Efficacy Results of FLUCELVAX Quadrivalent (ccIIV4) in Subjects ≥2 years to <18 years

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OUTLINE

- Background
- Phase III Randomized Clinical Trial
  - Objectives
  - Design
  - Location & Demographics
  - Results
    - Efficacy
    - Safety
- Conclusion
BACKGROUND

• Cell-based influenza vaccines avoid egg adaptation, thus potentially resulting in a closer match to selected vaccine strains by FDA/WHO¹

• ccIIV4 was licensed for the prevention of influenza in subjects ≥4 years of age by the U.S. Food and Drug Administration (FDA) in 2016 based on immunogenicity and safety data

• This is the first efficacy study with a quadrivalent cell-based influenza vaccine in a pediatric population and is a FDA requirement to demonstrate efficacy in this population

¹. Pérez Rubio A & Eiros JM. Hum Vaccin Immunother. 2018;14:1874–1882
STUDY OBJECTIVES

• **Primary:** Demonstrate vaccine efficacy (VE) of ccIIV4 in preventing influenza vs non-influenza comparator vaccine†
  • **SUCCESS:** Lower limit of the 2-sided 95% confidence interval for VE exceeds 20%

• **Secondary:** Demonstrate VE of ccIIV4 in preventing influenza due to any and vaccine-matched strains

• Immunogenicity: Characterization of immune response by HI and MN assays in a subset of subjects

• **Safety and Tolerability:** Solicited and unsolicited adverse events throughout the study

†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals
VACCINE TRIAL DESIGN

• Double Blind Placebo Controlled Trial / Randomized in a 1:1 fashion
  • ccIIV4 60 μg/0.5 mL pre-filled syringe, IM
    ✓ Season 1 - ccIIV4 Southern Hemisphere 2017
    ✓ Season 2 - ccIIV4 Northern Hemisphere 2017/2018
    ✓ Season 3 - ccIIV4 Northern Hemisphere 2018/2019

• Non-Influenza Comparator
  ✓ Menveo: conjugate MenACWY (CRM₁₉₇) vaccine, 0.5 mL, IM
  ✓ Second dose placebo 0.9% saline, 0.5 mL, IM

• Previously Vaccinated (2/3 of study population)
  • Any subject 9 yrs. to <18 yrs., or any subject 2 yrs. to <9 yrs. who had received 2 or more flu vaccines prior to enrollment

• Previously Not Vaccinated (1/3 of study population)
  • Any subject 2 yrs. to <9 yrs. who had not received 2 or more doses of flu vaccine prior to enrollment
### SEASON 1
**S HEMISP. 2017**
- PHILIPPINES 1800
- THAILAND 400
- AUSTRALIA 195
**TOTAL 2395**

### SEASON 2
**N HEMISP. 2017/18**
- ESTONIA 600
- FINLAND 319
**TOTAL 919**

### SEASON 3
**N HEMISP. 2018/19**
- ESTONIA 598
- POLAND 298
- LITHUANIA 292
- FINLAND 7
- SPAIN 5
**TOTAL 1200**

**PARTICIPATING COUNTRIES**

**8 PARTICIPATING COUNTRIES**

**39 SITES**

**4514 TOTAL ENROLLMENT**
## DEMOGRAPHICS AND BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
<th></th>
<th>ccIIV4 N=2258</th>
<th>Control† N=2256</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>8.7 (4.0)</td>
<td>8.9 (4.1)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>1152 (51.0)</td>
<td>1174 (52.0)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>1106 (49.0)</td>
<td>1082 (48.0)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>1106 (49.0)</td>
<td>1100 (48.8)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>1140 (50.5)</td>
<td>1139 (50.5)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>11 (0.5)</td>
<td>15 (0.7)</td>
</tr>
<tr>
<td><strong>Prior vaccination status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previously vaccinated, n (%)</td>
<td>1488 (65.9)</td>
<td>1487 (65.9)</td>
</tr>
<tr>
<td>Not previously vaccinated, n (%)</td>
<td>770 (34.1)</td>
<td>769 (34.1)</td>
</tr>
<tr>
<td><strong>Season</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SH 2017, n (%)</td>
<td>1199 (53.1)</td>
<td>1196 (53.0)</td>
</tr>
<tr>
<td>NH 2017-2018, n (%)</td>
<td>459 (20.3)</td>
<td>460 (20.4)</td>
</tr>
<tr>
<td>NH 2018-2019, n (%)</td>
<td>600 (26.6)</td>
<td>600 (26.6)</td>
</tr>
</tbody>
</table>
**PRIMARY OBJECTIVE: ABSOLUTE VACCINE EFFICACY**
RT-PCR CONFIRMED INFLUENZA

Any strain, across seasons

<table>
<thead>
<tr>
<th></th>
<th>ccIIV4 N=2257</th>
<th>Control† N=2252</th>
<th>aVE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any strain</td>
<td>n (attack rate)</td>
<td>n (attack rate)</td>
<td></td>
</tr>
<tr>
<td>Overall RT-PCR-confirmed cases</td>
<td>175 (7.8)</td>
<td>364 (16.2)</td>
<td>54.6 (45.7, 62.1)</td>
</tr>
</tbody>
</table>

- ccIIV4 prevented RT-PCR confirmed influenza (any Influ. A or B strain), with an absolute vaccine efficacy of 54.6%
- Pre-specified criterion for success was met

The lower bound of the 95% CI exceeded 20%
†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals
**SECONDARY OBJECTIVE: ABSOLUTE VACCINE EFFICACY**
**CULTURE-CONFIRMED INFLUENZA BY ANY STRAIN VS MATCHED STRAIN**

<table>
<thead>
<tr>
<th>Strain</th>
<th>% (95% CI) Any</th>
<th>% (95% CI) Matched</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>60.8 (51.3, 68.5)</td>
<td>63.6 (53.6, 71.5)</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>82.3 (70.3, 89.4)</td>
<td>82.1 (69.9, 89.3)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>43.4 (17.7, 61.1)</td>
<td>45.5 (5.9, 68.5)</td>
</tr>
<tr>
<td>Type B</td>
<td>51.2 (32.7, 64.6)</td>
<td>NA</td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>NA</td>
<td>51.6 (32.5, 65.3)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>NA</td>
<td>NA†</td>
</tr>
</tbody>
</table>

‡Not estimable, due to insufficient circulating strain.

aVE, absolute vaccine efficacy; CI, confidence interval; NA, not available; RT-PCR, reverse transcription polymerase chain reaction.
SOLICITED LOCAL AND SYSTEMIC ADVERSE EVENTS

Subjects reporting solicited AEs, %

Local AEs

- Tenderness
  - Any: 28.7, 25.4
  - Severe: 1.0, 1.4

- Pain
  - Any: 23.8, 19.0
  - Severe: 0.7, 1.2

- Erythema
  - Any: 19.3, 21.2
  - Severe: 0.2, 0.8

- Induration
  - Any: 12.7, 13.1
  - Severe: 0.1, 0.3

- Ecchymosis
  - Any: 7.5, 6.3
  - Severe: 0.0, 0.0

Systemic AEs

- Headache
  - Any: 16.7, 15.5
  - Severe: 1.0, 0.6

- Fatigue
  - Any: 15.9, 16.3
  - Severe: 1.0, 1.0

- Sleepiness
  - Any: 14.9, 17.6
  - Severe: 0.9, 1.8

- Irritability
  - Any: 13.8, 10.8
  - Severe: 0.2, 0.5

- Fever
  - ≥38°C: 5.3, 4.5
  - ≥40°C: 0.3, 0.2

†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals
‡Collected on diary card for subjects age ≥6 years only;
§Collected on diary card for subjects aged 2 to <6 years only.
AE, adverse event; ccIIIV4, cell-based quadrivalent influenza vaccine.
FLUCELVAX Quadrivalent (ccIIV4) CONCLUSIONS

• First efficacy study with a cell-derived quadrivalent influenza vaccine in the Pediatric and Adolescent population (2-18 years)

• Overall vaccine efficacy was 54.6% (95% CI 45.7, 62.1)†

• ccIIV4 was well tolerated, with similar rates of solicited and unsolicited adverse events between the two vaccination groups

†The lower bound of the 95% CI exceeded 20%
CI, confidence intervals
Thank you
# Absolute Vaccine Efficacy by Season

**First-Occurrence RT-PCR- or Culture-Confirmed Influenza**

<table>
<thead>
<tr>
<th>Season</th>
<th>Season 1</th>
<th>Season 2</th>
<th>Season 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QIVc N=1198</td>
<td>Comparator N=1193</td>
<td>aVE(^a) (95%CI)</td>
</tr>
<tr>
<td>Any Strain - Number of cases (attack rate)</td>
<td>89 (7.4)</td>
<td>193 (16.2)</td>
<td>56.58 (44.18; 66.22)</td>
</tr>
<tr>
<td>Type A</td>
<td>48 (4.0)</td>
<td>101 (8.5)</td>
<td>54.15 (35.35; 67.48)</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>6 (0.5)</td>
<td>42 (3.5)</td>
<td>86.16 (67.45; 94.12)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>30 (2.5)</td>
<td>55 (4.6)</td>
<td>46.20 (16.06; 65.52)</td>
</tr>
<tr>
<td>Type B</td>
<td>42 (3.5)</td>
<td>92 (7.7)</td>
<td>55.95 (36.55; 69.42)</td>
</tr>
</tbody>
</table>

Source: Table 14.2.0.1.3.1.

Abbreviations: aVE = absolute vaccine efficacy; CI = confidence interval; Men ACWY = meningococcal (Serogroup ACWY) conjugate vaccine; QIVc = cell-derived quadrivalent subunit influenza virus vaccine.

\(^a\) Adjusted aVE is presented.

Note 1: The non-influenza comparator is meningococcal (Serogroup ACWY) conjugate vaccine. Previously vaccinated subjects under 9 years of age received 1 vaccination (QIVc or Men ACWY) on Day 1. For subjects under 9 years of age who had not been previously vaccinated, 2 vaccinations were administered; the comparator vaccine group received Men ACWY on Day 1 followed by a saline placebo vaccine on Day 29, whereas the QIVc group received 2 QIVc vaccinations on Days 1 and 29.