Bezlotoxumab Decreases CDI Recurrence and is Associated with a Reduction in 30-Day Readmissions: European Analysis

Introduction and Purpose

- It has been estimated that *Clostridium difficile* causes 172,000 infections each year across the 27 countries of the European Union among individuals ≥2 years of age.1 However, these data do not take into account a recently documented 70% increase in incidence of *C. difficile* infection (CDI) and considerable scope for missed diagnoses across Europe.2

- Although initial antibiotic treatment of primary CDI is often successful, recurrence occurs in up to 35% of patients after treatment.3 After first recurrence, patients have a 40% chance of a second recurrence, with the risk increasing with further recurrences.4

- MODIFY I and MODIFY II were global, randomized, double-blind, placebo-controlled trials of the efficacy and safety of bezlotoxumab (a human monoclonal antibody against a *C. difficile* toxin B) alone and in combination with standard of care (SOC) for the prevention of CDI recurrence in adults receiving antibiotic treatment (metronidazole or vancomycin) for *C. difficile* infection.5 Both studies evaluated bezlotoxumab substantially reduced recurrent CDI and had a safety profile similar to placebo. The addition of actoxumab did not improve efficacy.

- Hospital readmissions are more common among patients with a CDI discharge diagnosis compared with patients who did not have a CDI discharge diagnosis.6 Patients with recurrent CDI are likely than patients without a recurrence to be readmitted to the hospital.7

- Hospital readmissions are a major driver of healthcare costs and can adversely affect patient outcomes.8

- MODIFY I and MODIFY II trials for the subgroup of subjects enrolled in the European region who were randomized to the bezlotoxumab or placebo groups.

Methodology

- The within-trial dataset for 30-day readmission is described in Figure 2.

- CDI recurrence: a new episode of *C. difficile* associated with a positive test result at the local or central laboratory for toxicologic *C. difficile* following clinical cure of the baseline CDI episode through 12 weeks following study medication infusion.

- All-cause 30-day readmission: the proportion of subjects attributed to a hospital readmission at the time of study medication infusion that had any readmission occurring within 30 days of discharge (post-hoc endpoint).

- CDI-associated readmission: a readmission having a primary or secondary discharge diagnosis described as "CDI" or "CDI recurrence".

Statistical Analysis

- Endpoint methods were estimated from the pooled MODIFY dataset for the subgroup of subjects enrolled in the European region who were randomized to the bezlotoxumab or placebo groups.

- Confidence intervals of the absolute difference between the bezlotoxumab and placebo groups were estimated using Mantel and Hennessey's methodology.

Results

- In the MODIFY trials, 781 subjects were treated with bezlotoxumab and 773 subjects received placebo and were included in the full analysis set population, which included all randomized patients who received study medication infusion; had a positive baseline stool test for toxigenic *C. difficile* and received SOC antibiotic treatment for CDI at time of study infusion.

- Bezlotoxumab decreased CDI recurrence: 521 (67.6%) of these subjects were enrolled in the European region (Figure 3) and were included in the CDI recurrence analysis (Figure 4).

Conclusions

- Bezlotoxumab was generally well tolerated. The types and incidence of adverse events (AEs) and serious AEs were similar across the bezlotoxumab and placebo groups.

- AEs were generally as expected considering the underlying disease severity, baseline co-morbidities, and age of the population studied.

Safety Outcomes

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References

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Disclosures

- Both authors report receiving standard honoraria from Merck for manuscript development.

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