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.

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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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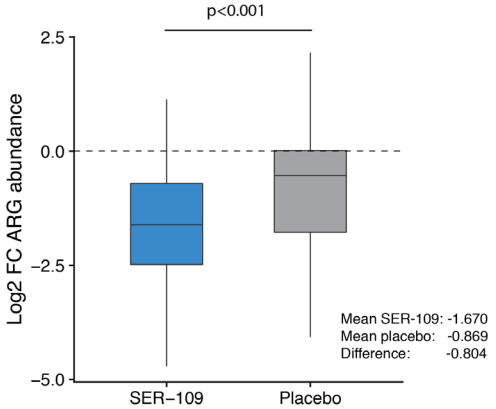
Background. The gastrointestinal microbiota is the first line of defense against colonization with antimicrobial resistant (AR) bacteria, particularly in vulnerable hosts with frequent antibiotic exposure. In a double-blind Phase 3 trial of rCDI patients, SER-109, an orally formulated consortia of purified 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.