POSTER NUMBER

P037

Efficacy and Safety of 1-L NER1006 Bowel Preparation in Patients With Inflammatory Bowel Disease: Analysis of 2 Phase 3 Studies

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INTRODUCTION

- Patients with inflammatory bowel disease (IBD) are at increased risk for development of dysplasia and colon cancer; therefore, screening/surveillance colonoscopy at guideline-recommended intervals is important[1]
- Adequate bowel preparation is critical for effectiveness of colonoscopy, including visualization of the cecum[2]
- NER1006 (Plenvu®, Salix Pharmaceuticals, Bridgewater, NJ), a 1-L polyethylene glycol (PEG)-based bowel preparation, is indicated in the United States for colon cleansing in preparation for colonoscopy in adults[3]
- The efficacy and safety of NER1006 bowel preparation using US Food and Drug Administration-approved dosing (2-day evening/morning [PM/AM] split dosing or 1-day morning [AM/AM] of colonoscopy split dosing) were demonstrated in two randomized, phase 3 studies (NOCT and MORA)[4,5]

OBJECTIVE

- The current post hoc data analysis was conducted to assess the efficacy and safety of 1-L NER1006 in an adult population who received this bowel preparation prior to colonoscopy, subgrouped by IBD diagnosis

METHODS

Study Design and Patients

- A pooled post hoc analysis was conducted of two phase 3, randomized, controlled, multicenter studies of adults undergoing screening, surveillance, or diagnostic colonoscopy (NOCT and MORA)[4,5]
- Adults (aged 18–85 years) undergoing colonoscopy were randomly assigned to NER1006 as a 2-day evening/morning (PM/AM) or 1-day morning/morning (AM/AM) split-dosing regimen (**Figure 1**)

Figure 1. NER1006 Bowel Preparation Dosing Regimens*[4,5]

	Day Before Colonoscopy	Day of Colonoscopy
NOCT	NER1006 (PM/AM) Dose 1: 6:00 PM	NER1006 (PM/AM) Dose 2: 6:00 AM
MORA	NER1006 (PM/AM) Dose 1: 6:00 PM	NER1006 (PM/AM) Dose 2: 6:00 AM
		NER1006 (AM/AM) Dose 1: 5:00 AM Dose 2: 7:00 AM

*The regimens allowed a light breakfast and light lunch on day before colonoscopy; in addition, for AM/AM dosing regimen, dinner of clear broth soup and/or plain yogurt was allowed. Administration of each dose was within (±) 2 hours of times indicated. The comparator arms of NOCT/MORA (oral sulfate solution/2 L polyethylene glycol plus ascorbate) were not included in the current analyses.

METHODS

- Minimum total NER1006 volume requirements were 64 oz, plus clear liquids ad libitum
- Patients with ongoing severe, acute IBD were excluded from the studies

Assessments

Efficacy

- Colon cleansing was assessed by independent, treatment-blinded central readers
- Two primary endpoints of the studies were overall bowel cleansing success rate and ascending colon/cecum high-quality cleansing rate[4,5] using the validated Harefield Cleansing Scale (HCS)[6]
  - Overall cleansing success was defined as HCS grade A/B (score of 3 or 4 [ie, clear liquid/empty and clean] in all 5 colonic segments or ≥1 segment scored as 2 [ie, brown liquid/removable semi-solid stools] and other segments scored as 3 or 4)[6]
  - High-quality cleansing in the ascending colon/cecum was defined as an HCS score of 3 or 4[4-6]
- Efficacy population: all randomly assigned patients excluding those who failed to meet entry criteria post-randomization and did not receive any study drug, confirmed per patient diary (modified full analysis set)

Safety

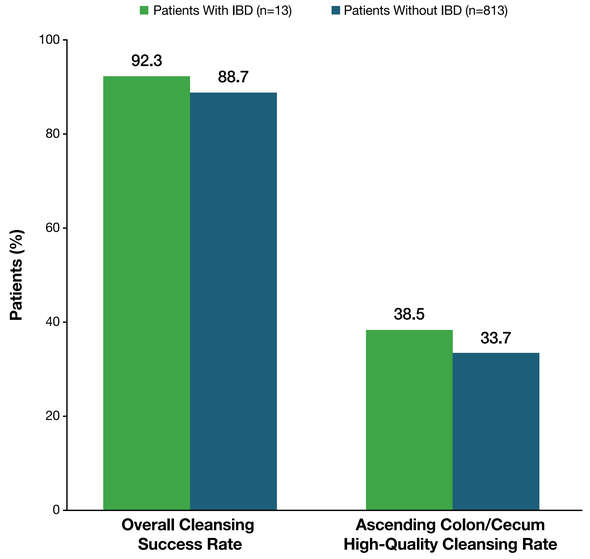
- Safety was determined through 7 ± 1 days post-colonoscopy
- Assessments included adverse event (AE) reporting, clinical laboratory evaluations, vital sign measurements, and physical examinations
  - Urinalysis and electrocardiogram were performed at screening and on the day of colonoscopy
- Safety population: all randomly assigned patients in whom it could not be ruled out that they received ≥1 dose of NER1006 (per patient diary)

RESULTS

- 13 patients with a medical history of IBD and 813 patients without a medical history of IBD were included in the efficacy analysis
  - The majority of patients with and without IBD received a NER1006 2-day split-dose regimen (61.5% and 66.8%, respectively)
- Overall cleansing success was achieved in 92.3% (12/13) of patients with IBD and 88.7% (721/813) of patients without IBD; high-quality cleansing of the ascending colon/cecum was observed in 38.5% (5/13) and 33.7% (274/813) of patients with and without IBD, respectively (**Figure 2**)

RESULTS

Figure 2. Overall Cleansing Success* and High-Quality Cleansing† of the Ascending Colon/Cecum in Patients With or Without IBD



*HCS grade A or B (score of 3 or 4 [ie, clear liquid/empty and clean] in all 5 colonic segments or score of 2 [ie, brown liquid/removable semi-solid stools] for ≥1 segment with a score of 3 or 4 for remaining segments).
†HCS score of 3 or 4 in the ascending colon/cecum.
HCS = Harefield Cleansing Score; IBD = inflammatory bowel disease.

- The safety population included 12 patients with IBD, based on post-colonoscopy diagnosis, and 781 patients without IBD (**Table**)
  - The most common AE in patients without IBD was nausea (6.0%)
  - 1 patient with IBD (NER 1006 1-day split-dose group) experienced a treatment-related AE (mild vomiting), which did not result in study discontinuation
  - 1 patient without IBD, also in the 1-day split-dose group, experienced a treatment-related AE that resulted in study discontinuation (moderate vomiting)

Table. Safety Profile

Parameter, n (%)	Patients With IBD (n=12)	Patients Without IBD (n=781)
Any AEs	1 (8.3)	166 (21.3)
Any drug-related AEs	1 (8.3)	109 (14.0)
AEs leading to discontinuation	0	1 (0.1)
Serious AEs*	0	3 (3.8)*
Drug-related serious AEs	0	0
Deaths	0	0
Most common AEs		
Nausea	0	47 (6.0)
Vomiting	1 (8.3)	44 (5.6)
Dehydration	0	13 (1.7)
Headache	0	11 (1.4)
Other AEs of interest		
Decreased GFR	0	5 (1.7)
Thirst	0	7 (0.9)

*Alcohol abuse (n=1), ileus (n=1), and procedural intestinal perforation (n=1).
AE = adverse event; GFR = glomerular filtration rate; IBD = inflammatory bowel disease.

CONCLUSIONS

- **Data support the overall efficacy and safety profile of 1-L PEG-based NER1006 bowel preparation in patients with IBD**
- **Future studies in patients with IBD are warranted, as thorough evaluation of the colonic mucosa is essential to assess disease activity, for the detection of polyps and other lesions, and for dysplasia surveillance**

REFERENCES: **1.** Shergill AK, et al. *Gastrointest Endosc.* 2015; 82:529-537 e521. **2.** Rex DK, et al. *Gastrointest Endosc.* 2015; 81:31-53. **3.** Plenvu® (polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride and potassium chloride for oral solution) [package insert]. Amsterdam, The Netherlands: Norgine BV; 2019. **4.** DeMicco MP, et al. *Gastrointest Endosc.* 2018;87(3):677-687. **5.** Bisschops R, et al. *Endoscopy.* 2019;51(1):60-72. **6.** Halphen M, et al. *Gastrointest Endosc.* 2013; 78:121-131.

ACKNOWLEDGMENTS: The phase 3 studies were supported by Norgine BV and current analyses were supported by Salix Pharmaceuticals. Medical writing and technical editorial assistance were provided under direction of the authors by Mary Beth Moncrief, PhD, and Sophie Bolick, PhD, Synchrony Medical Communications, LLC, West Chester, PA. Funding for this assistance was provided by Salix Pharmaceuticals.

DISCLOSURES: DMP reports being a consultant for Ambu, Inc., Olympus Inc., and Salix Pharmaceuticals. CO reports being a consultant for AbbVie Inc. and Salix Pharmaceuticals. CA is an employee of Salix Pharmaceuticals. CGA reports being on the speakers' bureau for Salix Pharmaceuticals.

Research funded by: Salix Pharmaceuticals