

P1435 **Translational study of the antibiofilm activity of lysin CF-301 in an infected haemodialysis catheter from patient with suspected *S. aureus* bacteraemia**

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**Background:** CF-301 is a novel, recombinantly-produced, bacteriophage-derived lysin (cell wall hydrolase) which is in Phase 2 of clinical development for the treatment of *S. aureus* bacteremia including endocarditis used in addition to standard-of-care antibiotics. In contrast to conventional antibiotics, CF-301 has potent activity against staphylococcal biofilms in vitro and in animal models. To explore the activity of CF-301 against *S. aureus* biofilms associated with human infections, CF-301 was tested on a colonized explanted hemodialysis catheter from a patient with suspected *S. aureus* bacteremia. This is the first study to assess CF-301 activity on biofilm formed in the setting of human disease.

**Materials/methods:** An infected hemodialysis catheter was removed as part of clinical care. Segments (1 cm) of the catheter were bisected and allotted into different treatment groups (n=3 segments/group) with CF-301, daptomycin (DAP) or CF-301 + DAP at the clinically relevant concentration of 1 µg/mL. After 18 h, samples were homogenized for quantitative plating on Tryptic Soy Agar and Mannitol Salt Agar with 4 µg/mL oxacillin (OXA). Isolates (n=16) from the pretreatment group were examined by 16S rRNA amplicon sequencing and used to determine MIC values for CF-301, DAP, and OXA.

**Results:** Quantitative plating results:

Study Groups	[CF-301] (µg/mL)	[DAP] (µg/mL)	Mean Log <sub>10</sub> CFU/g*
Pretreatment	0	0	2.94
Buffer	0	0	2.88
CF-301	1	0	<LOD
DAP	0	1	3.76
CF-301+DAP	1	1	<LOD

\*The limit-of-detection (LOD) is 0.7 Log<sub>10</sub> CFU/g

CF-301 eradicated the biofilm at 1 µg/mL whereas DAP alone did not clear biofilm at 1 µg/mL. The addition of CF-301 and DAP resulted in clearance of the biofilm. The catheter biofilm included methicillin-resistant staphylococci (OXA MIC = 32-256 µg/mL), including *S. aureus*, *S. epidermidis*, and *S. capitis*.

**Conclusions:** A clinically relevant concentration of CF-301, alone and in addition to DAP, eradicated staphylococcal biofilm which formed inside a hemodialysis catheter in the setting of a human clinical

infection, whereas an analogous concentration of DAP alone did not. These data provide important translation of the previously reported potent efficacy of CF-301 against biofilms formed in vitro and in animal models, to biofilms formed in the setting of human disease.