

Session: P097 Understanding and managing Clostridium difficile

**Category: 5c. New antibacterial agents: clinical trials**

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## **Efficacy of bezlotoxumab in patient with recurrent Clostridium difficile infection: pooled analysis of data from the MODIFY trials**

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**Background:** Therapies for recurrent CDI, particularly in patients experiencing multiple recurrences, are needed. The CDI recurrence (rCDI) rate after an initial episode of CDI is ~25% after treatment with metronidazole or vancomycin, with risk of recurrence increasing to 40-60% in patients who have recurrent disease. MODIFY I/II were two independent global trials of the efficacy and safety of bezlotoxumab (bezlo: a human monoclonal antibody against *C. difficile* toxin B), each of which showed that a single 10 mg/kg IV dose of bezlo was superior to placebo at preventing rCDI among patients with primary or recurrent CDI given standard of care (SoC) antibiotic therapy.

**Material/methods:** This was an analysis of pooled data from the MODIFY trials to estimate clinical cure and rCDI through 12 weeks in subgroups of patients with 0, 1, or  $\geq 2$  episodes of CDI prior to the presenting CDI episode. Clinical cure was defined as receipt of a  $\leq 14$ -day regimen of SoC AND no diarrhoea during the 2 consecutive days following completion of SoC. CDI recurrence was defined as a new episode of diarrhoea associated with a positive stool test for toxigenic CDI in patients who achieved clinical cure of the presenting CDI episode. The 95% confidence intervals for the difference in clinical cure and rCDI rates between bezlo and placebo were calculated.

**Results:** Overall, 1526 patients were included in the analyses: 1018 (67%) had 0 prior episodes, 282 (18%) had 1 prior episode, and 226 (15%) had  $\geq 2$  prior episodes. Baseline characteristics were generally similar between treatment groups. A higher proportion of patients with recurrent CDI at study entry were  $\geq 65$  years of age (59%; 302/508) compared with those with primary CDI (47%; 475/1018) and a higher proportion of patients with primary disease were inpatients (72%; 291/508) compared with patients with recurrent CDI (57%; 736/1018). The proportion of patients who achieved clinical cure was generally similar between treatment groups across subgroups defined by prior CDI episodes (Table). In both treatment groups, the rCDI rate was higher in patients with 1 or more prior CDI episodes compared with patients with primary CDI (Table). Treatment with bezlo reduced the rCDI rate compared with placebo in patients with recurrent CDI, including those with multiple prior recurrences.

**Conclusions:** In patients with recurrent CDI, bezlo was associated with a marked decrease in the proportion of patients with rCDI over a 12-week period compared with placebo (~14% absolute difference). This antitoxin antibody shows promise as an adjunct to SoC therapy in the prevention of rCDI in patients with recurrent disease.

Number of Prior CDI Episodes	Bezlo % (n/N)	Placebo % (n/N)	Adjusted Difference (95% CI)
Clinical Cure in the mITT Population			
0	81.5 (424/520)	80.3 (400/498)	1.1% (-3.7, 6.0)
1	75.3 (113/150)	82.6 (109/132)	-7.8% (-17.2, 1.9)
$\geq 2$	81.0 (81/100)	81.7 (103/126)	-1.1% (-12.2, 9.5)
rCDI in the mITT Population who Achieved Clinical Cure			
0	16.3 (69/424)	26.5 (106/400)	-10.3% (-15.9, -4.7)
1	27.4 (31/113)	41.3 (45/109)	-14.4% (-25.8, -0.8)
$\geq 2$	35.8 (29/81)	51.5 (53/103)	-13.6% (-28.5, 1.9)

mITT: modified intent to treat=patients receiving study infusion with a positive stool test for toxigenic *C. difficile*, and receiving SoC within 1 day of bezlo