Colon Cleansing Efficacy and Safety of 1L NER1006 in Patients with Mild to Moderate Renal Impairment: Post Hoc Analysis of Randomized Phase 3 Clinical Trials

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Premise

Effective bowel preparation is critical for the diagnostic and therapeutic success of colonoscopy. Pre-procedural bowel cleansing is an important step for the detection of adenomas.¹

For patients with chronic kidney disease, bowel preparations may increase the risk of electrolyte imbalance or worsen renal function. Polyethylene glycol (PEG) based solutions pass through the bowel without absorption or secretion. Only PEG-based bowel preparations are recommended for patients with renal failure.²

NER1006 is the first 1L PEG-based bowel preparation. It is a taste-optimized combination of two different formulations, designed to maximize adherence and to work synergistically for bowel cleansing.¹ The efficacy and safety of NER1006 have been established in a Phase 3 clinical trial program, consisting of three large, European and US, multicenter, randomized, treatment-blinded central reader-assessed, active-controlled trials.^{3–5} NER1006 is not contraindicated in patients with renal impairment and no special dosage adjustment of NER1006 is deemed necessary in patients with mild to moderate renal impairment.

Objective

In the present post hoc analysis, the randomized NER1006 Phase 3 clinical trials assessed the colon cleansing efficacy of NER1006 in renally impaired versus non-renally impaired patients.

Methods

Patients

The three Phase 3 clinical trials in the NER1006 clinical development program were MORA, NOCT and DAYB and assessed the efficacy, safety, and tolerability of NER1006 compared with various licensed bowel preparations (Figure 1).^{3–5} Patients in these studies were males and females aged 18-85 years who required a screening, surveillance or diagnostic colonoscopy.

For the purpose of this post-hoc analysis, patients were stratified into creatinine clearance rate (CrCl) groups: normal renal function (\geq 90mL/min), mild renal insufficiency (\geq 60 to \geq 90mL/ min), or moderate renal insufficiency (≥ 30 to ≥ 60 mL/min). Patients with severe renal insufficiency were excluded. The efficacy analysis included patients with a documented renal status and colonoscopy data.

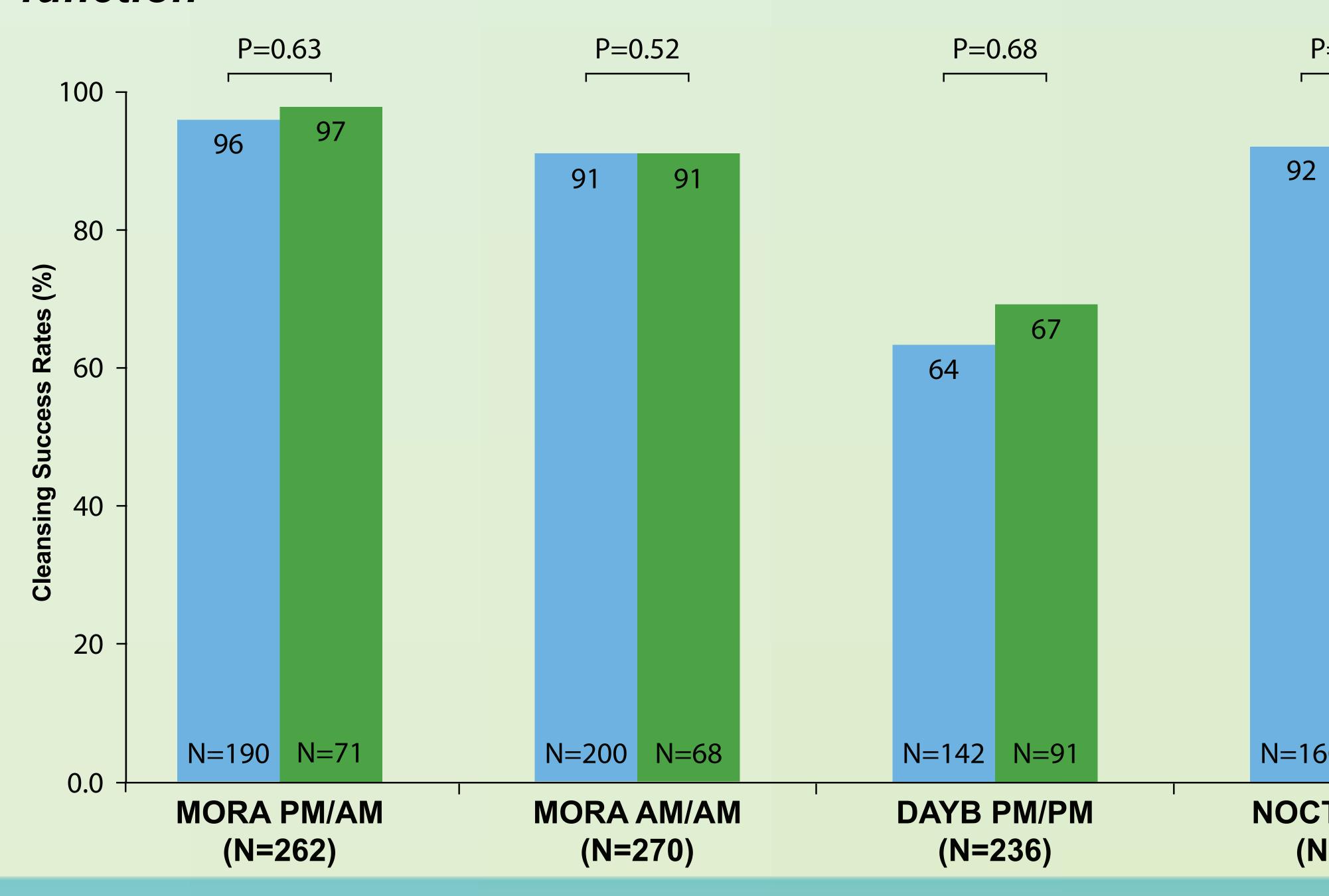
Author disclosure information: Cesare Hassan: an investigator in the DAYB study and received honoraria from Norgine Ltd for advisory board attendance, no other conflicts of interest; Hannah Thompson: employee of Norgine; Soniya Mokashi: employee of

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rati			ad bowel AYB, MORA	Table 1. Summaryand moderate renacombined NER100	l impairme	nt group a	nd normal	renal func		
BEFORE	DAYB	MORA		Number of patients (%)						
	SPMC (AM/PM) Dose 1: 08:00 NER1006 (PM/PM) Dose 1: 18:00				2-Day (N=524)		1-Day (N=504)		Overall (N=1028)	
					All TEAEs	Related TEAEs	All TEAEs	Related TEAEs	All TEAEs	Related TEAEs
	SPMC (AM/PM) Dose 2: 14:00–16:00	NER1006 (PM/AM) Dose 1: 18:00	NER1006 (PM/AM) Dose 1: 18:00	Renal insufficiency						
	NER1006 (PM/PM)	2L PEG + Asc (PM/AM)	Trisulfate (PM/AM)	Mild	77 (22.6)	48 (14.1)	49 (15.3)	42 (13.1)	126 (19.1)	90 (13.6)
	Dose 2: 20:00	Dose 1: 18:00	Dose 1: 18:00	Moderate	5 (35.7)	3 (21.4)	5 (29.4)	4 (23.5)	10 (32.3)	7 (22.6)
YOF		NER1006 (PM/AM) Dose 2: 06:00	NER1006 (PM/AM) Dose 2: 06:00	None	36 (21.7)	19 (11.4)	34 (21.4)	21 (13.2)	70 (21.5)	40 (12.3)
		2L PEG + Asc (PM/AM) Dose 2: 06:00NER1006 (AM/AM) Dose 1: 05:00NER1006 (AM/AM) Dose 2: 07:00	<section-header></section-header>	Endpoints Cleansing efficacy was assessed by treatment blin central readers using the Harefield Cleansing Scale (H The HCS scores the five segments of the colon to give overall colon cleansing grade ranging from A to D. Gra A and B were judged as successful cleansing.			Among 1134 randomized patients, 1016 patients were			
dium picos	ulfate + magnesium citrate; P	EG, polyethylene glycol; Asc,	ascorbate				^			

SPMC, sodium picosulfate + magnesium citrate; PEG, polyethylene glycol; Asc, ascorba

Statistics

T-tests were used to assess differences between the groups.

Figure 2. Percentage of NER1006 patients with successful overall cleansing, according to the HCS, in patients with renal-impairment versus normal renal

Norgine; Joost Drenth: received honoraria from Norgine Ltd for advisory board attendance and an investigator for the DAYB study. Acknowledgements: The authors would like to thank the MORA, DAYB and NOCT study groups for their contributions and TVF

Communications for help with the preparation of this poster. References: **1**. Bisschops R et al. Endoscopy. 2016; 150(4):S1269– 70; **2.** Lee J et al. Medicine (Baltimore). 2016 Sep; 95(36): e4755; **3.** DeMicco MP et al. Gastrointest Endosc. 2018; 87(3):677–687.e3;

P=0.69 _____ Mild/Moderate (CrCl 30-<90 mL/min) Normal (CrCl 90+mL/min) N=160 N=94 NOCT PM/AM (N=255)

Cleansing success rates

No significant difference was observed in the overall cleansing success rates between the mild and moderate renal impairment group versus the normal renal function group in all 3 trials (Figure 2).

Safety

Safety was assessed in 1028 patients. The type of treatment emergent adverse events (TEAEs) were generally consistent between all three CrCl groups (Table 1).

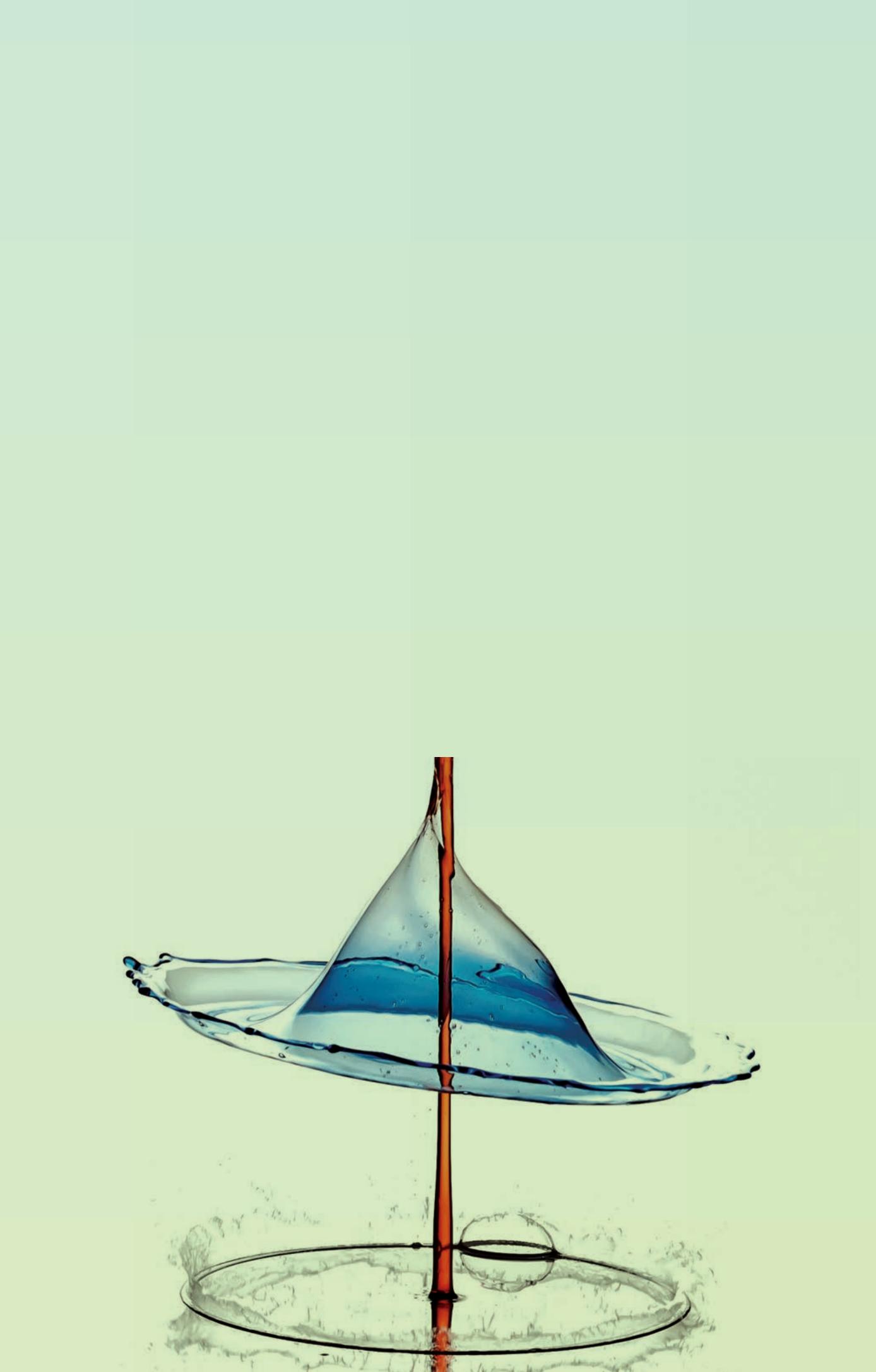
The most common TEAEs in all patient groups were gastrointestinal, i.e. nausea, vomiting, and dehydration.

Higher frequencies of patients with moderate renal disease had TEAEs compared with patients with mild or no renal disease, which may reflect the disease state in this subgroup.

4. Bisschops R, et al. Endoscopy. 2019; 51(1):60–72 **5.** Schreiber S et al. Endoscopy. 2019; 51(1):73–84.

Conclusions

- The current efficacy and safety findings support the use of NER1006 as a bowel preparation in patients with mild to moderate renal impairment.
- Adverse reactions in patients with mild or moderate renal impairment were similar to those in patients with normal renal function.
- The most common TEAEs seen in patients with normal renal function and mild and moderate renal insufficiency belonged to the gastrointestinal system organ class.



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