

# A Pilot Study of the Efficacy and Tolerability of AST-120 in the Treatment of Active Pouchitis

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## Background

Bacterial overload and associated bacterial toxins, as well as increased production of deconjugated bile acids are speculated to play an important role in the pathogenesis of acute pouchitis. While the majority of patients with pouchitis respond favorably to antibiotic therapy, many relapse frequently and non-absorbable and non-antibiotic-based agents are desirable to reduce bacterial resistance and systemic adverse effects associated with long-term antibiotic exposure. AST-120, an oral adsorbent licensed to Ocera Therapeutics, San Diego, CA, is comprised of highly adsorptive, porous, carbon microspheres with the ability to adsorb small molecular weight toxins, inflammatory mediators, and harmful bile acids. The aim of this pilot study was to evaluate efficacy and tolerability of AST-120 in the treatment of active pouchitis.

## Methods

### Study Protocol:

Open-label study in which all eligible patients received AST-120 in 2g sachets (oral) tid for 4 weeks.

Eligible patients were recruited from a subspecialty Pouchitis Clinic.

### Endpoints

The primary efficacy endpoint was remission as defined by a PDAI score < 7 points; the main secondary endpoint was clinical response, defined by a reduction in PDAI score of > 3 points. Cleveland Global Quality of Life (range 0 - 1 with one being the best) and Short Inflammatory Bowel Disease Questionnaire (range 0 - 70, with 70 being the best) were also assessed before and after the trial.

### Key Inclusion Criteria:

1. Ileal pouch-anal anastomosis performed after colectomy for ulcerative colitis;
2. Active pouchitis with Pouchitis Disease Activity Index (PDAI) scores > 7 points;
3. Discontinuation of antibiotic therapy for at least 2 weeks;

## Results

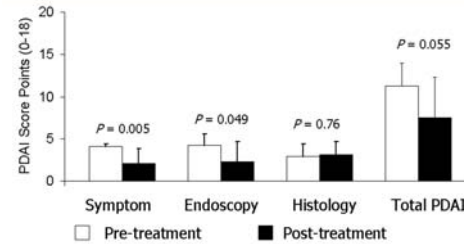


Figure 1. Pre- and post-therapy Pouchitis Disease Activity Index (PDAI) Subscores and Total Scores

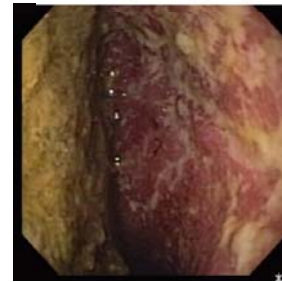


Figure 1A. Active Pouchitis Before AST-120

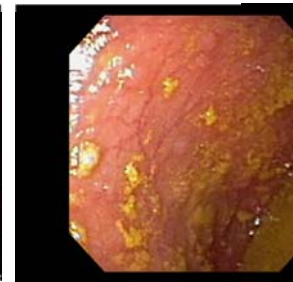


Figure 1B. Resolved Pouchitis After a 4-Week Course of AST-120

### Key Exclusion Criteria:

1. Patients previously treated with infliximab or any investigational immunomodulator;
2. Patients whose medical condition would not allow a 4 week treatment without antibiotics, probiotics, and nutritional agents;
3. Patients undergoing chemotherapy for the treatment of cancer;
4. Crohn's disease of the pouch, including inflammatory, fibrostenotic, or fistulizing phenotypes, based on the previously established diagnostic criteria (Shen B, et al. Am J Gastroenterol 2006 in press);
5. Active specific infection of the pouch: CMV, infection, C. difficile infection;
6. History of non-inflammatory disease of the pouch: decreased pouch compliance, irritable pouch syndrome, afferent or efferent limb obstruction;
7. Isolated Cuffitis;
8. Strictures of the pouch inlet or outlet;
9. Ileal pouch patients with familial adenomatous polyposis, known Celiac Disease, Primary Sclerosing Cholangitis (PSC) with or without liver transplant; PSC with or without Actigall or Urso therapy;
10. History of lactose intolerance;
11. Needing oral or topical steroid treatment or 5-ASA agents;
12. Active use of cholestyramine, NSAIDs or aspirin;

- A total of 10 patients were enrolled in the first cohort: 9 completed the trial. One patient dropped out due to a viral upper respiratory infection 2 days after entry.
- Demographic and clinical data for the 9 patients are listed in Table 2.
- Of the 9 patients, 4 (44.4%) had clinical remission (PDAI < 7) and 5 (55.6%) achieved clinical response (reduction in PDAI > 3 points).
- AST-120 effect on the different components of the PDAI score are illustrated in Figure 1.
- There was numerical, but not statistically significant, improvement in quality of life scores. The pre- vs. post- Cleveland Global Quality of Life scores were  $0.58 \pm 0.19$  and  $0.59 \pm 0.20$ , respectively ( $P = 0.924$ ). The pre- and post- Short Inflammatory Bowel Disease Questionnaire scores were  $42.1 \pm 12.1$  and  $44.7 \pm 10.3$ , respectively ( $P = 0.63$ ).
- The agent was well tolerated; one patient had transient mild elevation of alkaline phosphatase.

Table 2. Demographic and Clinical Data (N = 9)

Characteristics	Value
Age, yrs SD	48.6 ± 10.0
Gender F: M	3:6
Family history of IBD	4 (44.4%)
Active smoker	1 (11%)
Ex-smoker	4 (44.4%)
Preoperative diagnosis- UC vs. indeterminate colitis	7:2
Pancolitis vs. left-side colitis	8:1
Indication for colectomy-Refractory disease vs. dysplasia	6:3
Stage of pouch surgery- 1 vs. 2 vs. 3 or more	1:1:7
J pouch vs. S pouch	8:1
Duration IBD (from diagnosis of IBD to data entry), yrs	16.5 ± 8.3
Duration of the pouch, yrs	6.8 ± 4.6

## Conclusions

A 4 week treatment with AST-120 in patients with active pouchitis led to a significant decrease in symptoms of pouchitis and endoscopy scores. AST-120 was well tolerated. 44.4% of the patients achieved clinical remission and 55.6% achieved a clinical response warranting further evaluation of AST-120 for treatment of pouchitis in controlled randomized studies.

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