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Comparative Assessment of Bowel Cleansing of 1 L Polyethylene Glycol Plus Ascorbate NER1006 Compared With 2 L Polyethylene Glycol Plus Ascorbate: A Phase 3, Randomized, Multicenter Trial

Michael S. Epstein, MD[1]; Raf Bisschops, MD, PhD[2]; Zeev Heimanson, PharmD[3]; Bharat Amlani, BPharm[4]; Prateek Sharma, MD[5]

[1]Digestive Disorders Associates, Annapolis, MD, USA; [2]KU Leuven, University Hospitals Leuven, Leuven, Belgium; [3]Salix Pharmaceuticals, Bridgewater, NJ, USA; [4]Norgine Ltd, Harefield, UK; [5]Veterans Affairs Medical Center and University of Kansas, Kansas City, KS, USA

INTRODUCTION

- High-quality colon cleansing before colonoscopy is important for maximizing detection of sessile serrated lesions; they are particularly harder to visualize in the ascending (right) colon where they may occur at a greater frequency than the rest of the colon[1,2]
- Many polyethylene glycol (PEG)-based bowel preparations require large volumes for dosing; recent research has focused on reducing such volume requirements while maximizing colon cleansing efficacy and tolerability[3,4]
- NER1006 (Plenvu®, Norgine Ltd, Hengoed, UK), the first 1 L PEG-based bowel preparation approved for bowel cleansing as a preparation for colonoscopy in adults in the United States[5] and in at least 21 European countries, is a combination of two different formulations, with a low preparation volume, optimized for effective bowel preparation and favorable taste[6]
  - Three multicenter, randomized, phase 3, active-controlled, non-inferiority studies (2 conducted in Europe [MORA and DAYB] and 1 in the United States [NOCT]) have demonstrated the efficacy and safety of NER1006 versus other bowel preps (2 L PEG plus ascorbate,[7] sodium picosulfate with magnesium citrate,[8] and oral sulfate [trisulfate] solution[6]) in patients undergoing colonoscopy

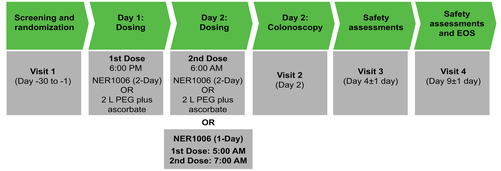
AIM

- Post hoc analysis to further evaluate the efficacy of NER1006 compared with 2 L PEG plus ascorbate bowel preparations in adults undergoing colonoscopy

METHODS

- Post hoc analysis of a phase 3, randomized, colonoscopist/central reader-blinded, noninferiority trial (MORA)
- Adults (18-85 y) undergoing colonoscopy were randomly assigned (1:1) to receive (Figure 1):
  - Evening/morning split dose of NER1006 or
  - Morning-only split dose of NER1006 (ie, 2 morning doses) or
  - Evening/morning split dose of 2 L PEG plus ascorbate (2 L PEG [MoviPrep®, Norgine Limited, Hengoed, UK])

Figure 1. MORA Study Design



EOS = end of study; PEG = polyethylene glycol.

METHODS

Assessments

- Bowel cleansing efficacy was assessed using the segmental scoring component of the Harefield Cleansing Scale (HCS; score of 0-4 for 5 segments of the colon) and overall colon and right colon Boston Bowel Preparation Scale scores (BBPS; score of 0-3 for 3 segments of the colon with a maximum overall score of 9; Table 1)

Table 1. Harefield Cleansing Scale and Boston Bowel Preparation Scale[9,10]

Score	Harefield Cleansing Scale*	Boston Bowel Preparation Scale†
0	Irremovable, heavy, hard stools	Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared
1	Semi-solid, only partially removable stools	Portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen due to staining, residual stool, and/or opaque liquid
2	Brown liquid/fully removable semi-solid stools	Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well
3	Clear liquid	Entire mucosa of colon segment seen well with no residual staining, small fragments of stool, or opaque liquid
4	Empty and clean	—

*5 segments scored: ascending colon (right colon), transverse colon, descending colon, sigmoid colon, and rectum.
†3 broad regions of the colon scored: right colon (includes ascending colon and cecum), transverse colon (includes hepatic and splenic flexures), and left colon (includes rectum, sigmoid colon, and descending colon).
Data from Halpen M, et al. *Gastrointest Endosc.* 2013;78(1):121-131 and Lai EJ, et al. *Gastrointest Endosc.* 2009;69(3 Pt. 2):620-625.[10]

- Analysis included patients who were randomly assigned to treatment who had readable colonoscopy videos for blinded central readers, excluding those who failed screening or had diary confirmation that they did not take any study drug
- Wilcoxon rank-sum test was used to compare treatment groups

RESULTS

- A total of 792 patients were included in the current analysis (Table 2)

RESULTS

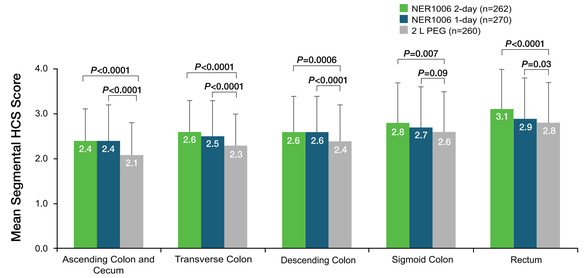
Table 2. Patient Demographics and Baseline Characteristics

Characteristic	NER1006 2-Day (n=262)	NER1006 1-Day (n=270)	2 L PEG (n=260)
Age, y, mean (SD)	56.6 (11.9)	54.8 (13.2)	54.3 (12.7)
≤65 y, n (%)	192 (73.3)	210 (77.8)	214 (82.3)
Male, n (%)	108 (41.2)	125 (46.3)	137 (52.7)
Race, n (%)			
White	256 (97.7)	267 (98.9)	257 (98.8)
Black	5 (1.9)	3 (1.1)	1 (0.4)
Other	1 (0.4)	0 (0)	2 (0.8)
BMI, kg/m^2*			
Mean (SD)	27.3 (4.8)	26.9 (4.3)	26.4 (4.2)
Median (range)	26.8 (16.4-46.5)	26.7 (16.2-40.6)	26.2 (16.9-40.3)
Reason for colonoscopy, n (%)			
Screening	134 (51.1)	137 (50.7)	129 (49.6)
Surveillance	63 (24.0)	57 (21.1)	60 (23.1)
Diagnostic	65 (24.8)	76 (28.1)	71 (27.3)

n=261 for NER1006 2-day group and n=258 for 2 L PEG group.
BMI = body mass index; PEG = polyethylene glycol; SD = standard deviation.

- Both NER1006 2-day and 1-day split dosing provided significantly higher (ie, better) mean HCS scores for nearly all 5 segments of the colon versus 2 L PEG plus ascorbate, including the right colon (ascending colon plus cecum; Figure 2)

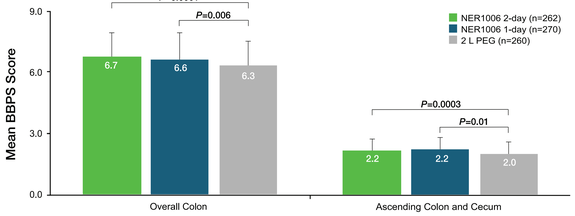
Figure 2. Mean HCS Scores by Colon Segment



Error bars represent standard deviation.
HCS = Harefield Cleansing Scale; PEG = polyethylene glycol.

- Significantly higher (ie, better) mean BBPS scores for the overall colon were observed with NER1006 2-day versus 2 L PEG (P=0.0001) and NER1006 1-day versus 2 L PEG (P=0.006; Figure 3)

Figure 3. Mean BBPS Scores for the Overall Colon and in the Ascending Colon/Cecum



Error bars represent standard deviation.
BBPS = Boston Bowel Preparation Scale; PEG = polyethylene glycol.

- Significant differences favoring NER1006 dosing regimens versus 2 L PEG were also observed for the mean BBPS scores for the ascending colon/cecum (right colon): 2 L PEG versus NER1006 2-day (P=0.0003) and NER1006 1-day (P=0.01; Figure 3)

CONCLUSIONS

- **Evening/morning split dosing and morning-only split dosing of the low-volume bowel preparation NER1006 provided significantly better colon cleansing overall and within various segments of the colon compared with 2 L PEG plus ascorbate in adults undergoing colonoscopy**
- **Improved ascending colon/cecum cleansing with NER1006 may help with detection of sessile serrated lesions, which requires high-quality bowel preparation[1]**

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DISCLOSURES: ME reports having participated as an investigator for Norgine Ltd.; serving as a consultant for Aspire Bariatrics and IM HealthScience; and serving on the speakers' bureau for Daiichi Sankyo, Pfizer, and Synergy Pharmaceuticals Inc. RB reports having participated as an investigator for Norgine Ltd; receiving honoraria from Norgine for speaking engagements; and participating on the Norgine advisory board. ZH reports being an employee of Salix Pharmaceuticals. BA reports being an employee of Norgine Ltd. PS has no disclosures to report.

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