PRECLINICAL RESULTS FOR A 25-VALENT PNEUMOCOCCAL CONJUGATE VACCINE USING A NOVEL LINKER PLATFORM TECHNOLOGY

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E-Poster(s): #754 (ISPPD-2022)

IVT PCV-25V - Product Development

- Animal TOX Completed
- CTA application in 2H2022 (Health Canada)
- FIH Phase I start 2H2022

Rationale for a Development of IVT PCV-25V

- IVT PCV-25V candidate containing capsular polysaccharides from the following 25 *S. pneumoniae* serotypes: **1, 2, 3, 4, 5, 6B, 6C, 7F, 8, 9N, 9V, 10A, 12F, 14, 15A, 15B, 16F, 18C, 19A, 19F, 22F, 23F, 24F, 33F, 35B**

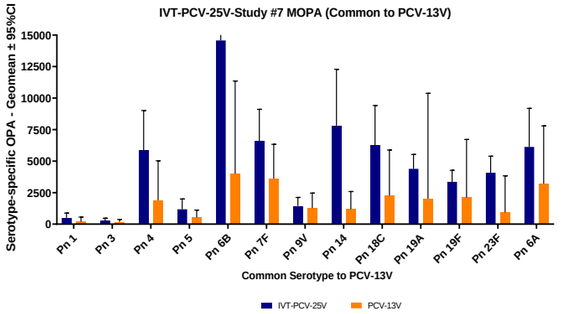
Serotype Selection based on:

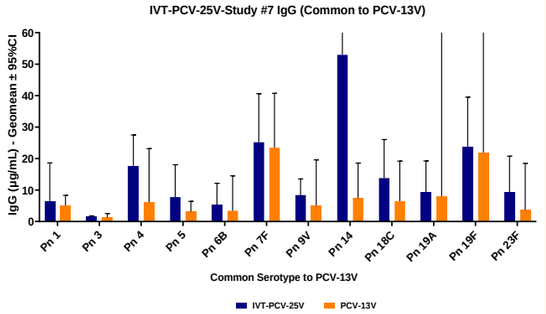
Inclusion of capsular polysaccharides from serotypes in currently licensed PCVs

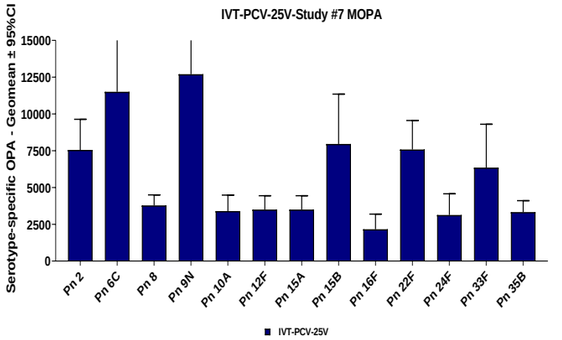
- Analysis of the most common IPD-causing isolates post-PCV introduction globally
- Frequency in Western Countries and Gavi-supported countries, potential for invasive diseases, for epidemics and known characterization of capsular polysaccharides
- PCVs with additional serotypes would offer great coverage for infants, children and adults, both in Western Countries and in Gavi-supported countries

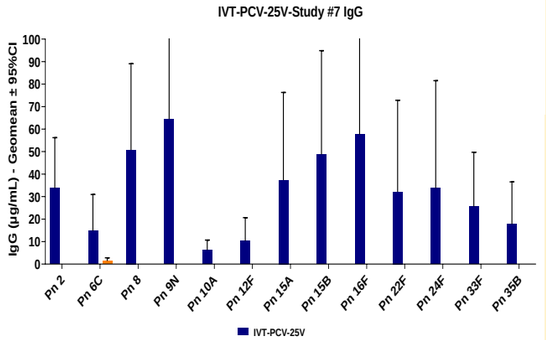
	1	5	6B	7F	9V	14	19F	23F	4	18C	6A	19A	3	22F	33F	8	10A	11A	12F	15B	9N	2	6C	15A	16F	24F	35B	17F	20	EU
Inventprise-PCV-25V	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6	1.4	0.4	0.7	7	13	7	2.2	14	3.2		6.8	1.1	5	0	2.5	3.3	1.5	2.3	1.3			81%
Prevnar-20V	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6	1.4	0.4	0.7	7	13	7	2.2	14	3.2	3.1	6.8	1.1										68%
Merck-15V	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6	1.4	0.4	0.7	7	13	7	2.2															40%
Prevnar-13V	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6	1.4	0.4	0.7	7	13																	31%
Pneumosil-10V	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6			0.7	7																		16%
Synflorix-10V	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6	1.4	0.4																				10%
Pneumovax-23V (PS)	0.7	0.1	0.6	1.6	0.8	2	1.6	0.6	1.4	0.4		7	13	7	2.2	14	3.2	3.1	6.8	1.1	5	0						1	1.2	75%

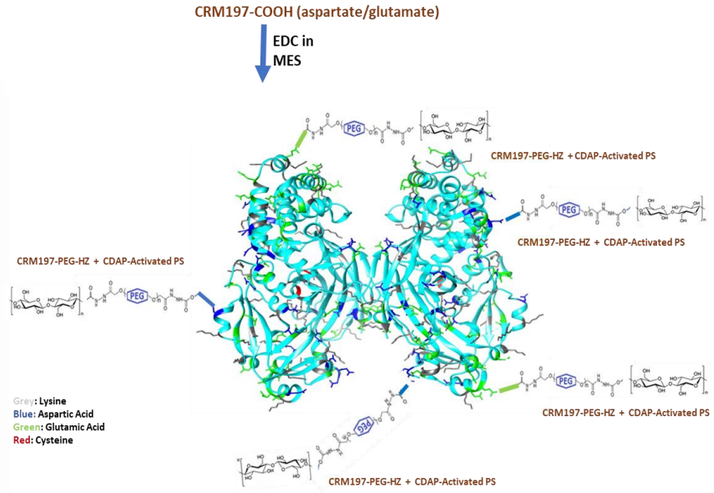
IVT PCV-25V elicits antibody against 6A serotype











Proposed indication

- Active immunization against invasive pneumococcal disease, pneumonia and otitis media caused by *Streptococcus pneumoniae* serotypes **1, 2, 3, 4, 5, 6B, 6C, 7F, 8, 9N, 9V, 10A, 12F, 14, 15A, 15B, 16F, 18C, 19A, 19F, 22F, 23F, 24F, 33F, 35B** in infants and children from 6 weeks up to 2 years of age
- With the inclusion of the linker technology, the PCV-25 vaccine has been shown (in animal studies) to result in HIGHER immunological titers and has more breadth covering the emerging strains.
- An age escalation study for adult/elderly is planned to take place following the completion of a Phase 1 study in adults aged 18-40 years. The Phase 1 study is planned to start in 2H2022.

A single dose (0.5 mL) of the 25-valent IVT PCV-25V vaccine contains:

- 2.2 µg of each saccharide, except for serotype 6B (4.4 µg); 0.02% polysorbate 80; 0.125 milligrams of aluminum as aluminum phosphate adjuvant; 20 mM histidine; 150 mM sodium chloride

25-valent IVT PCV-25V vaccine

- Compared immunogenicity (IgG and MOPA) of Inventprise's 25-valent PCV with Prevnar 13 in New Zealand White rabbits
- The polysaccharide antibody responses (both IgG and MOPA) for the serotypes contained in Prevnar 13 were higher in the 25-valent conjugate formulation treatment group than they were for the Prevnar 13 treatment group
- Additionally, the 12 new serotypes in the 25-valent conjugate formulation show antibody responses that are of a similar level to that seen for the traditional 13 serotypes
- The amount of CRM_{197} antibody was less in **25-valent IVT PCV-25V** , and PEG antibodies were not detected

The manufacturing process developed by Inventprise produces PS, CRM_{197} and conjugates with high yields decreasing the cost of the vaccine

Conjugation Technology

- Homo-bifunctional Hydrazide-PEG-Hydrazide (HZ-PEG-HZ) linker
- The carrier protein and polysaccharide are activated using CDAP chemistry, and the polysaccharide is covalently connected to the other end of the PEG linker
- Rationale for including a HZ-PEG-HZ linker:
- Elicit significantly higher IgG and functional OPA titers compared to the same PS-conjugate without the linker in preclinical studies
- May be due to increased availability of antigenic PS epitopes as a result of reduced steric shielding
- May also cause steric shielding of antigenic epitopes of the carrier, thus reducing the carrier's immunogenicity, which in turn may prevent suppression of the immune response to the PS epitopes ("carrier suppression")
- Positive safety profile of PEG in approved pegylated biopharmaceuticals

Pneumococcal Polysaccharides

- Pneumococcal isolates were obtained from the National Institute for Communicable Diseases (NICD), Johannesburg, South Africa and the Centers for Disease Control and Prevention (CDC), Atlanta, USA

Carrier Protein

- Recombinant CRM_{197} expressed in *E.coli*