PERFORMANCE OF LICENSED MENINGOCOCCAL VACCINES AGAINST HYPERVIRULENT MENC STRAINS: AN INTERESTING *POST-HOC* ANALYSIS

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BACKGROUND

- This *post-hoc* analysis was triggered by the evidence of an increase in invasive meningococcal disease (IMD) incidence in Tuscany (Italy) in 2015/16 (**Figure 1** and **2**), with the most common bacterial isolates being hypervirulent strains belonging to meningococcal serogroup C (MenC) clonal complexes cc11 and cc334.[1,2]

Figure 1. Annual distribution of MenC IMD cases by outcome between Jan 2000 – Feb 2016 (n=111) in Tuscany (Italy): a substantial increase observed in 2015

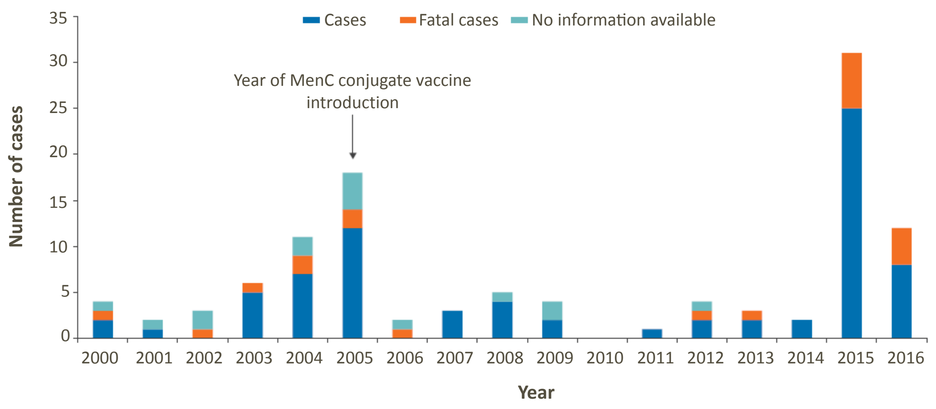
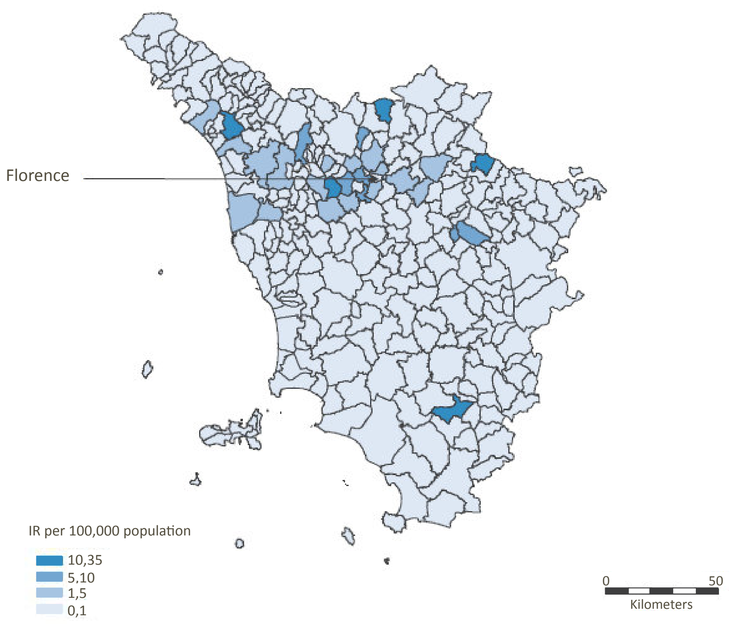


Figure 2. Incidence rate (IR) of MenC IMD cases by municipality of symptom onset in Tuscany (Italy) between Jan 2015 – Feb 2016 (n=43)



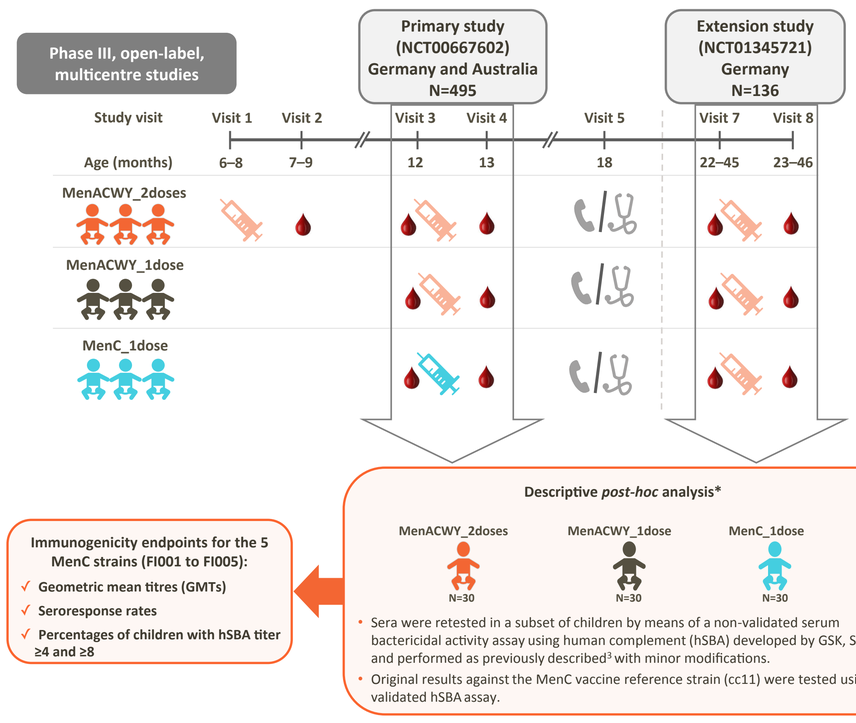
n, number of cases. Stefanelli P, et al. Euro Surveill. 2016; 21(12):pii=30176 under the terms of Creative Commons Attribution 4.0 international license (CC BY 4.0).

AIM

- The goal of this *post-hoc* analysis was to assess antibody titres against five MenC hypervirulent field strains (FI001 to 005; **Table 1**) in sera from children enrolled in previous trials where they were primed with either the quadrivalent meningococcal CRM_{197}-conjugate vaccine (MenACWY-CRM; *Menveo*, GSK) or the monovalent MenC CRM_{197}-conjugate vaccine (MenC-CRM; *Menjugate*, GSK) and who received a MenACWY-CRM booster dose.

METHODS

Figure 3. Sera from a subset of children who participated in 2 clinical studies were selected for this *post-hoc* analysis.



N, number of children in the according-to-protocol dataset for immunogenicity; 💉, MenACWY-CRM; 💉, MenC-CRM; 🩸,blood draw; 🩺, phone call or clinical visit; *on sera collected at visits 3, 4, 7 and 8 in a subset of study participants; seroresponse rate defined as hSBA titre ≥8 at visit 4 for children with titres <4 at visit 3 or a ≥4-fold increase in hSBA titres at visit 4 for children with titres ≥4 at visit 3.

References

1. Stefanelli P, et al. Euro Surveill. 2016; 21(12):pii=30176; **2.** Fazio C, et al. [Abstract EMGM2019-13159]; **3.** Borrow R, et al. Clin Diagn Lab Immunol. 2005; 12(8):970–6.

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CONCLUSIONS

- This *post-hoc* analysis showed that both MenACWY-CRM and MenC-CRM are able to elicit immune responses and immunological memory against hypervirulent cc11 and cc334 MenC strains responsible for outbreaks of IMD.
- Overall, there was a trend to higher antibody titres against FI002, FI003 and FI004 than against FI001 and FI005 hypervirulent field strains.
- hSBA GMTs were high after the MenACWY-CRM booster dose in all groups, with a trend to higher responses in children primed with MenC-CRM which was expected considering that MenC-CRM contains twice as much MenC antigen (10 µg) per dose as MenACWY-CRM and is also adjuvanted with aluminium hydroxide.
- Irrespective of the strain tested or the identity and number of doses of priming vaccine, hSBA titres ≥4 (not shown) and ≥8 were detected in almost all sera (≥96.7%) following a MenACWY-CRM booster dose.

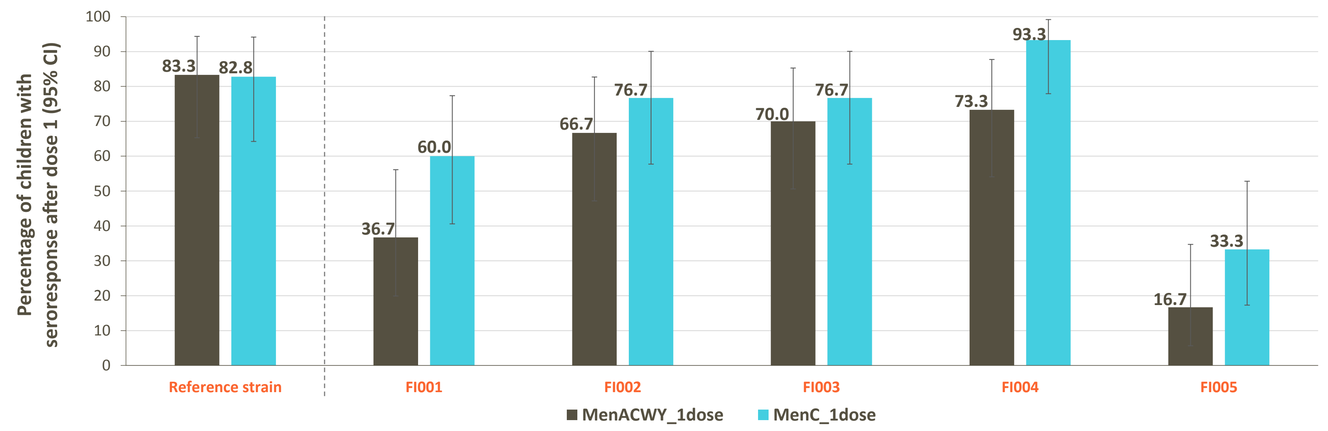
RESULTS

Table 1. Core gene analysis of the five MenC hypervirulent field strains isolated from IMD cases showed that four strains (FI001 to FI004) belonged to cc11 and one (FI005) to cc334

Strain	Clonal complex	Finetype	*penA* allele	*porB* allele	fHbp subvariant	NHBA peptide	*nadA*
FI001	11	C:P1.5-1,10-8:F3-6:ST-11(cc11)	398	2-2	1.13	20	allele 164 with 1 del, IS1301
FI002	11	C:P1.5-1,10-8:F3-6:ST-11(cc11)	248	2-2	1.13	20	allele 164 with 1 del, IS1301
FI003	11	C:P1.5-1,10-8:F3-6:ST-11(cc11)	398/248	2-2	1.13	20	allele 164 with 1 del, IS1301
FI004	11	C:P1.5-1,10-8:F3-6:ST-11(cc11)	398/248	2-2	1.13	20	allele 164 with 1 del, IS1301
FI005	334	C:P1.7,14-3:F3-9:ST-1031(cc334)	162/599	2-227	2.19	6	no

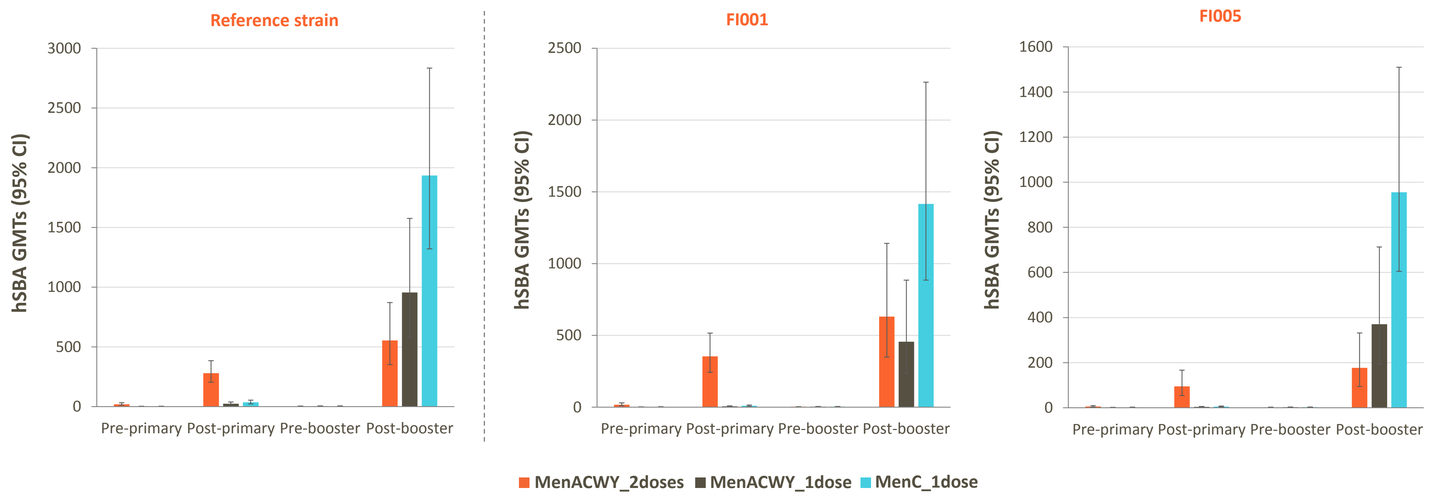
penA, gene encoding penicillin-binding protein 2; ***porB***, gene encoding porin B; **fHbp**, factor H binding protein; **NHBA**, neisserial heparin binding antigen; ***nadA***, gene encoding *Neisseria* adhesin A; **del**, deletion; **IS**, insertion

Figure 4. MenC hypervirulent field strains: post-primary seroresponse rates tended to be higher in the MenC_1dose group than in the MenACWY_1dose group



CI, confidence interval. Results against reference strains obtained on the same subset of children presented for descriptive comparison only.

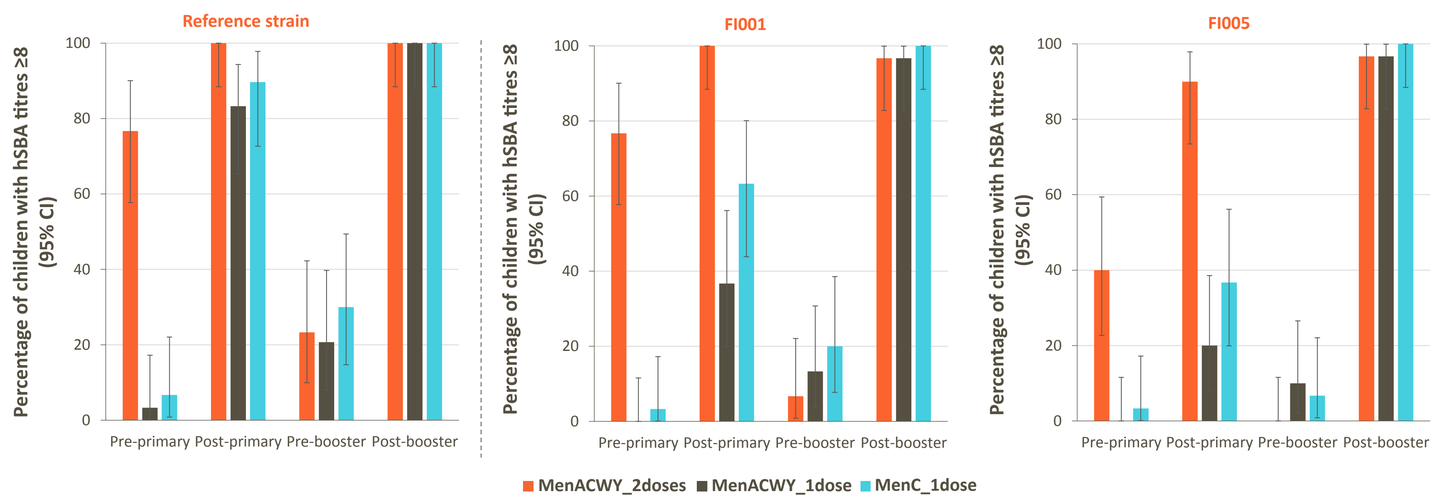
Figure 5. MenC hypervirulent field strains: hSBA GMTs were highest in the MenACWY_2doses group after primary vaccination and increased in all groups following the booster dose, with a trend to higher following MenC-CRM priming



Results against reference strains obtained on the same subset of children presented for descriptive comparison only.

- The post-primary hSBA GMTs for the FI002-004 strains were higher in MenACWY-CRM_2dose group (337.8 [FI002] – 588.1 [FI004]) than those observed in MenACWY_1dose (10.8 [FI002] – 27.2 [FI004]) and MenC_1 dose (18.4 [FI002] – 47.4 [FI004]) groups. GMTs increased >217-fold after booster vaccination compared to pre-booster in all groups (geometric mean ratio ranging from 217.8 [FI002, MenACWY_1dose group] to 977.8 [FI004, MenC_1dose group]).

Figure 6. Irrespective of the MenC hypervirulent field strain tested or the identity and number of doses of priming vaccine, hSBA titres ≥8 were detected in almost all sera tested (≥96.7%) following the MenACWY-CRM booster dose.



Results against reference strain obtained on the same subset of children presented for descriptive comparison only.

- hSBA titres ≥8 were observed in almost all sera tested (≥96.7%) following the MenACWY-CRM booster dose for the strains FI002 and FI003 and in all sera after the booster dose for FI004.

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