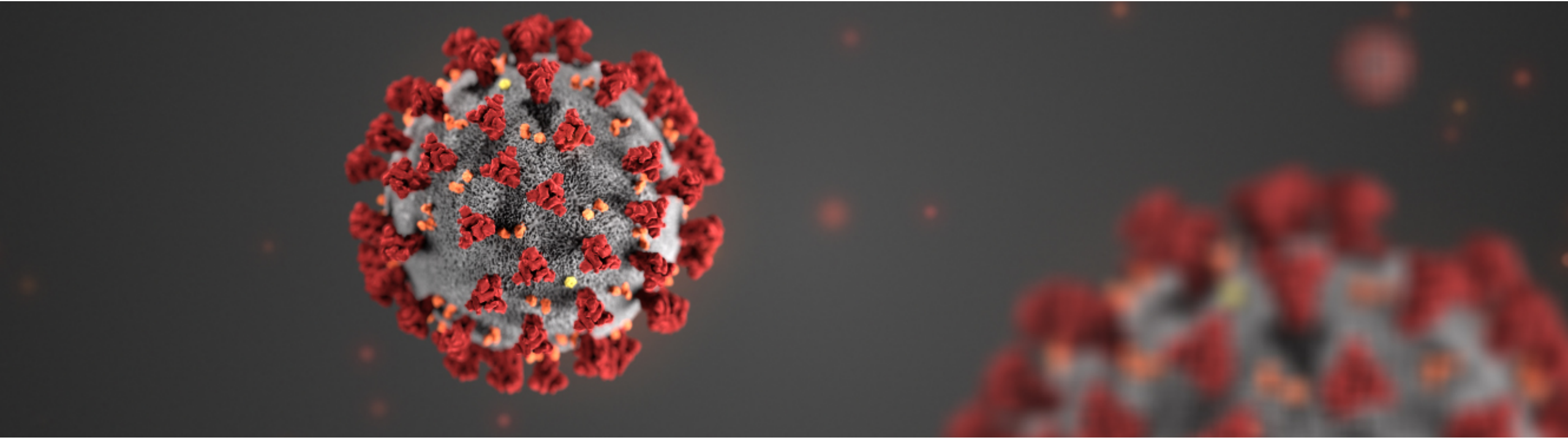
Graphic source: https://www.research.ox.ac.uk/Article/2020-07-19-the-oxford-covid-19-vaccine

Human adenovirus 26 (Ad.26) vector

- Nonreplicating
- Used in other vaccines (Ebola vaccine)
- Ad.26 Ebola vaccine used in broad populations, including pregnant women and children
- Previous exposure to the vector could reduce effectiveness

Chimpanzee adenovirus vector

- Nonreplicating
- Chimpanzee adenovirus vector circumvents preexisting immunity to human adenovirus



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Efficacy after dose 1

Phase III data

Pfizer-BioNTech COVID-19 vaccine

- Most (98%) recipients received 2 doses of the Pfizer-BioNTech vaccine
- Efficacy of **52.4**% (29.5–68.4%) noted between dose 1 and dose 2
- Additional data in UK press statement (not included in submission to FDA or CDC):
  - Cases from day 15-day 21: VE of **89**% (52-97%)
  - Follow-up only until day **21**

Moderna COVID-19 vaccine

- Most (97%) recipients received 2 doses of the Moderna vaccine
- Efficacy of **69.5**% (43.5–84.5%) noted between dose 1 and dose 2
- Additional data from Moderna Phase III trial:
  - Non-randomized sample of persons who only received 1 dose: VE of **92**% (66–98%),
  - Median follow-up only **28** days

SARS-CoV-2 Variants

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- Some changes (e.g.,E484K) affect polyclonal/monoclonal antibody neutralization

Emerging SARS-CoV-2 Variants | CDC