Novel 1L Polyethylene Glycol (PEG)-Based Bowel Preparation NER1006 Achieves Higher Quality Bowel Cleansing with Low Mandated Total Fluid Volume Intake: A Post-hoc Analysis versus Standard 2L PEG + Ascorbate

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Introduction

Colorectal cancer (CRC) screening reduces the incidence and mortality of CRC, and colonoscopy remains the gold standard screening method in terms of diagnostic sensitivity and specificity.[1–5] However, full visualization of the colonic mucosa is required during colonoscopy to ensure that lesions can be detected, and successful visualization is dependent on effective pre-procedural bowel preparation.[6–9] Clinical colonoscopy guidelines recommend that colonoscopy should be repeated if the bowel preparation is inadequate.[10,11]

Bowel preparations based on polyethylene glycol 3350 (PEG) plus electrolyte solutions are well-established.[12–17] Inclusion of ascorbic acid/sodium ascorbate (Asc) in PEG-based bowel preparations adds to the laxative effect of PEG while also enabling a total volume reduction.[12–14] Compared to 4L PEG-based preparations, 2L PEG + Asc bowel preparation halved the required preparation volume intake for patients, increasing convenience while still providing effective bowel cleansing.[15–17]

It was hypothesized that a further reduction in preparation volume for a PEG-based bowel preparation could be achieved through an increased ascorbate component. An initial clinical study exploring new low-volume PEG + Asc split-dosing bowel preparations identified two novel test formulations suitable for further clinical investigation.

The OPT study (ClinicalTrials.gov identifier: NCT01714466)[18] was a Phase 2 trial that compared taste- and flavor-optimized versions of these formulations to 2L PEG + Asc to asses their relative clinical efficacy, safety, and pharmacodynamic and pharmacokinetic properties.

OPT had two parts, evaluating five experimental low-volume PEGs versus 2L PEG + Asc. The best-performing low-volume bowel preparation candidate from Part 2 of OPT, NER1006, demonstrated 100% bowel cleansing success, as measured by a treatment-blinded colonoscopist using the validated Harefield Cleansing Scale (HCS, Figure 1).[9]

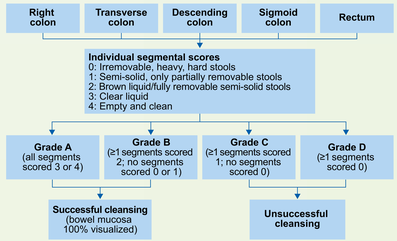
Objective
This analysis set out to measure the high-quality cleansing rate (Grade A cleansing criterion on the HCS, i.e. a cumulative bowel preparation score of ≥15 with segmental scores of ≥3) of NER1006 against the control bowel preparation, 2L PEG + Asc, by the respective patient's total fluid intake.

Methods

Patients
Part 2 of OPT enrolled patients aged 55–75 years (or 40–70 years with CRC risk factors) who were scheduled to undergo a screening colonoscopy. Patients were randomized 1:1:1:1 to receive one of three low-volume PEGs or 2L PEG; the present analysis includes the NER1006 and 2L PEG + Asc arms only. Table 1 shows the dose composition, overnight split-dosing schedules, and required fluid volumes in these NER1006 and 2L PEG + Asc treatment arms.

Endpoints
The overall bowel cleansing success rate versus preparation volume was evaluated. Treatment-blinded colonoscopists assessed the bowel cleansing quality using the HCS (Figure 1), which has a maximum cumulative score of 20.

Figure 1: Summary of cleansing assessment on the HCS[9]



The total fluid volume intake for each patient was calculated as total required fluid volume (preparation volume + required additional clear fluid volume) + voluntary ad libitum fluid intake.

Results

Patient baseline demographics
Sixty patients underwent screening colonoscopy: 30 patients per preparation protocol. Patient baseline demographics are shown in Table 2.

Results of post hoc analysis
Figure 2 shows the bowel cleansing success of the 60 patients in this analysis, according to cumulative segmental score on the HCS, plotted by each patient's total fluid volume intake.

97% (29/30) of NER1006-treated patients achieved cumulative segmental scores of ≥15 (all Grade A high-quality cleansing, with segmental scores of ≥3), compared to 37% (11/30) of 2L PEG + Asc-treated patients, who showed higher cleansing variability.

Table 2. Patient baseline demographics

	NER1006 (n=30)	2L PEG + Asc (n=30)
Mean age, years (SD)	60.0 (6.3)	58.8 (6.1)
Male, n (%)	13 (43.3)	14 (46.7)
White or Caucasian, n (%)	30 (100.0)[a]	30 (100.0)
Mean BMI, kg/m² (SD)	25.9 (3.4)	25.4 (3.4)

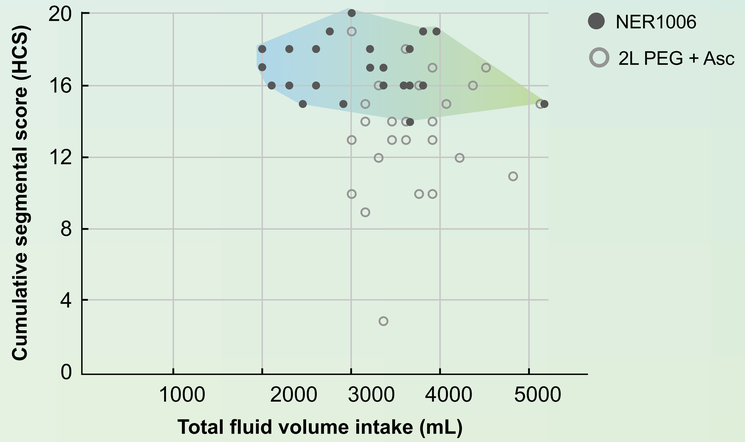
[a]One subject was described as both Hispanic or Latino, and White/Caucasian
BMI, body mass index; SD, standard deviation

Table 1. Composition and required fluid volumes of NER1006 and 2L PEG + Asc

Dosing regimen	NER1006		2L PEG + Asc	
Dose intake start time	5–6pm	7–8am	5–6pm	7–8am
Dose composition* (g)				
PEG3350	100.0	40.0	100.0	100.0
Sodium sulfate	9.0	–	7.5	7.5
Sodium ascorbate	–	48.1	5.9	5.9
Ascorbic acid	–	7.5	4.7	4.7
Fluid volume (mL)				
Preparation	500	500	1000	1000
Preparation, Total	1000		2000	
Required additional fluid	500	500	500	500
Required additional fluid, Total	1000		1000	
Required fluid, Total	2000		3000	

*Osmotically active ingredients only. All formulations included balanced electrolytes sodium chloride and potassium chloride. Total required fluid volume = bowel preparation reconstituted volume + required additional clear fluid volume. Patients were allowed to consume additional clear fluid as needed, in addition to the total required fluid volume.

Figure 2. Total fluid volume intake versus cumulative segmental cleansing score
One data point per patient. Total fluid volume = total required fluid volume + voluntary ad libitum clear fluid volume.



The total fluid volume intake (mean ± SD) was 3004±718mL for the NER1006 group and 3667 ±530mL for the 2L PEG + Asc group (P<0.001). Total fluid volume intake was not correlated to cleansing quality above 2L for NER1006, and half of NER1006 patients (15/30) chose to drink less than 3L of fluid in total.

The incidence of treatment-emergent adverse events (TEAEs) was similar between treatment arms; gastrointestinal events were the most common type. Most TEAEs were related to the investigational product, and of mild intensity. There were no serious adverse events (AEs) or deaths during the study, and no other significant AEs.

Discussion

- Overnight split-dosing with NER1006 can achieve clinically useful bowel cleansing with low total volume intake.
- NER1006 achieved its cleansing success mostly at the high-quality level and at a significantly lower total fluid intake than standard 2L PEG + Asc.

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