T1064 ONE-YEAR TREATMENT CONTINUATION WITH ALOSETRON IS HIGH IRRESPECTIVE OF IBS-D SEVERITY CRITERIA

Jean Paul A. Nicandro,[1] Pat Tennis,[2] Paul Shin,[1] Peter Hickman,[2] Lee Bennett,[2] Kelly Hollis,[2] Elizabeth Andrews[2]

[1]Clinical & Medical Affairs, Prometheus Laboratories Inc., San Diego, CA; [2]Pharmacoepidemiology & Risk Management, RTI Health Solutions, Research Triangle Park, NC.

INTRODUCTION

- Alosetron is a potent and selective 5-hydroxytryptamine type 3 (5HT3) receptor antagonist.
- Pharmacologic actions of alosetron at 5HT3 receptors modulate processes related to the pathophysiology of IBS, such as decreasing abdominal pain from visceral hypersensitivity, slowing colonic transit, and reducing gastrointestinal secretions.
- Treatment with alosetron has been associated with improvements in quality of life, productivity, and treatment satisfaction.
- Alosetron was reintroduced in Nov 2002 for treatment of female patients with severe, chronic diarrhea-predominant irritable bowel syndrome (IBS-D), under a Risk Management Program (RMP) intended to assure safe use of alosetron.
- A key component of the RMP is the Patient Follow-Up Study.
- The aim of this analysis was to evaluate characteristics and treatment patterns of female patients with chronic IBS-D from the alosetron Patient Follow-Up Study stratified by patient-reported severity criteria met.

METHODS

Patient Follow-Up Study

- Data were collected from an ongoing postmarketing study (Figure 1) conducted by RTI Health Solutions and Prometheus Laboratories Inc.[1,2]
- The study was designed to evaluate and monitor:
  - Characteristics of patients treated with alosetron.
  - Trends in treatment patterns (patient use, physician prescribing).
  - Patient knowledge of risks/benefits of treatment.
- Provides long-term data on alosetron therapy in the clinical practice setting.

Study Population

- All alosetron patients enrolled in the Patient Follow-Up Study from Nov 2002 to Jun 2009.
- Analyses were limited to enrolled patients who fulfilled the following FDA-approved prescribing criteria:
  - Female with chronic IBS-D (≥6 months).
  - Reported at least one of three of the following severity criteria:
    - Painful stomach cramps/bloating.
    - Accidents or fecal incontinence.
    - Experienced restricted activities of daily living such as difficulty in leading normal home/work or social life.

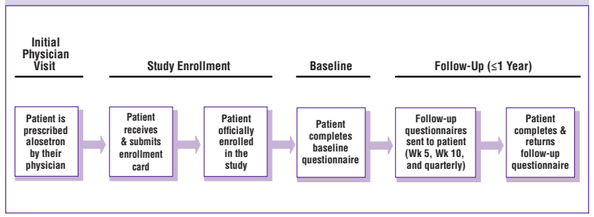
Study Surveys and Questionnaires

- Assessed alosetron dosage, treatment, and knowledge of risks/benefits.
- Administered at baseline and predefined time points during follow-up (Figure 1).
- IBS history, symptoms, IBS impact on activities of daily living, prior treatment(s), alosetron dosage, prescribing program for Lotronex (PPL) requirements, and physician interaction were assessed.

Statistical Analysis

- All categorical variables were described as counts and percentages, and continuous variables were summarized by mean, median, standard deviation, minimum, and maximum.
- Percentages describing patient characteristics do not include missing responses in the denominator; all analyses were performed using SAS for Windows statistical software (Cary, NC).
- To account for loss to follow-up, percentage discontinuation at specified timepoints was estimated with Kaplan Meier survival methods, with discontinuation as the outcome of interest.
- P-values are based on log-rank tests of equality between any of the three IBS-D severity groups.

Figure 1. Patient Follow-Up Study

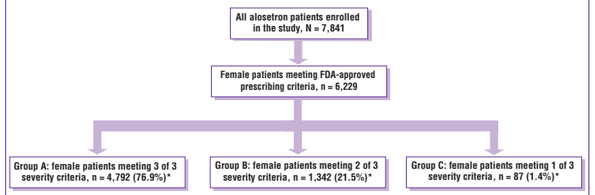


RESULTS

Patient Follow-Up Study

- Overall, a total of 7,841 patients enrolled in the study as of June 30, 2009 (Figure 2).
  - Distribution of Females/Males: F 92.4%; M 7.6%.
  - Mean follow-up time: 312.6 ± 231.8 days (10.3 months).
  - 1-year completion rate: 50.3% (n = 3,952 patients).
- Of enrolled female patients, 87.8% met FDA-approved prescribing criteria (n = 6,229).
  - In female patients meeting label criteria, the majority of patients (76.9%) reported experiencing all three IBS-D severity symptoms (Figure 2).
  - Most female patients reported trying other IBS-D therapies that did not provide adequate relief (Figure 3).
- Baseline demographics (Table 1).
  - Patients in Groups A and B were most similar in characteristics.
  - Compared with Groups A/B, patients in Group C generally:
    - Evenly distributed across age categories.
    - Attained higher level of education.
    - Less likely to be prescribed alosetron by gastroenterologists.
    - Less likely to be obese (BMI ≥30 kg/m2).

Figure 2. Stratification by IBS-D Severity Criteria

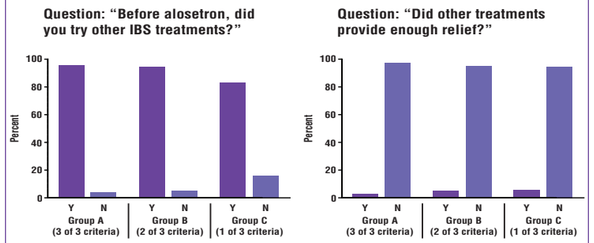


*Patients in Groups A, B, and C do not total 100% as some patients did not complete questionnaires. Denominator = 6,229.

Table 1. Baseline Demographics

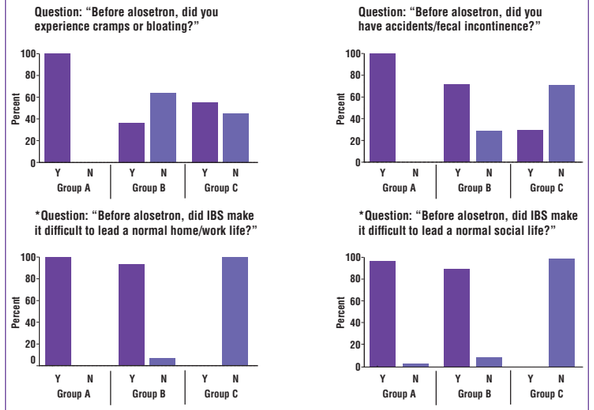
Characteristic	IBS-D Severity Groups			All Groups	All Patients
	Group A (%) (n = 4,792)	Group B (%) (n = 1,342)	Group C (%) (n = 87)	(%) (n = 6,229)	(%) (N = 7,841)
Age (yr)					
<18	0.3	0.5	0.0	0.3	0.4
18-44	32.7	27.6	34.4	31.6	31.3
45-64	50.1	47.3	37.9	49.3	48.5
≥65	17.0	24.8	27.5	18.8	19.8
Race					
Caucasian	96.1	96.0	92.8	96.0	95.6
Non-Caucasian	3.9	4.0	7.2	4.0	4.4
Attained some college education or higher	71.1	73.6	82.8	71.8	72.0
Alosetron prescribed by gastoenterologist	78.6	77.5	72.3	78.3	78.6
BMI ≥30 kg/m2	29.1	23.4	17.9	27.7	27.4

Figure 3. Responses to Baseline Pretreatment Questions (n = 6,229)



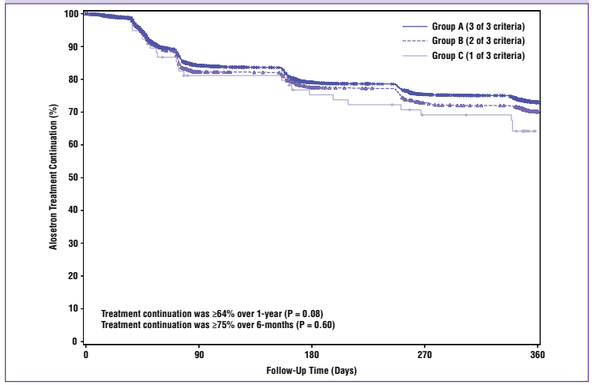
- Patients in Groups A and B had similar responses to IBS-D severity questions (Figure 4):
  - In Group A, ≥98% of patients responded positively to all IBS-D severity questions.
  - In Group B, ≥71% of patients responded positively to IBS-D severity questions, except for cramps and bloating, where the majority (64%) of patients did not experience the symptom.
- In Group C, only cramps and bloating were experienced by the majority (55%) of patients (Figure 4).
  - None reported difficulty with daily activities (home/work, social).

Figure 4. Comparison of Responses to Baseline IBS-D Severity Questions (n = 6,229)



*Yes response to either or both of these questions represented a restriction of daily living.

Figure 5. Treatment Continuation with All Alosetron Groups was ≥64% Over 1-Year



- The most common alosetron dosages at treatment initiation, maintenance, and discontinuation were 1 mg QD and 1 mg BID.
  - <10% of patients used other dosages.
  - The majority of patients were prescribed 1 mg QD at treatment initiation.
  - After initiation, some patients titrated up from lower dosages to 1 mg BID.

CONCLUSIONS

- Analysis provides key insights into real-world use of alosetron in clinical practice:
  - In patients meeting FDA-approved prescribing criteria, one-year treatment continuation with alosetron was high (≥64%) among all three groups.
  - Despite key differences in IBS-D symptoms reported at baseline, high treatment continuation suggests female patients with IBS-D are experiencing long-term benefits of alosetron.
  - Inadequate response to other IBS-D therapies was a prominent characteristic of female patients treated with alosetron.
- Alosetron appears to be predominantly prescribed to the most severe subset of female patients with IBS-D (Group A), which may be driven by:
  - Lack of education on alosetron risks/benefits provided to physicians (gastroenterologists, PCPs) and patients.
  - Negative perceptions of alosetron by physicians and/or their patients.
- Consistent with previous observations[1], participating patients report safe use of alosetron:
  - Most alosetron patients fulfilled FDA-approved prescribing criteria.

REFERENCES

1. Miller D, Bennett L, Hollis K, et al. A patient follow-up survey programme for alosetron: assessing compliance to and effectiveness of the risk management programme. *Aliment Pharmacol Ther.* 2006;24(5):869-878.
2. Tennis P, Andrews E, Hickman P, et al. The relationship between dosing of alosetron and discontinuation patterns reported by patients participating in a follow-up programme. *Aliment Pharmacol Ther.* 2007;25(3):317-322.