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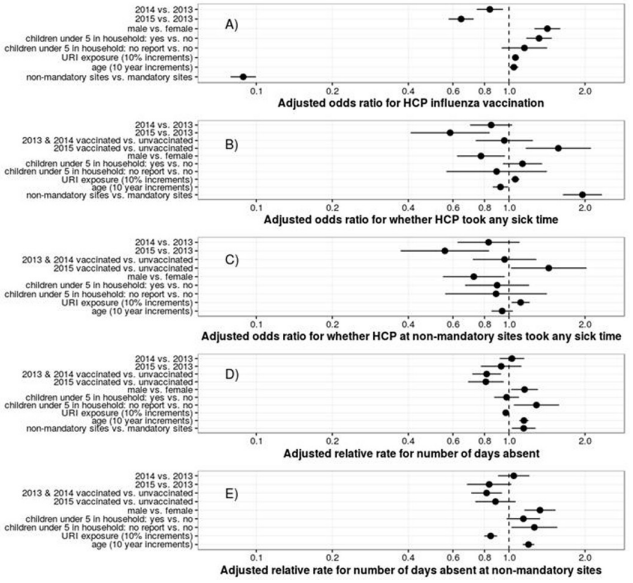
Background. We analyzed data from health care personnel (HCP) participating in the multicenter, cluster randomized Respiratory Protection Effectiveness Clinical Trial (ResPECT) obtained over three viral respiratory (influenza) illness seasons (2012–2015) at three university health systems where influenza vaccination was mandated, and four Veterans Affairs (VA) health systems where it was encouraged but not mandated, to determine the incidence and duration of symptomatic influenza like illness (SILI) associated absenteeism.

Methods. Participants reported SILI daily, vaccination status, and days absent from work due to SILI weekly throughout a 12 week period during the peak viral respiratory illness season each year. Adjusted effects of vaccination and other modulating factors on absenteeism rates were estimated using multivariable regression models.

Results. Overall 97.1%, 96.3%, and 92.1% of participants reported being vaccinated during each of the three study years where the vaccine was mandated, while 67.9%, 63.3%, and 60.4% reported vaccination at sites where it was encouraged but not mandated. The percent of HCP claiming any sick days at mandatory sites was estimated to be 5.9% lower than at non-mandatory sites (95% CI, -12.5, -1.4; $P = 0.02$). Among HCP who reported at least one sick day, the mean number of symptomatic sick days at mandatory sites was 0.74 lower than at non-mandatory sites (95% CI, -1.37, -0.37, $P < 0.01$). After adjusting for possible confounding factors (e.g., season, vaccination statues, mandatory or non-mandatory vaccination site, age, children at home) the relative rate of sick days taken by vaccinated compared with unvaccinated subjects was reduced in the entire cohort of HCP and in the vaccinated compared with unvaccinated subset of HCP from non-mandatory sites (see Figure).

Conclusion. We conclude that influenza vaccination rates are increased and SILI-related absenteeism is decreased at sites where influenza vaccination is mandated and that this should be one of the factors taken into consideration when healthcare facilities make decisions about influenza vaccination policies.

Figure: Adjusted Odds Ratio for Vaccination Status and Taking Any Sick Time, Adjusted Relative Rate of Sick Days Taken.



Disclosures. **All authors:** No reported disclosures.

1462. Transcriptome Analysis in Human Breast Milk and Blood after Inactivated or Attenuated Influenza Immunization

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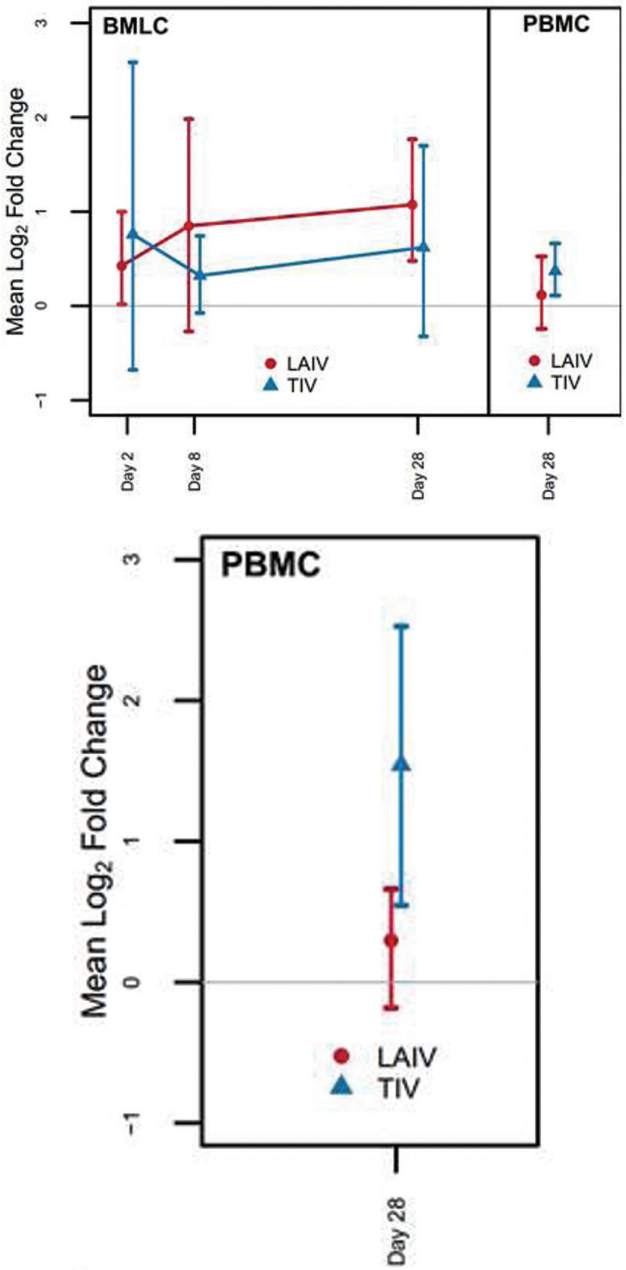
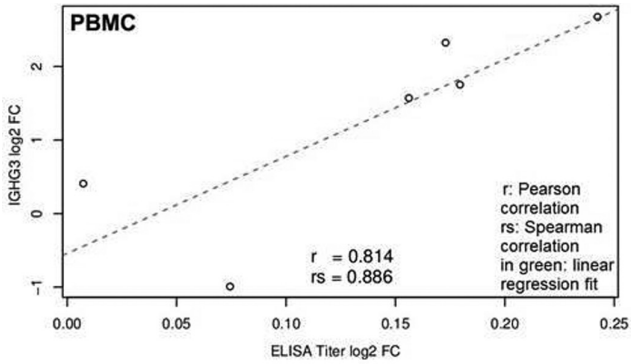
Background. The goal of this study was to identify transcriptomic signatures (RNA-Seq) in human peripheral blood mononuclear cells (PBMCs) and breast milk lymphocyte cells (BMLCs) in response to trivalent inactivated influenza vaccine (TIV) or live attenuated influenza vaccine (LAIV).

Methods. We performed a randomized, double-blind study in breastfeeding women who received either LAIV and intramuscular placebo, or TIV and intranasal placebo. A subset of subjects with available samples (LAIV, $n = 10$ and TIV, $n = 6$) was used for this study. Human milk was collected on days 0, 2, 8, and 28, and blood samples were collected on days 0 and 28. PBMC and BMLC RNA was extracted for RNA-Seq and differentially expressed (DE) gene analysis.

Results. We identified a total of 382 DE BMLC genes in the LAIV group, most of which were up-regulated at day 28. DE genes were preferentially involved in innate immune signaling pathways including cytokine-cytokine receptor interaction, TNF signaling, and NF-kappa B signaling. For TIV, 3 DE genes were identified of which 2 (*IL1A* and *IL1B*) overlapped with LAIV. Response time trends for co-expressed gene clusters by vaccine group showed that LAIV generally induced an early (day 2) up-regulation of innate immune signaling pathway genes, while TIV induced peak innate immune signaling gene responses ahead of LAIV (day 8 vs. day 28). A group of known interferon-alpha/β-inducible genes (*IFIT3*, *OAS3*, *IFI44L*, *MX1*, *OAS2*, *IFIT1*, *IFI6*) showed higher responses at day 2 for TIV but stronger peak levels by day 28 for the LAIV group (Fig 1). While no such innate immune signaling responses were observed in PBMCs at day 28, we identified an up-regulation of IgG gene *(IGHG1* and *IGHG3*) expression in the TIV group (Fig 2).

Conclusion. We observed increased innate immune signaling responses in BMLC but not in PBMC at day 28 for the LAIV group. We hypothesize that breastfeeding extends the innate response to LAIV via mucosal immunity. Gene cluster time trends indicated an earlier innate immune signaling response for TIV. The day 28 increase in *IGHG3* gene expression levels in TIV group PBMCs was correlated with corresponding increases in serum ELISA IgG titers for the influenza B antigen (Fig 3). Additional studies are required to investigate the differences in innate response signaling seen for BMLC and PBMC in this study.





Disclosures. **All authors:** No reported disclosures.

1463. Enhanced Potency and Durability of Antibody Response to Seasonal Trivalent Inactivated Influenza Vaccine (TIV) Combined with a Novel Water-in-Oil Adjuvant System at Reduced Hemagglutinin (HA) Doses

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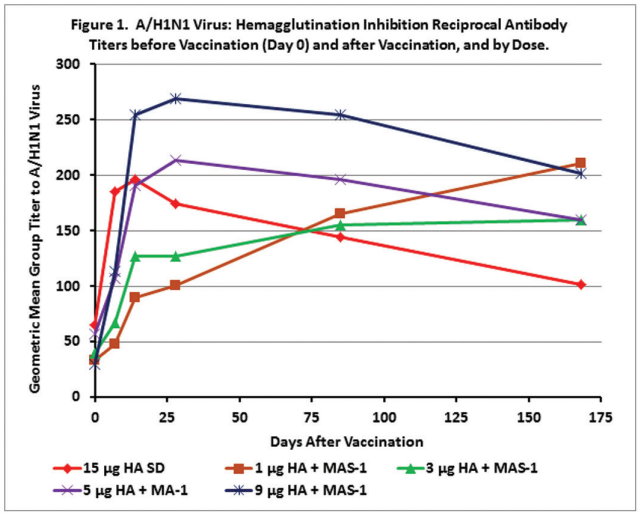
Background. New influenza vaccines are needed to increase vaccine efficacy against infection and illness. Adjuvants may allow HA dose-sparing while increasing the antibody response. MAS-1 is an investigational low viscosity, free-flowing, water-in-oil emulsion-based adjuvant delivery system with stable nanoglobular droplets whether manufactured in bulk or at point-of-use (POU). MAS-1 oily vehicle is stable for at least 5 years at room temperature, in bulk or POU vials.

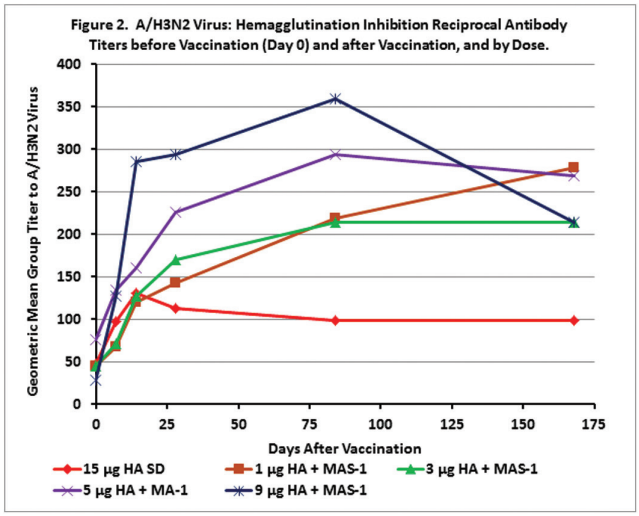
Methods. A phase 1, double-blind, single-center, safety and immunogenicity, HA dose escalation trial was conducted. 1, 3, 5 or 9 µg per HA from the licensed 2014/15 seasonal TIV prepared POU with a fixed dose of MAS-1 adjuvant in 0.3 mL emulsion compared with standard dose (SD, 15 µg per HA) TIV in 0.5 mL was injected IM on day 1. Safety was measured by reactogenicity, adverse events, and safety labs. Serum hemagglutination inhibition (HAI) antibody titers were measured at 5 time points post-vaccination.

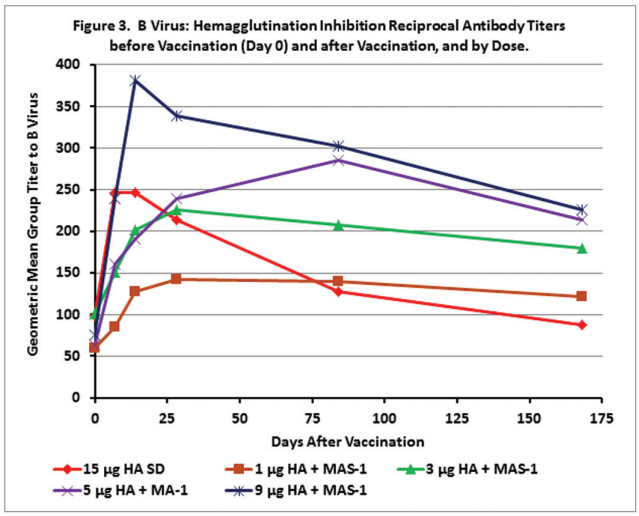
Results. 72 subjects, age 18–47 years, were randomly assigned to either adjuvanted vaccine or TIV in a 2:1 ratio. The 1 and 3 µg per HA cohorts were enrolled together, then the 5 µg follo wed by the 9 µg per HA cohorts. Common injection site reactions were mild tenderness (74%) and pain (54%), resolving by 5 days post-vaccination. Common systemic reactions were mild headache (36%), myalgia (19%), malaise (18%) and fatigue (18%) through day 14 post-vaccination. Safety labs were not concerning. Geometric mean antibody titers against component strains were higher, of longer duration and peaked later in the adjuvanted vaccine groups than with SD TIV (Figures 1 – 3). Seroconversion rates (%) had a similar pattern:

Vaccine	Subjects (N)	Days Post-Vaccination	A/H1(%)	A/H3 (%)	B (%)
1µg HA+MAS-1	12	14	25	33.3	25
		28	33.3	41.7	41.7
		84	50	60	40
3µg HA+MAS-1	12	14	33.3	25	25
		28	33.3	50	33.3
		84	33.3	50	16.7
5µg HA+MAS-1	12	14	41.7	41.7	50
		28	50	58.3	50
		84	50	58.3	58.3
9µg HA+MAS-1	12	14	66.7	50	66.7
		28	66.7	50	66.7
		84	75	75	66.7
15µg HA SD TIV	24	14	29.2	45.8	25
		28	25	33.3	20.8
		84	13	26.1	8.7

Conclusion. MAS-1 adjuvant provided HA dose-sparing without significant systemic or local safety concerns, higher HAI antibody titers and seroconversion rates for a longer duration than SD TIV, and could conceivably contribute to greater vaccine efficacy.







Disclosures. **G. J. Gorse**, Nova Immunotherapeutics Limited: Principal Investigator at Saint Louis University, Funding to Saint Louis University for the clinical study; **S. Grimes**, Mercia Pharma, Inc.: Employee and Principal Scientist, Salary; **H. Buck**, Nova Immunotherapeutics Limited: Consultant, Consulting fee; **H. Mulla**, Nova Immunotherapeutics Limited: Employee, Salary; **P. White**, Nova Immunotherapeutics Limited: Employee, Salary; Mercia Pharma, Inc.: Shareholder, Licensing agreement or royalty; **P. Blackburn**, Mercia Pharma, Inc.: President and CSO, Salary