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Paper Poster Session

New agents in clinical development against gram-positive bacteria

Activity of Debio 1452 against *Staphylococcus* spp. collected in 2013/2014

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**Background:** Debio 1452 is the active moiety of the prodrug Debio 1450, which is currently in Phase 2 clinical development for staphylococcal infections. Debio 1450 (is an oral first in class antibiotic specifically targeting staphylococcus species through FabI inhibition. Due to its unique mechanism of action, Debio 1450 should preserve the human microbiome and reduce associated complications such as *Clostridium difficile* related colitis and diarrhea and candidiasis. The current study evaluated the activity of this agent against methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA) and other staphylococci including coagulase negative staphylococci collected from various geographical locations during 2013 – 2014.

**Material/methods:** A total of 821 clinical isolates collected during the period 2013 / 2014 from European, North American, Latin America and Asian hospitals were tested. Of these, 402, 258, 95 and 66 were MRSA, MSSA, *S. epidermidis* and other *Staphylococcus* species, respectively. Minimal inhibitory concentrations (MICs) for Debio 1452 and eight antibiotic comparators were determined following CLSI guidelines.

**Results:** Summary results for Debio 1452 are shown in the Table. Debio 1452 was the most active agent tested with MIC<sub>90</sub> for all *S. aureus* (n = 660), all MRSA (n = 402) and all MSSA (n = 258) of 0.008, 0.008 and 0.015 mg/L, respectively. The overall range for all *S. aureus* (n = 660) was ≤ 0.001 – 0.25 mg/L. Debio 1452 showed similar activity against all *S. aureus*, MRSA and MSSA sub-groups with respect to geographical origin. Against *S. epidermidis* (n = 95), Debio 1452 was again the most active agent with an MIC<sub>90</sub> and MIC range of 0.03 and 0.008 – 0.5 mg/L, respectively. Against other *Staphylococcus* species (a total of 11 species), MIC<sub>90</sub> and MIC range of 0.015 and 0.004 – 0.5 mg/L, respectively. Activity was not affected by resistance to comparator antimicrobials.

Organism	Debio 1452 MIC (mg/L):			
	MIC <sub>50</sub>	MIC <sub>90</sub>	Min	Max
<i>S. aureus</i> (660)	0.004	0.008	≤ 0.001	0.25
MRSA (402)	0.004	0.008	≤ 0.001	0.25
MSSA (258)	0.008	0.015	0.002	0.25
<i>S. epidermidis</i> (95)	0.015	0.03	0.008	0.5
Other staphylococci (66)	0.015	0.06	0.004	0.5

**Conclusions:** Debio 1452 exhibited excellent *in vitro* activity against all clinical isolates tested in the study. In the present study Debio 1452 exhibited superior activity as compared with other agents and no cross-resistance to other antimicrobials was observed, consistent with historical data. Further studies are warranted in support of clinical development of Debio 1450 for staphylococcal infections.