MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE (4CMENB) MAY ELICIT FUNCTIONAL IMMUNITY AGAINST SEROGROUP A STRAINS

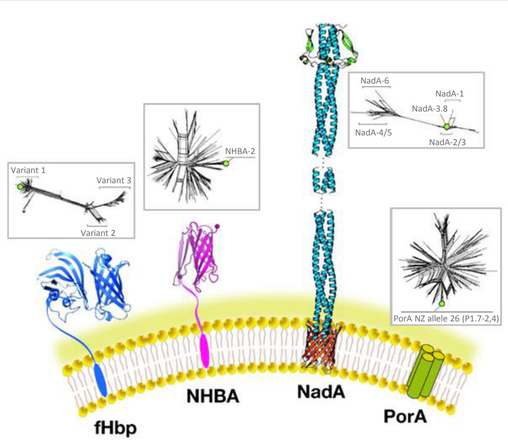
Alessia Biolchi, Maria Giuliani, Sara Tomei, Laura Santini, Elena Mori, Daniela Toneatto, Rita La Gaetana, Marzia Monica Giuliani, Mariagrazia Pizza

GSK, Siena, Italy

BACKGROUND AND AIM

- 4CMenB vaccine (*Bexsero*, GSK) is currently indicated for immunisation against invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B (MenB).[1]
- However, genes encoding the 4CMenB vaccine antigens are also present and expressed in strains belonging to other meningococcal serogroups.[2]
- We have recently demonstrated that sera from infants immunised with 4CMenB were able to kill 109 out of 147 genetically diverse isolates (collected in Europe and Brazil) belonging to meningococcal serogroups C, W and Y.[3]

Are antibodies raised by 4CMenB immunisation able to kill non-MenB strains?



4CMenB vaccine contains 4 antigens and is designed for broad coverage against MenB strains.

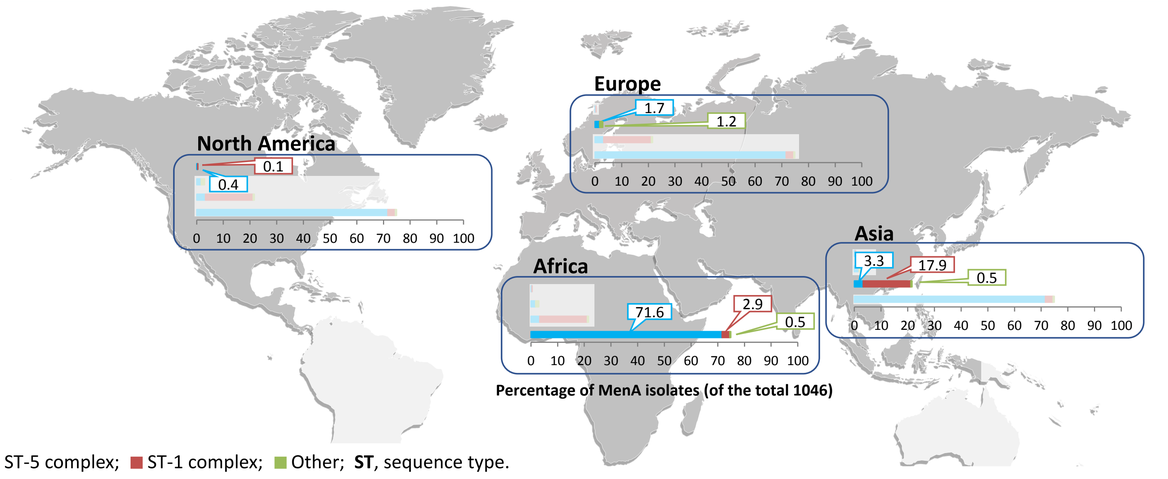
AIM OF THE STUDY: Adolescent sera taken after 4CMenB immunisation was tested to investigate the coverage against meningococcal serogroup A (MenA) strains.

fHbp, factor H binding protein; **NHBA**, Neisserial Heparin Binding Antigen; **NadA**, *Neisseria* adhesin A; **PorA**, porin A.

METHODS

- Sera derived from adolescents vaccinated with 2 doses of 4CMenB (NCT02212457) were tested in serum bactericidal antibody assay using human complement (hSBA) against a panel of strains representative of the current MenA epidemiology.
- The strain panel was selected based on the frequency of genetic profiles (clonal complex and 4CMenB antigen typing) in a dataset of MenA isolates, collected in different countries between 2000–2016, and available in PubMLST database.

The majority of ST-5 complex strains have been isolated in Africa, while ST-1 complex strains are mostly present in Asia. Presence of MenA in Europe and USA is very low.

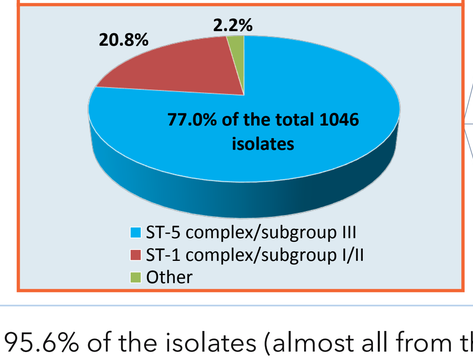


ST-5 complex; ST-1 complex; Other; **ST**, sequence type.

MATERIALS

Selection and characteristics of MenA strain isolates

- **1046 MenA isolates** from PubMLST
  - selection of the strains panel was based on the genetic profile of 4CMenB antigens (available for approximately 300 strains)
- **All MenA strains** were highly clonal



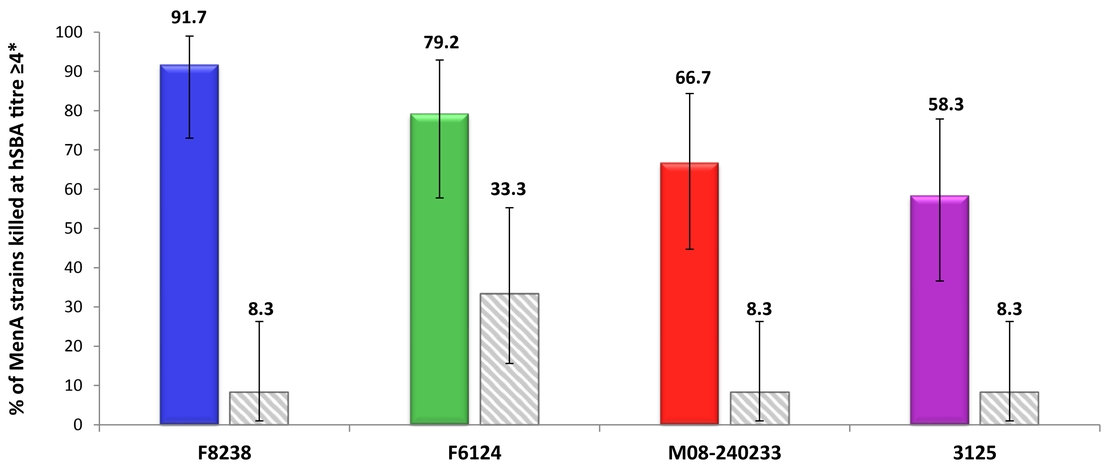
- Isolates belonging to **ST-5 complex/subgroup III**
  - carried the genes encoding for fHbp variant 1.5, NadA and PorA VR2 10
- Isolates belonging to **ST-1 complex/subgroup I/II**
  - carried the genes encoding for fHbp variant 1.4 and PorA VR2 9
  - did not carry the *nadA* gene
- **Selection for hSBA testing**
  - **3 strains from the ST-5 complex/subgroup III**
  - **1 strain from the ST-1 complex/subgroup I/II**

Strains	Clonal complex name	ST	PorA VR1	PorA VR2	fHbp	NHBA	NadA
F8238	ST-5 complex/subgroup III	5	20	9	1.5	27	8
F6124	ST-5 complex/subgroup III	5	20	9	1.5	27	8
M08-240233	ST-5 complex/subgroup III	4789	20	9	1.5	126	8
3125	ST-1 complex/subgroup I/II	7776	5-1	2-2	1.4	29	no

- 95.6% of the isolates (almost all from the ST-5 complex) for which the *nhbA* gene was sequenced had alleles encoding for the NHBA peptide 126.

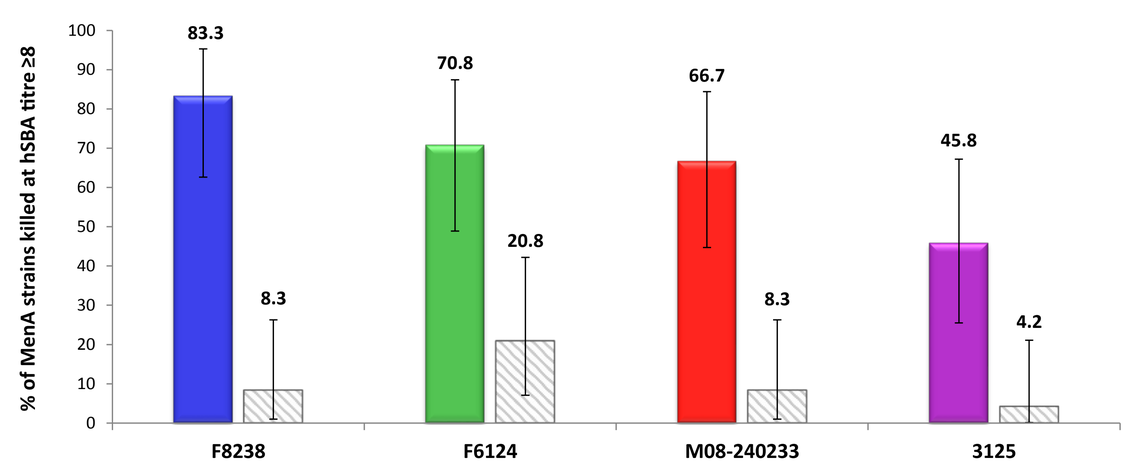
RESULTS

The percentage of MenA strains killed at **hSBA titre ≥4*** by adolescent post-immunisation sera ranged between 58.3% and 91.7%.

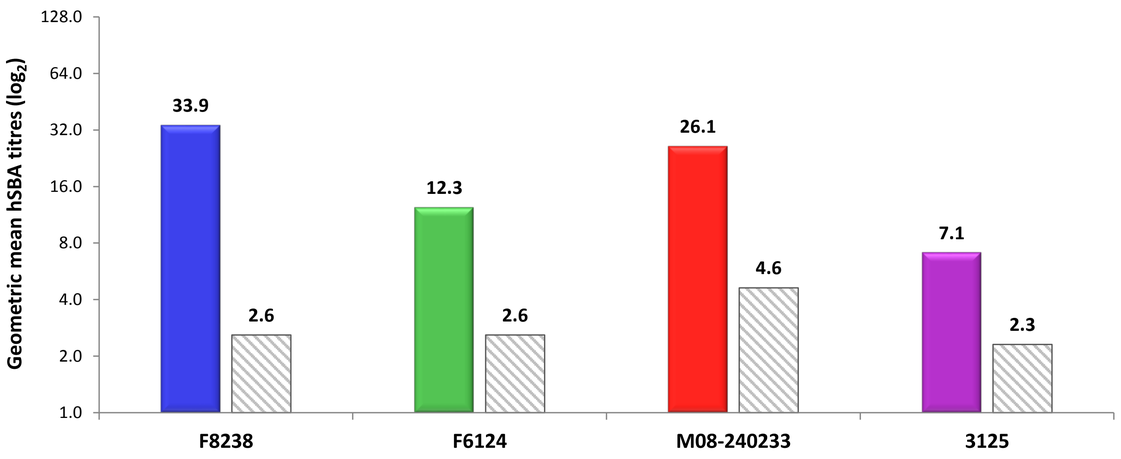


1 month post-dose 2 of 4CMenB vaccine; baseline; *accepted correlate of protection.

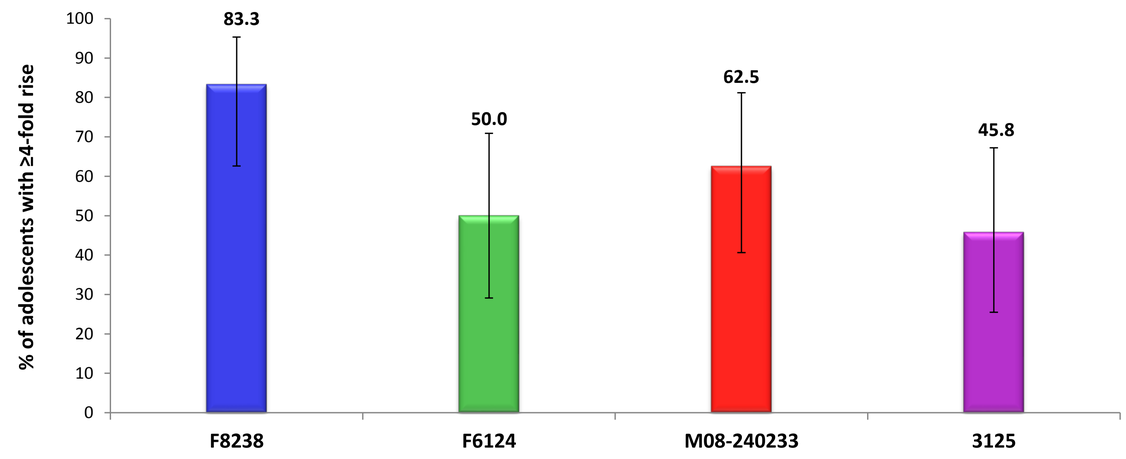
The percentage of MenA strains killed at **hSBA titre ≥8** by adolescent post-immunisation sera ranged between 45.8% and 83.3%.



Geometric mean hSBA titres tested against the 4 strains at 1 month post-dose 2 versus baseline



The percentage of adolescents with ≥4-fold rise in hSBA titres at 1 month post-dose 2 versus baseline ranged between 45.8% and 83.3%.



CONCLUSIONS

Sera from adolescents vaccinated with 4CMenB showed hSBA activity against MenA strains.

These results further support the evidence that 4CMenB vaccination may have an impact on meningococcal disease caused by serogroups other than MenB.

References
1. EMA. Bexsero Assessment Report. 2012. Product Information;
2. A. Bianchi et al. J Prev Med Hyg. 2015;56:E140–3;
3. M Pizza et al. ESPID, Slovenia, 2019. Abstract number: ESPID19-0255.

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Presenting author: Alessia Biolchi; alessia.x.biolchi@gsk.com

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