Same-Day Morning-Only Dosing of 1 L NER1006, a Polyethylene Glycol Bowel Preparation, Nearly Doubles the Chance of High-Quality Cleansing Versus Standard 2 L Polyethylene Glycol and Ascorbate

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INTRODUCTION

- Adequate bowel cleansing in preparation for colonoscopy improves outcomes, including adenoma and polyp detection rates[1]
  - Furthermore, high-quality bowel cleansing is required for detection of sessile serrated polyps, which are more difficult to detect with lower-quality cleansing[2]
- 1 L NER1006 (Plenvu; Salix Pharmaceuticals) is indicated in the United States for cleansing of the colon in preparation for colonoscopy in adults and may be administered as PM/AM (2-day) or AM/AM (1 day [morning-only]) split dosing[3]
- A same-day morning-only regimen may offer patients a convenient and less disruptive alternative to 2-day split-dosing regimens[4]

OBJECTIVE

- To compare colon cleansing efficacy of 1 L NER1006 (administered as an AM/AM [morning-only] split-dosing regimen) versus 2 L polyethylene glycol (PEG) plus ascorbate (administered as a PM/AM [2-day] split-dosing regimen)

METHODS

- Post hoc analysis of a multicenter, randomized, phase 3 clinical trial (ClinicalTrials.gov identifier: NCT02273167)[5]
- Patients were randomly assigned (1:1) to receive NER1006 administered as a 1-day, AM/AM split-dosing regimen or 2 L PEG plus ascorbate (MoviPrep; Norgine) administered as a PM/AM (2-day) split-dosing regimen[5]
- Central readers, who were blinded to treatment assignment, evaluated bowel cleansing quality strictly using the Boston Bowel Preparation Scale (BBPS)[5]
- BBPS utilizes a 4-point scoring system to assess 3 colonic regions: right colon (including the cecum and ascending colon), transverse colon (including the hepatic and splenic flexures), and left colon (including the descending colon, sigmoid colon, and rectum)[6]
  - The 4-point scoring system ranges from 0 ("unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared") to 3 ("entire mucosa of colon segment seen well with no residual staining, small fragments of stool, or opaque liquid")
  - Each colon segment is individually scored and the results are summed (total score, 0 ["unprepared colon"] to 9 ["perfectly clean colon with no residual liquid"])
- Definitions of colon cleansing success:
  - Adequate cleansing: BBPS score ≥2 in each of the 3 regions
  - High-quality cleansing: BBPS score ≥2 in each region and overall BBPS score ≥7
- Treatment groups were compared using a two-sided t-test
- Time-adjusted multiple logistic regression analysis was conducted to assess potential predictors of adequate and high-quality colon cleansing success
  - Variables included age, male sex, height, weight, body mass index, type of colonoscopy (screening, surveillance), adherence, time lapse (time between last dose of bowel preparation to start of colonoscopy), and use of NER1006 bowel preparation
    - Adherence was defined as the study drug compliance rate according to patient diaries, regardless of the amount of additional fluids consumed, for a rating of 0 = <75% of each dose of bowel preparation; 1 = ≥75% of each dose of bowel preparation; or 2 = 100% of each dose of bowel preparation

RESULTS

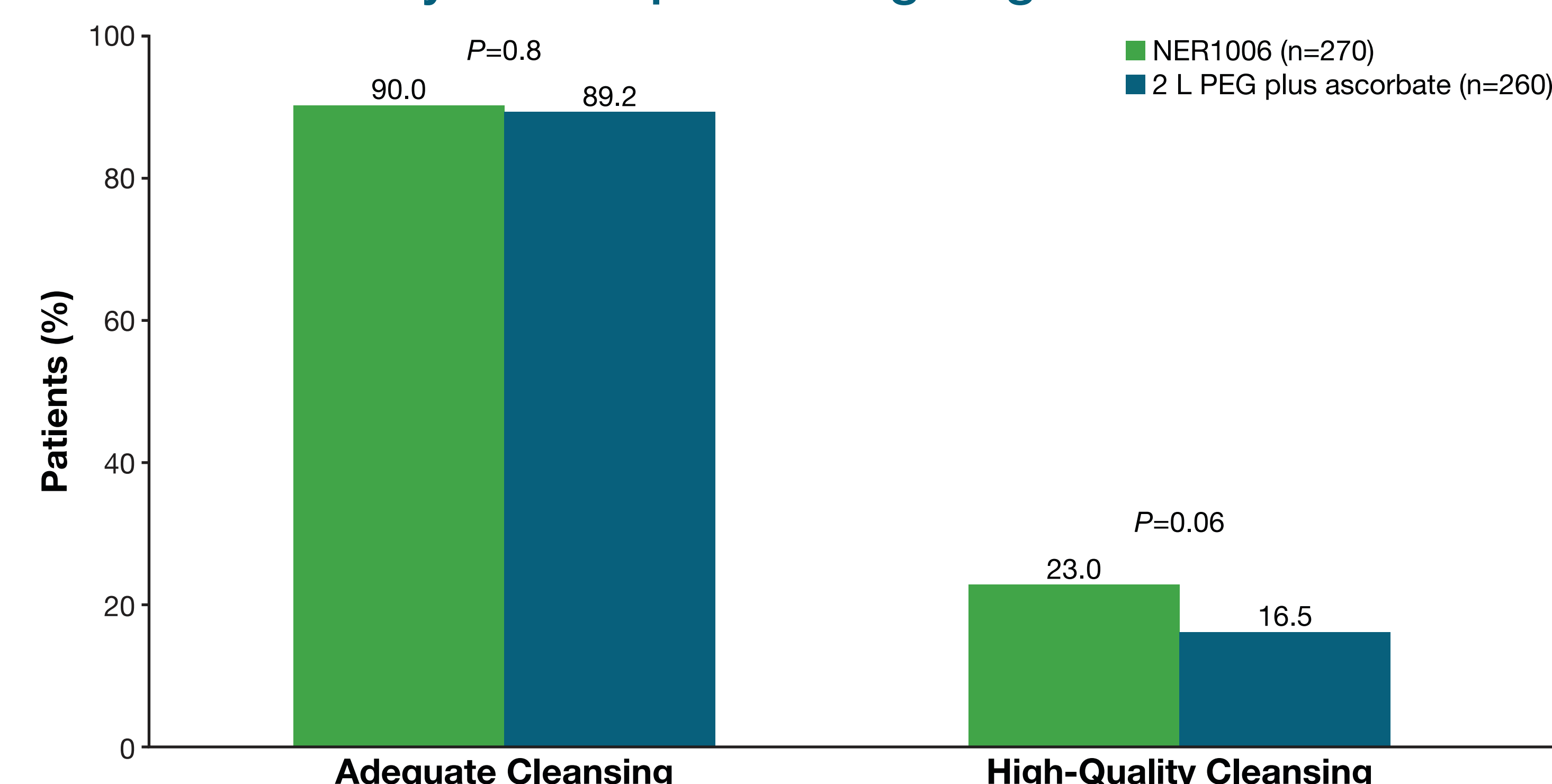- 530 patients were included in the analysis (NER1006 [n=270]; 2 L PEG plus ascorbate [n=260]; Table)

Table. Demographic and Baseline Characteristics

Parameter	NER1006 AM/AM Split-Dosing Regimen (n=270)	2 L PEG Plus Ascorbate PM/AM Split-Dosing Regimen (n=260)
Age ≤65 y, n (%)	210 (77.8)	214 (82.3)
Male sex, n (%)	125 (46.3)	137 (52.7)
Race, n (%)		
White	267 (98.9)	257 (98.8)
Black	3 (1.1)	1 (0.4)
Other	0	2 (0.8)
BMI, kg/m², mean (SD)	26.9 (4.3)*	26.4 (4.1)†
Reason for colonoscopy, n (%)		
Diagnostic	76 (28.1)	71 (27.3)
Screening	137 (50.7)	129 (49.6)
Surveillance	57 (21.1)	60 (23.1)
Time lapse, h, mean (SD)‡	5.4 (1.7)§	5.4 (2.1)¶

Data from Manning J, et al.[7]
*n=268. †n=256. ‡Time between last dose of bowel preparation to start of colonoscopy. §n=266. ¶n=253.
BMI = body mass index; PEG = polyethylene glycol; SD = standard deviation.

- The percentage of patients with adequate colon cleansing was similar between NER1006 and 2 L PEG plus ascorbate (Figure 1)
- The percentage of patients with high-quality colon cleansing was numerically greater with NER1006 versus 2 L PEG plus ascorbate, although the difference was not statistically significant (Figure 1)
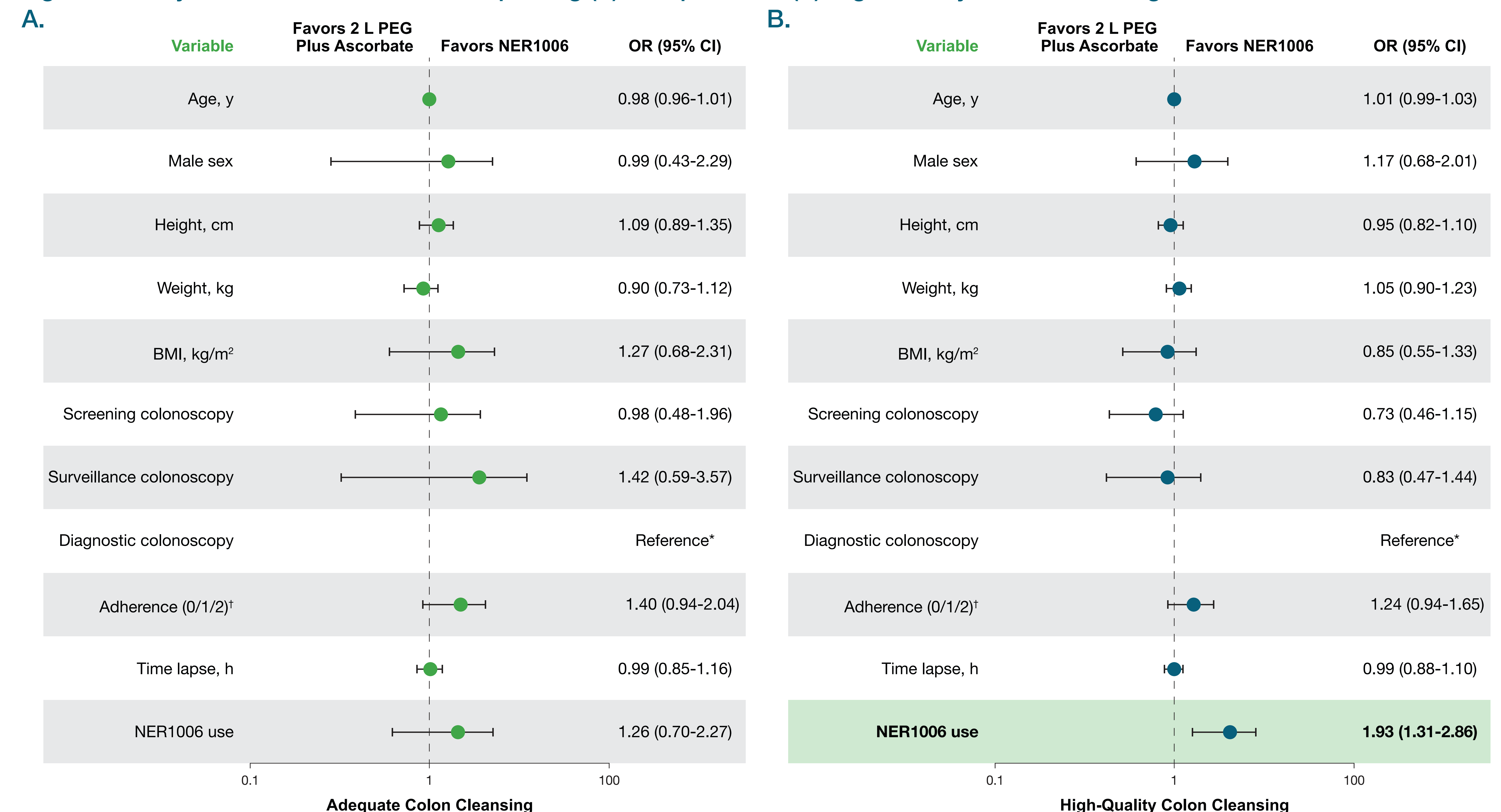
Figure 1. Adequate and High-Quality Colon Cleansing Rates With 1 L NER1006 AM/AM (Morning-Only) or 2 L PEG Plus Ascorbate 2-Day PM/AM Split-Dosing Regimen

Adequate Cleansing: NER1006 (n=270) 90.0; 2 L PEG plus ascorbate (n=260) 89.2; P=0.8
High-Quality Cleansing: NER1006 23.0; 2 L PEG plus ascorbate 16.5; P=0.06

PEG = polyethylene glycol.

- Although no specific variables were significantly associated with the odds of achieving adequate colon cleansing (Figure 2A), the NER1006 AM/AM morning-only regimen was significantly associated with achieving high-quality colon cleansing (Figure 2B; unadjusted, P<0.001; with Bonferroni correction for 11 assessed variables, P=0.01)

Figure 2. Analysis of Potential Variables Impacting (A) Adequate and (B) High-Quality Colon Cleansing Success

A. Adequate Colon Cleansing

Variable	Favors 2 L PEG Plus Ascorbate / Favors NER1006	OR (95% CI)
Age, y		0.98 (0.96-1.01)
Male sex		0.99 (0.43-2.29)
Height, cm		1.09 (0.89-1.35)
Weight, kg		0.90 (0.73-1.12)
BMI, kg/m²		1.27 (0.68-2.31)
Screening colonoscopy		0.98 (0.48-1.96)
Surveillance colonoscopy		1.42 (0.59-3.57)
Diagnostic colonoscopy		Reference*
Adherence (0/1/2)†		1.40 (0.94-2.04)
Time lapse, h		0.99 (0.85-1.16)
NER1006 use		1.26 (0.70-2.27)

B. High-Quality Colon Cleansing

Variable	Favors 2 L PEG Plus Ascorbate / Favors NER1006	OR (95% CI)
Age, y		1.01 (0.99-1.03)
Male sex		1.17 (0.68-2.01)
Height, cm		0.95 (0.82-1.10)
Weight, kg		1.05 (0.90-1.23)
BMI, kg/m²		0.85 (0.55-1.33)
Screening colonoscopy		0.73 (0.46-1.15)
Surveillance colonoscopy		0.83 (0.47-1.44)
Diagnostic colonoscopy		Reference*
Adherence (0/1/2)†		1.24 (0.94-1.65)
Time lapse, h		0.99 (0.88-1.10)
NER1006 use		1.93 (1.31-2.86)

*Diagnostic group was used as a reference in the multivariate regression mode.
†According to patient diary, and regardless of additional fluids consumed, 0 = adherence rate <75% of each dose of bowel preparation; 1 = adherence rate ≥75% of each dose of bowel preparation; and 2 = adherence rate of 100% of each dose of bowel preparation.
BMI = body mass index; CI = confidence interval; OR = odds ratio; PEG = polyethylene glycol.

CONCLUSIONS

- The 1 L NER1006 AM/AM (morning-only) split-dosing bowel preparation regimen was associated with improved high-quality colon cleansing compared with 2 L PEG plus ascorbate PM/AM (2-day) split-dosing regimen
- Findings suggest that NER1006 administered the morning of colonoscopy may offer a highly effective and convenient alternative to a traditional overnight split-dosing regimen of 2 L PEG plus ascorbate

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