Breakpoints and Drug Exposure Are Inevitably Closely Linked

J. W. C. Alffenaar,a* O. W. Akkerman,b* M. S. Bolhuis,a* M. J. Boeree,c W. C. M. de Lange,b*e T. S. van der Werfd

University of Groningen, University Medical Center Groningen, Department of Clinical Pharmacy and Pharmacology, Groningen, The Netherlands;a University of Groningen, University Medical Center Groningen, Pulmonary Diseases and Tuberculosis, Groningen, The Netherlands;b Radboud University Medical Center and University Lung Centre Dekkerswald, Nijmegen, The Netherlands;c University of Groningen, University Medical Center Groningen, Department of Internal Medicine, Groningen, The Netherlands;d Tuberculosis Center Beatrixoord, Haren, The Netherlands*e

It was with great interest that we read the article by Gumbo and colleagues titled “Redefining Multidrug-Resistant Tuberculosis Based on Clinical Response to Combination Therapy” (1). The authors performed a classification and regression tree (CART) analysis showing that MIC cutoff values above which therapy failure was observed are significantly lower than current breakpoints for isoniazid (INH) and rifampin (RIF). The consequence of the finding might be that the rate of multidrug-resistant tuberculosis (MDR TB) is much higher than previously assumed (1).

The impact to revise the definition of MDR TB based on these new critical concentrations will not only be statistical. Many patients will receive a second-line treatment regimen for at least 20 months that will be accompanied by a budget impact based on direct and indirect medical costs. The clinical outcome for these “new” MDR TB patients who will be treated with a second-line treatment regimen of drugs with unclear efficacy and more toxicology than standard treatment and treatment with high-dose INH and RIF. The publication of Gumbo and coworkers once again showed that new dosing strategies with currently available drugs are urgently needed to turn the tide of the MDR TB epidemic. It becomes clearer every day that drug susceptibility was and is important to be able to select an appropriate MDR TB treatment regimen (7) and in addition tailor treatment further by optimizing drug exposure in patients (8).

REFERENCES

Address correspondence to J. W. C. Alffenaar, j.w.c.alffenaar@umcg.nl.
For the author reply, see doi 10.1128/AAC.04688-14.
Copyright © 2015, American Society for Microbiology. All Rights Reserved. doi:10.1128/AAC.04485-14