SAFETY AND IMMUNOGENICITY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE (MenACYW-TT) ADMINISTERED AS A SINGLE DOSE IN A BROAD AGE RANGE (12 MONTHS AND ABOVE)

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- Quadrivalent meningococcal conjugate vaccines offer protection against 4 of the most invasive *N. meningitidis* serogroups - A, C, Y and W (W-135).
- MenACYW-TT is an investigational quadrivalent meningococcal vaccine conjugated to Tetanus Toxoid and intended for use in a broad age population (6 weeks of age and older).
- Summary of safety and immunogenicity in ages 12 months and above is presented. Studies in ages less than 12 months are ongoing
- We evaluated the safety and immunogenicity of MenACYW-TT conjugate vaccine compared to licensed quadrivalent conjugate meningococcal vaccines (MCV4-TT; Nimenrix®, MCV4-CRM; Menveo®, MCV4-DT; Menactra®*) in toddlers (12-23 months), children (2-9 years), adolescents (10-17 years) and adults (18-55 years); and licensed quadrivalent meningococcal polysaccharide vaccine (MPSV4; Menomune®) in adults ≥ 56 years of age.

* Not licensed in Europe

- A total of 3 phase II and 6 phase III studies, administering the vaccine as a single dose, were conducted globally [USA, Europe (Finland, Germany, Spain, Hungary), South Korea, Thailand, Russia and Mexico) in a broad age range (12 months and above).
- All but one studies evaluated MenACYW-TT conjugate vaccine vs a licensed standard of care comparator vaccine to demonstrate immune non-inferiority or describe the immunogenicity responses.
- Statistical hypothesis of immune non-inferiority was evaluated on the endpoint considered relevant by the health authority of the country where the study was conducted. Data presented in this poster will focus on seroprotection results.
- Co-administration with age specific vaccines was also evaluated in adolescents [tetanus toxoid, reduced diphtheria toxoid, acellular pertussis (Tdap) vaccine and Human Papillomavirus (4vHPV) vaccine] and toddlers [measles, mumps rubella (MMR), varicella (V), Pneumococcal 13-valent Conjugate Vaccine (PCV13), diphtheria, tetanus, acellular pertussis, poliomyelitis, Hepatitis B and *Haemophilus influenzae* type b conjugate vaccine (DTaP-IPV-HB-Hib)].
- Serum bactericidal assays with human (hSBA) and baby rabbit [(rSBA) in a subset of subjects] complement were used to evaluate antibodies at baseline and 30 days after vaccination.
- Safety data were collected up to 30 days or 6 months post-vaccination.

Table 1: Overview of Clinical Development

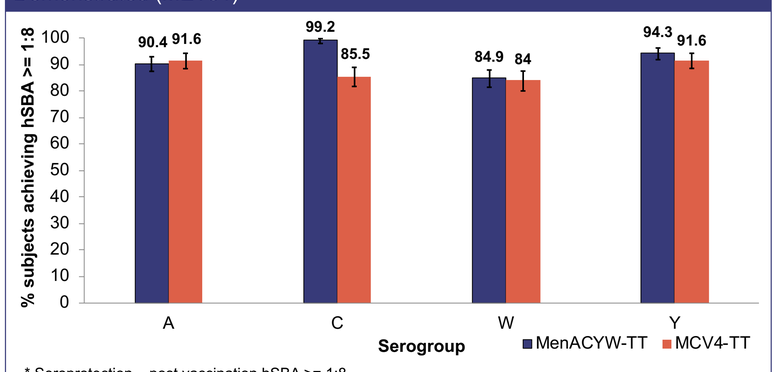
Age Range	Study Code	Phase	Country/ Region	Comparator	Sample size
12-23 months	MET54	II	Finland	Nimenrix®	188
	MET51	III	Finland, Germany, Spain & Hungary	Nimenrix®	918
	MET57	III	South Korea, Thailand, Mexico, Russia	N/A	1183
2-9 yrs	MET35	III	USA	Menveo®	1000
10-17 yrs	MET50	II*	USA	Menveo®	1715
10-55 yrs	MET43	III	USA	Menactra®	3344
15 yrs +	MET56	III	USA	Menactra®	810
56 yrs+	MET44	II	USA	Menomune®	301
	MET49	III	USA	Menomune®	907

* Pivotal data using investigational product identical to phase III lots

Summary of Immunogenicity Findings

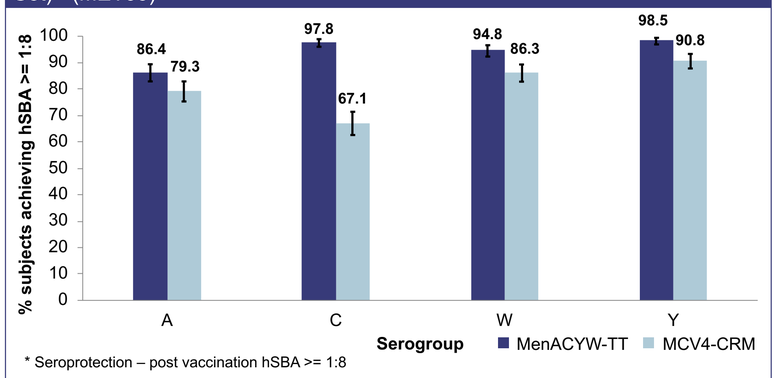
- Non-inferiority of immune responses was demonstrated between MenACYW-TT conjugate vaccine and comparator vaccines for all four serogroups across all ages, based on percentages of participants achieving hSBA vaccine seroresponse at Day 30 compared to baseline (children, adolescents, adults and elderly) or percentages of participants achieving hSBA ≥ 1:8 at Day 30 (toddlers).
- The percentages of participants with post vaccination hSBA ≥ 1:8 (seroprotection) were higher or comparable to comparator for all serogroups in subjects vaccinated with MenACYW-TT conjugate vaccine across all age groups.
- The percentages of participants with post vaccination rSBA ≥ 1:128 were comparable or higher for all serogroups in subjects vaccinated with MenACYW-TT conjugate vaccine vs comparator vaccine. (data not shown)
- Co-administration of MenACYW-TT conjugate vaccine, MMR+V, PCV13 and DTaP-IPV-HB-Hib vaccines did not generate evidence suggestive of clinically significant interference in toddlers (12 – 23 months). (data not shown)
- Co-administration of MenACYW-TT conjugate vaccine, Tdap and HPV4 vaccines did not generate evidence suggestive of clinically significant interference in adolescents (10-17 years). (data not shown)

Figure 1: Percentage of Combined Meningococcal Vaccine Naïve and MenC Vaccine Primed Subjects (12-23 Months) Achieving hSBA Seroprotection* at D30 After Vaccine (Per Protocol Analysis Set) – Immune Non-inferiority# Demonstrated (MET51)



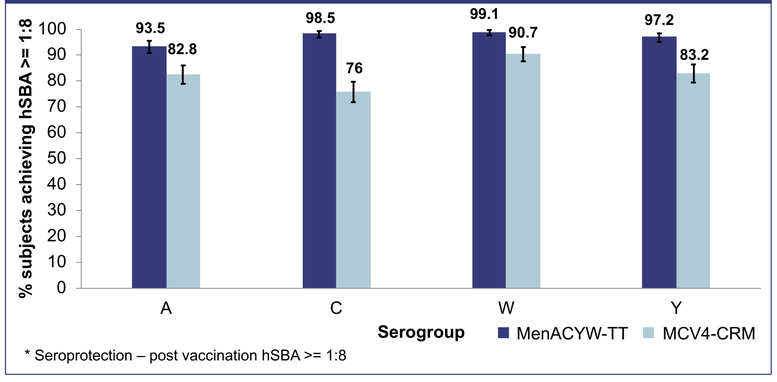
* Seroprotection – post vaccination hSBA >= 1:8
# Non-inferiority concluded if the lower limit of the two-sided 95%CI of the proportion difference is >-10%

Figure 2: Percentage of Meningococcal Vaccine Naïve Subjects (2-9 Years) Achieving hSBA Seroprotection* at D30 After Vaccine (Per Protocol Analysis Set) - (MET35)



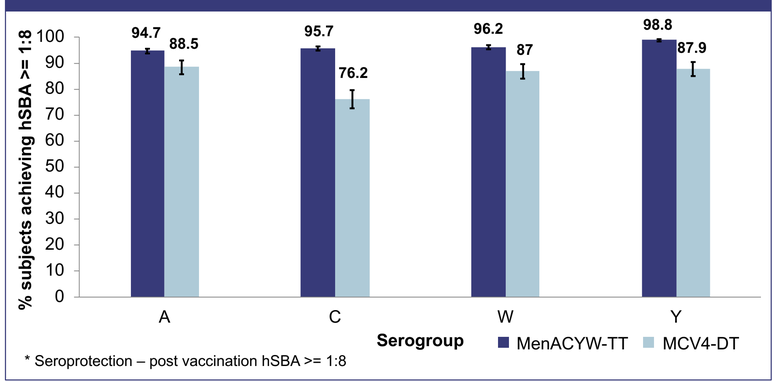
* Seroprotection – post vaccination hSBA >= 1:8

Figure 3: Percentage of Meningococcal Vaccine Naïve Subjects (10-17 Years) Achieving hSBA Seroprotection* at D30 After Vaccine (Per Protocol Analysis Set) – (MET50)



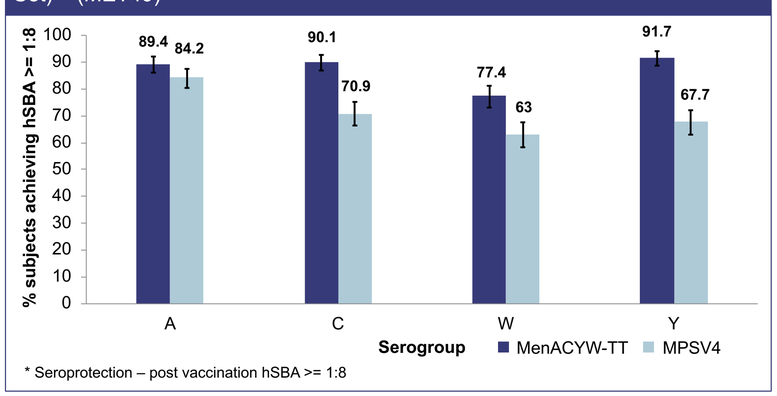
* Seroprotection – post vaccination hSBA >= 1:8

Figure 4: Percentage of Meningococcal Vaccine Naïve Subjects (10-55 Years) Achieving hSBA Seroprotection* at D30 After Vaccine (Per Protocol Analysis Set) – (MET43)



* Seroprotection – post vaccination hSBA >= 1:8

Figure 5: Percentage of Meningococcal Vaccine Naïve Subjects (56 Years +) Achieving hSBA Seroprotection* at D30 After Vaccine (Per Protocol Analysis Set) – (MET49)



* Seroprotection – post vaccination hSBA >= 1:8

Summary of Safety Findings

- Overall, the safety profiles of MenACYW-TT and standard of care vaccines were comparable across all ages.
- No safety concerns were identified.
- There were no related AEs leading to study discontinuation and no related serious adverse events among MenACYW-TT recipients.
- Post-vaccination rates of severe reactions were low for all vaccines.
- There were no important changes in the safety profiles of the concomitant vaccines when given with MenACYW-TT.

Figure 6: Safety Profile of MenACYW-TT is Comparable to That of Licensed Vaccine in Age Group 12-23 Months (MET51)

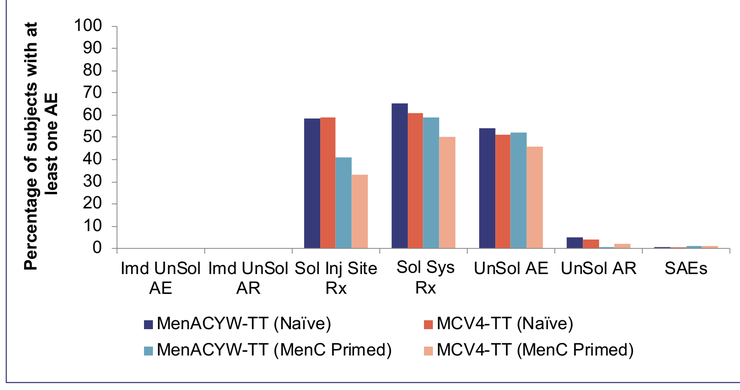


Figure 7: Safety Profile of MenACYW-TT is Comparable to That of Licensed Vaccine in Age Group 2-9 Years (MET35)

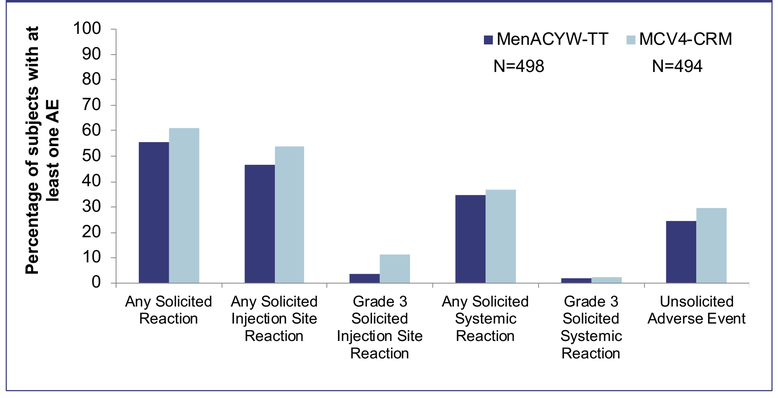


Figure 8: Safety Profile of MenACYW-TT is Comparable to That of Licensed Vaccine in Age Group 10-17 Years (MET50)

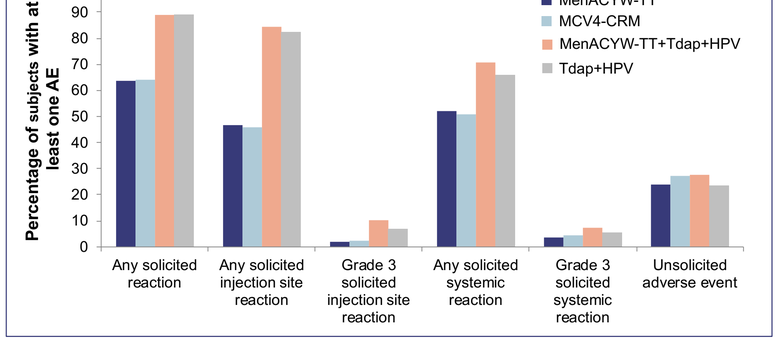
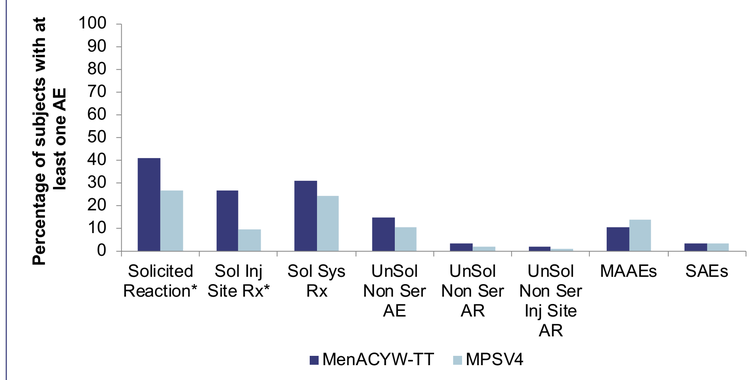


Figure 9: Safety Profile of MenACYW-TT is Comparable to That of Licensed Quadrivalent Polysaccharide Vaccine in Age Group ≥56 Years (MET49)



Sol Inj Site Rx – Solicited injection site reaction; Sol Sys Rx – Solicited systemic reaction; UnSol Non Ser AE – Unsolicited non serious adverse event; UnSol Non Ser AR – Unsolicited non serious adverse reaction; UnSol Non Ser Inj Site AR – Unsolicited non serious injection site adverse reaction; MAAEs – medically attended adverse events; SAEs – serious adverse events

- **MenACYW-TT was well tolerated and no safety concerns were identified.**
- **MenACYW-TT demonstrated a non-inferior immune response compared to the standard of care quadrivalent conjugate or polysaccharide meningococcal vaccines in a broad age range of 12 months and above.**
- **MenACYW-TT demonstrated higher or comparable seroprotection rates compared to the standard of care quadrivalent conjugate or polysaccharide meningococcal vaccines in a broad age range of 12 months and above including elderly.**
- **This vaccine will be a global option for the prevention of invasive meningococcal disease in a broad age range.**

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