to childhood vaccination recommendations and targeted vaccination of recommended at-risk groups can prevent future hepatitis A outbreaks of any transmission pattern.

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

LB11. Rapid Rise in Decreased Susceptibility to Azithromycin among *Shigella* Isolates in the United States: A Look at National Surveillance Data, 2011–2017

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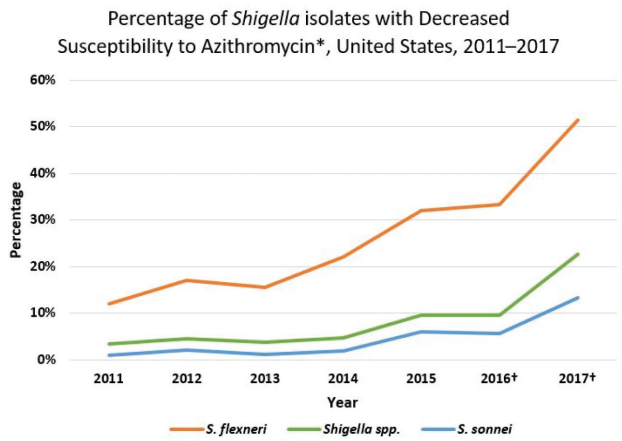
Background. *Shigella* spp. cause ~500,000 illnesses in the United States annually. Antibiotics are recommended for immunocompromised patients and shorten the duration of illness, thus limiting spread. First-line treatments include ciprofloxacin (CIP) and azithromycin (AZM). CIP resistance is a growing problem in the United States; decreased susceptibility to AZM (DSA) has been reported globally, particularly among men who have sex with men (MSM). We reviewed National Antimicrobial Resistance Monitoring System (NARMS) data to determine DSA trends among *Shigella* isolates in the United States.

Methods. Health departments nationwide forward every 20th *Shigella* isolate to CDC NARMS for antimicrobial susceptibility testing using broth microdilution. We defined CIP resistance using CLSI clinical breakpoints and DSA using epidemiological cutoff values where available. We performed whole genome sequencing on isolates from 2016 and screened the sequences for resistance determinants using ResFinder 3.0.

Results. To date, we have tested 3,044 *Shigella* isolates collected during 2011–2017. Overall, 264 isolates (9%) had DSA, increasing from 3% in 2011 to 23% in 2017; 41 (16%) were also CIP resistant. The odds of DSA increased by 1.5 (95% confidence interval [CI] 1.4–1.6) annually. DSA was more common among adult males (OR 21.2, CI 14.9–30.3), in isolates from the West census region (OR 2.4, CI 1.8–3.2), and in *S. flexneri* (OR 8.2, CI 6.3–10.7). Of 543 sequenced isolates, 52 (10%) had DSA; of these, 31 (60%) contained both *mph(A)* and *erm(B)* genes, 17 (33%) contained *mph(A)* only, and 4 (8%) had no identified macrolide-resistance mechanism.

Conclusions. In 2017, nearly 1 in 4 *Shigella* isolates tested had DSA, a 7-fold increase since 2011. This rapid rise in DSA parallels that seen in other countries, where resistance to other clinically relevant drugs is high and macrolides are no longer useful as empiric treatment. The increased risk of DSA in adult males is consistent with previous reports of DSA *Shigella* in MSM. The resistance genes observed are typically plasmid-mediated and can be transferred to other bacteria. Public health strategies to mitigate the spread of resistant *Shigella* should include antibiotic stewardship and novel approaches for sexually transmitted infection prevention in MSM.



*Criteria for decreased susceptibility to azithromycin (DSA) were based on the non-wild-type epidemiological cutoff values set by CLSI for *Shigella sonnei* (MIC ≥32 µg/mL) and *Shigella flexneri* (MIC ≥16 µg/mL). For remaining *Shigella* species, we defined DSA using the NARMS-established breakpoint of MIC ≥32 µg/mL.
† Preliminary data

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

LB12. Safety and Efficacy of Fidaxomicin and Vancomycin in Pediatric Patients with *Clostridium difficile* Infection: Phase III, Multicenter, Investigator-blind, Randomized, Parallel Group (SUNSHINE) Study

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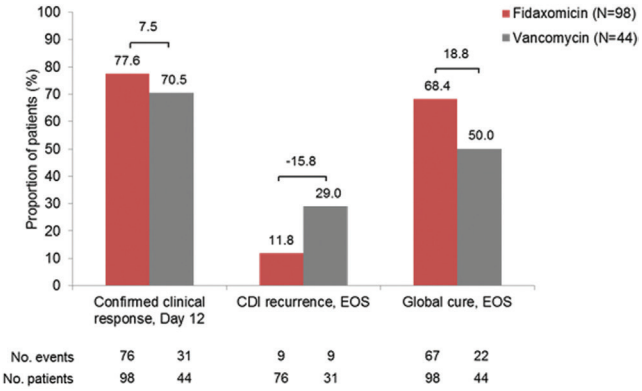
Background. *Clostridium difficile* infection (CDI), a common cause of antibiotic-associated diarrhea, leads to substantial healthcare burden. In children and young adults, the incidence of CDI is increasing. Fidaxomicin (FDX) is a narrow-spectrum macrocyclic antibiotic treatment for CDI in adults, but pediatric data are limited. The primary objective of our study was to investigate safety and efficacy of FDX and vancomycin (VAN) in children.

Methods. Patients aged <18 years with new laboratory-confirmed CDI and diarrhea (watery diarrhea for patients aged <2 years, and ≥3 unformed bowel movements in 24 hours for patients aged ≥2 years) were enrolled in a randomized, investigator-blinded study. Participants were randomized (2:1) to 10 days of treatment with either FDX (oral suspension 32 mg/kg/day or tablets 200 mg BID) or VAN (oral liquid 40 mg/kg/day or capsules 125 mg QID). Concurrent use of other antibiotic treatment for CDI was not permitted. Randomization was stratified by age group. The primary efficacy endpoint was confirmed clinical response (CCR) at Day 12 (absence of diarrhea for 2 consecutive days on treatment and remaining well until treatment discontinuation). Other efficacy endpoints were also evaluated.

Results. Of 142 patients in the full analysis set (FDX n = 98; VAN n = 44), 30 were aged <2 years, 48 were aged 2 to <6 years, 36 were aged 6 to <12 years and 28 were aged 12 to <18 years. At baseline, 28.6% of the FDX arm and 22.7% of the VAN arm had prior confirmed CDI. Overall, 73.5% of the FDX arm and 75.0% of the VAN arm had ≥1 treatment-emergent adverse event. There were three deaths in the FDX arm during the study and two deaths in the VAN arm after end of study (post-Day 40); none were related to treatment. There was a trend to improved CCR and other efficacy outcomes for FDX (figure) and this was statistically significant for global cure (adjusted difference 18.8%; 95% CI 1.5%, 35.3%).

Conclusions. There was a consistent trend for improved efficacy outcomes with FDX compared with VAN, as shown by the adjusted treatment differences, although the small sample size precluded conclusions on most outcome differences.

Figure.



Results are given for the Full Analysis Set: all patients with confirmed CDI who were randomized and received at least one dose of study medication. End of study (EOS) occurred 30 days after the end of 10-day treatment. Confirmed clinical response (CCR) was defined as absence of watery diarrhea symptoms for patients <2 years of age or improvement in the number and character of bowel movements (i.e. <3 unformed bowel movements per day) for patients ≥2 years of age, along with no further requirement for CDAD therapy within 2 days after completion of study drug. Recurrence was defined as recurrence of diarrhea to an extent that was greater than that reported on the last day of study drug, and positive direct or indirect test for the presence of toxigenic *C. difficile* in stool that required (in the investigator's opinion) further anti-infective CDI treatment. Global cure was defined as positive CCR without CDI recurrence until EOS. Bars show adjusted treatment differences calculated using a stratified Cochran-Mantel-Haenszel method

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LB13. *Candida auris* in NYC: A Health System's Experience Treating the Emerging Drug-Resistant Yeast

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Background. *Candida auris* is emerging multidrug-resistant yeast that can cause serious infections with published mortality rates as high as 60%. It was first recognized in 2009 and has been reported in over a dozen countries. The current United States outbreak was identified in 2016 with New York City (NYC) as the epicenter. The aim of this evaluation was to describe the clinical infections and outcomes with *C. auris* in a large health system in NYC.

Methods. Cases were identified from clinical specimens collected December 2015–June 2018 from the Mount Sinai Hospital Clinical Microbiology Laboratory, the central laboratory for the Mount Sinai Health System, which encompasses seven hospitals across NYC. All *C. auris* isolates were confirmed by the New York State Department of Health Wadsworth Center. Medical charts were reviewed. A case was included if *C. auris* grew from a sterile body site, an antifungal treatment was initiated or the patient expired before the yeast was identified on Gram stain.

Results. Twenty-nine possible cases were identified with 23 meeting the case definition. These cases included 19 bloodstream infections (BSI), two intra-abdominal abscesses, one skin soft tissue infection, and one otitis externa. Using the MIC breakpoints recommended by the Centers for Disease Control and Prevention, 100% of isolates tested were susceptible to caspofungin, 29% were susceptible to amphotericin B, and 17% were susceptible to fluconazole. Nineteen patients received antifungal treatment, 13 with caspofungin monotherapy and four with sequential therapy of caspofungin followed by an azole (three with fluconazole, one with posaconazole). Fifteen (65%) patients expired within 90 days of the positive culture. Fourteen of the deaths were in candidemic patients, despite that eight (57%) of these patients had documented microbiologic clearance after appropriate therapy. The 90-day mortality rate was 74% for BSI.

Conclusions: This case series is the largest reported in the United States. Candidemia was the most common site of infection and had a very high 90-day mortality rate, despite sterilization of the blood. These findings highlight the significant morbidity and mortality associated with *C. auris* and the need to focus efforts on rapid diagnostics and infection prevention.

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

LB14. Safety and Immunogenicity of High-Dose Quadrivalent Influenza Vaccine Administered by Intramuscular Route in Subjects Aged 65 Years and Older

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Background. Older adults (≥65 years of age) remain at increased risk of influenza because they do not respond to standard dose influenza vaccines as well as younger adults. A high dose, inactivated trivalent influenza vaccine, IIV3-HD, containing four times the antigen content (60 µg hemagglutinin per influenza strain) of standard-dose influenza vaccines has been available in the United States since 2010. Two distinct B influenza lineages (Victoria and Yamagata) have co-circulated for over a decade, making it difficult to predict which will predominate the next season. IIV4-HD has been developed to address the frequent influenza B strain mismatches by incorporating a strain from each B lineage. This pivotal Phase III study evaluated the safety and immunogenicity of IIV4-HD as compared with two IIV3-HD vaccines.

Method. A randomized, modified double-blind, multicenter study (NCT03282240) was conducted in 2670 healthy subjects in the United States, who were randomly assigned to receive IIV4-HD, a licensed IIV3-HD, or an IIV3-HD with the alternate B influenza strain. Using the hemagglutinin inhibition (HAI) assay at baseline and 28 days after vaccination, post-vaccination geometric mean titers and seroconversion rates were measured. Safety data were collected through 6 months post-vaccination.

Result. IIV4-HD was noninferior to the licensed IIV3-HD and the investigational IIV3-HD (containing the alternate B strain) for all four influenza strains as assessed by HAI GMTs and seroconversion rates. Moreover, IIV4-HD induced a superior immune response (HAI GMTs and seroconversion rates) compared with the immune response induced by the IIV3-HD that does not contain the corresponding B strain. Reactogenicity profiles were comparable across all study groups. Most unsolicited adverse events were of Grade 1 or Grade 2 intensity. One serious adverse event considered related by the Investigator was reported in the IIV4-HD group.

Conclusion. Vaccination of adults 65 years of age and older with IIV4-HD was found to be noninferior to two IIV3-HD vaccines with a similar safety profile. The addition of a second B lineage strain does not adversely affect the safety or immunogenicity profile of IIV4-HD compared with IIV3-HD.

Disclosures. **L. J. Chang**, Sanofi Pasteur: Employee, Salary. **Y. Meng**, Sanofi Pasteur: Employee, Salary. **H. Janosczyk**, Sanofi Pasteur: Employee, Salary. **V. Landolfi**, Sanofi Pasteur: Employee, Salary. **H. K. Talbot**, Sanofi Pasteur: Investigator, Research grant. Gilead: Investigator, Research grant. MedImmune: Investigator, Research grant. Vaxinnate: Safety Board, none. Seqirus: Safety Board, none.

LB15. Vaccine Effectiveness of Flucelvax Relative to Inactivated Influenza Vaccine During the 2017–18 Influenza Season in Northern California

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Background. In June 2018, the CDC reported that influenza vaccine effectiveness (VE) against A(H3N2) influenza virus for the 2017–2018 season was ~24%. This lower than expected VE was hypothesized to be partially related to genetic changes arising in the vaccine virus during passage in eggs. Flucelvax™ (Seqirus) is a cell culture-based inactivated influenza vaccine (ccIIV) which is not manufactured in eggs. We investigated whether the VE of ccIIV against influenza A differed from that of egg-based IIV (ebIIV) during the 2017–2018 influenza season.

Methods. The study included all Kaiser Permanente Northern California members aged 4–64 years. We identified all individuals who were positive for influenza by polymerase chain reaction (PCR). This cohort analysis estimated the relative VE of ccIIV vs. ebIIV by comparing the ccIIV vaccinees vs. the ebIIV vaccinees with respect to the risk of PCR-confirmed influenza. We separately estimated the absolute VE of ccIIV and ebIIV by comparing each group of vaccinees with unvaccinated individuals. We used Cox regression with a calendar timeline, stratified by birth year, and adjusted for facility, race, years of membership, prior season influenza vaccine, co-morbidities, and number of inpatient admits in the prior year. We calculated VE as 1 – hazard ratio (HR).

Results. Of the 3,015,891 members aged 4–64 years, 1,017,314 were vaccinated. Of these, 932,874 (91.7%) received ebIIV and 84,440 (8.3%) received ccIIV. Most ebIIV (86.2%) was trivalent. Comparing ccIIV with ebIIV, the adjusted relative VE against influenza A was 6.8% (95% CI: 11.2, 21.9; $P = 0.43$). The adjusted absolute VE vs. unvaccinated of ccIIV was 30.2% (95% CI: 17.1, 41.3; $P < 0.0001$) and of ebIIV was 17.9% (95% CI: 12.1, 23.3; $P < 0.0001$).

Conclusion. Both cell-culture and egg-based IIV vaccines showed relatively low effectiveness during the 2017–2018 influenza season in which A(H3N2) predominated. The findings of this study show there was no significant difference in the effectiveness of cell-culture IIV compared with egg-based IIVs. Improvements in influenza vaccines will require ongoing monitoring of vaccine effectiveness.

Disclosures. **N. P. Klein**, GSK: Investigator, Research support. Sanofi Pasteur: Investigator, Research support. Merck: Investigator, Research support. Pfizer: Investigator, Research support. Protein Science: Investigator, Research support. MedImmune: Investigator, Research support. Dynavax: Investigator, Research support.

LB16. Phase 3 Trial of Baloxavir Marboxil in High-Risk Influenza Patients (CAPSTONE-2 Study)

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Background. Baloxavir marboxil (BXM), an oral selective cap-dependent endonuclease inhibitor, is effective and safe for treating acute influenza in otherwise healthy patients.

Method. We conducted an international, randomized, double-blind, placebo (PLC)- and oseltamivir (Os)-controlled treatment study in patients at higher risk (HR) of influenza complications. Inclusion criteria included age ≥12 years, fever + influenza symptoms of ≤48 hours duration, and presence of at least 1 HR factor adapted from CDC criteria. Patients were randomized (1:1:1) to a single oral dose of BXM (40/80 mg for BW </≥80 kg), PLC, or 75 mg Os BID for 5 days. The primary endpoint was time to improvement of influenza symptoms (TTIIS) in those with RT-PCR confirmed influenza (ITTI population). Secondary endpoints included infectious virus detection in serial nasopharyngeal swabs, prescription of antibiotics, and influenza-related complications.

Result. Among 2,184 randomized patients, 1,163(53%) comprised the ITTI population (47.9% A/H3N2, 6.9% A/H1N1, 41.6% B). The most common risk factors were asthma or chronic lung disease (39.2%) and age ≥65 years (27.4%). TTIIS was significantly shorter in BXM than PLC (median 73.2 hours vs. 102.3 hours, $P < 0.0001$) and numerically shorter than Os (81.0 hours, $P = 0.8347$). TTIIS in BXM patients with A/