Paper - Annual Meeting

Paper Session: RCT and Other
Prospective Studies I

Treatment of Orthopaedic Infections: A Phase 2a Study to Assess Safety, Tolerability and Clinical Activity of Intrasurgical Administration of MBN-101 to Infected Bone

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Purpose: Pravibismane, the broad-spectrum antimicrobial/antibiofilm agent in MBN-101, potentially promotes more rapid/complete resolution of orthopaedic infections. The primary study objective was to evaluate safety of MBN-101 in patients with orthopaedic infections. Secondary objectives were evaluation of clinical activity and pharmacokinetics.

Methods: This was a randomized, single-blind, placebo-controlled, multicenter study evaluating single escalating doses of MBN-101 applied locally to infected osteosynthesis or osteomyelitis sites during revision surgery. Three cohorts of 8 subjects, randomized 3:1, received MBN-101 at doses of 0.5, 1.5, and 5.0 µg/cm2 or placebo. Eligible[subjects had prior operative fracture fixation or arthrodesis with subsequent osteomyelitis and hardware contamination. Revision surgery was performed that included obtaining cultures, debridement, and irrigation with or without hardware removal/replacement. MBN-101 or placebo was administered directly to exposed bone and hardware within the infected site prior to closure. Systemic antibiotics were administered. Surgical site and safety assessments were conducted through week 12 post-treatment. Clinical activity was assessed as number/timing of treatment failures and serious interventions.

Results: 29 subjects were randomized and 25 subjects treated with MBN-101 (n = 18) or placebo (n = 7). MBN-101 was tolerated at all doses. The highest dose group had no serious adverse events (SAEs) and had lower treatment emergent adverse events (TEAEs) versus placebo and other MBN-101 groups. TEAEs occurred in 83.3, 66.7, 16.7% of subjects in 0.5, 1.5, 5.0 µg/cm2 MBN-101 and 85.7% of placebo. SAEs occurred in 66.7, 33.3, 0.0% of subjects in 0.5, 1.5, 5.0 µg/cm2 MBN-101 and 42.9% of placebo. None of the SAEs and only 1 mild TEAE per MBN-101 (16.7%) and placebo (14.3%) group were considered related to study drug. Systemic exposure was very low to undetectable at all dose levels. Positive, non-statistical efficacy trends were observed. Week 12 treatment failure rates were lower in all MBN-101 groups: 16.7%, 33.3%, and 16.7% in the 0.5, 1.5, 5.0 µg/cm2 versus 42.9% of placebo. No serious interventions occurred in the 5.0 µg/cm2 MBN-101 versus 33.3% of 0.5 and 1.5 µg/cm2 and 14.3% of placebo. Pravibismane had potent in vitro efficacy against all isolated pathogens, including those with multidrug resistance.

Conclusion: MBN-101 was safe and trended toward efficacy in the treatment of contaminated hardware and bone after fracture fixation. Pravibismane has potential to provide a safe, novel antimicrobial/antibiofilm approach to treatment of orthopaedic infections and thus warrants continuing clinical investigation.