Activity of the Novel Engineered Antimicrobial Peptide PLG0206 against Staphylococci and Enterococci that Cause Periprosthetic Joint Infections

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INTRODUCTION: PLG0206 is an investigational, engineered cationic antimicrobial peptide designed to overcome the shortcomings of other natural antimicrobial peptides (AMPs), such as toxicity and limited activity. PLG0206 has recently been shown to be well tolerated and safe when administered via IV in a Phase 1 study. The initial proposed indication for this peptide is the treatment of periprosthetic joint infections (PJI) via irrigation due to a broad spectrum of activity and anti-biofilm properties. This study evaluated the activity of PLG0206 and comparator antimicrobials against staphylococci and enterococci, causes of periprosthetic joint infections, from the IHMA repository of isolates collected from various worldwide locations in 2019.

METHODS: Isolates tested included *Enterococcus faecalis* (77), *E. faecium* (75), methicillin-resistant *Staphylococcus aureus* (MRSA, 180), methicillin-susceptible *S. aureus* (MSSA, 121), and 152 coagulase-negative staphylococci (CoNS) comprised of *S. epidermidis* (113), *S. haemolyticus* (31), *S. hominis* (4), *S. lugdunensis* (1), *S. saprophyticus* (2), and *S. simulans* (1). Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution in cation-adjusted Mueller Hinton broth (CA-MHB), except for PLG0206 which was tested in RPMI medium due to plate-reading difficulties with CA-MHB. The susceptibility of comparators was determined using the 2022 Clinical and Laboratory Standards Institute (CLSI) breakpoints. Multidrug-resistant (MDR) was defined as resistance to ≥3 antibacterial classes.

RESULTS: When tested in RPMI, 18 *E. faecalis*, 29 *E. faecium*, 9 *S. aureus* and 7 CoNS were unable to grow. Summary MIC and susceptibility data for PLG0206 and comparators just including those isolates able to grow in RPMI are shown in the Table. Identical MIC_{50} and MIC_{90} values were obtained for PLG0206 when tested against MDR *E. faecium* (38), MDR CoNS (63) and MDR MRSA (67). Insufficient numbers of MDR MSSA (7) and MDR *E. faecalis* (4) were tested to accurately evaluate.

DISCUSSION AND CONCLUSION: PLG0206 was the most potent antimicrobial overall (based on MIC_{50} and MIC_{90}) against enterococci and CoNS and compared well with the comparators against MRSA and MSSA. These data support the evaluation of this novel antimicrobial peptide as a treatment option for periprosthetic joint infections, including those caused by MDR strains.