

Should Carbapenem be Used for Elective Colorectal Surgery in Developing Countries?

Anucha Apisarntharak, M.D.*

To Editor,

In a recent industry-sponsored study, Itani and colleagues reported the superiority of ertapenem over cefotetan for adverse events after elective colorectal surgery.¹ Of the 1,002 patients randomly assigned to study groups, 901 (451 in the ertapenem group and 450 in the cefotetan group) qualified for the modified intention-to-treat analysis, and 672 (338 in the ertapenem group and 334 in the cefotetan group) were included in the per-protocol analysis. After adjustment for strata, in the modified intention-to-treat analysis, the rate of overall prophylactic failure was 40.2 percent in the ertapenem group and 50.9 percent in the cefotetan group (absolute difference, -10.7%; 95% confidence interval [CI], -17.1 to -4.2); in the per-protocol analysis, the failure rate was 28.0 percent in the ertapenem group and 42.8 percent in the cefotetan group (absolute difference, -14.8%; 95% CI, -21.9 to -7.5). Both analyses fulfilled statistical criteria for the superiority of ertapenem. In the modified intention-to-treat analysis, the most common reason for failure of prophylaxis in both groups was surgical-site infection: 17.1 percent in the ertapenem group and 26.2 percent in the cefotetan group (absolute difference, -9.1; 95% CI, -14.4 to -3.7).

While I congratulate the investigators on the completion of such an extensive study, important

considerations should be made prior to the translation of this study finding into practice, especially in developing countries. First, the adverse event rates of 40 percent for ertapenem and 51 percent for cefotetan, while similar to historical controls, suggest that measures beyond antimicrobial prophylaxis need to be prioritized for these elective colorectal surgical cases. Several of the independent risks in the final model suggest potentially modifiable risks such as pre-operative weight reduction, appropriate hair removal, tobacco cessation, and improved surgical techniques to reduce inadvertent perforation and fecal spillage. Second, it is probably true that a single dose of antimicrobial prophylaxis is less likely to produce the emergence of drug-resistant microorganisms than is repeated administration. However, only 67 percent of surgeons discontinued antibiotic prophylaxis within 24 hours of surgery, and thus carbapenem resistance associated with widespread use of ertapenem prophylaxis is of concern.²⁻⁴ Third, excess costs of a new drug need to be considered in practice-change scenarios, especially in developing countries. Furthermore, in developing countries a few, if any, antibiotic control programs exist, multidrug-resistant Gram-negative bacilli are prevalent and the duration of post-operative antibiotic use often goes unchecked.⁵⁻⁶ I, therefore, emphasize the need of caution as the

*Division of Infectious Diseases, Faculty of Medicine, Thammasart University Hospital, Pratumthani 12120, Thailand.

Received for publication: January 24, 2007.

Reprint request: Anucha Apisarntharak, M.D., Division of Infectious Diseases, Faculty of Medicine, Thammasart University Hospital, Pratumthani 12120, Thailand.

E-mail: anapisarn@yahoo.com

Keywords: Carbapenems, surgical prophylaxis, colorectal surgery, developing countries

findings in this study are balanced with anticipated ongoing drug supplies and future antibiotic prophylaxis guidelines.

References

1. Itani KM, Wilson SE, Awad SS, Jensen EH, Finn TS, Abramson MA. Ertapenem versus cefotetan prophylaxis in elective colorectal surgery. *N Engl J Med* 2006;355:2640-51.
2. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis* 2006;43:322-30.
3. Dinubile MJ, Friedland I, Chan CY, et al. Bowel colonization with resistant gram-negative bacilli after antimicrobial therapy of intra-abdominal infections: observations from two randomized comparative clinical trials of ertapenem therapy. *Eur J Clin Microbiol Infect Dis* 2005;24:443-9.
4. Elliott E, Brink AJ, van Greune J, Els Z, Woodford N, Turton J, et al. In vivo development of ertapenem resistance in a patient with pneumonia caused by *Klebsiella pneumoniae* with an extended-spectrum beta-lactamase. *Clin Infect Dis* 2006;42:e95-98.
5. Apisarnthanarak A, Danchaivijitr S, Bailey TC, Fraser VJ. Inappropriate antibiotic use in a tertiary care center in Thailand: an incidence study and review of experience in Thailand. *Infect Control Hosp Epidemiol* 2006;27:416-20.
6. Apisarnthanarak A, Danchaivijitr S, Khawcharoenporn T, et al. Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clin Infect Dis* 2006;42:768-75.