Advances in Vaccine Development for Meningococcal Serogroup B Disease

Philipp Oster, MD
Head, Development of Meningococcal B Vaccines
Novartis Vaccines & Diagnostics

Meningitis Research Foundation
November 7-8, 2007
London, UK

Key Points

- *N. meningitidis* serogroup B has high incidence and causes meningitis outbreaks in many regions of the world
- Reverse vaccinology is an innovative approach to identifying novel antigens as vaccine candidates against meningococcal serogroup B (MenB)
- The Novartis MenB vaccine is the first based on recombinant proteins to induce a robust bactericidal immune response against a broad panel of disease-causing strains
- The Novartis MenB vaccine is immunogenic and safe in adults and infants

Limitations of Conventional Approaches to Vaccinology for Prevention of MenB Disease

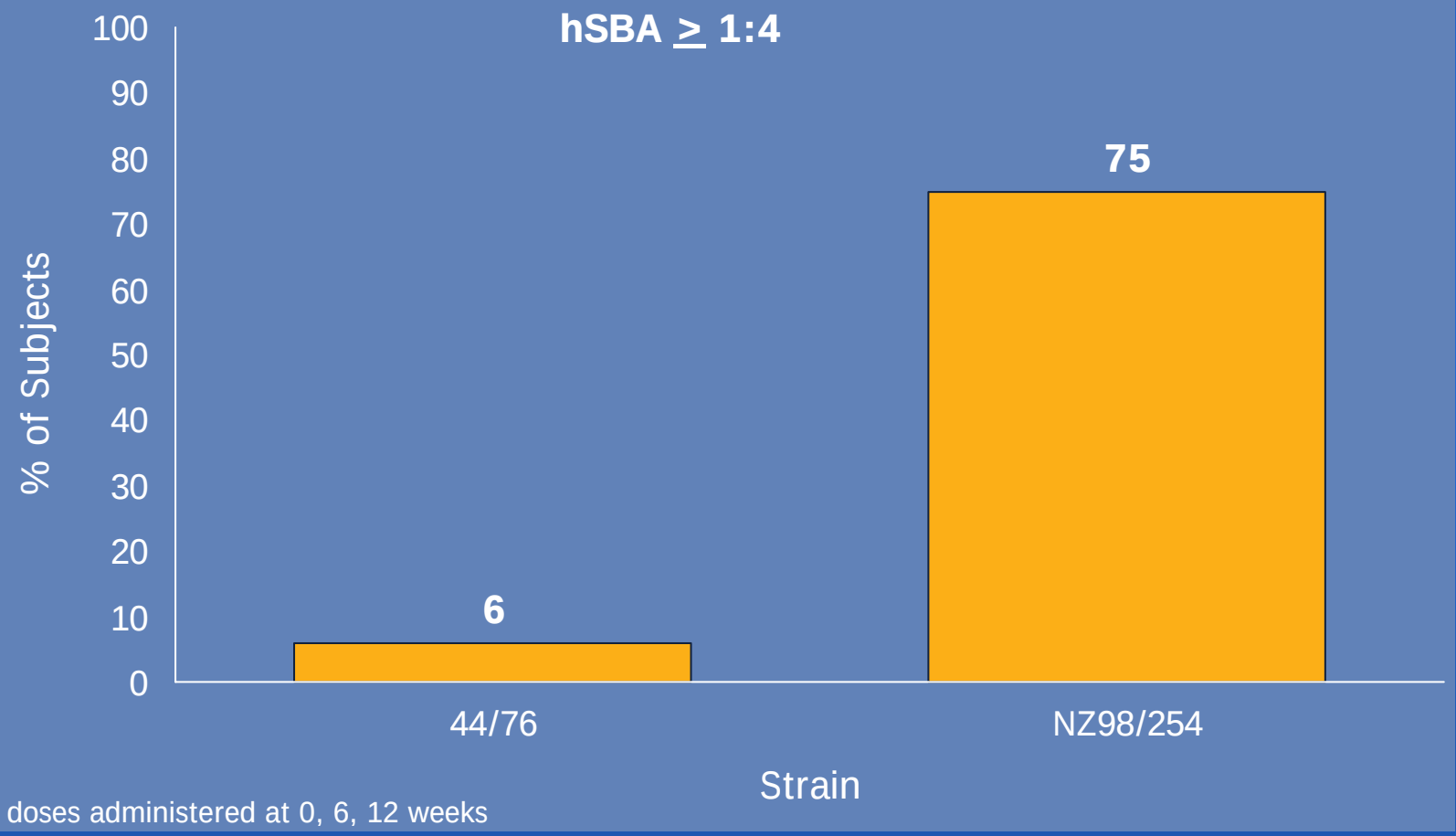
- Capsular Approaches
  - Plain polysaccharide vaccines[1,2]
    - Poorly immunogenic
    - Risk of autoimmunity
  - N-propionylated polysaccharide conjugates[3]
    - No functional activity of vaccine induced antibodies

- Non-Capsular Approaches[4]
  - OMV vaccines[5,6]
    - Sequence and antigen variability
    - Protection only against homologous strain
  - With the exception of NspA, all the surface-exposed proteins described during the past 3 decades are limited by antigenic variability.[7]

1. Häyrinen J et al. *J Infect Dis.* 1995; 171:1481-1490. 2. Finne J et al. *J Immunol.* 1987; 138:4402-4407. 3. Bruge J et al. *Vaccine.* 2004; 22:1087-1096. 4. Pizza M et al. *Science*. 2000; 287:1816-1820. 5. Zimmer SM and Stephens DS. *Curr Opin Investig Drugs*. 2007; 7:733-739. 6. Poolman JT. *Infect Agents Dis*. 1995; 4:13-28. 7. Martin D et al. *J Exp Med*. 1997; 185:1173-1183.

Immunogenicity MeNZB™ OMV Vaccine

Phase II 16-24 month old toddlers: Post 3rd dose*

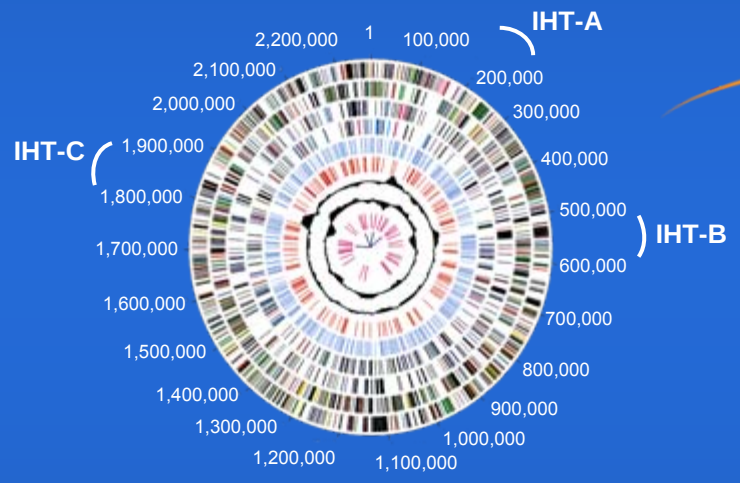


*3 doses administered at 0, 6, 12 weeks

Wong S et al. *Pediatr Infect Dis J.* 2007; 26:345-350.

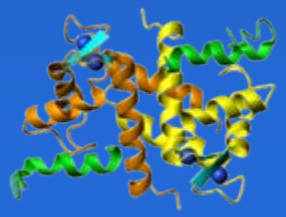
Reverse Vaccinology Approach

Based on the genome sequence of MC58, **600** ORFs that potentially encoded novel surface exposed or exported proteins were identified



~350 proteins successfully expressed in *E.coli*, purified, and used to immunize mice

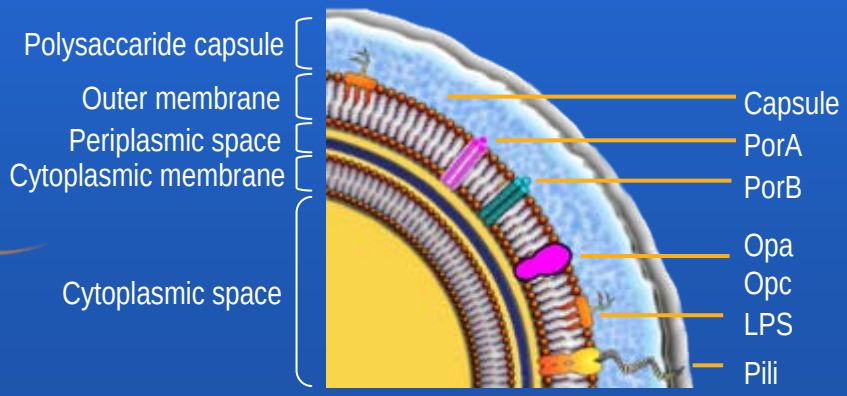
expression and purification



purified proteins

immunizations

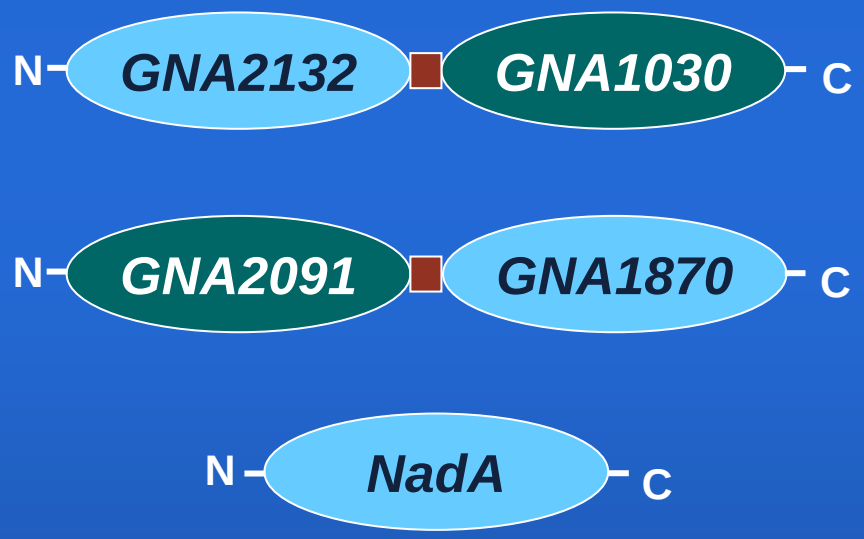
91 novel surface-exposed proteins identified



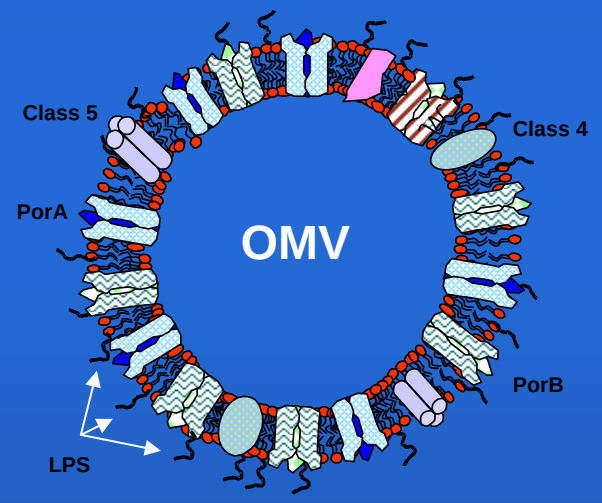
28 novel protein antigens with bactericidal activity were identified

Protein Antigen Combinations in an Effective Serogroup B Vaccine

3 protein antigens (2 fusion proteins and one single polypeptide)



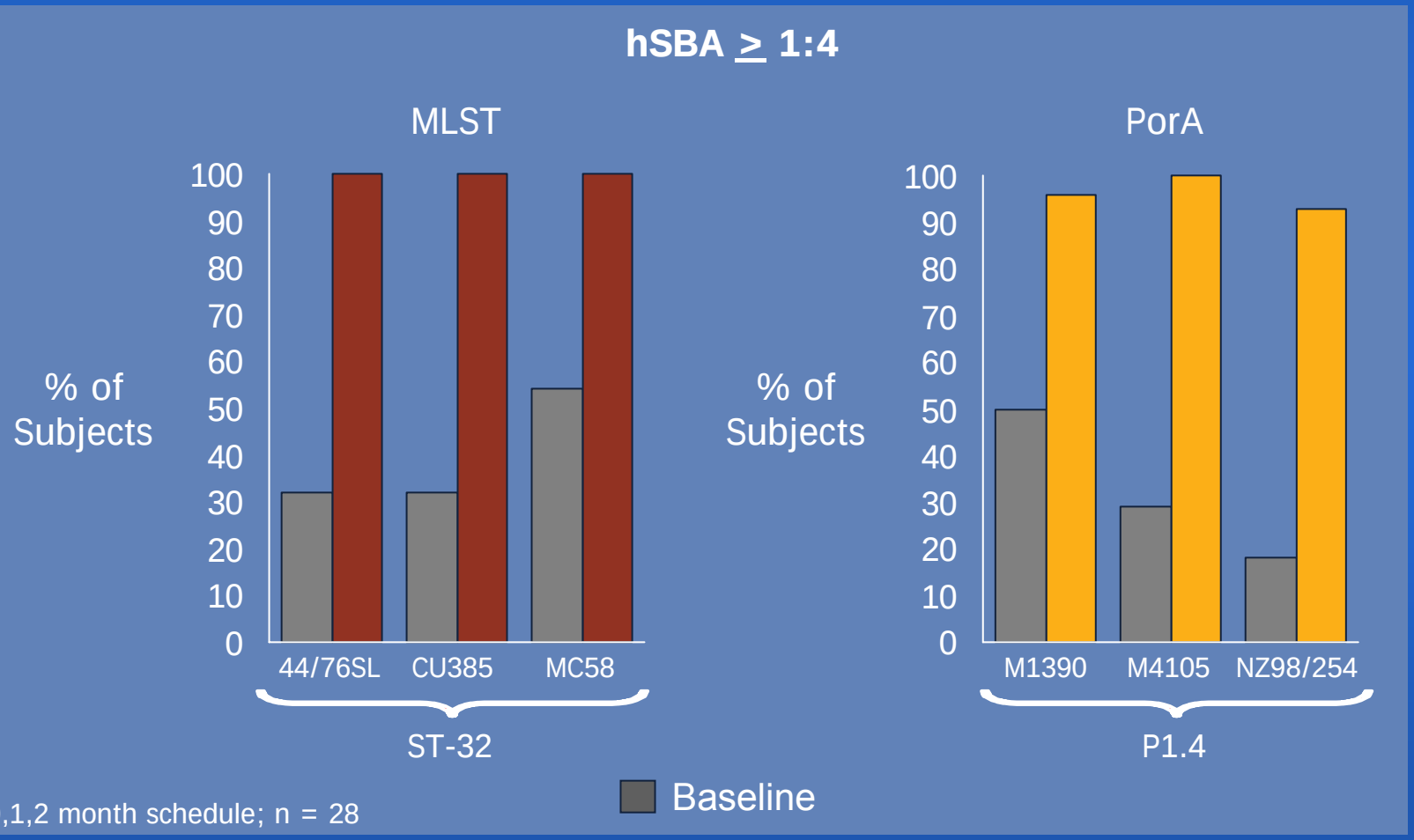
Outer Membrane Vesicle (OMV) component (NZ PorA is P1.4)



Giuliani MM et al. *PNAS*. 2006; 103:10834-10839.

Reverse Vaccinology: Proof of Concept

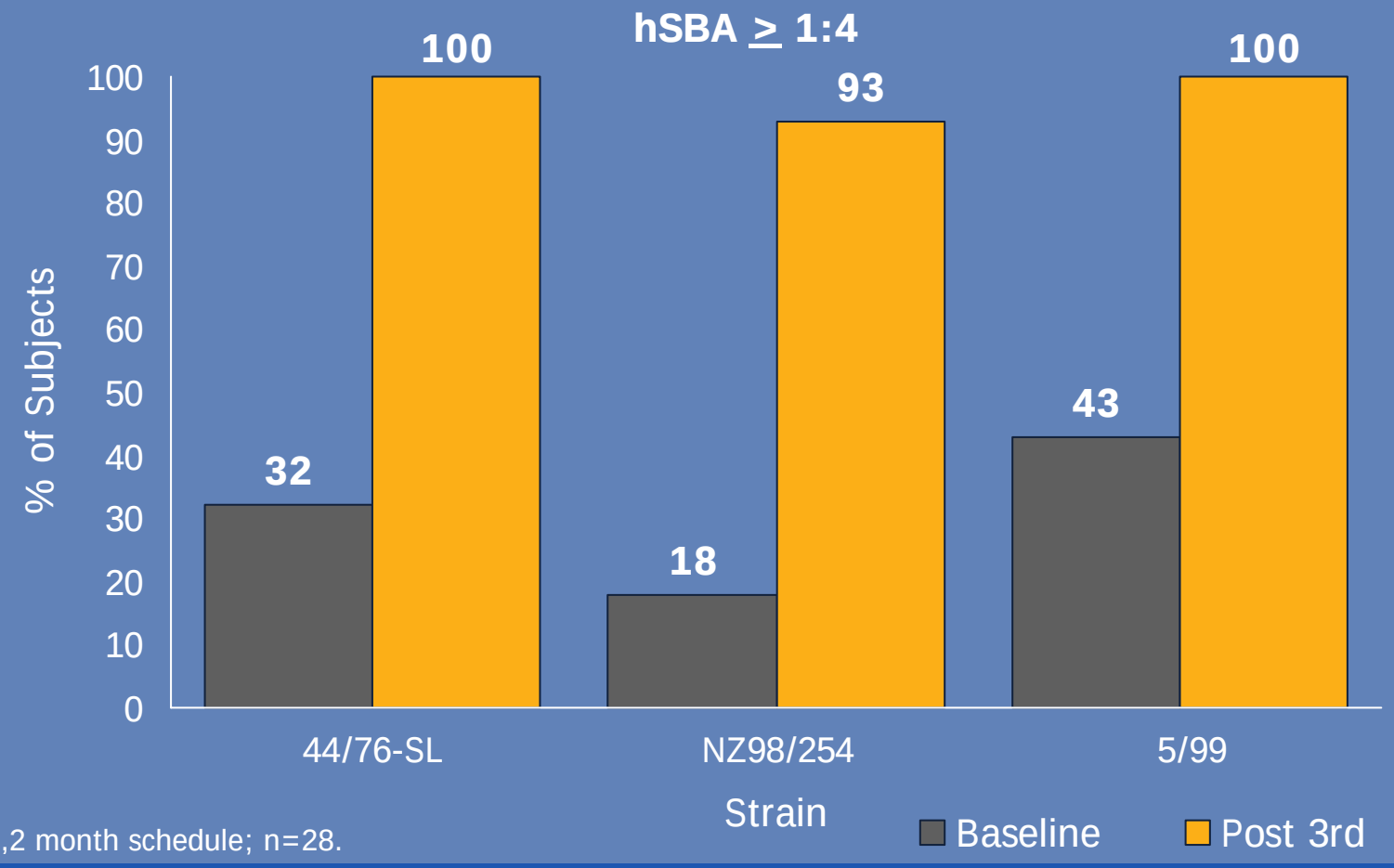
Phase I Adults: 1-month post 3rd dose*



*0,1,2 month schedule; n = 28

Novartis MenB Vaccine Immunogenicity Results in Adults

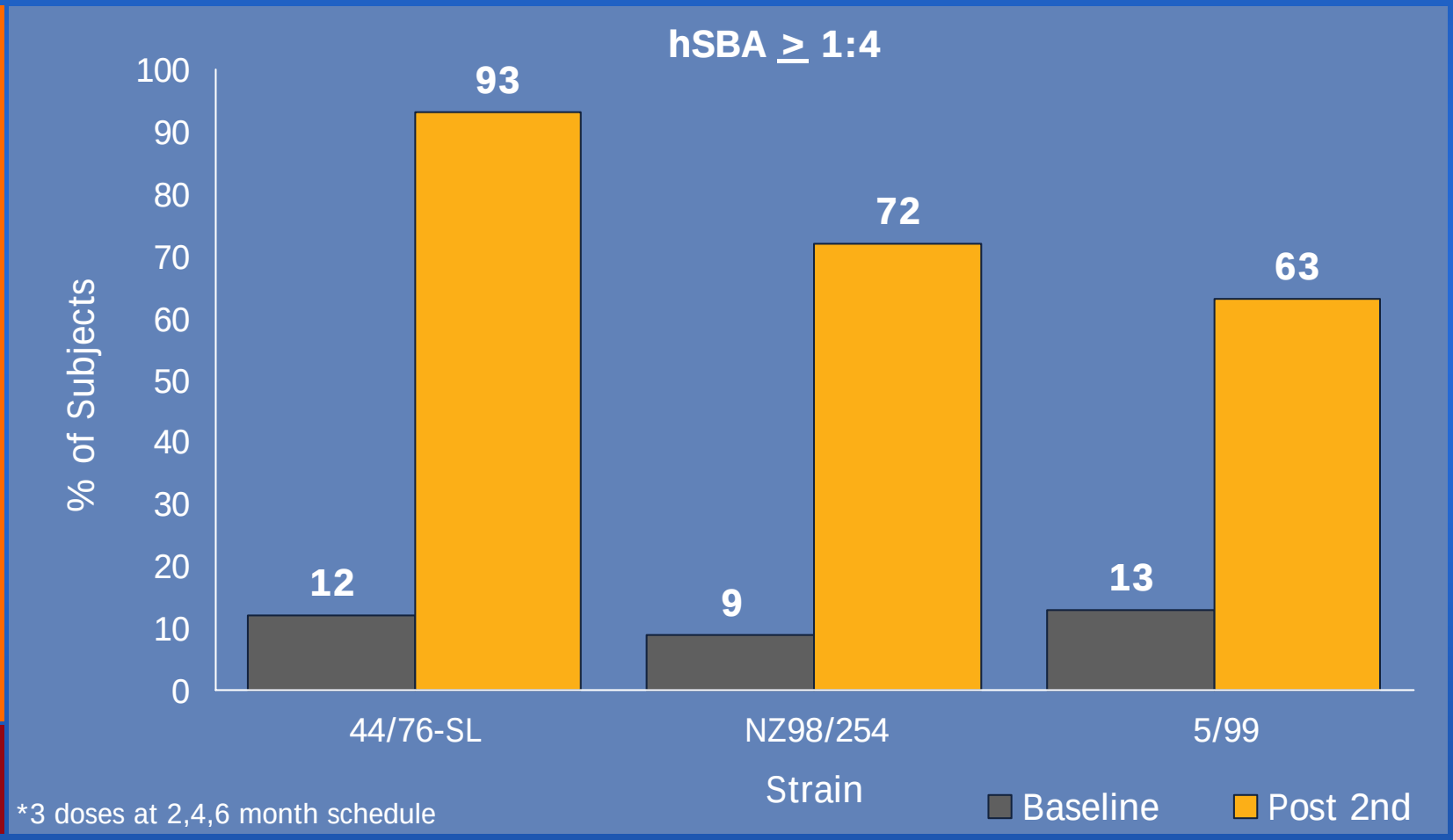
Phase I Adults Study: Post 3rd dose* for 3 reference strains



*0,1,2 month schedule; n=28.

Novartis MenB Vaccine Immunogenicity Results in Infants *(Interim Data)*

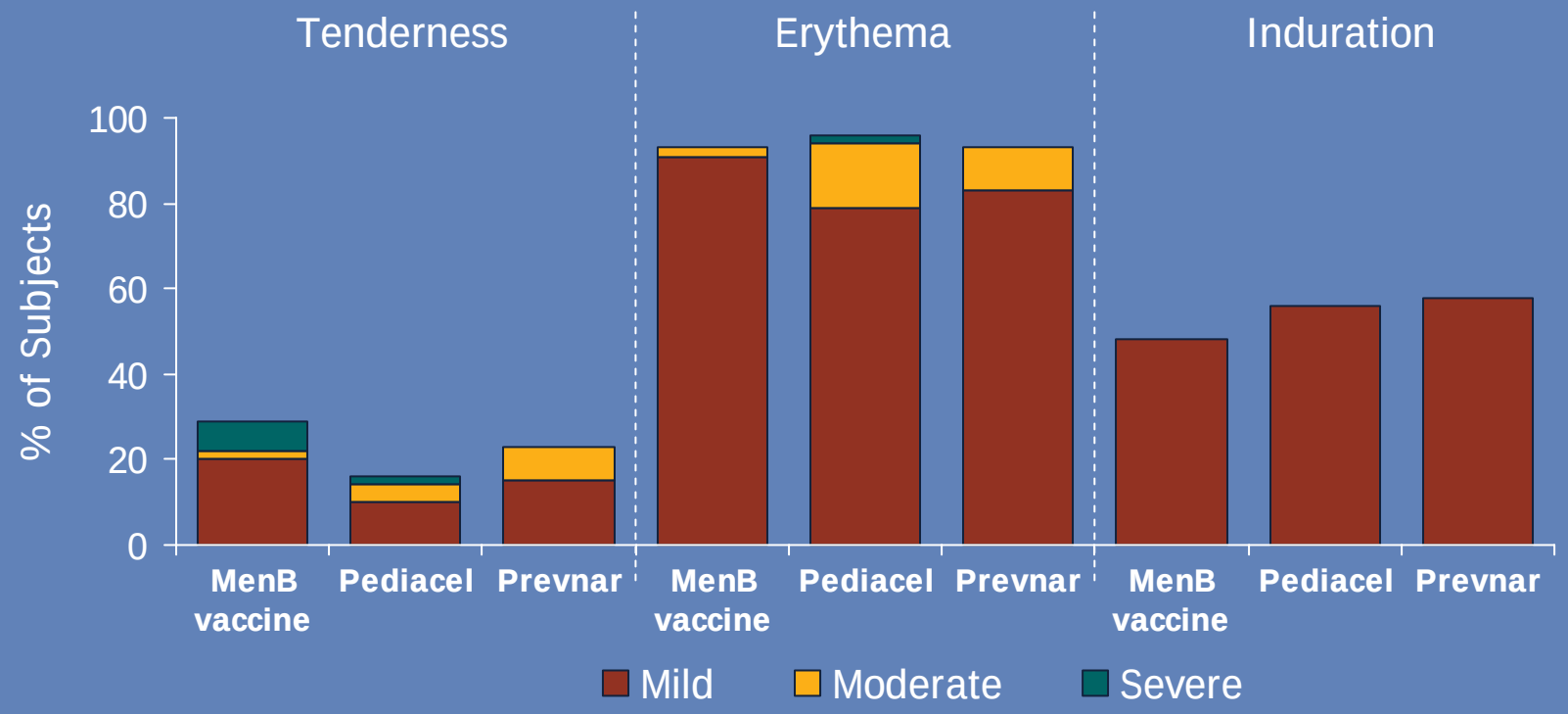
Phase II Infants Study UK: Post 2nd dose* for 3 reference strains



*3 doses at 2,4,6 month schedule

Novartis MenB Vaccine Comparable Local Reactions *(Interim Data)*

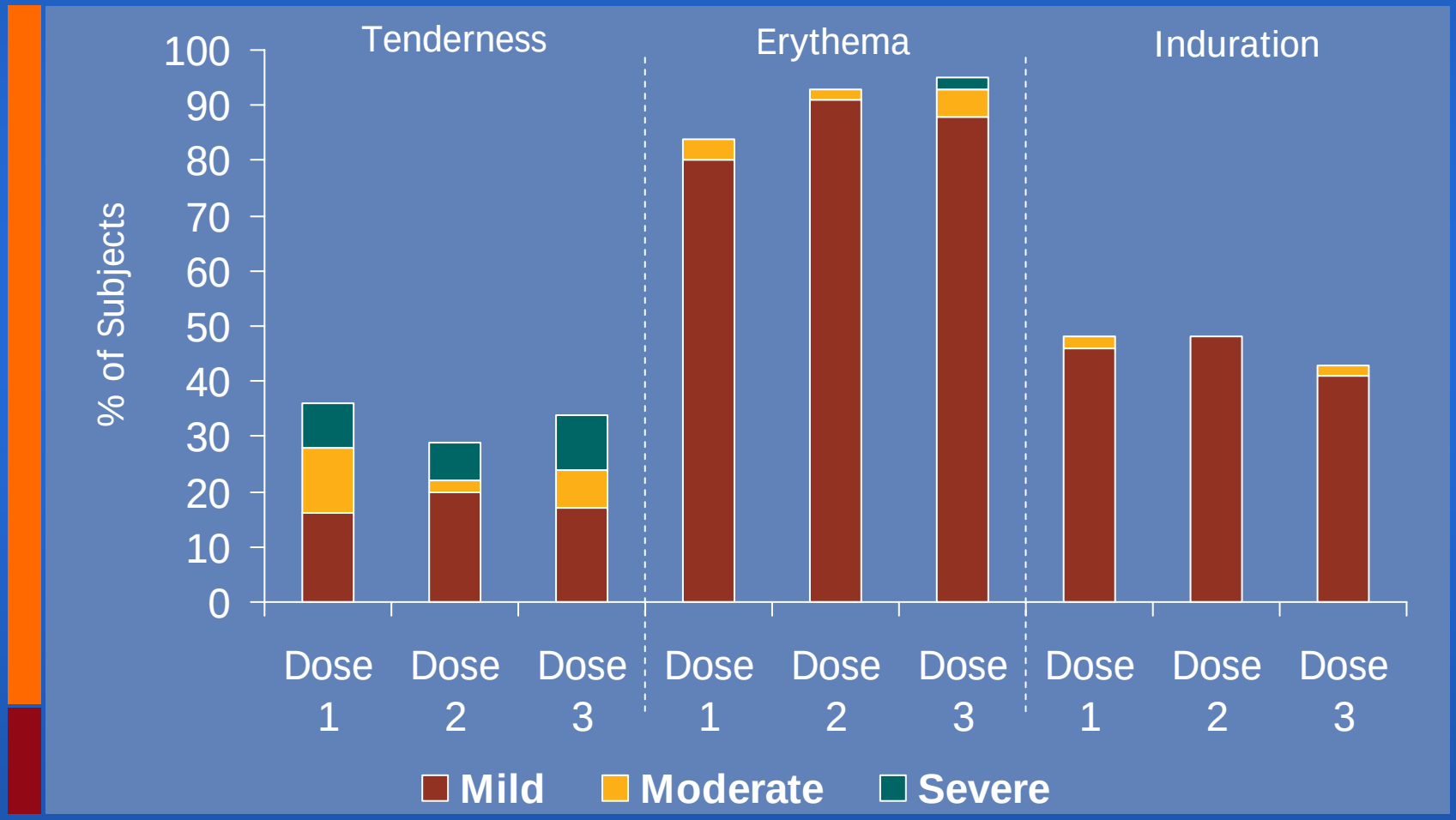
Phase II Infants Study UK: Post 2nd dose



Visit	Month of age	MenB vaccine	Pediacel ®	Prevnar ®
3	4	2nd dose (N=46)	3rd dose (N=49)	2nd dose (N=48)

Novartis MenB Vaccine Local Reactions Post Each Dose *(Interim Data)*

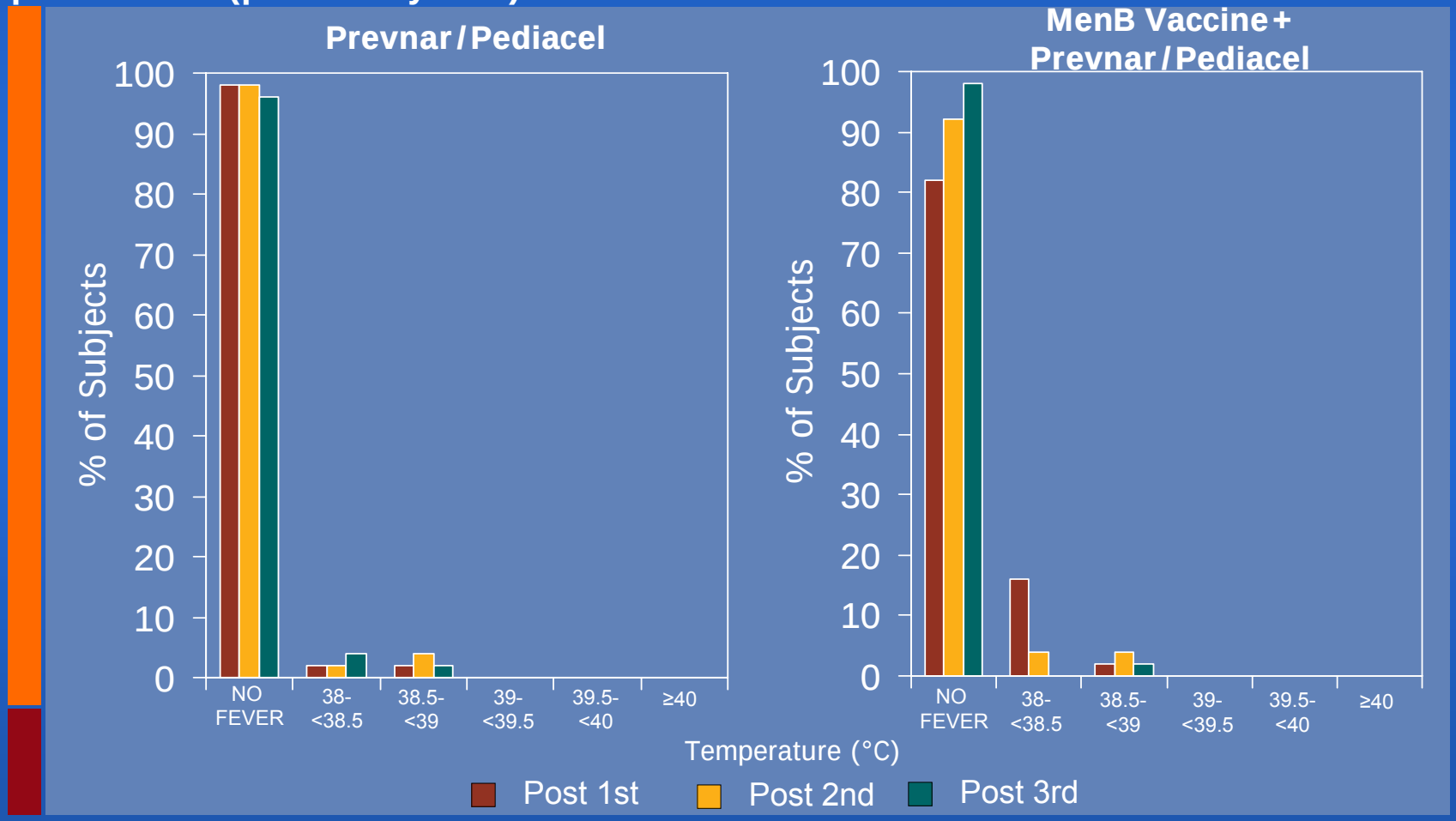
Phase II Infants Study UK



Novartis MenB Vaccine Systemic Reaction: Fever

Phase II Infants Study UK *(Interim Data)*

More fever seen post 1st dose vs other routine vaccines, comparable post 2nd dose and post 3rd dose (preliminary data)*



*Fever data were collected within 48 hours of vaccination

Summary

- *N. meningitidis* serogroup B
  - Highest incidence in many regions of the world
  - Causes outbreaks and is unpredictable
- Reverse vaccinology is an effective approach to identifying novel vaccine candidates against serogroup B
- Novartis MenB vaccine
  - Developed from the analysis of the meningococcal genome
  - Induces a robust bactericidal immune response
  - Immunogenic and safe in adults and infants
  - Vaccine moving into Phase III clinical trials
- The Novartis MenB vaccine is the first vaccine based on recombinant proteins to demonstrate bactericidal immune response in adults and infants

Advances in Vaccine Development for Meningococcal Serogroup B Disease

Philipp Oster, MD
Head, Development of Meningococcal B Vaccines
Novartis Vaccines & Diagnostics

Meningitis Research Foundation
November 7-8, 2007
London, UK