

ORIGINAL ARTICLE

# 대장내시경 전처치를 위한 2개의 1 L 폴리에틸렌 글리콜-아스코르빅산 장정결제 비교: 전향적 무작위 연구

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## Comparison of Two Types of 1-L Polyethylene Glycol-ascorbic Acid as Colonoscopic Bowel Preparation: A Prospective Randomized Study

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**Background/Aims:** Recently, 1-L polyethylene glycol-ascorbic acid (PEG-Asc) has been used to reduce the volume of preparation agents in colonoscopy. This clinical trial aimed to compare the efficacy and safety of two types of 1-L PEG-Asc (CleanViewAL<sup>®</sup> [Tae Joon Pharmaceutical Company, Seoul, Korea] and Plenvu<sup>®</sup> [Norgine, Harefield, United Kingdom]) in average-aged adults.

**Methods:** This study was a prospective, randomized, non-inferiority, open-label, phase 4 clinical trial. The primary endpoint was the efficacy evaluated using the Boston bowel preparation scale (BBPS), and the secondary endpoint was clinical safety.

**Results:** In total, 173 patients were assigned to either the CleanViewAL<sup>®</sup> (n=84) or Plenvu<sup>®</sup> (n=89) group. Overall cleansing successes of 97.6% (82/84) and 98.8% (88/89) were achieved in the CleanViewAL<sup>®</sup> group and in the Plenvu<sup>®</sup> group, respectively, showing that CleanViewAL<sup>®</sup> has similar bowel cleansing efficacy to Plenvu<sup>®</sup> (95% CI, -0.052 to 0.027; p=0.207). The total BBPS score was 8.67±1.00 and 8.70±0.76 in the CleanViewAL<sup>®</sup> group and Plenvu<sup>®</sup> group, respectively (p=0.869). The most common adverse symptom was nausea, and no adverse symptoms requiring hospitalization were reported in either group. There were no cases of critical hyponatremia and liver dysfunction exceeding the common terminology criteria for adverse events grade I. An overall satisfaction score (scale of 1 to 10) showed no difference between the two groups (p=0.289). However, the CleanViewAL<sup>®</sup> group showed a higher taste satisfaction score (scale of 1 to 5) than the Plenvu<sup>®</sup> group (CleanViewAL<sup>®</sup>: 2.90±0.91, Plenvu<sup>®</sup>: 2.60±0.86, p=0.028).

**Conclusions:** Both types of 1-L PEG-Asc, CleanViewAL<sup>®</sup> and Plenvu<sup>®</sup>, are effective and safe bowel cleansing agents in average-aged adults. CleanViewAL<sup>®</sup> was preferred in terms of taste satisfaction. (Korean J Gastroenterol 2022;80:85-92)

**Key Words:** Polyethylene glycols; Ascorbic acid; Colonoscopy; Cathartics

## INTRODUCTION

Colonoscopy is an important diagnostic and therapeutic

tool for various colonic diseases because it allows visualization of the mucosa of the entire large intestine.<sup>1,2</sup> Effective bowel cleansing is essential before performing a colonoscopy

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to ensure accurate diagnosis and treatment.<sup>3,4</sup> Poor bowel preparation can lead to longer procedure times that could make the patients uncomfortable and cause missed lesions; this is a major cause of interval cancer.<sup>5-7</sup> Patient compliance with bowel cleansing agents and efficacy are correlated with the adequacy of bowel preparation.<sup>8</sup> Therefore, efforts have been made to develop bowel cleansing agents with a low volume for patient compliance. Currently, diverse bowel cleansing agents, such as polyethylene glycol (PEG) and sodium phosphate (NaP), oral sulfate solution (OSS), and sodium picosulfate with magnesium citrate (SPMC) are used in preparation for colonoscopy.<sup>3,9-13</sup>

However, low volume agents, such as NaP, OSS, and SPMC, can cause dehydration and electrolyte imbalance, such as hyponatremia in elderly patients,<sup>14,15</sup> and are reported to have worse preparation quality than the PEG.<sup>15-17</sup> In contrast, the PEG solution has become the preferred bowel cleansing agent owing to its safety and efficacy. On the other hand, its large volume and poor taste can cause several adverse effects, such as abdominal fullness, nausea, vomiting, and abdominal pain, which can reduce patient compliance.<sup>11,15,16</sup> A PEG-ascorbic acid (PEG-Asc) formulation was developed to reduce the volume of PEG that needs to be ingested and improve the taste. In this PEG-Asc formulation, ascorbic acid was added to the existing PEG formulation.<sup>18</sup> Currently, the split dose of 2-L PEG-Asc is the most widely used standard bowel cleansing method worldwide.<sup>19,20</sup>

Recently, several 1-L PEG-Asc variations have been developed, which have a lower volume (total 2-L including free water 1-L) than conventional 2-L PEG-Asc (total 3-L including free water 1-L) and are more tolerable for the patient. This leads to improved patient compliance. Indeed, several studies assessed the efficacy and safety of 1-L PEG-Asc compared to conventional 2-L PEG-Asc, showing a favorable colon cleansing efficacy with comparable safety.<sup>21-23</sup> Therefore, the use of 1-L PEG-Asc is expanding, and several 1-L PEG-Asc agents have been introduced with diverse compositions of PEG3350 contents, electrolytes, and ascorbate (Supplementary Table 1). On the other hand, few studies have investigated the efficacy, safety, and compliance of 1-L PEG-Asc agents and their satisfaction with them, particularly in clinical practice.

This study compared the efficacy, safety, and patient satisfaction of two types of 1-L PEG-Asc (CleanViewAL<sup>®</sup> [Tae Joon Pharmaceutical Company, Seoul, Korea] and Plenvu<sup>®</sup>

[Norgine, Harefield, United Kingdom]) as bowel cleansing agents in healthy adults.

## SUBJECTS AND METHODS

### 1. Study design

This prospective, randomized, non-inferiority, open-label, phase 4 clinical trial was conducted at Inje University Seoul Paik Hospital from September 2020 to December 2021. The bowel preparation agent was assigned randomly to the patients as follows: CleanViewAL<sup>®</sup> (test group) or Plenvu<sup>®</sup> (control group) at least 2 days before the procedure day according to a computer generated randomization table (in blocks of 10). The study protocol was approved by the Institutional Review Board (IRB) of Seoul Paik Hospital (IRB No. 2020-07-006), and written informed consent was obtained from all patients before enrollment. This study is registered at the Clinical Research Information Service (CRIS, <http://cris.nih.go.kr>) number KCT0007163.

### 2. Patients

Eligible patients who visited the hospital for colonoscopy and had no experience of 1-L PEG-Asc were enrolled in the study. The inclusion criteria were as follows: 1) men and women aged  $\geq 20$  years and  $\leq 60$  years, and 2) voluntary agreement with the study protocol. Patients meeting any of the following criteria were excluded: 1) age  $< 20$  or  $> 60$  years; 2) cognitive impairment or inability to provide informed consent for the study (for example, language barrier); 3) bowel obstruction; 4) severe constipation (bowel movement  $< 3$  times/week); 5) history of gastrointestinal tract surgery, 6) severe underlying diseases, such as liver cirrhosis, inflammatory bowel disease, heart failure, coronary heart disease, and chronic kidney disease; 7) pregnant or lactating woman; 8) a history of hypersensitivity to bowel cleansing agents.

### 3. Endoscopic procedure

Written informed consent for the colonoscopy procedure was obtained from all patients. All colonoscopies were performed using either CF-H260, CF-Q260, or CF-HQ290 (Olympus Optical Co., Ltd., Tokyo, Japan) by three experienced endoscopists (J.S.M., Y.S.K., T.Y.P.) who had performed more than 500 colonoscopies per year. After diet restriction for at

least 3 days, bowel cleansing was performed using the split-dose method, and the colonoscopy examinations were performed within 5-7 hours of administering the last cleansing agent. In the split-dose method, 500 mL of cleansing agent was ingested with additional 500 mL water on the night before colonoscopy and 500 mL cleansing agent on the day of the colonoscopy, followed by an extra 500 mL water. As the pre-endoscopic preparation, conscious sedation was performed using midazolam (0.05-0.1 mg/kg) and propofol (0.5-1 mg/kg). The analgesic agent meperidine (25 mg) and hyoscine-N-butylbromide (intravenous 5 mg) were administered to inhibit peristalsis if there were no contraindications for these agents.<sup>24</sup>

The cecal intubation time, colonoscopy withdrawal time, Boston bowel preparation scale (BBPS),<sup>24,25</sup> and the size of polyps were recorded by the endoscopists. To minimize the variability of BBPS, an inter-colonoscopist assessment was performed through an endoscopic image review.

#### 4. Outcome assessment

The primary endpoint was efficacy and evaluated using the BBPS in both groups. The BBPS score was measured for each colon segment, and the total BBPS score was obtained by adding each segment score (Supplementary Fig. 1).<sup>24,25</sup> Bowel cleansing success was defined as a total BBPS  $\geq 6$  with a partial BBPS  $\geq 2$  in each segment. In addition, the detection rates of polyps and adenomas were calculated in both groups to measure the efficacy of bowel cleanliness.

The secondary endpoint was the assessment and comparison of safety between the two bowel preparation agents. Safety was evaluated based on adverse symptoms using a questionnaire and laboratory tests. Possible symptoms included paresthesia, dizziness, nausea, vomiting, abdominal pain, and fullness. The laboratory tests included sodium (Na), potassium (K), chloride (Cl), BUN, creatinine (Cr), AST, and ALT levels before and after bowel preparation. The Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 is used to define the meaningful results of the laboratory tests measuring blood biochemistry.<sup>26</sup> The CTCAE displays grades 1-5 with a unique clinical description of severity for each adverse event based on general guidelines (Supplementary Table 2).<sup>26</sup> All grades were included as adverse events.

Patient satisfaction was determined using a questionnaire. Satisfaction with taste, the volume of the cleansing agent,

and the overall satisfaction with the bowel preparation method were investigated. The overall satisfaction was evaluated using a 0-10-point rating scale. The specific satisfaction with "taste" and "volume" was evaluated further using a 1-5-point rating scale.

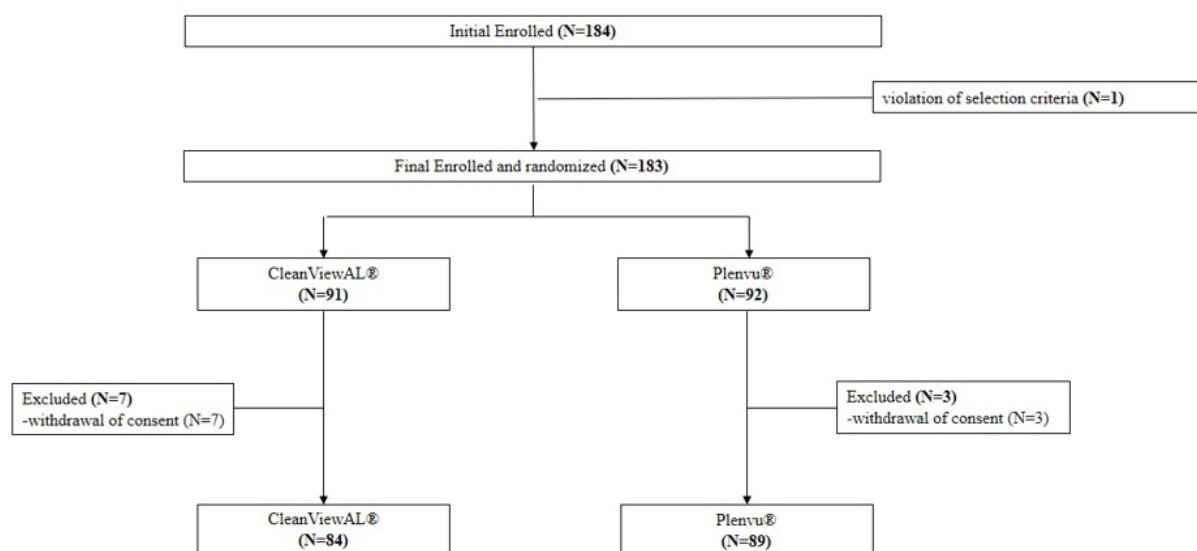
#### 5. Statistical analyses

The success rate of bowel cleansing when the reference drug Plenvu<sup>®</sup> was used as a cleansing agent was assumed to be 90% - based on a previous study.<sup>23</sup> The clinically acceptable maximum difference in effectiveness (non-inferiority margin) between CleanViewAL<sup>®</sup> (test drug) and Plenvu<sup>®</sup> (control drug) was set to 15%. The non-inferiority margin of 15% is a commonly used value as the maximum clinically acceptable error in existing studies to evaluate the effectiveness of colon cleansers. A non-inferiority test was used to compare the BBPS of CleanViewAL<sup>®</sup> to Plenvu<sup>®</sup>. Assuming a dropout rate of 5%, a statistical power of 0.75, and  $\alpha=0.05$ , 92 patients were required per group, totaling 184 patients. For the differences between the groups, continuous variables were analyzed using an independent *t*-test, and categorical variables were analyzed using a chi-square test or Fisher's exact test. A paired *t*-test was used to evaluate the change in laboratory test results measuring blood biochemistry before and after bowel preparation. The statistical significance was set to  $p<0.05$ . Statistical analysis was performed using SPSS version 25.0 (IBM Co., Armonk, NY, USA).

## RESULTS

#### 1. Baseline characteristics

One hundred and eighty-four patients eligible for this study were enrolled; one patient was excluded due to a violation of the selection criteria. Therefore, 183 patients were assigned randomly to the two groups: 91 patients in the CleanViewAL<sup>®</sup> group and 92 patients in the Plenvu<sup>®</sup> group. In the end, 84 patients in the CleanViewAL<sup>®</sup> group and 89 patients in the Plenvu<sup>®</sup> group were evaluated (Fig. 1). There were no significant differences in age, sex, BMI, or average stool frequency per week. The most common reason for a colonoscopy in both groups was regular screening (46.4% and 51.7%) (Table 1).



**Fig. 1.** Flow chart of enrolled patients. Eighty-four patients in the CleanViewAL<sup>®</sup> group and 89 in the Plenvu<sup>®</sup> group completed the present study.

**Table 1.** Baseline Characteristics

	CleanViewAL <sup>®</sup> Group (n=84)	Plenvu <sup>®</sup> Group (n=89)	p-value
Age (years)	48.49±8.92	49.22±9.05	0.592
Sex (male)	54 (64.3)	57 (64.0)	0.974
BMI (kg/m <sup>2</sup> )	23.90±3.14	24.70±3.56	0.120
Average stool frequency per week	7.63±3.82	7.81±4.60	0.776
Indications for colonoscopy			
Screening	39 (46.4)	46 (51.7)	0.489
Bowel habit change	17 (20.2)	20 (22.5)	0.720
Melena/hematochezia	7 (8.3)	1 (1.1)	0.031
Abdominal pain	4 (4.8)	7 (7.9)	0.403
Anemia	1 (1.2)	0 (0.0)	0.486
Polyp surveillance	15 (17.9)	12 (13.5)	0.428
Other	1 (1.2)	3 (3.4)	0.621

Values are presented as number (%) or mean±standard deviation.  
BMI, body mass index.

**Table 2.** Efficacy of the Bowel Cleansing Agent

	CleanViewAL <sup>®</sup> (n=84)	Plenvu <sup>®</sup> (n=89)	p-value
BBPS (total)	8.67±1.00	8.70±0.76	0.869
Ascending colon	2.84±0.45	2.80±0.43	0.498
Transverse colon	2.93±0.30	2.96±0.21	0.487
Descending colon	2.90±0.37	2.94±0.28	0.415
Polyp detection rate	51 (60.7)	56 (62.9)	0.765
Adenoma detection rate	35 (41.7)	36 (40.4)	0.871
Adenoma detection rate for screening colonoscopy	14/39 (35.9)	18/46 (39.1)	0.759
Size of adenoma <sup>a</sup>	0.583±0.24	0.647±0.29	0.307
Cecal intubation time (min)	10.64±6.93	9.52±6.26	0.266
Withdrawal time (min)	19.70±10.74	19.08±9.69	0.690

Values are presented as number (%) or mean±standard deviation.

BBPS, Boston bowel preparation scale; min, minutes.

<sup>a</sup>Size of adenoma is based on the largest adenoma.

## 2. Bowel cleansing efficacy

An overall cleansing success of 97.6% (82/84) and 98.8% (88/89) was achieved in the CleanViewAL<sup>®</sup> group and Plenvu<sup>®</sup> group, respectively, indicating that both cleansing agents showed excellent bowel cleansing efficacy. Moreover, the bowel cleansing success rate of the CleanViewAL<sup>®</sup> group was not inferior to that of the Plenvu<sup>®</sup> group (95% CI, -0.052 to 0.027;  $p=0.207$ ) using a non-inferiority margin of 15%.

The total BBPS scores were  $8.67 \pm 1.00$  and  $8.70 \pm 0.76$  in the CleanViewAL<sup>®</sup> group and Plenvu<sup>®</sup> group, respectively ( $p=0.869$ ). There was no significant difference in BBPS be-

tween the two groups for each segment of the colon. The adenoma detection rate (ADR) in both groups exceeded 40%, indicating successful bowel preparation and good quality colonoscopy (Table 2).<sup>27</sup> The ADR among patients for screening colonoscopy was approximately 35-40%.

## 3. Safety

In both groups, total adverse symptoms were reported in 46.4% (39/84) and 56.2% (50/89), respectively ( $p=0.200$ ), and most of the symptoms were mild. Nausea is the most common symptom in both groups (Table 3).

**Table 3.** Adverse symptoms in the CleanViewAL<sup>®</sup> and Plenvu<sup>®</sup> groups

	CleanViewAL <sup>®</sup> (n=84)	Plenvu <sup>®</sup> (n=89)	p-value
All symptoms	39 (46.4)	50 (56.2)	0.200
Nausea	21 (25.0)	28 (31.5)	0.346
Vomiting	7 (8.3)	13 (14.6)	0.197
Abdominal pain	0 (0.0)	0 (0.0)	
Dizziness	2 (2.4)	4 (4.5)	0.683
Fullness/bloating	6 (7.1)	4 (4.5)	0.527
Anal irritation	2 (2.4)	0 (0.0)	0.234
Sleep disturbance	1 (1.2)	1 (1.1)	1.000
Paresthesia	0 (0.0)	0 (0.0)	

Values are presented as number (%).

**Table 4.** Laboratory Test Results Using the CTCAE Grade after Bowel Cleansing

	CleanViewAL <sup>®</sup> pre	CleanViewAL <sup>®</sup> post	p-value <sup>c</sup>	Plenvu <sup>®</sup> pre	Plenvu <sup>®</sup> post	p-value <sup>d</sup>
Sodium (Na) <sup>a</sup>	138.03 $\pm$ 1.66	137.83 $\pm$ 2.57	0.564	137.84 $\pm$ 2.28	140.53 $\pm$ 3.11	0.007
Hyponatremia grade 1		0 (0.0)			5 (5.7)	
Hyponatremia grade 1		9 (11.0)			3 (3.4)	
Potassium (K) <sup>a</sup>	4.12 $\pm$ 0.39	4.35 $\pm$ 0.43	0.000	4.02 $\pm$ 0.31	4.04 $\pm$ 0.37	0.710
Hyperkalemia grade 1		3 (3.7)			2 (2.3)	
Hypokalemia grade 1		0 (0.0)			2 (2.3)	
Chloride (Cl) <sup>a</sup>	104.20 $\pm$ 2.26	108.65 $\pm$ 2.73	0.001	103.78 $\pm$ 2.19	107.47 $\pm$ 3.27	0.005
Hyperchloremia		19 (23.2)			10 (11.5)	
Hypochloremia		0 (0.0)			0 (0.0)	
BUN <sup>a</sup>	14.82 $\pm$ 4.33	13.99 $\pm$ 4.03	0.055	13.75 $\pm$ 3.34	13.80 $\pm$ 3.52	0.918
Cr <sup>a</sup>	0.79 $\pm$ 0.15	0.90 $\pm$ 0.18	0.000	0.78 $\pm$ 0.16	0.85 $\pm$ 0.19	0.000
eGFR <sup>b</sup>	105.78 $\pm$ 22.05	92.85 $\pm$ 20.95	0.000	109.92 $\pm$ 27.35	100.25 $\pm$ 23.89	0.000
AST <sup>a</sup>	28.61 $\pm$ 11.15	35.71 $\pm$ 14.24	0.000	28.06 $\pm$ 12.82	42.18 $\pm$ 22.69	0.000
ALT <sup>a</sup>	28.28 $\pm$ 17.78	33.43 $\pm$ 18.62	0.000	30.87 $\pm$ 21.24	41.09 $\pm$ 30.03	0.000

Values are presented as number (%) or mean $\pm$ standard deviation.

CTCAE, common terminology criteria for adverse events; BUN, blood urea nitrogen; Cr, creatinine; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ALT, alkaline phosphatase.

<sup>a</sup>The N of lab values was 82 in the CleanViewAL group and 87 in the Plenvu group; <sup>b</sup>eGFR calculated by the Cockcroft-Gault equation; <sup>c</sup>This is the paired *t*-test p-value of the changes in laboratory test results measuring biochemistry before and after bowel preparation in the CleanViewAL group; <sup>d</sup>This is the paired *t*-test p-value of the changes in laboratory test results measuring biochemistry before and after bowel preparation in the Plenvu group.

**Table 5.** Patient's Satisfaction with the Bowel Cleansing Agent

	CleanViewAL <sup>®</sup> (n=84)	Plenvu <sup>®</sup> (n=89)	p-value
Overall satisfaction (scale 0-10)	6.95±2.15	6.60±2.15	0.289
Taste (scale 1-5)	2.90±0.91	2.60±0.86	0.028
Volume (scale 1-5)	3.28±0.95	3.20±0.94	0.602

Values are presented as mean±standard deviation. Satisfaction scale is larger when satisfaction is higher.

A comparison of the blood test results before and after bowel preparation showed a significant trend of an elevated sodium level after bowel preparation in the Plenvu<sup>®</sup> group ( $p=0.007$ ) but not in the CleanViewAL<sup>®</sup> group ( $p=0.564$ ). On the other hand, there were no cases exceeding hypernatremia CTCAE grade I or hyponatremia CTCAE grade I in either group. Regarding other parameters, both groups showed a significant increase in chloride, Cr, AST, and ALT after bowel preparation, but these changes were mild and did not exceed the CTCAE grade I. The estimated glomerular filtration rate (eGFR) showed a significant decrease in both groups after bowel preparation, but post-eGFR in both groups was within the normal range. Mild hyperkalemia was observed in three patients in the CleanViewAL<sup>®</sup> group and two patients in the Plenvu<sup>®</sup> group without clinical symptoms, and they resolved spontaneously (Table 4).

#### 4. Patient satisfaction

The overall satisfaction scores were similar in both groups ( $p=0.289$ ). When satisfaction regarding "taste" was surveyed, the CleanViewAL<sup>®</sup> group showed a significantly higher taste satisfaction score than the Plenvu<sup>®</sup> group (CleanViewAL<sup>®</sup>:  $2.90\pm0.91$ , Plenvu<sup>®</sup>:  $2.60\pm0.86$ ,  $p=0.028$ ) (Table 5).

## DISCUSSION

Effective bowel cleansing for colonoscopy is associated with an accurate diagnosis, safe inspection, and appropriate treatments, e.g., in removing precancerous lesions.<sup>3,7</sup> Many factors affect the quality of the colonoscopy besides bowel preparation agents, such as patients' age, degree of physical activity, adherence to instructions, underlying disease, continuing medical education of the endoscopist, instrument quality, and withdrawal times.<sup>6,27,28</sup> On the other hand, among the several factors mentioned, the bowel cleansing agent is considered the most important factor, and the discomfort experienced

in the bowel preparation process affects patient compliance. Therefore, studies on bowel cleansing agents are continuously being conducted. Although the PEG solution has an excellent cleansing effect and safety evaluation, its large volume makes patients uncomfortable. 1-L PEG-Asc products are being developed to reduce the volume of bowel cleansing agents. Plenvu<sup>®</sup> is the first 1-L PEG-Asc that has reduced the PEG3350 content and increased the ascorbate content (instead of the 2-L PEG-Asc). Phase 3 studies have compared the safety and effectiveness of bowel cleansing between Plenvu<sup>®</sup> and other bowel preparation agents.<sup>29,31</sup> In the MORA study, which compared Plenvu<sup>®</sup> with the split-dose method of 2-L PEG-Asc, Plenvu<sup>®</sup> showed superior colon cleansing efficacy with comparable safety and tolerability.<sup>21,30</sup> In other studies, Plenvu<sup>®</sup> was as effective as OSS or SPMC in achieving overall bowel cleansing success. Only the adverse event rates were slightly higher with Plenvu<sup>®</sup> than with OSS, and Plenvu<sup>®</sup> showed superior high-quality cleansing of the right colon compared with SPMC.<sup>29,31</sup> Right colon preparation is essential because detection of adenoma and serrated polyps is more difficult in the right colon than in other areas of the colon.<sup>27</sup> Moreover, multicenter, observational phase 4 studies also confirmed that 1-L PEG-Asc (Plenvu<sup>®</sup>) could be a reasonable substitute for 2-L PEG-Asc.<sup>23,32</sup> In previous studies, no serious side effects were found with Plenvu<sup>®</sup>, but because a small volume causes diarrhea, hypernatremia may occur when dehydrated because of high doses of sodium ascorbate and sodium sulfate.<sup>31</sup> CleanViewAL<sup>®</sup> is 1-L PEG-Asc with a reduced sodium content compared to Plenvu<sup>®</sup>. In the present study, the efficacy and safety of 1-L PEG-Asc products were evaluated, and comparisons were made between CleanViewAL<sup>®</sup> (1-L PEG-Asc) and Plenvu<sup>®</sup> (1-L PEG-Asc). The total BBPS scores of both groups were similar and remarkably high ( $8.67\pm1.00$  in the CleanViewAL<sup>®</sup> group and  $8.70\pm0.76$  in the Plenvu<sup>®</sup> group [ $p=0.869$ ]), indicating that both 1-L PEG-Asc agents are very effective in terms of bowel cleansing. In addi-

tion, the CleanViewAL<sup>®</sup> group is not inferior to the Plenvu<sup>®</sup> group in aspects of bowel cleansing. In the present study, aged patients and patients with underlying diseases, such as IBD or renal dysfunction, were excluded owing to the lack of experience with 1-L PEG-Asc agents in the Seoul Paik Hospital. On the other hand, recent studies reported the effectiveness and safety of 1-L PEG-Asc agents in diverse settings, such as in patients with IBD<sup>33</sup> and even in elderly patients and patients with renal dysfunction.<sup>34</sup>

Both groups showed sufficient ADR (over 40%). The ADR was calculated in patients with screening colonoscopy, and 35.9% and 39.1% were observed in the CleanViewAL<sup>®</sup> group and Plenvu<sup>®</sup> group, respectively. Only patients under 60 years were enrolled in this study due to safety concerns in aged patients, which resulted in an ADR lower than 40%. On the other hand, an ADR of approximately 40% in this study population is reasonable considering the average age. In all, both 1-L PEG-Asc agents can be used to achieve successful bowel cleansing. The overall satisfaction was also similar in the two groups; however, the CleanViewAL<sup>®</sup> group had a significantly higher “taste” satisfaction score than Plenvu<sup>®</sup> ( $p=0.028$ ). The increased ascorbic acid in CleanViewAL<sup>®</sup> might make it taste better than Plenvu<sup>®</sup>.

Regarding safety, no cases of severe adverse events that required hospitalization were observed in either group. In terms of laboratory test result changes, the Plenvu<sup>®</sup> group showed significant elevation in sodium levels after bowel cleansing, whereas CleanViewAL<sup>®</sup> showed no difference in sodium levels before and after bowel cleansing. This may be due to differences in the sodium contents between the two products (Supplementary Table 1). In addition, sodium, chloride, creatinine, eGFR, and liver function test (AST, ALT) also showed significant differences before and after bowel cleansing in both groups, but there were no cases of critical changes exceeding CTCAE grade I. In addition, there was no clinical symptom related to these laboratory changes. Therefore, these two agents are safe for bowel cleansing in average-aged patients. In the present study, CleanViewAL<sup>®</sup> was not inferior to Plenvu<sup>®</sup> in terms of bowel cleaning and tolerability in adults without chronic disease, suggesting that CleanViewAL<sup>®</sup>, like Plenvu<sup>®</sup>, can be an alternative to 2-L PEG-Asc in average-aged patients.

This study had some limitations. First, the dropout rate was predicted to be 5%; however, the COVID-19 pandemic affected

the patient dropout rate. Several patients canceled their colonoscopy appointment during the COVID-19 pandemic period. Therefore, the final dropout rate was increased to 5.46% (10/183); the CleanViewAL<sup>®</sup> group (7.69%, 7/91) had a higher dropout rate than the Plenvu<sup>®</sup> group (3.26%, 3/92), despite the patients being assigned randomly to the two groups. However, the efficacy demonstrated by the BBPS score was very similar in both groups, suggesting that CleanViewAL<sup>®</sup> group is not inferior to that of the Plenvu<sup>®</sup> group. Second, this study was conducted in an open-label, single-center manner. It is surmised that the open-label method can affect the patient’s satisfaction. Nevertheless, patients with no experience of 1-L PEG-Asc were included in this study. Therefore, previous experience may affect the “volume” satisfaction score but not that of “taste”. Third, this study only included average-aged patients. Although a few studies reported the efficacy and safety of 1-L PEG-Asc for aged patients or patients with chronic disorders,<sup>33,34</sup> the authors have limited experience on 1-L PEG-Asc for aged patients or patients with chronic disorders. With the safety concerns, aged patients and patients with chronic disorders were excluded from this study. Therefore, using 1-L PEG-Asc for aged patients or patients with chronic disorders cannot be guaranteed.

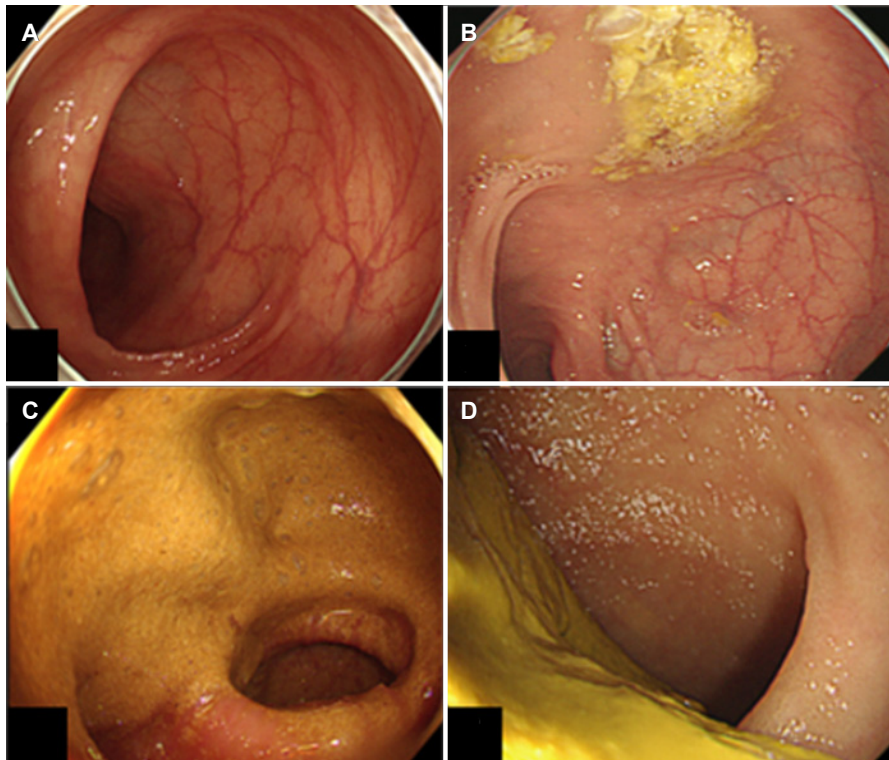
In conclusion, compared to the standard 2-L PEG-Asc regimen, both 1-L PEG-Asc agents have a much smaller volume for the patient to consume and less volume to make the patient uncomfortable. These findings suggest that both types of 1-L PEG-Asc, CleanViewAL<sup>®</sup> and Plenvu<sup>®</sup>, are effective and safe bowel cleansing agents in average-aged adults. CleanViewAL<sup>®</sup> was preferred in terms of “taste” satisfaction.

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**Supplementary Fig. 1** The Boston bowel preparation scale.<sup>25</sup> (A) Segment score=3: The entire mucosa of the colon segment was observed well with no residual staining, small fragments of stool or opaque liquid. (B) Segment score=2: Minor amount of residual staining, small fragments of stool or opaque liquid, but the mucosa of the colon segment was observed well. (C) Segment score=1: A portion of the mucosa of the colon segment can be seen, but other areas of the colon segment were not observed well due to staining, residual stool, or opaque liquid. (D) Segment score=0: Unprepared colon segment with mucosa not observed due to solid stool that cannot be cleared.

**Supplementary Table 1.** Supplement Facts of the Two Bowel Preparation Agents

Supplement facts	CleanViewAL <sup>®</sup>	Plenvu <sup>®</sup>
PEG3350	160 g	140 g
Potassium chloride	1 g	2.2 g
Sodium chloride	2.7 g	5.2 g
Sodium sulfate anhydrous	18 g	9 g
Ascorbic acid	40.6 g	7.54 g
Sodium ascorbate	9.4 g	48.11 g

PEG, polyethylene glycol.

**Supplementary Table 2.** Definition of the CTCAE Grade<sup>26</sup>

Grade	Definition
1	Asymptomatic or mild symptoms; clinical or diagnostic observations only
2	Minimal, local, or noninvasive intervention indicated
3	Severe or medically significant but not immediately life threatening
4	Life threatening consequences; urgent intervention indicated
5	Death related to adverse event

CTCAE, common terminology criteria for adverse events.