COVID-19 Vaccines for Children

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US Effort in Trials for Special Populations

- Goal: “SARS CoV2 vaccine for whole of US population”
- USG will provide resources for vaccine trials in pregnant women and pediatrics
- Company can elect to be the sponsor
- Protocols must be approved by USG partners with NIAID, BARDA, engaged on protocol team
- Protocol chairs will include NIAID-funded investigators
- USG partners and company will jointly oversee operationalization of the studies
- Joint oversight team (BARDA, NIAID, Company) will resolve conflicts
Rationale for Pediatric SARS CoV2 Vaccine Trials

- Pediatric burden of disease is significant
- Disproportionate burden among children in minority communities
- Indirect effects to the child and society (school, development, etc)
- Continued burden if we wait for natural “herd” effects
- Data suggests that vaccination prevents asymptomatic carriage, thus reversing pandemic more rapidly
- Safety data are best collected in clinical trials

Table 1. Numbers of hospitalizations and deaths for COVID-19 in comparison to varicella, rubella, hepatitis A, and rotavirus in pre-vaccine era*

<table>
<thead>
<tr>
<th>Virus</th>
<th>Hospitalizations/year</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19</td>
<td>19.4 per 100,000 age 0-4 yrs 11.4 per 100,000 age 5-17 yrs Through 10/10/2020</td>
<td>185 children Age ≤ 18 yrs Through 12/16/2020</td>
</tr>
<tr>
<td>Varicella</td>
<td>4-13 per 100,000 Age &lt; 20 yrs Years 1988 – 1995</td>
<td>50 children per year Age&lt; 15 yrs Years 1970-1994</td>
</tr>
<tr>
<td>Rubella</td>
<td>Not available</td>
<td>17 children per year All ages Years 1966 – 1968</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>107 hospitalized children Age &lt; 15 yrs Year 2005</td>
<td>3 children per year Age &lt; 20 yrs Years 1990 – 1995</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>55,000 - 70,000 children Age &lt; 5 yrs Years 1993 – 2002</td>
<td>20 – 60 children per year Age &lt; 5 yrs Years 1999 - 2007</td>
</tr>
<tr>
<td>Influenza</td>
<td>34-92 per 100,000 age 0–4yrs 20-41 per 100,000 age 5-17 yrs for 2016 – 2020 season</td>
<td>110-192 children per year Years 2016 – 2020</td>
</tr>
</tbody>
</table>

Updated table courtesy of Evan Anderson
Vaccine clinical development: Children

<table>
<thead>
<tr>
<th>Platform/Design</th>
<th>mRNA: encodes stabilized spike; lipid NP</th>
<th>mRNA: encodes 2P-stabilized spike; lipid NP</th>
<th>Replication incompetent Ad26; stabilized spike</th>
<th>Replication incompetent ChAdOx1 chimp Ad; wild type spike</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose/ Schedule Adults</td>
<td>IM 2 doses X 30 µg 21 days apart</td>
<td>IM 2 doses 100 µg 28 days apart</td>
<td>IM 1 dose at 5 x 10^{10} vp (also testing 2 doses (0, 56 days))</td>
<td>IM 2 doses at 5 x 10^{10} vp, (0, 28 days)</td>
</tr>
<tr>
<td>Current Status</td>
<td>EUA ages 16 and up</td>
<td>EUA ages 18 and up</td>
<td>Phase 3 adults</td>
<td>Phase 3 adults</td>
</tr>
<tr>
<td>Adolescents</td>
<td>Fully enrolled</td>
<td>TeenCOVE</td>
<td>Start 4-6wks after results from adult trials</td>
<td>Begin Early 2021</td>
</tr>
<tr>
<td>Younger Children</td>
<td>Planning early 2021</td>
<td>Planning early 2021</td>
<td>Planning early 2021</td>
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</tr>
<tr>
<td>Comments</td>
<td>Platform used widely in teens, infants, children</td>
<td></td>
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</tr>
</tbody>
</table>

Others supported by USG: Novavax (Ph3 enrolling), Sanofi
Approaches to label indication for vaccination in age 12-17 yr old cohort

- Expand age eligibility in adult efficacy trials (Pfizer/BioNTech)
- Stand-alone trial for safety (Moderna TeenCOVE)
- Expand age eligibility in Phase 2 trials for immunogenicity/safety

TeenCOVE Study

Figure 1: Study Schema

mRNA-1273 Phase 2/3 Adolescent (12 to <18 yo) Study

Abbreviations: D = day; DME = Data Safety Monitoring Event; IT = intent analysis; iv = intravenous; IV = intravenous; LM = local monitoring; V = visit; yo = year old
Example: dose-ranging study in children, infants to <12 years

- Protocols in development
- 3 age groups:
  - 6 to <12 years
  - 2 to < 6 years
  - Infants to < 2 years
- May relatively large N for safety if novel platform
- May test multiple dose levels
  - Full, half, and quarter doses considered by age group