Safety and Immunogenicity of an Investigational Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) When Co-administered With Other Vaccines in Healthy Adolescents

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Speaker Disclosure

	No, nothing to disclose
√	Yes, please specify:

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*
Sanofi Pasteur					x		x	

Background on MenACYW-TT

- Disease burden due to *Neisseria meningitidis* in adolescents and young adults is high and mortality rates can be twice as high than for general population.
- The elevated incidence seen in adolescence and young adults is probably related to increased transmission through social activities and through living in close quarters.
- Vaccine coverage is not easy to attain in adolescents. Since a combined diphtheria-tetanus-acellular pertussis vaccine and HPV vaccine are also given routinely during adolescence in many countries, co-administration with MenACYW-TT may improve vaccination coverage.
- Quadrivalent meningococcal conjugate vaccines offer protection against 4 of the most clinically important *N. meningitidis* serogroups: A, C, W, and Y.
- The MenACYW-TT conjugate vaccine is an investigational quadrivalent meningococcal (serogroups A, C, W, Y) vaccine intended for use in individuals 6 weeks of age and older.

MET50 Study Overview

Phase II, pivotal, randomized, open-label, parallel group study in meningococcal vaccine naive adolescents, evaluated concommitant administration of Tdap and HPV4

Primary Objective

To demonstrate noninferior immunogenicity to MCV4-CRM by vaccine seroresponse measured by serum bactericidal assay using human complement

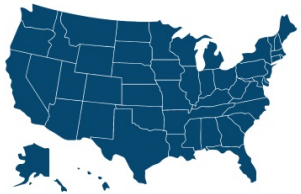
Study Period

FVFS JULY 2014

LVLS OCTOBER 2015

1715

Adolescents (10-17 years)



40

study sites

Investigational Product used in MET50 was identical to the one used in Phase III studies

MET50 Vaccination Schedule

Group	Day 0	Day 60	Day 180
1	MenACYW-TT		
2	MCV4-CRM (Menveo®)		
3	MenACYW-TT Tdap (Adacel®) HPV4 (Gardasil®)	HPV4 (Gardasil®)	HPV4 (Gardasil®)
4	Tdap (Adacel®) HPV4 (Gardasil®)	HPV4 (Gardasil®)	HPV4 (Gardasil®)

Demographics: Gender and Age

The randomized groups were balanced by age and gender.

(N= number of evaluable subjects)	MenACYW-TT (N= 503)	MCV4-CRM (N= 501)	MenACYW-TT Tdap+HPV (N= 392)	Tdap+HPV (N= 296)	**Overall** (N= 1692)
Males	243 (48.3%)	272 (54.3%)	201 (51.3%)	155 (52.4%)	871 (51.5%)
Females	260 (51.7%)	229 (45.7%)	191 (48.7%)	141 (47.6%)	821 (48.5%)
Mean age (years)	11.4	11.4	11.1	11.1	11.1

Number of evaluable subjects is based on the Safety Analysis Set.

Safety

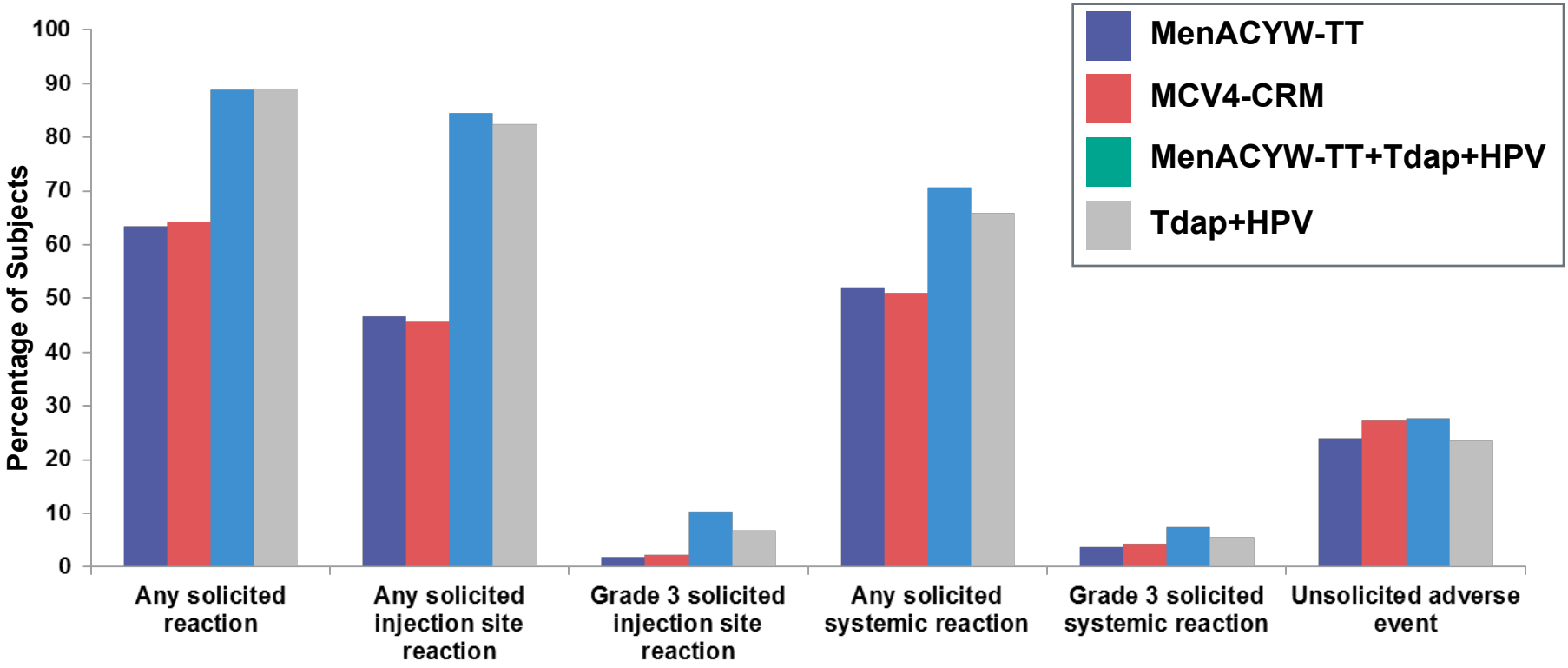
MET50 Safety Overview

MenACYW-TT was well-tolerated in the study.

	MenACYW-TT (N= 503)	MCV4-CRM (N= 501)	MenACYW-TT Tdap+HPV (N= 392)	Tdap+HPV (N= 296)
Immediate* unsolicited AE	3 (0.6%)	1 (0.2%)	3 (0.8%)	3 (1.0%)
AE leading to study discontinuation	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SAE (within 30 days)	2 (0.4%)	1 (0.2%)	0 (0.0%)	1 (0.3%)
SAE (entire study)	4 (0.8%)	4 (0.8%)	4 (1.0%)	4 (1.4%)
Fatal	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Number of evaluable subjects is based on the Safety Analysis Set.
***Within 30 mins; AE: adverse event; SAE: serious adverse event; (N= number of evaluable subjects)**

MET50 Solicited and Unsolicited Reactions Overview



Similar solicited reaction and unsolicited AE rates observed after MenACYW-TT and MCV4-CRM

MET50: Summary of Safety Results

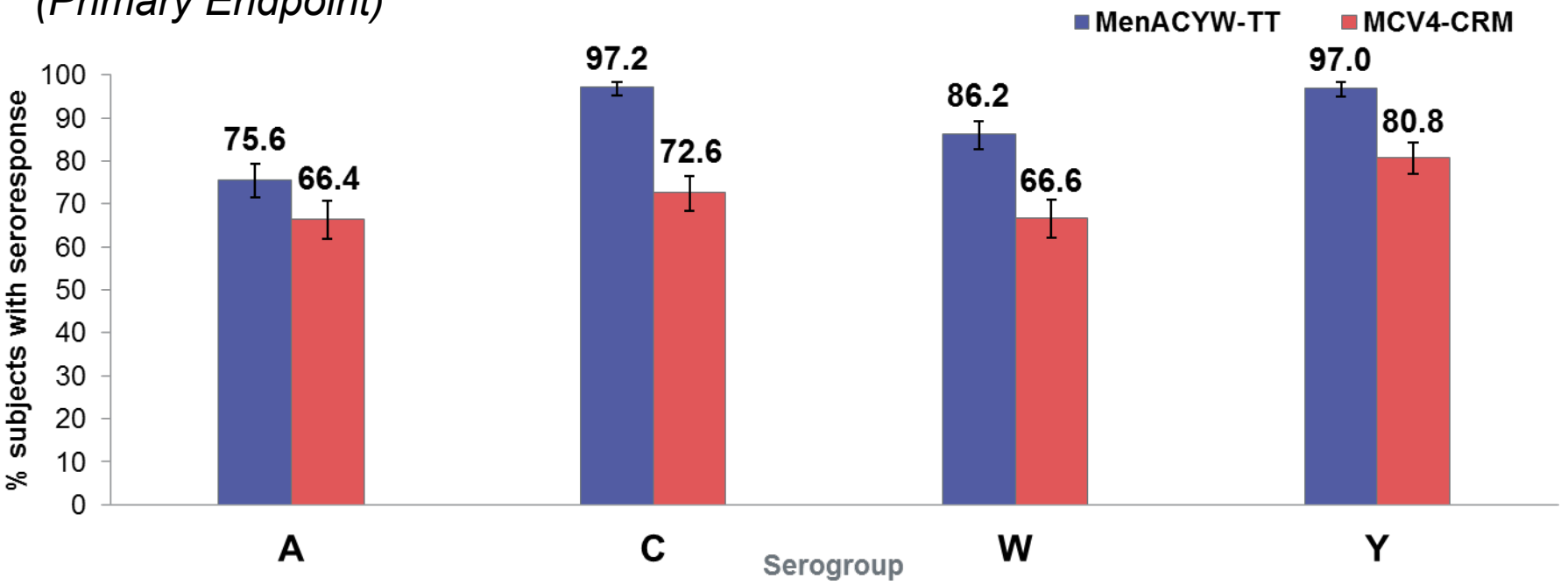
MenACYW-TT was well-tolerated in the study.

- Overall, vaccination with MenACYW-TT among adolescents was found to be safe with no safety concerns identified when given alone or concomitantly with Tdap and HPV vaccines.
- MenACYW-TT was well tolerated with no immediate hypersensitivity reactions, no related SAEs, and no deaths.
- The safety profile of MenACYW-TT was comparable to that of licensed MCV4-CRM when given alone, while the local & systemic reactogenicity was found to be higher when MenACYW-TT was given with Tdap and HPV vaccines.
  - Reactogenicity remained comparable to control Tdap+HPV Group

Immunogenicity

Seroresponse (hSBA): MenACYW-TT vs MCV4-CRM

Non-inferior hSBA vaccine seroresponse of MenACYW-TT vs MCV4-CRM (Primary Endpoint)

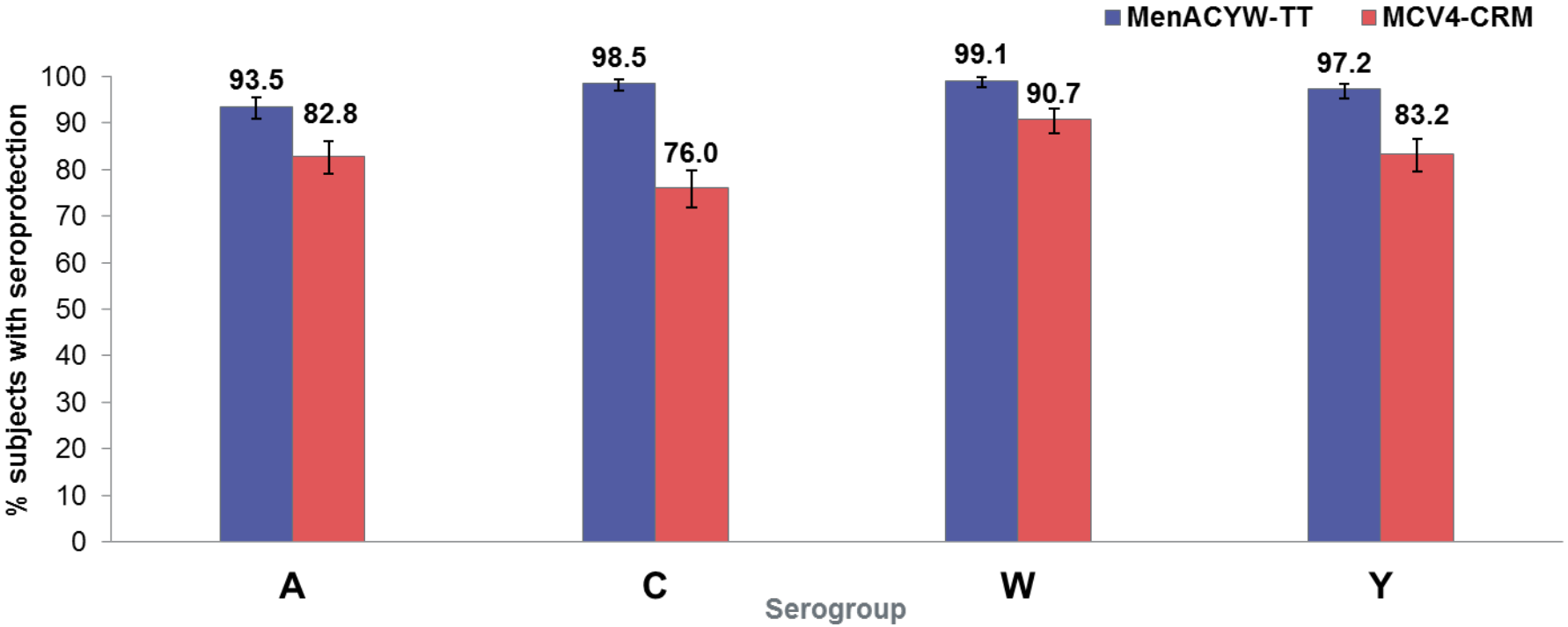


Vaccine seroresponse as assessed by hSBA for serogroups A, C, W, and Y is defined as:

- **For a subject with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:8.**
- **For a subject with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer.**

Seroprotection (hSBA): MenACYW-TT vs MCV4-CRM

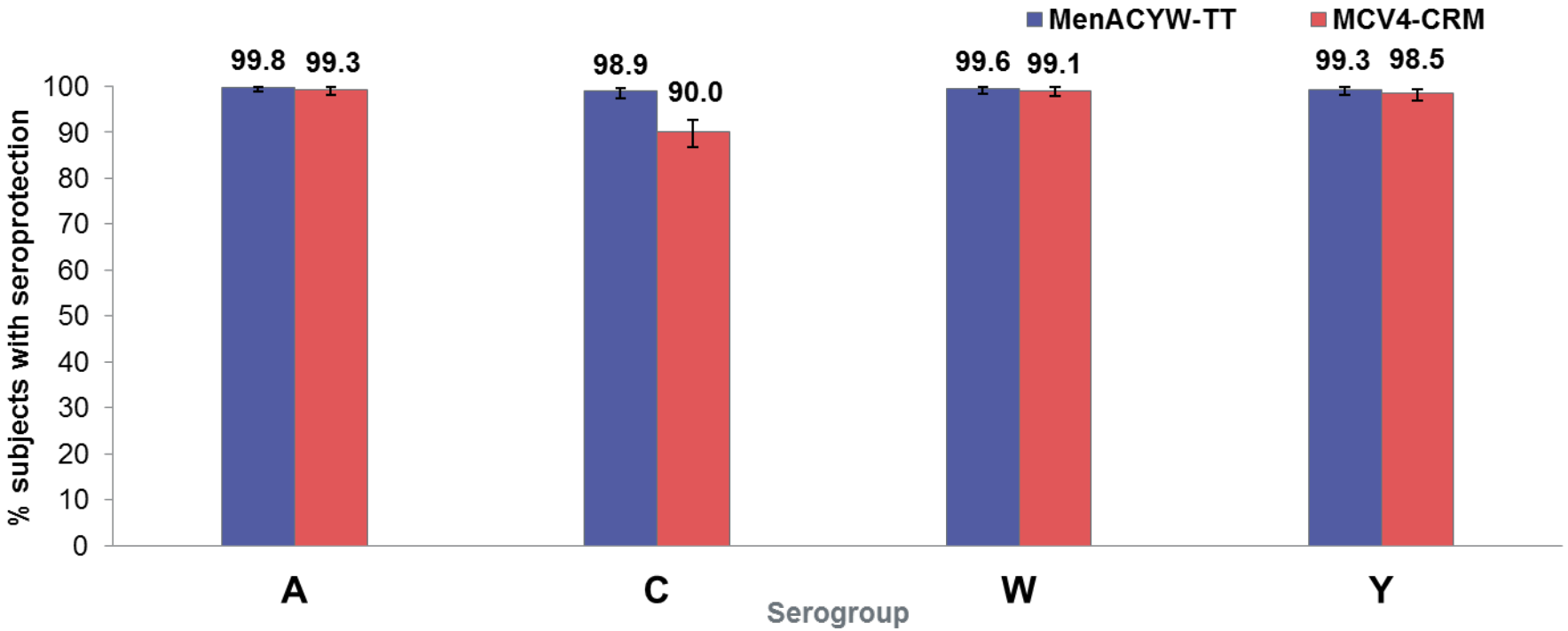
Higher hSBA seroprotection after MenACYW-TT for all 4 serogroups



hSBA Vaccine seroprotection for serogroups A, C, Y, and W is defined as a post-vaccination titer ≥ 1:8.

Seroprotection (rSBA): MenACYW-TT vs MCV4-CRM

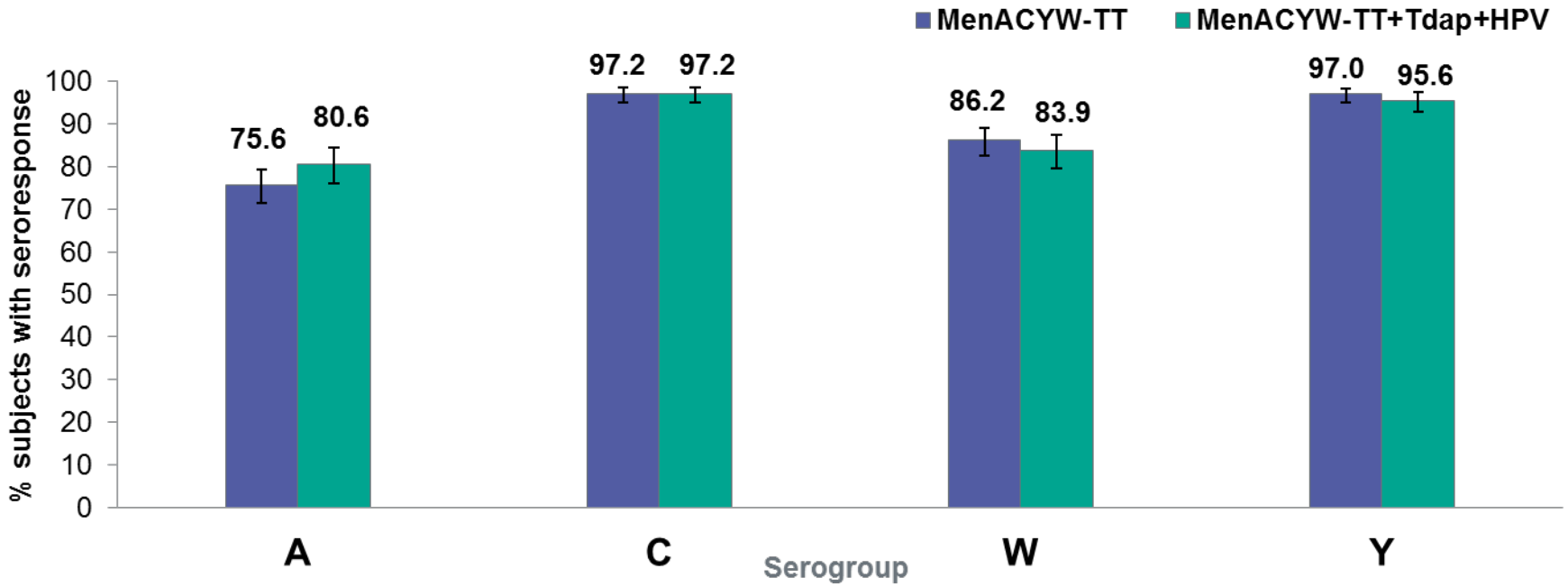
Similar rSBA seroprotection rates



rSBA Vaccine seroprotection for serogroups A, C, Y, and W is defined as a post-vaccination titer ≥ 1:128.

Seroresponse (hSBA): MenACYW-TT alone vs with Tdap/HPV

Non-inferior hSBA seroresponse of MenACYW-TT alone vs MenACYW-TT+Tdap+HPV



Vaccine seroresponse as assessed by hSBA for serogroups A, C, W, and Y is defined as:

- **For a subject with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:8.**
- **For a subject with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer.**

Tdap: MenACYW-TT with or without Tdap/HPV (PPAS)

Pertussis GMC

	MenACYW-TT + Tdap + HPV (N= 360)			Tdap + HPV (N= 263)			Group 3/Group 4 GMC3 / GMC4	
Antigen	**GMC**	95% CI	**Vaccine Response** (%)	**GMC**	95% CI	**Vaccine Response** (%)	Ratio	2-sided 95% CI for ratio
PT	37.5	(33.8; 41.7)	**67.3**	44.4	(39.5; 49.9)	**78.2**	0.845	(0.722; 0.990)
FHA	180	(168; 194)	**92.1**	242	(218; 268)	**89.4**	0.746	(0.661; 0.842)
PRN	200	(177; 225)	**94.7**	265	(231; 304)	**96.6**	0.753	(0.627; 0.903)
FIM	339	(285; 403)	**92.2**	499	(414; 601)	**95.4**	0.679	(0.525; 0.878)

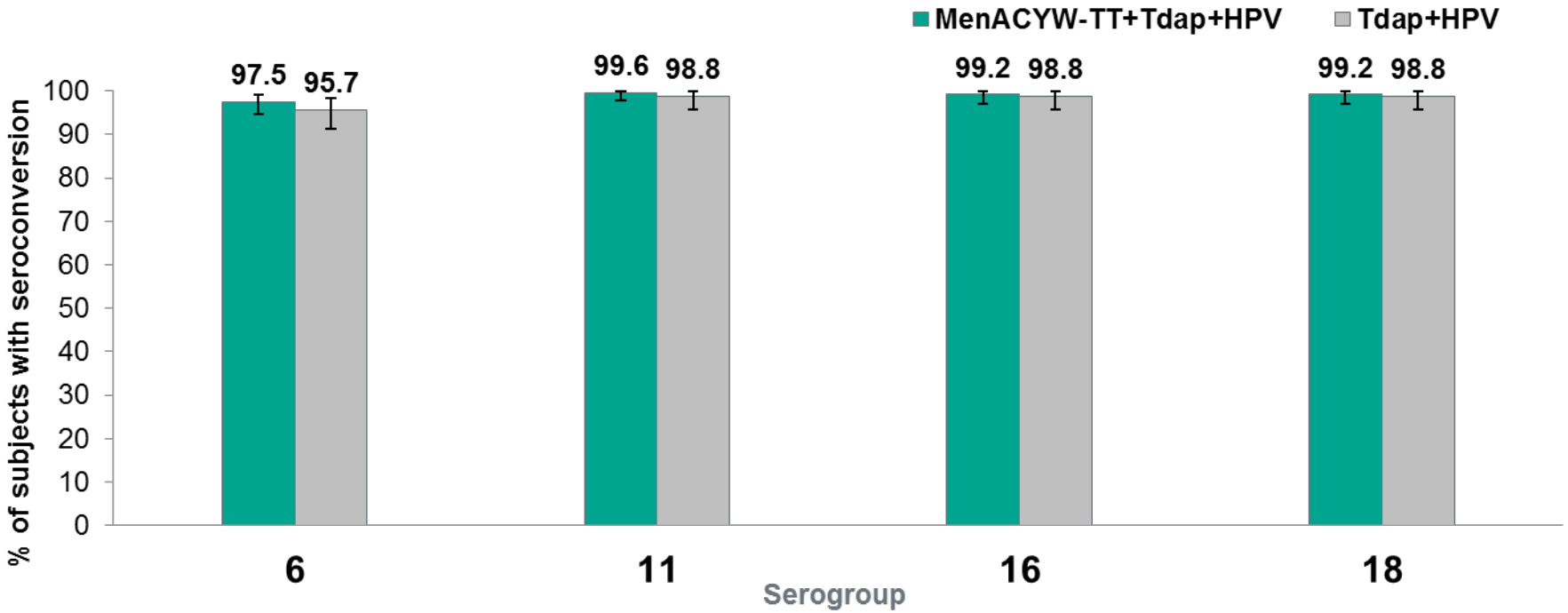
Pertussis vaccine response defined as ≥ 4 x baseline concentration, if the anti-pertussis antibody concentration at baseline (D0) is < 4 x lower limit of quantitation (LLOQ) **OR** ≥ 2 x baseline concentration, if the anti-pertussis antibody concentration at baseline (D0) was ≥ 4 x LLOQ.

Non-inferior diphtheria and tetanus responses between groups.

Pertussis response trends similar to those observed with other MCV4 vaccines.

HPV Seroconversion

Non-inferior HPV seroconversion of MenACYW-TT+Tdap+HPV vs Tdap+HPV



Seroconversion is changing serostatus from seronegative to seropositive. Cutoff values for HPV seropositivity are >= 20 mMU/mL for types 6 and 16, >= 16 mMU/mL for type 11, and >= 24mMU/mL for type 18.

Summary of Immunogenicity Results

- MenACYW-TT was non-inferior to MCV4-CRM by the hSBA vaccine seroresponse for all 4 serotypes.
- MenACYW-TT administered alone was non-inferior to when administered concomitantly with Tdap and HPV vaccines by the hSBA vaccine seroresponse for all 4 serotypes.
- Responses to diphtheria, tetanus, PT, and HPV were non-inferior when Tdap and HPV were administered alone to when MenACYW-TT was given together with Tdap and HPV.
  - Response trends observed for pertussis antigen were similar to those observed with other licensed MCV4 vaccines.
- MenACYW-TT and MCV4-CRM induced comparable immune responses as measured by the rSBA vaccine seroprotection.

Conclusion

- MenACYW-TT vaccine was well tolerated and generated an immune response that was non-inferior to the licensed MCV4 -CRM vaccine.
- The immunogenicity and safety profiles were comparable when vaccine was administered with or without Tdap and HPV vaccines in meningococcal vaccine naïve adolescents.

THANK YOU

BACK UP

MET50 Overview

Study Vaccine(s)	MenACYW-TT	MCV4-CRM	MenACYW-TT Tdap + HPV4	Tdap + HPV4
	Group 1	Group 2	Group 3	Group 4
Safety Analysis Set	503	501	392	296
Per Protocol Analysis Set	463	464	360	263

Dipththeria and Tetanus: MenACYW-TT with Tdap/HPV (PPAS)

Noninferior diphtheria and tetanus responses between groups.

	MenACYW-TT + Tdap + HPV (N= 360)		Tdap + HPV (N= 263)		Group 3 - Group 4	
Antigen	%*	95% CI	%*	95% CI	Difference (%)	2-sided 95% CI for difference
Diphtheria	97.8	(95.7; 99.0)	98.9	(96.7; 99.8)	-1.1	(-3.3; 1.3)
Tetanus	99.7	(98.5; 100.0)	99.6	(97.9; 100.0)	0.1	(-1.2; 1.9)

*Proportions of subjects achieving concentration >= 1.0 IU/mL for tetanus and diphtheria