PUBLICATION CARD

Immunogenicity and safety of a quadrivalent meningococcal tetanus toxoid conjugate vaccine (MenACYW-TT) in healthy toddlers in Finland

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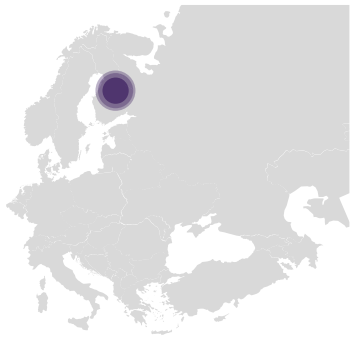
INTRODUCTION

- In Europe, despite a slow decline in incidence rate of IMD between 2000 and 2016, the age standardised rate of IMD was 0.64 per 100,000, with a case fatality rate of 10.4% in 2016
- 90% of reported cases of IMD in Europe were caused by serogroups B, C, W and Y in 2016
- Currently, MCV4-CRM and MCV4-TT are the only conjugate quadrivalent vaccines licensed in Europe to protect against IMD



OBJECTIVE

- To evaluate the immunogenicity and safety of **MenACYW-TT** compared with licensed vaccine **MCV4-TT**, in healthy toddlers

METHODS

STUDY DESIGN

Phase II
randomised, open-label descriptive study, conducted across
8 centres
in Finland

AGE OF PARTICIPANTS

Meningococcal vaccine-naïve toddlers aged
>12 to <24 months

INTERVENTION

188 healthy toddlers
were randomised 1:1 to receive one dose of MenACYW-TT (n=94) or MCV4 control (n=94)

MenACYW-TT and **MCV4-TT** contained 10 µg and 5 µg of each serogroup (A, C, Y, and W) and
55 µg and 44 µg of tetanus toxoid protein carrier per dose, respectively

STUDY DURATION

31 March 2015 — 19 August 2015

ASSESSMENTS

SAFETY[a]

- Participants were observed for 30 minutes after vaccination (for immediate unsolicited AEs)
- Parents/legal guardians recorded solicited AEs up to 7 days, and unsolicited AEs until 30 days after vaccination in diary card

IMMUNOGENICITY[b]

- Blood samples were collected pre-vaccination on Day 0 and post vaccination on Day 30
- hSBA and rSBA[c] GMTs, seroprotection[d] and seroresponse[e] were measured for each serogroup (A, C, Y, and W)
- GMCs of anti-tetanus antibodies were measured by ELISA both pre- and post vaccination

RESULTS

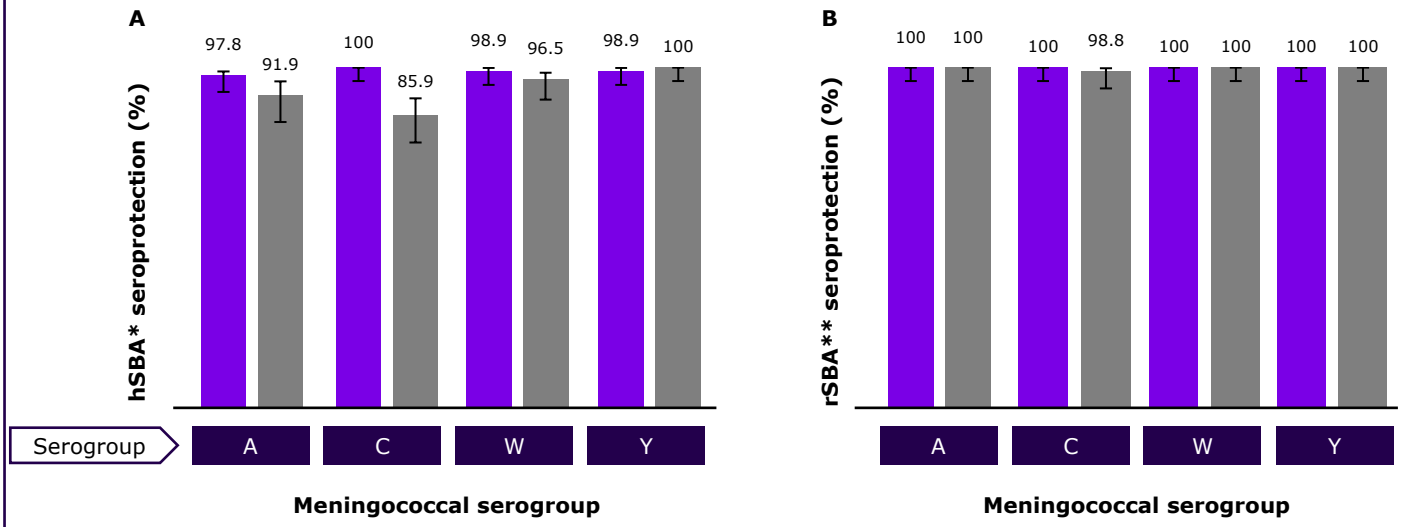
SAFETY (n=188)

- There were no immediate unsolicited AEs or reactions after vaccination in either vaccine group
- Solicited AEs up to 7 days after vaccination were comparable (79.8% in MenACYW-TT group vs 83.0% in MCV4-TT group)
- No unsolicited non-serious injection-site ARs were reported following administration of MenACYW-TT, but these events were reported in 3.2% of toddlers who received MCV4-TT
- There were no AEs, SAEs or ARs that led to discontinuation of the study, and there were no reported deaths

IMMUNOGENICITY[b]

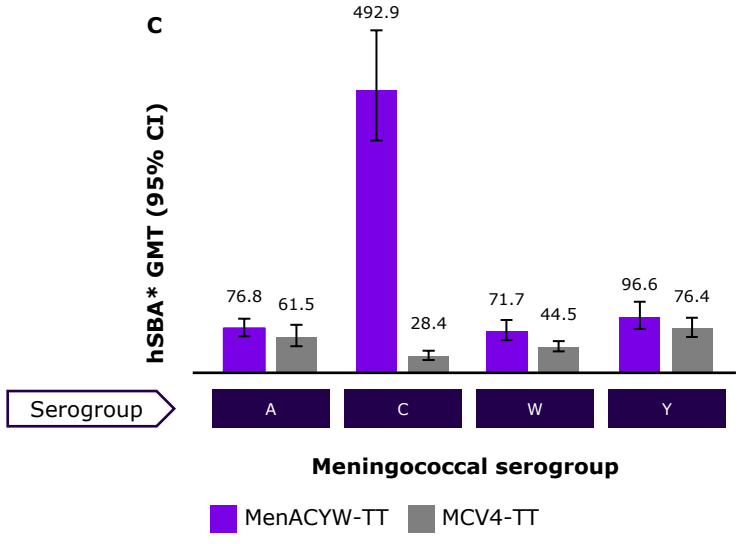
- By Day 30, hSBA and rSBA GMTs for all serogroups had increased with notable difference in serogroup C between MenACYW TT group (492.9 with hSBA and 2440.1 with rSBA) and MCV4-TT group (28.4 with hSBA and 418.6 with rSBA)
- The proportion of participants with seroprotection at Day 30 was >90% for each serogroup in both vaccine groups
- hSBA vaccine seroresponse at Day 30 was similar in both groups for serogroups A, W and Y, but was higher for serogroup C in the MenACYW-TT group (100%) than in the MCV4-TT group (86.0%)
- At baseline, the rSBA seroresponse for serogroup A was higher in the MenACYW-TT group (33.0%) compared with the MCV4-TT group (17.4%). However, at Day 30 the seroresponse for serogroup A was lower in the MenACYW-TT group (91.2%) compared to the MCV4-TT group (98.8%), but was similar for the other serogroups (C, W and Y)
- GMCs of anti-tetanus antibodies measured by ELISA were similar in both groups

Proportion of participants with vaccine seroprotection at Day 30 against meningococcal serogroups A, C, W and Y (PPAS)



*hSBA seroprotection was defined as titre <8 at baseline with post-vaccination titre ≥8 or titre is ≥8 at baseline with a ≥4-fold increase at post vaccination
**rSBA seroprotection was defined as titre <8 at baseline with post-vaccination titre ≥32 or titre is ≥8 at baseline with a ≥4-fold increase at post vaccination

Geometric mean titers at Day 30 post-vaccination as assessed by hSBA (PPAS)



The error bars represent the upper and lower values of the 95% CI

LIMITATIONS

- Due to the differences in the appearances of the vaccines, this was an open-label design that could incur the risk of bias; however, laboratory technicians were blinded to vaccine assignment
- There was a slightly imbalanced gender ratio (52.1% males and 47.9% females), which is known to have an effect on immunogenicity as males have been found to be more susceptible to IMD compared to females

KEY MESSAGES

1. MenACYW-TT generated a comparable immune response to the licensed MCV4-TT vaccine
2. MenACYW-TT is well tolerated and has a comparable safety profile with MCV4-TT
3. MenACYW-TT has the potential to be considered as an alternative vaccination option

[a]Safety analyses were based on the SAS, which included all participants who received at least one dose of study vaccine and had any safety data available;

[b]Immunogenicity analyses were based on the PPAS, which included all participants who received at least one dose of the study vaccine, had at least one valid serology result and were without major pre-defined protocol deviations

[c]hSBA and rSBA assays were performed in global clinical immunology labs, Sanofi and Public Health England labs, respectively;

[d]Seroprotection is defined as hSBA titres and post vaccination rSBA titres of ≥1:8;

[e]Seroresponse defined as % of subjects with post-vaccination titre ≥1:8 if baseline titre is <1:8 or ≥four-fold increase if baseline titre is ≥1:8;

Glossary: AE, adverse event; **AR,** adverse reaction; **ELISA,** enzyme-linked immunosorbent assay; **GMC,** geometric mean concentration; **GMT,** geometric mean titre; **hSBA,** human serum bactericidal assay; **IMD,** invasive meningococcal disease; **MCV4-CRM,** quadrivalent meningococcal vaccine conjugated to the diphtheria toxin mutant CRM197; **MCV4-TT,** quadrivalent meningococcal vaccine; **MenACYW-TT,** quadrivalent meningococcal tetanus toxoid conjugate vaccine; **PPAS,** per-protocol analysis set; **rSBA,** rabbit serum bactericidal assay; **SAE**, serious adverse event; **SAS,** safety analysis set

References: Vesikari T, *et al.* Immunogenicity and safety of a quadrivalent meningococcal tetanus toxoid conjugate vaccine (MenACYW-TT) in healthy toddlers: a Phase II randomized study. *Hum Vaccin Immunother*. 2020;16(6):1306–12. [NCT03205358 https://clinicaltrials.gov/ct2/show/NCT03205358] [Last accessed August 2020].

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