Background. Anti-bacterial monoclonal antibodies can serve as a new treatment modality for difficult to treat infections. AR-105 is a fully human IgG1 monoclonal antibody (mAb) that binds to an extracellular polysaccharide epitope of Pseudomonas aeruginosa (PA) and was shown to mediate in vitro complement-dependent opsonophagocytic killing. AR-105 is currently being tested in a global Phase 2 clinical trial as an adjunctive treatment to standard of care antibiotics in ventilator-associated pneumonia patients. Here we present pre-clinical efficacy and clinical safety data for AR-105.

Methods. Efficacy in nonclinical studies against PA pneumonia was tested in prophylactic and therapeutic mouse models, either as a stand-alone therapy or in combination with antibiotics. Mice were dosed intranasally or by intravenous infusion with AR-105 post or prior to infection with PA and survival or lung bacteriology were monitored. In a clinical Phase 1 open-label study, 16 healthy volunteers received 2, 8, or 20 mg/kg of AR-105. Adverse events, immunogenicity, and pharmacokinetic (PK) profiles were evaluated for up to 84 days following administration.

Results. In the animal models, AR-105 reduced lung bacterial counts in a dose-dependent manner, and improved survival (80% in the treated group vs. 0% in the control group). Combination of AR-105 with antibiotics was more effective than monotherapy. In the Phase 1 study, no serious adverse events (AE) were observed in any cohort. Few AE were deemed related to the investigational drug, and all were mild and transient. AR-105 was found to be well tolerated in healthy volunteers with no anti-drug antibodies (ADA) detected. The PK profile was comparable with other human IgG1 mAbs, exhibiting a serum half-life of approximately 20 days.

Conclusion. AR-105 was confirmed to be effective in PA pneumonia animal models, either as stand-alone therapeutic or in combination with antibiotics. In the Phase 1 clinical study, AR-105 was shown to be safe and well-tolerated, with a PK profile similar to that of other IgG1 mAbs. AR-105 is a promising drug candidate for therapy of PA pneumonia.

AR-105 (Aerucin) reduces Bacterial Lung Counts in a Prophylactic Mouse Model

Disclosures. All authors: No reported disclosures.

675. Efficacy of Human-Simulated Bronchopulmonary Exposures of Cefepime and Zidexbacum (WCK 5222) Against Multidrug-Resistant (MDR) Pseudomonas aeruginosa (PSA) in a Neutropenic Mouse Pneumonia Model

James M. Kidd, PharmD; Kamila Abdelraouf, PhD; David P. Nicolau, PharmD; Hartford Hospital, Hartford, Connecticut

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs Thursday, October 3, 2019: 12:15 PM

Background. WCK 5222 combines cephampe (FEP) with zidebactam (ZID), a bicycloacyl hydrazide β-lactam enhancer which binds PBPs in PSA and inhibits class A and C β-lactamases. The in vivo efficacy of human-simulated bronchopulmonary exposures of WCK 5222 against MDR PSA, a recalcitrant pneumonia-causing pathogen with few treatment options, was investigated in a neutropenic mouse pneumonia model.

Methods. Thirteen clinical isolates of MDR PSA with FEP MIC ≥64 mg/L were studied in neutropenic CD-1 mice. FEP, ZID, and WCK 5222 MICs were measured by broth microdilution in triplicate. For in vivo experiments, lungs were intranasally inoculated with 10^3–10^4 CFU/mL bacterial suspensions. Human-simulated regimens (HSR) of FEP and ZID alone and in combination which achieved epithelial lining fluid (ELF) exposures in mice approximating human ELF exposures after doses of 2 g FEP/1 g ZID as a 1 hour infusion at steady state were developed. For each regimen, groups of 6 mice were dosed subcutaneously 2 hours after inoculation for 24 hours, then sacrificed. Vehicle-dosed control mice were sacrificed at the start (0 hour) and end (24 hours) of the dosing period. Lungs were aseptically harvested and bacterial CFU/lungs were determined.

Results. FEP MIC was >64 mg/L for all isolates, while ZID and WCK 5222 MICs ranged from 4–512 and 4–32 mg/L, respectively. Mean bacterial growth for all isolates at 0 hour was 6.68 ± 1.09, CFU/lungs. Mean changes ± SD in bacterial density at 24 hours compared with 0 hour controls for 12 isolates with WCK5222 MIC ≤16 mg/L were 2.08 ± 1.09, 1.09 ± 0.98, –0.92 ± 1.45, and –2.13 ± 0.75, for control, FEP, ZID, and WCK5222, respectively. Against these isolates, ZID yielded >1 log CFU/lungs reduction in 11/12 and >2 log CFU/lungs reduction in 9/12. All isolates showed growth or stasis on FEP.

Conclusion. Human-simulated bronchopulmonary exposures of WCK5222 is effective against MDR PSA at MIC up to 16 mg/L. These data support the clinical development of WCK5222 for the treatment of pseudomonal lung infections, but further studies of PSA with high WCK5222 MIC are necessary to delineate the susceptibility breakpoint.

Disclosures. All authors: No reported disclosures.

676. Health-Related Quality of Life (HRQoL) as Measured by the 12-Item Short Form (SF-12) Among Adults With Community-Acquired Bacterial Pneumonia (CABP) Who Received Either Lefamulin (LEF) or Moxifloxacin (MOX) in Two Phase 3 Randomized, Double-Blind, Double-Dummy Clinical Trials (LEAP 1 and 2)

Thomas Lodise, PharmD, PhD; Sam Colman, MSc; Elizabeth Alexander, MD, MSc, FIDSA; Daniel Stein, MD; David Fitts, MPH, PhD; Lisa Goldberg, MS; Jennifer Schranz, MD; Albany College of Pharmacy and Health Sciences, Albany, New York; Covance Market Access Services, Inc., Gaithersberg, Maryland; 'Nabavra Therapeutics US, Inc., King of Prussia, Pennsylvania

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs Thursday, October 3, 2019: 12:15 PM

Background. Interest in patient health experience as part of a benefit–risk assessment for new drug approvals is increasing. Patient-centeredness, a key metric in the 2010 Affordable Care Act, is also a growing area of focus in healthcare. LEF, a new anti-biotic in development for treating adults with CABP, was noninferior to MOX based on clinical response endpoints in LEAP 1 and 2. HRQoL was prospectively incorporated and evaluated in both studies via SF-12, a well-known survey that measures general health status in 8 domains (physical function, role limitations due to physical