Stock Options. **P. Radspinner**, FluGen: Board Member and Founder, Salary and Stock Options. **R. Aitchison**, FluGen: Consultant, Consulting fee. **P. Bilsel**, FluGen: Employee, Salary and Stock Options.

1971. A Randomized, Double-Blind, Placebo-Controlled Trial to Assess the Safety and Tolerability of a Respiratory Syncytial Virus (RSV) Neutralizing Monoclonal Antibody (MK-1654) in Healthy Subjects

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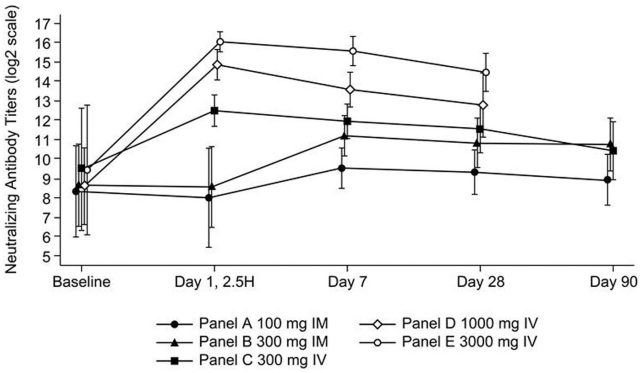
Background. Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection and hospitalization in infants. Prophylaxis for RSV infection is only recommended for the highest risk infants, leaving the majority of infants unprotected. MK-1654 is a fully human monoclonal antibody targeting the RSV fusion (F) protein with Fc domain mutations to extend half-life that is being developed to provide passive immunity against RSV in infants. The safety profile, development of anti-drug antibodies (ADAs), serum neutralizing antibody (SNA) titers, and pharmacokinetics (PK) in healthy adult volunteers receiving single-ascending doses of MK-1654 was evaluated.

Methods. In this double-blinded ongoing Phase 1 study, healthy adults of non-childbearing potential (19 to 59 years) were randomized in a 3:1 ratio to receive a single dose of MK-1654 or placebo (0.9% sodium chloride injection, USP) as a bolus intramuscular injection (IM) or in an intravenous infusion (IV) for at least 2.5 hours. Dose levels included 100 and 300 mg IM, and 300, 1,000, and 3,000 mg IV. Standard methods were used to assess safety and tolerability. Serum was tested for ADAs and RSV A SNA titers at time points up to day 120 and up to day 90, respectively. MK-1654 adult PK and estimated PK for infants will be reported separately.

Results. A total of 152 subjects (male = 117, female = 35) have been enrolled (mean age = 41 years). No deaths, serious adverse events, discontinuations due to AEs, clinically significant laboratory AEs, or dose-dependent pattern of drug-related AEs were reported. Sixty-six subjects reported 181 clinical AEs (97.8% mild and 2.2% moderate in intensity). The most common AEs (≥5%) were headache, nasal congestion, vessel puncture site hemorrhage, oropharyngeal pain, rhinorrhea and nausea. No treatment emergent ADAs have been identified through time points tested. Administration of MK-1654 resulted in a dose-dependent increase in RSV A SNA titers through Day 90 (figure). Updated safety, SNA titers and ADAs will be provided.

Conclusion. MK-1654 was generally well tolerated at doses up to 300 mg IM and up to 3,000 mg IV and resulted in a dose-dependent increase in SNA titers, reflecting biologically active MK-1654 in the serum. No treatment emergent ADAs have been observed.



Disclosures. **A. Aliprantis**, Merck: Employee and Shareholder, Salary and stock options. **D. Wolford**, Merck: Employee and Shareholder, Salary and stock options. **L. Caro**, Merck: Employee and Shareholder, Salary and stock options. **B. Maas**, Merck: Employee and Shareholder, Salary and stock options. **H. Ma**, Merck: Employee and Shareholder, Salary and stock options. **K. Vora**, Merck: Employee, Salary. **D. Geng**, Merck: Employee and Shareholder, Salary and stock options. **R. Railkar**, Merck: Employee and Shareholder, Salary and stock options. **A. Lee**, Merck: Employee and Shareholder, Salary and stock options. **L. Sterling**, Merck: Investigator, Research grant. **E. Lai**, Merck: Employee and Shareholder, Salary and stock options.

1972. Safety and Immunogenicity of 15-Valent Pneumococcal Conjugate Vaccine (PCV-15) Compared with PCV-13 in Healthy Older Adults Previously Vaccinated With 23-Valent Pneumococcal Polysaccharide Vaccine (PPV23)

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Background. Safety and immunogenicity of a new formulation of PCV-15 (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19F, 19A, 22F*, 23F, 33F*) was evaluated in adults ≥65 years of age previously vaccinated with PPV23.

Methods. Study subjects who received PPV23 at least 1 year prior to study entry received a single dose of either PCV-15 or PCV-13 (125/arm) and were followed for safety for 14 days postvaccination. Serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) and opsonophagocytic activity (OPA) geometric mean titers (GMTs) were measured immediately prior and 30 days postvaccination. NCT02573081

Results. Safety profiles were comparable between PCV-15 and PCV-13 recipients. Following vaccination, serotype- specific antibody responses for the 13 shared serotypes were generally comparable between recipients of PCV- 15 and PCV-13 for IgG GMCs and geometric mean fold rises (GMFRs), OPA GMTs and GMFRs, and percentages of subjects with ≥4-fold-rise from baseline. Recipients of PCV-15 had numerically higher IgG GMCs and OPA GMTs than PCV-13 recipients for two serotypes unique to PCV-15 (22F, 33F).

Conclusion. PCV-15 was generally well tolerated when given as a single dose to adults ≥65 years of age previously vaccinated with PPV23. Following vaccination, serotype-specific IgG GMCs and OPA GMTs were comparable between recipients of PCV-15 and PCV-13 for 13 shared serotypes.

*Not shared serotypes with PCV-13

Disclosures. **U. Buchwald**, Merck: Employee and Shareholder, Salary and stock options. **J. Peterson**, Merck: Investigator, Research grant. **H. Stacey**, Merckl: Investigator, Research grant. **K. Julien**, Merck: Investigator, Research grant. **T. Sterling**, Merck: Employee and Shareholder, Salary and stock options. **M. Bruch**, Merck: Employee and Shareholder, Salary and stock options. **G. Tamms**, Merck: Employee and Shareholder, Salary and stock options. **J. Li**, Merck: Employee and Shareholder, Salary and stock options. **A. Pedley**, Merck: Employee and Shareholder, Salary and stock options. **K. Nolan**, Merck: Employee and Shareholder, Salary and stock options. **P. Benner**, Merck: Employee and Shareholder, Salary and stock options. **C. Abeygunawardana**, Merck: Employee and Shareholder, Salary and stock options. **M. Winters**, Merck: Employee and Shareholder, Salary and stock options. **M. Kosinski**, Merck: Employee and Shareholder, Salary and stock options. **J. Stek**, Merck: Employee and Shareholder, Salary and stock options. **L. Musey**, Merck: Employee and Shareholder, Salary and stock options.

1973. A Meta-Analysis of the Effectiveness of LAIV4 and IIV against Influenza A/H3N2 Strains in Children 2–18 Years of Age During the 2016–2017 Season

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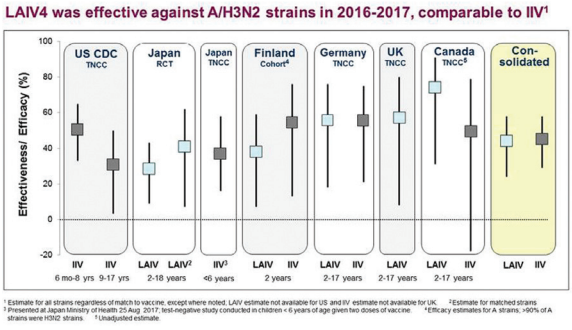
Background. The effectiveness of the quadrivalent live attenuated influenza vaccine (LAIV4) and inactivated influenza vaccines (IIV) has been evaluated in recent seasons using a number of different study designs (e.g., randomized controlled studies [RCT], cohort studies and test-negative case–control [TNCC] studies). Effectiveness estimates from these studies have, in general, had very broad confidence intervals reflecting the small numbers of cases reported. We conducted a meta-analysis to more precisely estimate the effectiveness of both vaccine types for the 2016–2017 season.

Methods. LAIV4 and IIV efficacy and effectiveness studies conducted over the 2016–2017 influenza season were identified from the published literature and through personal communication with the study investigators. Effectiveness estimates from all available study designs were included in the meta-analysis to maximize use of all available data and because all studies included methods to minimize bias. The analysis provided average estimates of the LAIV4 and IIV efficacy across countries. A sensitivity analysis limited to TNCC studies was also conducted. Only effectiveness results for A/H3N2 strains were combined as circulation of other strains was minimal. The meta-analyses used a random effects model. Heterogeneity testing was performed.

Results. Seven studies conducted in children in the United States, Japan, Finland, Germany, thr UK, and Canada were identified including four TNCC studies, one cohort study and one RCT (Figure 1). Individual effectiveness estimates ranged from 29% to 74% for LAIV4 and from 31% to 56% for IIV. Heterogeneity testing for H3N2 strains was not statistically significant. The consolidated effectiveness estimate across studies for LAIV4 was 44% (95% CI: 24, 58) and for IIV was 45% (95% CI: 29, 58). Estimates for the sensitivity analysis limited to TNCC studies were 61% (95% CI: 40, 74) and 43% (95% CI: 32, 52) for LAIV4 and IIV, respectively.

Conclusion. Despite variability in estimates across studies, both LAIV4 and IIV showed moderate and comparable effectiveness in children for circulating H3N2 strains during the 2016–2017 influenza season.



¹ Estimate for all strains regardless of match to vaccine, except where noted. LAIV estimate not available for US and IIV estimate not available for UK. ² Estimate for matched strains. ³ Presented at Japan Ministry of Health 25 Aug 2017; test-negative study conducted in children < 6 years of age given two doses of vaccine. ⁴ Efficacy estimates for A strains, >90% of A strains were H3N2 strains. ⁵ Unadjusted estimate.

Disclosures. **R. Mallory**, MedImmune: Employee, Salary. **A. Bandell**, AstraZeneca: Employee, Salary. **C. S. Ambrose**, AstraZeneca: Employee, Salary. **J. Yu**, GSK: Employee, Salary and Stockholder.

1974. Ceftriaxone-Sulbactam-EDTA vs. Meropenem in PLEA (a Phase 3, Randomized, Double-Blind Trial): Outcomes by Baseline MIC in Adults With Complicated Urinary Tract Infections or Acute Pyelonephritis

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Background. Ceftriaxone–sulbactam–disodium EDTA (CSE) is being developed for Gram-negative infections caused by multidrug-resistant (MDR) bacteria. PLEA was a Phase 3, double-blind, multicenter, randomized study of CSE vs. meropenem (MR) for treatment of adults with complicated urinary tract infections (cUTI) or acute pyelonephritis (AP). Non-inferiority of CSE over MR at the EMA/FDA primary endpoints has been reported. The effect of baseline MIC on clinical and microbiological outcome at the test of cure (TOC) visit was investigated.

Methods. Adult patients were randomized 1:1 to receive either CSE (1 g ceftriaxone/500 mg Sulbactam/37 mg EDTA) every 12 h or MR 1g every 8 hours as 30 minutes IV infusion for 5–14 days. Oral step-down therapy was not allowed. Prior to dosing, urine specimens were collected, and MICs were conducted using CLSI methods for both study drugs. Patients that were nonsusceptible to MR were not included in the mMITT population.

Results. Of 230 subjects randomized, 143 (62.2%) were included in the mMITT population. Baseline Enterobacteriaceae was found in 131 (91.6%) patients, 67/74 (90.5%) in CSE and 64/69 (92.8%) in MR arm. Mean duration of IV therapy was 7 days. Favorable clinical and microbiological outcomes were observed in ≥90% patients for all MICs across the two study groups, with the exception of MIC 1 µg/mL in MR (associated with >20% failures). Overall, both clinical cure and microbiological eradication rates were higher in CSE as compared with MR (95.9% Vs. 89.9% and 94.6% vs. 88.4% respectively) (Table 1).

CSE			MR		
MIC (µg/mL)	Clinical Cure *n/N* (%)	Microbiological Eradication *n/N* (%)	MIC (µg/mL)	Clinical Cure *n/N* (%)	Microbiological Eradication *n/N* (%)
<0.25	16/16 (100)	16/16 (100)	<0.25	20/22 (90.9)	21/22 (95.4)
0.25	4/4 (100)	4/4 (100)	0.25	12/12 (100)	11/12 (91.7)
0.5	3/3 (100)	2/3 (66.7)	0.5	14/14 (100)	13/14 (92.7)
1	9/10 (90)	9/10 (90)	1	16/21 (76.2)	16/21 (76.2)
2	23/23 (100)	23/23 (100)			
4	16/17 (94.1)	16/17 (94.1)			
8	0/1 (0)	0/1 (0)			
Overall	71/74 (95.9)	70/74 (94.6)	Overall	62/69 (89.9)	61/69 (88.4)

Conclusion. CSE showed a high *in vitro–in vivo* correlation of >97% for MICs up to 4 µg/mL and is a potential new treatment option in patients with cUTI or AP.

Disclosures. **P. Mandale**, Venus Medicine Research Centre: Employee, Salary. **M. A. Mir**, Venus Medicine Research Centre: Employee, Salary. **S. Chaudhary**, Venus Medicine Research Centre: Employee and Shareholder, Salary. **M. Chaudhary**, Venus Medicine Research Centre: Board Member and Shareholder, Salary. **A. Pyasi**, Venus Medicine Research Centre: Employee, Salary.

1975. 1 g vs. 2 g Daily Intravenous Ceftriaxone in the Therapy of Community-onset Pneumonia: A Propensity Score Analysis From a Data of Japanese Multicenter Registry

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Background. Community-acquired pneumonia (CAP) is one of the most common infectious diseases and is an important cause of mortality and morbidity worldwide. The prognosis of CAP in adults is associated with factors such as age, comorbidities, vital signs, laboratory data, and other factors on admission. Usually, ceftriaxone (CTRX) is used to treat CAP. However, whether 1 or 2 g of CTRX daily has better efficacy remains unclear.

Methods. This study is an analysis of prospectively registered data from four Japanese hospitals for patients with community-onset pneumonia (COP) from September 2011 to August 2014 (the Adult Pneumonia Study Group-Japan: APSG-J). Subjects who were initially treated solely with 1 g or 2 g of CTRX were enrolled. Propensity score was estimated from the 33 pretreatment variables including age, sex, weight, comorbidities, medications, risk factors for aspiration, whether background was consistent with CAP or not, vital signs, laboratory data, and findings of a chest x-ray. The primary endpoint was cure rate, for which a noninferiority analysis was performed with a margin of 0.05. The secondary outcomes included in-hospital mortality, duration of antibiotic treatment, and length of hospital stay, which were assessed using superiority analyses.

Results. Of the 3,817 adult subjects with pneumonia who were registered in the APSG-J study, 290 and 216 were initially treated solely with 1 g or 2 g of CTRX, respectively. Propensity score matching was used to finally extract 175 subjects in each group. Overall, the cure rate was 94.6% in the 1 g group and 93.1% in the 2 g group (risk difference, 1.5 percentage points; 95% confidence interval [CI], −3.1 to 6.0; $P = 0.009$ for noninferiority). The in-hospital mortality rate was 4.7% and 4.0% ($P = 0.740$ for superiority), length of hospital stay was 17 and 26 days ($P < 0.001$ for superiority), and duration of antibiotic treatment was 8 and 10 days ($P = 0.002$ for superiority) in the 1 g and 2 g groups, respectively.

Conclusion. Propensity score-matched analysis of multicenter cohort data from Japan revealed that the cure rate for COP patients treated with 1 g of CTRX was non-inferior to that in the patients treated with 2 g of CTRX.

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

1976. Pooled Analysis of Safety Data From Phases 2 and 3 Clinical Trials Evaluating Eravacycline in Complicated Intra-Abdominal Infections

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Background. Eravacycline is a novel, fully synthetic fluorocycline antibiotic that was evaluated in three comparator-controlled studies for the treatment of complicated intra-abdominal infections (cIAI). The objective of this analysis was to evaluate the safety profile of eravacycline 1 mg/kg IV q12h for the treatment of cIAI.

Methods. Pooled data from one phase 2 and two phase 3 (IGNITE1 and IGNITE4) clinical trials in cIAI were analyzed. Patients in the trials were randomized to receive eravacycline 1 mg/kg IV q12h, ertapenem 1 g IV q24h, or meropenem 1 g IV q8h for 4–14 days. Overall treatment-emergent adverse events (TEAEs), serious TEAEs, and laboratory assessments were evaluated.

Results. Five hundred seventy-six patients were treated with eravacycline 1 mg/kg IV q12h and 547 patients with comparators (ertapenem and meropenem). Demographic and baseline characteristics were similar among the groups. Overall summary and common TEAEs are presented in Table 1. None of the serious TEAEs or those leading to death were related to the study drug. Clinically notable laboratory abnormalities were relatively uncommon and occurred at similar frequencies in eravacycline- and comparator-treated patients.

Table 1. Overall Summary of Treatment Emergent Adverse Events—Eravacycline Phases 2 and 3 Clinical Studies

	Eravacycline 1 mg/kg IV q12h, *N* = 576, *n* (%)	Comparators[a], *N* = 547, *n* (%)
Any TEAEs	217 (37.7)	152 (27.8)
Nausea	40 (6.9)	5 (0.9)
Vomiting	20 (3.5)	13 (2.4)
Diarrhea	13 (2.3)	8 (1.5)
Infusion phlebitis	13 (2.3)	1 (0.2)
Pyrexia	11 (1.9)	11 (2.0)
Anemia	7 (1.2)	12 (2.2)
Treatment-related TEAEs	71 (12.3)	20 (3.7)
TEAEs leading to discontinuation from study drug	9 (1.6)	12 (2.2)
Serious TEAEs	33 (5.7)	33 (6.0)
TEAEs leading to death	7 (1.2)	7 (1.3)

[a]Comparators include ertapenem 1 g IV q24h and meropenem 1 g IV q8h.