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P1661 Murepavadin activity tested against contemporary (2016-2017) clinical isolates of extensively drug-resistant (XDR) Pseudomonas aeruginosa

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Background: Murepavadin (POL7080) represents the first member of a novel class of outer membrane protein targeting antibiotics (OMPTA), being developed by Polyphor for the treatment of serious infections by Pseudomonas aeruginosa. Murepavadin acts by binding to the lipopolysaccharide transport protein D (LptD) and is being developed for the treatment of hospital-acquired and ventilator-associated pneumonia caused by Pseudomonas aeruginosa.

Materials/methods: A total of 528 XDR *P. aeruginosa* isolates were collected in 2016–2017 through the SENTRY Antimicrobial Surveillance Program from 30 medical centres in 19 European nations (n=272) and 69 medical centres located in North America (n=256). Isolates were categorised as XDR when susceptible per CLSI criteria to ≤2 of the following antimicrobial classes: antipseudomonal cephalosporin, carbapenem, broad-spectrum penicillin/β-lactamase-inhibitor combination, fluoroquinolone, aminoglycoside, and polymyxin. Isolates were collected mainly from patients with pneumonia (61%), skin and soft tissue infections (20%), and bloodstream infections (9%). Susceptibility testing was performed by reference broth microdilution method, and EUCAST and CLSI interpretative criteria were applied.

Results: Murepavadin (MIC50/90, 0.12/0.25 mg/L) inhibited 98.5% of isolates at ≤1 mg/L and was 8-fold more active than colistin (MIC50/90, 1/2 mg/L; Table). Only 5 isolates (0.9%) exhibited murepavadin MIC values >2 mg/L; 3 isolates from the United States and 2 from Europe (Spain and United Kingdom). Among the comparator agents tested, colistin was the most active compound (MIC50/90, 1/2 mg/L; 93.6% susceptible), followed by ceftolozane-tazobactam (MIC50/90, 2/>32 mg/L; 69.8% susceptible), tobramycin (MIC50/90, >8/>8 mg/L; 42.6% susceptible), and amikacin (MIC50/90, 16/>32 mg/L; 42.5/57.7% susceptible [EUCAST/CLSI]). Susceptibility rates for meropenem, piperacillin-tazobactam, and ceftazidime were 6.6%, 7.0%, and 20.6%, respectively. Murepavadin was active against isolates nonsusceptible (NS) to colistin (n=34; MIC50/90, 0.25/0.25 mg/L; highest MIC, 0.5 mg/L) and/or ceftolozane-tazobactam (n=164; MIC50/90, 0.12/0.25 mg/L; 99.4% inhibited at ≤1 mg/L). All tobramycin-NS isolates (n=303) were inhibited at ≤1 mg/L of murepavadin.

Conclusions: Murepavadin exhibited good activity against a large collection of clinical XDR *P. aeruginosa* isolates from Europe and North America, including isolates NS to colistin, ceftolozane-tazobactam, and/or tobramycin.

	Number of isolates (cumulative %) inhibited at murepavadin MIC (mg/L) of:							
Organism subset (n)	**≤0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**>4**
All (528)	126 (23.9)	239 (69.1)	127 (93.2)	21 (97.2)	7 (98.5)	3 (99.1)	1 (99.2)	4 (100.0)
Colistin-NS (34)	2 (5.9)	10 (35.3)	21 (97.1)	1 (100.0)				
Ceftolozane-tazobactam-NS (164)	45 (27.4)	65 (67.1)	46 (95.1)	6 (98.8)	1 (99.4)	0 (99.4)	0 (99.4)	1 (100.0)
Tobramycin-NS (303)	73 (24.1)	145 (71.9)	72 (95.7)	9 (98.7)	4 (100.0)			