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633. Preliminary Results from a Phase 1 Single Ascending-Dose Study Assessing Safety, Serum Viral Neutralizing Antibody Titers (sVNA), and Pharmacokinetic (PK) Profile of ADG20: an Extended Half-Life Monoclonal Antibody Being Developed for the Treatment and Prevention of Coronavirus Disease (COVID-19)

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Background. ADG20 is a fully human IgG1 monoclonal antibody engineered to have high potency and broad neutralization against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other SARS-like CoVs with pandemic potential by binding to a highly conserved epitope in the receptor-binding domain (RBD) of the spike protein. The Fc region of ADG20 has been modified to provide an extended half-life. ADG20 is in clinical development for the treatment and prevention of COVID-19.

Methods. This is an ongoing Phase 1, randomized, placebo (PBO)-controlled, single ascending-dose study of ADG20 administered intramuscularly (IM) or intravenously (IV) to healthy adults aged 18–50 years with no evidence of prior or current SARS-CoV-2 infection. Participants were randomized 8:2 in 3 cohorts (N=10/cohort: n=8 ADG20, n=2 PBO): ADG20 300 mg IM, 500 mg IV, and 600 mg IM. Safety, tolerability, PK, and sVNA titers were assessed up to 3 months post dose. Serum ADG20 concentrations were measured with a validated hybrid ligand binding liquid chromatography–mass spectrometry (MS)/MS assay. sVNA titers against authentic SARS-CoV-2 were determined by a plaque reduction neutralization assay.

Results. Overall, 30 participants received ADG20 (n=24) or PBO (n=6). Blinded safety data for all cohorts and PK/sVNA titer data for the 300 mg IM cohort are reported. Through a minimum of 10 weeks post dose, no study drug-related adverse events (AEs), serious AEs, injection site reactions, or hypersensitivity reactions were reported. The observed preliminary PK profile was dose proportional, consistent with an extended half-life monoclonal antibody, and well predicted by translational physiologically-based PK modeling. The measured 50% sVNA titer (MN50; geometric mean [coefficient of variation, %]) was 1382 (32.7%) 13 days after a single 300 mg IM dose. These values are within the range of peak serum neutralizing antibody titers reported for COVID-19 mRNA vaccines.

Conclusion. A single dose of ADG20, up to 600 mg IM, was well tolerated. Preliminary PK and sVNA titer profiles support the ongoing Phase 2/3 trials of ADG20 at a 300 mg IM dose for the prevention of COVID-19 (EVADE: NCT04859517) and treatment of ambulatory patients with mild to moderate COVID-19 (STAMP: NCT04805671).

Disclosures. **Helen Paguntalan, MD**, **Adagio Therapeutics, Inc.** (Scientific Research Study Investigator) **Zoltán Magyarics, MD, PhD**, **Adagio Therapeutics, Inc.** (Consultant) **Lynn E. Connolly, MD, PhD**, **Adagio Therapeutics, Inc.** (Employee) **Ellie Hershberger, PharmD**, **Adagio Therapeutics, Inc.** (Employee) **Kristin Narayan, PhD**, **Adagio Therapeutics, Inc.** (Employee) **Deepali Gupta, BS**, **Adagio Therapeutics, Inc.** (Employee) **Paul G. Ambrose, PharmD**, **Adagio Therapeutics, Inc.** (Employee) **Frank Engler, PhD**, **Adagio Therapeutics, Inc.** (Independent Contractor) **Ed Campanaro, BSN, MSHS**, **Adagio Therapeutics, Inc.** (Employee) **Anita F. Das, PhD**, **Adagio Therapeutics, Inc.** (Consultant) **Pete Schmidt, MD**, **Adagio Therapeutics, Inc.** (Employee)

634. Investigational Microbiome Therapeutic SER-109 Reduces Recurrence of *Clostridioides difficile* Infection (CDI) Compared to Placebo, Regardless of Risk Factors for Recurrence

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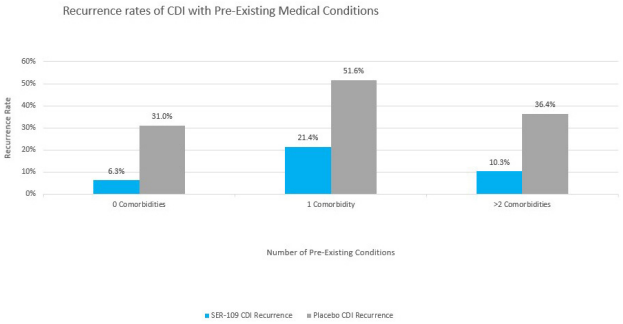
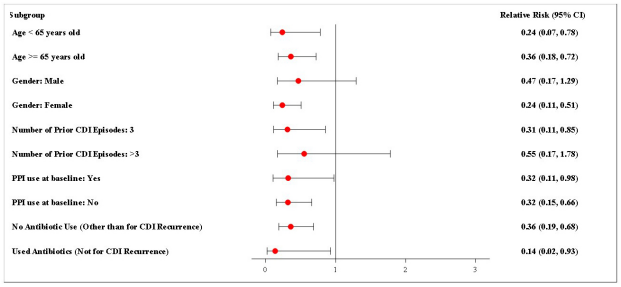
Background. Several demographic and clinical characteristics, including age, sex, medication use and presence of comorbid conditions are considered risk factors for recurrent CDI (rCDI). We examined the efficacy of an investigational purified oral microbiome therapeutic, SER-109, versus placebo in an exploratory analysis of subgroups of patients with risk factors for recurrence who enrolled in ECOSPOR III, a double-blind, placebo controlled trial.



Forest Plot of Relative Risks for Recurrence at Week 8 for Selected Baseline Characteristics in the ITT population



Methods. Patients with ≥ 3 CDI episodes were treated with SER-109 or placebo (four capsules daily for three days) following standard treatment of CDI. The primary efficacy objective was to demonstrate superiority of SER-109 versus placebo in reducing rCDI up to 8 weeks after treatment. In this exploratory analysis, we analyzed the rate of CDI recurrence among SER-109 treated subjects compared to placebo in subgroups defined by rCDI baseline risk factors: proton-pump inhibitor use, number of CDI recurrences, prior FMT history, presence of comorbid conditions and exposure to non-CDI antibiotics after dosing. We also analyzed the rate of CDI recurrence among SER-109 treated subjects by age (≥ 65 and ≤ 65) and gender, which were pre-specified.

Results. Of 281 patients screened,182 were enrolled. Overall recurrence rates were lower in SER-109 treated patients compared to placebo (12.4% vs 39.8%, respectively); relative risk (RR), 0.32 [95% CI, 0.18-0.58; P< 0.001 for RR< 1.0:P< 0.001 for RR< 0.833]. Co-morbidities including diabetes, renal disease, malignancy, cardiac disease, COPD/asthma, colitis, or immunocompromised status were observed in most patients in the overall study population; 33.5%, 32.4% and 34.1% had 0, 1, or ≥ 2 comorbidities. SER-109 was consistently observed to show greater benefit than placebo in reducing CDI recurrence in all subgroups regardless of the presence or absence of the rCDI risk factor (Fig 1).

Conclusion. Regardless of risk factor status, SER-109 reduced recurrence of CDI compared to placebo. Most subjects in ECOSPOR III had co-morbidities consistent with the broad inclusion criteria in this Phase 3 trial. Despite a high proportion of patients with co-morbidities in ECOSPOR III, SER-109 significantly reduced the risk of recurrence compared to placebo.

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636. A Phase I Study to Evaluate the Safety, Tolerability, and Immunogenicity of a Live, Attenuated, Quadrivalent Dengue Vaccine (V181)

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