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Dalbavancin Activity against Bacterial Isolates from Pediatric Patients: Results from the International Dalbavancin Evaluation of Activity (IDEA) Program for the United States and Europe (2019–2021)

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CONCLUSIONS

Dalbavancin showed potent *in vitro* activity against a large collection of Gram-positive isolates from pediatric patients, independent of patient age and geographic region (US and Europe).

Only 13 of 4,487 (0.3%) isolates exhibited a dalbavancin MIC >0.25 mg/L, all of which were vancomycin-resistant *E. faecium*.

These *in vitro* results support further clinical development of dalbavancin for treatment of Gram-positive infections in children.

INTRODUCTION

- Dalbavancin is a lipoglycopeptide approved in the United States (US; 2014) and Europe (2015) to treat skin and skin structure infections in adults with a convenient parenteral administration of either a single dose of 1500 mg or a dose of 1000 mg followed by 500 mg a week later.
- As of July 2021, dalbavancin is approved for treating pediatric patients (from birth) with ABSSSI in the US. It is still under evaluation for pediatric approval in Europe.
- We evaluated dalbavancin *in vitro* spectrum and potency against Gram-positive isolates from pediatric patients.

MATERIALS AND METHODS

- A total of 4,487 organisms were consecutively collected (1/patient) from 66 medical centers located in the US (*n*=3,098; 32 centers) and Europe (*n*=1,389; 34 centers from 18 countries: Belarus, Belgium, Czech Republic, France, Germany, Hungary, Ireland, Israel, Italy, Poland, Portugal, Russia, Slovenia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom).
- Isolates were determined to be clinically significant based on local guidelines and were submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA).
- Isolates were tested for susceptibility by broth microdilution following guidelines in the Clinical and Laboratory Standards Institute (CLSI) M07 (2018).
- The dalbavancin breakpoints approved by the US FDA and/or CLSI for indicated species were applied (i.e., an MIC ≤0.25 mg/L), and breakpoint criteria for comparator agents were from the CLSI M100 (2021).

RESULTS

- Dalbavancin showed complete activity against *S. aureus* (100.0% susceptibility), with a highest MIC value of 0.12 mg/L (Table 1) and consistent activity against all age groups: $MIC_{50/90}$ of 0.03/0.03 mg/L for the US and Europe as well as the MSSA and MRSA subsets.
- MRSA rates were higher in the US (32.4% overall) than Europe (14.0%; Table 2).
- In the US, the MRSA rate was lowest in the 13–17 year old (yo) group (25.0%); whereas, in Europe, MRSA rates were slightly lower in the 2–5 yo group (11.5%) compared to the other age groups (14.1%–14.8%; Table 2).
- Ceftaroline was consistently active against *S. aureus* isolates from all age groups, with susceptibility rates ranging from 99.4% (13–17 yo) to 99.8% (2–5 yo) in the US and from 95.3% (≤1 yo) to 100.0% (2–5 yo) in Europe (Table 2).
- Dalbavancin showed consistent activity against *S. pneumoniae* from all age groups ($MIC_{50/90}$ of 0.008/0.015 mg/L for all age groups in the US and Europe) with a highest MIC value of 0.06 mg/L (1 isolate; Table 1).
- All *S. pneumoniae* isolates were susceptible to ceftaroline, and susceptibility to ceftriaxone (at ≤1 mg/L; non-meningitis breakpoint) ranged from 92.7% (13–17 yo) to 100.0% (≤1 yo), or 97.8% overall (Table 2).
- Dalbavancin was also highly active against BHS, coagulase-negative staphylococci (CoNS), *Enterococcus faecalis*, viridans group streptococci, and vancomycin-susceptible *E. faecium*, but showed limited activity against vancomycin-resistant *E. faecium* (Table 1).

Table 1. Antimicrobial activity of dalbavancin tested against organisms from pediatric patients

Organism (no. of isolates)	No. and cumulative % of isolates inhibited at dalbavancin MIC (mg/L) of:											MIC_{50}	MIC_{90}
	≤0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	>2		
S. aureus (2,633)	2 0.1	11 0.5	518 20.2	2,046 97.9	55 >99.9	1 100.0						0.03	0.03
MSSA (1,922)	2 0.1	11 0.7	404 21.7	1,465 97.9	40 100.0							0.03	0.03
MRSA (711)		0 0.0	114 16.0	581 97.7	15 99.9	1 100.0						0.03	0.03
S. pneumoniae (689)	30 4.4	387 60.5	249 96.7	22 99.9	1 100.0							0.008	0.015
β-hemolytic streptococci (584)	174 29.8	185 61.5	181 92.5	36 98.6	8 100.0							0.008	0.015
CoNS (240)	0 0.0	5 2.1	59 26.7	108 71.7	52 93.3	14 99.2	2 100.0					0.03	0.06
E. faecalis (200)			18 9.0	149 83.5	33 100.0							0.03	0.06
Viridans group streptococci (102)	45 44.1	20 63.7	22 85.3	12 97.1	2 99.0	1 100.0						0.008	0.03
E. faecium (39)			5 12.8	9 35.9	7 53.8	4 64.1	1 66.7	1 69.2	1 71.8	1 74.4	10 100.0	0.06	>2
VAN-S (≤4 mg/L) (26)			5 19.2	9 53.8	7 80.8	4 96.2	1 100.0					0.03	0.12

Abbreviations: MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; VAN-S, vancomycin-susceptible.

Table 2. Antimicrobial activity of dalbavancin and comparator agents against *S. aureus* and *S. pneumoniae* stratified by age group

Organism / Antimicrobial	% Susceptible per CLSI by region and age group									
	United States by age group in years old					Europe by age group in years old				
	≤1	2–5	6–12	13–17	All (≤17)	≤1	2–5	6–12	13–17	All (≤17)
S. aureus (no.)	(594)	(433)	(496)	(336)	(1,859)	(257)	(122)	(220)	(175)	(774)
Dalbavancin	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Ceftaroline	99.7	99.8	99.6	99.4	99.6	95.3	100.0	99.1	98.3	97.8
Oxacillin	61.3	65.8	71.6	75.0	67.6	85.2	88.5	85.9	85.7	86.0
Clindamycin	96.3	92.1	93.8	90.5	93.6	96.1	99.2	96.8	96.0	96.8
Erythromycin	47.6	51.7	52.4	56.2	51.4	78.2	78.7	69.5	60.0	71.7
Levofloxacin	81.1	77.4	81.7	84.2	80.9	93.4	95.1	90.4	91.4	92.4
TMP-SMX	98.0	98.8	100.0	99.1	98.9	100.0	100.0	99.5	100.0	99.9
S. pneumoniae (no.)	(132)	(203)	(100)	(30)	(465)	(61)	(91)	(47)	(25)	(224)
Dalbavancin	—[a]	—[a]	—[a]	—[a]	—[a]	—[a]	—[a]	—[a]	—[a]	—[a]
Ceftaroline	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Ceftriaxone[a]	99.2	99.0	98.0	90.0	98.3	96.7	97.8	95.7	96.0	96.9
Penicillin[a]	98.5	98.0	98.0	86.7	97.4	95.1	94.5	93.6	96.0	94.6
Amoxillin-clavulanate	97.7	97.0	98.0	86.7	96.8	91.8	95.6	95.7	92.0	94.2
Erythromycin	50.8	57.1	55.0	70.0	55.7	80.3	72.5	70.2	72.0	74.0
Levofloxacin	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
TMP-SMX	61.4	68.0	72.0	76.7	67.5	63.9	62.6	66.0	64.0	64.1

[a] Breakpoints have not been established.
Abbreviation: TMP-SMX, trimethoprim-sulfamethoxazole.

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