Our objective was to examine whether an PCT algorithm compared with standard practice would reduce antibiotic exposure in patients with LRTI [pneumonia and acute exacerbations of chronic obstructive pulmonary disease (AECOPD)] in an American urban academic hospital.

Methods. From April 17, 2017 until November 1, 2017, consecutive patients admitted to a medicine service were enrolled in the PCT intervention if they were receiving antibiotics for LRTI and gave consent. Providers were encouraged to discontinue antibiotics using a PCT algorithm with predefined cutoffs. Serum PCT was measured in the hospital laboratory once daily. Results and recommendations were communicated to providers by study team and in the medical record. Control patients were selected by reviewing charts for patients admitted to a medicine service for LRTI from December 1, 2016 to April 16, 2017. The primary endpoint was median antibiotic duration. Overall adverse outcomes at 30 days comprised death, transfer to an intensive care unit, antibiotic side effects, *Clostridium difficile* infection, disease- specific complications, and new antibiotic prescription for LRTI after discharge.

Results. 174 patients were enrolled in the intervention group and 200 patients in the control group. Intervention group providers complied with the PCT algorithm in 75% of encounters. The rate of overall adverse outcomes was similar in PCT and control groups (21.8% vs. 23.5%; difference, –0.02; 95% CI, –0.10 to 0.07). PCT-guided therapy reduced the median antibiotic duration for pneumonia from 7 days to 6 (P = 0.05), and AECOPD from 4 days to 3 (P = 0.01). Noncompliance with the PCT algorithm resulted in 260 excess antibiotic days in 44 patients.

Conclusion. In our center, 75% adherence to a PCT-guided algorithm safely reduced the duration of antibiotics for treating LRTI. Incentivizing providers to comply with PCT-guided algorithms could lead to further reductions in antibiotic use.

Disclosures. **J. Townsend**, BRAHMS: Grant Investigator, Research grant.

1969. Comparison of Adverse Event Rates Between Patients Treated With Ceftaroline or Ceftriaxone

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Background. At the VA St. Louis Health Care System 17.3% of patients treated with ceftaroline developed an adverse drug reaction (ADR). This evaluation compares ADR rates between patients treated with ceftaroline and those treated with ceftriaxone.

Methods. This was a retrospective, single-center cohort study of patients treated with ceftaroline or ceftriaxone at the VA St. Louis Health Care System between October 29, 2010 and March 28, 2017. Patients included received at least two doses of either medication and were treated for osteomyelitis, acute bacterial skin and skin structure infections, blood stream infections, pneumonia, infective endocarditis, septic arthritis, prosthetic joint infections, or an empyema. Once identified, patients were matched 1:1 utilizing the nearest neighbor method accounting for age, indication, and duration of therapy. The primary and secondary outcomes were the composite of any ADR while on therapy and any ADR leading to therapy discontinuation, respectively. Adverse reactions evaluated were rash, neutropenia, acute kidney injury, eosinophilia, thrombocytopenia, transaminitis, and hyperbilirubinemia.

Results. There were 75 unique ceftaroline-treated and 312 ceftriaxone-treated patients identified. After propensity score matching, 50 patients per group were included and analyzed. The mean age of patients was 65.4 and 63.4 years (P = 0.47), and the mean duration of therapy was 14.5 and 17 days (P = 0.90), ceftriaxone compared with ceftaroline respectively. Any ADR occurred in 20% (10/50) of patients treated with ceftriaxone and 16% (8/50) of patients treated with ceftaroline (P = 0.60). One patient (2%) treated with ceftriaxone and 16% (8/50) treated with ceftaroline had therapy discontinued for an ADR (P = 0.03). The most common ADR was eosinophilia (3/50) in the ceftriaxone group and rash (5/50) in the ceftaroline group. In multivariate regression, ceftaroline therapy was identified as an independent risk factor for development of an ADR requiring discontinuation (OR 10.2; 95% CI 1.19–87.8), P = 0.03).

Conclusion. There was no difference in the development of any ADR between patients treated with ceftriaxone or ceftaroline, but patients treated with ceftaroline had more ADRs leading to therapy discontinuation.

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

1970. Phase 1 Clinical Trial of Intranasal Immunization with M2-Deficient, Single Replication, Live Influenza Vaccine (M2SR): Safety and Immune Response in Adults

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Background. Influenza vaccines are needed with greater effectiveness and breadth of coverage. FluGen is developing M2SR (*M2* deficient Single *R*eplication), an investigational, live virus vaccine. M2SR contains the internal proteins of donor A/Puerto Rico/8/34 and hemagglutinin (HA) and neuraminidase (NA) selected from targeted Type A influenza strains. M2SR undergoes only a single round of infection in the respiratory epithelium but evokes an immune response profile similar to wild-type influenza viruses. In influenza naïve and pre-immune ferrets, M2SR protects against multiple influenza A subtypes.

Methods. A Phase 1, first-in-human, randomized, placebo-control study (FluGen-H3N2-V001; ClinicalTrials.gov identifier NCT02822105) was conducted at a single USA site, with 96 adults, ages 18–49 years. Study vaccine contained HA and NA from A/Brisbane/10/2007 (H3N2). Study volunteers received a single intranasal (IN) inoculation with either M2SR at dose levels of 10^6, 10^7 or 10^8 $TCID_{50}$ or saline placebo (N = 24/cohort). Study subjects were evaluated for virus replication and solicited local and systemic reactions for 7 days, all adverse events (AE) for 28 days and serious AE (SAE) for 180 days.

Results. No infectious virus was detected in nasal swabs from any vaccinated subject. The most commonly reported AE was mild nasal rhinorrhea/congestion during the first 7 days after vaccination (Figure 1). No subject had fever or a severe reaction to the vaccine. No SAEs were reported. At least one AE was reported among 29%, 58%, and 83% of M2SR subjects administered 10^6, 10^7, or 10^8 $TCID_{50}$, respectively, and 46% among placebo subjects. There were no notable imbalances among study groups for other events. T- and B-cell responses, including influenza-specific serum and mucosal antibody responses were detected at a significantly higher frequency among vaccine than placebo subjects (Figure 2).

Conclusion. M2SR vaccine was safe and well tolerated at all dose levels, generated a dose-response effect for humoral (HA antibody) and mucosal antibodies against both homologous and heterologous influenza variants, and elicited robust T-cell responses. No infectious virus was detected in nasal swabs from any vaccinated subject.

Figure 1. Common adverse events first 7 days post-vaccination

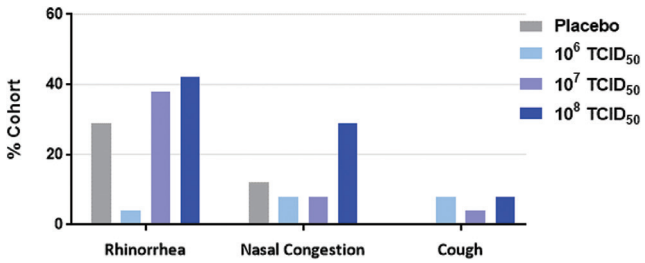

Figure 2. Influenza-specific immune responses

Disclosures. **J. Eiden**, FluGen, Inc.: Consultant, Consulting fee and Stock Options. **G. Gordon**, FluGen: Consultant, Consulting fee. **C. Fierro**, FluGen: Investigator, Fee for service. **R. Belshe**, FluGen: Consultant, Consulting fee and Stock Options. **H. Greenberg**, FluGen: Consultant, Consulting fee and Stock OpTions. **D. Hoft**, FluGen: Research Contractor, Fee for service. **Y. Hatta**, FluGen: Employee, Salary and Stock Options. **M. Imboden**, FluGen: Employee, Salary and Stock Options. **M. Moser**, FluGen: Employee, Salary and Stock Options. **R. Herber**, FluGen: Employee, Salary and Stock Options. **D. Boltz**, FluGen: Research Contractor, fee for service. **M. Tary-Lehmann**, FluGen: Research Contractor, Fee for service. CTL: Founder and Owner, Salary. **Y. Kawaoka**, FluGen: Founder, Stock Options. **G. Neumann**, FluGen: Founder,

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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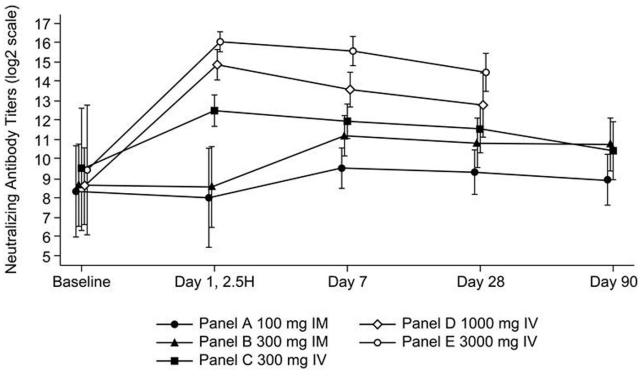
Background. Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection and hospitalization in infants. Prophylaxis for RSV infection is only recommended for the highest risk infants, leaving the majority of infants unprotected. MK-1654 is a fully human monoclonal 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.