COVID-19 Vaccine Development

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We need to develop multiple vaccine platforms.

No single vaccine platform can be manufactured at enough scale to immunize the 4.4 billion adult population on the planet and 3 billion children. - 220 million adults in US alone.

Use known platforms to cover the field scientifically. Manufacturing scalability is a key factor.

Coordinated USG effort to involve global vaccine manufacturing companies.

There must be an unprecedented coordinated approach to test, manufacture the vaccine at scale, and deliver the vaccine into peoples’ arms throughout the world.
**Goal of OWS Program: To Assess Major Vaccine Platforms to COVID-19**

**Platform Vaccine Technologies**

- **Protein vaccines**
  - soluble prefusion trimer (Sanofi/GSK)
  - transmembrane bound spike nanoparticle (Novavax)

- **Viral vector vaccines**
  - Ad26 vector
  - ChimpAdOx1

- **RNA and DNA technology**
### Immunogenicity Data from Phase 1 Clinical Trials

<table>
<thead>
<tr>
<th></th>
<th>Moderna 100 ug 2 dose</th>
<th>ChAdOx1 nCoV-19 2 dose</th>
<th>Ad26 1 dose 5x10^{10} VP</th>
<th>Novavax 5 ug/50 ug 2 dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spike GMT</strong></td>
<td></td>
<td>1:1,000</td>
<td>596</td>
<td></td>
</tr>
<tr>
<td><strong>Live virus neut GMT</strong></td>
<td></td>
<td>1:400</td>
<td>1:214</td>
<td></td>
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<tr>
<td><strong>Pseudovirus neut GMT</strong></td>
<td></td>
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*The data are not in the same lab.*
The full development pathway for an effective vaccine for SARS-CoV2 will require that industry, government, and academia collaborate in unprecedented ways, each adding their individual strengths. . . . We further discuss a collaborative platform for conducting harmonized, randomized controlled vaccine efficacy trials. This mechanism aims to generate essential safety and efficacy data for several candidate vaccines in parallel, so as to accelerate the licensure and distribution of multiple vaccine platforms and vaccines to protect against COVID-19.
Organizational Structure of OWS Clinical Trials Program

Harmonized Efficacy Trials

- Platform 1: RNA
- Platform 2: ChAdOx1
- Platform 3: Ad26
- Platform 4: Nanoparticle
- Platform 5: Pre-fusion Spike Recombinant Protein

Collaborating clinical trial networks (CoVPN)

Harmonized endpoint data collection

Common Labs
1. Defining infection from disease
2. Quantitative immune responses to spike and spike epitopes
3. T-cell responses

Corelates of protection analyses within and cross protocols

Common DSMB

1. Defining infection from disease
2. Quantitative immune responses to spike and spike epitopes
3. T-cell responses
## COVID-19 Prevention Network Phase 3 Efficacy Trial Timeline

<table>
<thead>
<tr>
<th></th>
<th>July</th>
<th>August</th>
<th>September</th>
<th>October</th>
<th>November</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderna</td>
<td>AstraZeneca</td>
<td>Johnson &amp; Johnson</td>
<td>Novavax</td>
<td>Sanofi</td>
</tr>
<tr>
<td></td>
<td>July 27</td>
<td>August 29</td>
<td>September 22</td>
<td>Early</td>
<td>Late</td>
</tr>
<tr>
<td></td>
<td>Pfizer</td>
<td>Paused Sept 9</td>
<td>Johnson &amp; Johnson</td>
<td>December</td>
<td>December</td>
</tr>
<tr>
<td></td>
<td>July 28</td>
<td></td>
<td></td>
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</table>
Balancing Harmonized Clinical Trial Design with Regulatory Realities

Main Goal: To evaluate each candidate vaccine with high veracity for safety and potential efficacy in reducing COVID-19 Disease.

- Each trial 30,000 persons; 150 disease endpoints
- Critical to enroll Black, LatinX and Tribal Communities into each trial
- Essential to evaluate vaccines in the epidemiological setting of persons at greatest risk of its complications; including comorbidities, age and race
WHAT’S THE CHALLENGE?

WE NEED OVER 125,000 VOLUNTEERS READY TO ROLL UP THEIR SLEEVES BY THE END OF 2020
Projected # Cases of COVID-19 in 30,000-person 2 Dose SARS-CoV-2 Vaccine Trial
This is how we designed the trial.
# Cases of COVID-19 in 30,000-person 2 Dose SARS-CoV-2 Vaccine Trial

This is how it is working out

**Enrollment Period**

**Safety Follow Up**

23 weeks
## mRNA Vaccines

<table>
<thead>
<tr>
<th>Pfizer Vaccine</th>
<th>Moderna Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prefusion spike transcript</td>
<td>Prefusion spike transcript</td>
</tr>
<tr>
<td>2 doses 21 days apart</td>
<td>2 doses 28 days apart</td>
</tr>
<tr>
<td>VE = 95%</td>
<td>VE = 94.5% efficacy</td>
</tr>
<tr>
<td>162 cases of symptomatic disease in placebo; 8 in vaccine group</td>
<td>90 cases of symptomatic disease in placebo; 5 in vaccine group</td>
</tr>
<tr>
<td>10 cases of severe disease; 9 in placebo, 1 in vaccine</td>
<td>11 cases of severe disease - all 11 in placebo group</td>
</tr>
<tr>
<td>VE 94% in those &gt;65</td>
<td>No difference in VE by age and ethnicity (20% endpoints in these groups)</td>
</tr>
</tbody>
</table>
• To have 2 large scale efficacy trials enrolled and completed independently, with such similar results, is remarkable.

• The spike part of the RNA transcript is essentially identical; allowing one to feel quite comfortable about the veracity of the efficacy data.

• The safety data from the trials needs to be made public, so one can evaluate it. Available data suggest the vaccines are well tolerated, more side effects with the second dose and somewhat lower severity of systemic side effects in older persons.

• The similarity of the data means either vaccine can do the job and should simplify that part of the distribution process.
Marvelous - but we are not done!

- Vaccines don’t save lines; vaccinating people saves lives!
- USG contracts for mRNA is 100 million doses from each company.
- Timeline uncertain, but supposedly we will get these cumulative 200 million by April / May 2021.
  - 25 million doses Pfizer and 15 million Moderna in December
  - 30 million doses Pfizer and 20 million Moderna in January
  - 35 million Pfizer and 25 million Moderna in February and March
  - This is enough for first responders, medical personnel, elderly, and staff in nursing homes; and getting close to the complete NAM 1B group
- We need the other vaccines for the rest of the adult populations, as well as kids and pregnant women, where experience is much greater with Ad26 vector and the recombinant protein vaccines with adjuvants.
- Keeping the ongoing trials, as well as creating way to test the Recombinant Protein Platforms post EUA, is critical for overall vaccine strategy and getting everyone back to school and work.
- This means keeping the AZ and Janssen trials intact until end of February / mid-March.
We do not know if the vaccine reduces acquisition of infection. Do persons still get infected after vaccination and if so, are they still infectious to others?
  • Shifting the disease spectrum from 75% symptomatic / 25% asymptomatic to 5% symptomatic / 95% asymptomatic

If this is the case, community spread and population-based effects will be highly dependent on vaccine coverage; individual cases of severe disease will likely occur – especially in underserved populations.
  • In HIV terms - U = U
  • In COVID-19 terms - does VEi = U?

On an individual level - do I still need to wear a mask after vaccination?
  • Until we find this out – yes!

The infectivity of this pathogen is formidable and defining the effect of these vaccines on infectivity and onward transmission is the next frontier for us to investigate.
Thank You

**Network Collaboration**
- HVTN Executive Management Team:
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- IDCRC
- David Montefiori

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- Francis Collins
- Hilary Marston
- Hugh Auchincloss

**OWS**
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- Mary Marovich
- Merlin Robb
- Tina Tong
- Julie Ake