



Knee explant analysis (KnEA) using PLG0206 in periprosthetic joint infection (KnEA Study)

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Introduction

- Prosthetic joint infections (PJI) are the most severe complications in total knee (TKA) arthroplasty.
- Five-year mortality of TKA PJI is 20% and irrigation and debridement is a method to manage PJI but fails in approximately 60% of cases (1).
- PLG0206 is a novel engineered cationic antimicrobial peptide being evaluated for treatment of PJI.
- PLG0206 is a broad-spectrum antimicrobial agent against multidrug resistant organisms, has rapid activity against biofilms, does not have significant local or systemic toxicity in animal models (2,3).
- This study evaluated the activity of PLG0206 against planktonic bacteria on *ex vivo* infected prosthesis following removal from patients with chronic PJI.

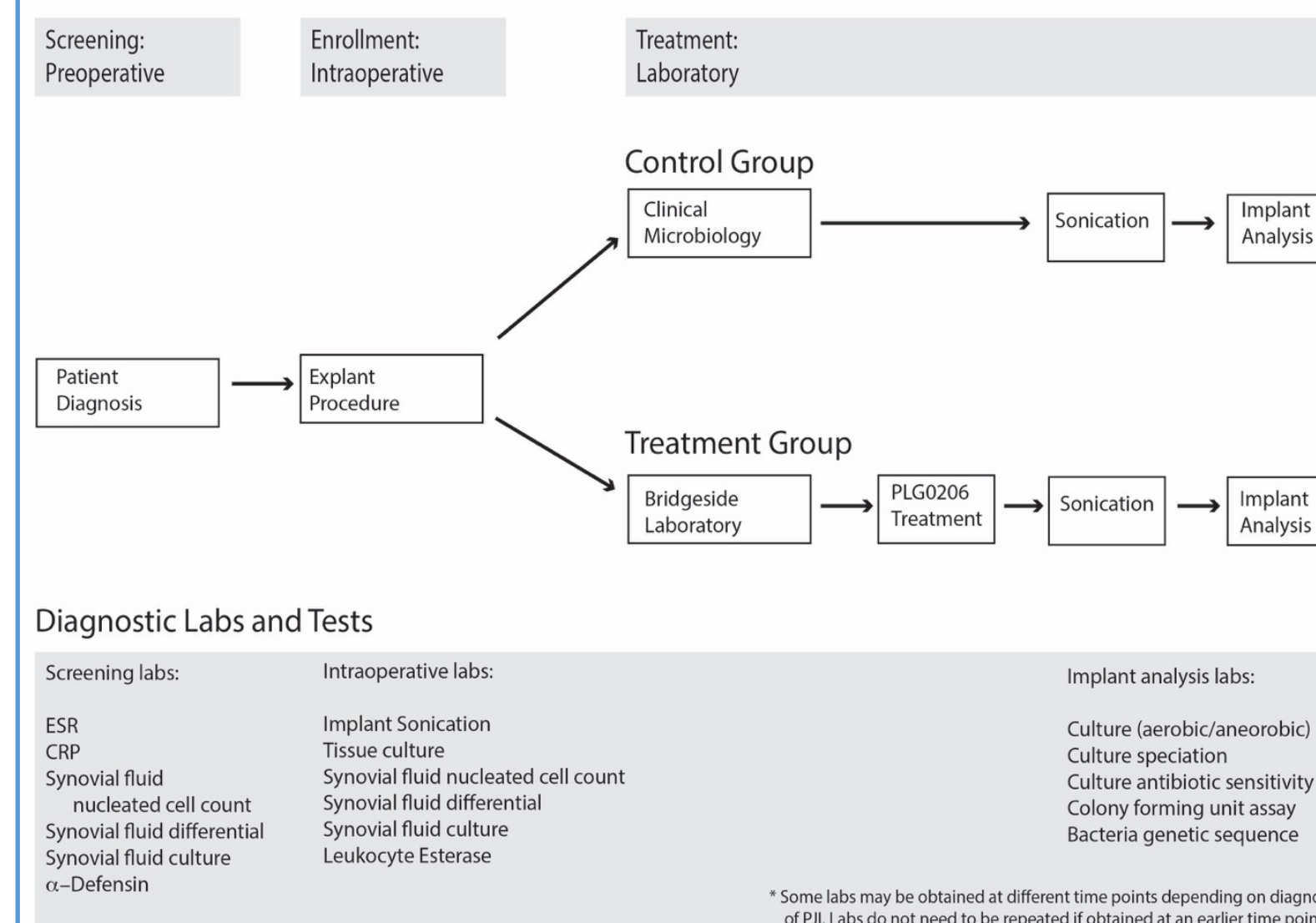
Methods

- This was a multi-center *ex vivo* study completed inside the University of Pittsburgh Medical Center Healthcare System.
- The inclusion criteria were: adults > 18 years, clinical diagnosis of bacterial PJI based on 2018 International Consensus Meeting criteria for PJI, surgery with removal (explant) of the infected implant components, and medical optimization for surgery.
- De-identified infected prosthetics were removed from 21 patients with chronic PJI, who despite receiving chronic suppressive oral antibiotics required a 2-stage revision procedure.
- PLG0206 remained frozen at $-20^{\circ}\text{C} \pm 5^{\circ}\text{C}$ until prosthetic was received.
- PLG0206 was diluted in PBS at a concentration of 1 mg/mL and adjusted to $\text{pH} 7.40 \pm .01$
- Removed prosthetics were then submersed *ex vivo* to an expected clinical exposure of PLG0206, 1 mg/mL, for ~15 minutes.
- Prosthetics were rinsed with 50 mL dPBS.

Methods

- Upon completion of the 15-minute exposure, the treated explant was placed into PBS + 1% Tween 20 and sonicated for 5 minutes
- The sonication solution was then plated for bacterial analysis including colony forming unit (CFU) enumeration.
- Remaining explanted implants from the same patient served as a control and was processed similarly but without exposure to PLG0206.
- The study occurred from 25 January 2021 to 5 August 2021.
- The study design is shown in the Figure below.

KnEA Study Design:
PLG0206 Explant Analysis



Results

- The Table shows the summary of culture and CFU log reduction among infected prosthetics exposed and not exposed to PLG0206

#	Culture	MDR	CFU/mL Untreated	CFU/mL Treated
1	<i>S. epidermidis</i>	clindamycin, erythromycin, gentamicin, oxacillin	5.00E+07	0
2	<i>S. epidermidis</i>	clindamycin, erythromycin, gentamicin, oxacillin	5.00E+07	0
3	<i>S. aureus</i> (MSSA)	none	N/A	0
4	<i>S. aureus</i> (MRSA)	oxacillin, erythromycin	5.00E+07	0
5	<i>S. hemolyticus</i>	clindamycin, gentamicin, oxacillin, rifampin, TMP/SMX	7.30E+02	0
6	<i>S. aureus</i> (MSSA)	none	5.00E+07	12,500
7	<i>S. caprae</i>	none	5.00E+07	0
8	<i>E. coli</i>	ampicillin, ampicillin/sulbactam	5.00E+07	60
9	<i>E. coli</i>	ampicillin, ampicillin/sulbactam	5.00E+07	30
10	<i>E. coli</i>	ampicillin, ampicillin/sulbactam	5.00E+07	3,510
11	<i>S. epidermidis</i>	none	5.00E+07	90
12	<i>H. parainfluenzae</i>	none	5.00E+07	0
13	<i>H. parainfluenzae</i>	none	5.00E+07	0
14	<i>E. faecalis</i>	none	5.00E+07	10
15	<i>S. aureus</i> (MRSA)	oxacillin, erythromycin		
16	<i>S. dysgalactiae</i>	n/a	n/a	0
17	<i>S. dysgalactiae</i>	n/a	n/a	60
18	<i>S. epidermidis</i>	penicillin	5.00E+07	0
19	<i>S. epidermidis</i>	oxacillin, tetracycline, TMP/SMX	5.00E+07	0
20	<i>S. epidermidis</i>	oxacillin, tetracycline, TMP/SMX	5.00E+07	320
21	<i>S. epidermidis</i>	oxacillin, tetracycline, TMP/SMX	5.00E+07	10

Results

- As shown in the Table, both Gram-positive and Gram-negative bacteria were identified from removed prosthetics during a 2-stage revision procedure for chronic PJI.
- S. epidermidis* (7/21; 33%), *S. aureus* (4/21; 19%) and *E. coli* (3/21; 14%) were the most common bacterial cause of chronic PJI.
- 12 of 21 (57%) bacteria were resistant to at least one antibiotic.
- 12 of 21 (57%) chronically infected prosthetics treated *ex vivo* to PLG0206 1 mg/mL were culture negative.
- Collectively, infected prosthetics exposed to PLG0206 demonstrated a mean $4\log_{10}$ reduction (range 2 to 7).

Conclusions

These findings support the ongoing development of PLG0206 as a local irrigation solution of at least 1 mg/mL concentration in the wound cavity for 15 minutes in patients undergoing treatment of a PJI occurring after total knee arthroplasty.

References

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