Achieving Successful Bowel Preparation (BBPS Score 2–3 per Segment) with Evening/Morning Split-Dosing Regimens of NER1006 versus Trisulfate: Post Hoc Analysis of a Phase 3 Trial

Authors: Michael Epstein¹, Bharat Amlani², Pradeep Bekal³

Introduction

The effectiveness of colonoscopy for colorectal cancer screening is critically dependent on effective pre-procedural bowel preparation.^{1,2} Successful cleansing is termed 'adequate' by clinical guidelines. US colonoscopy guidelines suggest that an adequate level of bowel cleansing is one NOCT (NCT02254486)⁷ was a US multicenter, that allows detection of lesions >5mm in size, and European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend that a minimum of 90% of colonoscopies, with a target of 95%, should have adequate-level preparation.^{3,4}

It was recently shown that a Boston Bowel Preparation Scale (BBPS, Table 1) score of 2 per bowel segment was non-inferior to segmental cleansing scores of 3 in the detection of lesions cleansing success and high-quality cleansing of >5mm. Therefore, BBPS scores of ≥ 2 per segment may be defined as adequate-level cleansing.⁵

Segment score		Description	
	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)⁹

NER1006 is the first 1L (32 fl oz) polyethylene glycol Figure 1: Study design (PEG) and ascorbate bowel preparation and is a patented taste-optimized combination of two different formulations, with a low preparation volume, optimized for effective bowel preparation.⁶

randomized, colonoscopist-blinded, Phase 3 trial, that compared NER1006 with Trisulfate solution in terms of cleansing efficacy in adults undergoing colonoscopy. Patients were randomized 1:1 to receive either NER1006 or Trisulfate solution, both administered as evening/morning split-dosing regimens (Figure 1).

The primary efficacy endpoints were overall bowel the right colon (ascending colon plus cecum), as assessed by treatment-blinded central readers using the validated Harefield Cleansing Scale (HCS).⁸ The central readers also scored the video recordings of each colonoscopy using the BBPS as the reference scale, as a supportive secondary endpoint.7,

Objective

This post hoc analysis reports the comparative rates of successful cleansing between the two dosing regimens of NER1006 and Trisulfate solution bowel preparation in patients with a readable video, using the BBPS as the reference scale.

Methods

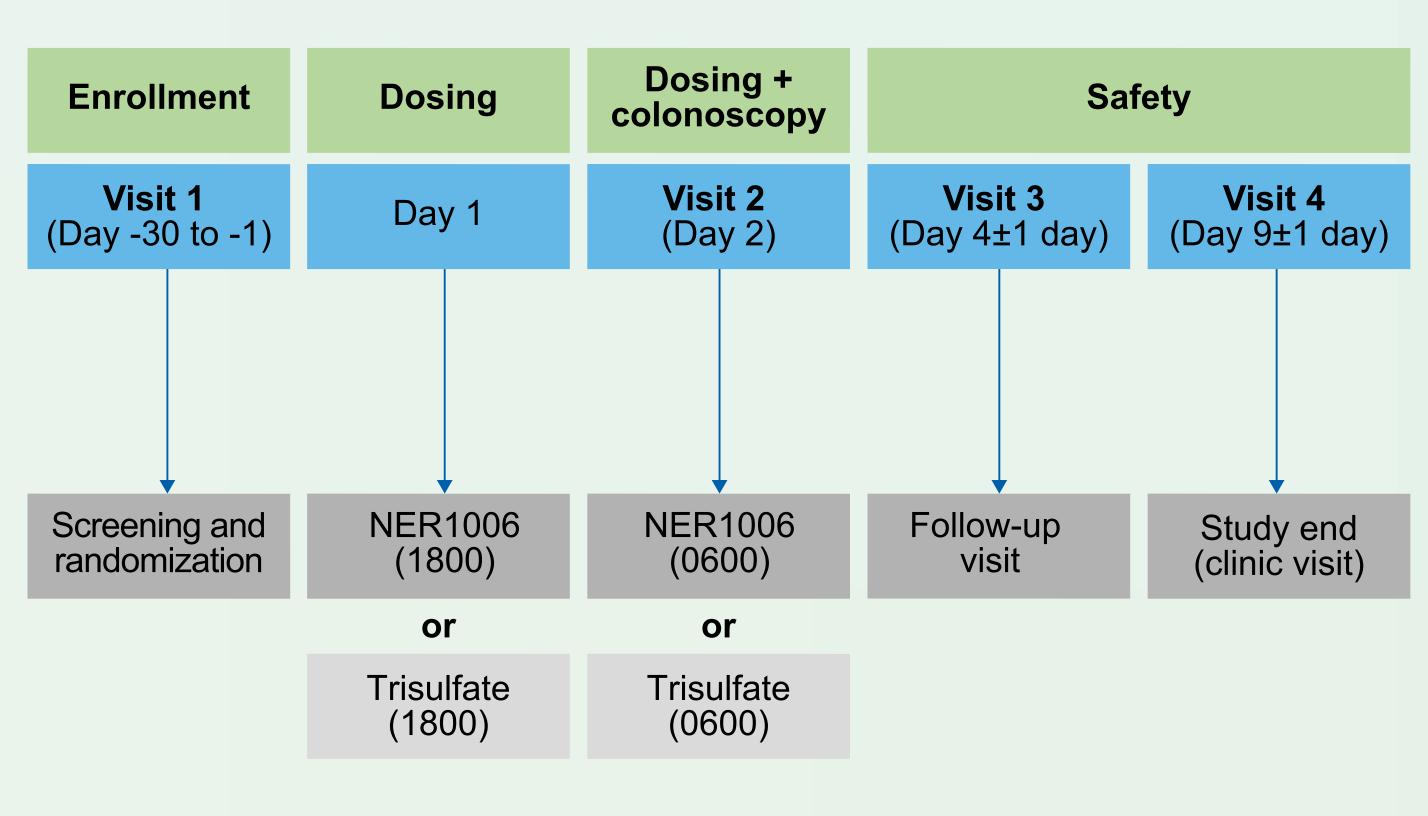
Patients

Patients (aged 18–85) were randomized (Figure 2). The original analysis was conducted in a modified full analysis set (mFAS) with imputation of missing primary efficacy outcomes as failures. The present analysis excluded patients with missing colonoscopy data or those who didn't have a readable video of the colonoscopy to create the mFAS2 (Figure 2).

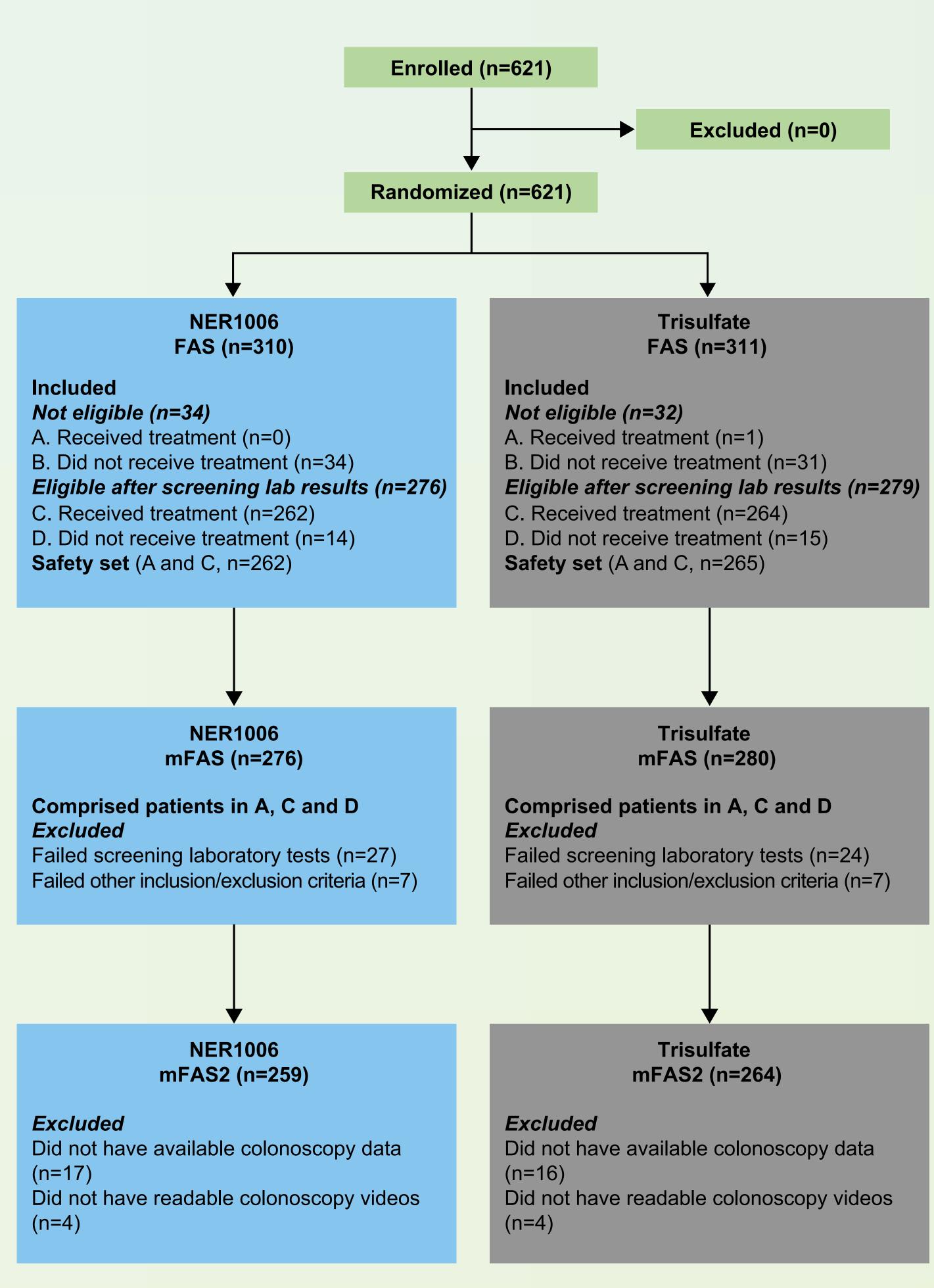
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Affiliations: ¹Digestive Disorders Associates, Annapolis, MD, USA; ²Medical Affairs, Norgine, Harefield, UK; ³Ohio GI & Liver Institute, Cincinnati, OH, USA







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

Endpoints

Cleansing was assessed by treatment-blinded central readers using the BBPS. Successful cleansing was defined as all segments with score ≥ 2 for the overall colon, and segmental score ≥ 2 for the right colon.

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

Baseline demographics

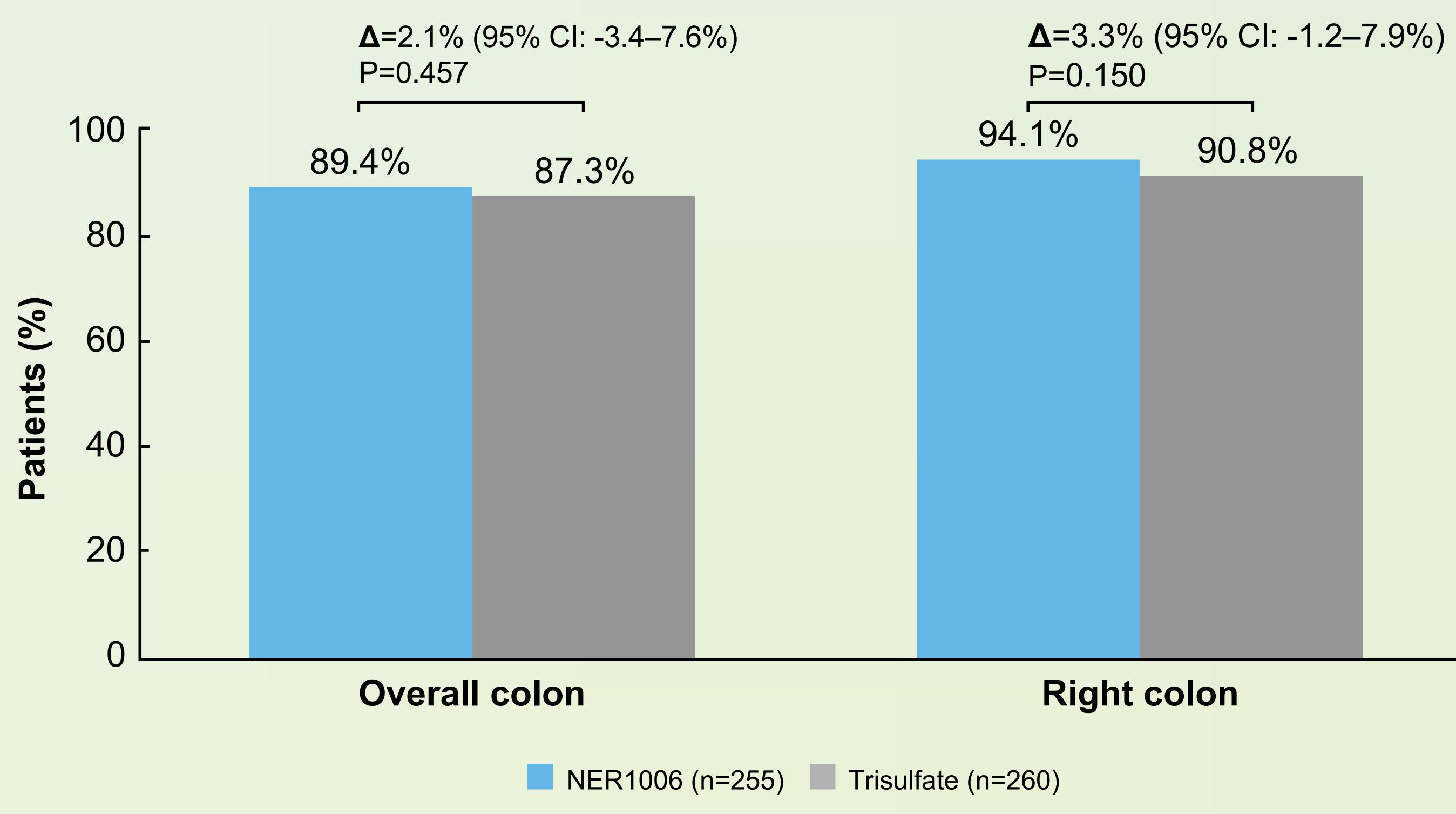
Of the 621 randomized patients, 515 patients had a readable video and were included in this analysis. The baseline demographics are summarized in Table 2.

Table 2. Baseline demographics

	NER1006 (n=255)	Trisulfate (n=260)	
Mean age, years (SD)	57.4 (10.3)	57.0 (10.1)	
P-value for mean age vs Trisulfate	0.642		
Age ≤65 years, n (%)	208 (81.6)	213 (81.9)	
Male, n (%)	129 (50.6)	145 (55.8)	
Race, n (%) White or Caucasian Black Asian Other	217 (85.1) 31 (12.2) 7 (2.7) 0 (0)	215 (82.7) 24 (9.2) 16 (6.2) 5 (1.9)	

Figure 3. Successful level cleansing of the overall colon and right colon (BBPS segmental scores ≥2) as determined by treatment-blinded central readers

NOCT Study Group: P



The results of this post hoc analysis are shown in Figure 3. A higher proportion of patients in the NER1006 group achieved successful overall bowel cleansing compared to those in the Trisulfate group: 89.4% (228/255) versus 87.3% (227/260), P=0.457.

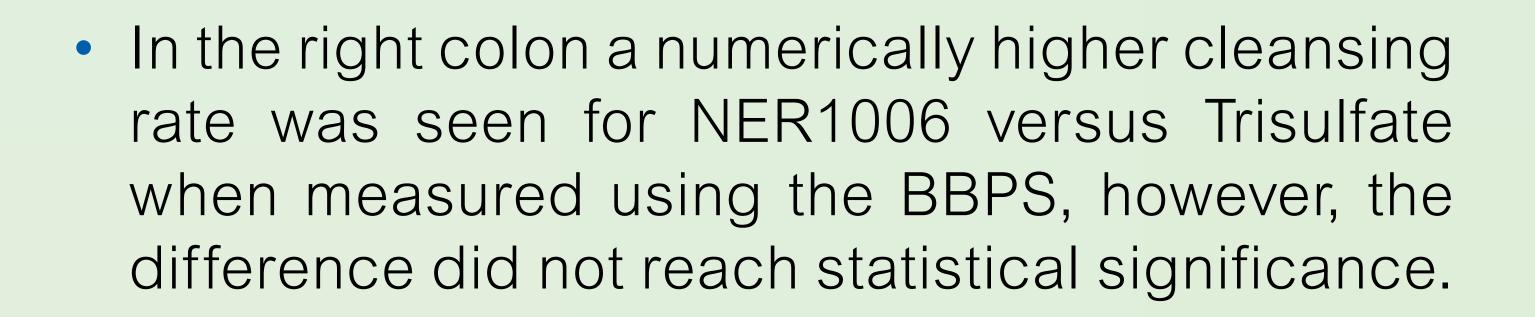
A higher proportion of patients in the NER1006 group achieved successful bowel cleansing in the right colon compared to those in the Trisulfate group: 94.1% (240/255) versus 90.8% (236/260), P=0.150.

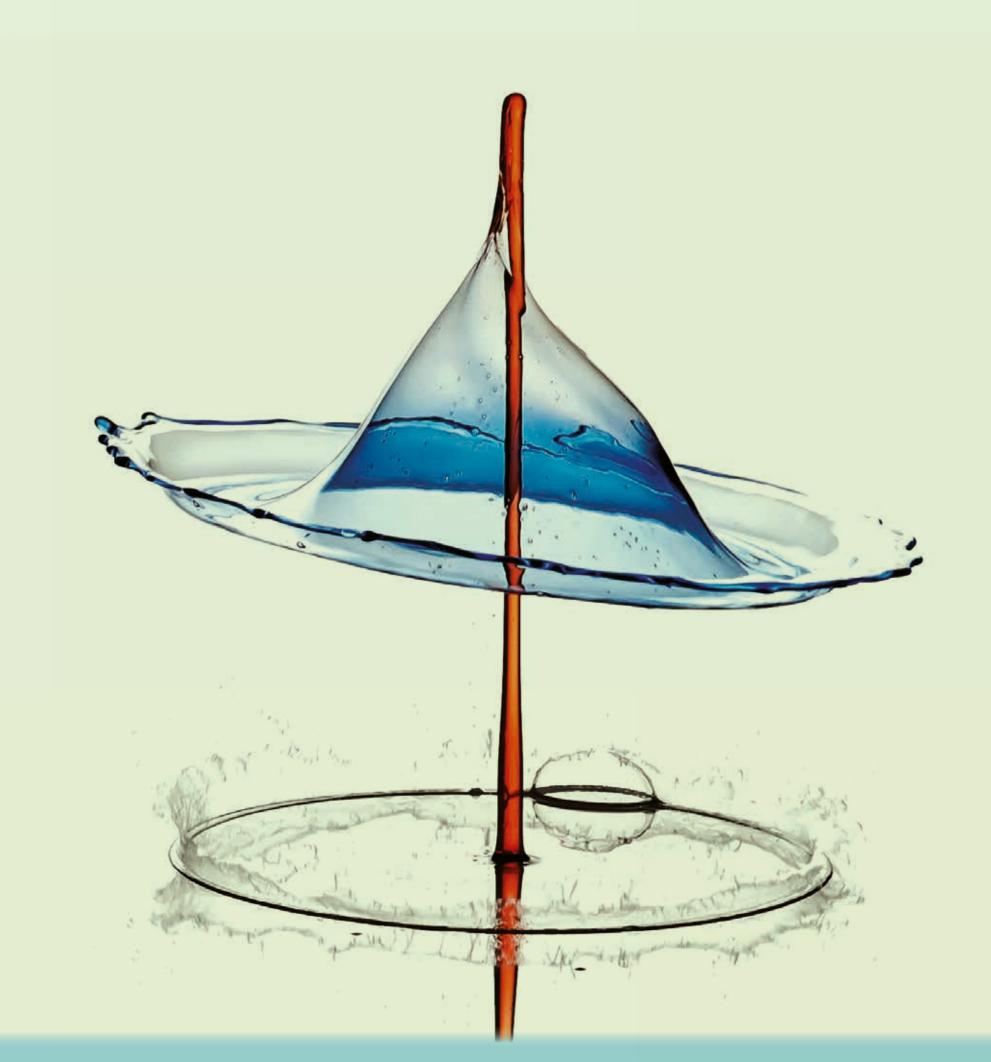
Discussion

- When used as an evening/morning split-dosing regimen, both NER1006 and Trisulfate solution delivered a consistent and very high level of adequate level cleansing success for both the overall colon and the right colon.

90.8%

LLP. Ogden, UT. USA: Barrett Levesque, Robarts, San Diego, CA, USA: Mahmoud Mosli, Robarts, Jeddah, Saudi





sultants For Clinical Research Inc, Cincinnati, OH, USA; Michael 👘 Arabia; Walter Reinisch, Robarts, Modling, Austria; Mariam S. Sauer, Trial Management Associates LLC, Raleigh, DeMicco, Associated Gastroenterology Medical Group, Anaheim, CA, USA; Michael Epstein, Digestive Disorders NC, USA; Mark Silv Associates, Annapolis, MD, USA; Robert Hardi, Chevy Chase Clinical Research, Mentor, OH, USA; Wayne L. Harper, Tucson, AZ, USA. Wake Research Associates LLC, Great Neck, NY, USA; Joseph B, Henderson, Cumberland Research Associates. NC, USA; Mark Silverberg, Robarts, Toronto, Canada; Kenneth E. Smith, Clinical Research Institute of Michigan,

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