

Supplemental Materials

TABLE S1. Frequency distribution of gepotidacin MICs ($\mu\text{g/ml}$) against *S. aureus* from lesion samples by visit (mMITT population).

Visit (n)	Number of isolates with indicated gepotidacin MIC											
	≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32	
Baseline (78)	0	10	50	13	2	1	0	1	0	0	1	
IV – Day 1 (3)	0	0	3	0	0	0	0	0	0	0	0	
IV – Day 2 (30)	0	5	19	5	0	0	0	1	0	0	0	
Early Efficacy (17)	0	4	12	1	0	0	0	0	0	0	0	
IV – Day 3 (4)	0	0	4	0	0	0	0	0	0	0	0	
IV – Day 4 (1)	0	0	1	0	0	0	0	0	0	0	0	
IV – Day 5 (3)	0	0	3	0	0	0	0	0	0	0	0	
IV – Day 6 (2)	0	0	2	0	0	0	0	0	0	0	0	
IV – Day 7 (1)	0	0	1	0	0	0	0	0	0	0	0	
IV – Day 8 (1)	0	0	1	0	0	0	0	0	0	0	0	
Oral – Day 1 (3)	0	0	3	0	0	0	0	0	0	0	0	
Oral – Day 7-10 (1)	0	0	0	1	0	0	0	0	0	0	0	
Overall Postbaseline (66)	0	9	49	7	0	0	0	1	0	0	0	

IV, intravenous; MIC, minimum inhibitory concentration; mMITT, modified microbiological intent-to-treat.

TABLE S2. Gepotidacin MICs against Gram-positive (other than *S. aureus*) and Gram-negative aerobic isolates recovered from pretreatment lesion samples (mMITT population).

Pathogen	Number of isolates	MIC range, min – max (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
Gram-positive aerobic pathogens (excluding <i>S. aureus</i>)^a	11	≤0.06 to 0.5	0.25	0.5
Gram-negative aerobic isolates				
<i>Klebsiella pneumoniae</i>	8	4 to 8	8	8
<i>Serratia marcescens</i>	3	8	NA	NA
<i>Escherichia coli</i>	1	4	NA	NA
<i>Enterobacter cloacae</i>	2	8 to 16	NA	NA
<i>Leclercia adecarboxylata</i>	1	4	NA	NA
<i>Acinetobacter</i> spp.	1	32	NA	NA
<i>Pseudomonas aeruginosa</i>	2	8	NA	NA
<i>Haemophilus</i> spp.	2	2	NA	NA
<i>Klebsiella oxytoca</i>	1	2	NA	NA

MIC, minimum inhibitory concentration; MIC₅₀, median minimum inhibitory concentration; MIC₉₀, 90th percentile minimum inhibitory concentration; mMITT, modified microbiological intent-to-treat.

^aOther Gram-positive aerobes included β-hemolytic *Streptococcus* groups A, F, and G; *Staphylococcus epidermidis*; *Staphylococcus lugdunensis*; and *Streptococcus viridans*.

TABLE S3. Multilocus sequence typing (MLST) of the 12 isolates selected for whole genome sequencing using 7 housekeeping genes in the *S. aureus* MLST database.

SampleID	<i>arcC</i>	<i>aroE</i>	<i>glpF</i>	<i>gmk</i>	<i>pta</i>	<i>tpi</i>	<i>yqil</i>	MLST	Gepotidacin
								Strain Type	MIC ($\mu\text{g/mL}$)
isolate138	12	1	37	15	11	1	40	1598	0.25
isolate139	3	3	1	1	4	4	3	8	8
isolate141	3	3	1	1	4	4	3	8	0.25
isolate144	3	3	1	1	4	4	3	8	0.25
isolate146	10	14	8	6	10	3	2	45	1
isolate151	3	3	1	1	4	4	3	8	0.25
isolate212	3	3	1	1	4	4	3	8	0.5
isolate584	3	3	1	1	4	4	3	8	0.12
isolate586	3	3	1	1	4	4	3	8	0.25
isolate713	3	3	1	1	4	4	3	8	>32
isolate825	1	1	1	1	1	1	1	1	0.25
isolate832	3	3	1	1	4	4	3	8	0.25

MIC, minimum inhibitory concentration; MLST, multilocus sequence typing.

TABLE S4. Microbiological response and outcomes at the early and posttherapy visits for Gram-positive pathogens (other than *S. aureus*) from pretreatment lesion samples (mMITT population).

Pathogen Microbiological response and outcome	Early efficacy visit				Posttherapy visit			
	750 mg q12h	1,000 mg q12h	1,000 mg q8h	Total	750 mg q12h	1,000 mg q12h	1,000 mg q8h	Total
Other Gram-positive pathogens								
Patients/pathogens, n/n	4/4	4/4	3/3	11/11	4/4	4/4	3/3	11/11
Microbiological success, n (%) [95% CI]	2 (50) [6.8, 93.2]	3 (75) [19.4, 99.4]	3 (100) [29.2, 100.0]	8 (73) [39.0, 94.0]	3 (75) [19.4, 99.4]	3 (75) [19.4, 99.4]	2 (67) [9.4, 99.2]	8 (73) [39.0, 94.0]
Eradication	2 (50)	2 (50)	0	4 (36)	-	-	-	-
Presumed eradication	0	1 (25)	3 (100)	4 (36)	3 (75)	3 (75)	2 (67)	8 (73)
Microbiological failure, n (%) [95% CI]	2 (50) [6.8, 93.2]	1 (25) [0.6, 80.6]	0	3 (27) [6.0, 61.0]	1 (25) [0.6-80.6]	1 (25) [0.6-80.6]	1 (33) [0.8-90.6]	3 (27) [6.0-61.0]
Persistence	1 (25)	1 (25)	0	2 (18)	-	-	-	-
Presumed persistence	1 (25)	0	0	1 (9)	0	1 (25)	0	1 (9)
Presumed recurrence	-	-	-	-	1 (25)	0	1 (33)	2 (18)

CI, confidence interval; mMITT, modified microbiological intent-to-treat; q8h, every 8 h; q12h, every 12 h.

Text S1. Clinical success/failure in Gram-negative isolates

Definitive conclusions on the role of gepotidacin in the clinical success or failure of patients with Gram-negative isolates could not be made. Of the 17 patients in the mITT population who had a Gram-negative aerobic isolate recovered from their baseline lesion specimen, only 3 who had a Gram-negative aerobic pathogen did not receive concomitant antibacterial therapy and also did not have a co-infecting pathogen. These patients included 1 patient in the 750 mg q12h treatment group with an *Escherichia coli* isolate with a gepotidacin MIC value of 4 µg/ml; 1 in the 1000 mg q12h treatment group with a *K. pneumoniae* isolate with a gepotidacin MIC value of 4 to 8 µg/ml; and 1 in the 1000 mg q8h treatment group with a *Haemophilus* spp. isolate with a gepotidacin MIC value of 2 µg/ml.