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Safety and Immunogenicity of Quadrivalent Meningococcal Conjugate Vaccine in 2 to 10 Year-Old Human Immunodeficiency Virus-Infected Children

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Abstract

Background—HIV-infected children are at increased risk of meningococcal infection and poor response to quadrivalent meningococcal conjugate vaccine (MCV4), but MCV4 has not been studied in pre-adolescent HIV-infected children.

Methods—The P1065 trial enrolled 2-10 year-old HIV-infected children with CD4 ≥25% to receive MCV4 at entry and at week 24. Rates of response (≥4-fold rise in rabbit serum bactericidal antibody [rSBA]) against each meningococcal serogroup [A, C, Y, W-135], geometric mean titers (GMT), and rates of seroprotection (rSBA titer ≥1:128) were determined from sera obtained at entry and weeks 4, 24, 28 and 72. Adverse events (AE) were assessed for 6 weeks after each MCV4 dose.

Results—At entry, 47% of the 59 participants were male, 56% black, 31% Latino, median age was 6 years, 88% were receiving antiretroviral therapy, and 75% had viral load <400 copies/mL.

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There were no serious AEs within 6 weeks after MCV4 doses; all vaccination reactions were mild. Response after a single MCV4 dose was high to serogroup A (92%) and W-135 (98%); responses improved after a second dose for serogroup C (43% to 80%) [p<0.0001] and Y (76% to 84%) [p=0.38]. By week 72, seroprotection rates were 93%, 91%, 78% and 46% for serogroups W-135, Y, A and C, respectively.

Conclusions—Two doses of MCV4 were safe and immunogenic in 2-10 year-old HIV-infected children. The second dose increased the proportion of children who made a response to serogroup C. Seroprotection waned substantially for serogroups A and C within one year of last MCV4 dose.

Keywords

Pediatric HIV infection; meningococcal vaccine; conjugate vaccine

Introduction

HIV infection in children increases the risk of infections with encapsulated bacteria while also impairing the development of protective immunity in response to vaccines.[1,2] In a recent South African study, the incidence and severity of meningococcal disease in HIV-infected adults and children of all ages were markedly higher than in the HIV-uninfected population. HIV-infected children were at more than 60-fold higher risk of meningococcal disease compared with HIV-uninfected children.[3] Highly active antiretroviral therapy (HAART) attenuates the risk of bacterial infection and improves the response to vaccines, but children receiving HAART continue to experience higher rates of bacterial infections and demonstrate poorer response to vaccines than their HIV-uninfected counterparts.[4-9]

In the United States, the CDC Advisory Committee on Immunization Practices (ACIP) has recommended quadrivalent (serogroups A, C, Y, and W-135) meningococcal polysaccharide conjugate vaccine (MCV4) as part of the routine immunization schedule for adolescents (11 years of age and older) since 2005.[10] This recommendation was later expanded to 2- to 10-year-old children with conditions that increase their risk of meningococcal infection.[11] MCV4 has been shown to be safe and well tolerated in HIV-infected youth but two MCV doses are needed to overcome lower response rates to a single vaccine dose, relative to those seen in HIV-uninfected youth, especially for serogroup C.[9,12] As a result, the ACIP now recommends that initial meningococcal immunization of those with HIV-infection consist of a two-dose primary series.[13]

There are no data about use of MCV4 in HIV-infected children younger than 11 years old. The objective of the present study was to provide safety and immunogenicity data for a two-dose series of MCV4 in 2-10 year old HIV-infected children, including levels of seroprotection out to 72 weeks from immunization initiation. Since routine HAART availability in the United States enables most HIV-infected children of this age to preserve or restore immunologic function, this study focused on children with CD4+ T-lymphocyte (CD4) values of at least 25%.[14]

Materials and Methods

P1065 Study Population

P1065 is a Phase I/II safety and immunogenicity trial of MCV4 in HIV-infected children and youth performed at 31 clinical sites of the International Maternal Pediatric Adolescent AIDS Clinical Trial (IMPAACT) network in the United States. Results for 11-24 year-old participants enrolled under Version 2.0 of the protocol have been reported elsewhere.[9,12] Eligibility criteria for Version 3.0 of the protocol were: (1) age of 2 to 10 years; (2) CD4

≥25% at screening; (3) on stable antiretroviral therapy (ART) or not receiving ART for at least 90 days prior to vaccination; (4) no personal or family history of Guillain-Barré Syndrome (GBS); and (5) no meningococcal polysaccharide vaccine within last 2 years and no MCV4 at any time. To ensure representation across the full age range, enrollment was limited to require that no more than 80% of the subjects were enrolled in either the 2-5 or 6-10 year-old age subgroups. Additional exclusion criteria included receipt of other killed vaccines within 2 weeks before entry, receipt of live vaccines within 4 weeks before entry, planned receipt of other vaccines within 2 weeks after entry, use of systemic immunosuppressant or immunomodulatory drugs, malignancy, hypersensitivity to MCV4 components, bleeding problems precluding intramuscular injection, or signs/symptom suggestive of GBS including areflexia in all 4 extremities, and presence of any new and unresolved grade 3 laboratory or clinical toxicity. Participants were enrolled between September and December of 2008.

P1065 Study Protocol

All sites received approval for the study through their local Institutional Review Boards (IRB). Participants or their parents/guardians signed an informed consent prior to participation; assent was obtained as required by local IRBs.

At study entry (Step 1), participants were administered MCV4 (Meningococcal [Serogroups A, C, Y and W-135] polysaccharide diphtheria toxoid conjugate vaccine -Menactra, Sanofi Pasteur Inc, Swiftwater, PA; 0.5 mL intramuscular injection). At week 24, participants who had not had adverse reactions that precluded further vaccine doses were entered on Step 2 and received a second dose of MCV4. Delay of second vaccine dose was permitted for febrile illness or other temporary conditions.

Participants were followed for 72 weeks after enrollment. Samples collected for the evaluation of immunogenicity were sent in batches to Sanofi Pasteur for analysis.

Safety

The outcome measures for safety objectives included the occurrence of documented reactions to the vaccine, ≥grade 3 adverse events (AEs) and suspected or proven GBS. AEs were graded according to the December 2004 DAIDS AE Grading Table[15] and were based on laboratory evaluations, signs and symptoms, local vaccine reactions, and adverse event reports. Participants were observed for 30 minutes post vaccination and were contacted by telephone at 3, 7, and 42 days after each vaccine administration. In addition, standardized questionnaires were administered during the study visits at 4, 24, 28, and 72 weeks after initial immunization. Signs and symptoms suggestive of GBS were collected on case report forms. The safety assessment reported here includes all enrolled participants who received at least one MCV4 dose.

Immunogenicity

The primary criterion for an immunogenic response was a ≥4-fold rise in functional serum bactericidal antibody (SBA) titer against each meningococcal serogroup [SG] (A, C, W-135, and Y). Serum was obtained at entry (pre-vaccine) and at weeks 4, 24, 28, and 72 on all participants. SBA assays using a baby rabbit complement source (rSBA) were performed at Sanofi Pasteur, Inc., as previously described.[16] Absolute rSBA titer ≥1:128 was classified as evidence of seroprotection; <1:8 as susceptible, and 1:8 to 1:64 as indeterminate.

Statistical Methods

Response rates for each serogroup were calculated based on at least a 4-fold rise in rSBA titer from pre-vaccine levels. In addition, the percents of participants with absolute rSBA

titer of at least 1:128 and the geometric mean titers (GMT) were calculated for each serogroup. Standard errors for response rates were based on the binomial distribution. The target sample size of 56 was chosen to have at least 50 evaluable participants, which would permit an estimate of the true response rate to within +/- 8% of an observed rate of 92%, to within +/- 9 % of an observed rate of 85% and to within +/- 12% of an observed rate of 70%.

Fisher's exact test (for binomial variables) and Chi-squared tests (for multinomial variables) were used to assess the association of participant characteristics with the immunogenic response to each serogroup and with having seroprotection (rSBA ≥1:128), and the association between age strata and subject characteristics. Results were not corrected for multiple comparisons. Among participants receiving two doses of MCV4, hyporesponsiveness (defined as a lower titer after the second vaccine dose than after the first vaccine dose) was assessed using within-subject comparisons of log base 2 titers at Weeks 4 and 28 for each serogroup using signed rank tests. Within-subject agreement in response at weeks 4 and 28 was assessed using McNemar's test.

Statistical analyses were conducted using SAS Version 9.2 (SAS Institute, Cary, NC). A two-sided significance level of 0.05 was used for statistical significance. All analyses are based on data submitted by November 16, 2010.

Results

Study Population

Fifty-nine participants, evenly distributed between those <6 years old (N=29) and those ≥6 years old (N=30), were enrolled between September and December 2008. Fifty-eight participants enrolled to Step 2 between February 2009 and June 2009 and received a second dose of MCV4; one subject was lost to follow-up before Step 2. At study entry, 47% of participants were male, 56% were black, and 31% were Hispanic/Latino (see Table, Supplemental Digital Content 1). Seventy-three percent had viral load < 400 copies/mL (median 75 copies/mL, IQR 50-625 copies/mL), the median screening CD4% was 36%, 14% of participants had a history of CDC Class C conditions, and 88% of participants were receiving HAART at study entry. There were no statistically significant differences in these characteristics between age strata. Viral load and CD4% were stable over the course of the study, with medians remaining constant at weeks 0, 24 and 72.

Safety

No participants developed GBS or other neurologic adverse events during the study. There were no adverse events reported in the 42 days following each MCV dose other than mild local pain, tenderness and/or redness reported by 5 participants, 4 (7%) in Step 1 and 1 (2%) in Step 2. The overall rate of new grade 3 or higher adverse events was 5% (3/59), including two neutropenia episodes and one fever; these events all occurred at least 24 weeks after an MCV4 dose and were deemed unrelated to vaccine.

Short-Term (4- and 24-Week) Immunogenicity

Of 59 participants who received the first dose of MCV4, 53 had entry and week 4 serology results and are included in the immunogenicity analyses. The six participants without serology results were more likely to be classified as CDC Class C at study entry (50% vs 9%, Fisher's exact test p=0.03) but were otherwise similar to those with serology results.

The proportions (95% Confidence Interval [CI]) of participants with 4-fold response at week 4 to serogroup A, C, W-135 and Y were 91% (79-97%), 43% (30-58%), 96% (87-99.5%),

and 77% (64-88%), respectively; all participants had ≥ 4-fold SBA titer rise to at least one serogroup. Response rates to the first dose of MCV4 were similar when limited to subjects with weeks 0, 4, and 28 serologic results (Table 1).

At study entry, 62% of participants had seroprotection (rSBA titer ≥ 1:128) to at least one serogroup (A, 23%; C, 11%; W-135, 6%; Y, 51%). However, many participants had undetectable rSBA titers at entry (A, 77%; C, 85%; W-135, 75%; Y, 25%). Four weeks after vaccination, all participants had seroprotection to at least one serogroup but seroprotection rates varied considerably by serogroup (A, 94%; C, 51%; W-135, 96%; Y, 89%) (Table 1). By week 24, the seroprotection rates (A, 83%; C, 35%; W-135, 88%; Y, 94%) were still substantially higher than at entry, but most participants lacked seroprotection for serogroup C. Seroprotection rates were similar when limited to subjects with weeks 0, 4, and 28 serologic results (Table 1). For all serogroups except Y, the median antibody titer was <1:8 at baseline; at Week 4, the median rSBA titer for all serogroups exceeded 1:128. At week 24, the median titers remained well above 1:128 for all serogroups except serogroup C, for which the median titer declined to below the limit of detection. Serogroup C had the lowest post-vaccination GMTs at both Weeks 4 and 24 (see Figure, Supplemental Digital Content 2; Table 2).

Immunogenicity of Second MCV4 Dose

The proportions (95% CI) with ≥ 4-fold rSBA titer rise relative to baseline at Week 28 for serogroups A, C, W-135 and Y were 88% (75-95%), 80% (66-90%), 100% (93-100%), 84% (70-93%), respectively. All participants had ≥ 4-fold SBA titer rise to at least one serogroup. Seroprotection (rSBA ≥ 1:128) rates at Week 28 for serogroups A, C, W-135 and Y were 96%, 80%, 100%, and 98%, respectively (Table 1).

Univariate Predictors of Response to Each MCV Dose

For each serogroup, week 4 responders were compared with non-responders by participant demographic and HIV-specific characteristics. For serogroup A, younger participants (2-5 years old) were more likely than older participants to have 4-fold response at week 4 (100% vs. 81%, p=0.05, Fisher's exact test). For serogroup W-135, participants with CD4% ≥30 were more likely than those with CD4%<30 to respond at Week 4 (100% vs. 83%, p=0.05, Fisher's exact test). For serogroup Y, females were more likely to respond than males (89% vs. 65%, p=0.05). When restricted to those with viral load <400 copies/mL or to those with entry rSBA < 1:8, the response rates were not significantly different from the overall response rates (Table 3). No other characteristics, including suppressed viral load, were associated with vaccine response.

As was true for response to serogroup A after the first MCV4 dose, participants in the younger age stratum (2 to <6 years old) were more likely than the older participants to have 4-fold response to serogroup A to the second dose of MCV4 (100% vs. 75%, p=0.01, Fisher's exact test). Participants with viral load <400 copies/mL at entry were more likely than those with entry viral load ≥ 400 copies/mL to respond to serogroup C after the second dose of MCV4 (89% vs. 57%, p=0.02, Fisher's exact test), but this association was not found for the other serogroups. The response rates to the second dose were similar to those of the overall study population when restricted to the subset of children with VL<400 cp/mL, or to the subset with rSBA<1:8. (Table 3). No other characteristics, including CD4 percentage, were associated with vaccine response. These analyses were exploratory and therefore not corrected for multiple comparisons. No characteristic was associated with response to more than one serogroup.

Seroprotection Rates Through Week 72

Of the 58 participants who received both doses of MCV4, 50 had both baseline and week 28 serology data; of those 50, 45 also had week 72 serology data. Participants with serology results were similar to those without serology (data not shown). The median titer for serogroup C at week 24 was the same as at entry, but the week 72 GMT was higher than at entry and at Week 4. For all other serogroups, the GMTs and median titers at Weeks 24 and 72 were equal to or lower than at Week 4 post-vaccination but higher than at study entry (Table 2). GMTs by serogroup over time are shown in the SDC 2 (Figure). At Weeks 24 and 72, the proportion of participants with seroprotection (rSBA≥ 1:128) was higher than at baseline for all serogroups; however, seroprotection rates at weeks 24 and 72 were lower than at week 4 for all serogroups except serogroup Y (Table 1).

The proportions (95% CI) of participants with titers ≥1:128 at Week 72 for serogroups A, C, W-135 and Y were 80% (65-90%), 45% (30-61%), 95% (85-99%), and 91% (78-97%), respectively. The only participant characteristic associated with seroprotection at week 72 was that black participants were more likely than others to have protective titers to serogroup C (63% vs. 26%, p=0.03, Fisher's exact test).

Comparison of titers at Weeks 4 and 28

In order to assess for hyporesponsiveness, defined as a lower titer after the second vaccine dose than after the first vaccine dose, within-subject comparisons of log base 2 titers at Weeks 4 and 28 were performed for each serogroup. There was no evidence of lower rSBA titer at week 28 compared with week 4 for any of the serogroups. For serogroup A, the median titers at week 28 were the same as at week 4. For the other three serogroups, median week 28 titers were significantly higher than those at week 4, with a median increase of two-fold for serogroup W-135 ($p<0.001$) and serogroup Y ($p=0.04$) and four-fold for serogroup C ($p<0.001$). The mean (SD) changes in $\log_2$-titers were increases of 1.5 (2.0), 2.1 (1.6) and 3.2 (3.0) for serogroups W-135, Y, and C, respectively, in contrast to a mean decrease of 0.3 (1.6) for serogroup A. For all serogroups except A, most participants who did not respond after dose 1 responded after dose 2 [SG C 64% (18/28), SG W-135 100% (1/1), SG Y 58% (7/12)]

Discussion

A two-dose series of MCV4 was safe and immunogenic in this group of 2- to 10-year-old HIV-infected children. Most children who did not respond to the first dose of MCV4 did respond after the second MCV4 dose. The two-dose series resulted in high levels of seroprotection against most serogroups even 48 weeks after the completion of the primary series (week 72). There was no evidence of hyporesponsiveness after a second dose, as has been observed after repeated doses of meningococcal polysaccharide vaccine.[17] These findings support the current ACIP recommendation for a two-dose primary MCV series for HIV-infected children, although the dosing interval of 24 weeks in the current study is longer than the 2-month interval recommended by ACIP.

It is reassuring that many of these children appear to acquire seroprotection naturally at rates of 6-53% (baseline seroprotection rates, depending on serogroup), similar to findings previously reported for HIV-infected adolescents and young adults in this study.[9] The response rate and seroprotection rate for serogroup C after the first MCV4 dose were much lower than the rates for the other serogroups; the second MCV4 dose markedly increased the response rate and seroprotection rate for serogroup C, though these remained lower than those for the other serogroups. In a study of healthy (HIV-uninfected) 2-10 year-old children, response rates to serogroups C and Y were somewhat lower than those for

serogroups A and W-135, and, similar to the current study, the levels of protection achieved against serogroup C relative to protection achieved against other serogroups was markedly lower (Table 3).[18] The second MCV4 dose in HIV-infected children in the current study raised the rate of seroprotection against serogroup C to a level similar to that seen after a single MCV4 dose in HIV-uninfected children, though levels remained suboptimal in both groups. Inferior serogroup C response was also observed in older HIV-infected children and youth whose immunologic status was similar to the younger HIV-infected children in the current study (Table 3); however, levels of response and protection to serogroup C were not inferior in a trial of HIV-uninfected adolescents.[16] Thus, studies of higher-dose vaccine, adjuvanted vaccine and other strategies to improve vaccine-induced protection against meningococcal serogroup C may be important for younger children and for HIV-infected children and youth of all ages.

Studies of MCV4 in healthy children suggest that it is somewhat more immunogenic and achieves higher rates of seroprotection in adolescents than in pre-adolescent children.[16,18] Among HIV-infected children and adolescents with baseline CD4 ≥ 25%, the response rate to serogroup C after the first dose of MCV4 was lower in the younger children than in youth, but the response to other serogroups after the first MCV dose and the response rate to all serogroups – including serogroup C – after the second MCV4 dose were similar for both age groups. Lower CD4, history of CDC class B/C disease, and higher viral load were independent predictors of poor response to a single dose of MCV4 in HIV-infected 11-24 year-olds, but that study group included youth with a broad range of these markers of poorer HIV control.[9] These factors were not consistently predictive of poorer MCV response in the current study of younger children, likely because this study limited enrollment to children with preserved or restored immunologic status. These findings are similar to the findings in other studies that examined response of HIV-infected children on effective HAART to a neo-antigen (primary hepatitis A vaccine series).[7] Taken together, these results support making a single set of recommendations for a 2-dose series for primary MCV immunization in HIV-infected children and youth with good immunologic status.

The durability of seroprotection is especially important for HIV-infected children as they approach the adolescent ages of increased risk of meningococcal infection compounded by their HIV-related potential for increased meningococcal infection risk.[13] Bactericidal antibodies wane substantially in healthy adolescents and healthy 2-10 year olds within 2-5 years after MCV4 immunization.[13,19] Furthermore, a CDC case-control study demonstrated that the overall efficacy of MCV4 immunization given in the prior five years was only 78% with efficacy decreasing as the interval since MCV4 administration increased: 58%, 91% and 95% efficacy for persons who received a single dose of MCV4 2-5, one and less than one year earlier, respectively.[13] In addition, MCV4 given five years after primary MCV4 immunization elicits a robust, “booster” response of bactericidal antibodies. These data form the basis of the current ACIP recommendation that healthy youth who receive their first MCV4 at 11-12 years old should receive a routine MCV4 booster dose at 16 years old age to enhance protection against meningococcal disease during the period of greatest age-related risk. In the current study, by week 72, the proportion of children protected against serogroups A and C declined substantially compared with the proportion with seroprotection at the time of completion of their two-dose primary series only 48 weeks earlier. The effectiveness of a booster MCV4 dose after a two-dose primary series is unknown, but this approach warrants study in HIV-infected children and is the focus of an ongoing extension of the P1065 protocol. Until those results are available, it would be prudent to provide a booster MCV4 at age 16 years to all HIV-infected children, whether or not they received a one-dose or two-dose primary MCV series. In addition, achieving high community uptake of MCV4 by non-immunocompromised children should provide herd immunity and decrease the disease burden in the HIV- infected children in that community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Response Rates and Seroprotection Rates to MCV4 by Serogroup*

Serogroup	% (n/N) participants with undetectable levels of rSBA titer at Baseline	% (n/N) ≥4-fold increase in rSBA titer at Week 4	% (n/N) ≥4-fold increase in rSBA titer at Week 28	% (n/N)* participants with rSBA titer ≥ 128				
				Baseline	Week 4	Week 24	Week 28	Week 72
A	80% (39/49)	92% (45/49)	88% (43/49)	20% (10/49)	96% (47/49)	84% (41/49)	96% (47/49)	80% (35/44)
C	86% (42/49)	43% (21/49)	80% (39/49)	10% (5/49)	49% (24/49)	33% (16/49)	80% (39/49)	45% (20/44)
W-135	76% (37/49)	98% (48/49)	100% (49/49)	6% (3/49)	98% (48/49)	90% (44/49)	100% (49/49)	95% (42/44)
Y	24% (12/49)	76% (37/49)	84% (41/49)	53% (26/49)	90% (44/49)	96% (46/48)	98% (48/49)	91% (40/44)

* Limited to **participants with at least weeks 0, 4, and 28 serology results.**

* The number of participants with serology results varies by serogroup

Table 2

Geometric Mean Titer (GMT) Through 72 Weeks^ by Serogroup

Serogroup	Geometric Mean Titer* (95% Confidence Limits)				
	Week 0 (n=49)	Week 4 (n=49)	Week 24 (n=49)	Week 28 (n=49**)	Week 72 (n=44)
A	12 (6,22)	3871 (2158, 6944)	689 (342, 1388)	3175 (1909, 5281)	488 (221, 1078)
C	8 (5, 12)	52 (24, 112)	28 (14, 54)	484 (250, 937)	65 (30, 140)
W-135	7 (5, 11)	783 (551, 1112)	573 (403, 816)	2167 (1558, 3014)	528 (358, 779)
Y	87 (45, 168)	1039 (614, 1757)	636 (418, 967)	1438 (1023, 2021)	488 (302, 789)

* Due to assay limitations, exact titers could not be provided for results <8 or >131,072. For purposes of calculating medians and geometric mean titers, results <8 were set equal to 4 and those >131,072 were set equal to 262,144.

** N=48 for serogroup Y

^ Limited to participants with serology results available from at least Weeks 0, 4 and 2

Table 3

Response Rates (Confidence Limits) and Seroprotection Rates (Confidence Limits) after One and Two Doses of MCV4 for 2-10 Year-old Participants with data for Weeks 4 and 28 (Current Report) Compared to 11-24 Year-old Participants (Earlier P1065 Cohort) with HIV Infection and 2-10 Year-Old Participants without HIV Infection

Study Cohort		After First MCV4 Dose (Week 4)				After Second MCV4 Dose (Week 28)			
		A	C	W-135	Y	A	C	W-135	Y
2-10 yrs, HIV-infected (current cohort)[1]	All (n=49)	92 (80, 98)	43 (29, 58)	98 (89, >99)	76 (61, 87)	88 (75, 95)	80 (66, 90)	100 (93, 100)	84 (70, 93)
	Entry titer <1:8	95 (83, 99) n=39	43 (28,59) n=42	100 (91, 100) n=37	100 (74, 100) n=12	95 (83, 99) n=39	86 (71, 95) n=42	100 (91, 100) n=37	100 (74, 100) n=12
	VL<400 (n=34)	91 (76, 98)	44 (27, 62)	100 (90, 100)	76 (59, 89)	85 (69, 95)	85 (69, 95)	100 (90, 100)	88 (73, 97)
	Seroprotection	96 (86, >99)	49 (34, 64)	98 (89, >99)	90 (78, 97)	96 (86, >99)	80 (66, 90)	100 (93, 100)	98 (89, >99)
11-24 yrs, HIV-infected (previous cohort)[2]	CD4%≥25, 2-Dose Group	85 (74, 92) n=65	66 (53, 77) n=65	88 (78, 95) n=66	76 (64, 85) n=66	86 (75, 93) n=63	75 (63, 85) n=65	92 (83, 97) n=66	82 (70, 90) n=66
	Seroprotection	95 (87, 99) n=66	64 (51, 75) n=66	83 (72, 91) n=66	79 (67, 88) n=66	95 (87, 99) n=64	68 (56, 79) n=66	91 (81, 97) n=66	88 (78, 95) n=66
2-10 yrs, Healthy[3]	All	99 (96, 100) n=279	88 (84, 91) n=338	96 (94, 98) n=400	86 (77, 93) n=87	-	-	-	-
	Seroprotection	97 (95, 100)	81 (78,100)	91 (88, 100)	93 (90, 100)	-	-	-	-

[1] All participants in 2-10 year-old cohort were required to have CD4%≥25% at baseline.

[2] Older cohort results presented for comparison[Ref # 12].

[3] Results from study of single MCV4 dose in healthy (HIV-uninfected) 2-10 year-old study presented for comparison; all with pre-vaccine rSBA titer <8) [Ref # 18].