candidate molecule is recombinant human plasma gelsolin (rhu-pGSN), an abun-
dant normal blood protein whose levels fall proportionally with disease severity.
Preservative with rhu-pGSN has beneficial effects in many pre-clinical models of
inflammation and injury, including pneumonia. We evaluated the effects of delaying
therapy with rhu-pGSN up to 48 hours after lethal intra-nasal pneumococcal challenge
in a murine model to more closely mimic realistic clinical circumstances.

**Methods.** Adult BL/6 mice were inoculated intra-nasally with S. pneumoniae
serotype 3 on day 0, followed by subcutaneous rhu-pGSN 24 hours later for evaluation of
bacterial clearance in lavage fluids. To assess effects on survival, rhu-pGSN was admin-
istered on days 2 and 3 after infection and effects monitored for 10 days. No antibiotics
or other interventions were given.

**Results.** Treatment with rhu-pGSN at 24 hours after infection improved bacter-
ic clearance, seen as reduction of bacterial CFUs in bronchoalveolar lavage fluid at 48
hours (% of initial inoculum, vehicle vs. rhu-pGSN: dose range 0.5–2 mgL; 30 ± 13
vs. 11 ± 7, n = 6 mice/group inocula range 0.3–1.8 x 10^8 CFU/mL/mice/group/trial, P = 0.01). In 3 separate trials, pGSN (0.5 mg s.c.) reduced weight loss and mortality (% survival, vehicle vs. pGSN: 40 vs. 80, vs. 25, 17 vs. 45; n ≥ 16/group, P = 0.02). Increasing the dose to 1 mg further improved survival from 17 to 71%.

**Conclusion.** rhu-pGSN can substantially improve survival in a murine model
of fatal pneumococcal pneumonia, even when administered as single doses on days 2
and 3 after infection without antibiotics. The data support further evaluation of pGSN
as adjunctive therapy for serious infections with diverse pathogens and in models of antibiotic-resistant pneumonia.

**Disclosures.** Z. Yang, BioAegis: Shared NIH grant to study plasma gelsolin, we receive plasma gelsolin for our lab studies; S. Levinson, BioAegis: BioAegis shares a grant to investigate plasma gelsolin with HSPH, Employee and Shareholder, Salary; T. Stellone, BioAegis: Consultant and Shareholder, portion of royalties from Hospital IP licensed to BioAegis; M. DiNubile, BioAegis: Employee and Shareholder, Consulting fee; L. Kobzick, BioAegis: Collaborator and We share a NIH grant on pGSN with BioAegis, we receive plasma gelsolin for our lab studies

1520. In Vitro Efficacy of Humanized Exposures of Cefiderocol Compared with Ceftazidime (FEP) and Meropenem (MEM) Against Gram-negative Bacteria in a Murine Thigh Model
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**Session:** 167. Preclinical Study with New Antibiotics and Antifungals

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**Background.** Cefiderocol (S-64926) is a novel siderophore cephalosporin under development by Shionogi (Osaka, Japan). Previous studies have demonstrated cefider-
ocol efficacy against a diverse population of Gram-negative bacteria with MICs ≤ 4 µg/

**Methods.** 15 Gram-negative isolates were studied. MICs were determined by broth microdilution in triplicate, using reference CLSI methods. Pharmacokinetic studies were

**Results.** Treatment with cefiderocol resulted in bacterial kill of 2.6 ± 0.5 and 2.1 ± 0.9 logCFU/mL, respectively, similar to that of FEP (2.6 ± 0.3) and MEM (2.2 ± 0.6). Against MEM and FEP resistant isolates, cefiderocol produced a mean (± SD) bacterial reduction of 1.5 ± 0.4 log CFU at 24 hours.

**Conclusion.** Cefiderocol humanized exposures produced antibacterial efficacy similar to MEM and FEP for susceptible pathogens, while also displaying activity
against Enterobacteriaceae, A. baumannii, and P. aeruginosa with phenotypic resist-
ance to the comparator β-lactams. These studies support the potential clinical utility of
cefdiderocol against these difficult-to-treat multidrug-resistant pathogens.

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