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1 L Polyethylene Glycol-Based NER1006 Is Efficacious as a Bowel Preparation for Colonoscopy in Patients With or Without Diabetes Mellitus: a Pooled Analysis of 2 Randomized, Phase 3 Studies

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INTRODUCTION

- Diabetes mellitus (DM) is an independent risk factor for inadequate bowel preparation for colonoscopy¹⁻³
- DM has been associated with slowed gastrointestinal (GI) motility and delayed gastric emptying⁴⁻⁵
- Although the exact mechanism for altered GI function in patients with DM is unclear, it is considered to be multifactorial⁴⁻⁶
- NER1006 (Plenvu[®], Norgine Ltd, Tir-Y-Berth Hengoed, United Kingdom) is a low-volume 1 L polyethylene glycol (PEG)-based bowel preparation indicated in the United States in 2018 for colon cleansing in preparation for colonoscopy in adults⁷
- The efficacy, safety, and tolerability of NER1006 were demonstrated in 2 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 [ам/ам] of colonoscopy split dosing)^{8,9}

OBJECTIVE

 To evaluate the efficacy of NER1006 bowel preparation in adults with DM compared with those without DM

METHODS

- A pooled post hoc analysis of two phase 3, randomized, double-blind, controlled, multicenter studies (NOCT/MORA)^{8,9} was conducted
- The current analysis included patients aged 18 to 85 years who underwent screening, surveillance, or diagnostic colonoscopy and received NER1006 as a 2-day pm/am split-dose bowel preparation regimen (Figure 1)^{8,9}
- All patients randomly assigned to NER1006 were included in the analysis except those who failed to meet entry criteria postrandomization and did not receive the study drug (as confirmed via patient diary entries)

Figure 1. NER1006 Bowel Preparation Dosing Regimen*^{8,9}



*A light breakfast and light lunch were permitted on the day before the colonoscopy. The NER1006 AM/AM split-dosing arm of the MORA study and the comparator arms of NOCT/MORA (oral sulfate solution/2 L polyethylene glycol plus ascorbate) were not included in the current analyses.

- Type 1 or type 2 DM was determined as part of medical history at the screening visit
- Bowel cleansing efficacy was evaluated via video review by central readers who were blinded to the treatment arm

METHODS

- Overall colon cleansing success rates were assessed using the Boston Bowel Preparation Scale (BBPS)¹⁰ and Harefield Cleansing Scale (HCS), both validated scales¹¹
- BBPS: successful bowel cleansing was defined as an overall score ≥ 6 with a score ≥ 2 in each of the 3 segments (right [ascending colon/cecum], transverse, and left colon [descending colon, sigmoid colon, rectum])
- HCS: successful bowel cleansing was defined as all 5 colonic segments scored as 3 (clear liquid) or 4 (empty and clean); or ≥ 1 segment scored as 2 (brown liquid/fully removable semi-solid stools) and other segments scored as 3 or 4 (ie, good/excellent)
- Good/excellent cleansing quality (colon segments free of stool; HCS score of 3 or 4) was also determined for the ascending colon
- Lesions were detected by onsite endoscopists who performed the colonoscopy and were blinded to treatment, and adenomas were confirmed by histopathology
- Overall and ascending colon adenoma detection rate (ADR) were calculated (number of patients with ≥ 1 adenoma divided by total population)
- P values were calculated using a 2-sided Fisher's exact test

RESULTS

 A total of 47 patients with type 1 or 2 DM and 504 patients without DM were included in the analysis (Table)

Table. Demographics and Baseline Characteristics

Parameter	Patients With Diabetes (n=47)	Patients Without Diabetes (n=504)
Age, y, mean (SD)	63.6 (7.9)	56.4 (11.2)
Sex, male, n (%)	26 (55.3)	229 (45.4)
Race, n (%)		
White	34 (72.3)	466 (92.5)
Black	10 (21.3)	33 (6.5)
Other	3 (6.4)	5 (1.0)
Weight, kg, mean (SD)	89.7 (14.7)	80.3 (17.7)

SD = standard deviation.

 Overall colon cleansing success rates with NER1006 were high and similar between patients with DM and patients without DM using the BBPS (78.7%) vs 87.3%; P=0.12) or HCS (78.7% vs 89.5%; P=0.05; Figure 2)

RESULTS



*Defined for HCS as all 5 colonic segments scored as 3 (clear liquid) or 4 (empty and clean); or ≥1 segment scored as 2 (brown liquid/fully removable semi-solid stools) and other segments scored as 3 or 4 (ie, good/excellent); defined for BBPS as an overall score ≥ 6 with score ≥ 2 in each of 3 segments (right, transverse, and left colon). 3BPS = Boston Bowel Preparation Scale; HCS = Harefield Cleansing Scale.

 Excellent or good cleansing quality in each colonic segment, based on the HCS, was achieved in a similar percentage of patients with DM or without DM (Figure 3)

Figure 3. NER1006 Excellent or Good Quality* Bowel Cleansing (HCS) in Patients With or Without Diabetes, by Colonic Segment



Patients with diabetes (n=47) Patients without diabetes (n=504)

*Defined as empty and clean or clear liquid observed in colonic segments. HCS = Harefield Cleansing Scale.

 The overall ADR was significantly higher in patients with DM compared with patients without DM (P=0.002) and similar to data for ADR in the ascending colon (P=0.18; Figure 4)

Figure 4. Overall and Ascending Colon Adenoma Detection Rates

 Limitations of this study include the small number of patients with DM and lack of stratification by type of DM



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