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Efficacy of 1 L NER1006 Bowel Preparation for Colonoscopy in Adults With Diabetes: A Pooled Analysis of Two Randomized, Phase 3 Studies

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INTRODUCTION

- Diabetes has been identified as an independent risk factor for inadequate bowel preparation for colonoscopy[1-3]
  - Diabetes negatively impacts gastrointestinal motility and gastric emptying, although the exact mechanism of gastrointestinal dysfunction is unclear and likely multifactorial[3,4]
- NER1006, a low-volume 1 L polyethylene glycol (PEG)-based bowel preparation (Plenvu®, Norgine Ltd, Tir-Y-Berth Hengoed, United Kingdom), is indicated in multiple countries for colon cleansing in preparation for colonoscopy in adults[5]
- Two randomized, phase 3 studies evaluating the US Food and Drug Administration-approved dosing regimens (2-day evening/morning [PM/AM] split dosing or 1-day morning [AM/AM] of colonoscopy split dosing) have demonstrated that NER1006 was efficacious and well tolerated[6,7]
- Given that diabetes is a risk factor of inadequate bowel preparation, a post hoc analysis of these two phase 3 trials was conducted to assess the cleansing quality and adenoma detection rate (ADR) with NER1006 versus oral sulfate solution (OSS) or 2 L PEG plus ascorbate (2 L PEG) in patients with diabetes

OBJECTIVE

- To examine the efficacy and safety of NER1006, administered as a PM/AM split-dosing regimen, in adults with diabetes

METHODS

- A pooled post hoc analysis was conducted of data from two phase 3, randomized, multicenter studies
  - NOCT study: NER1006 versus OSS[6]
  - MORA study: NER1006 versus 2 L PEG[7]
- Modified full analysis (mFAS) population included adults (aged 18–85 years) undergoing colonoscopy who received a PM/AM split-dose bowel preparation regimen (**Figure 1**)[6,7]
  - All randomly assigned patients were included in the mFAS population except those who failed to meet entry criteria postrandomization and also did not receive study drug (confirmed per patient diary)

Figure 1. Bowel Preparation Dosing Regimen*†[6,7]

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 prescribing information/summary of product characteristics. 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 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; 2 L PEG = 2 L polyethylene glycol plus ascorbate.

METHODS

- Colon cleansing success was assessed by treatment-blinded central readers using 2 validated scales[6,7]:
  - Boston Bowel Preparation Scale (BBPS)[8]: success defined as score ≥6 overall and ≥2 in each colonic segment (right [ascending colon/cecum], transverse, and left colon [descending colon, sigmoid colon, and rectum])
  - Harefield Cleansing Scale (HCS)[9]: success defined as all 5 colonic segments scored 3 (clear liquid) or 4 (empty and clean) or ≥1 segment scored 2 (brown liquid/fully removable semi-solid stools) with other segments scored 3 or 4 (ie, good/excellent)
    - Good/excellent cleansing quality (colon segments free of stool; score 3 or 4) was also determined for each colon segment
- Lesions were detected by site endoscopists and adenomas were confirmed by histopathology
  - Overall ADR was defined as the number of patients with ≥1 adenoma divided by total number in the mFAS population
- Differences in cleansing quality and ADR between treatment groups were determined using Fisher's exact test
- Safety was monitored through Day 7 ± 1 after colonoscopy

RESULTS

- 92 adults with type 1 or 2 diabetes, reported as part of medical history, were included in the current analysis (**Table**)

Table. Demographic and Baseline Characteristics

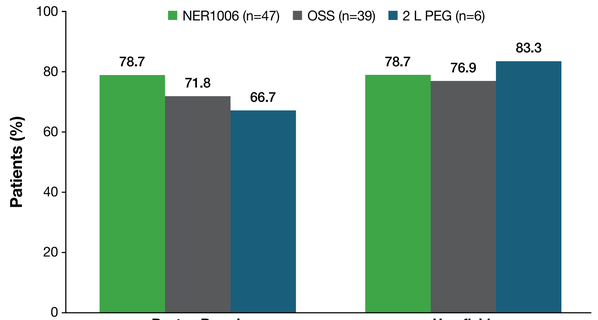
Parameter	NER1006 (N=47)	OSS (N=39)	2 L PEG (N=6)
Age, y			
Mean (SD)	63.6 (7.9)	59.8 (7.1)	63.8 (7.5)
Range	50–86	49–77	56–75
Male sex, n (%)	26 (55.3)	28 (71.8)	3 (50.0)
Race, n (%)			
White	34 (72.3)	33 (84.6)	6 (100.0)
Black	10 (21.3)	4 (10.3)	0
Asian	3 (6.4)	1 (2.6)	0
Other	0	1 (2.6)	0

OSS = oral sulfate solution; 2 L PEG = 2 L polyethylene glycol plus ascorbate; SD = standard deviation.

RESULTS

- There were no significant differences in the overall cleansing success rate in patients with diabetes for NER1006 compared with OSS or 2 L PEG when assessed by BBPS or HCS (**Figure 2**)

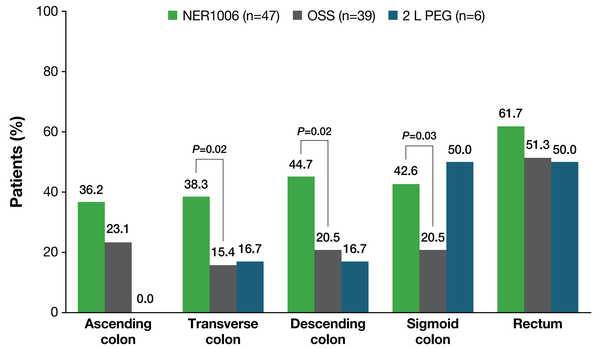
Figure 2. Overall Cleansing Success Rates in Patients With Diabetes



P>0.05 for NER1006 versus OSS or versus 2 L PEG.
OSS = oral sulfate solution; 2 L PEG = 2 L polyethylene glycol plus ascorbate.

- Good/excellent cleansing quality in each colonic segment was achieved by a similar percentage of patients with diabetes receiving NER1006 versus OSS or 2 L PEG, with statistical differences favoring NER1006 relative to OSS for 3 segments of the colon (**Figure 3**)
  - Differences were significant for NER1006 versus OSS for the transverse (*P*=0.02), descending (*P*=0.02), and sigmoid (*P*=0.03) colon

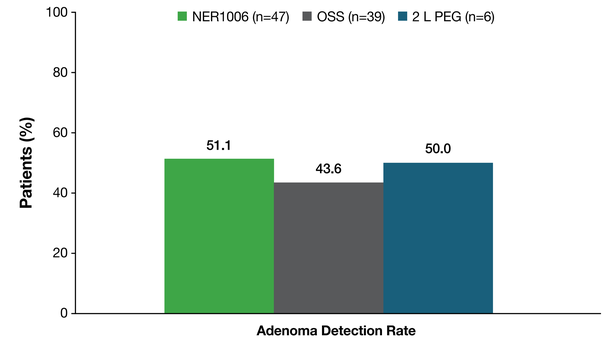
Figure 3. Excellent or Good Quality Bowel Cleansing (HCS) in Patients With Diabetes, by Colonic Segment



P>0.05 for NER1006 versus OSS or versus 2 L PEG, unless otherwise indicated.
HCS = Harefield Cleansing Scale; OSS = oral sulfate solution; 2 L PEG = 2 L polyethylene glycol plus ascorbate.

- The overall ADR in patients with diabetes was similar for NER1006 versus comparators (**Figure 4**)

Figure 4. Overall Adenoma Detection Rate in Patients With Diabetes



P>0.05 for NER1006 versus OSS or versus 2 L PEG.
OSS = oral sulfate solution; 2 L PEG = 2 L polyethylene glycol plus ascorbate.

- NER1006 was well tolerated in patients with diabetes
  - No adverse events (AEs) were reported by >1 patient in any treatment group and no AEs led to study discontinuation
  - There was one serious AE (ileus) in a patient receiving NER1006; this AE was considered unrelated to treatment
  - A similar incidence of drug-related AEs was observed with NER1006 (4.8%) and OSS (5.7%); 1 (16.7%) of 6 patients in 2 L PEG had a drug-related AE

CONCLUSIONS

- **Although limited by a small number of patients, this analysis supports that NER1006 is efficacious and well tolerated as a bowel preparation in adults with diabetes undergoing colonoscopy**

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