Evidence for the use of Synflorix™ in a 2 + 1 immunization schedule

Dr. Lode SCHUERMAN
Global Clinical Research & Development

PHiD-CV 2+1 immunogenicity data

- Evidence for the use of PHiD-CV (pneumococcal non-typeable *Haemophilus influenzae* Protein D-Conjugate Vaccine) in a 2+1 schedule comes from 2 sets of data:
  1. Direct comparison of PHiD-CV 2+1 vs PHiD-CV 3+1 (*Silfverdal S. et al. PIDJ 2009; 28: e276-e282*)
  2. Post dose 2 data from a head-to-head comparative study with PHiD-CV and 7vCRM (*Wysocki J. et al. PIDJ 2009; 28: S77-S88*)

PHiD-CV 2+1 immunogenicity data

Please note an error in the abstract book (p17)

Sero-type	% 22F-ELISA Ab concentration ≥ 0.2 µg/mL				% OPA ≥ 8			
	Study-002		Study-011		Study-002		Study-011	
	PHiD-CV Post-2	PHiD-CV Post-3	PHiD-CV Post-2	PCV7 Post-2	PHiD-CV Post-2	PHiD-CV Post-3	PHiD-CV Post-2	PCV7 Post-2
1	97.4	98.7	95.8	4.2	60.8	62.9	48.8	0.0
4	98.0	99.3	98.7	99.3	100	99.2	97.8	95.6
5	96.1	100.0	96.5	2.1	82.6	90.8	74.6	0.0
6B	55.7	63.1	64.1	30.8	74.4	88.9	63.0	35.2
7F	96.7	99.3	98.6	6.4	90.6	98.5	96.8	0.0
9V	93.4	99.3	96.1	96.6	100	100	98.5	99.3
14	96.1	100.0	99.4	97.9	98.5	100	97.1	93.3
18C	96.1	99.3	87.8	97.3	82.8	96.2	59.8	77.0
19F	92.8	96.1	96.2	99.3	87.0	93.8	84.3	67.9
23F	69.3	77.6	75.0	74.7	86.3	97.7	97.1	87.8

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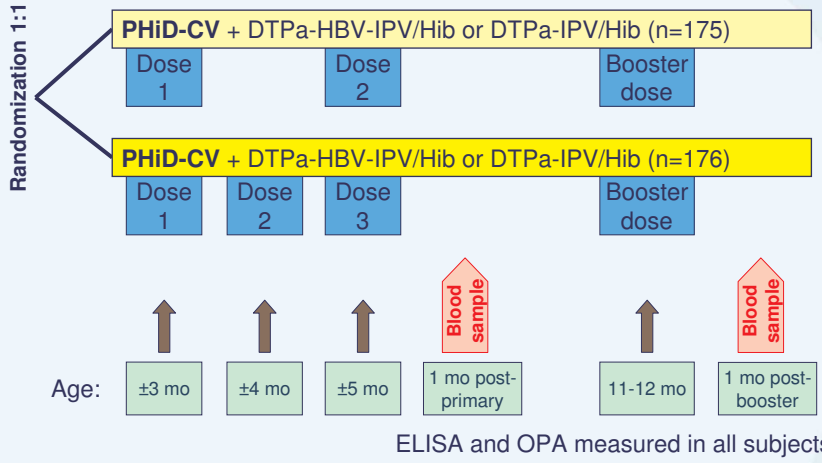
PHiD-CV 2+1 vs PHiD-CV 3+1

Open, randomized trial in Sweden, Denmark, Norway and Slovakia



ELISA and OPA measured in all subjects

Silfverdal S. et al. PIDJ 2009; 28: e276-e282

PHiD-CV - Pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine; Synflorix™; DTPa-HBV-IPV/Hib: Infanrix™ hexa (Sweden and Slovakia) and DTPa-IPV/Hib: Infanrix™ IPV-Hib (Denmark and Norway); are trademarks of the GlaxoSmithKline group of companies

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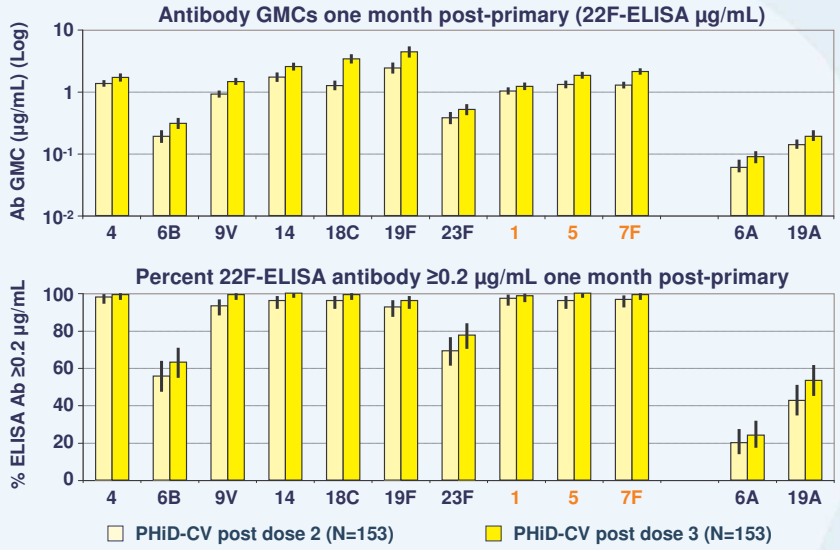
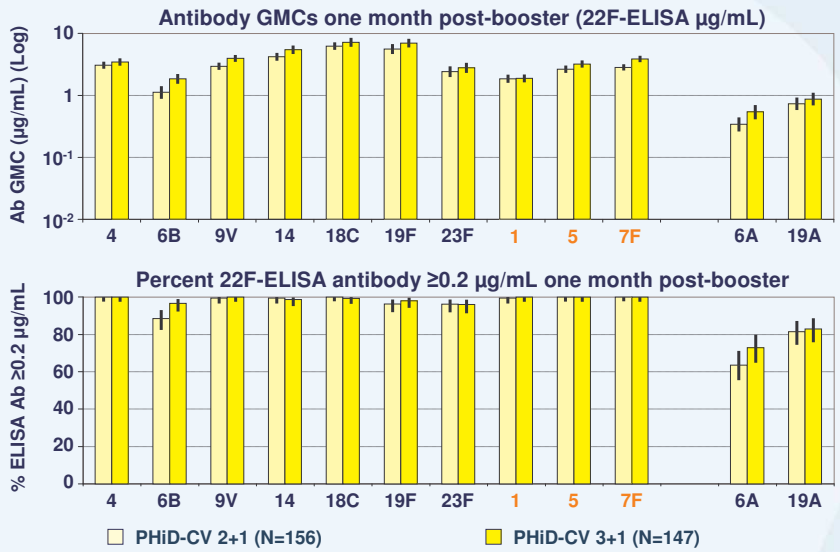
Post-primary PHiD-CV immunogenicity (post dose 2 vs post dose 3)



Silfverdal S. et al. PIDJ 2009; 28: e276-e282

Post-booster PHiD-CV immunogenicity (2+1 vs 3+1)



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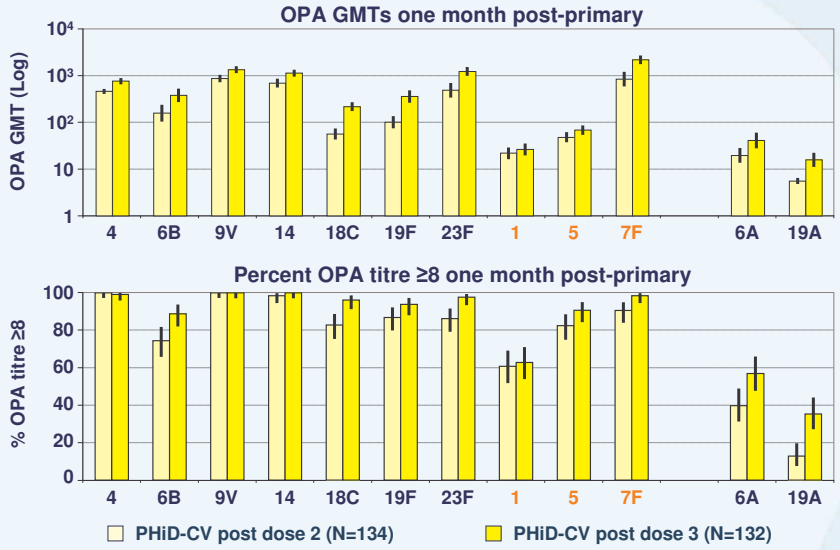
Post-primary PHiD-CV immunogenicity (post dose 2 vs post dose 3)



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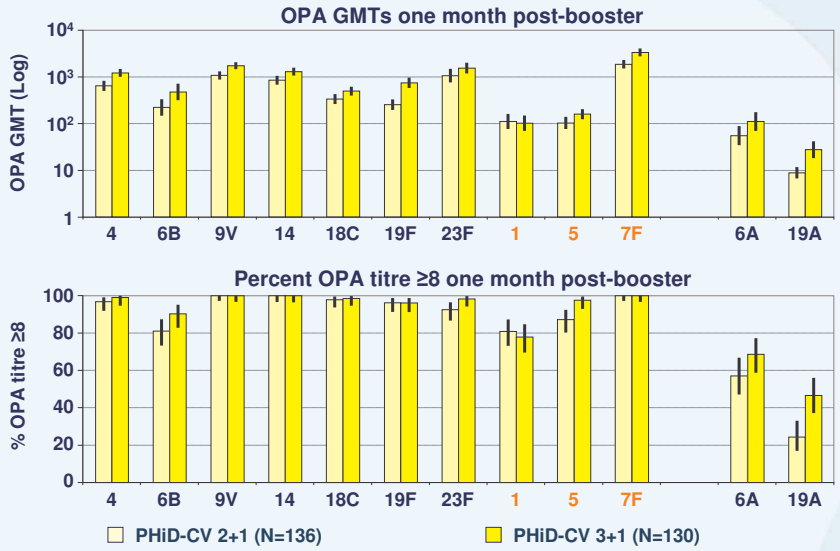
Post-booster PHiD-CV immunogenicity (2+1 vs 3+1)



Silfverdal S. et al. PIDJ 2009; 28: e276-e282

Conclusion on PHiD-CV 2+1 versus 3+1

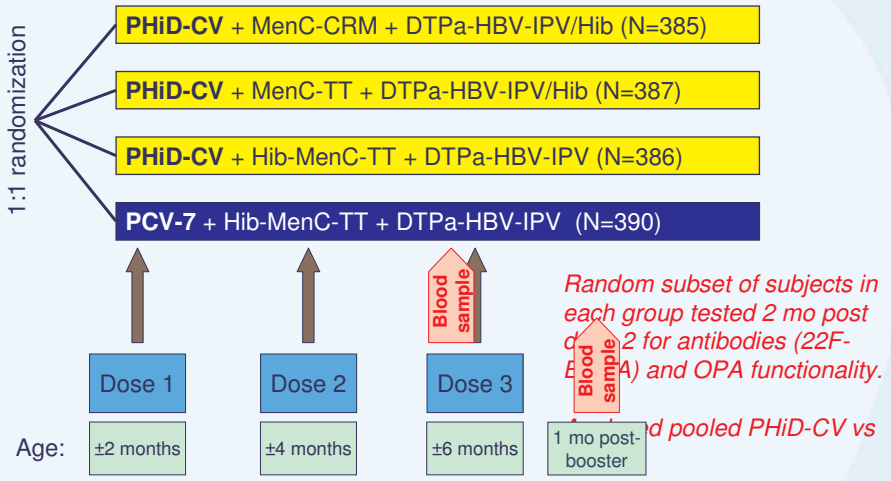
- Lower anti-pneumococcal responses with the 2+1 schedule compared to the 3+1 schedule for several serotypes
- These findings are consistent with results in similar studies conducted with CRM-conjugate vaccines
- OPA responses also lower in 2+1 schedule compared to 3+1 schedule

  Note: No OPA responses were so far reported for pneumococcal conjugate vaccines administered according to a 2+1 immunization schedule

Kaythy H. et al., PIDJ 2005; 24: 108-114 – Goldblatt D. et al., PIDJ 2006; 25: 312-19 – Esposito S. et al., Vaccine 2005; 23: 1703-1708 – Sigurdartottir S. et al., Vaccine 2008; 26: 4178-86 – Givon-Lavi N. et al., ISPPD-6 2008, Reykjavik, P3-049 – Sanders E. et al., MINOES trial, ISPPD-6 2008, Reykjavik, P3-069 – Rodenburg GD. et al., ISPPD-6 2008, Reykjavik, P3-074 – Southern J. et al., ESPID 2008, Graz, Austria; ISPPD-6 2008, Reykjavik, Iceland – Silfverdal S., et al. PIDJ 2009; 28: e276-e282

Post dose 2 PHiD-CV vs post dose 2 PCV-7

Open, randomized trial in Poland, Germany and Spain

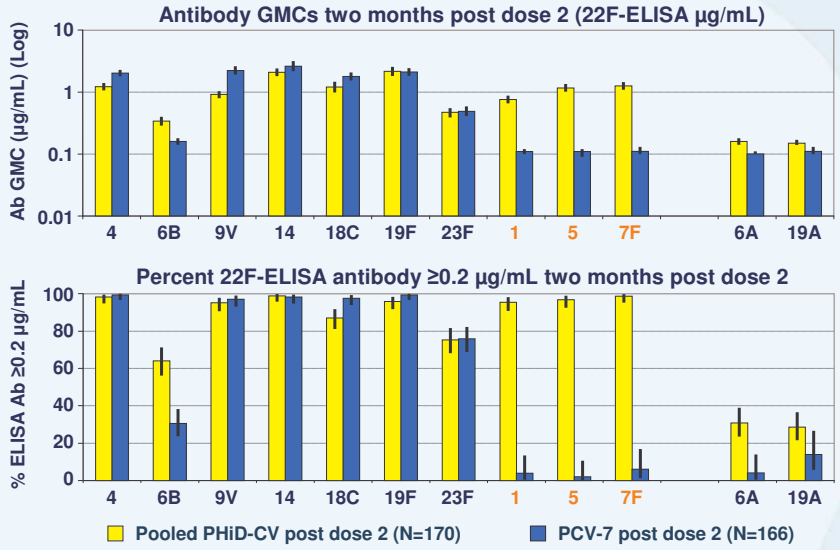


Random subset of subjects in each group tested 2 mo post d… 2 for antibodies (22F-E… A) and OPA functionality.

…d pooled PHiD-CV vs

7vCRM: *Prevenar*™/*Prevnar*™, Wyeth; **Menc-CRM:** *Meningitec*™, Wyeth; **Menc-TT:** *NeisVac*-C™, Baxter; **Hib-Menc-TT**: *Menitorix*™, GSK; **DTPa-HBV-IPV/Hib**: *Infanrix hexa*™, GSK; **DTPa-HBV-IPV:** *Infanrix penta*™, GSK

Post dose 2 PHiD-CV vs post dose 2 PCV-7



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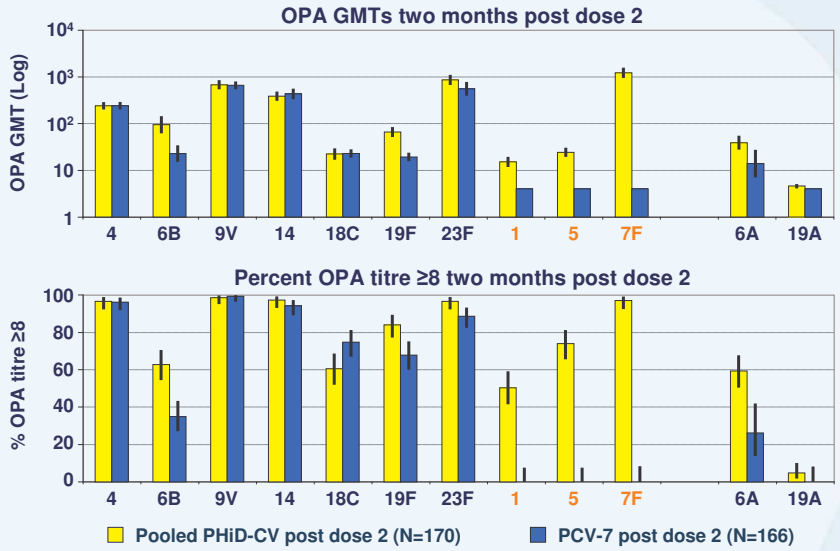

Wysocki J. et al. PIDJ 2009; 28: S77-S88

Conclusions 2+1 schedule

- Available efficacy data for pneumococcal conjugate vaccines are all based on 3-dose primary vaccination, with or without booster.
- Lower anti-pneumococcal antibody responses were observed with the 2+1 PCV-7 schedule compared to 3+1 for some serotypes (mainly for 6B and 23F). No OPA data available so far.
- Lower antibody and OPA responses when PHiD-CV used according to 2+1 schedule compared to 3+1. *(Silfverdal S. et al. PIDJ 2009; 28: e276-e282)*
- Countries that introduced PCV7 according to a 2-dose primary schedule have reported significant reductions in IPD (although some breakthrough cases for serotype 6B were observed).
- Immune responses (ELISA and OPA) following 2 primary doses of PHiD-CV were comparable to those following 2 doses of the licensed PCV-7 (but 6B responses were clearly lower for PCV-7).
  (Wysocki J. et al. PIDJ 2009; 28: S77-S88)