

problems, bodily pain, general health, vitality, social function, role limitations due to emotional problems, and mental health).

**Methods.** An exploratory analysis evaluated HRQoL in patients who received LEF or MOX in LEAP 1 (IV-PO treatment) and LEAP 2 (PO-only treatment). SF-12 was measured at baseline (BL) and test-of-cure (TOC; 5–10 days after last study drug dose). SF-12 outcomes assessed included the 8 domains, physical component summary (PCS), and mental component summary (MCS) scores. SF-12 scores were normalized to the 2009 US population reference mean (SD) of 50 (10). A 3-point change on any scale represents a clinically meaningful difference.

**Results.** Analysis included 1,215 patients (LEF  $n = 607$ ; MOX  $n = 608$ ). At BL, all mean SF-12 scores in both treatment groups were well below the US reference mean, indicating a low HRQoL level, consistent with the acute illness of the study population (figure). Clinically meaningful and significant improvements from BL to TOC were observed in all domain, PCS, and MCS scores in both groups. Mean scores were close to the reference mean, indicating an average HRQoL level. No significant differences in mean score improvements from BL to TOC were seen for LEF vs. MOX. SF-12 score improvements at TOC across predefined subgroups (age, sex, number of comorbidities, study, and PORT risk class) were comparable between treatment groups.

**Conclusion.** Our data indicate that adults with CABP experienced HRQoL improvements with LEF that were comparable with MOX, and treatment with either agent resulted in return to normal HRQoL. When combined with overall study results, these data suggest LEF as a potential alternative to MOX for treatment of adults with CABP.

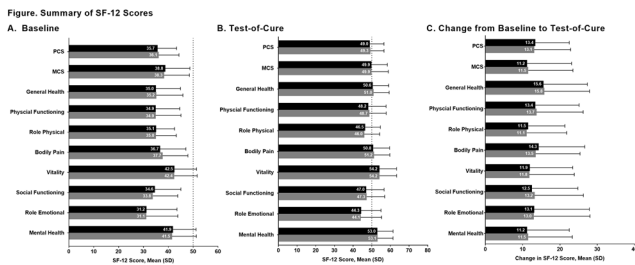


Figure. Summary of SF-12 Scores. MCS=mental component summary; PCS=physical component summary. Higher SF-12 domain, PCS, and MCS scores indicate better health-related quality of life. Dotted line indicates the 2009 US population reference mean of 50.

**Disclosures.** All authors: No reported disclosures.

### 677. Activity of Novel $\beta$ -Lactamase Inhibitor QPX7728 Combined with $\beta$ -Lactam Agents When Tested Against Carbapenem-Resistant *Enterobacteriaceae* (CRE) Isolates

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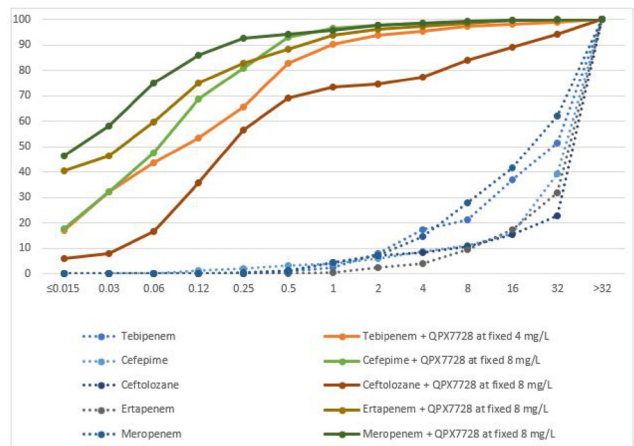
**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs  
**Thursday, October 3, 2019: 12:15 PM**

**Background.** CREs have been described worldwide and these isolates are often multidrug resistant with few therapeutic options remaining active against them. New  $\beta$ -lactam (BL)/ $\beta$ -lactamase inhibitor (BLI) combinations recently approved are active against KPC and some OXA-48 producers, but not against isolates producing metallo- $\beta$ -lactamases (MBLs). We evaluated the activity of QPX7728 (QPX), a novel BLI paired with various BLs against a collection of CRE isolates characterized for the presence of carbapenemases.

**Methods.** A total of 508 CRE clinical isolates were susceptibility (S) tested by reference broth microdilution methods against meropenem (MER), tebipenem (TEB), cefepime (FEP), ceftolozane (TOL), and ertapenem (ETP), and meropenem (MEM) combined with QPX at fixed 2, 4, and 8 mg/L. Agents were provided by Qpex Biopharma except for FEP, ETP, and MEM. Carbapenemases were detected using PCR/sequencing or whole-genome sequencing.

**Results.** All BLs had limited activity against CRE isolates ( $MIC_{50/90} \geq 32 / >32$  mg/L) and QPX lowered the MIC for all agents (figure). Against 157 isolates carrying serine-carbapenemase (SCarb) genes (153 KPC-producers), MEM or ETP plus QPX at fixed 4 or 8 mg/L displayed  $MIC_{50}$  at  $\leq 0.03$  mg/L and  $MIC_{90}$  ranging from 0.12 to 0.5 mg/L. QPX lowered the FEP or TOL  $MIC_{50}$  to  $\leq 0.25$  mg/L and  $MIC_{90}$  to 0.25, 0.5 or 1 mg/L depending on the BLI concentration. Over 98.0% of the 150 isolates harboring OXA-48-like genes were inhibited by FEP, TOL, ETP or MEM plus QPX at  $\leq 2$  mg/L. Similarly, MEM, FEP, TOL and ETP + QPX inhibited  $>98.0\%$  of the 51 CREs that did not carry carbapenemases at  $\leq 2$  mg/L when using a higher BLI concentration. The activity of FEP ( $MIC_{50/90}$ , 0.06/1 mg/L), ETP ( $MIC_{50/90}$ , 0.03/4 mg/L), and MEM ( $MIC_{50/90}$ ,  $\leq 0.015/2$  mg/L) was mostly restored when 8 mg/L of QPX was combined with these agents and tested against 150 MBL-producing isolates.

**Conclusion.** QPX restored the activity of several BLs when tested against 508 CRE isolates that include 157 harboring SCarb, 150 OXA-48-like-producers, and 150 MBL-producing isolates. Further development of this BLI with inhibitory activity against all carbapenemase types seems warranted.



**Disclosures.** All authors: No reported disclosures.

### 678. Galactomannan Is a Biomarker of APX001 (Fosmanogepix) Efficacy in Treating Experimental Invasive Pulmonary Aspergillosis

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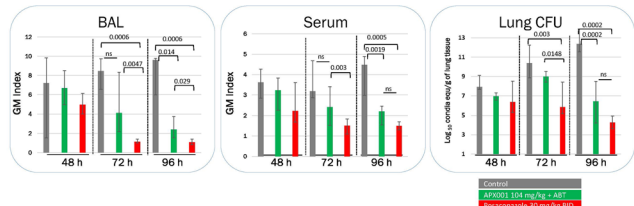
**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs  
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**Background.** Invasive pulmonary aspergillosis (IPA) is a serious fungal infection afflicting immunocompromised patients. Galactomannan (GM) detection in biological samples using the Platelia ELISA has been shown to predict therapy response by azoles, and polyenes. We previously reported on the activity of APX001 (fosmanogepix) in treating murine IPA. Here, we investigated the potential use of GM as a biomarker of APX001 efficacy in an immunosuppressed murine model of IPA.

**Methods.** ICR mice ( $n = 8$ /group) were immunosuppressed with cyclophosphamide and cortisone acetate on days -2, and +3, relative to infection with *Aspergillus fumigatus* via inhalation. Treatment with placebo (diluent control), APX001 (104 mg/kg, PO, a human equivalent dose), or posaconazole (POSA, 30 mg/kg, BID [equivalent to 6x the humanized dose]) began 16-hour post-infection and continued daily. To extend the half-life of APX001, mice were administered 50 mg/kg of the cytochrome P450 inhibitor 1-aminobenzotriazole (ABT) 2 hours prior to APX001 administration. Mice were sacrificed 48-, 72-, or 96-hour post-infection and their lungs, bronchoalveolar lavage (BAL) and sera were collected. Lung fungal burden was determined by conidial equivalent (CE) using qPCR, while GM was determined using the Platelia ELISA.

**Results.** Compared with placebo, APX001 or POSA treatment resulted in a gradual decrease in tissue fungal burden over time with APX001 or POSA showing significant reduction as early as 96 and 72 hours, respectively ( $P < 0.005$ ). Although the super-therapeutic dose of POSA resulted in faster reduction in lung fungal burden after 72 hours, both drugs resulted in similar reduction ( $\sim 6-7$  log) in lung CE vs. placebo after 96 hours. Changes in GM levels in BAL or serum samples mirrored reductions in lung CFU with significant decrease seen after 96 hours or 72 hours for APX001 or POSA, respectively, vs. placebo ( $P < 0.02$ ) (figure).

**Conclusion.** A human equivalent dose of APX001 and a super humanized dose of POSA resulted in a time-dependent reduction of lung fungal burden and GM levels when compared with placebo. These results show that GM can be used as a biomarker of APX001 efficacy in immunosuppressed mice.



**Disclosures.** All authors: No reported disclosures.

### 679. In vitro Activity of Cefiderocol (CFDC), a Novel Siderophore Cephalosporin, Against Difficult-to-Treat-Resistant (DTR) Gram-Negative Bacterial Pathogens From the Multi-National Sentinel Surveillance Study, SIDERO-WT (2014–2017)

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