LATE BREAKER ABSTRACT

LB-1. A Randomized Trial of High-dose Influenza Vaccine in Adult Solid-Organ Transplant Recipients

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Background. The annual influenza vaccine is recommended for solid-organ transplant recipients (SOTR) although studies have shown suboptimal immunogenicity. Influenza vaccine containing higher dose antigen may lead to greater immunogenicity in this population.

Method. We conducted a randomized, observer-blind trial comparing the safety and immunogenicity of high dose (HD; FluzoneHD, Sanofi) vs. standard dose (SD; Fluviral, GSK) influenza vaccine in adult SOTR. Patients were randomized 1:1 to receive the 2016–2017 influenza vaccine. Preimmunization and 4-week postimmunization sera underwent strain-specific hemagglutination inhibition assay for the three vaccine strains and an additional B strain not included in the vaccine.

Result. We randomized 172 patients and 161 (84 HD; 77 SD) were eligible for analysis. Median age was 57 years (range 18–86) and time from transplant was 38 (range 3–1402) months. Types of transplant were kidney 67 (39.0%), liver 38 (22.1%), lung 25 (14.5%), heart 23 (13.3%), and combined 19 (11.0%). Seroconversion to at least one of the three vaccine antigens (primary outcome) was present in 78.6% vs. 55.8% in HD vs. SD vaccine, respectively ($P < 0.001$). Seroconversion to A/H1N1, A/H3N2, and B strains were 40.5% vs. 20.5%, 57.1% vs. 32.5%, and 58.3% vs. 41.6% in HD vs. SD vaccine ($P = 0.006$, 0.002, 0.028, respectively). Postimmunization geometric mean titers of A/H1N1, A/H3N2, and B strains were significantly higher in the HD group ($P = 0.007$, 0.002, 0.033). Independent factors associated with seroconversion to at least one vaccine strain were the use of HD vaccine and being on mycophenolate doses less than 2 g daily ($P = 0.003$, 0.013, respectively). Seroconversion rate to the B strain not included in the trivalent study vaccine was also higher in the HD vaccine group (33.3% vs. 14.1%, $P = 0.004$). Local and systemic adverse events were similar for the two vaccines. Biopsy-proven rejection was seen in 3.4% vs. 1.2% in HD vs. SD groups, respectively ($P = 0.62$). Two patients in the SD vaccine group and one in the HD group developed influenza infection during the follow-up.

Conclusion. High-dose vaccine demonstrated significantly better immunogenicity than SD vaccine in adult transplant recipients and may be the preferred influenza vaccine for this population.

Disclosures. **D. Kumar**, Sanofi: Speaker's Bureau, Speaker honorarium. Pfizer: Speaker's Bureau, Speaker honorarium. GSK: Grant Investigator, Grant recipient.

LB-2. Cap-dependent Endonuclease Inhibitor S-033188 for the Treatment of Influenza: Results from a Phase 3, Randomized, Double-Blind, Placebo- and Active-Controlled Study in Otherwise Healthy Adolescents and Adults with Seasonal Influenza

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Background. Cap-dependent endonuclease (CEN) resides in the PA subunit of influenza virus polymerase and mediates the "cap-snatching" process during viral mRNA biosynthesis. S-033188 is a potent, selective, small molecule inhibitor of CEN. Here we report clinical and virologic outcomes from a global Phase 3 study CAPSTONE-1.

Method. This was a multicenter, randomized, double-blind, placebo- and active-controlled study. Key eligibility criteria included 12–64 years of age, fever (axillary temperature ≥38.0°C), ≥1 general symptom and ≥1 respiratory symptom (moderate to severe), and ≤48 hours from symptom onset. Patients between 20 and 64 years of age were randomized in 2:2:1 ratio to receive a single oral administration of S-033188, placebo, or 75 mg oseltamivir BID for 5 days. Patients between 12 and 19 years of age were randomized in 2:1 ratio to receive either a single oral administration of S-033188 or placebo. The primary efficacy endpoint was time to alleviation of influenza symptoms (TTAS) in the infected intent to treat population. Viral titer and RNA content were determined from pre- and postdose nasal/throat swabs.

Result. A total of 1436 patients were randomized. TTAS was significantly shorter in the S-033188 group than that in the placebo group (median TTAS: 53.7 hours vs. 80.2 hours, $P < 0.0001$). Median time to cessation of viral shedding was 24 hours in patients treated with S-033188, compared with 72 hours in those treated with oseltamivir ($P < 0.0001$) and 96 hours for placebo ($P < 0.0001$). Patients in the S-033188 group had significantly greater reductions from baseline in both viral titer and RNA content than those in oseltamivir or placebo groups at all time-points until Day 3 (compared with oseltamivir) or Day 5 (compared with placebo). S-033188 was generally well tolerated, with overall incidence of treatment-emergent adverse events lower than that seen with oseltamivir.

Conclusion. Treatment with S-033188 was superior to placebo in alleviating influenza symptoms, and superior to both oseltamivir and placebo in virologic outcomes. Safety profile of S-033188 compared favorably with that of oseltamivir.

Disclosures. **S. Portsmouth**, Shionogi Inc.: Employee, Salary. **K. Kawaguchi**, Shionogi & Co., Ltd.: Employee, Salary. **M. Arai**, Shionogi & Co Ltd: Employee, Salary. **K. Tsuchiya**, Shionogi & Co., Ltd.: Employee, Salary. **T. Uehara**, Shionogi & Co., Ltd.: Employee, Salary.

LB-3. Possible Impact of Wide-scale Vaccination Against Serogroup B Neisseria Meningitidis on Gonorrhea Incidence Rates in One Region of Quebec, Canada

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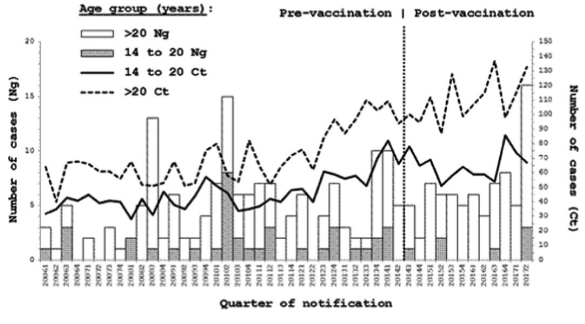
Background. Owing to a persistent increase of serogroup B *Neisseria meningitidis* (Nm) invasive infections in the Saguenay-Lac-Saint-Jean (SLSJ) region of the province of Quebec (Canada) since 2006, a wide-scale vaccination campaign of individuals aged 6 months to 20 years was conducted between May and December 2014 using the 4-component protein-based meningococcus serogroup B vaccine (4CMenB). Components of this vaccine have shown to potentially cross-react with *Neisseria gonorrhoeae* (Ng). The study objective was to assess the impact of the vaccination campaign on Ng incidence rate (IR).

Methods. Ng cases notified to public health authorities during prevaccination period (January 2006 to June 2014) and postvaccination period (July 2014 to June 2017) were analyzed. The impact of this mass campaign was estimated by a Poisson regression model, including the year (11 July–June categories), age (14–20 vs. 21 years and older), and the intervention (0 by default and 1 in those 14–20 years in the period of July 2014 to June 2017).

Results. Overall vaccine coverage was 82% in the target group. A total of 231 Ng cases were reported among persons 14 years and older (IR: 8.4/100,000 person-years) of the SLSJ region from January 2006 to June 2017. A decrease in the Ng number of cases and IR among individuals 14–20 years was observed during the post-vaccination period whereas it increased in those 21 years and older (figure). Estimate of vaccination impact was an Ng risk reduction of 59% (95% CI: −22% to 84%; $P = 0.1$). During the same period, *Chlamydia trachomatis* (Ct) infections increased among persons of both age groups in the SLSJ region.

Conclusion. Although the estimate of the impact of the campaign was not statistically significant, possibly due to limited size of the study population and the low incidence of the disease, it is congruent with results of a case–control study in New Zealand showing an OMV-MeNZB vaccine effectiveness of 31%. A higher effectiveness of 4CMenB is a plausible hypothesis as three additional proteins also found in Ng are included in the vaccine used in the SLSJ region. The results of this ecologic study suggest cross-protection of 4CMenB vaccine against Ng infections. Further studies on this topic are warranted.

Figure. Ng and Ct infections per quarter and by age group, SLSJ, January 2006 to June 2017.



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