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Electrolyte Shifts of NER1006 Bowel Preparation for Colonoscopy in the Elderly Are Transient and Well Tolerated

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INTRODUCTION

- Safety during bowel preparation administration for colonoscopy is important, especially in the elderly (eg, increased risk of adverse effects related to concurrent medical conditions)[1,2]
- Polyethylene glycol (PEG)-based bowel preparations have been preferentially considered in the elderly[1,2]
  - Some concerns with bowel preparations in the elderly include tolerability of large volumes, adherence, and risk of dehydration[2-4]
  - Electrolyte disturbances are generally uncommon with PEG-based bowel preparations; however, abnormalities in sodium homeostasis have been reported in patients ≥50 years of age[3]
- The low-volume 1 L PEG-based bowel preparation NER1006 (Plenvu®, Norgine Ltd, Tir-Y-Berth Hengoed, United Kingdom) was approved in the United States in 2018 and is indicated for colon cleansing in preparation for colonoscopy in adults
  - NER1006 has been shown to be efficacious and well tolerated in 3 randomized, phase 3, active comparator, noninferiority trials[5-7]
- To further evaluate the safety profile of NER1006 evening/morning split-dosing in the elderly, a subgroup analysis by age was conducted[5]

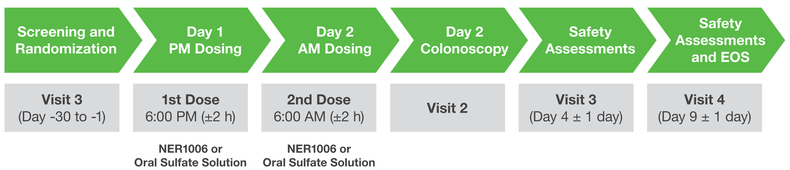
OBJECTIVE

- To further assess the safety of NER1006 in the elderly (>65 years of age)

METHODS

- In the NOCT (nocturnal pause arm) phase 3 study, adults (aged 18–85 years) undergoing colonoscopy were randomly assigned to receive NER1006 or oral sulfate solution (OSS; SuPrep® Bowel Prep Kit, Braintree Laboratories, Inc., Braintree, MA)[5]
  - For each prep, patients took the evening dose starting at ~6:00 PM and the morning dose starting at ~6:00 AM (Figure)[5]
  - Each bowel prep dose was administered as 16 oz (~500 mL)
  - Additional clear fluids
    - In the NER1006 group, patients were to consume 16 oz (~500 mL) of additional clear fluids after each dose and could drink clear fluids ad libitum
    - In the OSS group, patients were to consume 32 oz (~1000 mL) of additional water after each dose in accordance with the US prescribing information
- The safety population included all patients who received ≥1 study dose; population was then subgrouped by age (≤65 and >65 years)
- Safety assessments included monitoring adverse events (AEs) and clinical laboratory testing
  - Plasma electrolyte levels were measured at baseline, Day 2 (day of colonoscopy), Day 4 ± 1, and Day 9 ± 1 (Figure)
  - Upper limit of normal laboratory values were: 145 mmol/L (sodium), 105 mmol/L (chloride), and 5 mmol/L (potassium)

Figure. Study Design



EOS = end of study.
Adapted with permission from DeMicco MP, et al. *Gastrointest Endosc.* 2018;87(3):677-687.[5]

RESULTS

- The safety population (n=527) included 262 patients in the NER1006 group and 265 in the OSS group; overall, 96 patients were >65 years of age (Table 1)

Table 1. Demographics, by Age Group

Parameter	Patients, ≤65 Years: NER1006 (N=214)	Patients, ≤65 Years: OSS (N=217)	Patients, >65 Years: NER1006 (N=48)	Patients, >65 Years: OSS (N=48)
Age, y, mean (SD)	54.2 (8.1)	53.8 (8.7)	72.3 (4.8)	70.6 (3.8)
Range	22–65	18–65	66–86	66–80
Gender, n (%)				
Female	113 (52.8)	121 (55.8)	22 (45.8)	29 (60.4)
Male	101 (47.2)	96 (44.2)	26 (54.2)	19 (39.6)
Race, n (%)				
White	174 (81.3)	175 (80.6)	47 (97.9)	44 (91.7)
Black	34 (15.9)	22 (10.1)	0	3 (6.3)
Asian	6 (2.8)	15 (6.9)	1 (2.1)	1 (2.1)
Other	0	5 (2.3)	0	0

OSS = oral sulfate solution; SD = standard deviation.

- In patients >65 years of age, the most common AEs were nausea (10.4%) and vomiting (8.3%) with NER1006 and decreased glomerular filtration rate (6.3%) with OSS (Table 2)
  - Hyperuricemia was not reported in either age or treatment group

Table 2. Adverse Event Profile, by Age Group

Patients With an AE, n (%)	Patients, ≤65 Years: NER1006 (N=214)	Patients, ≤65 Years: OSS (N=217)	Patients, >65 Years: NER1006 (N=48)	Patients, >65 Years: OSS (N=48)
Any AE	55 (25.7)	38 (17.5)	17 (35.4)	11 (22.9)
Serious AEs	1 (0.5)	1 (0.5)	0	0
AE leading to discontinuation	0	1 (0.5)	0	0
Treatment-related AE	30 (14.0)	19 (8.8)	9 (18.8)	6 (12.5)
Most common AEs*				
Nausea	13 (6.1)	5 (2.3)	5 (10.4)	0
Vomiting	12 (5.6)	7 (3.2)	4 (8.3)	0
Dehydration	5 (2.3)	1 (0.5)	3 (6.3)	0
Decreased GFR	4 (1.9)	2 (0.9)	0	3 (6.3)

*Reported in ≥3 patients aged >65 years in either treatment group.
AE = adverse event; GFR = glomerular filtration rate; OSS = oral sulfate solution.

- Mean baseline sodium levels in age subgroups were similar between the 2 treatments (Table 3)
  - On Day 2 prior to the colonoscopy procedure, the mean change in sodium concentration from baseline was higher in NER1006 groups versus OSS, but was similar by Day 4

Table 3. Changes in Plasma Sodium Levels, by Age Group

Assessment*	Patients, ≤65 Years: NER1006 (N=214)	Patients, ≤65 Years: OSS (N=217)	Patients, >65 Years: NER1006 (N=48)	Patients, >65 Years: OSS (N=48)
Baseline, mean (SD), mmol/L	141.0 (2.4)	141.0 (2.5)	140.5 (2.5)	140.4 (2.4)
Day 2, n†	213	216	47	46
Mean (SD), mmol/L	144.5 (2.8)	141.0 (2.8)	145.1 (2.3)	141.6 (2.8)
Mean (SD) change from baseline, mmol/L	3.5 (2.9)‡	0	4.4 (2.5)‡	1.2 (2.1)
Day 4, n	210	208	46	47
Mean (SD), mmol/L	141.3 (2.3)	141.0 (2.5)	141.1 (2.4)	140.6 (2.7)
Mean (SD) change from baseline, mmol/L	0.3 (2.4)	0	0.4 (2.1)	0.2 (2.0)
Day 9, n	170	186	36	34
Mean (SD), mmol/L	141.3 (2.1)	140.8 (2.8)	141.4 (3.1)	140.6 (2.5)
Mean (SD) change from baseline, mmol/L	0.3 (2.3)§	-0.2 (2.5)	0.7 (2.6)	0.2 (2.3)

*Plasma sodium ULN = 145 mmol/L.
†Prior to colonoscopy.
‡P<0.0001 vs OSS.
§P=0.05 vs OSS.
OSS = oral sulfate solution; SD = standard deviation; ULN = upper limit of normal.

- A greater percentage of patients aged >65 years with normal baseline sodium levels had high sodium levels (>145 mmol/L) on Day 2 with NER1006 (48.9%) versus OSS (6.5%); shifts were transient and 95.7% (44/46) of all NER1006-treated patients aged >65 years had normal sodium levels by Day 4 (Tables 3 and 4)
  - On Day 2, no patients were found to have hyponatremia in the NER1006 group
  - On Day 2 (day of colonoscopy), no patients who received general anesthesia experienced sodium levels >155 mmol/L (mild elevation above upper limit of normal)
- In patients aged ≤65 years in the NER1006 group, 37.6% had a shift in sodium levels from normal at baseline to high at Day 2 versus 3.7% with OSS; by Day 4, 94.8% (199/210) of all NER1006-treated patients had normal sodium levels (Tables 3 and 4)
- Chloride levels transiently increased from baseline in 27.7% (aged >65 years) and 19.2% (aged ≤65 years) of patients at Day 2 treated with NER1006; 93.5% (43/46) and 91.0% (191/210) of NER1006 patients had normal levels by Day 4 (Table 4)
- At least 95% of NER1006-treated patients in both age groups had normal potassium levels from baseline through Day 9 (Table 4)
- No electrolyte shifts resulted in clinical sequelae

Table 4. Patients With Electrolyte Shifts From Baseline, by Age Group

Electrolyte	Patients, ≤65 Years, n (%): Normal to Low: NER1006 (N=214)	Normal to Low: OSS (N=217)	Normal to High: NER1006 (N=214)	Normal to High: OSS (N=217)	Patients, >65 Years, n (%): Normal to Low: NER1006 (N=48)	Normal to Low: OSS (N=48)	Normal to High: NER1006 (N=48)	Normal to High: OSS (N=48)
Sodium*								
Day 2†	0	3 (1.4)	80 (37.6)	8 (3.7)	0	0	23 (48.9)	3 (6.5)
Day 4	2 (1.0)	0	8 (3.8)	6 (2.9)	0	0	1 (2.2)	1 (2.1)
Day 9	0	4 (2.2)	1 (0.6)	6 (3.2)	0	0	5 (13.9)	0
Chloride‡								
Day 2†	0	15 (6.9)	41 (19.2)	3 (1.4)	0	2 (4.3)	13 (27.7)	1 (2.2)
Day 4	3 (1.4)	4 (1.9)	5 (2.4)	2 (1.0)	0	0	3 (6.5)	1 (2.1)
Day 9	3 (1.8)	3 (1.6)	5 (3.0)	2 (1.1)	1 (2.8)	2 (5.9)	4 (11.1)	1 (2.9)
Potassium§								
Day 2†	1 (0.5)	5 (2.3)	6 (2.8)	4 (1.9)	0	1 (2.2)	0	1 (2.2)
Day 4	4 (1.9)	2 (1.0)	1 (0.5)	2 (1.0)	0	0	1 (2.2)	0
Day 9	2 (1.2)	2 (1.1)	0	2 (1.1)	0	0	1 (2.8)	0

*Plasma sodium ULN = 145 mmol/L.
†Prior to colonoscopy.
‡Plasma chloride ULN = 105 mmol/L.
§Plasma potassium ULN = 5 mmol/L.
OSS = oral sulfate solution; ULN = upper limit of normal.

CONCLUSIONS

- **NER1006 was well tolerated regardless of age group**
- **Transient increases in sodium and chloride levels were observed on the day of colonoscopy, but changes were not associated with clinically meaningful sequelae and levels returned to normal in most patients by Day 4**
  - **Mild increases in electrolyte levels may potentially be addressed by adequate hydration in appropriate patients**

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DISCLOSURES: MSE reports acting as a principal investigator in research for Investigative Clinical Research; acting as a safety advisor for Aspire Bariatrics; serving as a consultant for Zx Pharma; and serving on the speakers' bureau for Ferring Pharmaceuticals Inc. and Otsuka America, Inc. SL and HF are employees of Salix Pharmaceuticals. BDC reports serving on the speakers' bureau, as a consultant, or as an advisory board member for Allergan plc, Ironwood Pharmaceuticals, Salix Pharmaceuticals, and Takeda Pharmaceutical Company Ltd (Shire).

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