

# SAFETY AND IMMUNOGENICITY OF A TETANUS TOXOID CONJUGATED QUADRIVALENT MENINGOCOCCAL VACCINE (MenACYW-TT) IN HEALTHY MENINGOCOCCAL VACCINE NAÏVE TODDLERS (12-23 MONTHS)

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## BACKGROUND

- Quadrivalent meningococcal conjugate vaccines offer protection against 4 of the most invasive *N. meningitidis* serogroups - A, C, Y and W
- MenACYW-TT (MenQuadfi®) is a quadrivalent meningococcal conjugate vaccine licensed for use in individuals 12 months of age and older in the EU and certain other countries
- Three randomized studies evaluated the safety and immunogenicity of MenACYW-TT when administered as a single dose in meningococcal vaccine-naïve toddlers
- We report the results pooled from these three randomized studies in this poster (EudraCT# 2018-001472-38, EudraCT# 2016-000749-30, EudraCT# 2017-001993-40)

## METHODS

### Source of Data for Pooled Analysis

- A Phase II study (MET54) was conducted in Finland in which 188 meningococcal vaccine-naïve toddlers received either MenACYW-TT or MCV4-TT [Nimenrix®]<sup>1</sup>
- A Phase III study (MET51) was conducted in Germany, Spain, Finland and Hungary. Overall, 609 meningococcal vaccine-naïve toddlers were recruited from Finland and Hungary and randomized to receive a single dose of either MenACYW-TT or MCV4-TT<sup>2</sup>
- A second Phase III study (MET57) conducted in South Korea, Thailand, Russia and Mexico, evaluated 1183 toddlers who received either a single dose of MenACYW-TT administered alone, or single dose of MenACYW-TT co-administered with routine pediatric vaccines, or routine pediatric vaccines alone. The routine pediatric vaccines administered varied according to country [DTaP-IPV-HB-Hib (Mexico); PCV13 (Russia) & MMR+V (South Korea and Thailand)]<sup>3</sup>

### Immunogenicity and Safety methods

- Serum bactericidal assays using human (hSBA) and baby rabbit (rSBA) complement were used to measure antibodies against meningococcal serogroups A, C, W and Y at baseline (D0) and 30 days (D30) after vaccination
- Safety data were collected for 30 days after the dose of vaccine
  - Immediate unsolicited adverse events (AEs) within 30 mins of vaccination
  - The interval for solicited adverse reactions (ARs) was between D0 and D7
  - Collection of solicited reactogenicity included daily measurement of body temperature and injection site erythema and swelling, as well as recording of the intensity for injection site tenderness, appetite lost, irritability, vomiting, abnormal crying and drowsiness
  - Unsolicited AEs, Adverse Events of Special Interest (AESIs)\* and Serious Adverse Events (SAEs) were collected throughout the studies

\*AESIs collected during the Phase III study in EU: seizures, Kawasaki disease, Idiopathic Thrombocytopenic Purpura & Guillain-Barre Syndrome

**Table 1: Participant disposition of the pooled meningococcal vaccine-naïve toddlers**

	MenACYW-TT Conjugate Vaccine (N=1174) <sup>1</sup>	MCV4-TT Control Vaccine (N=382) <sup>2</sup>	MenACYW-TT Conjugate Vaccine (N=691) <sup>3</sup>	MCV4-TT Control Vaccine (N=400) <sup>4</sup>
<b>Gender</b>				
Male n(%)	647 (55.1%)	196 (51.3%)	380 (55.0%)	202 (50.5%)
Female n(%)	527 (44.9%)	186 (48.7%)	311 (45.0%)	198 (49.5%)
<b>Age (months)</b>				
Mean (SD)	15.9 (3.21)	16.7 (3.43)	16.2 (3.39)	16.7 (3.42)
Min:Max	12.0;24.0	12.0;24.0	12.0;24.0	12.0;24.0
Median	15.3	16.0	15.0	16.0

<sup>1</sup>Per-Protocol Analysis Set (MET51, MET54 and MET57) – for immunogenicity evaluation

<sup>2</sup>Per-Protocol Analysis Set (MET51 and MET54) – for immunogenicity evaluation

<sup>3</sup>Safety Analysis Set (MET51, MET54 and MenACYW-TT administered alone recipients from MET57) – for safety evaluation

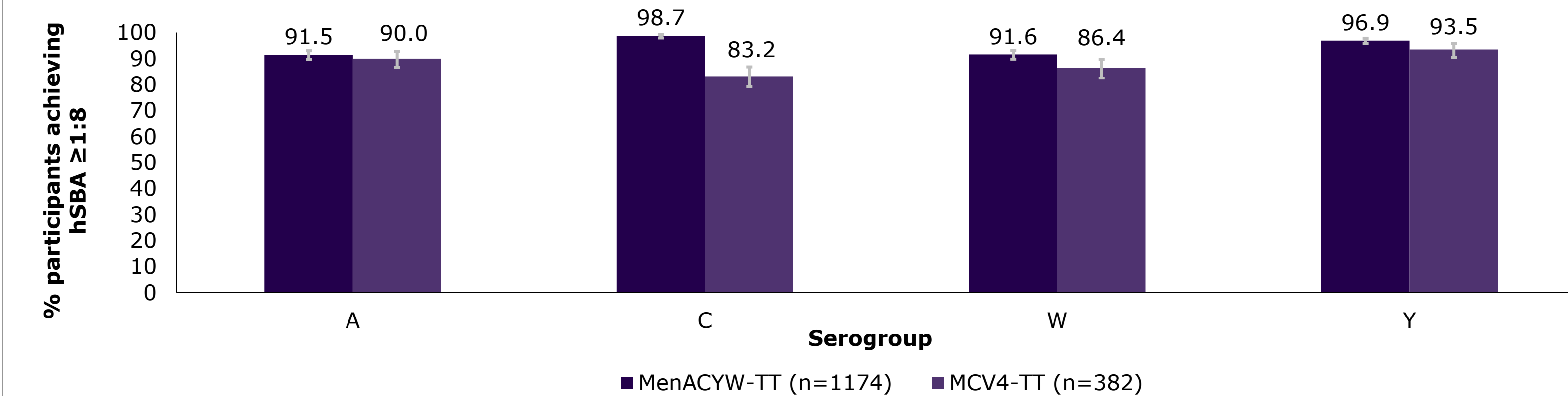
<sup>4</sup>Safety Analysis Set (MET51 and MET54) – for safety evaluation

## RESULTS

### Summary of Immunogenicity Findings

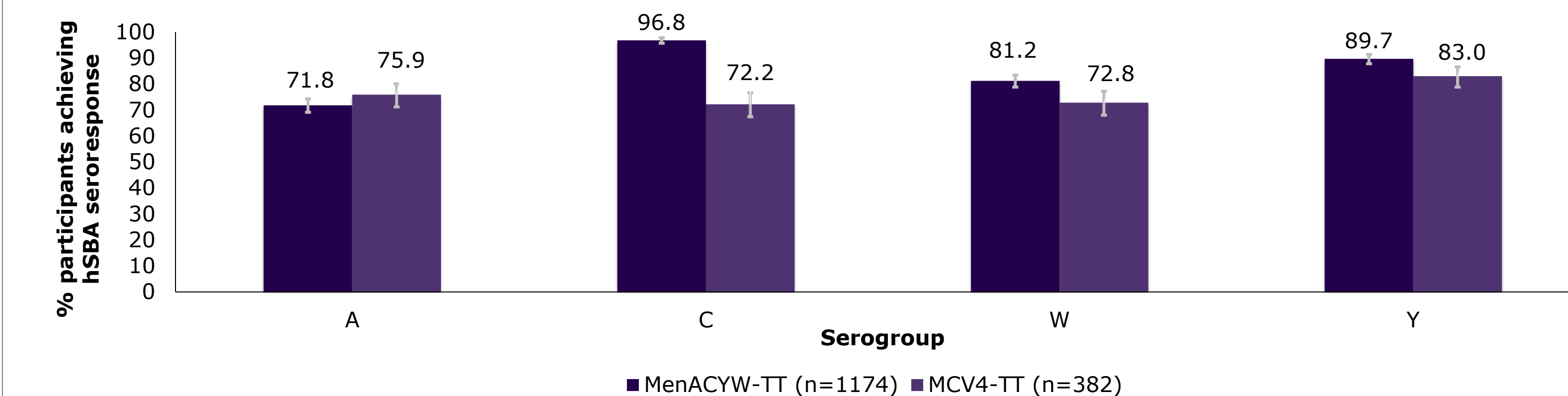
- In the pooled population at D30, the majority (≥ 91.5%) of toddlers who received MenACYW-TT had hSBA titers ≥ 1:8 (seroprotection) across all 4 serogroups
- Higher seroprotection rates for serogroups C, W and Y, and comparable rates for serogroup A, were observed in toddlers who received MenACYW-TT compared to those who received MCV4-TT (**Figure 1**)
- Higher hSBA vaccine seroresponse for serogroups C, W and Y, and comparable seroresponse for serogroup A, were observed in toddlers who received MenACYW-TT compared to those who received MCV4-TT (**Figure 2**)
- Higher GMT at D30 after vaccination for serogroups C, W and Y, and comparable GMT for serogroup A, were observed in toddlers who received MenACYW-TT compared to those who received MCV4-TT (**Figure 3**)

**Figure 1: Percentage of Meningococcal Vaccine-Naïve Toddlers Achieving hSBA Seroprotection\* at D30 after Vaccination (Per Protocol Analysis Set – Pooled MET51, MET54 and MET57)**



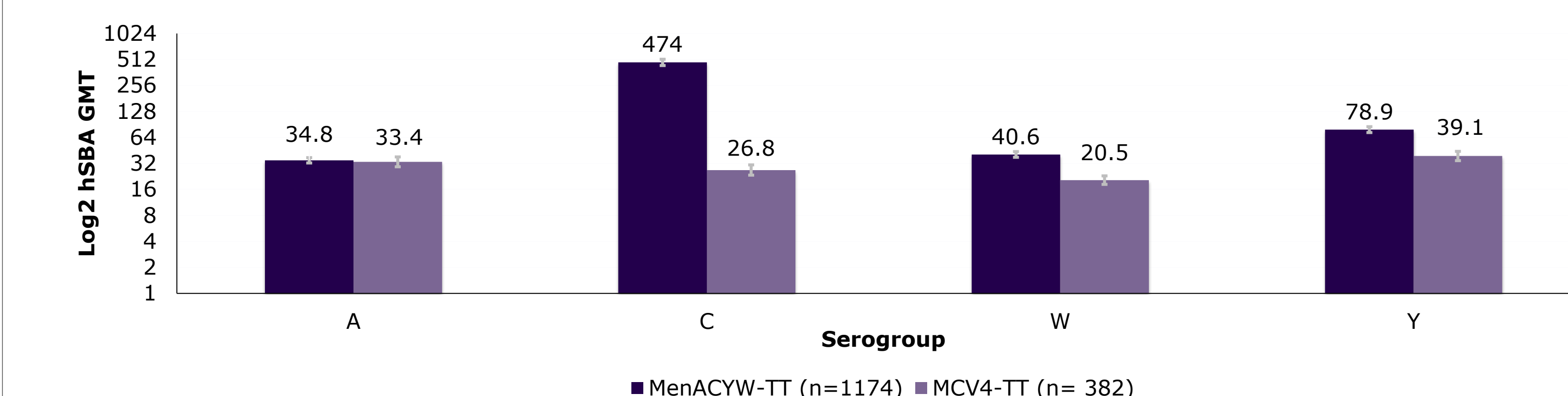
\*Seroprotection: post vaccination hSBA ≥1:8  
hSBA: Serum Bactericidal Assay using human complement  
D30: 30 days post vaccination

**Figure 2: hSBA Seroresponse\* Rates in Meningococcal Vaccine-Naïve Toddlers at D30 Post Vaccination (Per Protocol Analysis Set - Pooled MET51, MET54 and MET57)**



hSBA: Serum Bactericidal Assay using human complement  
D30: 30 days post vaccination  
\* Vaccine Seroresponse rate: Post vaccination titer ≥1:16 if pre vaccination titer is <1:8 or ≥4 fold rise in post vaccination titer if pre vaccination titer is ≥1:8

**Figure 3: hSBA Geometric Mean Titers in Meningococcal Vaccine-Naïve Toddlers at D30 Post Vaccination (Per Protocol Analysis Set - Pooled MET51, MET54 and MET57)**



hSBA: Serum Bactericidal Assay using human complement  
GMT: Geometric Mean Titer  
D30: 30 days post vaccination

**Table 2: Percentage of Meningococcal Vaccine-Naïve Toddlers Achieving rSBA Titer ≥1:128 at D30 Post Vaccination (Per Protocol Analysis; Subset of Vaccines; Pooled MET51, MET54 and MET57)**

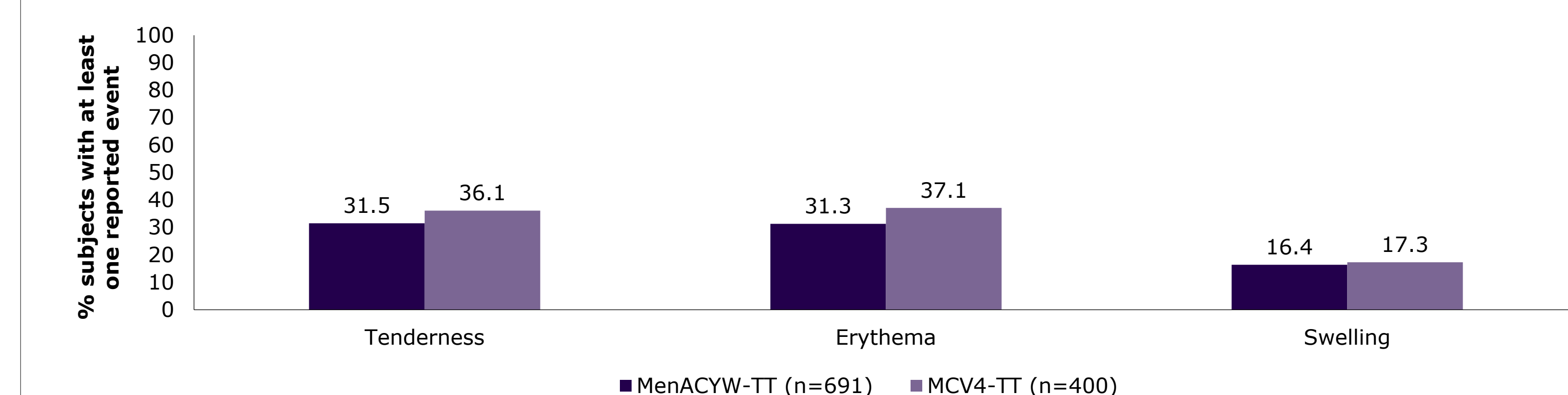
Serogroups	MenACYW-TT % (95% CI) (N=544)	MCV4-TT % (95% CI) (N=189)
A	98.3 (96.9; 99.2)	100 (98.1; 100.0)
C	99.6 (98.7; 100.0)	93.7 (89.2; 96.7)
W	99.1 (97.9; 99.7)	100 (98.1; 100.0)
Y	99.1 (97.9; 99.7)	99.5 (97.1; 100.0)

CI: Confidence interval  
rSBA: Serum Bactericidal Assay using baby rabbit complement

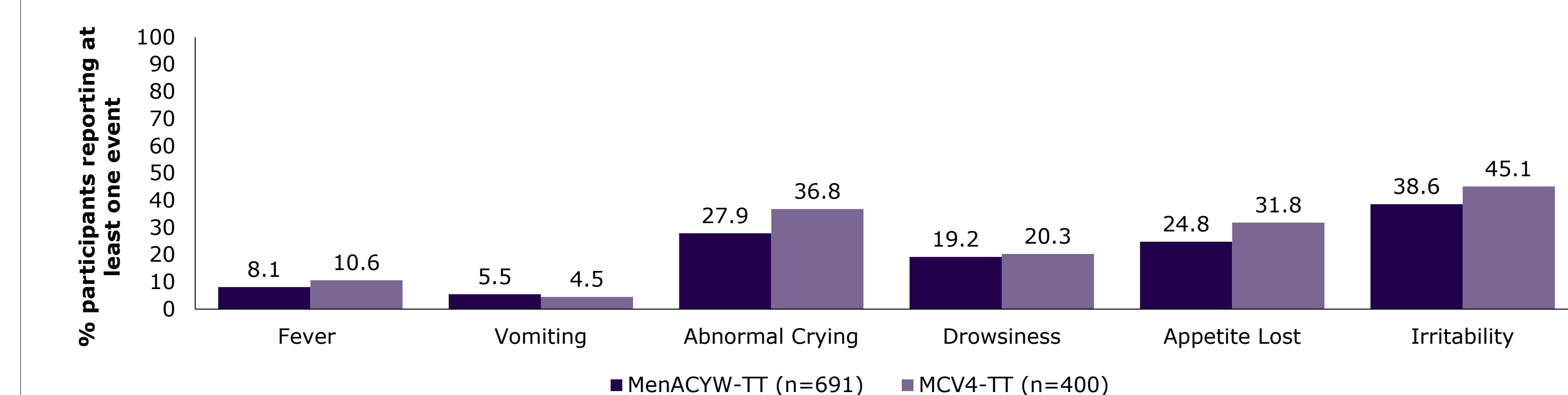
### Summary of Safety Findings in Meningococcal Vaccine-Naïve Toddlers (Descriptive Analysis)

- Since 2 out of the 3 studies contributing to the analysis were active controlled studies (using MCV4-TT), the safety profile of MCV4-TT vaccine (n=400) is based on pooled data from MET54 and MET51, and the safety profile of MenACYW-TT (n=691) is based on pooled data from MET54, MET51 and MET57 (only participants who received the MenACYW-TT vaccine without routine vaccines)
- Overall, the safety profiles of MenACYW-TT and MCV4-TT were generally comparable
- The percentages of subjects who reported at least 1 solicited injection site reaction tended to be lower in MenACYW-TT [47% (95%CI 43.2; 50.8)] vs MCV4-TT recipients [57.6% (52.6; 62.5)]
- The percentages of subjects who reported at least 1 solicited systemic reaction tended to be lower for MenACYW-TT [54.4% (50.6; 58.2)] vs MCV4-TT recipients [62.9% (58; 67.7)]
- The percentages of subjects who reported at least 1 unsolicited AE were comparable between MenACYW-TT [46.7% (43; 50.5)] and MCV4-TT recipients [53.5% (48.5; 58.5)]
- There were no immediate AEs or ARs and no vaccine-related SAEs reported from the studies contributing to this pooled analysis

**Figure 4: Solicited Injection Site reactions Following Vaccination in Meningococcal Vaccine-Naïve Toddlers (Safety Analysis Set- Pooled MET51, MET54 and MET57)**



**Figure 5: Solicited Systemic Reactions Following Vaccination in Meningococcal Vaccine-Naïve Toddlers (Safety Analysis Set- Pooled MET51, MET54 and MET57)**



## CONCLUSIONS

- The results observed with the data pooled across studies are consistent with the results observed in the individual studies
- MenACYW-TT vaccine was well tolerated and demonstrated a strong immune response when administered as a single dose to meningococcal vaccine-naïve toddlers

### ACKNOWLEDGEMENTS

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- The authors would also like to respectfully acknowledge the contributions of Dr. Jose Luis Arredondo-Garcia to the MET57 study and the field of vaccine research. Dr. Garcia tragically succumbed to COVID related complications in 2020
- The studies were sponsored by Sanofi

### AUTHORS AND CONFLICT OF INTEREST

- TV received funding to his institute from Sanofi for the conduct of this study, has received honoraria from Sanofi for advisory boards. BS has no conflicts to declare. LN-B, K-HK, KL, and WJ have no conflict of interest to declare. JLA-G received Sanofi resources to carry out this project through his institution. BZ, DC, JP, SBC, JP, DN, EJ and MSD are employees of Sanofi, and may hold shares and/or stock options in the company. JO and DVV were employees of Sanofi during the conduct of the study and may hold shares and/or stock options in the company

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This data was earlier presented at the 39th Annual Meeting of the European Society of Paediatric Infectious Diseases (ESPID); 24th to 29th May 2021