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1 L NER1006 Improves High-Quality Colon Cleansing and Mean Polyp Detection Versus Oral Sulfate Solution and 2 L Polyethylene Glycol Plus Ascorbate

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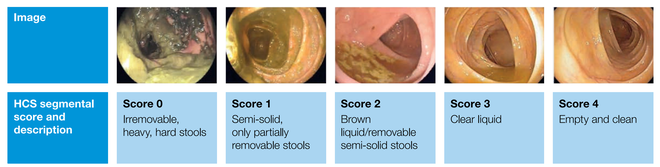
INTRODUCTION

- Up to ~11% of colorectal cancer (CRC) cases are interval cancer, occurring 6 to 60 months postcolonoscopy (ie, before next recommended colonoscopy)[1-4]
  - Interval CRC may occur due to procedural issues during the colonoscopy, such as missed neoplasia, inadequate examinations (eg, poor bowel preparation, incomplete colonoscopy), or incomplete lesion resection[5,6]
- The quality of bowel preparation is a key factor in achieving a successful colonoscopy and optimization of lesion detection
  - The US Multi-Society Task Force defined bowel preparation quality to be adequate if it allows detection of polyps >5 mm and recommends that healthcare providers aim for adequate bowel preparation rates in ≥85% of colonoscopies[7]
  - With commonly used bowel preparation scales, such as the Boston Bowel Preparation Scale and Harefield Cleansing Scale (HCS), patients may achieve an "adequate" cleansing score despite the presence of stool in the colon[8,9]
  - High-quality (eg, stool-free) cleansing is now known to improve polyp and adenoma detection[10,11]
- NER1006 (Plenvu®, Norgine Ltd, Tir-Y-Berth Hengoed, UK) is the first 1 L polyethylene glycol (PEG)-based bowel preparation and is approved in 29 countries and prescribed to >1 million patients worldwide
  - It was approved by the US Food and Drug Administration in 2018 for colon cleansing in preparation for colonoscopy in adults
- Two randomized, phase 3, non-inferiority studies demonstrated that NER1006 improves high-quality colon cleansing,[8,12] and reported adenoma detection rates that exceeded the ≥25% minimum performance target for asymptomatic, average-risk patients ≥50 years undergoing screening colonoscopy[7]
- It is unclear whether NER1006 primarily reduces the amount of stool that needs to be removed (see HCS score = 2 [Figure 1]; in favor of stool-free HCS score = 3) or amount of clear liquid that needs to be removed (see HCS score = 3 [Figure 1]; in favor of the empty and clean HCS score = 4)
- A post hoc analysis was conducted to assess segmental high-quality cleansing with NER1006 versus oral sulfate solution (OSS) and 2 L PEG plus ascorbate (2 L PEG) and resulting mean polyp detection rates

Figure 1. Harefield Cleansing Scale[12]



HCS = Harefield Cleansing Scale.
Reprinted with permission from Bisschops R, et al. *Endoscopy*. 2019;51(1):60-72.[12]

OBJECTIVE

- To characterize segmental high-quality cleansing with NER1006 and determine the effect of bowel cleansing quality on the mean rate of polyp detection per patient

METHODS

- Post hoc analysis of data from 2-day split-dosing (PM/AM) arms of two phase 3, randomized trials of adults aged 18 to 85 years (Figure 2)[8,12]
  - NOCT (Nocturnal Pause Arm): NER1006 versus OSS
  - MORA (Morning Arm): NER1006 versus 2 L PEG

Figure 2. Bowel Preparation Dosing Regimen for Two Phase 3 Trials*†[8,12]

NOCT		MORA	
Day Before Colonoscopy	Day of Colonoscopy	Day Before Colonoscopy	Day of Colonoscopy
NER1006 (PM/AM) Dose 1: 6:00 PM	NER1006 (PM/AM) Dose 2: 6:00 AM	NER1006 (PM/AM) Dose 1: 6:00 PM	NER1006 (PM/AM) Dose 2: 6:00 AM
OSS (PM/AM) Dose 1: 6:00 PM	OSS (PM/AM) Dose 2: 6:00 AM	2 L PEG (PM/AM) Dose 1: 6:00 PM	2 L PEG (PM/AM) Dose 2: 6:00 AM

*OSS and 2 L PEG dietary restriction were consistent with their summary of product characteristics/prescribing information. NER1006 regimens allowed a light breakfast and light lunch. OSS regimen allowed only a light breakfast the day prior to the procedure; 2 L PEG + ascorbate regimen allowed for meals, including a light dinner, on the day before colonoscopy.
†NER1006 AM/AM split-dosing arm in MORA study was not included in the current analyses.
MORA = morning arm; NOCT = nocturnal pause arm; OSS = oral sulfate solution; PEG = polyethylene glycol.

- Bowel cleansing efficacy was assessed by treatment-blinded central readers using the validated HCS (Figure 1)[12,13]
  - Five segments of the colon were scored using the HCS and classified: score of 0 to 1 (failure), 2 (adequate), or 3 to 4 (high quality)
- Presence of polyps were detected during colonoscopy by site endoscopists
- Segmental HCS scores and distribution and mean number of polyps per patient (in patients grouped by ≥1 to ≥10 polyps) were analyzed per treatment group
  - Mean number of polyps per patient was also assessed in pooled NER1006 group versus pooled OSS and 2 L PEG group
- A 1-sided t-test was used to assess between-treatment differences
  - For HCS = 2 in which outcomes were reversed, *P* values were reported as 1-sided *P* value for clarity

RESULTS

- Of 1103 patients from NOCT and MORA, 1037 (94.0%) comprised the primary analysis population (n=5185 segments)
  - 1015 of 1037 patients in the primary analysis population had documented lesion counts and demographics and baseline characteristics were available (Table)

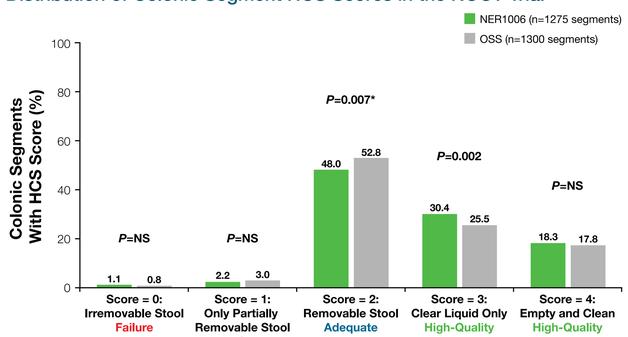
Table. Demographics and Baseline Characteristics*

	NOCT		MORA	
Parameter	NER1006 (N=251)	OSS (N=258)	NER1006 (N=256)	2 L PEG (N=250)
Age, y, mean (SD)	57.2 (10.3)	57.0 (10.1)	56.5 (11.8)	54.0 (12.7)
Sex, n (%)				
Female	128 (51.0)	145 (56.2)	108 (42.2)	133 (53.2)
Male	123 (49.0)	113 (43.8)	148 (57.8)	117 (46.8)
Race, n (%)				
White	214 (85.3)	213 (82.6)	250 (97.7)	247 (98.8)
Black	30 (12.0)	24 (9.3)	5 (2.0)	1 (0.4)
Asian	7 (2.8)	16 (6.2)	0	2 (0.8)
Other	0	5 (2.0)	1 (0.4)	0
BMI, kg/m^2, mean (SD)	29.6 (5.6)	29.7 (6.1)	27.4 (4.8)	26.4 (4.2)
Reason for colonoscopy, n (%)				
Diagnostic	28 (11.2)	27 (10.5)	63 (24.6)	67 (26.8)
Screening	147 (58.6)	155 (60.1)	131 (51.2)	124 (49.6)
Surveillance	76 (30.3)	76 (29.5)	62 (24.2)	59 (23.6)

*1015 of 1037 patients in the primary analysis population who had documented lesion counts.
BMI = body mass index; OSS = oral sulfate solution; PEG = polyethylene glycol; SD = standard deviation.

- In the NOCT trial (Figure 3), a larger percentage of stool-free (HCS score = 3) colonic segments were observed in the NER1006 group versus OSS (30.4% [388/1275] vs 25.5% [331/1300]; *P*=0.002); the percentage of segments with an HCS score = 4 (empty and clean) were similar

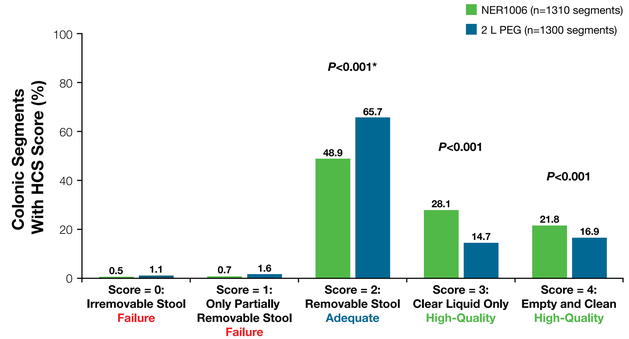
Figure 3. Distribution of Colonic Segment HCS Scores in the NOCT Trial



*1-sided *P* value (1-0.993).
HCS = Harefield Cleansing Scale; OSS = oral sulfate solution.

- In addition, in the MORA trial (Figure 4), a larger percentage of stool-free (HCS score = 3) colonic segments were observed in the NER1006 versus 2 L PEG (28.1% [368/1310] vs 14.7% [191/1300]; *P*<0.001); a significant difference favoring NER1006 was also observed for HCS score = 4

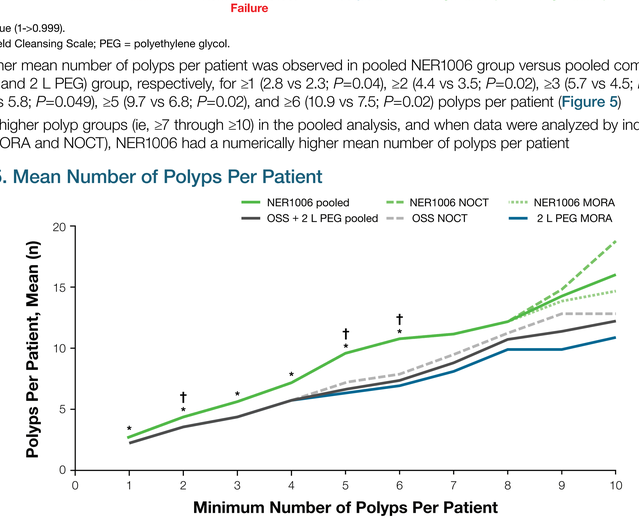
Figure 4. Distribution of Colonic Segment HCS Scores in the MORA Trial



*1-sided *P* value (1->0.999).
HCS = Harefield Cleansing Scale; PEG = polyethylene glycol.

- A higher mean number of polyps per patient was observed in pooled NER1006 group versus pooled comparator (OSS and 2 L PEG) group, respectively, for ≥1 (2.8 vs 2.3; *P*=0.04), ≥2 (4.4 vs 3.5; *P*=0.02), ≥3 (5.7 vs 4.5; *P*=0.03), ≥4 (7.3 vs 5.8; *P*=0.049), ≥5 (9.7 vs 6.8; *P*=0.02), and ≥6 (10.9 vs 7.5; *P*=0.02) polyps per patient (Figure 5)
  - In higher polyp groups (ie, ≥7 through ≥10) in the pooled analysis, and when data were analyzed by individual trial (MORA and NOCT), NER1006 had a numerically higher mean number of polyps per patient

Figure 5. Mean Number of Polyps Per Patient



*Pooled NER1006 versus pooled comparator (OSS and 2 L PEG), *P*<0.05.
†Pooled NER1006 versus 2 L PEG (MORA trial), *P*<0.05.
OSS = oral sulfate solution; PEG = polyethylene glycol.

CONCLUSIONS

- **Finding multiple polyps in a patient during colonoscopy can be challenging**
- **NER1006 improves high-quality cleansing versus OSS or 2 L PEG, primarily by delivering more stool-free segments in the colon**
- **The high-quality bowel cleansing observed with the 1 L PEG NER1006 enabled detection of more polyps per patient during colonoscopy versus comparators**

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DISCLOSURES: MSE reports acting as a principal investigator in research for Investigative Clinical Research; serving as a consultant for IM Health Science; and serving on the speakers' bureau for Pfizer Inc. JH and BA are employees of Norgine Ltd. CH reports being an investigator for Norgine Ltd; and receiving honoraria from Norgine for speaking engagements and advisory board participation.

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