Temporal Trends in Compliance With the Alosetron Risk Management Program

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BACKGROUND

Under a Risk Management Program (RMP) intended to assure safe use, alosetron was reintroduced in November 2002 for treatment of female patients with severe diarrhea-predominant irritable bowel syndrome (IBS) who have not responded to conventional therapy, whose IBS symptoms are chronic, and for whom other explanatory gastrointestinal medical conditions have been ruled out. These patients have one or more of the following severity criteria:

1. Frequent and severe abdominal pain/discomfort
2. Frequent bowel urgency or fecal incontinence
3. Disability or restriction of daily activities due to IBS

Physicians are recommended to begin treatment at the lowest dosage (0.5 mg twice daily) for 1 month to mitigate the occurrence of constipation, a common adverse event associated with alosetron. Based on patient response, the dosage of alosetron can be increased up to 1 mg twice daily.

RMP requirements include the following:

- Physicians
  - Enroll in the prescribing program
  - Counsel each patient regarding risks and benefits of treatment
  - Sign a physician–patient agreement (PPA) form
  - Affix a blue program sticker to alosetron prescriptions
  - Report serious adverse events to the sponsor
- Patients
  - Sign the PPA
- Pharmacists
  - Dispense a medication guide
  - Verify the presence of the blue sticker for new prescriptions of alosetron

A key component of the RMP is a cohort study that has been conducted by RTI Health Solutions in which all users of alosetron have the opportunity to participate through a continuous enrollment process. Information is collected by the patients through questionnaires. The primary objectives of the study are:

- To measure how well physicians and patients are following the RMP requirements for prescribing and using alosetron
- To measure how well patients comprehend the information provided to them
- To monitor temporal trends in compliance with the alosetron RMP

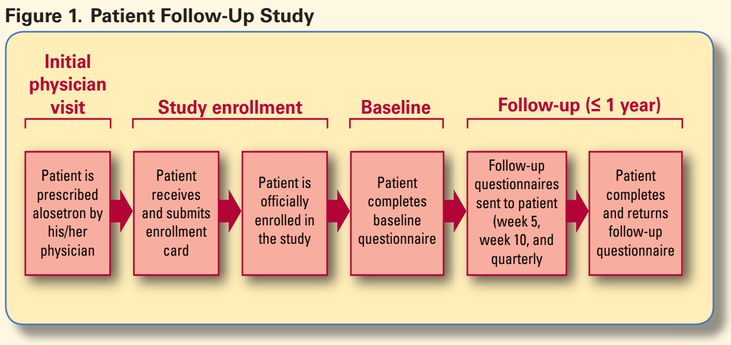
Participation and questionnaire responses have been analyzed on a semiannual basis since 2004.

Results on compliance and dosing have been published.[1,2] The aim of the current analysis is to present temporal trends in compliance with the alosetron RMP from the cohort study.

METHODS

- Patients are invited to complete and return a pre-enrollment card, located in every medication package for alosetron or obtained from a prescribing physician.
- Patient enrollment and follow-up are shown in Figure 1.
- Patients had the option to complete the questionnaire by phone through 2007.
- Data are collected on a customized schedule based on the patients' alosetron start date.

Figure 1. Patient Follow-Up Study



Baseline Data Collected

- IBS history, symptoms, impact on quality of life, and treatment before alosetron
- Current dosage of alosetron and frequency of use
- Patient interaction with prescribing physician
- Comprehension of educational materials (added to baseline questionnaire in 2004)

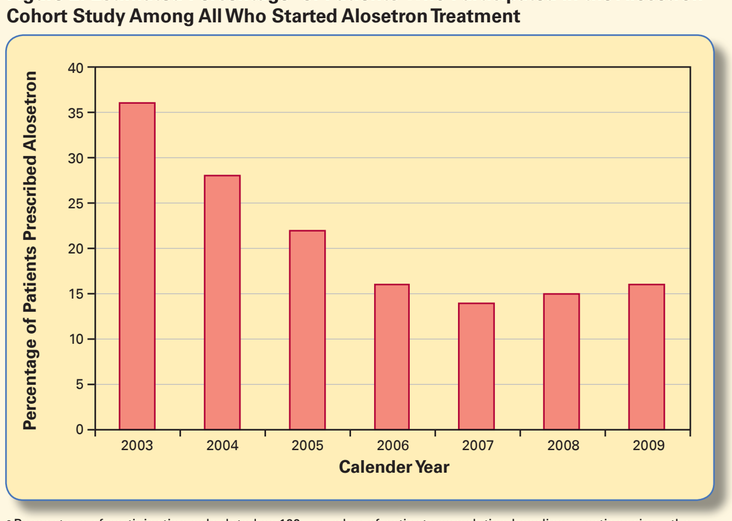
Follow-Up Assessments (5 weeks, 10 weeks, and Quarterly Up to 1 Year) Data Collected

- Current dosage of alosetron and frequency of use
- Continued interaction with the prescribing physician

RESULTS

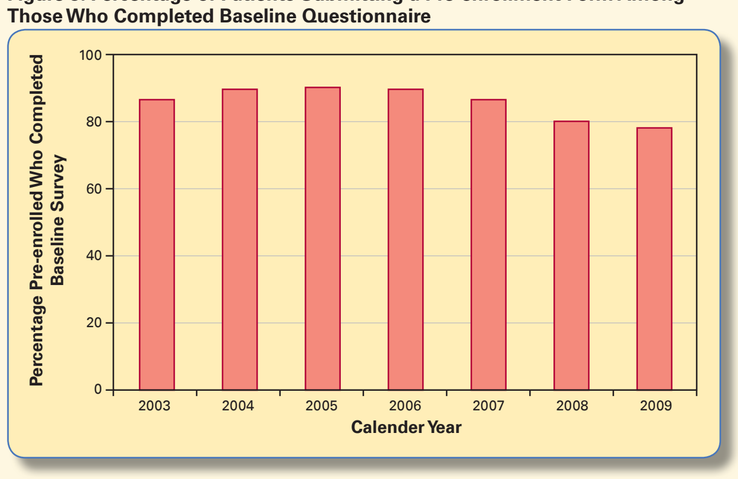
- As of December 31, 2009, 8,096 patients enrolled in the cohort study by completing a baseline form. Overall, 97% were white and 92% female. The distribution of age at enrollment was 32% < 45 years, 48% 45-64 years, and 20% ≥ 65 years. There has been little variation in demographic characteristics over time.

Figure 2. Estimated Percentage[a] of Patients Who Participated in the Alosetron Cohort Study Among All Who Started Alosetron Treatment



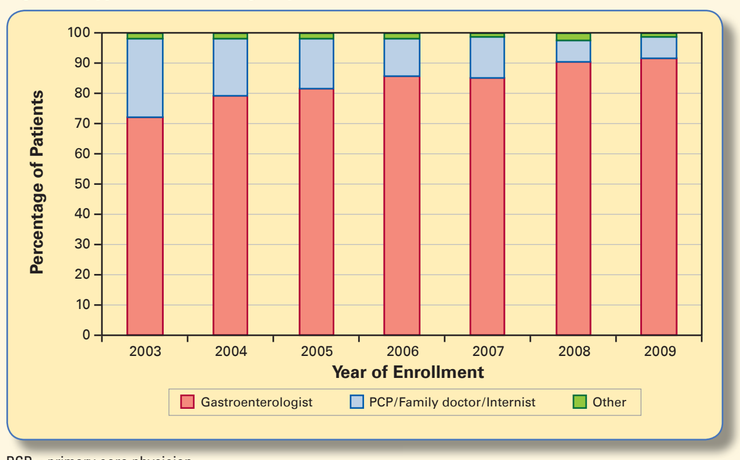
[a] Percentage of participation calculated as 100 × number of patients completing baseline questionnaire ÷ the number of US patients prescribed alosetron estimated from retail sales data.

Figure 3. Percentage of Patients Submitting a Pre-enrollment Form Among Those Who Completed Baseline Questionnaire



- Among those completing a baseline questionnaire, response to follow-up remained high over the follow-up period (> 95% each year)

Figure 4. Type of Prescribing Physician at Baseline



PCP = primary care physician.

Figure 5. Percentage of Enrolled Patients Meeting Full Eligibility Criteria at Baseline

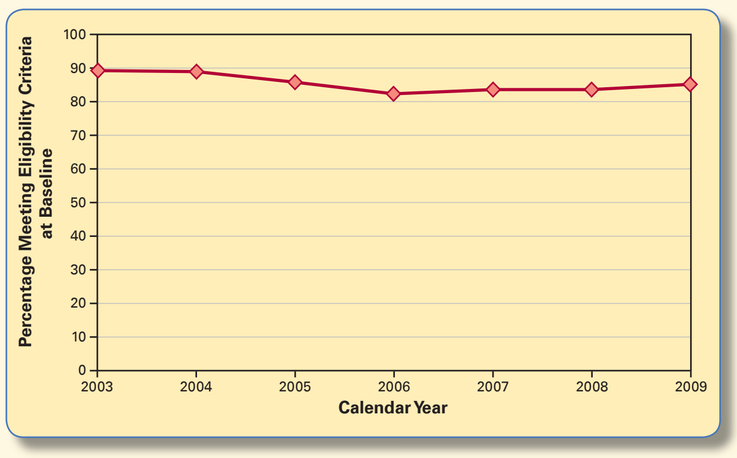


Figure 6. Number of Severity Criteria Met Among Patients Classified As Meeting Full Eligibility Criteria

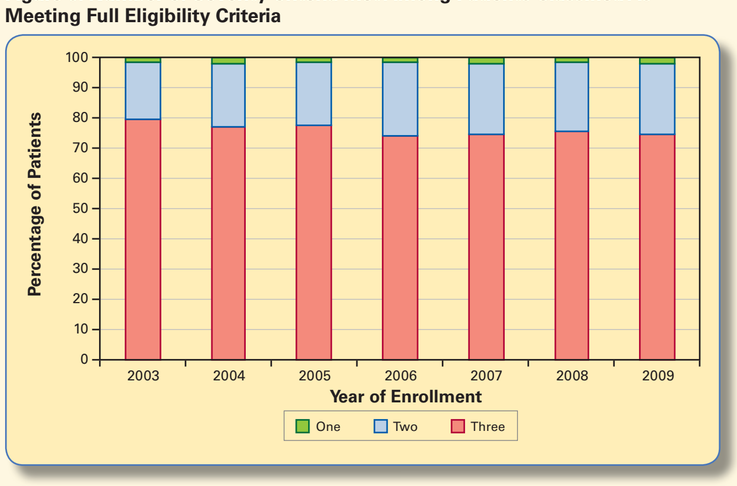


Figure 7. Compliance With RMP Elements at Baseline, Cumulative Over Entire Study Period

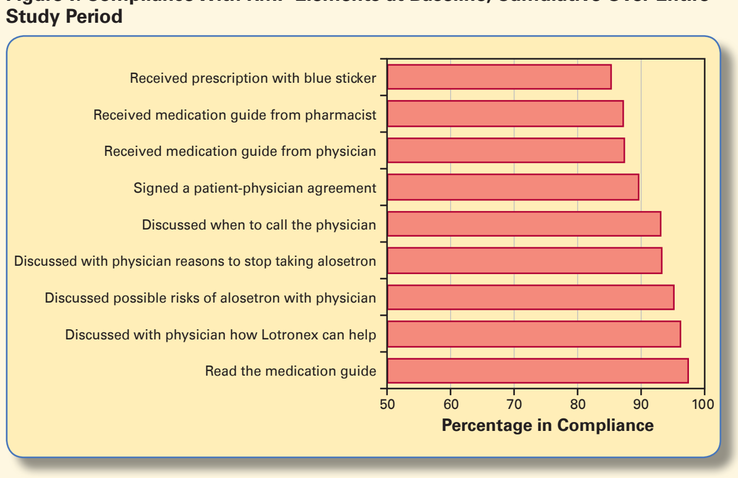
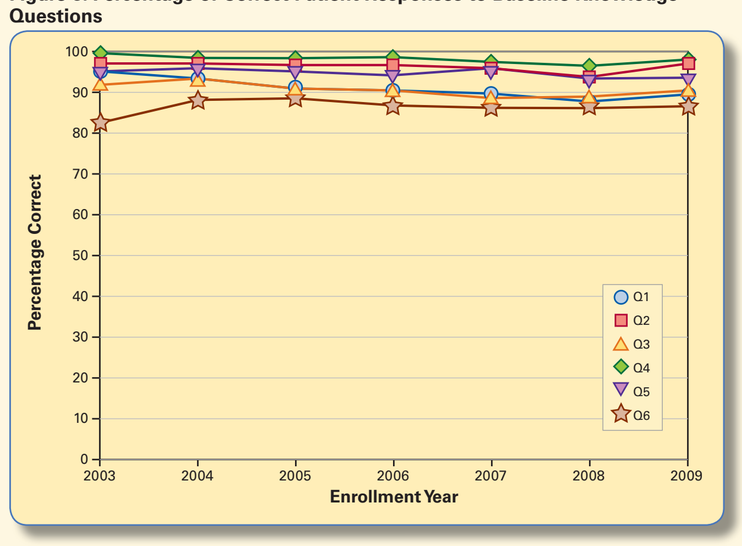


Table 1. Dose at Baseline Stratified by Year of Enrollment

Dosage	2003 (%)	2004 (%)	2005 (%)	2006 (%)	2007 (%)	2008 (%)	2009 (%)
Two (1 mg) per day	68	53	37	33	29	17	9
One (1 mg) as needed	0	4	5	2	3	2	1
One (0.5 mg) per day	0	15	23	24	24	31	33
Two (0.5 mg) per day	0	2	20	27	28	44	51
One (0.5 mg) as needed	0	1	1	0	2	1	1
Other	32	25	14	14	14	6	5

Figure 8. Percentage of Correct Patient Responses to Baseline Knowledge Questions



Correct Answers to Multiple Choice Questions

Q1. New or worsening pain in the bowels is a sign that a patient could be experiencing a serious problem related to alosetron.

Q2. If a patient experiences new or worsening pain in the bowels, the best action to take is to stop taking alosetron and call physician.

Q3. Blood in the stool is a sign that a patient could be experiencing a serious problem related to alosetron.

Q4. If there is blood in the stool, the best action to take is to stop taking alosetron and call physician.

Q5. Constipation is a sign that a patient could be experiencing a serious problem related to alosetron.

Q6. If a patient becomes constipated, the best action to take is to stop taking alosetron and call physician.

DISCUSSION

- Temporal trends in reported responses at baseline are very useful for understanding the characteristics of patients and compliance with the efforts to minimize patient risk.
- Since inception of the alosetron RMP, most participants in the study have consistently met eligibility criteria over time.
- Among participants, patient-reported awareness of and compliance with aspects of the RMP was high across all years of the RMP.
- Patient understanding of safety messages in the medication guide has been consistently high (> 82% for each question) every year of the RMP. Of the participating patients, more are now reporting that they are being prescribed alosetron by gastroenterologists (72% in 2003 vs. 92% in 2009).
- The proportion of alosetron patients who enrolled in the program was higher in the first 3 years than in subsequent years. This may be attributed to reduced efforts over time by physicians to encourage patients to participate in the program.
- The percentage of patients meeting all three severity criteria has decreased somewhat over time (80% to 75% of eligible patients). This decrease is at least partially related to the corresponding increase in prescribing of alosetron by gastroenterologists, who are more likely to possess greater familiarity and comfort with the clinical requirements of treating patients with alosetron. However, the majority of patients prescribed alosetron still meet all three severity criteria.

LIMITATIONS

- Study patients may not necessarily represent all users of alosetron. However, we identified no data to suggest that they do not. Comparisons of participants with national prescription data show similar distributions of age, sex, geographic region, and specialty of prescribers. Enrollment through cards provided via prescriptions was high (~ 50%) throughout the study. Thus, it appears that participation may have been high regardless of physician compliance (although there was no quantitative evaluation of this).
- Response rates are estimated from prescription data, from which new starts of alosetron can be a challenge to estimate nationally.
- By design, this study uses a passive recruitment process. Thus, the sample population is unknown until the patients initiate contact with the program.
- All questionnaire data are self-reported by patients and not confirmed by their physicians.

STRENGTHS

- The program provides real-time monitoring of RMP compliance through the experience of the patients.
- The program has now been evaluated for over 7 years and suggests consistent effectiveness of and compliance with the RMP over time.

CONCLUSIONS

The study demonstrated high compliance and little variation in compliance with the RMP among participants in the cohort study over the 7 years since initiation.

REFERENCES

1. Tennis P, Andrews E, Hickman P, Miller D, Hollis K, Cook S. The relationship between dosing of alosetron and discontinuation patterns reported by patients participating in a follow-up programme. Aliment Pharmacol Ther. 2007;25:317-22
2. Miller D, Bennett L, Hollis K, Tennis P, Andrews E. A patient follow-up survey programme for alosetron: assessing compliance to and effectiveness of the risk management program me. Aliment Pharmacol Ther. 2006;24:869-78

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