Meropenem-Vaborbactam (VABOMERE): Outcomes in Subjects with Renal Impairment in Phase 3 Studies TANGO I and II

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Abstract

Introduction

Meropenem-vaborbactam (MV-VBA) is being developed for the treatment of serious gram-negative infections, which often occur in patients with renal impairment. Studies of non-renal impaired patients have shown clinical response in patients with renal impairment. The TANGO (Trials of Agents forication in Renal Gnos) program included Phase 3 trials designed to demonstrate comparable outcomes in subjects with and without renal function impairment compared to products reported reduced clinical response in patients with renal impairment. The results of the TANGO I and II studies are presented in this report.

Methods

TANGO I and II were Phase 3, double-blind, randomized, controlled trials evaluating MV-VBA (500 mg q12h + 2 g q8h via IV) for the treatment of complicated urinary tract infection (cUTI)/acute pyelonephritis (AP) (Figure 1).

• TANGO I was a Phase 3, multicenter, double-blind, randomized trial comparing MV-VBA to Meropenem (500mg q6h) for the treatment of complicated urinary tract infection (cUTI)/acute pyelonephritis (AP) (Figure 1). TANGO I was a randomized, open-label, controlled study in which 313 subjects were treated with MV-VBA (156) or Meropenem (157). Subjects were treated for 7 days (500mg q12h) and 14 days (500mg q6h) or until resolution of symptoms and laboratory abnormalities. Outcomes were compared according to baseline renal function (CrCl ≥50 mL/min and <50 mL/min). The CrCl was derived from an estimated creatinine clearance, calculated using the Cockcroft-Gault equation.

Results

In TANGO I, outcomes with MV-VBA and Meropenem were comparable in efficacy outcomes across all infection types in patients with or without renal impairment. In patients with CrCl ≥50 mL/min, 112/156 (71.8%) of subjects treated with MV-VBA achieved clinical cure and eradication at End of Treatment (EOT). In patients with CrCl <50 mL/min, 54/57 (94.7%) of subjects treated with MV-VBA achieved clinical cure and eradication at EOT. There was no statistically significant difference in clinical response between subjects with and without renal impairment (p=0.2602). A summary of adverse events in subjects with renal impairment in TANGO I and II is presented in Table 4.

Background

• Meropenem-vaborbactam (MV-VBA) was developed for the treatment of serious gram-negative infections, which often occur in patients with renal impairment.
• Studies of non-renal impaired patients have shown clinical response in patients with renal impairment.
• The TANGO (Trials of Agents forication in Renal Gnos) program included Phase 3 trials designed to show that the drug is safe and effective in patients with renal function impairment.
• Here we report clinical response of subjects with renal impairment in the TANGO trials.

Table 1. Dose Reduction Scheme for Renal Adjusted Dosing

Table 2. Baseline Demographics in Subjects with Renal Impairment, TANGO I and II

Table 3. Efficacy Outcomes in Subjects with Renal Impairment, TANGO I and II

Table 4. Adverse Events in Subjects with Renal Impairment, TANGO I and II

Conclusions

• Based upon observations from the TANGO studies, 11.5% of patients with cUTI have underlying renal impairment; this incidence is doubled (21%) in patients with CRE infection.
• In TANGO I overall success at EDVT and TOC were similar between treatment groups regardless of baseline renal function.
• In TANGO II, 8.5% cUTI during EDVT were lower in patients with renal impairment vs. those with no renal impairment but remained higher in the MV-VBA arm vs. Best Available Therapy.
• There is no evidence of decreased safety associated with MV-VBA in patients with renal impairment.
• MV-VBA is safe and effective treatment for serious gram-negative infections in impaired patients. The dosage should be adjusted as recommended in the USPI.

Disclosures

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