Safety and immunogenicity of a booster dose of Trumenba (MenB-FHbp)

Paul Balmer, PhD
Medical Development, Scientific and Clinical Affairs Pfizer Vaccines
MenB-FHbp (Trumenba) indication and dosing recommendations

Trumenba is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B in individuals 10 through 25 years of age\(^1\)

**ACIP Dosing Recommendations**\(^2\)

- For persons at increased risk* for meningococcal disease and for use during serogroup B meningococcal disease outbreaks, ACIP recommends that 3 doses of Trumenba be administered at 0, 1–2, and 6 months.
- When given to healthy adolescents who are not at increased risk* for meningococcal disease, ACIP recommends that 2 doses of Trumenba should be administered at 0 and 6 months.

*Increased risk defined as persons with persistent complement component deficiencies, persons with anatomic or functional asplenia, microbiologists routinely exposed to isolates of *N. meningitidis*, persons identified as at increased risk because of a serogroup B meningococcal disease outbreak.

MenB-FHbp: Composition and evaluation of breadth of coverage against diverse MenB strains

- Pfizer’s MenB vaccine is based on a surface-exposed factor H binding protein (FHbp)
  - Expressed in > 95% of invasive MenB strains
  - FHbp sequences segregate into two genetically and immunologically distinct subfamilies, A and B
  - MenB-FHbp contains two lipidated FHbp variants (A05 and B01), one from each subfamily

- Breadth of coverage against diverse MenB strains evaluated by hSBA
  - Established correlate to predict protection
  - 4 MenB strains representative of prevalent strains in the US used to determine hSBA responses
  - The FHbp variants expressed (A22, A56, B24, B44) are not matched to the vaccine components

<table>
<thead>
<tr>
<th>Strain ID (Variant)</th>
<th>ST Clonal Complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMB80 (A22)</td>
<td>cc41/44</td>
</tr>
<tr>
<td>PMB2001 (A56)</td>
<td>cc213</td>
</tr>
<tr>
<td>PMB2948 (B24)</td>
<td>cc32</td>
</tr>
<tr>
<td>PMB2707 (B44)</td>
<td>cc269</td>
</tr>
</tbody>
</table>

MenB-FHbp: Persistence and booster data

### Primary Studies

**Study 1012**<sup>1</sup>
- Phase 2 Trial
- Age: 11 to 18 years
- MenB-FHbp: 2 doses at 0,6 m
- MenB-FHbp: 3 doses at 0,2,6 m

**Study 1010**<sup>2</sup>
- Phase 2 Trial
- Age: 11 to 18 years
- MenB-FHbp: 3 doses at 0,2,6 m

**Study 1015**<sup>3</sup>
- Phase 2 Trial
- Age: 10 to 12 years
- MenB-FHbp: 3 doses at 0,2,6 m

**Control**

---

**Persistence and Booster study**

**STUDY 1033**<sup>4,5</sup>
- Enrolled from Primary Study into Phase 3 Extension

   - MenB-FHbp: Persistence and booster data
   - MenB-FHbp: 3 doses at 0,2,6 m

- Persistence Stage through 48 months
  - n=116
  - n=114
  - n=40
  - n=123
  - n=70

- Booster Stage
  - MenB-FHbp vaccination at 48 months and persistence up to 26 months*
  - n=64
  - n=59
  - n=33

---

*Persistence of booster response was evaluated up to 12 months for participants from Study 1010 and 26 months for participants from Study 1012
Safety profile following a MenB-FHbp booster dose was similar to that observed following the primary series*

- Pain at the injection site was the most commonly reported local reaction, reported by 84.4% to 93.5% of subjects.

- Fatigue (51.9% to 65.6%) and headache (37.5% to 56.3%) were the most commonly reported systemic events.

- 3.7% to 12.5% of subjects reported ≥1 AE:
  - 3 subjects reported related AEs:
    - Mild worsening of psoriasis (0.6m Group)
    - Influenza like illness, classified as a SAE (0.2m Group)
    - Moderate dizziness (0.2, 0.6m Group)

- No reported SAEs during persistence phase post booster (up to 26m).

*Subjects from Studies 1010 and 1012 who received a booster dose.

Data on File (Nov 2018), Pfizer, Inc
MenB-FHbp 2-dose schedule

Current recommended schedule for healthy adolescents aged 16-23 years of age
Proportion of individuals with hSBA responses $\geq 1:4$ to 4 representative MenB strains following the 2-dose (0,6 months) MenB-FHbp primary series and a booster at 48 months

% of subjects with hSBA titer $\geq 1:4$

*Pre first dose of primary series; 48m Post Primary; 24m Post Primary series, 26m Post Booster.
Number of subjects with valid and determinate hSBA titer for the given strain ranged from 405-424 at baseline (before 1st dose of MenB-FHbp Study 1012), 103-115 Stage 1 mITT population (12 months and 24 month Post Primary), Booster Stage mITT population 63-64 at 48 months Post Primary and 42-45 at 26 months Post Booster.
Proportion of individuals with hSBA responses ≥1:4 against all 4 representative MenB strains following the 2-dose (0,6 months) MenB-FHbp primary series and a booster dose at 48 months

% of subjects with hSBA titer ≥1:4 for all 4 diverse test strains

<table>
<thead>
<tr>
<th></th>
<th>Pre Primary</th>
<th>Pre Booster</th>
<th>1m</th>
<th>12m</th>
<th>24m</th>
<th>26m†</th>
<th>48m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Primary</td>
<td>0.9</td>
<td>73.4</td>
<td>17.4</td>
<td>17.9</td>
<td>23.8</td>
<td>23.8</td>
<td></td>
</tr>
<tr>
<td>Post Booster</td>
<td>23.8</td>
<td>91.8</td>
<td>62.7</td>
<td>42.1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Pre first dose of primary series; 48m Post Primary; †24m Post Primary series, 26m Post Booster.
Number of subjects with valid and determinate hSBA titer for the given strain ranged from 95-110 Stage 1 mITT population (before dose 1 to 24 months Post Primary), Booster Stage mITT population 59-63 at before booster to 12 months Post Booster and 38 at 26 months Post Booster.
MenB-FHbp 3-dose schedule

Current recommended schedule for those identified at high risk of MenB disease
Proportion of individuals with hSBA responses to 4 diverse MenB strains following the 3-dose (0,2,6 months) MenB-FHbp primary series compared to a control* group

% of Subjects with hSBA Titer ≥1:4

*Control = MenACWY/TdaP/Saline.

Number of subjects with valid and determinate hSBA titer for the given strain ranged from 94-122 MenB-FHbp and 51-69 Control group Stage 1 mITT population (1 month to 48 months Post Primary).

Data on File (Nov 2018), Pfizer, Inc
Proportion of individuals with hSBA responses ≥1:4 to 4 diverse MenB strains following the 3-dose (0,2,6 months) MenB-FHbp primary series and booster at 48 months

% of subjects with hSBA titer ≥1:4

*Pre first dose of primary series; 48m Post Primary; †24m Post Primary series, 26m Post Booster.
Number of subjects with valid and determinate hSBA titer for the given strain ranged from 417-426 at baseline (before 1st dose of MenB-FHbp Study 1012), 102-111 Stage 1 mITT population (12 months and 24 month Post Primary), Booster Stage mITT population 56-58 at 48 months Post Primary and 30-35 at 26 months Post Booster.

Data on File (Nov 2018), Pfizer, Inc
Immune response and antibody persistence above the threshold of protection for all 4 test strains following the **3-dose (0,2,6 months)** MenB-FHbp primary series and booster dose.

<table>
<thead>
<tr>
<th></th>
<th>Post Primary</th>
<th>Post Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre Primary</td>
<td>1.9</td>
<td>29.6</td>
</tr>
<tr>
<td>Pre Booster</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1m</td>
<td>84.3</td>
<td>100</td>
</tr>
<tr>
<td>12m</td>
<td>18.8</td>
<td>63.3</td>
</tr>
<tr>
<td>24m</td>
<td>19.1</td>
<td>46.4</td>
</tr>
<tr>
<td>26m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>48m</td>
<td>29.6</td>
<td></td>
</tr>
</tbody>
</table>

*Pre first dose of primary series; 48m Post Primary; †24m Post Primary series, 26m Post Booster.

Number of subjects with valid and determinate hSBA titer for the given strain ranged from 101-108 Stage 1 mITT population (before dose 1 to 24 months Post Primary), Booster Stage mITT population 49-54 at before booster to 12 months Post Booster and 28 at 26 months Post Booster.

Data on File (Nov 2018), Pfizer, Inc
Summary of hSBA response after 2- and 3-dose MenB-FHbp primary series and booster dose

Schematic representation of range of hSBA responses ≥1:4 and antibody persistence to 4 representative MenB strains following the 2- or 3-dose primary series and a booster

The data on persistence of protective responses against diverse strains expressing non-matched FHbp variants after the primary series and a booster provide further insights on the optimal way to use MenB-FHbp and prevent MenB disease in adolescents.

Number of subjects with valid and determinate hSBA titre for the given strain ranged from 405-424 at baseline (before 1st dose of MenB-FHbp Study 1012), 103-115 Stage 1 mITT population (12 months and 24 month Post Primary), Booster Stage mITT population 63-64 at 48 months Post Primary and 42-45 at 26 months Post Booster for 2-dose group and 417-426 at baseline, 102-111 Stage 1 mITT population (12 months and 24 month Post Primary), and Booster Stage mITT population 56-58 at 48 months Post Primary and 30-35 at 26 months Post Booster.

## Data interpretation

### For High Risk Groups

- These data suggest that a 3-dose series followed by a booster dose will enhance persistence of breadth of coverage (Timing of booster dose to be established)

### For Individuals at Increased Risk Due to an Outbreak

- Potential for administration of a single dose of MenB-FHbp for those previously vaccinated with a primary series of MenB-FHbp

---

The Data on Persistence of Protective Responses against Diverse Strains Expressing Non-matched FHbp Variants Post Booster Provide Further Insights on the Optimal Way to Use MenB-FHbp and Prevent MenB Disease in Adolescents