NAIIS – DEVELOPING COVID-19 VACCINES IN RECORD TIME

November 8, 2021
SETH TOBACK, MD, FAAP

NVX-CoV2373 Vaccine Design

1. SARS-CoV-2 Spike gene inserted into insect virus
   The full-length, stabilized Spike gene is engineered into baculovirus.

2. SF9 cells infected
   Recombinant baculovirus infects S. frugiperda (SF9) in the insect cell expression system.

3. Spike gene enters SF9 cell nucleus
   Spike DNA is transcribed.

4. SF9 cells produce Spike
   Spike protein are expressed in their native trimer confirmation.

5. Nanoparticle formation
   Spike protein trimers are harvested. Vaccine nanoparticles assemble as six protein trimers arrange around a Poly saccharide (PS80) core.

6. Final vaccine
   Vaccine nanoparticles are mixed with Matrix-M™ adjuvant to create ready-to-use NVX-CoV2373 vaccine.
**PREVENT-19 Phase 3 Trial**

Enrollment complete: adult and pediatric cohorts in follow-up

Top-line adult randomized efficacy and safety results available for review

Randomized, observer-blinded, placebo-controlled trial evaluating efficacy, immunogenicity and safety.

- Primary endpoint: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose

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Enrollment and Diversity

29,949 adult participants enrolled

119 sites in US and Mexico

Pediatric expansion enrollment complete

- 21.5% Latin American
- 11.0% African American
- 6.2% Native American
- 4.4% Asian American

*Enrollment and diversity data is representative of the main study population (participants >18 years) and does not include pediatric expansion participants.*
High-Level Safety Summary Through Crossover

Serious and Severe adverse events were infrequent and balanced

<table>
<thead>
<tr>
<th>Event</th>
<th>NVX-CoV2373 N=19,729</th>
<th>Placebo N=9,853</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any treatment-emergent adverse event</td>
<td>16.3%</td>
<td>14.8%</td>
</tr>
<tr>
<td>Any medically attended adverse event</td>
<td>7.0%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Any severe treatment-emergent adverse event</td>
<td>1.3%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Adverse events of special interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potentially immune-mediated</td>
<td>0.1%</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td>COVID-19 related</td>
<td>&lt;0.1%</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td>Serious treatment emergent adverse events</td>
<td>0.9%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Deaths</td>
<td>0.02%</td>
<td>0%</td>
</tr>
</tbody>
</table>

No single adverse event occurred in more than 1% of vaccine group

Reactogenicity 7 Days After Dose 1 and Dose 2

Pain and Tenderness most common local symptom ≤ 3 days’ duration
Fatigue, Headache, and Muscle Pain most common systemic symptom ≤ 2 days’ duration
**Primary Endpoint: PCR-Confirmed Mild, Moderate, or Severe COVID-19 Illness Occurring ≥7 Days After Second Dose in Baseline Seronegative Participants**

<table>
<thead>
<tr>
<th></th>
<th>NVX-CoV2373 (n=17,298)</th>
<th>Placebo (n=8,077)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>14</td>
<td>63</td>
</tr>
<tr>
<td>Mild</td>
<td>14</td>
<td>49</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td><strong>Vaccine Efficacy</strong></td>
<td><strong>90.4%</strong> (95% CI: 82.9; 94.6)</td>
<td></td>
</tr>
</tbody>
</table>

- Statistical success criteria included lower bound of 95% CI >30%
- 82% of cases caused by Variants of Concern and Variants of Interest
- All breakthrough cases in the vaccine group were mild

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**Key Secondary Endpoint: Efficacy Against Variants NOT Currently Considered Variants of Concern or Variants of Interest**

<table>
<thead>
<tr>
<th></th>
<th>NVX-CoV2373 (n=17,312)</th>
<th>Placebo (n=8,127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Vaccine Efficacy</strong></td>
<td><strong>100%</strong> (95% CI: 85.84; 100)</td>
<td></td>
</tr>
</tbody>
</table>

- Statistical success criteria included lower bound of 95% CI >30%
- Sequence not available for 23 cases: 21 mild (8 in vaccine, 13 in placebo), 1 moderate in placebo, and 1 severe in placebo
Secondary Endpoint: PCR-confirmed Moderate or Severe COVID-19 Illness Occurring ≥7 days After Second Dose in Baseline Seronegative Participants

Efficacy for viral isolates NOT currently considered Variants of Concern/Interest

<table>
<thead>
<tr>
<th></th>
<th>NVX-CoV2373 (n=17,312)</th>
<th>Placebo (n=8,126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Vaccine Efficacy 100% (95% CI: 87.0; 100)

- Post-hoc analysis for severe disease only VE = 100% (95% CI 34.8; 100)
- An additional 6 COVID-19 hospitalizations (including 1 death) occurred in the placebo group but were not included in the efficacy analysis because PCR samples were not evaluated in the central lab

High Levels of Efficacy Maintained Against Variants of Concern and Variants of Interest

Efficacy for viral isolates considered Variants of Concern/Interest

<table>
<thead>
<tr>
<th></th>
<th>NVX-CoV2373 (n=17,312)</th>
<th>Placebo (n=8,140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>7</td>
<td>41</td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>31</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Vaccine Efficacy 92.6% (95% CI 83.6; 96.7)
Secondary Endpoint: Subgroup Analysis in High-Risk Population

Vaccine efficacy in high-risk population

<table>
<thead>
<tr>
<th></th>
<th>NVX-CoV2373 (n=16,493)</th>
<th>Placebo (n=7,737)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Efficacy</td>
<td>91.0% (95% CI: 83.6; 95.0)</td>
<td>62</td>
<td>13</td>
</tr>
</tbody>
</table>

High Risk Defined as:
- > 65 years of age
- <65 years of age with obesity, chronic kidney disease, chronic lung disease, cardiovascular disease, Type 2 diabetes
- Life circumstances with frequent COVID-19 exposure (e.g., meat packing plants) or densely populated living conditions

NVX-CoV2373 Efficacy Summary

- Results from 2 independent efficacy analyses demonstrate statistically significant efficacy
  - Final UK Phase 3 (N=15,187) VE = 89.7% (95% CI: 80.2; 94.6)\(^1\)
    - Blend of B.1.1.7 variant and non-B.1.1.7 variants
  - Final US Phase 3 (N=25,452) VE = 90.4% (95% CI: 82.9; 94.6)\(^2\)
    - Blend of variants with B.1.1.7 being the most predominant
- Efficacy estimates from post hoc analysis varied with level of drift from prototype sequence used in NVX-CoV2373
  - Alpha VE = 86.3% to 93.6%\(^1,2\)
  - Non-VOC/VOI VE = 96.4% to 100%\(^1,2\)
  - Beta VE = 51.0%\(^3\)
  - Severe disease VE = 100%\(^2\)
  - Moderate/Severe disease VE = 86.9% to 100%\(^2,4\)
  - Delta Immunogenicity (next few slides)
- Adolescent data (12-17 years) will be available shortly

\(^1\) Heath et al., NEJM 2021
\(^2\) Dunkle et al., medRxiv 2021
\(^3\) Shinde et al., NEJM 2021
Robust Anti-Spike IgG Responses
Vaccination on Day 0 and 21 with boost on Day 189

Titers increased ~4.6-fold compared to peak response seen after primary vaccination series.

Boosted Anti-spike IgG Responses
Greater than Observed in Phase 3 Studies

UK Phase 3 Efficacy
- non-B.1.1.7: 96%
- B.1.1.7: 86%
- All strains: 90%

PREVENT-19 Efficacy
- Non-VoI/VoC: 100%
- B.1.1.7: 94%
- All strains: 90%

† Indicates post hoc analysis

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Functional hACE2 Inhibition Responses Increased for All Variants with a Single Booster Dose of NVX-CoV2373
Post-boost consistency suggests maturation of immune response

NVX-CoV2373 Investigational Vaccine Candidate
Administration and Storage

- Two 0.5 mL doses 3 to 4 weeks apart via intramuscular injection.
- Administer using 1-mL syringe and standard 22- to 25-gauge needle.
- No reconstitution or dilution required.
- Each multi-dose vial contains 10 doses (0.5 mL/dose).
- Store in refrigerator at 2°C to 8°C (36°F to 46°F); do not freeze.
- Does not contain preservative; store opened vial between 2°C to 25°C for up to 6 hours after first puncture.
- Proposed use: 18 years old and up, primary 2-dose series
- Timeline: 110 million doses, US regulatory submission-rolling
THANK YOU