

Session: P097 Understanding and managing *Clostridium difficile*

**Category: 5a. Mechanisms of action, preclinical data & pharmacology of antibacterial agents**

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**Activity of cadazolid and other antibiotics against clinical isolates of *Clostridium difficile* collected from European hospitals in 2014/2015**

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**Background:** Cadazolid is a novel antibacterial currently in phase III clinical trials for the treatment of *C. difficile* infections. This study evaluated the activity of cadazolid and other compounds against recent clinical isolates of *C. difficile* from Europe.

**Material/methods:** A total of 652 clinical isolates of *C. difficile* were collected in 2014/2015 from Belgium (1 site), Czech Republic (2), France (9), Germany (3), Hungary (1), Poland (1), Romania (3), Spain (5), Sweden (1) and the United Kingdom (3). Minimum inhibitory concentrations (MICs) for cadazolid and antibiotic comparators were determined by agar dilution following CLSI guidelines. MIC<sub>50</sub> and MIC<sub>90</sub> (concentrations to inhibit 50% & 90% of isolates, respectively) were calculated. Susceptibility was evaluated using CLSI breakpoints for anaerobes, except for vancomycin and metronidazole where EUCAST breakpoints for *C. difficile* were used.

**Results:** Summary MIC results (mg/L) and % susceptibility (where available) against all 652 isolates are shown in the Table below. Cadazolid MIC values were very consistent between countries with MIC<sub>50</sub> and MIC<sub>90</sub> of 0.5 mg/L in each country except Sweden where MIC<sub>50</sub> was 0.25 mg/L. The highest cadazolid MIC was 1 mg/L for one isolate from Spain.

Antibiotic	Breakpoints <sup>1</sup> (S  R)	% Susceptible	MIC <sub>50</sub>	MIC <sub>90</sub>	Min MIC	Max MIC
Cadazolid	NB <sup>2</sup>	-	0.5	0.5	0.12	1
Clindamycin	≤2   4   ≥8	7.2	8	> 32	≤0.06	> 32
Fidaxomicin	NB	-	0.25	0.5	0.03	1
Imipenem	≤4   8   ≥16	0.6	> 16	> 16	4	> 16

Linezolid	NB	-	2	4	≤0.25	32
Metronidazole	≤2   -   ≥4	99.9	0.5	1	≤ 0.06	4
Moxifloxacin	≤2   4   ≥8	59.8	2	32	≤0.5	> 32
Tigecycline	NB	-	0.12	0.12	≤0.015	2
Vancomycin	≤2   -   ≥4	97.2	1	2	≤0.25	4

1. S, susceptible; I, intermediate; R, resistant breakpoints (mg/L)

2. NB, no breakpoint available

**Conclusions:** Cadazolid was very active against the European *C. difficile* isolates collected in 2014 and 2015 with MICs over a very narrow range between 0.12 and 1 µg/ml with a clear mode MIC of 0.5 mg/L across and within all 10 countries which contributed isolates. Based on MIC<sub>90</sub> cadazolid was more potent than vancomycin and metronidazole and equal to fidaxomicin. Susceptibility was very low to imipenem and clindamycin (0.6 and 7.2%, respectively) and also moxifloxacin showed low susceptibility (59.8%). These *in vitro* data support the continued investigation of cadazolid as an alternative therapy for *C. difficile*-associated diarrhoea.