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 (BV) is being developed for the treatment of complicated urinary tract infections (cUTI) due to known or suspected gram-negative pathogens, including those with decreased susceptibility to carbapenems. BV is a β-lactam/β-lactamase inhibitor combination product approved for patients with renal impairment. This paper presents the specific population analyses of Meropenem-Vaborbactam in patients with renal impairment enrolled in the TANGO I and II studies.

Methods: Meropenem-Vaborbactam (BV) was compared to treatment with Meropenem alone in two phase 3 clinical studies: TANGO I and TANGO II in subjects treated with BV (50 mg/kg IV q8h) plus Meropenem 1 g q8h for complicated urinary tract infection (cUTI) or acute pyelonephritis (AP) (T) or Meropenem 1 g q8h for complicated intra-abdominal infection (cIAI) (P). Baseline renal function was calculated using the Cockcroft-Gault equation. Outcomes were assessed in the efficacy population (subjects who received ≥75% of study drug and had at least one post-baseline bacterial isolate). Results were assessed through end of treatment (EOT).

Results: Subjects with renal impairment (CrCl <50 mL/min) enrolled in the TANGO trials. Studies of some recently approved beta-lactam/β-lactamase inhibitors have demonstrated a similar safety profile across patients with renal impairment. Overall, these findings suggest that BV may offer a safe and effective treatment option in subjects with renal impairment.

Conclusions: Based upon observations from the TANGO studies, 11.5% of patients with cUTI underling renal impairment; this incidence is reduced (21%) in patients with CRE infection.

Table 1. Baseline Demographics in Subjects with Renal Impairment (CrCl ≤50 mL/min) for both TANGO I and II in the Modified Intent-to-Treat (MITT) population are shown in Table 2.

Table 2. Baseline Demographics in Subjects with Renal Impairment (CrCl ≤50 mL/min) for both TANGO I and II in the Modified Intent-to-Treat (MITT) Population.

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.

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Background

• Meropenem-Vaborbactam (BV; VABOMERE) was developed to address the global threat of carbapenem-resistant gram-negative infections, which often occur in patients with renal impairment.
• Studies of some recently approved beta-lactam/β-lactamase inhibitor combination products reported improved clinical outcomes in patients with renal impairment. The TANGO trial demonstrated that BV was as effective as Meropenem alone (Meropenem 1 g q8h) in the treatment of uncomplicated urinary tract infection (UTI) due to extended-spectrum β-lactamase-producing Enterobacteriaceae (APF) [1].

Methods

• TANGO I was a Phase 3, multicenter, double-blind, randomized study evaluating BV and Meropenem as a treatment for the treatment of uncomplicated urinary tract infection (cUTI) due to extended-spectrum β-lactamase-producing Enterobacteriaceae (APF) [1]. TANGO I was a randomized, open-label, parallel-group study. Meropenem 1 g q8h was administered to subjects with creatinine clearances <60 mL/min. The BV dosage was adjusted in patients with creatinine clearances <50 mL/min in TANGO I, according to the Cockcroft-Gault equation. Here we report clinical responses of subjects with renal impairment enrolled in the TANGO trials.

Figure 1. Study Scheme for TANGO I.

Figure 2. Study Scheme for TANGO II.

Figure 3. Overall Success by Timepoint in Subjects with Renal Impairment, TANGO I (n=MITT).

Figure 4. Clinical Cure Rates Across All Infection Types by Timepoint in Subjects with Renal Impairment, TANGO II (n=MITT).