# Achieving Successful Bowel Preparation (BBPS Score 2–3 per Segment) with Evening/Morning or Morning-Only Split-Dosing Regimens of NER1006 versus 2L Polyethylene Glycol with Ascorbate: Post Hoc Analysis of a Phase 3 Trial

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# Introduction

The effectiveness of colonoscopy for colorectal cancer screening is critically dependent on successful pre-procedural bowel preparation.<sup>1,2</sup> Successful cleansing is termed 'adequate' by Phase 3, randomized, colonoscopist-blinded clinical guidelines. US colonoscopy guidelines non-inferiority study, conducted to compare the screening and suggest that an adequate level of bowel cleansing is one that allows detection of lesions >5mm size, and European Society of Gastrointestinal + Asc) in adults undergoing colonoscopy. Patients Endoscopy (ESGE) guidelines recommend that a minimum of 90% of colonoscopies, with a target of 95%, should have adequate-level preparation.<sup>3,4</sup>

A Boston Bowel Preparation Scale (BBPS, Table 1) score of  $\geq 2$  per bowel segment has been proposed as 'adequate' for the detection of lesions >5mm in size.<sup>5</sup> Therefore, BBPS scores of  $\geq 2$  per segment may be defined as 'adequate' or 'successful' cleansing for colonoscopy.

NER1006 is the first 1L (32 fl oz) polyethylene glycol (PEG) and ascorbate bowel preparation and is a patented taste-optimized combination of two

Segment score		Description	
Inadeqate	0	Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared.	
	1	Portion of mucosa of the colon segment seen, but other areas of the colon segment not well-seen due to staining, residual stool and/or opaque liquid.	
	2	Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well.	
	3	Entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid.	

# Table 1: Boston Bowel Preparation Scale (BBPS)<sup>9</sup>

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different formulations, with a low preparation volume, Figure 1: Study design optimized for effective bowel preparation.<sup>6</sup>

MORA (NCT02273167)<sup>7</sup> was a European multicenter, **Visit 1** (Day -30 to -1) **Day 1** efficacy, safety and tolerability of NER1006 versus 2L PEG and ascorbate bowel preparation (2L PEG were randomized (1:1:1) to receive either (1) NER1006 as an evening/morning split-dosing regimen (N2D), (2) NER1006 as a morning-only dosing regimen (N1D), or (3) 2LPEG + Asc bowel preparationas an evening/morning split-dosing regimen.

The primary efficacy endpoints were overall bowel cleansing success and high-quality cleansing of the right colon (ascending colon plus cecum), as assessed by treatment-blinded central readers using the validated Harefield Cleansing Scale (HCS).<sup>8</sup> As with the HCS, central readers also scored the video recordings of each colonoscopy using another validated scale, the BBPS, as a secondary endpoint.<sup>7,9</sup>

# Objective

This post hoc analysis reports the comparative rates of successful cleansing between the two dosing regimens of NER1006 and 2L PEG + Asc bowel preparation in patients who had a readable colonoscopy video, using BBPS as the reference scale.

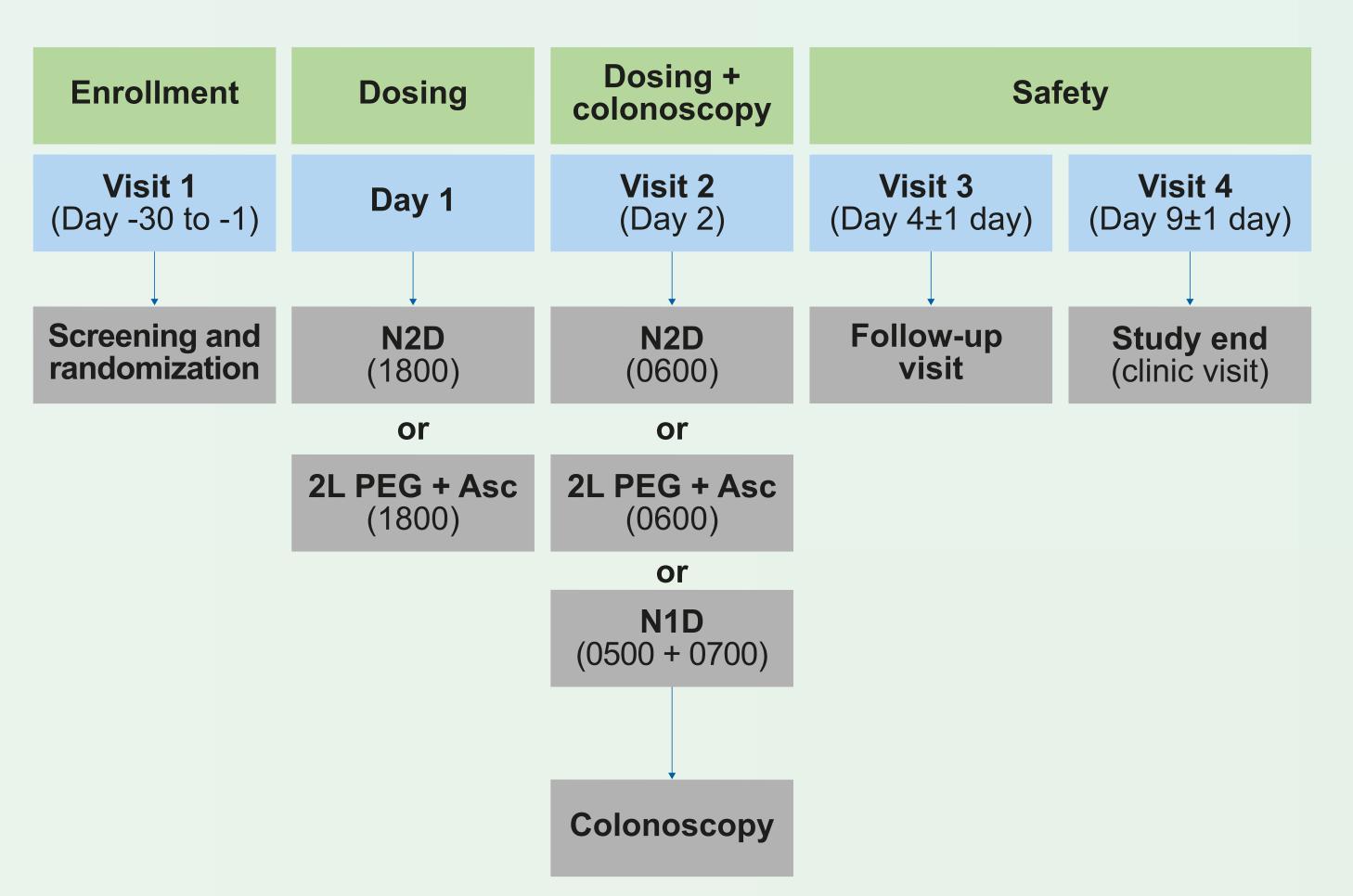
# Methods

# Patients

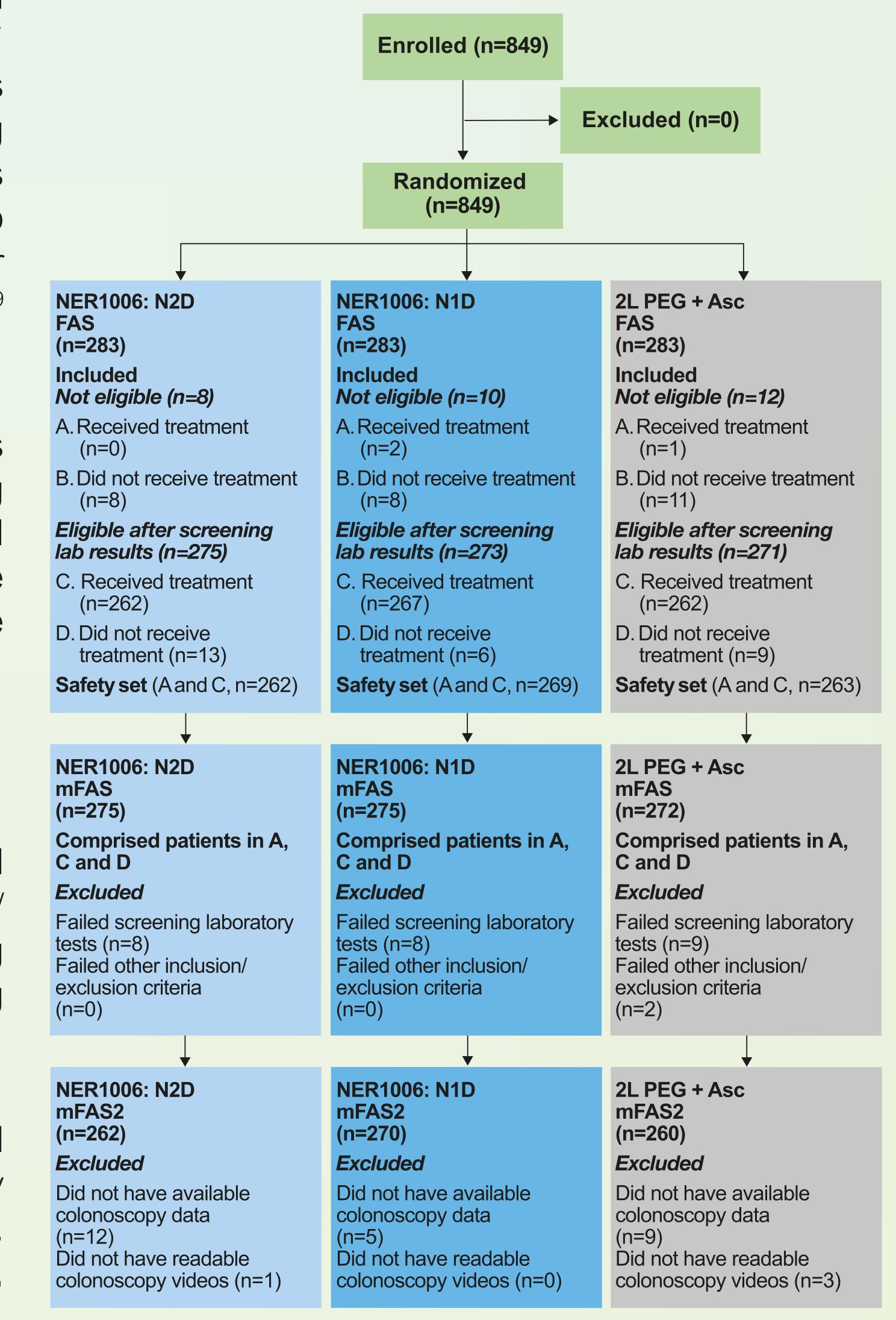
In total, 849 patients (aged 18–85) were randomized in a 1:1:1 ratio to receive: i) NER1006 as an evening/ morning split-dose (N2D), ii) a morning-only dosing regimen (N1D), or iii) 2L PEG + Asc administered using (n=0) an evening/morning split-dose regimen (Figure 1).

The primary analysis was conducted in the modified full analysis set (mFAS). mFAS patients without primary efficacy data were conservatively imputed as failures. The present analysis has excluded such patients, creating the mFAS2 set (Figure 2).

**References: 1.** Lin JS *et al.* Agency for Healthcare Research and Quality com/patents/WO2004037292A1; 7. Bisschops R *et al.* Gastroenterology 2016; (US); 2016 Jun. Report No.: 14-05203-EF-1; 2. Doubeni CA et al. Gut 2016; 150(4): S1269–70; 8. Halphen M et al. Gastrointest Endosc 2013; 78(1): 121– pii: gutjnl-2016-312712; **3.** Lieberman DA *et al.* Gastroenterology 2012; 143(3): 31; **9.** Lai EJ *et al.* Gastrointest Endosc 2009; 69(3 Pt 2): 620–5; **10.** Hassan C 844–57; **4.** Kaminski MF *et al.* Endoscopy 2017; 49(4): 378–97; **5.** Clark BT *et al. et al.* Endoscopy 2013; 45: 142–150. Gastroenterology 2016; 150(2): 396–405; 6. Barras N and Cox ID 2004 google.



### Figure 2: Patient disposition



FAS: full analysis set; mFAS: modified full analysis set

### Endpoints

Cleansing success was assessed by central readers using the BBPS. Analyses were performed for successful levels of cleansing in both the overall colon (defined as all segments  $\geq 2$ ) and for the right colon (defined as segmental score  $\geq 2$ ).

### **Statistics**

All analyses were carried out using the statistical package R v3.1.3 (The R Foundation, 2015) and confidence intervals and the t-statistic for each mean difference were calculated, and P-values estimated.

# Results

### Patient baseline demographics

Of the 849 randomized patients, 792 patients had a readable video and were included in this analysis. The patient baseline demographics are summarized in Table 2.

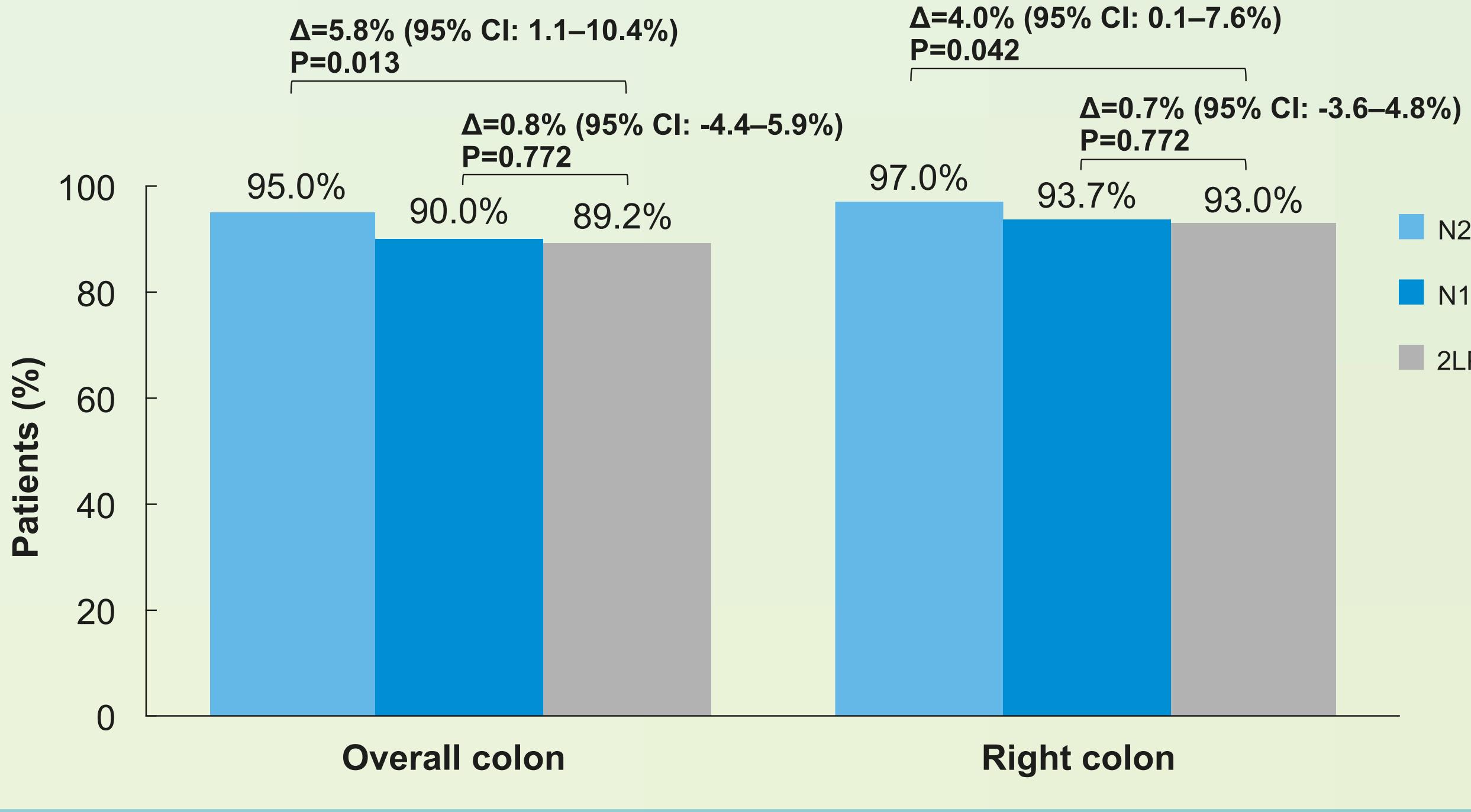
### Results of post hoc analysis

The results of this post hoc analysis are shown in Figure 3. A significantly higher proportion of patients in the N2D group achieved successful overall bowel

#### Table 2. Patient baseline demographics

	N2D (n=262)	N1D (n=270)	2L PEG + Asc (n=260)
Mean age, years (SD)	56.6 (11.9)	54.8 (13.2)	54.3 (12.7)
<b>P-value</b> for mean age vs 2L PEG + Asc	0.038	0.654	
<b>Age ≤65 years,</b> n (%)	192 (73.3)	210 (77.8)	214 (82.3)
<b>Male,</b> n (%)	108 (41.2)	125 (46.3)	137 (52.7)
<b>Race,</b> n (%) White or Caucasian Black Asian Other	256 (97.7) 5 (1.9) 0 (0) 1 (0.4)	267 (98.9) 3 (1.1) 0 (0) 0 (0)	257 (98.8) 1 (0.4) 2 (0.8) 0 (0)
<b>Mean BMI,</b> kg/m <sup>2</sup> (SD)	27.3 (4.8)	26.9 (4.3)	26.4 (4.2)
Reason for colonoscopy, n (%) Screening Surveillance Diagnostic	134 (51.1) 63 (24.0) 65 (24.8)	137 (50.7) 57 (21.1) 76 (28.1)	129 (49.6) 60 (23.1) 71 (27.3)

# Figure 3: Adequate-level cleansing of the overall colon and right colon (BBPS segmental scores 2–3) as determined by treatment-blinded central readers



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- N2D (n=262)
- N1D (n=270)
- 2LPEG + Asc (n=260)

cleansing compared to those in the 2L PEG + Asc group: 95.0% (249/262) versus 89.2% (232/260), P=0.013.

Rates of successful cleansing in the N1D group were comparable to the 2L PEG + Asc group (90.0%) [243/270] vs 89.2% [232/260], respectively, P=0.772).

Successful bowel preparation in the right colon was achieved in 97.0% (254/262) of patients treated in the N2D group, 93.7% (253/270) of patients in the N1D group, and 93.0% (242/260) of patients treated with 2L PEG + Asc (P=0.042 and P=0.772, for N2D and N1D vs 2L PEG + Asc, respectively).

### Discussion

- NER1006 demonstrated an exceptionally high rate of adequate-level bowel cleansing efficacy.
- A significant improvement was shown for both the overall colon and the clinically relevant right colon versus 2L PEG + Asc when both were administered using the same dosing regimen.
- The morning-only dosing regimen of NER1006 delivered a very high success rate, similar to that of 2L PEG + Asc.
- In line with clinical guidelines, high rates of successful bowel cleansing may reduce the need for repeat colonoscopies and improve the efficiency of colonoscopy procedures.<sup>3,10</sup>



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