

ALTERNATIVE VIEWPOINTS

Economic Analysis of Alvimopan—A Clarification and Commentary

Timothy J. Bell, M.H.A., Sara A. Poston, Pharm.D., Michael D. Kraft, Pharm.D.,
Anthony J. Senagore, M.D., and Lee Techner, D.P.M.

Key Words: alvimopan, ileus, gastroenterology, surgery outcomes.
(*Pharmacotherapy* 2013;33(5):e81–e82)

We congratulate Dr. Touchette and colleagues for their economic analysis of alvimopan.¹ We wanted to clarify the questions and concerns they raised about our previous economic analysis of alvimopan.² They expressed concern about inconsistencies in our patient numbers. Our total number of patients represented pooled data from all patients in the modified intent-to-treat populations from four phase III North American efficacy trials who underwent bowel resection and received placebo or alvimopan 12 mg (labeled indication and dose).^{3–6} This population was described previously by Dr. Wolff and colleagues⁷ and is also noted in the sponsor's United States Food and Drug Administration (FDA) briefing document used for the alvimopan advisory committee meeting (Table 12.3.1; studies 14CL302, 14CL308, 14CL313, and 14CL314).⁸

We did not include data from patients who received alvimopan 6 mg or from patients who underwent total abdominal hysterectomy

(nonapproved dose and indication). However, these patients were included in the first three phase III trials; as such, it appears that the data inputs used by Dr. Touchette and colleagues included data from these patients in addition to patients who underwent bowel resection. Furthermore, they did not include the largest and most recently published phase III efficacy study that evaluated alvimopan 12 mg only in patients who underwent bowel resection (labeled dose and indication).⁶ This study was included in our economic evaluation.²

In North America, hospital discharge is closely linked to gastrointestinal recovery. Therefore, treatments that accelerate gastrointestinal recovery may shorten hospital length of stay. Review of the European phase III efficacy study showed that hospital length of stay was not linked to gastrointestinal recovery,⁹ likely due to regional variation in practice patterns along with other differences that may impact decisions on hospital discharge. Therefore, we did not include these data in our economic analysis nor was it included in the FDA's evaluation of the drug for hospital discharge end points.

We used two sources to estimate total hospital costs for the pooled data in our analysis (day-specific hospital cost estimates for bowel resection procedures from Premier's Perspective Comparative Database and costs published in the 2007 U.S. Census Bureau statistical abstract for 2004, converted to 2007 dollars).² Despite using different data inputs, different patient data, and a different analytic approach, Dr. Touchette and colleagues' overall results were consistent with the conclusions from our analysis. Furthermore, these results are consistent with results of other

From Global Health Economics and Outcomes Research, Pfizer Inc., New York, New York (T.J. Bell); GlaxoSmith-Kline, Research Triangle Park, North Carolina (S.A. Poston); the Department of Pharmacy, University of Michigan Health System, and the University of Michigan College of Pharmacy, Ann Arbor, Michigan (M.D. Kraft); the Division of Colorectal Surgery, Department of Surgery, University of Southern California, Los Angeles, California (A.J. Senagore); and Cubist Pharmaceuticals, Lexington, Massachusetts (L. Techner).

For questions or comments, contact Michael D. Kraft, Pharm.D., BCNSP, Department of Pharmacy, University of Michigan Health System, Room 302, Victor Vaughan Building, 1111 East Catherine Street, Ann Arbor, MI; e-mail: mdkraft@umich.edu.

large database or institutional analyses of alvimopan.^{10–12} Overall, the results of these analyses suggest that use of alvimopan as indicated may be cost-beneficial provided that length of stay is reduced.

References

1. Touchette DR, Yang Y, Tiryaki F, Galanter WL. Economic analysis of alvimopan for prevention and management of postoperative ileus. *Pharmacotherapy* 2012;32(2):120–8.
2. Bell TJ, Poston SA, Kraft MD, Senagore AJ, Delaney CP, Techner L. Economic analysis of alvimopan in North American phase III efficacy trials. *Am J Health Syst Pharm* 2009;66:1362–8.
3. Wolff BG, Michelassi F, Gerkin TM, et al. Alvimopan, a novel, peripherally acting [mu] opioid antagonist: results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial of major abdominal surgery and postoperative ileus. *Ann Surg* 2004;240:728–34, discussion 734–5.
4. Viscusi ER, Goldstein S, Witkowski T, et al. Alvimopan, a peripherally acting mu-opioid receptor antagonist, compared with placebo in postoperative ileus after major abdominal surgery: results of a randomized, double-blind, controlled study. *Surg Endosc* 2006;20:64–70.
5. Delaney CP, Weese JL, Hyman NH, et al. Phase III trial of alvimopan, a novel, peripherally acting, mu opioid antagonist, for postoperative ileus after major abdominal surgery. *Dis Colon Rectum* 2005;48:1114–25; discussion 1125–6; author reply 1127–9.
6. Ludwig K, Enker WE, Delaney CP, et al. Gastrointestinal tract recovery in patients undergoing bowel resection: results of a randomized trial of alvimopan and placebo with a standardized accelerated postoperative care pathway. *Arch Surg* 2008;143:1098–105.
7. Wolff BG, Weese JL, Ludwig KA, et al. Postoperative ileus-related morbidity profile in patients treated with alvimopan after bowel resection. *J Am Coll Surg* 2007;204:609–16.
8. Adolor Corporation. Entereg (alvimopan) capsules for postoperative ileus (POI), FDA advisory panel briefing document, 14 December 2007. Available from <http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4336b1-02-Adolor.pdf>. Accessed May 4, 2012.
9. Büchler MW, Seiler CM, Monson JRT, et al. Clinical trial: alvimopan for the management of post-operative ileus after abdominal surgery: results of an international randomized, double-blind, multicentre, placebo-controlled clinical study. *Aliment Pharmacol Ther* 2008;28:312–25.
10. Delaney CP, Craver C, Gibbons MM, et al. Evaluation of clinical outcomes with alvimopan in clinical practice: a national matched-cohort study in patients undergoing bowel resection. *Ann Surg* 2012;255:731–8.
11. Poston S, Broder MS, Gibbons MM, et al. Impact of alvimopan (Entereg) on hospital costs after bowel resection: results from a large inpatient database. *P & T* 2011;36:209–20.
12. Absher RK, Gerkin TM, Banares LW. Alvimopan use in laparoscopic and open bowel resections: initial clinical results in a large community hospital system. *Ann Pharmacother* 2010;44:1701–8.

Authors' Reply

We thank Dr. Kraft and colleagues for their commentary. The information included in this commentary does help to clarify some of the issues we had difficulty resolving at the time of our publication.

Daniel R. Touchette, Pharm.D., M.A.
on behalf of
Yoojung Yang, Pharm.D., M.S.
Funda Tiryaki, Pharm.D., M.S.
William L. Galanter, M.D., Ph.D.