Improved High-Quality Colon Cleansing With 1 L NER1006 Versus 2 L Polyethylene Glycol + Ascorbate or Oral Sulfate Solution

Marc E. Sher, MD, FACS, FASCRS[1]; Prateek Sharma, MD[2]; Alessandro Repici, MD[3]; Howard Franklin, MD[4]; Daniel C. Baumgart, MD[5]

[1]Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA; [2]University of Kansas School of Medicine, Kansas City, KS, USA; [3]Humanitas University, Milan, Italy; [4]Salix Pharmaceuticals, Bridgewater, NJ, USA; [5]University of Alberta, Edmonton, Alberta, Canada

BACKGROUND

- Colonoscopy requires bowel cleansing for visualization of the gut mucosa, and high-quality cleansing is important for maximizing lesion detection to improve patient outcomes[1,2]
- NER1006 (Plenvu®, Norgine Limited, Hengoed, UK) is a low volume, 1 L polyethylene glycol (PEG) bowel preparation approved in the United States in 2018 for colon cleansing prior to colonoscopy in adults[3]
- The efficacy and safety of NER1006 has been demonstrated in three phase 3 trials[4-6]
  - Primary efficacy endpoints employed treatment-blinded central readers, a method used to minimize inter-reader variability[7]
- However, in real-world clinical practice, site endoscopists assess the level of bowel cleansing before making clinical decisions

AIM

- Post hoc analysis to investigate the cleansing quality of NER1006 versus 2 L PEG + ascorbate (asc) or oral sulfate solution (OSS) assessed, as in clinical practice (ie, real-world cleansing performance), by site endoscopists

METHODS

- Data were analyzed from two phase 3, multicenter, randomized, noninferiority trials (morning arm [MORA] and nocturnal pause arm [NOCT]) in adults (18-85 y) scheduled to undergo a colonoscopy (Figure 1)[5,6]
  - MORA (NER1006 vs 2 L PEG + asc [MoviPrep®, Norgine Limited, Hengoed, UK]) administered as 2-day evening/morning split (PM/AM) or 1-day morning-only dosing (AM/AM)[5]
  - NOCT (NER1006 vs OSS [trisulfate] solution [SuPrep® Bowel Prep Kit, Braintree Laboratories, Inc., Braintree, MA]) administered as 2-day (PM/AM) split dosing[6]

Figure 1. Bowel Prep Dosing Regimens for the Two Phase 3 Trials*[5,6]

*2 L PEG and OSS were administered per their summary of product characteristics/prescribing information. 2 L PEG + asc PM/AM regimen allowed for meals, including a light dinner, on the day before colonoscopy; OSS regimen allowed only breakfast the day prior to the procedure. Both PM/AM and AM/AM NER1006 regimens allowed a light breakfast and light lunch and NER1006 AM/AM regimen also allowed a light dinner.
asc = ascorbate; MORA = morning arm; NOCT = nocturnal pause arm; OSS = oral sulfate solution; PEG = polyethylene glycol.

METHODS

- 3 patient populations were analyzed
  - **mFAS:** modified full analysis set (all randomized patients except those who failed to meet entry criteria post-randomization and did not receive any study drug [per patient diary]) with imputed failures included
  - **mFAS2:** modified full analysis set with imputed failures excluded
  - **mFAS100:** patients in the mFAS population with 100% treatment adherence to bowel prep regimen
- Bowel cleansing was assessed by site endoscopists using the validated Harefield Cleansing Scale (HCS)[8]
  - 5-segment assessment (right colon [ascending colon/cecum], transverse colon, descending colon, sigmoid colon, and rectum); each segment individually scored from 0 (irremovable, heavy, hard stools) to 4 (empty and clean)
  - Grade A = all 5 segments scored 3 or 4; grade B = ≥1 segment scored 2, remaining segments scored 3 or 4; grade C = ≥1 segment scored 1, remaining segments scored 2, 3, or 4; grade D = ≥1 segment scored 0
- Overall successful cleansing defined as HCS grades A or B, overall high-quality cleansing defined as HCS grade A, and high-quality cleansing of individual colon segments defined as HCS segmental scores of 3 or 4
- P values comparing NER1006 with 2 L PEG + asc or OSS were estimated using a one-sided Student's t-test

RESULTS

- 1378 adults were included in the mFAS population, 1319 in mFAS2 population, and 1047 in the mFAS100 population (Table)
  - mFAS and mFAS2 populations have been previously described[5,6]

RESULTS

- Overall cleansing success in the 3 populations was significantly higher with NER1006 PM/AM dosing (92.7%–97.5%) versus 2 L PEG + asc PM/AM dosing (87.9%–93.0%; Figure 2)

Figure 2. Overall Bowel Cleansing Success*
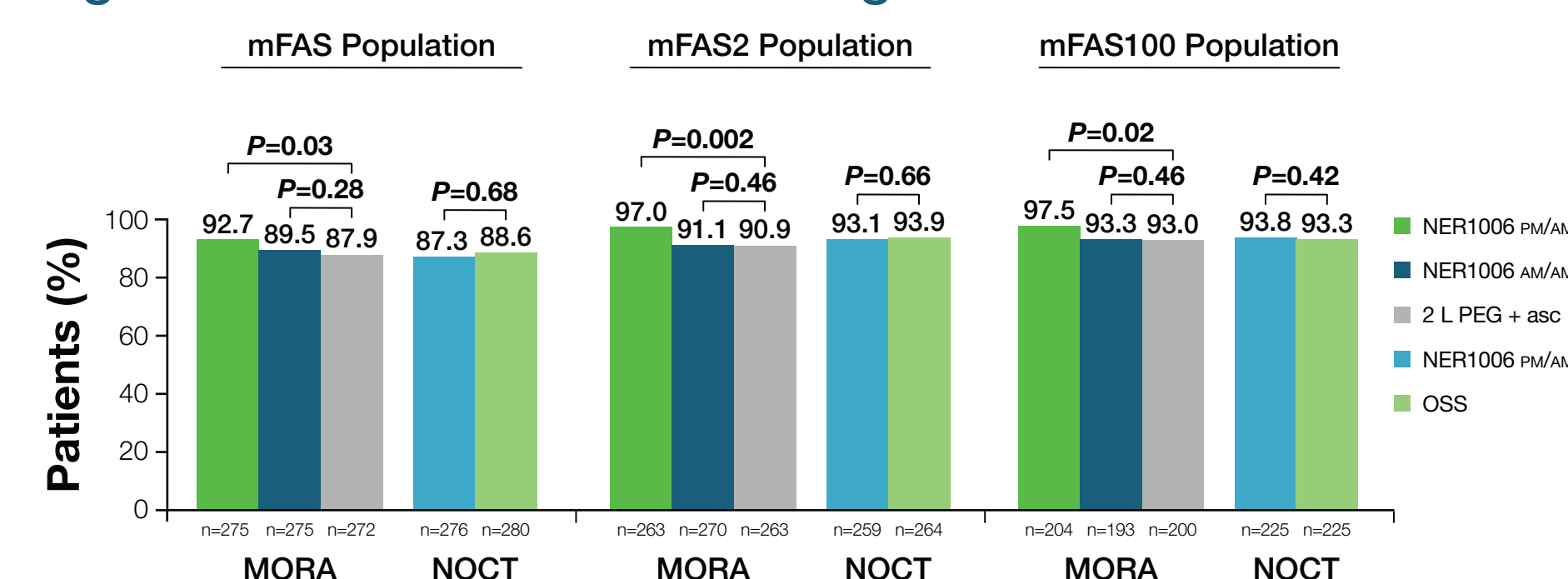
*Overall successful cleansing defined as Harefield Cleansing Scale score of grades A or B.
mFAS = modified full analysis set including imputed failures; mFAS2 = modified full analysis set excluding imputed failures; mFAS100 = patients in mFAS with 100% treatment adherence; MORA = morning arm; NOCT = nocturnal pause arm; OSS = oral sulfate solution; PEG = polyethylene glycol.

- Overall high-quality cleansing rates were also significantly higher for NER1006 PM/AM (68.0%–72.1%) and NER1006 AM/AM (64.0%–68.4%) versus 2 L PEG + asc PM/AM (50.7%–56.0%; Figure 3)

Figure 3. Overall High-Quality Bowel Cleansing Success*
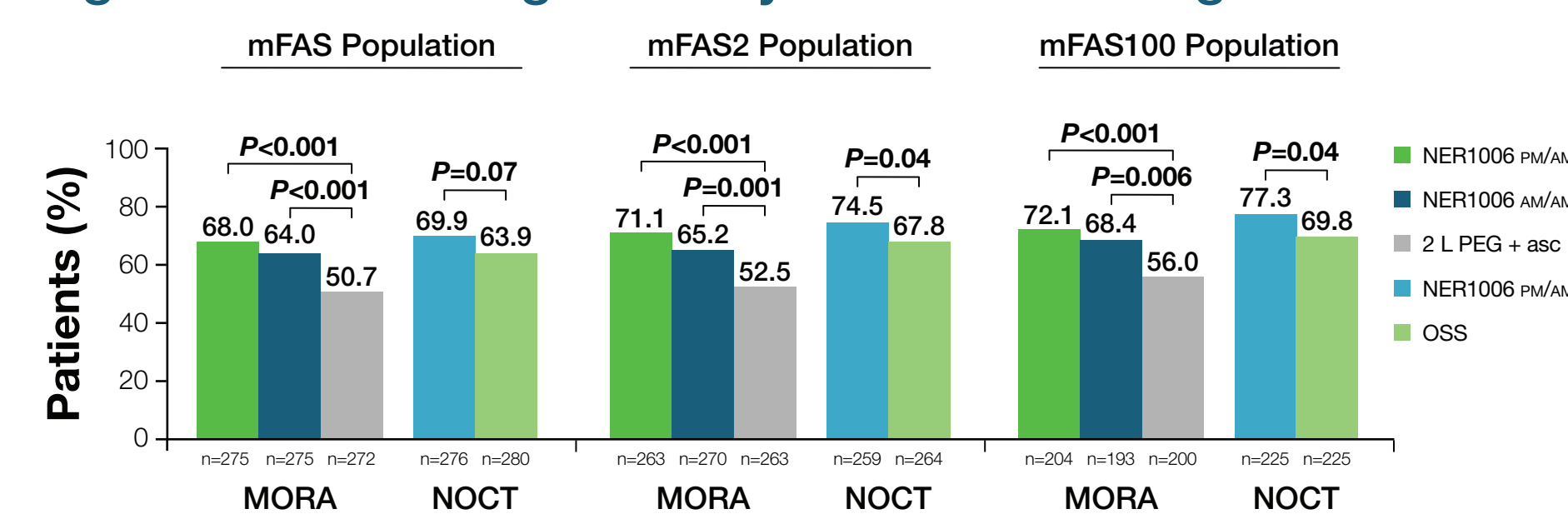
*High-quality bowel cleansing success defined as Harefield Cleansing Scale score grade A.
mFAS = modified full analysis set including imputed failures; mFAS2 = modified full analysis set excluding imputed failures; mFAS100 = patients in mFAS with 100% treatment adherence; MORA = morning arm; NOCT = nocturnal pause arm; OSS = oral sulfate solution; PEG = polyethylene glycol.

- A higher percentage of high-quality colon segments was observed with NER1006 PM/AM (82.5%–87.1%) and NER1006 AM/AM (79.3%–84.4%) versus 2 L PEG + asc PM/AM (70.4%–76.3%), and with NER1006 PM/AM (82.7%–89.5%) versus OSS (78.1%–84.4%; Figure 4)

Figure 4. Percentage of Segments With High-Quality Cleansing*
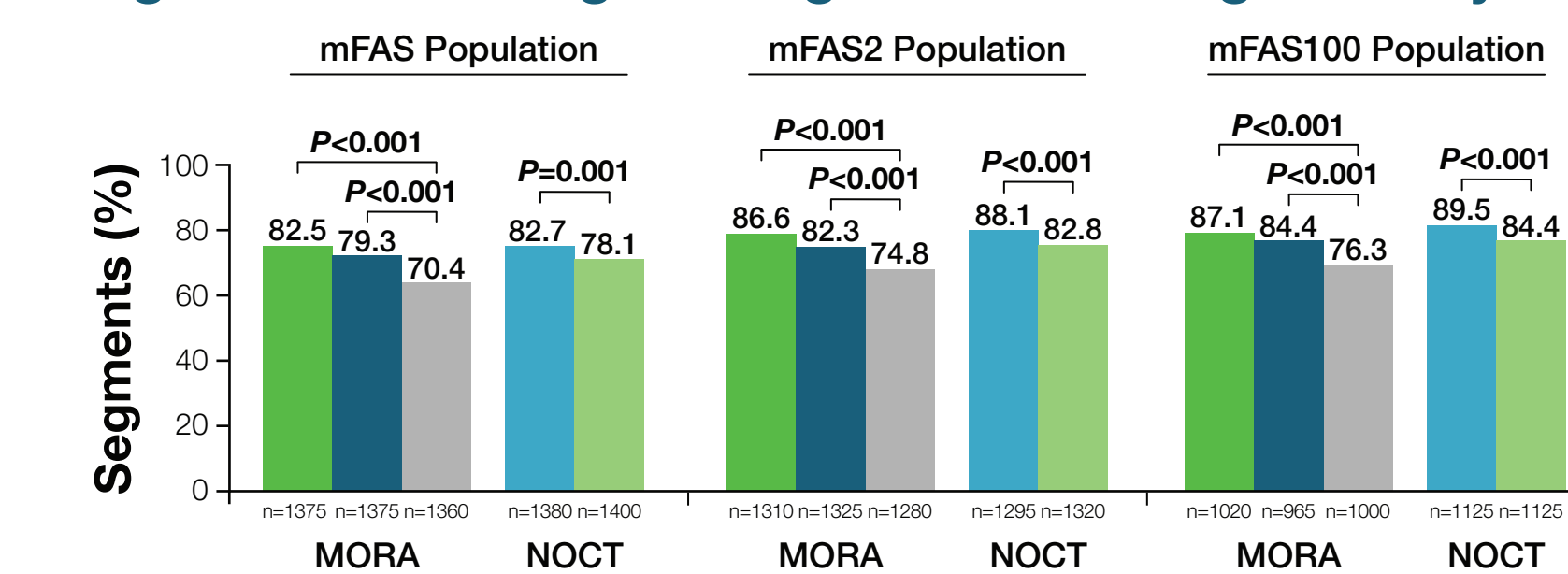
*Segment with a Harefield Cleansing Scale score of 3 or 4.
mFAS = modified full analysis set including imputed failures; mFAS2 = modified full analysis set excluding imputed failures; mFAS100 = patients in mFAS with 100% treatment adherence; MORA = morning arm; NOCT = nocturnal pause arm; OSS = oral sulfate solution; PEG = polyethylene glycol.

- For 100% adherent patients (mFAS100) with overall cleansing failure (HCS grade C or D), NER1006 PM/AM provided a higher rate of patients with ≥1 high-quality segment than OSS (85.7% [12/14 patients] vs 46.7% [7/15]; P=0.01) and a higher percentage of segments with high-quality cleansing than OSS (45.7% [32/70 segments] vs 22.7% [17/75]; P=0.002) in the overall treatment group

CONCLUSIONS

- When assessed by site endoscopists, NER1006 (Plenvu) delivered greater high-quality, HCS grade A cleansing than either 2 L PEG + asc (MoviPrep) or OSS (SuPrep)
- Given its low volume and high-quality cleansing outcomes, NER1006 should be considered an important option for bowel preparation before colonoscopy

Table. Patient Demographics and Baseline Characteristics of mFAS100 Population

| Characteristic	MORA			NOCT	
	NER1006 PM/AM (n=204)	NER1006 AM/AM (n=193)	2 L PEG + asc (n=200)	NER1006 PM/AM (n=225)	OSS (n=225)
Age ≤65 y, n (%)	152 (74.5)	148 (76.7)	167 (83.5)	187 (83.1)	183 (81.3)
Male, n (%)	89 (43.6)	93 (48.2)	111 (55.5)	118 (52.4)	135 (60.0)
Race, n (%)					
White	200 (98.0)	192 (99.5)	198 (99.0)	189 (84.0)	183 (81.3)
Black	3 (1.5)	1 (0.5)	0	30 (13.3)	22 (9.8)
Other	4 (0.5)	0	2 (1.0)	6 (2.7)	20 (8.9)
BMI, kg/m², mean (SD)	27.1 (4.6)*	27.1 (4.2)	26.4 (4.0)†	29.6 (5.5)	29.8 (6.2)
Reason for colonoscopy, n (%)					
Screening	99 (48.5)	99 (51.3)	98 (49.0)	134 (59.6)	139 (61.8)
Surveillance	49 (24.0)	33 (17.1)	40 (20.0)	64 (28.4)	63 (28.0)
Diagnostic	56 (27.5)	61 (31.6)	62 (31.0)	27 (12.0)	23 (10.2)

*Data missing for 1 patient.
†Data missing for 2 patients.
BMI = body mass index; mFAS100 = patients in mFAS with 100% treatment adherence; MORA = morning arm; NOCT = nocturnal pause arm; OSS = oral sulfate solution; PEG = polyethylene glycol; SD = standard deviation.

REFERENCES: 1. Johnson DA, et al. *Gastroenterology.* 2014;147(4):903-924. **2.** Pontone S, et al. *United European Gastroenterol J.* 2016;4(6):778-783. **3.** Plenvu® (polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride and potassium chloride for oral solution) [package insert]. Hengoed, UK: Norgine Limited; 2018. **4.** Schreiber S, et al. *Endoscopy.* 2019;51(1):73-84. **5.** Bisschops R, et al. *Endoscopy.* 2019;51(1):60-72. **6.** DeMicco MP, et al. *Gastrointest Endosc.* 2018;87(3):677-687. **7.** Kane SV, et al. *Gastrointest Endosc.* 2016;83:198-200. **8.** Halphen M, et al. *Gastrointest Endosc.* 2013;78(1):121-131.