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Session: 311. Vaccination II - Other
Saturday, October 5, 2019: 3:45 PM

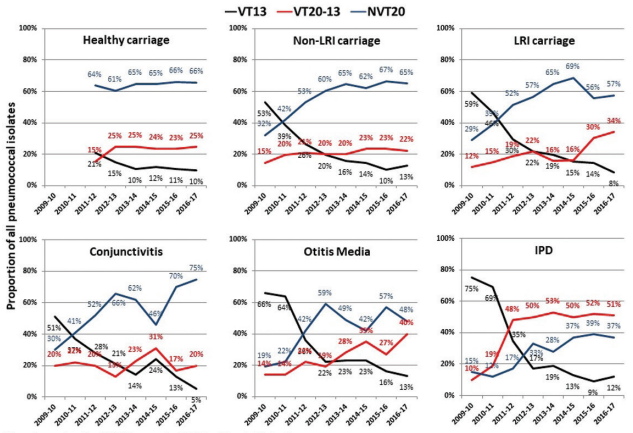
Background. PCV13 implementation in children resulted in a substantial decline in carriage of and disease by vaccine serotypes (VT13). However, disease caused by non-PCV13 serotypes (NVT) is still relatively prevalent and even increasing, leading to an effort to develop a 20-valent vaccine (PCV20), containing the additional 7 serotypes: 8, 10A, 11A, 12F, 15B/C, 22F, 33F (VT20-13). We assessed dynamics of VT13, VT20-13, and non-PCV20 (NVT20) in nasopharyngeal carriage, respiratory infections, and IPD in children < 2 years following PCV13 implementation.

Methods. Multiple prospective, population-based surveillance projects, conducted in Israel between 2009 and 2017 were used. We studied isolates from IPD; otitis media (OM); conjunctivitis; carriage in healthy children; carriage during lower respiratory tract infections with chest radiography examination (LRI); and carriage during non-LRI illnesses. We added data from healthy children in the community since 2011. Prevalence rate ratios were calculated, comparing VT13, VT20-13 and NVT20 rates in late-PCV13 (2015–2017) vs. early-PCV (2009–2011) periods.

Results. Overall, 9,089 episodes were recorded. VT13 declined significantly in all 6 groups by 75–86% (Figures 1 and 2). Proportions of VT20-13 significantly increased in all groups, excluding conjunctivitis. The highest increases were observed in IPD, OM, and carriage during LRI. In 2015–2017, VT20-13 consisted 24%, 23%, and 19% of carriage in healthy children, carriage in non-LRI illness, and conjunctivitis, respectively, vs. 51%, 33%, and 32% in IPD, OM, and carriage during LRI. VT20-13 rapidly became the leading fraction in IPD. NVT20 proportions increased in all groups.

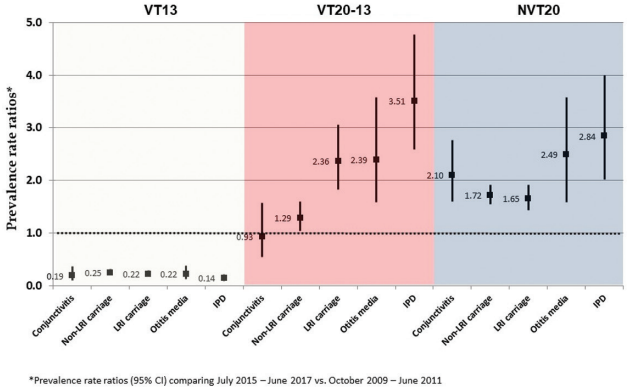
Conclusion. (1) PCV13 implementation resulted in a substantial increase in NVT carriage and disease; (2) In IPD, VT20-13 became the dominant group; (3) The increases in the proportion of VT20-13 seen in OM and carriage during LRI was significantly higher than in conjunctivitis and in carriage without LRI.

Figure 1: Dynamics of pneumococcal carriage, conjunctivitis, otitis media (OM) and IPD (proportion of VT13, VT20-13 and NVT20 of all pneumococcal isolates) in children <24 months, Israel, October 2009 through June 2017



*Prevalence rate ratios (95% CI) comparing Jul15-Jun17 vs. Oct09-Jun11

Figure 2: Prevalence rate ratios of VT13, VT20-13 and NVT20 of all pneumococcal isolates in carriage, conjunctivitis, otitis media (OM) and IPD in children <24 months, Israel: comparing July 2015 – June 2017 vs. October 2009 – June 2011



*Prevalence rate ratios (95% CI) comparing July 2015 – June 2017 vs. October 2009 – June 2011

Disclosures. **All Authors:** No reported Disclosures.

2904. Protective Efficacy of Nucleic Acid Vaccines Against Transmission of Zika Virus During Pregnancy in Mice

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Session: 311. Vaccination II - Other
Saturday, October 5, 2019: 4:00 PM

Background. Zika virus (ZIKV) caused an epidemic of microcephaly and congenital malformations in 2015–2016, prompting the development of ZIKV vaccines. Plasmid DNA and modified mRNA lipid nanoparticle-encapsulated (mRNA-LNP) vaccines were among the first to reach human clinical trials, where their evaluation is ongoing. Few studies have evaluated vaccine efficacy in the setting of infection during pregnancy, and there is an open question around antibody-dependent enhancement (ADE) of flaviviral disease due to cross-reactive fusion loop epitope (FLE) antibodies.

Methods. Female C57BL/6J mice and human STAT2 knock-in (hSTAT2-KI) mice were immunized with plasmid DNA (VRC5283) or mRNA-LNP (Moderna Inc.) vaccines encoding the ZIKV prM-E genes. Antibody responses were assayed, and immunized mice were mated and WT mice were transiently immunocompromised by administration of interferon blocking antibody, followed by ZIKV challenge. 1 week post-infection, ZIKV burden was measured via qRT-PCR. ZIKV-specific memory B cell (MBC), long-lived plasma cell (LLPC), and CD8+ T cell vaccine responses were also assayed.

Results. VRC5283 and mRNA-LNP vaccines were highly immunogenic, eliciting serum neutralizing EC50 responses >1:10,000, and markedly reduced placental ZIKV burden and fetal transmission. An improved mRNA-LNP construct with higher immunogenicity correlated with reduced placental viral burden. Significantly, an FLE-mutant mRNA-LNP vaccine yielded comparable EC50 responses without compromising vaccine efficacy; sera from these mice did not enhance dengue virus infection *in vitro*. Both VRC5283 and mRNA-LNP vaccines elicited MBC, LLPC, and CD8+ T cell responses, although MBC and LLPC responses were greater after mRNA-LNP immunization. Surprisingly, low-level ZIKV infection of the placenta and a minority of fetal heads were observed despite robust neutralizing antibody responses, which was not seen in the immunocompetent hSTAT2-KI model.

Conclusion. Nucleic acid vaccines were highly immunogenic and protective against vertical ZIKV transmission during pregnancy in mice. These data support and inform the ongoing clinical development of these vaccines in humans.

Disclosures. **All Authors:** No reported Disclosures.

2905. Long-term Immunological Persistence of the Adjuvanted Recombinant Zoster Vaccine: Clinical Data and Mathematical Modeling

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Session: 311. Vaccination II - Other
Saturday, October 5, 2019: 4:15 PM

Background. The adjuvanted recombinant zoster vaccine (RZV, GSK), administered to adults ≥ 50 years of age (YOA) demonstrated ≥ 90% efficacy against herpes zoster across all age cohorts. Vaccine-specific immune responses elicited by two RZV doses in adults ≥ 60 YOA have been shown to persist above pre-vaccination levels at least up to 9 years after initial vaccination. Here we present persistence of the humoral and cellular immunity and safety up to 10 years after initial vaccination as well as data from mathematical modeling, performed to predict immune persistence up to 15 years.

Methods. This phase IIIB, open-label extension trial (NCT02735915) included 70 participants who had received two RZV doses in the initial trial (NCT00434577) and builds on a previous extension trial (NCT01295320). Cellular and humoral immune responses up to year 10 after an initial 2-dose vaccination schedule are presented here. Additionally, prediction of immunological persistence at year 15 was assessed by mathematical modeling (Piecewise, Power-law, Fraser), using the individual subject values for available data up to year 10.

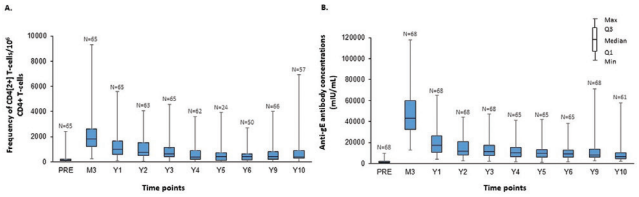
Results. The median frequency of varicella-zoster virus glycoprotein E (gE)-specific CD4+ T-cells expressing ≥ 2 activation markers plateaued at 3.3-fold above pre-vaccination levels starting around year 4 up to year 10 post-initial vaccination. Anti-gE antibody concentrations plateaued starting around year 3 up to year 10 post-initial vaccination.Ten years after initial vaccination, humoral responses remained 5.9-fold higher as compared with pre-initial vaccination levels (Figure 1). No relevant safety events were identified during the study (year 9–10 post-initial

vaccination). In line with previous modeling data, the year 10 analysis predicts that both cellular and humoral immune responses will remain above pre-vaccination levels for at least 15 years after initial vaccination (Figures 2 and 3).

Conclusion. In adults vaccinated when ≥ 60 YOA, humoral and cellular immune responses induced by two RZV doses persist above pre-vaccination levels for at least 10 years post-initial vaccination. Mathematical modeling predicts a maintained vaccine-related immune response for at least 15 years after initial vaccination.

Funding. GlaxoSmithKline Biologicals SA.

Figure 1. Median frequencies of gE-specific CD4[2+] T-cells (A, assessed by intracellular cytokine staining) and median anti-gE antibody concentrations (B, assessed by ELISA) up to 10 years after initial vaccination (According-to-protocol cohort for persistence)



PRE, before vaccination in the initial study; **M**, month after the initial vaccination; **Y**, year after the initial vaccination; **N**, number of adults with available results; **Q1**, first quartile; **Q3**, third quartile; **min**, minimum; **max**, maximum.

Figure 2. Statistical modeling for prediction of the gE-specific CD4[2+] T-cell frequency up to 15 years after initial vaccination

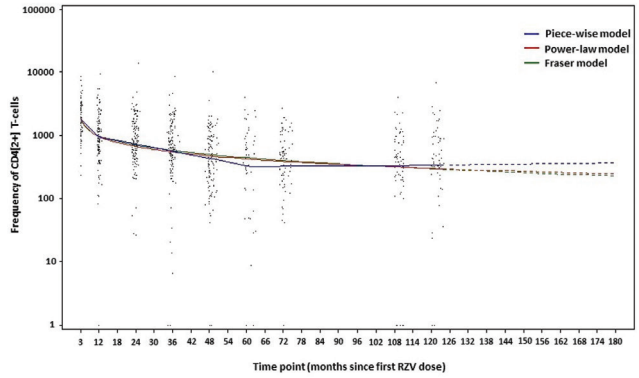
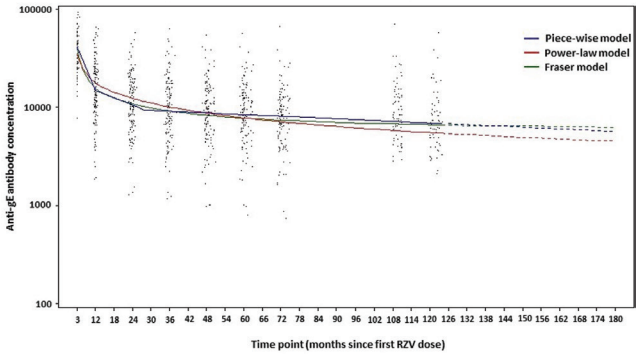


Figure 3. Statistical modeling for prediction of anti-gE antibody concentrations up to 15 years after initial vaccination



Disclosures. **All Authors:** No reported Disclosures.