Meningokok Enfeksiyonları ve Asılları

Dr Bennett Lee
Global Lead Medical Affairs (Meningitis)
Novartis Vaccines & Diagnostics AG

PUADER Conference
Antalya, Turkey
May 4, 2013
### Conjugate Vaccines Have Several Advantages Over Polysaccharide Vaccines

<table>
<thead>
<tr>
<th>Property</th>
<th>Polysaccharide</th>
<th>Conjugate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune memory/Booster effect</td>
<td>−</td>
<td>✓</td>
</tr>
<tr>
<td>Hyporesponsiveness with repeated dosing</td>
<td>✓</td>
<td>−</td>
</tr>
<tr>
<td>Reduction of carriage*†</td>
<td>−</td>
<td>✓</td>
</tr>
<tr>
<td>Contributes to herd effect*</td>
<td>−</td>
<td>✓</td>
</tr>
<tr>
<td>Effective in infants</td>
<td>−</td>
<td>✓</td>
</tr>
</tbody>
</table>

*As evidenced by meningococcal serogroup C conjugate vaccines.
†Effect of MENVEO on nasopharyngeal colonization and carriage not yet established; Carriage study ongoing.

## İnvasiv Meningokokal Hastalığı – Bazı Aşı Seçenekleri

<table>
<thead>
<tr>
<th>Aşı Adı</th>
<th>Firma</th>
<th>Ruhsat Yeri</th>
<th>Güncel Endikasyonu</th>
</tr>
</thead>
<tbody>
<tr>
<td>MenACWY-CRM</td>
<td>Novartis</td>
<td>Türkiye</td>
<td>2 yaş ve üzeri tek doz</td>
</tr>
<tr>
<td>MenACWY-D</td>
<td>sanofi pasteur</td>
<td>Türkiye</td>
<td>9-23 ay arasında 3 aya ile 2 doz</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2-11 yaş tek doz</td>
</tr>
<tr>
<td>MenACWY-TT</td>
<td>GSK</td>
<td>Türkiye’de Ruhsatlı Değil</td>
<td></td>
</tr>
<tr>
<td>4CMenB</td>
<td>Novartis</td>
<td>Türkiye’de Ruhsatlı Değil</td>
<td></td>
</tr>
</tbody>
</table>

MENVEO —Meningococcal Conjugate Vaccine Against Serogroups A, C, W-135 and Y

- Chemical conjugation of meningococcal polysaccharides to protein carriers
- Immunologic improvements over polysaccharide vaccines

CRM=cross-reacting material.

Does MENVEO affect carriage?

Data from the Novartis – UK collaborative study on the potential of Menveo and Bexsero to reduce nasopharyngeal Carriage of Neisseria meningitidis will be presented at ESPID 2013 (Milan Italy)
4CMenB
Meningococcal Group B Vaccine (rDNA, component, adsorbed)

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Bexsero (4CMenB) is not licensed for use in Turkey
Infants <1 Year of Age Are at Greatest Risk for Meningococcal Disease

*Europe,* 2009

N=4637.

*Countries: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom. No data available from Liechtenstein.

A Significant Proportion of Disease in Infants Is Due to Serogroup B

United Kingdom, 2006–2010

The Development of a Broadly Protective MenB Vaccine Has Been Challenging

Capsular Vaccines

- Poorly immunogenic\(^1,2\)
  - Structural homology between the B polysaccharide and human tissue, leading to immunological tolerance\(^1,2\)

OMV-based Vaccines

- Immunogenic and proven effective for a single serogroup B strain\(^3,4\)
- Limited in ability to help protect against different meningococcal serogroup B strains\(^3,4\)
  - >8000 MenB strains exist\(^5\)

4CMenB Consists of 4 Antigenic Components Chosen to Achieve Broad Protection

- **fHbp: factor H binding protein**
  - Binds factor H, which enables bacterial survival in the blood\(^1,2\)

- **NHBA: neisseria heparin-binding antigen**
  - Binds heparin, which may promote bacterial survival in the blood\(^7\)
  - Present in virtually all strains\(^6,7\)

- **NadA: neisserial adhesin A**
  - Promotes adherence to and invasion of human epithelial cells\(^3-5\)
  - May be important for colonisation\(^4\)

- **NZ PorA P1.4: porin A**
  - Major outer membrane vesicle protein—induces strain-specific bactericidal response\(^8\)

Combining antigens that target different steps of meningococcal pathogenesis is likely to optimize MenB vaccine effectiveness

*From Neisseria meningitidis serogroup B strain NZ 98/254 measured as amount of total protein containing the PorA P1.4.*

4CMenB Has Been Studied in Large Clinical Studies Starting in Early Infants Through Adults

Approximately 7800 subjects (from 2 months of age) received at least 1 dose of the vaccine*

**Infants and children 2 months to <2 years of age**
- 5850 received at least 1 dose of 4CMenB
- 3285 received booster dose in second year of life

**Children 2 to 10 years of age**
- 250 were included

**Adolescents and adults ≥11 years of age**
- 1703 were included

*4CMenB was evaluated in 13 studies, including 9 randomised controlled clinical trials.
Data on file, Novartis Vaccines and Diagnostics, Inc.
### 4CMenB Is Indicated in the EU for Active Immunisation of Individuals Starting From 2 Months of Age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Primary Immunisation</th>
<th>Intervals Between Primary Doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants 2–5 months of age</td>
<td>3 doses each of 0.5 ml, with the first dose given at 2 months of age*</td>
<td>Not less than 1 month</td>
<td>1 dose between 12 and 23 months†</td>
</tr>
<tr>
<td>Unvaccinated infants 6–11 months of age</td>
<td>2 doses each of 0.5 ml</td>
<td>Not less than 2 months</td>
<td>1 dose in second year of life; interval of at least 2 months between primary series and booster†</td>
</tr>
<tr>
<td><strong>Children</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated children 12–23 months of age</td>
<td>2 doses each of 0.5 ml</td>
<td>Not less than 2 months</td>
<td>1 dose with an interval of 12–23 months between primary series and booster†</td>
</tr>
<tr>
<td>Children 2–10 years of age</td>
<td>2 doses each of 0.5 ml</td>
<td>Not less than 2 months</td>
<td>Need not established</td>
</tr>
<tr>
<td><strong>Adolescents and Adults</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adolescents (from 11 years of age) and adults‡</td>
<td>2 doses each of 0.5 ml</td>
<td>Not less than 1 month</td>
<td>Need not established</td>
</tr>
</tbody>
</table>

*The first dose should be given at 2 months of age. The safety and efficacy of the vaccine in infants less than 8 weeks of age has not yet been established. No data are available.

†The need for, and timing of, further booster doses has not yet been determined.

‡There are no data in adults above 50 years of age.


4CMenB Induced a Protective Immune Response in Infants after a 2-4-6-12 Month Dosing Schedule

2-4-6-12 month dosing schedule with routine vaccines

**Blood drawn at 7 months, N=1149–1152.**

**Blood drawn at 13 months, N=421–424.**

**N=100.**

4CMenB Induced a Protective Immune Response in Infants after a 2-3-4-12 Month Dosing Schedule

2-3-4-12 month dosing schedule with routine vaccines

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**Blood drawn at 5 months, N=273–275.**

†Blood drawn at 13 months, N=83–86.

‡Blood drawn at 5 months, N=112; blood drawn at 13 months, N=67.

No Clinically Relevant Interference Was Demonstrated When 4CMenB Was Administered With Routine Vaccines to Infants

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Lower limit for 95% CI for difference in seroresponders</th>
<th>Non-inferiority criteria met† (concomitant use with BEXSERO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>−1</td>
<td>YES</td>
</tr>
<tr>
<td>Tetanus</td>
<td>−2</td>
<td>YES</td>
</tr>
<tr>
<td>Pertactin</td>
<td>−8</td>
<td>YES</td>
</tr>
<tr>
<td>Pertussis toxin</td>
<td>−5</td>
<td>YES</td>
</tr>
<tr>
<td>FHA</td>
<td>−8</td>
<td>YES</td>
</tr>
<tr>
<td>Polio 1</td>
<td>−5</td>
<td>YES</td>
</tr>
<tr>
<td>Polio 2</td>
<td>−11</td>
<td>NO*</td>
</tr>
<tr>
<td>Polio 3</td>
<td>−4</td>
<td>YES</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>−5</td>
<td>YES</td>
</tr>
<tr>
<td>PRP-Hib</td>
<td>−3</td>
<td>YES</td>
</tr>
</tbody>
</table>

<table>
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<tr>
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<th>Non-inferiority criteria met† (concomitant use with BEXSERO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotype 4</td>
<td>−4</td>
<td>YES</td>
</tr>
<tr>
<td>Serotype 6B</td>
<td>−4</td>
<td>YES*</td>
</tr>
<tr>
<td>Serotype 9V</td>
<td>−2</td>
<td>YES</td>
</tr>
<tr>
<td>Serotype 14</td>
<td>−4</td>
<td>YES</td>
</tr>
<tr>
<td>Serotype 18C</td>
<td>−3</td>
<td>YES</td>
</tr>
<tr>
<td>Serotype 19F</td>
<td>−3</td>
<td>YES</td>
</tr>
<tr>
<td>Serotype 23F</td>
<td>−8</td>
<td>YES</td>
</tr>
</tbody>
</table>

*Inconsistent results were seen across studies for responses to inactivated poliovirus type 2 (shown here) and pneumococcal conjugate serotype 6B (not shown) and lower antibody titres to the pertussis pertactin antigen were also noted, but these data do not suggest clinically significant interference.

†Criteria met for LL 95% CI for difference in seroresponders >−10%. Blood drawn at 7 months.

‡N=238–248; §N=242–243.

In General, When Given Separately, Rates of Local Reactions Were Comparable to Routine Vaccines

Solicited local reactions when 4CMenB given separately from routine vaccines—post-dose 1

*No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series;
Hatched lines represent severe. Erythema, swelling and induration were categorized as severe if local reaction was >50 mm. Tenderness was categorized as severe if subject cried when injected limb was moved.
†Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib; 4CMenB: N=626; Routine: N=613.

In General, When Given Separately, Rates of Systemic Reactions Were Comparable to Routine Vaccines

Solicited systemic reactions when 4CMenB given separately from routine vaccines—post-dose 1

*No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series;

Fever was categorized as severe if temperature was ≥40°C. All other reactions were categorized as severe if subject was unable to perform normal daily activities.

†Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib; 4CMenB: N=626–627; Routine: N=612.

When Given Concomitantly, Some Systemic Reactions Were Greater Than Those Seen With Routine Vaccines Alone

Solicited systemic reactions when 4CMenB given with or without routine vaccines—post-dose 1

*No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series;

Fever was categorized as severe if temperature was ≥40°C. All other reactions were categorized as severe if subject was unable to perform normal daily activities.

†Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib; 4CMenB+Routine 2-4-6: N=624; 4CMenB alone 2-4-6: N=626–627; Routine alone 3-5-7: N=612.

When Given Concomitantly, Some Systemic Reactions Were Greater Than Those Seen With MenC+Routine or Routine Vaccines Alone

Solicited systemic reactions when 4CMenB given with routine vaccines—post-dose 1

*No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series;

Fever was categorized as severe if temperature was ≥40°C. All other reactions were categorized as severe if subject was unable to perform normal daily activities.

†Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib; 4CMenB+Routine: N=2478; MenC+Routine: N=490; Routine: N=659.


When Fever* Occurred, It Generally Followed a Predictable Pattern, With the Majority Resolving the Day After Vaccination
4CMenB given with or without routine vaccines

*Fever was defined as axillary temperature ≥38°C.
Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.

Phase IIb in Infants
Study V72P12 in EU Countries
Prophylactic Paracetamol at the Time of and Closely After Vaccination Reduced Fever
4CMenB given concomitantly with routine infant vaccines

Post-dose 1* (of 2-3-4 month dosing schedule)

<table>
<thead>
<tr>
<th>Time</th>
<th>NPP</th>
<th>PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

% of subjects

- 38.5°C–<39°C
- 39°C–<40.0°C
- ≥40°C

*NPP: no prophylactic paracetamol (N=182); PP: with prophylactic paracetamol (N=178-179).
Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.

*Similar results were observed with subsequent doses of the vaccination series.

Predicted Coverage of MenB Strains Indicates 4CMenB Has the Potential to Impact MenB Disease

*All invasive capsular group B isolates tested. †Down weighted with respect to outbreak strains from Oregon. ‡Represents about 53% of capsular group B cases.

Summary

- Serogroup B affects mainly infants, is easily misdiagnosed, can kill within 24 hours of onset and may cause serious, lifelong disabilities despite appropriate treatment.

- Vaccination is the best prevention against an aggressive disease that leaves little time for intervention.

- 4CMenB is indicated (in the EU) for active immunisation of individuals from 2 months of age and older against invasive meningococcal disease caused by *Neisseria meningitidis group B*.

- In clinical studies, 4CMenB has demonstrated a protective immune response in infants, children, adolescents and adults with or without routine vaccines.

- MATS results from 8 European countries, Australia, United States, Brazil and Canada on nearly 2590 MenB strains estimate that 66% to 91% would be covered by 4CMenB.

- Predicted coverage of MenB strains by 4CMenB has the potential to impact the incidence of MenB disease in these regions.
BACKUP

PUADER Conference
Antalya, Turkey
May 4, 2013
The Role of MENVEO® (Meningococcal Group A,C,W135 and Y conjugate vaccine) in the Prevention of Meningococcal Disease

Dr Bennett Lee
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Menveo is a licensed trademark of Novartis AG
Conjugate Vaccines Have Several Advantages Over Polysaccharide Vaccines

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*As evidenced by meningococcal serogroup C conjugate vaccines.
†Effect of MENVEO on nasopharyngeal colonization and carriage not yet established; Carriage study ongoing.

MENVEO — Meningococcal Conjugate Vaccine Against Serogroups A, C, W-135 and Y

- Chemical conjugation of meningococcal polysaccharides to protein carriers
- Immunologic improvements over polysaccharide vaccines

CRM = cross-reacting material.

MENVEO Elicited Comparable or Higher Immune Responses in Children 2–10 Years of Age at 1 and 12 Months Post-vaccination Compared With MenACWY-PS

1 dose MENVEO or MenACWY-PS given at age 2–10 years\textsuperscript{1,2}

\textbf{Serogroup}

*Statistically significant difference; †A: n=253; C: n=252; W-135: n=249; Y: n=250; ‡A: n=238; C: n=240; W-135: n=237; Y: n=239.

Blood drawn at one and 12 months post-vaccination.

hSBA=human serum bactericidal assay.

MENVEO Elicited Robust Protective Immune Responses in Children 2–10 Years of Age

Data for individual groups 2–5 years and 6–10 years

1 dose of MENVEO given at age 2–5 years

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>Sero-responders (%)</th>
<th>MENVEO†</th>
<th>MenACWY-D‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>72</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>60</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>W-135</td>
<td>72</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>66</td>
<td>45</td>
<td></td>
</tr>
</tbody>
</table>

1 dose of MENVEO given at age 6-10 years

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>Sero-responders (%)</th>
<th>MENVEO†</th>
<th>MenACWY-D‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>77</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>63</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>W-135</td>
<td>57</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>58</td>
<td>39</td>
<td></td>
</tr>
</tbody>
</table>

†2–5 years, n=593–607; 6–10 years, n=542–554.
‡2–5 years, n=600–615; 6–10 years, n=533–541.

Blood drawn at one month post-vaccination.
The clinical significance of the differences in immune response seen in this study is not known.
**MENVEO Elicited Robust Protective Immune Responses in Children 2–10 Years of Age Compared With MenACWY-D**

*Data for individual groups 2–5 years and 6–10 years*

**1 dose of MENVEO given at age 2–5 years**\(^{1,2}\)

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>MENVEO†</th>
<th>MenACWY-D‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>72±1.4</td>
<td>78±1.4</td>
</tr>
<tr>
<td>C</td>
<td>68±1.4</td>
<td>64±1.4</td>
</tr>
<tr>
<td>W-135</td>
<td>90±1.7</td>
<td>75±1.7</td>
</tr>
<tr>
<td>Y</td>
<td>76±1.6</td>
<td>57±1.6</td>
</tr>
</tbody>
</table>

**1 dose of MENVEO given at age 6-10 years**\(^{1,2}\)

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>MENVEO†</th>
<th>MenACWY-D‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>77±1.5</td>
<td>83±1.5</td>
</tr>
<tr>
<td>C</td>
<td>77±1.5</td>
<td>74±1.5</td>
</tr>
<tr>
<td>W-135</td>
<td>91±1.7</td>
<td>84±1.7</td>
</tr>
<tr>
<td>Y</td>
<td>79±1.6</td>
<td>63±1.6</td>
</tr>
</tbody>
</table>

*Noninferiority criteria met.
Blood drawn at one 12 month post-vaccination.
The clinical significance of the differences in immune response seen in this study is not known.

MENVEO Elicited Comparable or Higher Seroresponse One Month Post-Vaccination Versus MenACWY-D in Adolescents

1 dose MENVEO or MenACWY-D given at age 11–18 years

n=1024–1483 per serogroup; ‡n=288–501 per serogroup.

*Noninferiority criterion met; §Statistically significant difference.

Per-protocol population.
Blood drawn at one month post-vaccination.
hSBA=serum bactericidal assay with human complement.
One Dose of MENVEO In Adolescents Resulted In Comparable or Higher Immune Responses Compared With MenACWY-D

1 dose of MENVEO or MenACWY-D given at age 11–18 years

Blood drawn at one month post-vaccination. hSBA=serum bactericidal assay with human complement.

*Statistically significant difference; †n=1024–1483; ‡n=288–501.

MENVEO Elicited Comparable or Higher hSBA GMTs Versus MenACWY-D at One Month Post-Vaccination in Adolescents

1 dose MENVEO or MenACWY-D given at age 11−18 years

*Noninferiority criterion met; †Statistically significant difference; ‡n=1024–1483 per serogroup; § n=288–501 per serogroup.

Per-protocol population. Blood drawn at one month post-vaccination.

hSBA=serum bactericidal assay with human complement.

MENVEO Elicited Comparable or Higher Protective Immune Responses One Month Post-Vaccination Versus MenACWY-D in Adults

1 dose MENVEO or MenACWY-D given at age 19–55 years

**Legend:**
- **MENVEO**
- **MenACWY-D**

**Serogroups:**
- A
- C
- W-135
- Y

**Graph:**
- *Statistically significant difference; †n=484–963 per serogroup; ‡n=292–321 per serogroup.
- Per-protocol population.
- hSBA= serum bactericidal assay with human complement.

1 dose MENVEO or MenACWY-PS given at age 56–65 years

MENVEO Elicited Comparable or Higher Immune Responses One Month Post-vaccination Versus MenACWY-PS in Older Adults

*Statistically significant difference; †n=82–84 per serogroup; ‡n=39–41.

Blood drawn at one month post-vaccination.

hSBA=serum bactericidal assay with human complement.


Subjects with hSBA≥1:8 (%)

Serogroup

A C W-135 Y

*Statistically significant difference; †n=82–84 per serogroup; ‡n=39–41.

Blood drawn at one month post-vaccination.

hSBA=serum bactericidal assay with human complement.

MENVEO Safety Studies

- 5 RCTs
- Reactogenicity profile and rates of AEs among subjects aged 11–55 years and 56–65 years who received MENVEO, were similar

3181 children (2–10 years of age) received MENVEO

- 4 clinical trials
- Most common adverse reactions generally persisted for 1 to 2 days and were not severe

6185 adolescents–older adults (11–65 years of age) received MENVEO

- 5 RCTs

RCTs=randomized controlled trials; AEs=adverse events.
Persistence of hSBA Titers Post-Vaccination Was Comparable or Higher in Adolescents Vaccinated With MENVEO Versus MenACWY-D

*Statistically significant difference of MENVEO from MenACWY-D; Naive group was statistically significantly lower than other groups for all serogroups; †Lines connecting data points indicate projected mean declines in proportion of subjects having serum bactericidal assay with human complement (hSBA) ≥1:8 ‡n=287–292; §n=200–202; ‖n=106-107. 1-month data1; 21-month data2; 36-month data3,4.


Phase III in Adolescents Study V59P13 and V59P13E1
A Booster Dose of MENVEO 5 Years Post–primary Vaccination in Adolescents Results in an Anamnestic Immune Response

Blood drawn 5 years post-primary vaccination and on days 8 and 29 post–booster vaccination.

Booster dose of MENVEO given to subjects previously vaccinated with MENVEO or MenACWY-PS; or primary dose of MENVEO given to meningococcal vaccine-naive adolescents.

GMT=geometric mean titer; hSBA=serum bactericidal assay with human complement.

Menveo is not licensed or approved in children below 2 years of age.
MenACWY-CRM Elicited a Robust Immune Response in Infants When Given as 4–dose Series

MenACWY-CRM given at 2, 4, 6 and 12 months of age

*Criteria met: LL of 2-sided 95% CI ≥80% (A) or ≥85% (C, W and Y); †n=182–212; ‡n=154–169; §n=84–86.

Blood drawn at 7 months (post-primary), 12 months (pre-boost) and 13 months (post-boost).

hSBA=serum bactericidal assay with human complement.

Generally Similar Immune Responses Demonstrated Between the Infant Series of DTaP, IPV, HBV and Coadministration With MenACWY-CRM

MenACWY-CRM and routine vaccines or routine vaccines alone, given at 2, 4 and 6 months of age

*Noninferiority criteria met: LL 95% CI ≥-10% (-5% for polio) for difference in seroresponders; †n=148-214; ‡n=98-102; §Routine vaccines: DTaP, IPV, Hib, HBV, PnC.

Blood drawn at 7 months (post-primary).

DTaP=diphtheria, tetanus, and pertussis; IPV=inactivated polio vaccine; HBV=hepatitis B vaccine; PRP=platelet rich plasma; Hib=Haemophilus influenzae type b; PnC=pneumococcal protein conjugate.

Generally Similar Immune Responses Demonstrated Between the Infant Series of Prevnar (7-valent) and Coadministration With MenACWY-CRM

MenACWY-CRM and Prevnar (7-valent) or Prevnar (7-valent) alone given at 2, 4 and 6 months of age*

*With other routine vaccines: DTaP, IPV, Hib, HBV; †n=181; ‡n=102; §Noninferiority criteria met: LL 95% CI ≥-10% for difference in percent of responders.

Blood drawn at 7 months (post-primary).

DTaP=diphtheria, tetanus, and pertussis; IPV=inactivated polio vaccine; Hib=Haemophilus influenzae type b; HBV=hepatitis B vaccine.

MenACWY-CRM Was Well Tolerated in Infants With Local Reactogenicity Similar to Routine Vaccines

All local reactions subsided within 4 days

Mild and Moderate Local Reactogenicity

- MenACWY-CRM+Routine vaccines
  - N=990–992

- Routine vaccines alone
  - N=503

- Severe


Phase III in Infants Study V59P14 US
MenACWY-CRM Was Well Tolerated in Infants With Systemic Reactogenicity Similar to Routine Vaccines

**Mild and Moderate Systemic Reactogenicity**

- **MenACWY-CRM+Routine vaccines**
  - N=989–990
- **Routine vaccines alone**
  - N=498–503

- **Severe**
- **Urticarial rash**
  (no severe category for this reaction)

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Does MENVEO affect carriage?

Data from the Novartis – UK collaborative study on the potential of Menveo and Bexsero to reduce nasopharyngeal Carriage of Neisseria meningitidis will be presented at ESPID 2013 (Milan Italy)
Summary

- MENVEO® has demonstrated an immune response in children after a vaccination schedule started at 2 months of age

- Demonstrated persistence of bactericidal antibodies out to 36 months

- No clinically significant differences were observed when Menveo was administered alone or with routine vaccines

- Well tolerated in all age groups studied