Fosfomycin for Injection (FOS) Versus (vs) Piperacillin-Tazobactam (PIP-TAZ) for Treating Complicated Urinary Tract Infections (cUTI) and Acute Pyelonephritis (AP): Further Analyses of the ZEUS Study

Evelyn J. Ellis-Grosse,1 David Skarinsky,1 Kristina Manvelian,1 Paul B. Eckberg,1 Anita F. Das,2 Keith S. Kaye3

1 Nabria Therapeutics US, Inc., King of Prussia, PA, USA; 2DAS Consulting, Guerneville, CA, USA; 3University of Michigan Medical School, Ann Arbor, MI, USA

INTRODUCTION

The efficacy of fosfomycin for injection (FOS; Figure 1) is a first-in-class injectable antimicrobial agent under evaluation by the US Food and Drug Administration (FDA) for the treatment of complicated urinary tract infection (cUTI), including acute pyelonephritis (AP) [9].

METHODS (continued)

The primary endpoint of overall success was defined as clinical cure and microbiologic eradication with few adverse events. The study compared FOS with standard-therapy (m-MITT) population at the test-of-cure (TOC) visit (Day 19–21).

RESULTS (continued)

Efficacy by Baseline PIP-TAZ Susceptibility

Baseline cUTI/AP caused by a PIP-TAZ-resistant pathogen was uncommon (n=14, 20.6% of PIP-TAZ) (Table 2).

- Among these patients, overall success rates at TOC were 78.6% (11/14) in the FOS group and 33.3% (5/15) in the PIP-TAZ group (Table 3).

- In patients infected with a PIP-TAZ-intermediate pathogen at baseline, overall success rates at TOC were 53.3% (1/2) and 62.5% (5/8) for the FOS and PIP-TAZ groups respectively (Table 3).

- In patients infected with a PIP-TAZ-susceptible pathogen at baseline, overall success rates at TOC were 84.7% (1/1) for FOS vs 56.7% (1/1) for PIP-TAZ (Table 2).

- Upon exclusion of those patients with a baseline pathogen resistant to PIP-TAZ, overall success rates were 63.5% (9/14) in the FOS group and 55.6% (9/16) in the PIP-TAZ group (treatment difference: 7.9%, 95% CI, 1.1 to 18.9).

RESULTS

Efficacy by 2016 FDA Guidance Reanalysis

In the original primary analysis based on the 2015 FDA cUTI Guidance, FOS was noninferior to PIP-TAZ based on the proposed noninferiority margin of 15% (Table 1).

- Use of the more stringent 2016 Guidance criteria for this analysis resulted in a slightly greater treatment difference that further favored FOS and had a 95% confidence interval (CI) with a lower bound above zero.

While success rates among FOS and PIP-TAZ were lower with the more stringent definition for microbial eradication or excluding patients with cUTI/AP caused by PIP-TAZ-resistant pathogens further support the robustness of FOS noninferiority to PIP-TAZ.

- FOS was associated with higher overall success rates in both post hoc analyses compared with PIP-TAZ.

- FOS may provide a useful treatment option for cUTI/AP, including for cases caused by PIP-TAZ-resistant and MDR pathogens.

CONCLUSIONS

- Reanalysis of the ZEUS primary endpoint using either a stricter definition for microbial eradication or excluding patients with cUTI/AP caused by PIP-TAZ-resistant pathogens further supports the robustness of FOS noninferiority to PIP-TAZ.

- FOS was associated with higher overall success rates in both post hoc analyses compared with PIP-TAZ.

- FOS may provide a useful treatment option for cUTI/AP, including for cases caused by PIP-TAZ-resistant and MDR pathogens.

REFERENCES


Acknowledgments

Funding for development of this poster was provided by Nabriva Therapeutics to C4 MedSolutions, LLC (Yardley, PA), a CME Outfitters, LLC Company.

Disclosures

Beverly A Shalom served as an CME during the design, evaluation, and analysis of the study and is currently a consultant or member of the board of directors Nabriva Therapeutics, Inc., Biotherapies, and VivaMed, Inc. He has served as a consultant for Nabriva Therapeutics, Inc., Biotherapies, and VivaMed, Inc. Yedid E. Bik le has been a consultant to Nabriva Therapeutics, Inc., Biotherapies, and VivaMed, Inc. He has served as a consultant to TruthPharm, Teleflex, Pharmasset, Corazyme, Amgen, Abbott, YDSTI, Genentech, Serono, and Abbott. Evelyn J. Ellis-Grosse has served as a consultant for Nabriva Therapeutics, Merck & Co., and Emerick & Co., and has received research grant funding from Merck & Co.