LATE BREAKER ABSTRACT

LB-1. A Randomized Trial of High-dose Influenza Vaccine in Adult Solid-Organ Transplant Recipients
Yoichi Natori, MD,1 Atul Humar, MD,1 Mika Shiotsuma, MD,1 Jacky Slomovic, BSc,2 Katja Hoschler, PhD,2 Victor Ferreira, PhD,2 Peter Ashton, MSC2
Coleson Rostein, MD,3 Lee Lilly, MD,4 Jeffrey Schiff, MD,5 Lansen Siftert, MD,6 Deepli Kumar, MD,7 Transplant Infectious Diseases, University Health Network, Toronto, ON, Canada; 2Transplantation, University of Toronto, Toronto, ON, Canada; 3University Health Network, Toronto, ON, Canada; 4Public Health England, London, UK; 5UHN, Toronto, ON, Canada

Session: 228. Late Breaker Oral Abstracts
Saturday, October 7, 2017: 10:30 AM

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; Fluzone HD, 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 (13.5%), and combined 11 (19.3%). 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/H1N2, 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, 0.033). 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
Saimon Porteous, MD,1 Keiko Kawaguchi, MS,2 Masatsugu Arai, MS,2 Kenji Tsuchiya, MS3 and Takeki Uehara, PhD2; Shionogi Inc., Flohram Park, New Jersey; 3Shionogi & Co., Ltd., Osaka, Japan; 2Shionogi & Co Ltd., Osaka, Japan

Session: 228. Late Breaker Oral Abstracts
Saturday, October 7, 2017: 10:30 AM

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), ≥21 general symptoms 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.

Results. A total of 1436 patients were randomized. TTAS was significantly shorter for 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 Gonorrhoea Incidence Rates in One Region of Quebec, Canada
Jean Longtin, MD,1 Rejean Dion, MD,1 Marc Simard, MSc,2 Jean-Francois Betalin Meli, MD,2 Yves Longtin, MD,1 Brigitte Lefebvre, PhD,3 Annie Claude-Leber, MD,4 MD,4 Genevieve Deceuninck, MD, MSc,1 Philippe De Wals, MD, PhD,14 INSPQ, Montreal, QC, Canada; 2Centre de recherche en épidémiologie, Université Laval, Québec, QC, Canada; 3CISSS du Saguenay-Lac-Saint-Jean, Saguenay, QC, Canada; 4Infectious Diseases & Microbiology, Jewish General Hospital, Montreal, QC, Canada; 5Microbiology, CIUSSS de l’est-de-l’île-de-Montréal, Montreal, QC, Canada; 6Social and Preventive Medicine, Laval University, Quebec City, QC, Canada

Session: 228. Late Breaker Oral Abstracts
Saturday, October 7, 2017: 10:30 AM

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: 14.0/100,000 person-years) in 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-MenNZB 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.
**Disclosures.** P. De Waal, GlaxoSmithKline: Grant Investigator and Scientific Advisor, Grant recipient and travel expenses. Pfizer: Grant Investigator and Scientific Advisor, Grant recipient and travel expenses. Sanofi-Pasteur: Grant Investigator and Scientific Advisor, Grant recipient and travel expenses. Novartis: Grant Investigator and Scientific Advisor, Grant recipient and travel expenses.

**LB-4. Phase 3 Randomized, Controlled Trial of Switching to Fixed-dose Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) from Boosted Protease Inhibitor-based Regimens in Virologically Suppressed Adults: Week 48 Results**

Eric Deja, MD;1 Edwin Dejesus, MD;2 Peter Ruane, MD;3 Gordon Crofoot, MD;4 Goodman Yosuchi, MD;5 Carine Creticos, MD;6 James K Rockstroh, MD7,8,9; Michaela Molina, PhD, MD;10 Ellen Koenig, MD;10 Ya-Pei Liu, PhD;8,11 Kristen Andreatta, PhD;8,12 Hiba Graham, Pharm D13,14; Andrew Cheng, MD PhD15; Hal Martin, MD, MPH;16 Erin Quirk, MD;17,18,19 1124 W Carson St., Harbor-UCLA Medical Center, Torrance, California; 2Endo Immunology, Orlando, Florida; 3Biontech; 4Clinical Research Group, Inc., Los Angeles, California; 5The Crofoot Research Center, Houston, Texas; 6Midland Florida Clinical Research Center, LLC, Deland, Florida; 7Howard Brown Health Center, Chicago, Illinois; 8Department of Medicine, I Bonn University Hospital, Venssburg, Germany; 9Department of Infectious Diseases, Saint-Louis Hospital, Paris, France; 10Medical, Inst Domin Estudio Virologico, Santo Domingo, Dominican Republic; 20Gilead Sciences, Foster City, California

**Session:** 228. Late Breaker Oral Abstracts

**Saturday, October 7, 2017: 10:30 AM**

**Background.** Boosted protease inhibitor regimens (bPIS) are effective and often used in HIV-infected individuals with difficulties with adherence, but they can have drug–drug interactions and GI adverse effects. Bictegravir (B), a novel, potent integrase strand-transfer inhibitor with a high bar admission to resistance and drug–drug interactions, was coformulated with the recommended nucleoside reverse transcriptase inhibitor backbone emtricitabine (FTC)/tenofovir alafenamide (F/TAF) and demonstrated high efficacy and tolerability in randomized studies in treatment-naive adults. This randomized, assessor blinded study assessed efficacy and safety of switching to B/F/TAF from a multi-tablet regimen containing a bPI.

**Methods.** HIV-infected adults suppressed on regimens of boosted atazanavir (ATV) or darunavir (DRV) + abacavir/lamivudine (ABC/3TC) or FTC/tenofovir disoproxil fumarate (TDF) were randomized 1:1 to continue their current bPI regimen or switch to open-label coformulated B/F/TAF (50/200/25 mg) once daily. Primary endpoint was proportion with HIV-1 RNA ≤50 copies/mL (c/mL) at W48 (FDA snap-shot). Noninferiority was assessed with 95.002% confidence intervals (CI) using a margin of 4%. Secondary endpoints included proportion with HIV-1 RNA <50 c/mL and safety in 12 weeks.

**Results.** A total of 577 participants were randomized and treated with B/F/TAF (n = 290) or current bPI regimens (n = 287): 17% women, 26% black, median age 48 years. Most were receiving a bPI with FTC/TDF (85%) at screening. At W48, switching to B/F/TAF was noninferior to continuing bPI with 1.7% in each group having HIV-1 RNA <50 c/mL (difference -0.002%; 95.002% CI: −2.5% to 2.5%, P = 1.00); the proportion with HIV-1 RNA <50 c/mL was 92.1% in B/F/TAF vs. 88.9% in bPI. No participant on DRV/ritonavir + ABC/3TC developed a treatment-emergent L74V mutation. Incidence of grade 3 or 4 AEs was similar (B/F/TAF 4%, bPI regimens 6%). No renal discontinuations or tubulopathy cases occurred with B/F/TAF.

**Conclusion.** Adults switching to B/F/TAF from a boosted PI maintained high rates of virologic suppression without resistance. B/F/TAF was safe and well tolerated.

---

**LB-5. The SEP-SEQ Trial: Clinical Validation of the Karius Plasma Next-Generation Sequencing Test for Pathogen Detection in Septic Patients**

Simone Thay, PhD;1 Hon Seng, BS2; Desiree Hollemon, MSN, MPH;3 David Hong, MD;4 Timothy Blawaukamp, PhD,5 Mickey Kertesz, PhD;5 Carine Ho, MD;6 Rosen Marra, BS;3 James Quinn, MD;7 and Samuel Yang, MD;8 Emergency Medicine, Stanford University Medical Center, Stanford, California; 9Karius, Inc., Redwood City, California

**Session:** 228. Late Breaker Oral Abstracts

**Saturday, October 7, 2017: 10:30 AM**

**Background.** Septic patients may die because of the broad range of potential pathogens. In up to 40% of cases, a causative pathogen is never identified. There is a need for improved diagnostic tests that can accurately identify the breadth of potential pathogens in septic patients.

**Methods.** We enrolled a prospective cohort of patients presenting to the hospital with signs and symptoms of sepsis. Plasma samples were collected for NGS testing at time of initial blood culture. Extracted plasma cell-free DNA was sequenced, human sequences removed and remaining reads aligned against a pathogen database consisting of viruses, bacteria, and eukaryotic pathogens. Relative abundance was estimated; pathogens present at high statistical significance were identified. NGS results were compared with a composite reference standard of all microbiology testing performed within 7 days of hospital admission.

**Results.** Of 286 patients enrolled, plasma NGS identified potential pathogens in 60.1% (172 of 286) of septic subjects including DNA viruses, bacteria (including fastidious/unculturable bacteria like *Mycobacterium tuberculosis*), and fungi. In contrast, the 286 subjects positive with initial broad blood culture and 38.1% (109 of 286) had a potential infectious etiology identified using a composite microbiology laboratory standard. The NGS plasma assay had a positive agreement of 86.7% (39 of 45) and 79.3% (78 of 98) compared with initial broad culture (after excluding contaminants) and the composite laboratory reference standard, respectively. After clinical adjudication, 81.4% (140 of 172) of the positive plasma NGS results were deemed to be consistent with the septic event. Of the remaining 32 subjects, 15 had NGS results that were plausible causes of sepsis but clinical were insufficient to confirm this. With a single blood draw, the Karius plasma NGS assay identified a broad range of pathogens incident to septic patients three times more often than blood culture and more often than all microbiology tests combined. This plasma NGS test can identify viruses, bacteria, and eukaryotic pathogens which can provide valuable information to help clinicians better target antimicrobial therapy for patients with sepsis.

**Conclusions.** With a single blood draw, the Karius plasma NGS assay identified a broad range of pathogens incidence to septic patients three times more often than blood culture and more often than all microbiology tests combined. This plasma NGS test can identify viruses, bacteria, and eukaryotic pathogens which can provide valuable information to help clinicians better target antimicrobial therapy for patients with sepsis.

---

**LB-6. Ethanol Lock Treatment and Secondary Prophylaxis for Central Line-Associated Bloodstream Infection in Pediatric Hematology and Oncology: A Randomized, Double-Blind, Placebo-Controlled, Intervention Trial**

Joshua Wolf, MBBS FRACP;1 Tom Connell, PhD;2 Kim J. Allison, BSN, MS1; Li Tang, PhD3;illee Richardson, PharmD;4 Kristeen Braun, BS5; Eloise Borello, BSNC;6 Amalie Gaur, MD;6 Hana Hakim, MD, MS7; Yin Su, MS6; Françoise Mecheinad, MD;6 Randall Hayden, MD;7 Paul Monagle, MBBS, MD;8 Leon Worth, MBBS, MD;9 Nigel Curtis, PhD10; Patricia M. Flynn, MD, MS5; 1Infectious Diseases, St. Jude Children’s Research Hospital, Memphis, Tennessee; 2Clinical Paediatrics, Murdoch Children’s Research Institute, Parkville, Victoria, Australia; 3St. Jude Children’s Research Hospital, Memphis, Tennessee; 4Bioanalytical, St. Jude Children’s Research Hospital, Memphis, Tennessee; 5Pharmaceutical Sciences, St. Jude Children’s Research Hospital, Memphis, Tennessee; 6Oncology, Royal Children’s Hospital Melbourne, Parkville, Victoria, Australia; 7Oncology, Royal Children’s Hospital Melbourne, Parkville, Victoria, Australia, 8Flinders University, Adelaide, South Australia; 9Department of Paediatrics, The University of Melbourne, Parkville, Australia, 10Department of Infectious Diseases, Royal Children’s Hospital, Melbourne, Victoria; 11Department of Infectious Diseases, Royal Childrens Hospital Melbourne, Parkville, Victoria, Australia; 12Department of Infectious Diseases, Royal Children’s Hospital Melbourne, Parkville, Victoria, Australia; 13Department of Paediatrics, The University of Melbourne, Parkville, Australia

**Session:** 228. Late Breaker Oral Abstracts

**Saturday, October 7, 2017: 10:30 AM**

**Background.** Central line-associated bloodstream infection (CLABSI) commonly affects children with cancer and hematological disorders, with significant attributable costs and mortality. Treatment failure, comprising persistent infection, infection relapse or new infection, occurs in ~50% of cases. Adjunctive ethanol lock therapy (ELT) has been proposed to prevent failure, but has never been tested in a prospective controlled study.

**Methods.** A prospective, dual-center, double-blind, block randomized, placebo-controlled trial of ELT (70% ethanol in water) for CLABSI, given as treatment (2 x 5 mL, once per week) for 24 weeks, in children with oncologic or hematologic disorders (NCT01742965). Risk of treatment failure was compared between intervention and control groups according to proportional and cumulative incidence models,