Intravenous Eravacycline with Transition to Oral Therapy for Treatment of Complicated Urinary Tract Infections (cUTI) Including Pyelonephritis: Results from a Randomized, Double-Blind, Multicenter, Phase 3 Trial (IGNITE2)

L Tsai, M Zerros, L Miller, P Tenke, A Marsh, J Mohr, K Luxpuek, P Hom

Trumphares Pharmacuticals, Watertown, MA; Henry Ford Hospital, Detroit, MI; Harbor-UCLA Medical Center, Los Angeles, California; John Ferrero South-Post Teaching Hospital, Budapest, Hungary

Abstract

Background: Eravacycline (ERV) is a novel anti-MRSA drug already approved for treatment of complicated urinary tract infections (cUTI) including pyelonephritis in the EU. This was a Phase 3 trial to compare safety and efficacy of ERV versus levofloxacin (LEV). The Per Protocol (PP) results are pending.

Methods: Randomized, double-blind, double-dummy, multicenter, prospective study. Eligible subjects were ≥18 years old with cUTI including pyelonephritis. A total of 304 subjects (152 ERV, 152 LEV) were randomized. Subjects received intravenous ERV 1,400 mg bid for 3-5 days, followed by oral ERV 250 mg q12h or LEV 750 mg q12h for 14 days. Primary endpoint was microbiological response at end of therapy (EOE) (modified intent-to-treat [mITT]). Secondary endpoints included clinical response at EOE, responder rates at other timepoints, safety and tolerability.

Results: Pathogen was Enterobacteriaceae in 91% of cases. Although intrapatient pathogen consistency was maintained throughout the study, 3.7% of patients switched pathogens. Overall, microbiological response at end of therapy was 90.9% for ERV and 86.8% for LEV (90.4% vs. 86.4% in ITT). Clinical response at EOE was 91.7% for ERV and 87.4% for LEV (91.5% vs. 87.2% in ITT). Combined responder rates through the end of therapy favored eravacycline; responder rates at subsequent timepoints favored levofloxacin. Risk of treatment failure was lower for eravacycline and higher for levofloxacin. EMA Co-primary endpoints were microbiological response at post-treatment visit (m-microIT) and microbiological success at post-treatment visit (m-microITT). Microbiological success rates at post-treatment visit were 95.4% for ERV and 82.6% for LEV (95.2% vs. 82.4% in m-microITT). ERV was associated with lower rates of any drug-related adverse event, drug-related TEAE, and SAE. Adverse events associated with treatment in >5% of subjects were hypertension (ERV 8.9%, LEV 26.6%), vomiting (ERV 8.9%, LEV 2.6%), and headache (ERV 5.3%, LEV 1.8%). Subjects treated with ERV had lower rates of all TEAE and SAE compared to LEV. A final analysis will be presented at the International Society of Antimicrobial Agents and Chemotherapy (ISAAC). Regulatory approval is pending.

Conclusions: Eravacycline was well tolerated and superior to LEV for cUTI including pyelonephritis. The study met the primary objective of non-inferiority for microbiological response at end of therapy, and also met the primary objective of equivalence for microbiological success at end of therapy. Eravacycline has the potential to be a first-line treatment option for complicated UTI including pyelonephritis.