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NER1006 1 Liter Polyethylene Glycol–Based Bowel Preparation Safety Profile in Patients With Mild or Moderate Renal Impairment: a Pooled Analysis of Two Phase 3 Trials

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INTRODUCTION

- NER1006 (Plenvu®, Salix Pharmaceuticals, Bridgewater, NJ), a 1 L polyethylene glycol (PEG)-based bowel preparation, was approved in the United States in 2018 for colon cleansing in preparation for colonoscopy in adults[1,2]
- Two randomized, phase 3 studies evaluating the US-indicated dosing regimens (2-day evening/morning [PM/AM] split dosing or 1-day morning [AM/AM] split dosing) demonstrated that NER1006 was efficacious and well tolerated[2,3]
- In patients with decreased renal function, bowel preparations may increase the risk of electrolyte imbalances or worsen renal function[1,4]
- Due to their iso-osmotic nature, PEG-based bowel preparations are generally preferred in patients with renal insufficiency[5,6]
- Data are limited on the safety profile of low-volume PEG products (eg, 1 L) in patients with renal insufficiency

OBJECTIVE

- To evaluate the safety profile of the 1 L PEG, NER1006, in adults undergoing colonoscopy, subgrouped by renal insufficiency

METHODS

- Data were pooled from two phase 3, randomized studies (NOCT and MORA)
- Patients (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[2,3]
- Per protocol, mild renal insufficiency was defined as creatinine clearance (CrCl) ≥60 to <90 mL/min/1.73 m^2 and moderate as CrCl ≥30 to <60 mL/min/1.73 m^2
  - Moderate renal insufficiency was an exclusion criterion in NOCT, and severe disease (CrCl <30 mL/min/1.73 m^2) was an exclusion criterion in both trials
- Safety (adverse events [AEs] and clinical lab testing) was assessed, per protocol, through 7 ± 1 days post-colonoscopy
- In a post hoc analysis, worsening renal function (ie, increase from baseline in creatinine >0.3 mg/dL or decrease from baseline in calculated CrCl of >25%) definition was derived from RIFLE (risk, injury, failure, loss, end-stage kidney disease) criteria
- The intent to treat (ITT) population included all patients randomly assigned to treatment; the safety population included those in the ITT population for whom it could not be ruled out that they had received ≥1 dose of NER1006 (based on patient diary)

RESULTS

- 524 and 269 adults were included in the NER1006 PM/AM and the NER1006 AM/AM groups, respectively (**Table 1**)
  - The majority of patients in each treatment group had mild-to-moderate renal insufficiency (67.6%–73.6%)

Table 1. Demographic and Baseline Characteristics (Safety Population)

Parameter	NER1006 PM/AM (n=524)	NER1006 AM/AM (n=269)
Age, y, mean (SD)	57.0 (11.1)	54.9 (13.2)
Age >65 y, n (%)	118 (22.5)	60 (22.3)
Sex, n (%)		
Male	243 (46.4)	124 (46.1)
Female	281 (53.6)	145 (53.9)
Race, n (%)		
White	477 (91.0)	266 (98.9)
Black	39 (7.4)	3 (1.1)
Asian	7 (1.3)	0
Other	1 (0.2)	0
BMI, mean (SD), kg/m^2	28.4 (5.3)*	26.9 (4.3)
Reason for colonoscopy, n (%)		
Screening	287 (54.8)	136 (50.6)
Surveillance	143 (27.3)	57 (21.2)
Diagnostic	94 (17.9)	76 (28.3)
Renal insufficiency status, n (%)		
Mild	340 (64.9)	184 (68.4)
Moderate	14 (2.7)	14 (5.2)
None	166 (31.7)	68 (25.3)
Unknown	4 (0.8)	3 (1.1)

*n=523.
BMI = body mass index; SD = standard deviation.

- The most common AEs during the study were gastrointestinal-related, regardless of renal function status (**Table 2**)

Table 2. AE Profile of Patients Treated With NER1006, by Renal Insufficiency Status (Safety Population)*

	Renal Insufficiency					
	NER1006 (PM/AM) Split-Dosing Regimen			NER1006 (AM/AM) Split-Dosing Regimen		
Patients, n (%)	Mild† (n=340)	Moderate‡ (n=14)	None (n=166)	Mild† (n=184)	Moderate‡ (n=14)	None (n=68)
Any AE	77 (22.6)	5 (35.7)	36 (21.7)	28 (15.2)	4 (28.6)	17 (25.0)
Drug-related AEs	48 (14.1)	3 (21.4)	19 (11.4)	24 (13.0)	4 (48.6)	12 (17.6)
AEs leading to discontinuation	0	0	0	0	0	1
Most common AEs§						
Nausea	22 (6.5)	1 (7.1)	10 (6.0)	11 (6.0)	1 (7.1)	2 (2.9)
Vomiting	18 (5.3)	0	9 (5.4)	12 (6.5)	2 (14.3)	4 (5.9)
Other AEs of interest						
Abdominal pain	1 (0.3)	1 (7.1)	1 (0.6)	1 (0.5)	0	0
Dehydration	7 (2.1)	0	2 (1.2)	2 (1.1)	0	2 (2.9)
Dry mouth	2 (0.6)	1 (7.1)	0	2 (1.1)	0	1 (1.5)
Fatigue	2 (0.6)	0	2 (1.2)	0	0	0
Feeling cold	0	0	0	0	0	1 (1.5)
Headache	6 (1.8)	0	3 (1.8)	2 (1.1)	0	0
Thirst	2 (0.6)	0	0	2 (1.1)	1 (7.1)	2 (2.9)

*All patients randomized to treatment in whom it could not be ruled out that they received NER1006 at least once, per patient diary.
†CrCl ≥60 to <90 mL/min/1.73 m^2.
‡CrCl ≥30 to <60 mL/min/1.73 m^2.
§Most common AEs reported in overall population of the NOCT and MORA studies.
AE = adverse event; CrCl = creatinine clearance.

- To assess a risk of worsening renal function, patients who showed an increase from baseline in creatinine >0.3 mg/dL or a decrease from baseline in calculated CrCl of >25% were identified
  - The number of patients, subgrouped by renal insufficiency, meeting 1 or both of these criteria was low, with no signal of renal injury related to NER1006 observed (**Table 3**)
- In addition, these changes did not persist; only 1 patient (baseline mild renal insufficiency; AM/AM split dose) with a change in renal function at Day 2 ± post-colonoscopy (**Table 3**) met the same criteria (for CrCl) at Day 7 ± 1 days post-colonoscopy

Table 3. Patients With Change in Renal Function*, by Renal Insufficiency Status (ITT Population)

	Renal Insufficiency, n/N (%)†					
	NER1006 (PM/AM) Split-Dosing Regimen			NER1006 (AM/AM) Split-Dosing Regimen		
Visit‡	Mild§	Moderate¶	None	Mild§	Moderate¶	None
Day of colonoscopy	6/332 (1.8)	1/15 (6.7)	8/164 (4.9)	4/172 (2.3)	0/15 (0)	3/69 (4.3)
2 ± 1 days post-colonoscopy	0/333 (0)	0/15 (0)	4/163 (2.5)	2/175 (1.1)	0/15 (0)	1/69 (1.4)
7 ± 1 days post-colonoscopy	5/256 (2.0)	0/12 (0)	2/136 (1.5)	2/147 (1.4)	0/11 (0)	1/54 (1.9)

*Increase from baseline in creatinine of >0.3 mg/dL and/or a decrease from baseline in calculated CrCl of >25% at the indicated visit. †N = number of patients within each group with serum creatinine and/or CrCl data at baseline and at indicated visit. ‡Per protocol for both studies, there were 4 study visits (visit 1 [screening/randomization], visit 2 [day of colonoscopy], visit 3 [2 ± 1 days post-colonoscopy], and visit 4 [7 ± 1 days post-colonoscopy]). §CrCl ≥60 to <90 mL/min/1.73 m^2. ¶CrCl ≥30 to <60 mL/min/1.73 m^2. CrCl = creatinine clearance; ITT = intent to treat.

CONCLUSION

- **Data support the overall safety profile of 1 L PEG-based NER1006 as a bowel preparation, including in patients with mild-to-moderate renal insufficiency**

REFERENCES: **1.** 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. **2.** DeMicco MP, et al. *Gastrointest Endosc.* 2018;87(3):677-687. **3.** Bisschops R, et al. *Endoscopy.* 2019;51(1):60-72. **4.** Lim YJ, et al. *World J Gastroenterol.* 2014;20(11):2741-2745. **5.** Johnson DA, et al. *Gastroenterology.* 2014;147(4):903-924. **6.** Connor A, et al. *Gut.* 2012;61(11):1525-1532.

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