Poster EA46 Activity of the novel engineered antimicrobial peptide PLG0206 against non-fermenting Gram-negative rods

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Peptilogics

INTRODUCTION

- PLG0206 is an investigational, engineered cationic antimicrobial peptide designed to overcome the shortcomings of other natural AMPs, such as toxicity and limited activity (1, 2). PLG0206 has recently been shown to be well tolerated and safe in a phase 1 study (3).
- This study evaluated the activity of PLG0206 and comparator antimicrobials against non-fermenting Gram-negative rods from the IHMA repository of isolates collected from various world-wide locations in 2019.

MATERIALS AND METHODS

- Isolates tested included *Acinetobacter baumannii* (298), *Pseudomonas aeruginosa* (300) and *Stenotrophomonas maltophilia* (150). The isolates were collected in 2019, with approximately one-third from Europe and the remainder from other regions (Figure 1). The isolates originated mainly from respiratory infections, but also included a variety of other infection types (Figure 2).
- Minimum inhibitory concentrations (MICs) were determined by Clinical and Laboratory Standards Institute (CLSI) broth microdilution methodology (4) in cation-adjusted Mueller Hinton broth (CA-MHB), except for PLG0206 which was tested in MOPS RPMI-1640 medium supplemented with 0.002% Tween-80 due to precipitation of PLG0206 observed in CAMHB.
- The susceptibility of comparators was determined using the 2022 CLSI breakpoints (5).
- Multi-drug-resistance (MDR) for *A. baumannii* and *P. aeruginosa* was defined as resistance to 3 or more of the antimicrobials tested by class of antimicrobial including aminoglycosides (amikacin, gentamicin or tobramycin), cephems (cefepime or ceftazidime), fluoroquinolones (levofloxacin or ciprofloxacin) and tetracyclines (doxycycline or tetracycline) or by individual antimicrobial for aztreonam, ampicillin/sulbactam, colistin, ceftazidime/avibactam, meropenem and piperacillin/tazobactam. MDR for *S. maltophilia* was defined as resistance to both ceftazidime and levofloxacin (the only agents tested with CLSI breakpoints).

FIGURE 1: Geographical location of the non-fermenting Gram-negative rods tested.

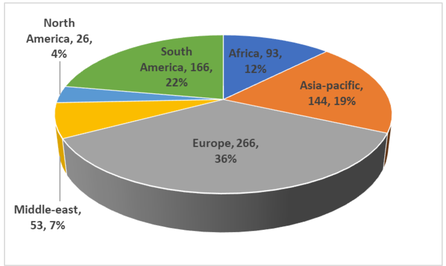

FIGURE 2: Infection source for non-fermenting Gram-negative rods tested.

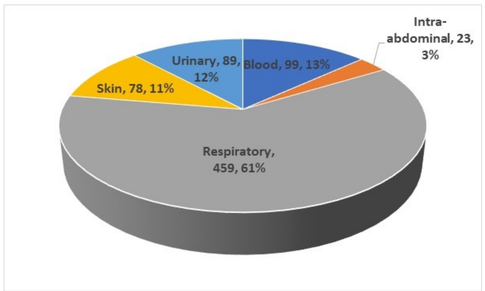

FIGURE 3: Cumulative % MIC distribution for PLG0206 against non-fermenting Gram-negative rods.

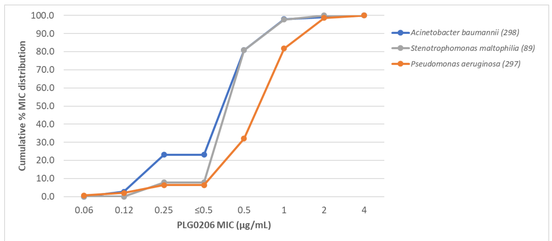

TABLE 1: Summary of activity of PLG0206 and comparators against non-fermenting Gram-negative rods

Antimicrobial	*A. baumannii* (n=298)					*P. aeruginosa* (n=297)					*S. maltophilia* (n=89)				
	MIC_{50}	MIC_{90}	%S	%I	%R	MIC_{50}	MIC_{90}	%S	%I	%R	MIC_{50}	MIC_{90}	%S	%I	%R
PLG0206	0.5	1	-	-	-	1	2	-	-	-	0.5	1	-	-	-
Amikacin	>64	>64	39.9	2.3	57.7	4	>64	85.2	2.4	12.5	>64	>64	-	-	-
Ampicillin/sulbactam (2:1)	32	>32	29.2	4.4	66.4	Not tested					Not tested				
Aztreonam	Not tested					8	>16	69.0	11.1	19.9	Not tested				
Aztreonam-avibactam (4 µg/ml)	Not tested					4	>16	-	-	-	Not tested				
Cefepime	>32	>32	26.2	2.3	71.5	4	>32	75.4	7.1	17.5	>32	>32	-	-	-
Ceftazidime	>32	>32	29.5	1.7	68.8	4	>32	71.4	5.7	22.9	>32	>32	33.7	3.4	62.9
Ceftazidime-avibactam (4 µg/ml)	Not tested					2	>16	87.2	-	12.8	Not tested				
Ciprofloxacin	>32	>32	27.2	0.3	72.5	0.12	16	76.1	4.0	19.9	4	16	-	-	-
Colistin	0.25	0.5	-	97.3	2.7	0.5	1	-	99.7	0.3	8	>32	-	-	-
Doxycycline	4	64	57.0	5.0	37.9	8	32	-	-	-	2	4	-	-	-
Gentamicin	>32	>32	38.3	3.4	58.4	1	>32	82.5	3.0	14.5	>32	>32	-	-	-
Levofloxacin	16	>32	28.2	5.4	66.4	0.5	32	69.4	9.1	21.5	2	8	79.8	7.9	12.4
Meropenem	64	>64	29.9	1.3	68.8	0.5	32	77.4	7.1	15.5	>64	>64	-	-	-
Meropenem-vaborbactam (8 µg/ml)	>32	>32	-	-	-	0.5	32	-	-	-	>32	>32	-	-	-
Piperacillin-tazobactam (4 µg/ml)	>128	>128	26.8	3.0	70.1	8	128	73.4	12.1	14.5	>128	>128	-	-	-
Tetracycline	32	>32	33.6	11.1	55.4	8	32	-	-	-	16	32	-	-	-
Tobramycin	16	>32	45.3	2.0	52.7	0.5	>32	84.5	0.7	14.8	>32	>32	-	-	-

TABLE 2: Summary of activity of PLG0206 and comparators against multi-drug-resistant (MDR) non-fermenting Gram-negative rods.

Antimicrobial	*A. baumannii* (n=216)					*P. aeruginosa* (n=70)					*S. maltophilia* (n=10)				
	MIC_{50}	MIC_{90}	%S	%I	%R	MIC_{50}	MIC_{90}	%S	%I	%R	MIC_{50}	MIC_{90}	%S	%I	%R
PLG0206	0.5	1	-	-	-	1	1	-	-	-	0.5	1	-	-	-
Amikacin	>64	>64	17.1	3.2	79.6	64	>64	42.9	5.7	51.4	>64	>64	-	-	-
Ampicillin/sulbactam (2:1)	>32	>32	3.2	5.6	91.2	Not tested					Not tested				
Aztreonam	Not tested					>16	>16	14.3	17.1	68.6	Not tested				
Aztreonam-avibactam (4 µg/ml)	Not tested					16	>16	-	-	-	Not tested				
Cefepime	>32	>32	0.5	2.3	97.2	32	>32	11.4	21.4	67.1	>32	>32	-	-	-
Ceftazidime	>32	>32	3.7	1.4	94.9	>32	>32	10.0	10.0	80.0	>32	>32	0.0	0.0	100.0
Ceftazidime-avibactam (4 µg/ml)	Not tested					16	>16	45.7	-	54.3	Not tested				
Ciprofloxacin	>32	>32	2.3	0.0	97.7	16	>32	28.6	7.1	64.3	16	>32	-	-	-
Colistin	0.25	0.5	-	96.8	3.2	1	1	-	98.6	1.4	16	>32	-	-	-
Doxycycline	16	64	41.7	6.9	51.4	16	>128	-	-	-	4	16	-	-	-
Gentamicin	>32	>32	15.7	4.2	80.1	32	>32	40.0	2.9	57.1	>32	>32	-	-	-
Levofloxacin	16	>32	2.8	7.4	89.8	16	>32	30.0	7.1	62.9	8	>32	0.0	0.0	100.0
Meropenem	>64	>64	3.2	1.9	94.9	16	>64	28.6	8.6	62.9	>64	>64	-	-	-
Meropenem-vaborbactam (8 µg/ml)	>32	>32	-	-	-	16	>32	-	-	-	>32	>32	-	-	-
Piperacillin-tazobactam (4 µg/ml)	>128	>128	0.9	2.3	96.8	128	>128	12.9	30.0	57.1	>128	>128	-	-	-
Tetracycline	>32	>32	11.6	13.9	74.5	0.5	1	-	-	-	0.5	0.5	-	-	-
Tobramycin	>32	>32	24.5	2.8	72.7	32	>32	38.6	2.9	58.6	>32	>32	-	-	-

RESULTS SUMMARY

- 3 *P. aeruginosa* and 61 *S. maltophilia* were unable to grow in RPMI, so all antimicrobial data presented exclude these isolates. All *A. baumannii* remained viable in RPMI.
- PLG0206 was very active against *A. baumannii, S. maltophilia,* and *P. aeruginosa* (Figure 3 & Table 1).
- PLG0206 retained activity against MDR isolates of *A. baumannii, P. aeruginosa* and *S. maltophilia* (Table 2).

CONCLUSIONS

- PLG0206 was the most active antimicrobial overall (based on MIC_{50} and MIC_{90}) against *S. maltophilia* and was the most active overall against *A. baumannii* and *P. aeruginosa* except for colistin. However, the use of colistin is not ideal due to its safety and tolerability profile, and recent breakpoint changes render all isolates to be of intermediate susceptibility to colistin at best.
- As a high proportion of *S. maltophilia* were unable to grow in RPMI, further work is underway to find an alternative test medium for PLG0206.
- These data suggest that this novel antimicrobial peptide could be a potential treatment option for these difficult to treat bacterial pathogens, including MDR strains.

References

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