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A Randomized, Assessor-blinded, Multicenter Study Demonstrates the Efficacy and Safety of a New Ready-to-drink Low Volume Bowel Preparation Prior to Colonoscopy

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BACKGROUND

- An effective bowel preparation is essential for an optimal screening colonoscopy[1-4]
- Approximately 20% of all colonoscopies show inadequate bowel preparation[4-6]
- Improper bowel preparation can lead to missed lesions at colonoscopy and early repeated colonoscopies[1-3,7]
- Patients may benefit from having a more convenient, ready-to-drink bowel preparation agent

OBJECTIVE

To evaluate the safety and efficacy of a new ready-to-drink, low volume colon preparation of sodium picosulfate, magnesium oxide, and citric acid (SPMC oral solution)

METHODS

Study Design

- Phase 3, randomized, assessor-blinded, multicenter, non-inferiority study comparing split-dose SPMC oral solution to split-dose sodium picosulfate, magnesium oxide, and citric acid powder (P/MC powder)
  - NCT03017235; 12 sites in the United States, 2 in Canada

Study Population

- Females and males, 18 to 80 years of age, undergoing elective colonoscopy
  - No pregnant or lactating females
- No known or suspected major gastrointestinal (GI) disorder, including GI obstruction, perforation, ileus, severe acute inflammatory bowel disease (IBD), or diverticulitis
- Not undergoing colonoscopy for foreign body removal or decompression
- No prior upper GI surgery
- Renal function >30 ml/min/1.73m^2
- No uncontrolled angina and/or myocardial infarction within last 3 months, congestive heart failure, uncontrolled hypertension, or ascites

Endpoints

- Primary endpoint was overall quality of colon cleansing as assessed by the Aronchick scale (AS; **Table 1**)
- Secondary endpoint was quality of cleansing of the right colon as assessed by the Boston Bowel Preparation Scale (BBPS; **Table 2**)
- Safety assessments included the rates of adverse events (AEs), laboratory evaluations, and electrocardiograms

Statistical Analysis

- Efficacy rate ("responders") by AS was the proportion of patients with "excellent" or "good" ratings
- Efficacy rate by BBPS was the proportion of patients with a segmental score of "3" or "2" in the right colon
- Prespecified non-inferiority (NI) margin for both efficacy endpoints was -8%
  - If both primary and secondary efficacy endpoints met NI, then pre-specified superiority testing for the primary endpoint was performed

METHODS

Table 1. Modified Aronchick Scale[8]

Grade[a]	Description
Excellent	>90% of mucosa seen, mostly liquid stool, minimal suctioning needed for adequate visualization
Good	>90% of mucosa seen, mostly liquid stool, significant suctioning needed for adequate visualization
Fair	>90% of mucosa seen, mixture of liquid and semisolid stool, could be suctioned and/or washed
Inadequate	<90% of mucosa seen, mixture of semisolid and solid stool, which could not be suctioned or washed

[a] Scoring was performed before any attempt of washing or suctioning

Table 2. Boston Bowel Preparation Scale[9]

Grade[a]	Description
3	Entire mucosa of colon segment seen well with no residual staining, small fragments of stool, or opaque liquid
2	Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well
1	Portion of mucosa of the colon segment seen, but other areas of the segment not well seen due to staining, residual stool, and/or opaque liquid
0	Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared

[a] Scoring was performed after any attempt of washing or suctioning

RESULTS

Table 3. Demographic Characteristics, mITT Population

	SPMC Oral Solution (N=448)	P/MC Powder (N=453)	Total (N=901)
Age (years), mean (SD)	57.2 (11.0)	57.1 (10.9)	57.2 (10.9)
<65 years, n (%)	324 (72.3)	340 (75.1)	664 (73.7)
Female, n (%)	252 (56.3)	250 (55.2)	502 (55.7)
Race, n (%)			
White	376 (83.9)	394 (87.0)	770 (85.5)
Black/African American	49 (10.9)	42 (9.1)	90 (10.0)
Asian	13 (2.9)	5 (1.1)	18 (2.0)
Other	7 (1.6)	8 (1.8)	15 (1.7)
BMI (kg/m^2), mean (SD)	29.7 (6.1)	29.9 (5.4)	29.8 (5.8)

Abbreviations: BMI, body mass index; mITT, modified intent-to-treat; P/MC, sodium picosulfate, magnesium oxide, and citric acid; SD, standard deviation; SPMC, sodium picosulfate, magnesium oxide, and citric acid

RESULTS

Table 4. Primary Efficacy Endpoint, Aronchick Scale, mITT Population

% (N)	SPMC Oral Solution (N=448)	P/MC Powder (N=453)	Total (N=901)
Excellent	53.8 (241)	46.4 (210)	50.1 (451)
Good	33.9 (152)	35.1 (159)	34.5 (311)
Fair	9.6 (43)	15.0 (68)	12.3 (111)
Inadequate	0.9 (4)	2.2 (10)	1.6 (14)
No Rating	1.8 (8)	1.3 (6)	1.6 (14)
Responders [95% CI]	**87.7 (393) [84.3, 90.6]**	**81.5 (369) [77.6, 84.9]**	**84.6 (762) [82.0, 86.9]**
Difference [95% CI]	6.3 [1.8, 10.9] P=.0067[a]		

Abbreviations: CI, confidence interval; mITT, modified intent-to-treat;
[a] P value associated with the test of superiority

- Efficacy rate by Aronchick scale was 87.7% Responders for SPMC oral solution and 81.5% Responders for P/MC powder

Table 5. Secondary Efficacy Endpoint, BBPS in Right Colon, mITT Population

% (N)	SPMC Oral Solution (N=448)	P/MC Powder (N=453)	Total (N=901)
3	51.6 (231)	44.4 (201)	47.9 (432)
2	42.6 (191)	45.3 (205)	44.0 (396)
1	4.0 (18)	8.4 (38)	6.2 (56)
0	0	0.7 (3)	0.3 (3)
No Rating	1.8 (8)	1.3 (6)	1.6 (14)
Responders [95% CI]	**94.2 (422) [91.6, 96.2]**	**89.6 (406) [86.4, 92.3]**	**91.9 (828) [89.9, 93.6]**
Difference [95% CI]	4.6 [1.1, 8.0] P=.0099[a]		

Abbreviations: CI, confidence interval; mITT, modified intent-to-treat
[a] P value associated with the test of superiority

- Efficacy rate by BBPS was 94.2% Responders for SPMC oral solution and 89.6% Responders for P/MC powder

Support

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RESULTS

Table 6. Responders by BBPS for Transverse and Left Colon, mITT Population

% (N)	SPMC Oral Solution (N=448)	P/MC Powder (N=453)	Total (N=901)
Transverse Colon			
Responders [95% CI]	96.0 (430) [93.7, 97.6]	94.0 (426) [91.4, 96.0]	95.0 (856) [93.4, 96.3]
Difference [95% CI]	1.9 [-0.9, 4.7]		
Left Colon			
Responders [95% CI]	94.6 (424) [92.1, 96.5]	91.2 (413) [88.2, 93.6]	**92.9 (837) [91.0, 94.5]**
Difference [95% CI]	3.5 [0.2, 6.7]		

Abbreviations: CI, confidence interval; mITT, modified intent-to-treat;

- The majority of patients using SPMC oral solution were Responders by BBPS in the transverse and left colon

Table 7. Treatment-emergent Adverse Events, Safety Population

% (N)	SPMC Oral Solution (N=448)	P/MC Powder (N=453)	Total (N=901)
Any TEAE[a]	84.4 (378)	84.8 (384)	84.6 (762)
Deaths	0	0	0
Serious TEAEs	2.0 (9)	1.3 (6)	1.7 (15)
TEAEs leading to study discontinuation	0	0	0
Severe TEAEs	2.5 (11)	2.2 (10)	2.3 (21)
Adverse Drug Reactions	13.2 (59)	16.8 (76)	15.0 (135)
Serious ADRs	0	0	0

Abbreviations: ADR, adverse drug reaction; TEAE, treatment-emergent adverse events
[a] All endoscopic findings were reported as TEAEs; malignancies were reported as serious TEAEs.

- No deaths and no serious TEAEs related to the study drug were reported

Disclosures

Dr. Hookey has participated in the speaker's bureau for Ferring Pharmaceuticals Inc. Dr. Bertiger has served as a consultant and has participated in the speaker's bureau for Ferring Pharmaceuticals Inc. Dr. Seifu, Ms. Ayala, Dr. Brogadir, and Dr. Dubcenco are employees of Ferring Pharmaceuticals Inc.

RESULTS

- The majority of patients tolerated SPMC oral solution well
- Patients reported that the bowel preparation tolerability was easy or acceptable (≥89%), with most willing to use this preparation in the future (≥81%), and not bothered by or only mildly bothered by bad taste in their mouth (≥83%)

Table 8. Treatment-emergent, Drug-related Gastrointestinal AEs, Safety Population

% (N)	SPMC Oral Solution (N=448)	P/MC Powder (N=453)	Total (N=901)
Nausea	3.1 (14)	2.9 (13)	3.0 (27)
Vomiting	1.3 (6)	0.7 (3)	1.0 (9)
Abdominal distension	0.4 (2)	0.7 (3)	0.6 (5)
Abdominal pain	0.7 (3)	0.2 (1)	0.4 (4)

Abbreviations: AE, adverse event

CONCLUSIONS

- **SPMC oral solution met the primary criteria of non-inferiority and further demonstrated superiority compared to P/MC powder**
- **The adverse event profiles of SPMC oral solution and P/MC powder were comparable**
- **A split-dose, ready-to-drink, low volume bowel preparation was efficacious in cleaning the colon, as assessed by the Aronchick Scale and Boston Bowel Preparation Scale**

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