Methods. To address low rates of HIV testing among PWUD, we evaluated the acceptability of a HIV self-testing program (OraQuick In-Home HIV Test by OraSure Technologies, Inc.) implemented at a health department in Louisville, Kentucky that services PWUD. Descriptive statistics were calculated for testing location, testing self-efficacy, reasons and motivations, ease of use, and preferences for future services.

Results. From May to June 2021, a total of 230 PWUD engaged with the program (average of 18 per day). Most participants (87.8%) self-tested at the health department with the help of study staff, while the other 12.2% tested at home and returned at a later time. Approximately 77% of participants reported the self-test kit made them feel better able to keep track of their HIV status compared to standard testing methods. The most common reasons for testing were wanting to know their status (85%), the test was free (37%), fast results (31%), more privacy (23%), and recent high-risk drug use and sexual behaviors (17%). Virtually all (97%) reported the test kits were very easy to use. For future availability of self-test kits through the health department, 33% reported they would use them monthly, 28% every three months, 22% every six months, and 17% annually. In terms of preference for future testing modality, 72% indicated a preference for taking the kits home, while the other 28% indicated a desire to test at the health department with help from staff.

Conclusion. Program participants found the self-test kits to be acceptable and easy to use. Implications for program implementation and future research will be discussed.

Disclosures. **Michelle Rose, MBA**, **Gilead Sciences Inc.** (Grant/Research Support) **Laura Guy, BS, CCRC**, **GILEAD Sciences** (Grant/Research Support, Research Grant or Support)

LB12. Exebacase Shows Rapid Symptom Resolution in a Phase 2 Study in Adult Patients with *Staphylococcus aureus* bacteremia

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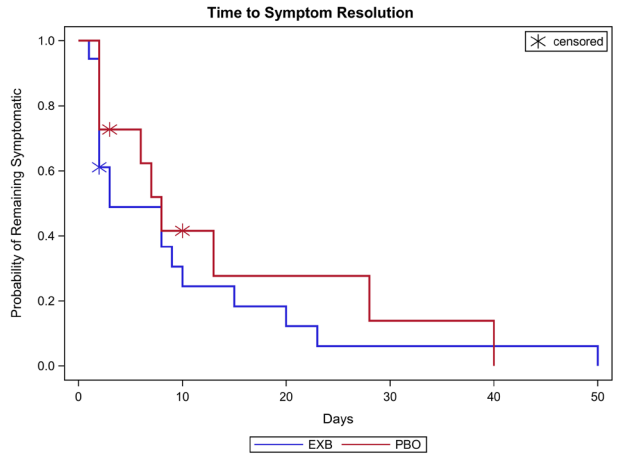
Background. Exebacase (EXB), a recombinantly-produced lysin (cell wall hydrolase), is the first direct lytic agent to advance into Phase 3 of clinical development for the treatment of bacteremia including infective endocarditis due to *Staphylococcus aureus*. The microbiologic attributes of EXB, including pathogen-targeted rapid bacteriolysis, and biofilm eradication are distinct from and synergistic with those of traditional antibiotics and underpin the therapeutic potential for EXB.

Methods. The Phase 2 trial was a randomized, double-blind, placebo-controlled multinational study. Patients were randomized (2:1) to receive a single 2-hour infusion of EXB or placebo (PBO) in addition to standard of care antibiotics. Time to resolution of symptoms (shortness of breath, sweating, fatigue and confusion) attributable to the bacteremia was analyzed using Kaplan-Meier methods. Time to resolution was defined as the number of days until all attributable symptoms were absent. If a new (not present at baseline) attributable symptom was present before the baseline symptoms resolved, this new symptom also had to be absent for symptoms to be considered resolved.

Results. A total of 86 patients (53 EXB and 33 PBO) had at least one attributable symptom present at baseline. Of these, symptoms resolved in 94.3% and 87.9% of EXB and PBO patients, respectively. The median time to resolution was 3 days for EXB and 6 days for PBO patients. Median days to symptom resolution in the MRSA group was 3 and 7 days for EXB and PBO patients, respectively, and 3 and 5 days for EXB and PBO patients in the MSSA group, respectively. Time to symptom resolution in MRSA patients in presented in Figure 1.

Figure 1. Time to Resolution of Symptoms in Patients with MRSA Bacteremia including Infective Endocarditis



Conclusion. The majority of EXB and PBO patients had symptom resolution. However, EXE patients achieved symptom resolution in 3 days compared with 6 days for PBO patients overall, and 7 days for PBO patients with MRSA. These data suggest that rapid bacteriolysis may translate to a clinical benefit for patients receiving EXB and aligns with a median length of hospital stay of 6 and 10 days among US MRSA patients that received EXE and PBO patients, respectively. (Fowler, et al, 2020).

Disclosures. **Cara Cassino, MD**, **ContraFect Corporation** (Employee) **Anita F. Das, PhD**, **Adagio** (Consultant)**AN2** (Consultant)**Cidara** (Consultant)**ContraFect** (Consultant)**Iterum** (Consultant)**MicuRx** (Consultant)**Paratek** (Consultant)**Union** (Consultant) **Joy Lipka, MS**, **ContraFect Corporation** (Consultant)

LB13. The Efficacy and Impact in Heathy Infants of Nirsevimab on Medically Attended RSV Lower Respiratory Tract Infection

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MELODY Study Group

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Background. Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection (LRTI) in infants. Nirsevimab is a single-dose monoclonal antibody with extended half-life that was shown to protect preterm infants 29 to < 35 weeks gestation against RSV LRTI. However, most medically attended (MA) cases occur in otherwise healthy, term infants for whom there is currently no effective RSV prevention strategy. We report the primary analysis of efficacy and safety, along with the impact of nirsevimab in late preterm and term infants (≥ 35 weeks gestation) in the phase 3 MELODY study (NCT03979313).

Methods. Infants were randomized 2:1 to receive one intramuscular injection of nirsevimab (50 mg if < 5 kg; 100 mg if ≥ 5 kg at dosing) or placebo entering their first RSV season. The primary endpoint was the incidence of MA RSV LRTI over 150 days postdose. Cases met predefined clinical criteria of disease severity and were confirmed by real-time reverse-transcriptase PCR. Safety was evaluated through 360 days postdose. Enrollment started on 23 July 2019 and was suspended following the declaration of the COVID-19 pandemic by the WHO on 11 March 2020.

Results. Overall, 1490 infants were randomized and included in the intent-to-treat population; 1465 (98%) completed the 150-day efficacy follow-up, and 1367 (92%) completed the 360-day safety follow-up. The incidence of MA RSV LRTI was 1.2% (n=12/994) in the nirsevimab group and 5.0% (n=25/496) in the placebo group, giving nirsevimab an efficacy of 74.5% (95% confidence interval [CI]: 49.6, 87.1; p< 0.0001). Nirsevimab averted 93.6 (95% CI 63.0, 124.0) MA LRTIs per 1000 infants dosed. Nirsevimab was well tolerated, with similar rates of adverse events (87.4% nirsevimab; 86.8% placebo) and serious adverse events (6.8% nirsevimab; 7.3% placebo) between groups.

Conclusion. In this phase 3 study, a single dose of nirsevimab protected late preterm and term infants against MA RSV LRTI over an RSV season with a favorable safety profile. Approximately 11 infants need to be immunized to prevent 1 case of LRTI; nirsevimab has the potential to be an important intervention to reduce the burden of RSV LRTI in healthy infants.

Disclosures. **Laura Hammitt, MD**, **MedImmune** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support)**Merck & Co., Inc.** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support)**Novavax** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support)**Pfizer** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support) **Laura Hammitt, MD**, MedImmune (Individual(s) Involved: Self): Grant/Research Support, Research grant to my institution; Merck (Individual(s) Involved: Self): Grant/Research Support, Research grant to my institution; Pfizer (Individual(s) Involved: Self): Grant/Research Support, Research grant to my institution **Ron Dagan, MD**, **Medimmune/AstraZeneca** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support)**MSD** (Consultant, Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member, Research Grant or Support, Speaker's Bureau)**Pfizer** (Consultant, Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member, Research Grant or Support, Speaker's Bureau) **Yuan Yuan, PhD**, **AstraZeneca** (Employee, Shareholder) **Shabhir A. Mahdi, PhD**, **BMGF** (Research Grant or Support)**EDCTP** (Research Grant or Support)**GlaxoSmithKline** (Research Grant or Support)**Melody** (Research Grant or Support)**Minervax** (Research Grant or Support)**Novavax** (Research Grant or Support)**SAMRC** (Research Grant or Support) **William J. Muller, MD, PhD**, **Ansun** (Scientific Research Study Investigator)**Astellas** (Scientific Research Study Investigator)**AstraZeneca** (Scientific Research Study Investigator)**Genentech** (Scientific Research Study Investigator)**Gilead** (Scientific Research Study

Investigator)**Janssen** (Scientific Research Study Investigator)**Karius** (Scientific Research Study Investigator)**Melinta** (Scientific Research Study Investigator)**Merck** (Scientific Research Study Investigator)**Nabriva** (Scientific Research Study Investigator)**Seqirus** (Scientific Research Study Investigator)**Tetraphase** (Scientific Research Study Investigator) **William J. Muller, MD, PhD**, Ansun (Individual(s) Involved: Self): Grant/Research Support; Astellas (Individual(s) Involved: Self): Research Grant or Support; AstraZeneca (Individual(s) Involved: Self): Grant/Research Support; BD (Individual(s) Involved: Self): Research Grant or Support; Eli Lilly (Individual(s) Involved: Self): Grant/Research Support; Gilead (Individual(s) Involved: Self): Grant/Research Support; Karius, Inc. (Individual(s) Involved: Self): Grant/Research Support, Scientific Research Study Investigator; Melinta (Individual(s) Involved: Self): Grant/Research Support; Merck (Individual(s) Involved: Self): Grant/Research Support; Moderna (Individual(s) Involved: Self): Grant/Research Support; Nabriva (Individual(s) Involved: Self): Grant/Research Support; Seqirus (Individual(s) Involved: Self): Consultant; Tetraphase (Individual(s) Involved: Self): Grant/Research Support **Heather J. Zar, PhD**, **AstraZeneca** (Grant/Research Support)**Novavax** (Grant/Research Support)**Pfizer** (Grant/Research Support, Advisor or Review Panel member) **Dennis Brooks, MD**, **AstraZeneca** (Employee) **Amy Grenham, MSc**, **AstraZeneca** (Employee, Shareholder) **Ulrika Wählby Hamrén, PhD**, **AstraZeneca R&D** (Employee, Shareholder) **Vaishali S. Mankad, MD**, **AstraZeneca** (Employee) **Therese Takas, BSc**, **AstraZeneca** (Employee, Other Financial or Material Support, Own stock in AstraZeneca) **Jon Heinrichs, PhD**, **AstraZeneca** (Shareholder)**Bristol Myers Squibb** (Shareholder)**J&J** (Shareholder)**Merck** (Shareholder)**Organon** (Shareholder)**Procter & Gamble** (Shareholder)**Sanofi** (Shareholder)**Sanofi Pasteur** (Employee) **Amanda Leach, MRCPCH**, **AstraZeneca** (Employee, Shareholder) **M. Pamela Griffin, MD**, **AstraZeneca** (Employee) **Tonya L. Villafana, PhD**, **AstraZeneca** (Employee)

LB14. Efficacy and Immunogenicity of an Ad26.RSV.preF-based Vaccine in the Prevention of RT-PCR-confirmed RSV-mediated Lower Respiratory Tract Disease in Adults Aged ≥65 Years: A Randomized, Placebo-controlled, Phase 2b Study

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CYPRESS

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Background. Respiratory syncytial virus (RSV) can cause serious lower respiratory tract disease (LRTD) in older adults. Despite a high burden of disease, there is currently no licensed vaccine for RSV. Here, we report the primary efficacy and immunogenicity results from a Phase 2b proof-of-concept trial of an Ad26.RSV.preF-based vaccine for the prevention of RSV-mediated LRTD in adults aged ≥65 years.

Methods. CYPRESS (NCT03982199) is a randomized, double-blind, placebo-controlled Phase 2b trial. Adults ≥65 years of age were randomized 1:1 prior to the RSV season to receive an Ad26.RSV.preF-based vaccine or placebo. Symptoms of acute respiratory infection (ARI) were collected through an RSV-specific patient-reported Respiratory Infection Intensity and Impact Questionnaire (RiiQ) and/or by a clinician assessment until the end of the RSV season. The primary endpoint was the first occurrence of RT-PCR-confirmed RSV-mediated LRTD according to any of 3 case definitions: (1) ≥3 symptoms of lower respiratory tract infection (LRTI), (2) ≥2 symptoms of LRTI, or (3) ≥2 symptoms of LRTI or ≥1 symptom of LRTI with ≥1 systemic symptom. The secondary endpoint was the first occurrence of any RT-PCR-confirmed RSV-mediated ARI. Immunogenicity assessments were performed in a subset of approximately 200 participants.

Results. A total of 5782 participants (2891 in each study arm) received study treatment (92.5% white, 57.7% female, median age 71 years). Vaccine efficacy was 80% (94.2% CI, 52.2–92.9%), 75% (50.1–88.5%), and 69.8% (43.7–84.7%) for case definition 1, 2, and 3, respectively (all *P* values < 0.001). Efficacy for any RSV-mediated ARI was 69.8% (95% CI, 42.7–85.1%). In the vaccine arm of the immunogenicity subset, geometric mean fold increase in antibody titers 14 days after vaccination was 13.5 for RSV neutralizing antibodies and 8.6 for RSV prefusion F-specific binding antibodies. Median frequency of RSV-F-specific INFγ T-cells increased from 34 to 444 SFC/10^6 PBMC 14 days after vaccination in the vaccine arm; no relevant changes were observed in the placebo arm.

Conclusion. In CYPRESS, the Ad26.RSV.preF-based vaccine was highly effective against RSV-mediated LRTD through the first RSV season and elicited robust humoral and cellular immune responses in adults aged ≥65 years.

Disclosures. **Ann R. Falsey, MD**, AstraZeneca (Individual(s) Involved: Self): Grant/Research Support; BioFire Diagnostics (Individual(s) Involved: Self): Grant/Research Support; Janssen (Individual(s) Involved: Self): Grant/Research Support; Merck, Sharpe and Dohme (Individual(s) Involved: Self): Grant/Research Support; Novavax (Individual(s) Involved: Self): Other Financial or Material Support, Paid DSMB member; Pfizer (Individual(s) Involved: Self): Grant/Research Support **Kristi Williams, PhD**, **Janssen R&D US** (Employee) **Efi Gymnopoulou, MSc**, **Janssen Infectious Diseases BV** (Employee) **Arangassery Rosemary Bastian, PhD**, **Janssen Vaccines & Prevention BV** (Employee) **Joris Menten, n/a**, **Janssen Infectious Diseases BV** (Employee) **Els De Paepe, MSc**, **Janssen Infectious Diseases BV** (Employee) **Hilde de Boer, MSc**, **Janssen-Cilag** (Employee) **Sjoukje Vandenberghe, n/a**, **Janssen Infectious Diseases BV** (Employee) **Eric Chan, PhD**, **Janssen Global Services, LLC** (Employee) **Jerald Sadoff, MD**, **Johnson & Johnson** (Employee, Shareholder) **Macaya Douoguih, MD, MPH**, **Janssen** (Employee) **Benoit Callendret, PhD**, **Janssen Vaccines & Prevention BV** (Employee) **Christy Comeaux, MD**, **Janssen Vaccines & Prevention BV** (Employee) **Esther Heijnen, MD**, **Janssen Vaccines & Prevention BV** (Employee)

LB15. SER-109, an Investigational Microbiome Therapeutic, Reduces Abundance of Antimicrobial Resistance Genes in Patients with Recurrent Clostridioides difficile Infection (rCDI) after Standard-of-Care Antibiotics

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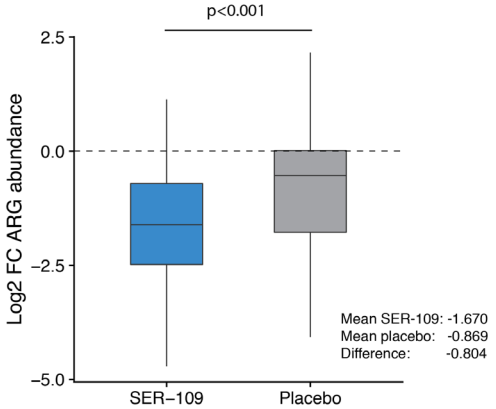
Background. The gastrointestinal microbiota is the first line of defense against colonization with antimicrobial resistant (AR) bacteria, particularly in vulnerable hosts with frequent antibiotic exposure. In a double-blind Phase 3 trial of rCDI patients, SER-109, an orally formulated consortia of purified Firmicutes spores, was superior to placebo in reducing CDI recurrence at week 8 post clinical resolution on standard-of-care (SoC) antibiotics. Overall recurrence rates were lower in SER-109 vs placebo (12.4% vs 39.8%, respectively) relative risk, 0.32 [95% CI, 0.18–0.58; p< 0.001 for RR< 1.0; p< 0.001 for RR< 0.833]. This is a post-hoc analysis examining the impact of SER-109 on antimicrobial resistance genes (ARGs) abundance in the intestinal microbiota compared to placebo.

Methods. Subjects with rCDI received SoC antibiotics, then were randomized 1:1 to SER-109 or placebo at baseline. Of 182 subjects, 140 who had paired stool samples at baseline and 1-week post-treatment were included in this analysis. ARG abundances and taxonomic profiles were generated from whole metagenomic shotgun sequencing. *t*-tests were used to compare changes in ARG abundance from baseline; mixed linear models were used to associate ARG and taxon abundances across time points.

Results. ARG abundance was reduced overall by week 1, with a significantly greater decrease in SER-109 subjects vs. placebo at week 1 (Fig. 1). Proteobacteria relative abundance were positively correlated with ARG abundance across all samples (Fig. 2), with the *Enterobacteriaceae* family associated with the abundance of 95 ARGs (all p < 0.05). *Enterococcaceae* relative abundance was associated with glycopeptide AR abundance (p < 0.001). At week 1, Proteobacteria relative abundance was significantly decreased from baseline in SER-109 subjects vs. placebo (p < 0.001). *Enterobacteriaceae* and *Enterococcaceae* relative abundances were also decreased from baseline in SER-109 subjects vs. placebo (p < 0.001 and p = 0.007, respectively).

Figure 1. Significant reduction in ARG abundance at week 1 from baseline in SER-109 treatment compared to placebo.



y-axis: Log_2 fold change of ARG abundance at week 1, compared to baseline, for subjects receiving SER-109 and placebo. Dotted line indicates no change from baseline. t-test used to compare log_2 FC distributions between SER-109 and placebo.