

An Engineered Antimicrobial Peptide, PLG0206, Reduces Biofilm Mass and Increases Survival in an Acute Rabbit Model of *S. aureus* Periprosthetic Joint Infection

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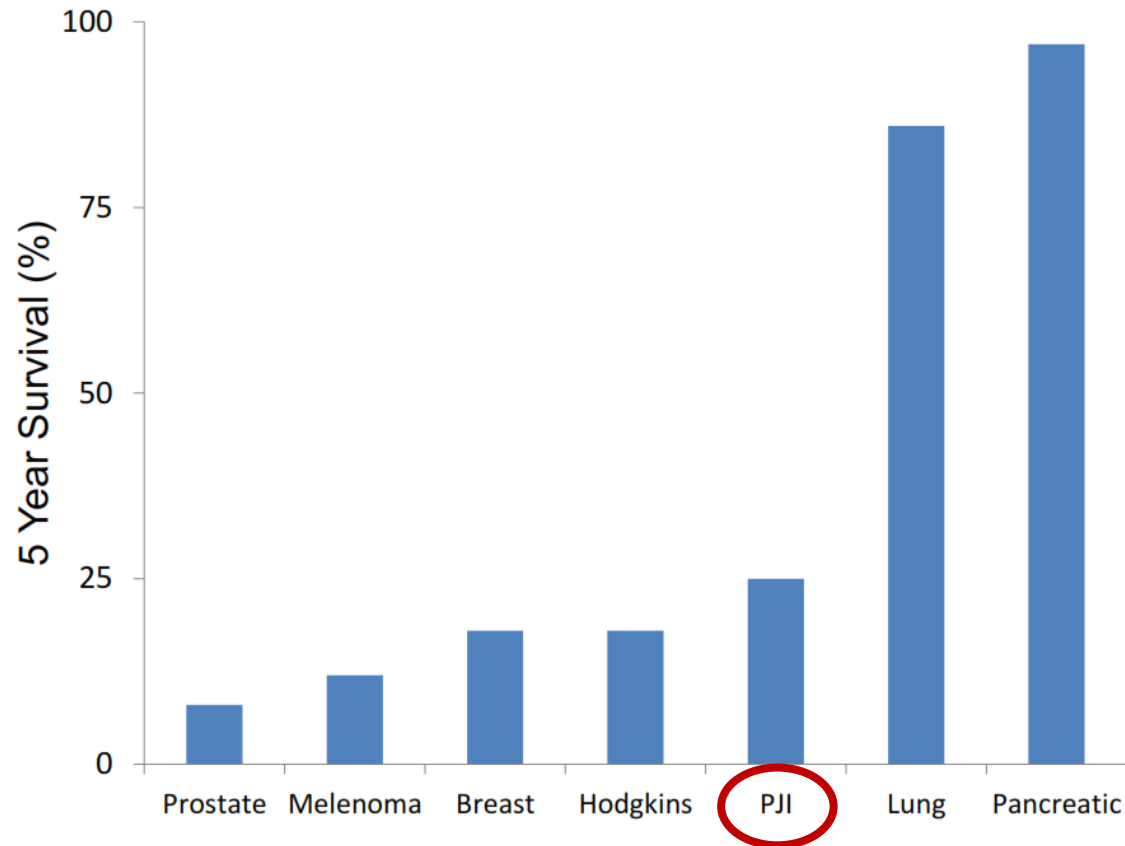
Author Disclosures

I and/or my co-authors have something to disclose:

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Background

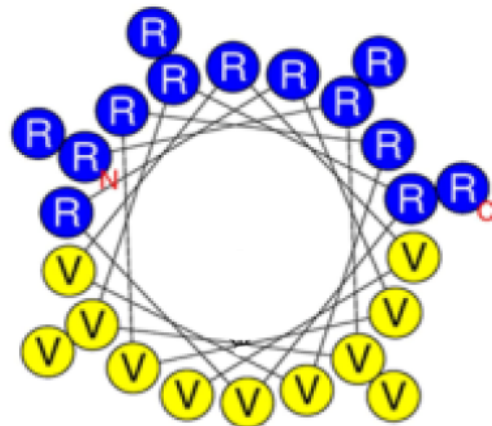


Author	Time	Study Design	Treatment	Mortality (n)
Parvizi	5yr	Observational	Mixed	25% (436)
Bedair	4yr	Matched Control	Two Stage	18% (88)
Urish	5yr	Observational	I&D	18% (385)

PJI has a mortality higher than some cancers

Background: PLG0206: A New Class of Antimicrobials

1	Biofilm Activity	Mandell 2017 Nature Sci Reports
2	Rapid Acting	Mandell 2017 Nature Sci Reports & AAOS 2022
3	Mechanism: Metabolic Independent Membrane Destabilization	Mandell 2017 Nature Sci Reports Kumagai 2019 Soft Matter
4	Broad Spectrum (ESKAPE)	AAOS 2022



R Arginine

V Valine

W Tryptophan

Purpose

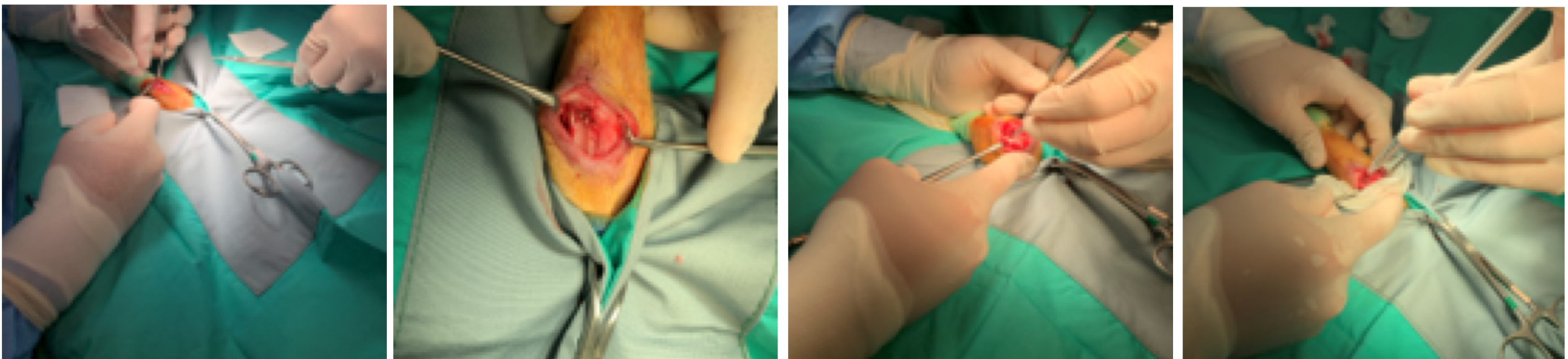
Objective: Determine PLG0206 activity in a large animal model

Hypothesis: Comparable to the murine model, PLG0206 will maintain antimicrobial activity in an acute rabbit model of *S. aureus* PJI

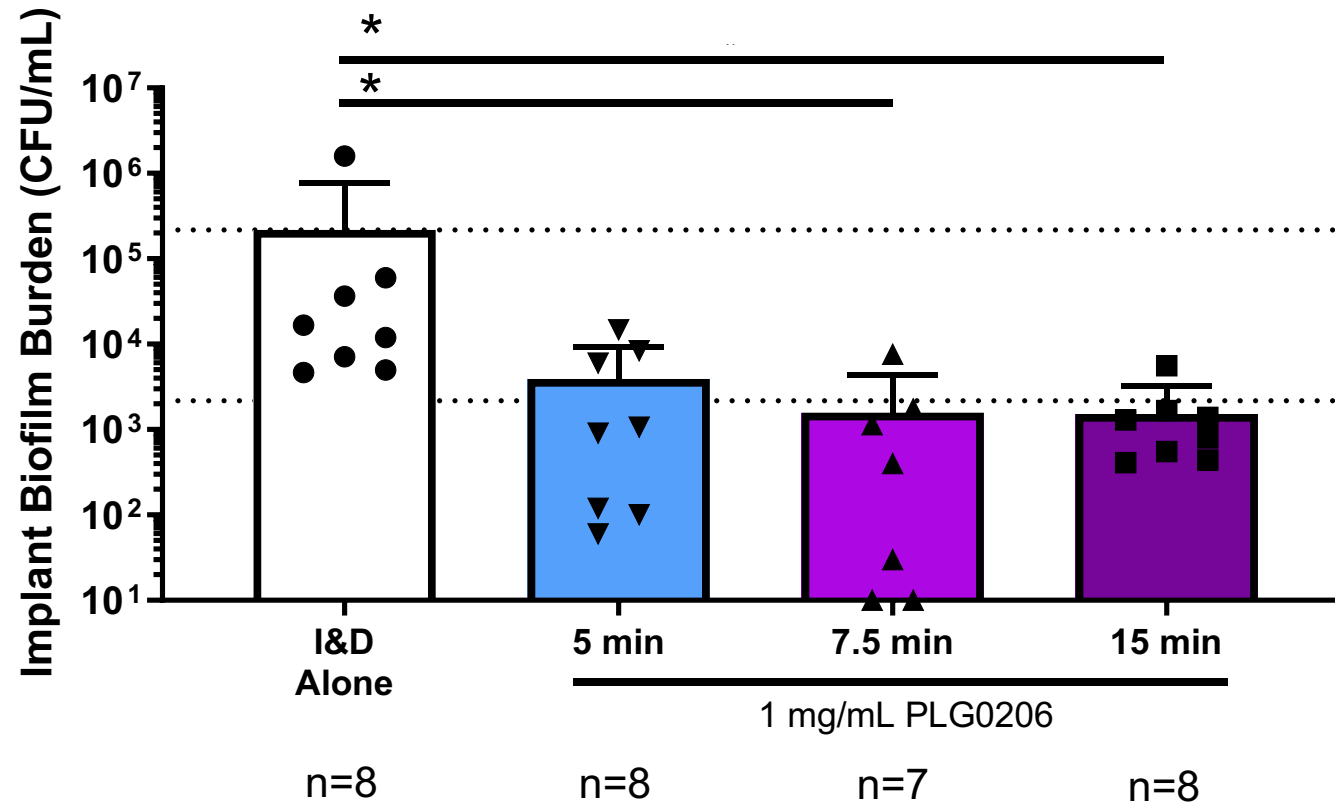
Logic: Incremental study to FDA phase 1B

Methods: Rabbit PJI Model

- Kirschner wire implant placed into the proximal tibia
- 2×10^6 CFU/ml *Staphylococcus aureus* injected into intra-articular space
- Wire placement was confirmed by X-ray
- Mature biofilm allowed to develop (2 days)
- I&D performed, treatments begin *in vivo*
- Groups: 1. I&D alone, 2. DAIR (I&D + cefazolin), 3. DAIR (I&D + cefazolin) + PLG0206



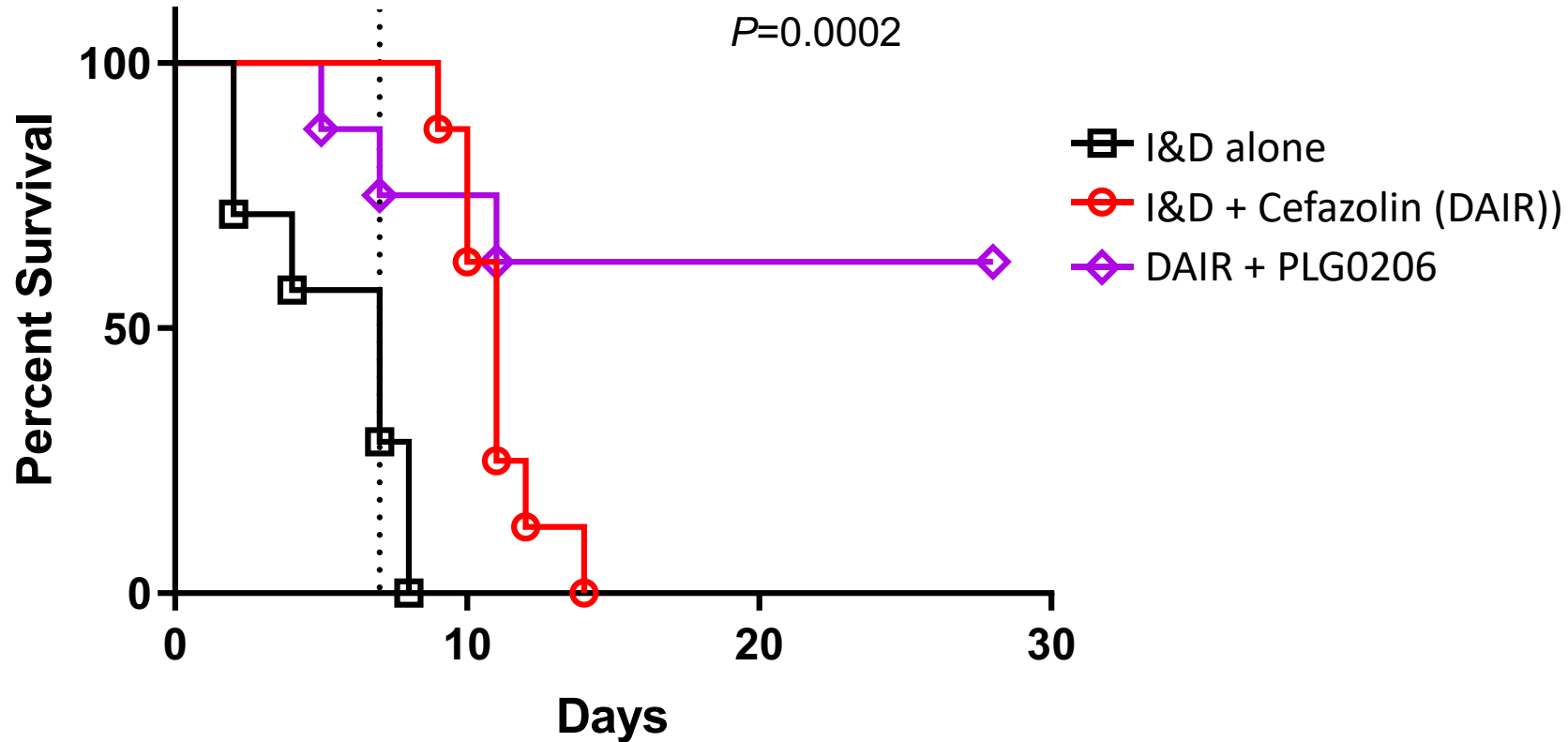
Results: Bacterial Burden of Implant *In vivo*



I&D results in a $>2 \log_{10}$ reduction in bacterial burden

* $p < 0.05$

Results: Survival Study



- I&D alone results in rapid 100% mortality
- I&D + cefazolin (DAIR) results in 100% mortality
- DAIR + PLG0206 results in 63% survival

Discussion

- Short term study: PLG0206 significantly reduced bacterial burden
- Combination therapy most successful: 63% survival to 28 days compared to cefazolin alone (0% survival)



DAIR (I&D + Cefazolin)



DAIR (I&D + Cefazolin) + PLG0206

PLG0206: A New Class of Antimicrobials

	Outcome	
1	Biofilm Activity	Mandell 2017 Nature Sci Reports
2	Rapid Acting	Mandell 2017 Nature Sci Reports & AAOS 2022
3	Broad Spectrum (ESKAPE)	AAOS 2022
4	Efficacy in Large Animal PJI	AAOS 2022
	Safety	
6	Systemic Safety & Pharmacokinetics	Phase I Clinical Study: ACTRN12618001920280 Huang AAC 2022
7	Acute Postop TKA PJI (Ongoing)	FDA Phase 1b; clinical.trial.gov: NCT05137314

Thank You



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