Update on COVID-19 Vaccines

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June 10, 2021
NIH Research on Coronavirus Disease 2019 (COVID-19)

- Therapeutics
- Diagnostics
- Natural History
- Vaccines
- Research Resources
- Basic Research
NIH Research on Coronavirus Disease 2019 (COVID-19)

Therapeutics

Diagnostics

Natural History

Vaccines

Research Resources

Basic Research
“The speed and efficiency with which these highly efficacious vaccines were developed and their potential for saving millions of lives are due to an extraordinary multidisciplinary effort involving basic, preclinical, and clinical science that had been under way—out of the spotlight—for decades before the unfolding of the COVID-19 pandemic.”
Role of NIH in the Development of COVID-19 Vaccines

- Basic, pre-clinical, and clinical research to develop vaccine platforms

- Stabilization of pre-fusion spike protein

- Extensive NIAID domestic and international clinical trials networks for HIV and influenza
Vaccine Construct
Vaccine Construct

Vaccine Immunogen

Vaccine Platform
Structure-Based Vaccine Design
Stable, Soluble Structure of HIV Envelope Trimer

Structure and Immune Recognition of Trimeric Pre-Fusion HIV-1 Env

M Pancera, M Connors, PD Kwong, et al.

Stabilized, soluble trimer crystal structure resolved in detail

Image courtesy of M Pancera, J Stuckey, PD Kwong.
Pre-Fusion F Protein Stabilized Using Structure-Based Vaccine Design

Structure-Based RSV Vaccine Shows Promise in Phase 1 Trial – “Precision Vaccinology”

- RSV fusion glycoprotein stabilized in prefusion conformation (DS-Cav1) used as immunogen

1 dose of DS-Cav1 induced large increases in RSV-neutralizing antibodies that were sustained for several months
Immunogenicity and Structures of a Rationally Designed Prefusion MERS-CoV Spike Antigen

Mutations

SARS-CoV-2 Spike protein
Pre-fusion form
(Stable)

SARS-CoV-2 Spike protein
Pre-fusion form
(Unstable)
Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation

D Wrapp, N Wang, KS Corbett, JA Goldsmith, C-L Hsieh, O Abiona, BS Graham, JS McLellan

Atomic-level structure of SARS-CoV-2 spike protein. Receptor binding domain is colored green.
Vaccine Platform Technologies

Genetic immunization (DNA and RNA vaccines)
- SARS, MERS, West Nile, Zika, RSV

Nanoparticles (viral protein on particle)
- Influenza, Malaria, RSV

Viral vector (e.g., VSV, adenovirus)
- Ebola, Marburg, Zika

Virus-like particle (VLP) (no RNA or DNA; non-infectious)
- Chikungunya, Zika, WEVEE

Recombinant protein
- Influenza, RSV

Adjuvants (e.g., AS01, MF59)

Selected Examples
Suppression of RNA Recognition by Toll-like Receptors: The Impact of Nucleoside Modification and the Evolutionary Origin of RNA

K Karikó, D Weissman et al.

Showed how to modify mRNA without triggering key inflammatory pathways, overcoming a key hurdle and paving the way for current vaccines
Comparative Seroprevalence and Immunogenicity of Six Rare Serotype Recombinant Adenovirus Vaccine Vectors from Subgroups B and D

P Abbink, DH Barouch et al.

rAd26 vectors proved the most immunogenic among the rare serotype rAd vectors studied, with promise for vaccine development.

Journal of Virology

May 2007, Volume 81 Issue 9
<table>
<thead>
<tr>
<th>Platform</th>
<th>Developer</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleic Acid (mRNA)</td>
<td>Moderna</td>
<td>EUA</td>
</tr>
<tr>
<td></td>
<td>BioNTech, Pfizer</td>
<td>EUA</td>
</tr>
<tr>
<td>Adenovirus Vector</td>
<td>Johnson &amp; Johnson</td>
<td>EUA</td>
</tr>
<tr>
<td></td>
<td>AstraZeneca</td>
<td>EUA TBD</td>
</tr>
<tr>
<td>Recombinant Protein</td>
<td>GSK, Sanofi, Novavax</td>
<td>Phase 3 clinical trial launched May 2021</td>
</tr>
<tr>
<td>and Adjuvant</td>
<td></td>
<td>EUA TBD</td>
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</table>
Science’s Breakthrough of the Year 2020: COVID-19 Vaccines
COVID-19 Vaccines are:

- Efficacious in clinical trials
- Effective in real-world settings
- Safe
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- Effective in real-world settings
- Safe
Pfizer/BioNTech Vaccine

Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine

FP Polack et al. for the C4591001 Clinical Trial Group

Efficacy: 95%

Moderna Vaccine

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

LR Baden et al. for the COVE Study Group

Efficacy: 94.1%
Johnson & Johnson (Janssen) Vaccine

Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against COVID-19

J Sadoff et al. for the ENSEMBLE Study Group

- 66% efficacy overall vs. moderate-to-severe COVID-19
  - 72% in United States
  - 68% in Brazil
  - 64% in South Africa

- 85% efficacy vs. severe disease across all regions studied
COVID-19 Vaccines are:

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Early Evidence of the Effect of SARS-CoV-2 Vaccine at One Medical Center

W Daniel, DK Podolsky et al.

- 23,234 employees of University of Texas Southwestern Medical Center, Dallas, TX; vaccination program initiated 12/15/2020
- 0.05% infection rate among fully vaccinated employees
Impact and Effectiveness of mRNA BNT162b2 Vaccine Against SARS-CoV-2 Infections and COVID-19 Cases, Hospitalisations, and Deaths Following a Nationwide Vaccination Campaign in Israel: An Observational Study Using National Surveillance Data

EJ Haas, S Alroy-Preis et al.
Effect of Robust COVID-19 Vaccination Program in Israel

Israel, population 9.1 million

COVID metrics for June 1, 2021
- New Cases: 17*
- New Deaths: 1*
- Hospitalized: 87

*7-day rolling average

Source: Our World in Data
Estimated Effectiveness of 2 Doses of Pfizer/BioNTech COVID-19 Vaccine Against 6 Outcomes, Israel

- All ages, 201.9 million person-years total
- B.1.1.7 variant accounted for ~95% of SARS-CoV-2 infections

Estimated adjusted effectiveness, ≥7 days after the second dose, Jan 24 to April 3, 2021

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effectiveness</th>
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<tbody>
<tr>
<td>SARS-CoV-2 infection</td>
<td>95.3%</td>
</tr>
<tr>
<td>Asymptomatic SARS-CoV-2 infection</td>
<td>91.5</td>
</tr>
<tr>
<td>Symptomatic COVID-19</td>
<td>97.0</td>
</tr>
<tr>
<td>COVID-19-related hospitalization</td>
<td>97.2</td>
</tr>
<tr>
<td>Severe or critical COVID-19-related hospitalization</td>
<td>97.5</td>
</tr>
<tr>
<td>COVID-19-related death</td>
<td>96.7</td>
</tr>
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### Estimated Effectiveness of 2 Doses of Pfizer/BioNTech COVID-19 Vaccine Against SARS-CoV-2 Infection, by Age Group, Israel

**Estimated adjusted effectiveness, ≥7 days after the second dose, Jan 24 to April 3, 2021**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>VE vs. SARS-CoV-2 infection</th>
</tr>
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<tbody>
<tr>
<td>All ages</td>
<td>95.3%</td>
</tr>
<tr>
<td>Age 16-44 years</td>
<td>96.1</td>
</tr>
<tr>
<td>Age 45-64 years</td>
<td>94.9</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>94.8</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td>95.1</td>
</tr>
<tr>
<td>Age ≥85 years</td>
<td>94.1</td>
</tr>
</tbody>
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Interim Estimates of Vaccine Effectiveness of Pfizer-BioNTech and Moderna COVID-19 Vaccines Among Health Care Personnel — 33 U.S. Sites, January–March 2021

- Test-negative design case-control study; 623 case-patients and 1,220 controls in 25 states
- Adjusted vaccine effectiveness (VE) of 2 doses of Pfizer-BioNTech or Moderna COVID-19 (measured ≥7 days after the second dose): 94% against symptomatic COVID-19
- VE after 1 dose: 82%
Real-World Effectiveness of Ad26.COV2.S Adenoviral Vector Vaccine for COVID-19

J Corchado-Garcia et al.

- Multi-state Mayo Clinic health system (MN, AZ, FL, WI, IA)
- After at least 2 weeks of follow-up, 3 of 1,779 people vaccinated with Johnson & Johnson vaccine tested positive for SARS-CoV-2 compared to 128 of 17,744 unvaccinated individuals
- Vaccine effectiveness: 76.7%
COVID-19 Vaccines are:

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- Effective in real-world settings
- Safe
Ensuring COVID-19 Vaccine Safety in the U.S.

- Clinical trials
- Expanded safety monitoring systems
  - CDC: V-safe
  - CDC: National Healthcare Safety Network (NHSN)
  - FDA: Other large insurer/payer databases
- Other safety monitoring systems
  - CDC and FDA: Vaccine Adverse Event Reporting System (VAERS)
  - CDC: Vaccine Safety Datalink (VSD)
  - CDC: Clinical Immunization Safety Assessment (CISA) Project
  - FDA and the Centers for Medicare and Medicaid Services: Medicare data
  - FDA: Biologics Effectiveness and Safety System (BEST)
  - FDA: Sentinel Initiative
  - DoD, VA systems

Impact of Viral Variants on Vaccine Effectiveness
Selected SARS-CoV-2 Variants

**B.1.1.7**
originally United Kingdom

**B.1.351**
originally South Africa

**P.1**
originally Brazil

**B.1.429/B.1.427**
originally California

**B.1.526**
originally New York

**B.1.617**
originally India
Effectiveness of the BNT162b2 COVID-19 Vaccine against the B.1.1.7 and B.1.351 Variants

LJ Abu-Raddad et al. for the National Study Group for COVID-19 Vaccination

- Mass vaccination campaign in Qatar; total n=385,853

- Vaccine effectiveness against any documented infection
  - B.1.1.7 -- 89.5% after 2 doses, 29.5% after 1 dose
  - B.1.351 -- 75.0% after 2 doses, 16.9% after 1 dose

- Vaccine effectiveness against severe, critical, or fatal disease
  - B.1.1.7 -- 100% after 2 doses, 54.1% after 1 dose
  - B.1.351 -- 100% after 2 doses, 0% after 1 dose
Improved Neutralization of SARS-CoV-2 Variants After 2nd Pfizer Vaccine Dose

1 dose

Week 2

Week 3

2 doses

Week 4 (1 week after 2nd dose)

Week 6 (3 weeks after second dose)

No. of vaccinees

BNT162b2-Elicited Neutralization against New SARS-CoV-2 Spike Variants

Y Liu, P-Y Shi et al.

- The newly emerged B.1.526, B.1.429, and B.1.1.7+E484K variants remain susceptible to neutralizing antibodies

- The E484K mutation (also found in the B.1.351 and B.1.526 lineages) caused little compromise to neutralization
Most individuals vaccinated with mRNA-1273 (Moderna vaccine), including older individuals, maintained binding and functional antibodies against SARS-CoV-2 variants B.1.1.7, B.1.351, P.1, B.1.429, and B.1.526 antibodies for >6 months.

“While the correlates of vaccine-induced protection are not yet known, our data are encouraging for the use of this vaccine in the face of viral variation.”
Update on the B.1.617 Variant

- The modest neutralization resistance of B.1.617.1 variant to vaccine-elicited antibodies suggests that current vaccines will be protective.

Selected references:

- **SARS-CoV-2 B.1.617 Emergence and Sensitivity to Vaccine-Elicited Antibodies**
  May 8, 2021
  I Ferreira, RK Gupta et al.

- **Infection and Vaccine-Induced Neutralizing Antibody Responses to the SARS-CoV-2 B.1.617.1 Variant**
  May 9, 2021
  V Edara, MS Suthar et al.

- **Neutralization Potential of Covishield Vaccinated Individuals Against B.1.617.1**
  May 12, 2021
  PD Yadav, B Bhargava et al.

- **The Spike Proteins of SARS-CoV-2 B.1.617 and B.1.618 Variants Identified in India Provide Partial Resistance to Vaccine-Elicited and Therapeutic Monoclonal Antibodies**
  May 14, 2021
  T Tada, NR Landau et al.
Press Release

May 22, 2021

Vaccines Highly Effective Against B.1.617.2 Variant after 2 Doses

From April 4 to May 16, 2021,

- 2 weeks after the second dose, Pfizer-BioNTech vaccine was 88% effective against symptomatic disease from B.1.617.2 variant and 93% effective against B.1.1.7 variant.

- 2 doses of AstraZeneca vaccine were 60% effective against B.1.617.2 and 66% effective against B.1.1.7.

- 3 weeks after first dose, both vaccines were 33% effective against symptomatic disease from B.1.617.2 and ~50% effective against B.1.1.7.
The Race is On

SARS-CoV-2

Vaccines