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# Low Risk of Hypokalemia in Adults Treated With the 1 Liter Polyethylene Glycol-Based Bowel Preparation NER1006: A Pooled Analysis of 2 Randomized Phase 3 Trials

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## INTRODUCTION

- Optimal bowel cleansing prior to colonoscopy is key for visualization of the colonic mucosa during diagnostic and screening procedures[1]
- Electrolyte disturbances (eg, hypokalemia) have been reported after use of low-volume bowel preparations (eg, polyethylene glycol [PEG]-based products), including rare reports of cardiac arrhythmia[2,3]
- Use of thiazide diuretics, which are used to treat hypertension, is an independent risk factor of hypokalemia[4], including being a significant risk factor after use of a low-volume PEG-based bowel preparation[5]
- In the United States, NER1006 (Plenvu, Salix Pharmaceuticals, Bridgewater, NJ) is a 1 L PEG-based bowel preparation indicated for cleansing of the colon prior to colonoscopy in adults[6]

## OBJECTIVE

- To evaluate the incidence of hypokalemia in patients who received NER1006 compared with other bowel preparations, including in a subgroup of patients taking thiazide diuretics

## METHODS

- Pooled post hoc analysis of two phase 3 clinical trials (NOCT [NCT02254486] and MORA [NCT02273167])[7,8]
- Adults randomly assigned to receive NER1006, or comparators oral sulfate solution (OSS [NOCT trial]) or 2 L PEG plus ascorbate solution (2 L PEG [MORA trial])[7,8]
  - Preparations were administered as evening/morning (PM/AM) split-dose regimen (MORA/NOCT) or morning/morning (AM/AM) split-dose regimen (MORA [NER1006 arm]; **Figure 1**)

### Figure 1. Bowel Preparation Dosing Regimens for the Two Phase 3 Trials*[7,8]

| | MORA | NOCT |
|---|---|---|
| Day before colonoscopy | NER1006 (PM/AM) Dose 1: "6:00 PM" | NER1006 (PM/AM) Dose 1: "6:00 PM" |
| | 2 L PEG + ascorbate (PM/AM) Dose 1: "6:00 PM" | OSS (PM/AM) Dose 1: "6:00 PM" |
| Day of colonoscopy | NER1006 (PM/AM) Dose 2: "6:00 AM" | NER1006 (PM/AM) Dose 2: "6:00 AM" |
| | 2 L PEG + ascorbate (PM/AM) Dose 2: "6:00 AM" | OSS (PM/AM) Dose 2: "6:00 AM" |
| | or NER1006 (AM/AM) Dose 1: "5:00 AM" Dose 2: "7:00 AM" | |

*2 L PEG and OSS were administered per their summary of product characteristics/prescribing information. Patients were allowed to begin consumption of each bowel preparation dose within a ±2-hour window of the indicated time (other activities were aligned to ensure colonoscopy was performed ≥2 hours after last fluid intake). 2 L PEG PM/AM regimen allowed for meals, including a light dinner, on the day before colonoscopy; OSS regimen allowed only breakfast the day prior to the procedure. Both NER1006 PM/AM and AM/AM regimens allowed a light breakfast and light lunch and NER1006 AM/AM regimen also allowed a light dinner. OSS = oral sulfate solution; PEG = polyethylene glycol.

- Serum potassium concentrations evaluated at screening, day of colonoscopy, and 7 days following colonoscopy
- Hypokalemia was defined as a serum potassium concentration <3.5 mmol/L
- All patients randomly assigned to a bowel preparation were included in the analysis, except the following:
  - Patients with pre-existing hypokalemia at screening
  - Patients who failed to meet individual trial[7,8] entry criteria postrandomization
  - Patients without a potassium measurement at Days 2 (day of colonoscopy) and 9 (7 days postcolonoscopy)
- Multiple logistic regression analysis was conducted to assess whether certain variables (eg, patient demographics, bowel preparation used, certain medication use) were risk factors for hypokalemia development

## RESULTS

- 1229 patients were included in the analysis (NER1006 PM/AM [n=493]; NER1006 AM/AM [n=243]; OSS [n=251]; 2 L PEG [n=242])
  - Patients in each group had a comparable mean age (range): NER1006 PM/AM, 57.0 y (18-86 y); NER1006 AM/AM, 55.0 y (20-79 y); OSS, 56.9 y (18-80 y); 2 L PEG, 54.0 y (22-84 y); percentage of males were 46.9%, 45.7%, 56.6%, and 50.4%, respectively
  - 68 (5.5%) of the 1229 patients were taking thiazide diuretics (NER1006 PM/AM [n=22]; NER1006 AM/AM [n=8]; OSS [n=26]; 2 L PEG [n=12])
- On the day of colonoscopy, the percentage of patients with hypokalemia who had received NER1006 ranged from 0% to 1.0% and for those who had received OSS or 2 L PEG, 2.4% to 2.9% (**Table**)
  - 7 days after colonoscopy, the percentage of patients with hypokalemia was ≤1.0% for the 4 groups (**Table**)

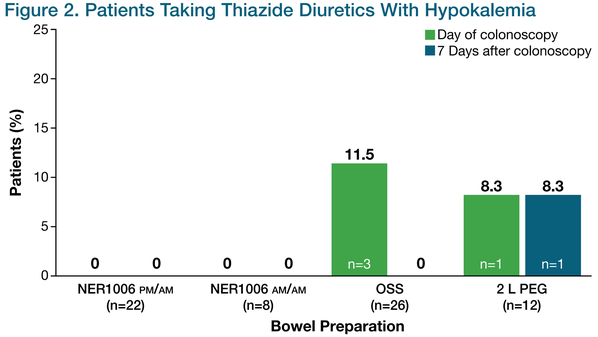
### Table. Incidence of Hypokalemia*

| Parameter | NER1006 PM/AM (n=493) | NER1006 AM/AM (n=243) | OSS PM/AM (n=251) | 2 L PEG PM/AM (n=242) |
|---|---|---|---|---|
| Screening potassium level, mM, mean (SD) | 4.4 (0.4) | 4.4 (0.4) | 4.3 (0.4) | 4.4 (0.4) |
| Patients with hypokalemia,* n (%) | | | | |
| Day of colonoscopy | 5 (1.0) | 0 | 6 (2.4) | 7 (2.9) |
| *P* value† | | 0.70 | 0.45 | 0.19 |
| 7 days after colonoscopy | 5 (1.0) | 2 (0.8) | 2 (0.8) | 1 (0.4) |
| *P* value† | | 0.99 | 0.99 | 0.83 |

*Serum potassium level <3.5 mmol/L. †*P* value versus NER1006 PM/AM group. OSS = oral sulfate solution; PEG = polyethylene glycol; SD = standard deviation.

- Among the 68 patients taking thiazide diuretics, no patients in the NER1006 PM/AM or NER1006 AM/AM groups had hypokalemia on the day of colonoscopy (**Figure 2**)

### Figure 2. Patients Taking Thiazide Diuretics With Hypokalemia




OSS = oral sulfate solution; PEG = polyethylene glycol.

- NER1006 use was not found to be a risk factor for development of hypokalemia on the day of colonoscopy (negative correlation [regression coefficient, -1.5]; *P*=0.02) or 7 days after colonoscopy (not significant [regression coefficient, 0.68]; *P*=0.36; **Figure 3**)

### Figure 3. Linear Regression and OR Analysis to Identify Variables Impacting Incidence of Hypokalemia*

| Dependent Variable | Day of Colonoscopy: Regression Coefficient (SE) | Day of Colonoscopy: OR (95% CI) | Day of Colonoscopy: *P* Value | 7 Days After Colonoscopy: Regression Coefficient (SE) | 7 Days After Colonoscopy: OR (95% CI) | 7 Days After Colonoscopy: *P* Value |
|---|---|---|---|---|---|---|
| Age, y | -0.02 (0.03) | 0.98 (0.93-1.03) | 0.16 | 0.03 (0.04) | 1.04 (0.96-1.13) | 0.40 |
| Colonoscopy† | | | | | | |
| Screening | -0.69 (0.68) | 0.50 (0.14-2.11) | 0.31 | 16.62 (1628) | — | 0.99 |
| Surveillance | -1.18 (0.92) | 0.31 (0.04-1.83) | 0.20 | 16.31 (1628) | — | 0.99 |
| Male | -0.43 (0.56) | 0.65 (0.21-1.93) | 0.44 | -0.19 (0.71) | 0.83 (0.19-3.32) | 0.79 |
| MORA trial participant | 1.02 (1.32) | 2.78 (0.20-32.62) | 0.44 | -1.56 (1.25) | 0.21 (0.02-2.37) | 0.21 |
| NER1006 use | **-1.50 (0.62)** | **0.22 (0.06-0.71)** | **0.02** | **0.68 (0.75)** | **1.98 (0.48-10.22)** | **0.36** |
| Screening K level‡ | -3.50 (0.99) | 0.03 (0.00-0.19) | 0.01 | -3.06 (1.14) | 0.05 (0-0.38) | 0.007 |
| Systolic BP‡ | -0.01 (0.03) | 0.99 (0.94-1.05) | 0.76 | 0.05 (0.03) | 1.05 (0.98-1.12) | 0.16 |
| Diastolic BP‡ | 0.04 (0.04) | 1.04 (1.00-1.13) | 0.32 | -0.05 (0.05) | 0.95 (0.87-1.04) | 0.25 |
| **Medical Conditions** | | | | | | |
| CVD | -16.41 (2576) | — | 0.99 | -16.63 (4276) | — | >0.99 |
| Diabetes | 0.54 (1.12) | 1.71 (0.09-11.01) | 0.63 | -16.81 (2637) | — | 0.99 |
| DVD | -0.09 (0.80) | 0.91 (0.16-4.00) | 0.91 | -0.23 (0.89) | 0.80 (0.11-4.07) | 0.80 |
| Hypertension | 0.34 (0.82) | 1.40 (0.28-7.21) | 0.68 | -1.04 (1.11) | 0.35 (0.03-2.90) | 0.35 |
| IBD | -16.87 (3203) | — | >0.99 | -14.94 (5192) | — | >0.99 |
| RI | 0.95 (0.59) | 2.59 (0.85-8.77) | 0.11 | -0.56 (0.73) | 0.57 (0.13-2.54) | 0.45 |
| **Medication Use** | | | | | | |
| Analgesics | 1.01 (0.64) | 2.74 (0.77-9.68) | 0.11 | 0.73 (0.90) | 2.08 (0.31-11.43) | 0.42 |
| General anesthetic | -1.56 (0.91) | 0.21 (0.03-1.13) | 0.09 | -0.68 (1.07) | 0.51 (0.06-4.16) | 0.53 |
| IV fluids | 1.91 (1.36) | 6.73 (0.62-119.77) | 0.16 | -0.56 (1.03) | 0.57 (0.08-4.89) | 0.59 |
| ML drugs | -15.58 (2353) | — | 0.99 | -16.42 (3692) | — | >0.99 |
| MS drugs | -13.79 (5932) | — | >0.99 | 2.83 (1.59) | 16.93 (0.44-330.49) | 0.08 |
| Sedation | -0.22 (0.72) | 0.81 (0.18-3.15) | 0.76 | -0.13 (1.08) | 0.88 (0.09-6.49) | 0.91 |
| Thiazides | 2.04 (0.77) | 7.72 (1.58-34.95) | <0.01 | 0.33 (1.20) | 1.39 (0.06-10.79) | 0.79 |


*Serum potassium level <3.5 mmol/L. †Diagnostic colonoscopy was not evaluated as a variable. ‡Continuous variable. BP = blood pressure; CI = confidence interval; CVD = cardiovascular disease; DVD = diverticular disease; IBD = inflammatory bowel disease; IV= intravenous; K = potassium; ML = motility lowering; MS = motility stimulating; OR = odds ratio; RI = renal insufficiency; SE = standard error.

## CONCLUSIONS

- **Incidence of hypokalemia after administration of NER1006 bowel preparation was low in this combined analysis of phase 3 trials and not significantly greater compared with OSS or 2 L PEG**
- **No patients in the NER1006 group taking thiazide diuretics met the criterion for hypokalemia on the day of or 7 days after colonoscopy**
- **NER1006 use was not found to be a risk factor for development of hypokalemia**

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