C0005

Impact of Pancrelipase on Stool Frequency and Consistency in Patients With Exocrine Pancreatic Insufficiency Due to Chronic Pancreatitis or Pancreatic Surgery: Analysis of Randomized Trial Patient-Reported Daily Symptoms

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OBJECTIVE

This study assessed the impact of pancrelipase delayed-release capsules on exocrine pancreatic insufficiency (EPI) symptoms as reported by patients through daily diaries

CONCLUSIONS

Stool frequency and consistency significantly improved in patients with EPI due to chronic pancreatitis or pancreatic surgery during 1-week treatment with pancrelipase vs placebo

Pancrelipase reduced the mean number of stools by 1.2/day, eliminated watery stools, and increased the number of patients with formed stools by 33% vs placebo

Patient-reported stool frequency and consistency can be utilized, along with nutritional markers, to guide response to pancreatic enzyme replacement therapy in treatment of EPI due to chronic pancreatitis or pancreatic surgery

References

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Disclosures

J.A. Barkin serves as an advisor and review panel member for AbbVie.

D. Harb, J. Kort, and J. Yu are full-time salaried employees of AbbVie and may own AbbVie stock or stock options.

J.S. Barkin serves as a consultant for AbbVie.

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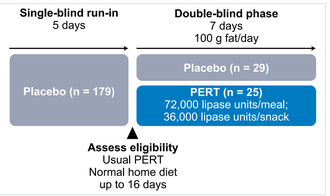
INTRODUCTION

- Patients with exocrine pancreatic insufficiency (EPI) experience maldigestive symptoms that negatively impact quality of life[1,2]
- The leading cause of EPI is chronic pancreatitis[1,3] and pancreatic enzyme replacement therapy (PERT) is the mainstay of EPI treatment[2]
- We previously reported efficacy for pancrelipase delayed-release capsules (CREON) for EPI due to chronic pancreatitis or pancreatic surgery assessed from randomization to the end of the double-blind treatment period[4]

METHODS

- Data from a double-blind, randomized phase 3 trial in patients with EPI due to chronic pancreatitis or pancreatic surgery are included (NCT00414908)[4]
  - This new post-hoc analysis focuses on the patient-reported EPI symptoms and stool consistency that were collected from daily patient diaries during the run-in period and the randomized period of the trial (**Figure 1**)
- After a 5-day placebo run-in period, patients were randomized to pancrelipase (CREON) (72,000 lipase units/meal; 36,000 lipase units/snack) or placebo for a 7-day double-blind period

Figure 1. Study Design



PERT, pancreatic enzyme replacement therapy.

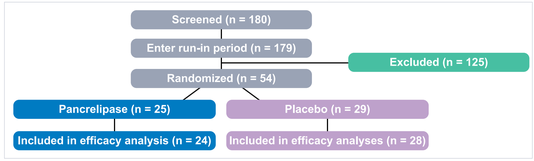
Endpoints and Statistical Analysis

- Patients completed a daily diary, reporting:
  - Stool frequency (number of stools)
  - Stool consistency (–1 = hard; 0 = formed/normal; 1 = soft; 2 = watery)
  - Flatulence (0 =none; 1 = mild; 2 = moderate; 3 = severe)
  - Abdominal pain (0 = none; 1 = mild; 2 = moderate; 3 = severe)
- Average of daily reported symptoms was calculated in each period and mean results are presented for each treatment group
- Two-sample *t* tests compared mean change from run-in to double-blind period between pancrelipase and placebo
- Population level marginal difference-in-difference models were used to assess differences in the change in the percentage of patients in symptom subgroups from run-in to double-blind period between pancrelipase and placebo

RESULTS

- A total of 54 patients were randomized and 52 patients (24 pancrelipase; 28 placebo) were included in the efficacy analysis (**Figure 2**)

Figure 2. Patient Disposition



- Among the 52 patients, 75% had EPI due to chronic pancreatitis and 25% had EPI due to pancreatic surgery
- Mean age was 51.7 years for pancrelipase and 50.4 years for placebo, 75% and 68% were male, respectively
  - Other baseline characteristics were similar between groups (**Table 1**)

Table 1. Baseline Demographics and Disease Characteristics of Randomized Patients

	Pancrelipase (n = 25)	Placebo (n = 29)
BMI, mean (SD), kg/m^2	23.4 (4.4)	22.2 (4.4)
White, n (%)	25 (100.0)	28 (96.6)
Region, n (%)		
United States	7 (28.0)	7 (24.1)
Eastern and central Europe	18 (72.0)	22 (75.9)
Duration of previous enzyme therapy, mean (SD), years	4.9 (5.4)	4.9 (6.7)
Baseline coefficient of fat absorption >50, n (%)	16 (64.0)	18 (64.3)

BMI, body mass index.

- A mean reduction of 1.2 stools/day (95% CI –2.284, –0.128) with pancrelipase vs placebo (P = .0296) was observed (**Table 2**)

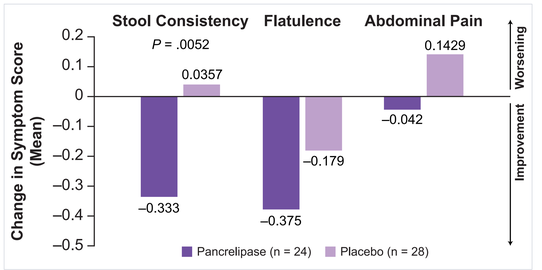
Table 2. Change in Stool Frequency

	Pancrelipase (n = 24)	Placebo (n = 27)[a]
Number of stools/day, mean (SD)		
Run-in placebo period	3.7 (2.41)	3.5 (1.40)
Double-blind treatment period	2.1 (0.85)	3.1 (1.33)
Change in number of stools/day, mean (SD)		
From run-in to double-blind period	–1.6 (2.39)	–0.4 (1.05)
Treatment difference (95% CI)	–1.206 (–2.284, –0.128) P = .0296	

[a]One patient with missing data was excluded.

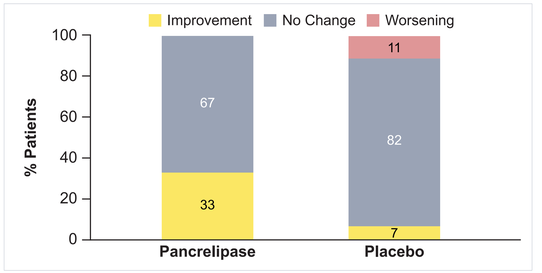
- A mean change in stool consistency score of –0.369 (95% CI –0.623, –0.115) with pancrelipase vs placebo (P = .0052) was observed (**Figure 3**)
- There was a trend towards improvement in flatulence and abdominal pain for pancrelipase vs placebo

Figure 3. Change in Symptom Score From Run-In to Double-Blind Period



- A shift analysis of change in stool consistency from run-in to double-blind period demonstrated (**Figure 4**):
  - Improvement in 33% of patients receiving pancrelipase and 7% of patients receiving placebo
  - Worsening in 0% of patients receiving pancrelipase and 11% of patients receiving placebo

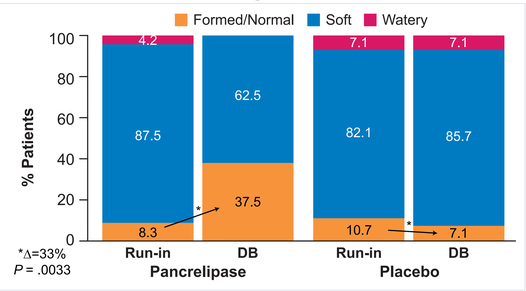
Figure 4. Shift Analysis of Stool Consistency Change From Run-in to Double-Blind Period



Pancrelipase, n = 24; Placebo, n = 28.

- In the formed/normal stools subgroups, absolute percentage change of patients from run-in to double-blind period was 33% greater for pancrelipase vs placebo (P = .0033; **Figure 5**)
- Use of pancrelipase also eliminated watery stools from run-in to double-blind period (**Figure 5**)

Figure 5. Percentage of Patients in Each Consistency Subgroup



Safety

- There were no serious adverse events (AEs) or deaths and no discontinuations due to AEs
- The most common AEs were gastrointestinal events and metabolism and nutritional disorders (**Table 3**)
- One patient in each group had treatment-emergent AEs (TEAEs) thought to be related to treatment
- One severe TEAE was recorded in the placebo group (abdominal pain)

Table 3. Treatment-Emergent Adverse Events in ≥2 Patients in Any System Organ Class in Either Treatment Group (Randomized Patients)

≥1 TEAE, n (%)	Pancrelipase (n = 25)	Placebo (n = 29)
	5 (20.0)	6 (20.7)
Gastrointestinal disorders	2 (8.0)	2 (6.9)
Abdominal pain	1 (4.0)	1 (3.4)
Abdominal discomfort	0	1 (3.4)
Abnormal feces	1 (4.0)	0
Flatulence	1 (4.0)	0
Frequent bowel movements	1 (4.0)	0
Vomiting	0	1 (3.4)
Metabolism and nutritional disorders	3 (12.0)	2 (6.9)
Diabetes mellitus inadequate control	1 (4.0)	0
Hyperglycemia	1 (4.0)	2 (6.9)
Hypoglycemia	1 (4.0)	1 (3.4)

TEAE, treatment-emergent adverse event.