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One-Liter NER1006 Is Efficacious as a Bowel Preparation for Colonoscopy in Patients Taking Concomitant Medications Known to Impact Prep Quality

David Poppers, MD, PhD[1]; Brooks D. Cash, MD[2]; David Bloom, RPh[3]; Christopher Allen, MS[3]; Prateek Sharma, MD[4]

[1]NYU Langone Health, New York, NY; [2]University of Texas Health Science Center at Houston, Houston, TX; [3]Salix Pharmaceuticals, Bridgewater, NJ; [4]University of Kansas School of Medicine and VAMC, Kansas City, KS

INTRODUCTION

- A high-quality tolerable bowel preparation is a critical component of successful colonoscopy, and an inadequate prep may lead to cecal intubation failure and missed lesion detection[1-3]
- Patient-specific factors such as medication use (eg, opioids, tricyclic antidepressants [TCAs]) can negatively impact bowel preparation quality[4,5]
  - Opioids may reduce bowel prep quality by decreasing motility directly, via opioid-receptor–mediated effects within the myenteric plexus, and indirectly, via centrally mediated sympathetic activation of alpha-2 receptors in the enteric nervous system[4]
  - The anticholinergic effects of TCAs may adversely affect bowel prep quality via blockade of enteric muscarinic receptors, resulting in a reduction in gastrointestinal motility[4]
- NER1006 is a low-volume (1L) polyethylene glycol (PEG)-based bowel prep (Plenvu®, Norgine Ltd, Tir-y-Berth, Hengoed, United Kingdom) indicated for colon cleansing in preparation for colonoscopy in adults[6]
  - NER1006 was efficacious and well tolerated in two randomized, phase 3 trials (NOCT[7] and MORA[8]) that evaluated the US Food and Drug Administration approved split-dosing regimens (2-day evening/morning [PM/AM] or 1-day morning/morning [AM/AM])
- Given that concurrent treatment with opioids and/or TCAs is a risk factor for inadequate bowel prep, a post hoc analysis of two NER1006 phase 3 trials was conducted to assess the cleansing quality of NER1006 vs 2L PEG plus ascorbate (2L PEG) in patients taking these concomitant medications

AIM

- To evaluate the efficacy of 1L NER1006 vs 2L PEG in patients stratified by use of concomitant medications that can adversely impact bowel prep quality

METHODS

- Data were pooled from two phase 3, randomized, noninferiority trials in adults aged 18–85 years undergoing colonoscopy who were randomly assigned to the PM/AM split-dose regimen of:
  - NER1006 (NOCT)
  - NER1006 or 2L PEG (MORA)
- Patients were stratified by concomitant use of opioid analgesics and/or TCAs, and data were analyzed post hoc
  - A concomitant medication was defined as a drug for which the end date was on or after the date of first dose of study drug
- Efficacy was assessed in all randomly assigned patients, except those failing to meet entry criteria postrandomization and those who did not receive any study drug; confirmed per patient diary (**Figure 1**)

Figure 1. Bowel Prep Dosing Regimens*†[7,8]

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

*2L PEG dietary restrictions were consistent with the summary of product characteristics/prescribing information. NER1006 regimens allowed a light breakfast and light lunch on the day before colonoscopy. 2L PEG regimen allowed for meals, including a light dinner, on the day before colonoscopy.
†Trisulfate solution arm in NOCT study and NER1006 AM/AM split-dosing arm in MORA study were not included in the current analyses.
MORA = morning arm; NOCT = nocturnal pause arm; 2L PEG = 2 liter polyethylene glycol plus ascorbate.

- Colon cleansing success was assessed by treatment-blinded central readers using 2 validated scales[7,8]
  - Boston Bowel Preparation Scale (BBPS)[9]: success defined as overall score ≥6, with score ≥2 in each colonic segment (right [ascending colon/cecum], transverse, and left [descending colon, sigmoid colon, and rectum] colon)
  - Harefield Cleansing Scale (HCS)[10]: success defined as all 5 colonic segments (ascending/transverse/descending/sigmoid/rectum) scoring 3 (clear liquid) or 4 (empty and clean) or ≥1 segment scored 2 (brown liquid/fully removable semi-solid stools) and other segments scored 3 or 4 (ie, good/excellent)
    - High quality (good/excellent) cleansing for each segment (colon segments free of stool; score 3 or 4) was also determined using the HCS
- Adenomas were detected by site colonoscopists and confirmed by histopathology
- *P* values were calculated using a Chi-square test
- Safety assessments included treatment-emergent adverse events (AEs) and monitored through Day 7 ± 1 postcolonoscopy
  - Safety population included all patients for whom it could not be ruled out (based on patient diary) that they received study medication at least once

RESULTS

- A total of 139 adults with concomitant use of opioids and/or TCAs were included (**Table 1**)

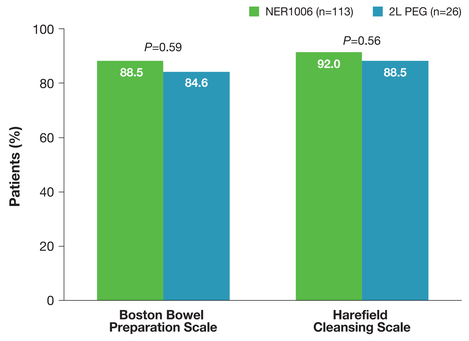
Table 1. Demographics and Baseline Characteristics

Parameter	NER1006 (n=113)	2L PEG (n=26)
Age, y		
Mean (SD)	55.7 (11.6)	54.6 (13.8)
Range	18–80	27–84
Male, n (%)	53 (46.9)	11 (42.3)
Race, n (%)		
White	102 (90.3)	26 (100.0)
Black	6 (5.3)	0
Asian	5 (4.4)	0
Most common concomitant medication class, n (%)*		
Opioid analgesic	113 (100)	26 (100)
Tricyclic antidepressant	6 (5.3)	1 (3.8)

*>1 patient. Patients may have been taking >1 medication.
2L PEG = 2 liter polyethylene glycol plus ascorbate.

- NER1006 and 2L PEG had a similar high overall colon cleansing success rate using the BBPS or the HCS (**Figure 2**)

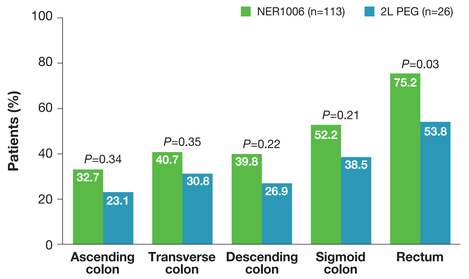
Figure 2. Overall Cleansing Success Rates in Patients Receiving Concomitant Opioids and/or Tricyclic Antidepressants



2L PEG = 2 liter polyethylene glycol plus ascorbate.

- A larger percentage of patients receiving concomitant opioids and/or TCAs had high-quality cleansing (HCS scores of good/excellent) in each colonic segment with NER1006 vs 2L PEG, with the difference being statistically significant in the rectum (**Figure 3**)

Figure 3. High-Quality Bowel Cleansing (HCS) in Patients Taking Concomitant Opioids and/or Tricyclic Antidepressants, by Colonic Segment



HCS = Harefield Cleansing Scale; 2L PEG = 2 liter polyethylene glycol plus ascorbate.

- Among patients taking concomitant opioids and/or TCAs, the percentage of those with ≥1 adenoma detected in the ascending colon was similar between the 2 bowel prep groups (9.7% and 15.4% for NER1006 and 2L PEG, respectively; *P*=0.40)
- Both preparations were well tolerated (**Table 2**)
  - Most commonly reported AEs were nausea, vomiting, and headache
  - No patients failed to complete the bowel preparation due to an AE

Table 2. Adverse Event Profile

AE, n (%)	NER1006 (n=112)	2L PEG (n=26)
≥1 AE	27 (24.1)	5 (19.2)
Discontinuation due to AE	0	0
≥1 Serious AE	1 (0.9)*	0
Most common AEs†		
Nausea	7 (6.3)	2 (7.7)
Vomiting	5 (4.5)	0
Headache	2 (7.7)	3 (2.7)
Abdominal tenderness	2 (1.8)	0
Dehydration	2 (1.8)	0
Fatigue	2 (1.8)	0
Hiatus hernia	2 (1.8)	0

*AE of ileus that was not considered by investigator to be related to study drug.
†Occurring in >1 patient in any treatment group.
AE = adverse event.

CONCLUSION

- 1L NER1006 was as effective as the higher-volume 2L PEG bowel preparation in adults undergoing colonoscopy and receiving concomitant opioid analgesics and/or TCAs, medications known to potentially impact bowel prep quality

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