Baxter

Single Priming Dose of NeisVac-C in Infants

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ABSTRACT

The current licensed infant immunization schedule for meningococcal serogroup C conjugated vaccines requires two doses, followed by a booster dose in the second year of life. Several clinical studies with NeisVac-C vaccine have suggested that high seroprotective titers in infants can be induced with a single priming dose. The aim of the present study was to assess the feasibility of a single priming dose of NeisVac-C® given at 4 or 6 months of age compared to the currently licensed two-dose priming schedule.

956 subjects were randomly assigned to three treatment groups to receive a single dose of NeisVac-C at 4 or 6 months of age, or two doses at 2 and 4 months of age. All subjects received a booster between 12 and 13 months of age. Concomitant vaccinations with Infanrix® hexa and Prevenar 13® were administered to all subjects at all timepoints.

Endpoint of the study was to demonstrate non-inferiority of seroprotection rates following a single priming dose as compared to a two-dose priming one month after the primary vaccination (rSBA ≥8), prior to the booster (rSBA ≥8), and one month after the booster (rSBA ≥128).

Rates of subjects with seroprotective antibody titers (rSBA ≥ 8) one month after primary vaccination was 99.6% in the 4 month dose group, 99.2% in the 6 month dose group, and 99.6% in the two-dose group. Prior to the booster, 78.0% and 90.7% of subjects had seroprotective antibody titers in the single dose groups (month 4 or month 6, respectively), compared to 67.8% in the two dose group.

One month after the booster, > 98.5% of subjects in all three dose groups showed rSBA titers ≥ 128, with no differences between the groups. Non-inferiority of the single dose regimen vs. two doses could be demonstrated.

Thus, a single priming dose given at age > 4 months, followed by a booster in the beginning of the second year of life, is expected to offer a degree of protection, which is comparable to that of the currently licensed 2-dose priming schedule.

INTRODUCTION

Meningococcal serogroup C conjugate vaccines (MCC) were successfully introduced in several countries 10-12 years ago. In the absence of controlled efficacy trials, various national vaccination schedules were adopted considering the specific regional epidemiological situation as well as practical and economic factors. Originally, in order to ensure an adequate immune response, the primary vaccination schedule for MCC vaccines in infants comprised three doses. Clinical trial experience later on provided evidence that the infant primary schedule could be reduced to two doses (Borrow 2003). As a result, a two-dose primary vaccination for NeisVac-C was licensed. Based on evidence for waning immunity after primary vaccination in infancy a booster vaccination in the second year of life has been added to the infant vaccination schedule.

Several clinical studies with a Tetanus-Toxoid conjugated MCC vaccine, which uses a de-O-acetylated polysaccharide, NeisVac-C® (Baxter Bioscience, Vienna, Austria), have suggested that high seroprotective titers in infants could be induced even with a single priming dose. The aim of the present study was to assess the feasibility of a single priming dose of NeisVac-C® given at either 4 or 6 months of age compared to the currently licensed two-dose priming schedule with vaccinations at 2 and 4 months of age.

OBJECTIVES

The objective of this study was to assess the feasibility of a single priming dose of NeisVac-C in infants (at either 4 or 6 months of age), as determined by immune response

STUDY PURPOSE

Demonstration of non-inferiority of seroprotection rates following a single priming dose (at either 4 or 6 months of age) as compared to a two-dose priming (at 2 and 4 months of age)

- one month after the primary vaccination (rSBA titers ≥8)
- prior to the administration of the booster vaccination (rSBA titers ≥8)
- one month after the booster vaccination (rSBA titers ≥128)

STUDY DESIGN

Subject Disposition				
dose group	**month 2**	**month 4**	**month 6**	**month 12-13**
group 1		NeisVac-C		NeisVac-C
group 2			NeisVac-C	NeisVac-C
group 3	NeisVac-C	NeisVac-C		NeisVac-C

Concomitant vaccinations with Prevenar 13® and Infanrix® hexa at 2, 4, 6 and booster between 12 and 13 months of age

MAIN INCLUSION CRITERIA

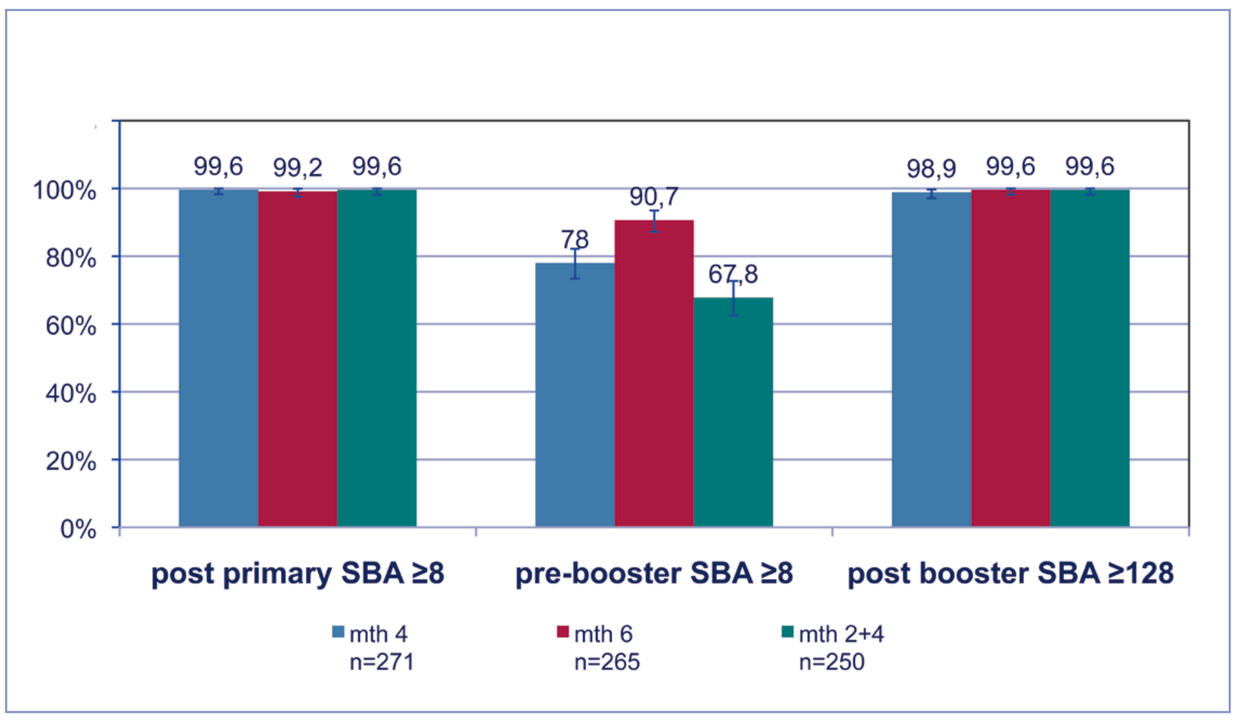
- Subject is an infant aged 8 to 11 weeks at the time of first vaccination
- Subject is clinically healthy as determined by the investigator's clinical judgment through collection of medical history and physical examination
- Subject was born at full term of pregnancy (≥ 37 weeks) with a birth weight ≥ 2.0 kg
- The parent(s) or legally authorized representative of the subject provides written consent for participation

MAIN EXCLUSION CRITERIA

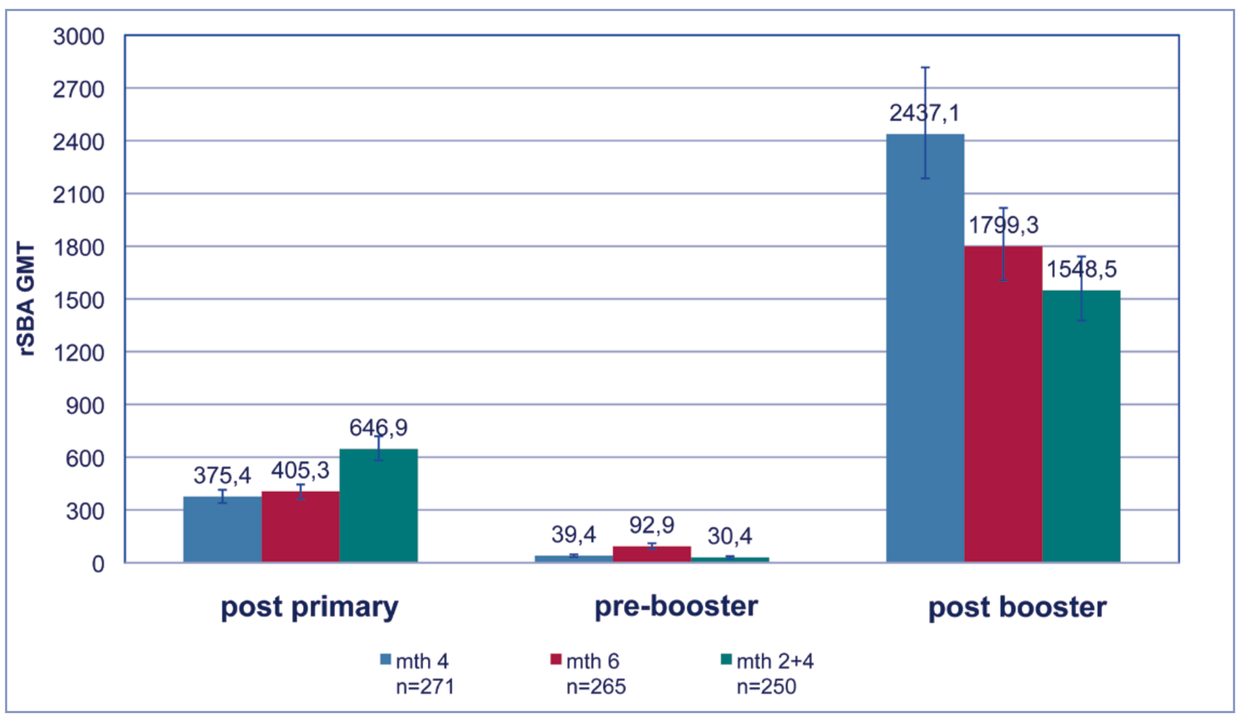
- History of severe allergic reactions or anaphylaxis, or a known sensitivity or allergy to any components of the vaccines
- Current or recent acute or chronic infection requiring systemic therapy (antibiotic or antiviral) or other prescribed treatment within the 2 weeks prior to the first study vaccination
- Rash or dermatologic condition which may interfere with injection site reaction rating
- Current or history of any significant cardiovascular, respiratory, hepatic, renal, metabolic, autoimmune, rheumatic, hematological, neurological, or neurodevelopmental disorder
- A disease, or a form of treatment, within 30 days prior to study entry, that could be expected to influence immune response
- Receipt of any blood products or immunoglobulins within 60 days of study entry
- Subject has received a live vaccine within 4 weeks or an inactivated or subunit vaccine within 2 weeks of the scheduled first vaccination;
- Subject has previously been vaccinated against meningococcal C disease;
- Subject has a known or suspected immune dysfunction;
- Subject has a functional or surgical asplenia (e.g. due to a pathologic hemoglobinopathy, leukemia, lymphoma, etc.);

RESULTS

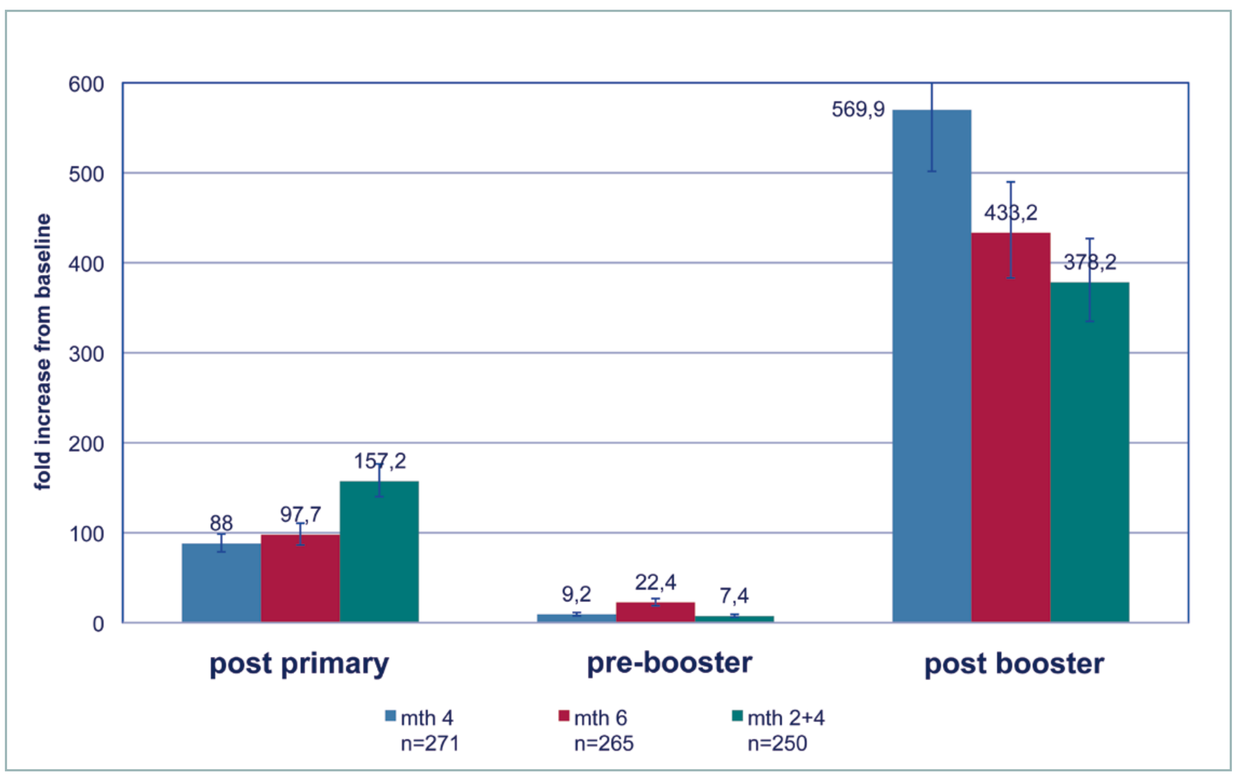
Seroprotection rates post primary, pre booster and post booster



rSBA GMTs post primary, pre booster and post booster



rSBA GMT fold increase vs. baseline post primary, pre booster and post booster



CONCLUSIONS

- Both single-dose schedules are non-inferior to the 2-dose schedule at all time points: one month after priming, prior to the booster, and one month post-booster
- Prior to the booster vaccination, the highest seroprotection rates and functional antibody titers were observed in the 6-month single-dose group
- The 4-month single-dose group showes significantly higher post-booster antibody titers compared to the remaining groups
- A single priming dose given at age > 4 months, followed by a booster in the beginning of the second year of life, is expected to offer a degree of protection, which is comparable to that of the currently licensed 2-dose priming schedule

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