Bowel preparation quality of NER1006 versus standard 2L PEG with ascorbate as assessed by colonoscopists at site: a post hoc analysis from a randomized controlled trial

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Introduction

Effective bowel preparation for colonoscopy is necessary to ensure that the full colonic mucosa can be visualized and lesions can be detected.[1–3] Suboptimal cleansing reduces lesion detection and may result in delayed treatment and repeat or prolonged procedures.[1–4]

US and European colonoscopy guidelines recommend early repeat procedures for patients with inadequate bowel preparation, with the European guidelines suggesting this happen the day after the initial colonoscopy, which reduces efficiency and increases costs.[5–7] Use of additional devices, such as colon irrigation pumps, is also recommended in patients with inadequate bowel preparation, which can increase the length of the procedure for the patient.[5,8]

NER1006 is the first 32 fl oz (1L) polyethylene glycol (PEG)-based bowel preparation, and is a patented combination of two different formulations, optimized for effective bowel cleansing.

The MORA study[9] was a European multicenter, randomized, colonoscopist-blinded, Phase III clinical trial that compared NER1006 to standard 2L PEG plus ascorbate (2L PEG + Asc) to assess the cleansing efficacy of the overall colon and high-quality cleansing of the 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 during the colonoscopy, 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 MORA study were males and females aged 18–85 years who required a screening, surveillance or diagnostic colonoscopy. In total, 849 patients were randomly assigned 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 an evening/morning split-dose regimen (Figure 1).

For the original efficacy analysis, a modified full analysis set (mFAS) of patients was used, for whom a missing primary efficacy outcome was imputed as 'failure'. In this post hoc analysis, a subset of the original mFAS population was used (mFAS2), which excluded patients who had missing data, with the aim of better reflecting data that would be available to colonoscopists in the clinic.

Figure 1. Study plan

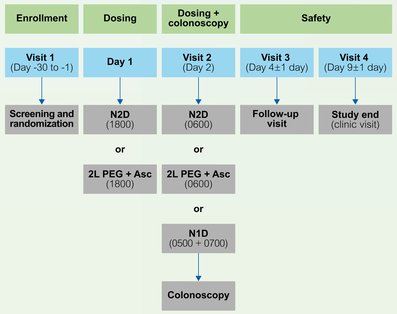


Figure 2. Summary of cleansing assessment on the HCS

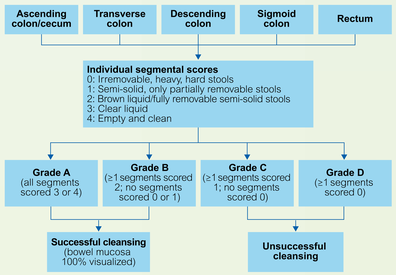
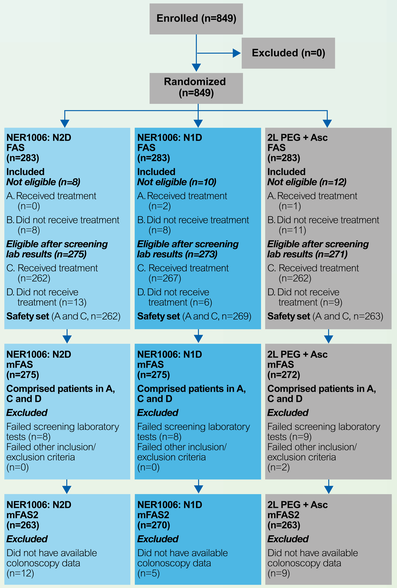


Figure 3. Patient randomization



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

Table 1. Characteristics of patients included in the mFAS2

	N2D (n=263)	N1D (n=270)	2L PEG + Asc (n=263)
Age, mean (standard deviation)	56.6 (11.8)	54.8 (13.2)	54.3 (12.7)
P-value for mean age vs 2L PEG + Asc	0.0343	0.6334	1
Age group, n (%)			
≤65 years	193 (73.4)	210 (77.8)	217 (82.5)
>65 years	70 (26.6)	60 (22.2)	46 (17.5)
Sex, n (%)			
Male	109 (41.4)	125 (46.3)	138 (52.5)
Female	154 (58.6)	145 (53.7)	125 (47.5)
Race, n (%)			
White or Caucasian	257 (97.7)	267 (98.9)	260 (98.9)
Black	5 (1.9)	3 (1.1)	1 (0.4)
Asian	0 (0)	0 (0)	2 (0.8)
Other	1 (0.4)	0 (0)	0 (0)

Figure 4. Overall colon assessment by site colonoscopists

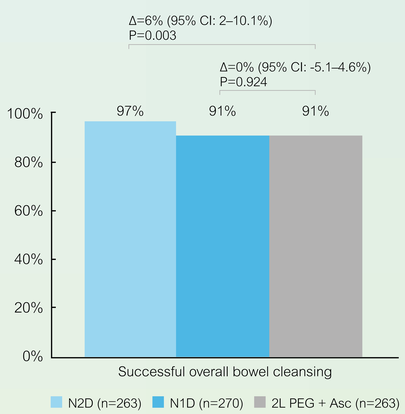
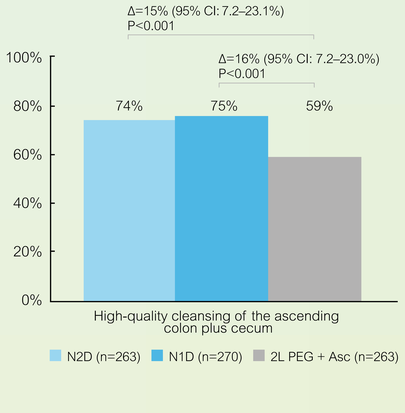


Figure 5. Ascending colon assessment by site colonoscopists



Endpoints

Cleansing was assessed according to the HCS.[10] 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 (Figure 2). Scores of 3 and 4 were judged as high-quality cleansing in the ascending colon plus cecum.

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 (CI) 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

Patient characteristics

Of the 849 randomized patients, 796 patients had an available cleansing score as assigned by the treatment-blinded site colonoscopist and were included in this analysis (Figure 3). The patient characteristics are summarized in Table 1.

Colonoscopist assessments

When both treatments were administered using an evening/morning split-dose regimen, the proportion of patients who achieved successful bowel cleansing was 97% (255/263) for N2D and 91% (239/263) for 2L PEG + Asc (P=0.003; 95% CI: 2.0–10.1%) (Figure 4).

By calculating the corresponding NNT, a total of 17 patients would need to be treated with NER1006 to achieve one additional patient with overall successful cleansing of the whole colon compared to 2L PEG + Asc.

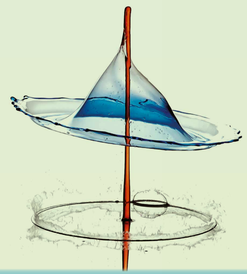
There were no significant differences in cleansing efficacy between N1D and 2L PEG + Asc, with 91% (246/270) of patients in the N1D group achieving overall colon cleansing success compared to 91% (239/263) for 2L PEG + Asc (P=0.924; 95% CI: -5.1–4.6%) (Figure 4).

A significantly higher proportion of patients in the N2D and N1D groups achieved high-quality cleansing of the ascending colon plus cecum, compared to patients in the 2L PEG + Asc group (N2D: P<0.001; 95% CI: 7.2–23.1% and N1D: P<0.001; 95% CI: 7.2–23.0%) (Figure 5).

The NNT for one additional patient to achieve high-quality cleansing of the ascending colon plus cecum compared to 2L PEG + Asc was 7 for N2D and 6 for N1D.

Conclusions

- When comparing evening/morning split-dose regimens, NER1006 showed a significantly increased rate of overall bowel cleansing compared to 2L PEG + Asc, when assessed by site colonoscopists. For every 17 patients treated with NER1006, one extra patient would have successful overall bowel cleansing compared to 2L PEG + Asc
- When administered as a morning-only dosing regimen, NER1006 had a rate of successful cleansing that was comparable to evening/morning split-dose 2L PEG + Asc
- Colonoscopists assessed both dosing regimens of NER1006 as having a significantly increased rate of high-quality cleansing of the ascending colon plus cecum when compared to 2L PEG + Asc
- Compared to treatment with 2L PEG + Asc, one additional patient would have achieved high-quality cleansing of the ascending colon plus cecum for every 7 patients treated with NER1006, administered as an evening/morning split-dose regimen, or for every 6 patients dosed with a morning-only dosing regimen
- Colonoscopist cleansing scores reflect the real-world clinical performance of the respective treatments analyzed here



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