Bowel Preparation Quality of NER1006 versus Oral Trisulfate Solution as Assessed by Colonoscopists at Site: a Post Hoc Analysis from a Randomized Controlled Trial

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Introduction

Successful bowel preparation prior to colonoscopy ensures that the full colonic mucosa can be clearly visualized.[1,2] Suboptimal cleansing reduces lesion detection, prolongs procedure time and could have a detrimental effect on clinical outcome.[1–4]

Clinical guidelines for colonoscopy recommend early repeat procedures for patients within adequate bowel cleansing.[3,5] European guidelines recommend that colonoscopy is repeated the following day, which reduces efficiency and increases the cost to healthcare providers.[3,6] The guidelines also recommend using bowel irrigation pumps, which can increase the length of the procedure for the patient.[3,7]

NER1006 is the first 1L (32 fl oz) polyethylene glycol (PEG)-based bowel preparation, and is a patented combination of two different formulations, optimized for effective bowel cleansing.[8] The lower volume of NER1006, compared to currently used preparations, is achieved through increasing the ascorbate component, and administering it in the second dose only.

NOCT (NCT02254486)[9] was a US multicenter, randomized, colonoscopist-blinded, Phase 3 trial that compared NER1006 to Trisulfate in terms of cleansing efficacy in the overall colon and high-quality cleansing in the right colon (ascending colon plus cecum), using the validated Harefield Cleansing Scale (HCS).[10]

In the study, initial evaluation of cleansing was performed by the treatment-blinded colonoscopist, followed by video evaluation by a treatment-blinded independent central reader. The central reader's score was used for the primary and secondary endpoint analyses.

Objective

The objective of this post hoc analysis was to examine the rates of successful cleansing as scored by the site colonoscopists, which may better reflect real-world use of NER1006, where central readers are not used.

Methods

Patients

Patients in the NOCT study were males and females aged 18–85 years who required a screening, surveillance or diagnostic colonoscopy. Patients were randomized into the study in a 1:1 ratio to receive NER1006 or Trisulfate, both administered using an evening/morning split-dosing regimen (Figure 1).

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 scores to create the mFAS2 (Figure 2).

Endpoints

Cleansing was assessed according to the HCS.[9] The HCS scores the five segments of the colon to give an overall colon cleansing grade ranging from A to D; grades A and B were judged as successful cleansing. High-quality cleansing of the right colon was defined as scores of 3 or 4 for that bowel segment.

Figure 1: Study design

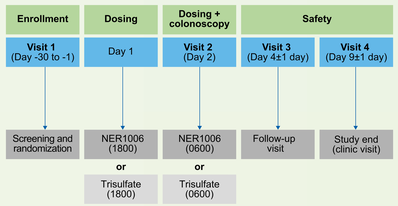
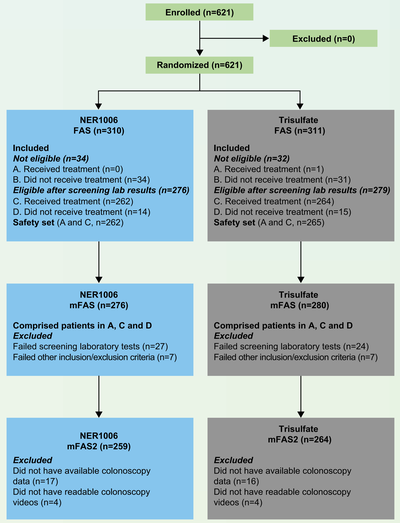


Figure 2: Patient disposition



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

Table 1. Baseline demographics

	NER1006 (n=259)	Trisulfate (n=264)
Mean age, years (SD)	57.5 (10.3)	56.9 (10.3)
P-value for mean age vs Trisulfate	0.528	
Age ≤65 years, n (%)	211 (81.5)	216 (81.8)
Male, n (%)	132 (51.0)	149 (56.4)
Race, n (%)		
White or Caucasian	218 (84.2)	219 (83.0)
Black	34 (13.1)	24 (9.1)
Asian	7 (2.7)	16 (6.1)
Other	0 (0)	5 (1.9)

Statistics

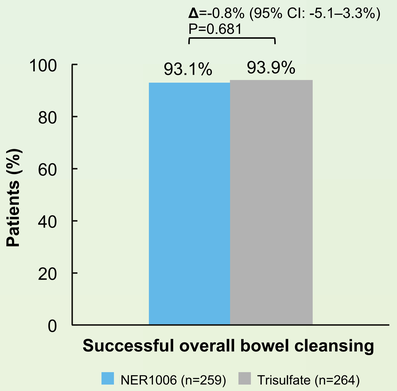
All analyses were carried out using the statistical package R v3.1.3 (The R Foundation, 2015). Colonoscopist-recorded scores were analyzed to determine rates of successful or failed cleansing. Confidence intervals and the t-statistic for each mean difference were calculated and P-values estimated. Numbers needed to treat (NNTs) were also calculated for each comparison.

Results

Baseline demographics

Of the 621 randomized patients, 523 patients had an available cleansing score as assigned by the treatment-blinded site colonoscopist and were included in this analysis (Figure 2). Table 1 shows a summary of patient demographics.

Figure 3: Overall bowel assessment by site colonoscopists



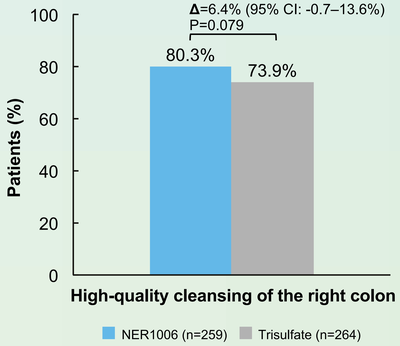
Colonoscopist assessments

Successful overall bowel cleansing was achieved in 93.1% (241/259) of patients who received NER1006 and 93.9% (248/264) of patients in the Trisulfate group, meaning the difference in the rate of successful cleansing between NER1006 and Trisulfate was -0.8% (95% CI: -5.1–3.3%, P=0.681) (Figure 3).

In the right colon, high-quality cleansing was achieved in 80.3% (208/259) of patients who received NER1006 compared to 73.9% (195/264) of patients who received Trisulfate, which was an improvement of 6.4% (95% CI: -0.7–13.6%, P=0.079) (Figure 4).

The corresponding NNT indicates that 17 patients would need to be treated with NER1006 to achieve one additional patient with high-quality cleansing of the right colon compared to Trisulfate.

Figure 4: Right colon assessment by site colonoscopists



Discussion

- For both preparations, site colonoscopist findings demonstrated similar very high rates of cleansing success for the overall colon (>93%) and high rates of high-quality cleansing of the right colon (>73%), however, statistical significance was not met in either comparison.
- The rates of cleansing success in the right colon reported by the site colonoscopists are notably higher than those previously reported by central readers.

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