Patient-Level Data Provide Additional Insight for Tigecycline All-Cause Mortality Meta-analysis

To the Editor—Prasad and colleagues [1] have now published the fifth study-level meta-analysis on tigecycline all-cause mortality that replicates initial analyses performed by Pfizer Inc [2]. Patient-level data have provided additional helpful information in the assessment of this clinical issue [3]. Pfizer has disclosed the patient-level analyses to regulatory agencies and it was the basis for an update to the US prescribing information in July 2010 [4].

Despite the demonstration of statistical homogeneity by Prasad and colleagues, study-level and patient-level data suggest substantial clinical heterogeneity [2] that
requires exploration to improve our understanding of the meta-analysis results [5, 6]. First, the hospital-acquired pneumonia and resistant pathogen trials accounted for 52% of the deaths in the meta-analysis, but contributed only 15% of patients to the overall population. Second, indication but not treatment was associated with all-cause mortality in the patient-level analyses of pooled data. Third, subjects with identified patient-level risk factors for mortality had different treatment outcomes depending on the treatment indication.

Finally, Prasad and colleagues’ association of all-cause mortality and tigecycline noncure is problematic. In the context of composite endpoints, including the use of mortality as part of the failure definition in clinical trials, an association between inferior antimicrobial activity and all-cause mortality using a meta-analysis is difficult to conclude [7, 8]. Conclusions regarding the benefit-risk of a drug should include all available data; however, the authors’ conclusions are based on limited information. Tigecycline remains an appropriate treatment option in its approved indications and Pfizer is committed to publishing patient-level analyses to provide clarity on this important clinical issue.

Notes

Acknowledgment. Assistance with editing and preparing this letter for submission was provided by Charlotte Kenreigh of UBC Scientific Solutions and was funded by Pfizer Inc.

Disclaimer. Both signatories to this letter are employees of Pfizer.

Potential conflicts of interest. All authors:
No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Paul C. McGovern and Alvaro Quintana
Pfizer Clinical Research, Pfizer Inc, Collegeville, Pennsylvania

References