Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of PRV-015 in Adult Patients with Non-Responsive Celiac Disease as an Adjunct to a Gluten-free Diet

Summary

EudraCT number	2020-000649-16
Trial protocol	NL ES
Global end of trial date	30 July 2024

Results information

Result version number	v1
This version publication date	13 August 2025
First version publication date	13 August 2025

Trial information

Trial identification

Sponsor protocol code	PRV-015-002B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04424927
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Provention Bio, Inc.
Sponsor organisation address	55 Broad Street, 2nd Floor, Red Bank, New Jersey, United States, 07701
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of PRV-015 in attenuating the symptoms of celiac disease in adult participants with nonresponsive celiac disease as measured by the Abdominal Symptoms domain of the celiac disease patient reported outcome (CeD PRO) questionnaire.

Protection of trial subjects:

Participants were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 August 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 32
Country: Number of subjects enrolled	United States: 187
Worldwide total number of subjects	226
EEA total number of subjects	33

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	215
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 39 centers in 4 countries. A total of 648 participants were screened between 24 August 2020 and 16 January 2024, of which 255 participants were screen failures and 5 participants discontinued before run-in period. Screen failures were mainly due to not meeting eligibility criteria.

Pre-assignment

Screening details:

A total of 388 participants entered the single-blind placebo run-in period and among them, 9 participants discontinued during run-in or were not dosed, and 27 participants were considered run-in failures. Another 126 participants were considered randomization failures. A total of 226 participants were enrolled and randomized in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matching with PRV-015 subcutaneous (SC) injection every 2 weeks (q2w) in double-blind treatment period for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo SC injection q2w for 24 weeks.

Arm title	PRV-015 100 mg

Arm description:

Participants received PRV-015 100 milligram (mg) SC injection q2w in double-blind treatment period for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	PRV-015
Investigational medicinal product code	
Other name	Ordesekimab, AMG 714
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PRV-015 100 mg SC injection q2w for 24 weeks.

Arm title	PRV-015 300 mg

Arm description:

Participants received PRV-015 300 mg SC injection q2w in double-blind treatment period for 24 weeks.

Arm type	Experimental

Investigational medicinal product name	PRV-015
Investigational medicinal product code	
Other name	Ordesekimab, AMG 714
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PRV-015 300 mg SC injection q2w for 24 weeks.

Arm title	PRV-015 600 mg

Arm description:

Participants received PRV-015 600 mg SC injection q2w in double-blind treatment period for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	PRV-015
Investigational medicinal product code	
Other name	Ordesekimab, AMG 714
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PRV-015 600 mg SC injection q2w for 24 weeks.

Number of subjects in period 1	Placebo	PRV-015 100 mg	PRV-015 300 mg
Started	57	56	57
Received treatment	57	56	57
Completed	51	47	51
Not completed	6	9	6
Consent withdrawn by subject	3	5	5
Unspecified	1	3	1
Lost to follow-up	1	1	-
Investigator or Sponsor judgement	1	-	-

Number of subjects in period 1	PRV-015 600 mg
Started	56
Received treatment	54
Completed	49
Not completed	7
Consent withdrawn by subject	6
Unspecified	-
Lost to follow-up	-
Investigator or Sponsor judgement	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching with PRV-015 subcutaneous (SC) injection every 2 weeks (q2w) in double-blind treatment period for 24 weeks.	
Reporting group title	PRV-015 100 mg
Reporting group description:	
Participants received PRV-015 100 milligram (mg) SC injection q2w in double-blind treatment period for 24 weeks.	
Reporting group title	PRV-015 300 mg
Reporting group description:	
Participants received PRV-015 300 mg SC injection q2w in double-blind treatment period for 24 weeks.	
Reporting group title	PRV-015 600 mg
Reporting group description:	
Participants received PRV-015 600 mg SC injection q2w in double-blind treatment period for 24 weeks.	

Reporting group values	Placebo	PRV-015 100 mg	PRV-015 300 mg
Number of subjects	57	56	57
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	41.0	41.9	39.0
standard deviation	± 14.53	± 14.82	± 12.25
Gender Categorical Units: Subjects			
Female	53	38	50
Male	4	18	7
Race Units: Subjects			
Black or African American	0	1	0
White	57	55	56
Not Reported	0	0	0
Unknown	0	0	0
Multiple	0	0	1
CeD PRO Abdominal Symptoms Domain Score			
The CeD PRO questionnaire was captured daily in the electronic (e)Diary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Abdominal Symptoms domain included abdominal cramping, abdominal pain, bloating and gas. Total score for abdominal symptoms domain range from 0 to 40. Higher scores indicated worse outcome.			
Units: Subjects			
Score: <3	13	13	13
Score: >=3	44	43	44
Stratification Factor Villous Height-to-Crypt Depth Ratio (VH:CD)			

The CeD PRO questionnaire was captured daily in the eDiary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Abdominal Symptoms domain included abdominal cramping, abdominal pain, bloating and gas. Total score for abdominal symptoms domain range from 0 to 40. Higher scores indicated worse outcome.			
Units: Subjects			
Score: <2	37	37	37
Score: >=2	20	19	20

Reporting group values	PRV-015 600 mg	Total	
Number of subjects	56	226	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	37.9		
standard deviation	± 12.58	-	
Gender Categorical Units: Subjects			
Female	45	186	
Male	11	40	
Race Units: Subjects			
Black or African American	0	1	
White	53	221	
Not Reported	2	2	
Unknown	1	1	
Multiple	0	1	
CeD PRO Abdominal Symptoms Domain Score			
The CeD PRO questionnaire was captured daily in the electronic (e)Diary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Abdominal Symptoms domain included abdominal cramping, abdominal pain, bloating and gas. Total score for abdominal symptoms domain range from 0 to 40. Higher scores indicated worse outcome.			
Units: Subjects			
Score: <3	13	52	
Score: >=3	43	174	
Stratification Factor Villous Height-to-Crypt Depth Ratio (VH:CD)			
The CeD PRO questionnaire was captured daily in the eDiary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Abdominal Symptoms domain included abdominal cramping, abdominal pain, bloating and gas. Total score for abdominal symptoms domain range from 0 to 40. Higher scores indicated worse outcome.			
Units: Subjects			
Score: <2	36	147	
Score: >=2	20	79	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching with PRV-015 subcutaneous (SC) injection every 2 weeks (q2w) in double-blind treatment period for 24 weeks.	
Reporting group title	PRV-015 100 mg
Reporting group description:	
Participants received PRV-015 100 milligram (mg) SC injection q2w in double-blind treatment period for 24 weeks.	
Reporting group title	PRV-015 300 mg
Reporting group description:	
Participants received PRV-015 300 mg SC injection q2w in double-blind treatment period for 24 weeks.	
Reporting group title	PRV-015 600 mg
Reporting group description:	
Participants received PRV-015 600 mg SC injection q2w in double-blind treatment period for 24 weeks.	

Primary: Absolute Change From Baseline in Celiac Disease Patient-Reported Outcome Abdominal Symptoms Domain Score Through Week 24

End point title	Absolute Change From Baseline in Celiac Disease Patient-Reported Outcome Abdominal Symptoms Domain Score Through Week 24
End point description:	
The CeD PRO questionnaire was captured daily in the eDiary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Abdominal Symptoms domain included abdominal cramping, abdominal pain, bloating and gas. Total score for abdominal symptoms domain range from 0 to 40. Higher scores indicated worse outcome. Baseline abdominal symptoms domain score was defined as the average of the daily scores for the last week of the placebo run-in period. The modified intent-to-treat (mITT) analysis set included all randomized participants who received at least 1 dose of double-blind treatment. Only participants with data collected at baseline and up to Week 24 are reported.	
End point type	Primary
End point timeframe:	
Baseline (average of Day -7 to Day -1) up to Week 24	

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	52
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.32 (-1.66 to -0.98)	-1.28 (-1.62 to -0.94)	-1.21 (-1.55 to -0.88)	-1.28 (-1.63 to -0.93)

Statistical analyses

Statistical analysis title	Treatment difference in CeD PRO questionnaire 1

Statistical analysis description:

Estimates/p-value are from a mixed model for repeated measures (MMRM) with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8543
Method	MMRM
Parameter estimate	Least square (LS) mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.52

Statistical analysis title	Treatment difference in CeD PRO questionnaire 2

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 300 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6552
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.59

Statistical analysis title	Treatment difference in CeD PRO questionnaire 3

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 600 mg

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8705
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.53

Secondary: Absolute Change From Baseline in Celiac Disease Patient-Reported Outcome Diarrhea and Loose Stool Domain Score Through Week 24

End point title	Absolute Change From Baseline in Celiac Disease Patient-Reported Outcome Diarrhea and Loose Stool Domain Score Through Week 24

End point description:

The CeD PRO questionnaire was captured daily in the eDiary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Diarrhea and loose stool domain included diarrhea and loose stool. Total score for diarrhea and loose stool domain range from 0 to 20. Higher scores indicated worse outcome. Baseline diarrhea and loose stool domain score was defined as the average of the daily scores for the last week of the placebo run-in period. The mITT analysis set included all randomized participants who received at least 1 dose of double-blind treatment. Only participants with data collected at baseline and up to Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (average of Day -7 to Day -1) up to Week 24

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	52
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.77 (-1.15 to -0.40)	-0.66 (-1.04 to -0.28)	-1.02 (-1.39 to -0.64)	-1.07 (-1.46 to -0.68)

Statistical analyses

Statistical analysis title	Treatment difference in CeD PRO questionnaire 1

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 100 mg

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6757
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.65

Statistical analysis title	Treatment difference in CeD PRO questionnaire 2

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 300 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3645
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	0.29

Statistical analysis title	Treatment difference in CeD PRO questionnaire 3

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 600 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2791
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.24

Secondary: Absolute Change From Baseline in Celiac Disease Patient-Reported Outcome Total Gastrointestinal (GI) Score Through Week 24

End point title	Absolute Change From Baseline in Celiac Disease Patient-Reported Outcome Total Gastrointestinal (GI) Score Through Week 24

End point description:

The CeD PRO questionnaire was captured daily in the eDiary. The questionnaire included 9 items: abdominal cramping, abdominal pain, bloating, gas, diarrhea, loose stool, nausea, headache and tiredness. Participants were asked to rate their symptom severity on an 11-point scale and scores range from 0 (not experiencing the symptom) to 10 (the worst possible symptom experience). Total GI domain included abdominal symptoms domain, diarrhea, loose stool and nausea. Total GI score range from 0 to 70. Higher scores indicated worse outcome. Baseline GI score was defined as the average of the daily scores for the last week of the placebo run-in period. The mITT analysis set included all randomized participants who received at least 1 dose of double-blind treatment. Only participants with data collected at baseline and up to Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (average of Day -7 to Day -1) up to Week 24

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	55	56	52
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.89 (-1.15 to -0.63)	-0.84 (-1.10 to -0.57)	-0.88 (-1.14 to -0.62)	-1.05 (-1.32 to -0.78)

Statistical analyses

Statistical analysis title	Treatment difference in CeD PRO questionnaire 1

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 100 mg
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7829
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.42

Statistical analysis title	Treatment difference in CeD PRO questionnaire 3

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 600 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4107
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.22

Statistical analysis title	Treatment difference in CeD PRO questionnaire 2

Statistical analysis description:

Estimates/p-value are from a MMRM with treatment, week, and treatment by week as fixed effects; continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio as covariates, and participant as a random effect.

Comparison groups	Placebo v PRV-015 300 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9503
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.38

Secondary: Absolute Change From Baseline in Intraepithelial Lymphocyte (IEL)

Density at Week 24

End point title	Absolute Change From Baseline in Intraepithelial Lymphocyte (IEL) Density at Week 24

End point description:

The small intestinal mucosal inflammation was measured by IEL density using immunohistochemistry. Baseline was defined as IEL density from the esophagogastroduodenoscopy biopsy conducted during the run-in period. The mITT analysis set included all randomized participants who received at least 1 dose of double-blind treatment. Only participants with data collected at baseline and Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day -28 up to Day -1) and Week 24

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	51	48
Units: cells/100 epithelial cells				
least squares mean (confidence interval 95%)	-0.39 (-3.82 to 3.03)	1.54 (-1.99 to 5.07)	-4.11 (-7.56 to -0.66)	-4.53 (-8.13 to -0.93)

Statistical analyses

Statistical analysis title	Treatment difference in IEL density 1

Statistical analysis description:

Estimates/p-value are from an analysis of covariance (ANCOVA) model with treatment as a fixed effect. Continuous baseline CeD PRO Abdominal Symptoms
domain score and baseline VH:CD ratio are included as covariates.

Comparison groups	Placebo v PRV-015 100 mg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4397
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	6.87

Statistical analysis title	Treatment difference in IEL density 2

Statistical analysis description:

Estimates/p-value are from an ANCOVA model with treatment as a fixed effect. Continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio are included as covariates.

Comparison groups	Placebo v PRV-015 300 mg

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1337
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-3.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.58
upper limit	1.15

Statistical analysis title	Treatment difference in IEL density 3

Statistical analysis description:

Estimates/p-value are from an ANCOVA model with treatment as a fixed effect. Continuous baseline CeD PRO Abdominal Symptoms domain score and baseline VH:CD ratio are included as covariates.

Comparison groups	Placebo v PRV-015 600 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1021
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-4.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.11
upper limit	0.83

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs) and Treatment-Emergent Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs) and Treatment-Emergent Adverse Events of Special Interest (AESIs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of study drug, whether or not considered related to the study drug. An SAE was defined as any AE that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. AESIs included severe opportunistic infections and hypersensitivity reactions of at least moderate severity. A TEAE was defined as an AE that occurred from the first dose of post-randomization study drug administration through the end of the study. The Safety analysis set included all participants who received at least 1 dose of the study drug post-randomization.

End point type	Secondary

End point timeframe:

From first dose of study drug administration (Day 1) up to 28 days after the last dose administration, 197 days

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	54
Units: participants				
Any TEAE	34	34	36	29
TEAE leading to study treatment discontinuation	1	1	2	0
Treatment-emergent SAE	1	0	0	1
Treatment-emergent AESI	2	1	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Important Changes in Hematology

End point title	Number of Participants With Potentially Clinically Important Changes in Hematology

End point description:

Blood samples were collected to determine the hematology laboratory important changes. The Safety analysis set included all participants who received at least 1 dose of the study drug post-randomization. Only participants with data collected are reported. CHG= Change from baseline hemoglobin.

End point type	Secondary

End point timeframe:

From first dose of study drug administration (Day 1) up to 28 days after the last dose administration, 197 days

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	53
Units: participants				
Hemoglobin: CHG <=-20	0	0	1	2
Neutrophils: <1	2	1	4	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Important Changes in Clinical Chemistry

End point title	Number of Participants With Potentially Clinically Important Changes in Clinical Chemistry

End point description:

Blood samples were collected to determine the clinical chemistry laboratory important changes. The Safety analysis set included all participants who received at least 1 dose of the study drug post-randomization. Only participants with data collected are reported. Here, ULN= Upper limit of normal, mmol/L= millimoles per liter and mcmol/L= micromoles per liter.

End point type	Secondary

End point timeframe:

From first dose of study drug administration (Day 1) up to 28 days after the last dose administration, 197 days

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	53
Units: participants				
Alanine Aminotransferase: >=3x ULN	1	4	1	2
Aspartate Aminotransferase: >=3x ULN	1	2	0	0
Chloride: >125 mmol/L	1	0	1	0
Creatinine: >=132 mcmol/L	1	1	0	0
Potassium: >6 mmol/L	0	0	2	1
Sodium: <125 mmol/L	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Important Changes in Urinalysis

End point title	Number of Participants With Potentially Clinically Important Changes in Urinalysis

End point description:

Urine samples were collected to determine the important changes in urine. The Safety analysis set included all participants who received at least 1 dose of the study drug post-randomization. Here, n= number of participants with data collected for each specific parameter and 99999= no participant was analyzed. Squamous Epithelial Cells= SEC, TNTC= Too numerous to count, LPF= Low power field and HPF= High power field.

End point type	Secondary

End point timeframe:

From first dose of study drug administration (Day 1) up to 28 days after the last dose administration, 197 days

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	53
Units: participants				
Bacteria: Present (n=54,51,55,47)	54	51	55	47
Crystals: Present (n=3,4,2,5)	3	4	2	5
Erythrocytes (/HPF): Many/TNTC (n=55,56,56,53)	1	0	4	3
Glucose: 3+/4+ (n=57,56,57,53)	1	2	1	0
Hyaline Casts (/HPF): Few/Moderate/Many(n=8,7,9,7)	3	2	3	0
Hyaline Casts (/LPF): Few/Moderate/Many(n=0,2,1,0)	99999	1	1	99999
Ketones: 3+ (n=57,56,57,53)	1	2	3	1
Leukocyte Esterase: 3+/4+ (n=57,56,57,53)	19	12	16	15
Leukocytes (/HPF): Many/TNTC (n=56,56,57,53)	11	3	9	7
Nitrite: Positive (n=57,56,57,53)	2	1	2	1
SEC (/HPF): Many/TNTC(n=54,54,54,49)	6	0	6	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Important Changes in Vital Signs and Body Weight

End point title	Number of Participants With Potentially Clinically Important Changes in Vital Signs and Body Weight

End point description:

Participant's vital signs and body weight were examined to determine the important changes. Vital signs included systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate. The Safety analysis set included all participants who received at least 1 dose of the study drug post-randomization. Here, mmHg= millimeters of mercury, DFB= Decrease from baseline and IFB= Increase from baseline.

End point type	Secondary

End point timeframe:

From first dose of study drug administration (Day 1) up to 28 days after the last dose administration, 197 days

End point values	Placebo	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	54
Units: participants				
SBP: <=95 mmHg and DFB >=20 mmHg	5	2	6	1
SBP: >=160 mmHg and IFB >=20 mmHg	2	1	0	1
DBP: >=110 mmHg and IFB >=10 mmHg	0	0	0	1

Heart Rate: <=50 bpm and DFB >=20 bpm	1	1	1	0
Heart Rate: >=120 bpm and IFB >=20 bpm	0	0	0	1
Body weight: >=5% DFB	8	11	9	7
Body weight: >=5% IFB	9	8	13	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-PRV-015 Antibodies

End point title	Number of Participants With Anti-PRV-015 Antibodies[1]

End point description:

Blood samples were collected to determine the presence of anti-drug antibodies by immunoassay. The Immunogenicity analysis set included participants who were randomized, dosed, and had at least 1 evaluable immunogenicity assessment. Here, n= number of participants with data collected at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4, 12, 22, 24 and 28

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated with the study drug are analyzed for this endpoint.

End point values	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	56	53	
Units: participants				
Baseline (n=52,52,50)	3	8	7	
Week 2 (n=53,56,51)	8	9	9	
Week 4 (n=52,51,48)	5	6	5	
Week 12 (n=51,51,53)	4	5	4	
Week 22 (n=49,49,48)	4	4	2	
Week 24 (n=49,51,49)	4	3	2	
Week 28 (n=50,52,48)	4	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentrations (Cmin) of PRV-015

End point title	Minimum Serum Concentrations (Cmin) of PRV-015[2]

End point description:

Blood samples were collected at specified timepoints to determine the Cmin. The Pharmacokinetic (PK) analysis set included participants who were randomized, dosed, and had at least 1 post-dose evaluable PK assessment. Here, n= number of participants with data collected at specific time point.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Weeks 2, 4, 8, 12, 16, 20, 22, 24 and 28

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants treated with the study drug are analyzed for this endpoint.

End point values	PRV-015 100 mg	PRV-015 300 mg	PRV-015 600 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	53	48	
Units: nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Pre-dose on Day 1 (n=52,51,48)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Week 2 (n=46,53,46)	8778 (± 74.1)	27820 (± 39.8)	66400 (± 46.1)	
Week 4 (n=36,43,39)	15140 (± 42.8)	51190 (± 42.1)	98420 (± 49.4)	
Week 8 (n=31,40,33)	21790 (± 46.4)	61990 (± 66.5)	142600 (± 43.7)	
Week 12 (n=28,33,32)	23630 (± 46.8)	73150 (± 56.5)	168300 (± 37.9)	
Week 16 (n=25,27,26)	22960 (± 46.7)	75830 (± 65.1)	166700 (± 44.9)	
Week 20 (n=20,25,21)	27000 (± 42.5)	74110 (± 67.8)	186400 (± 51.2)	
Week 22 (n=20,22,21)	25410 (± 36.2)	73120 (± 64.2)	181000 (± 55.6)	
Week 24 (n=18,18,18)	26680 (± 40.3)	72400 (± 49.6)	160500 (± 47.5)	
Week 28 (n=26,25,27)	10210 (± 58.0)	32810 (± 80.0)	69370 (± 78.3)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug administration (Day 1) up to 28 days after the last dose administration, 197 days

Adverse event reporting additional description:

The Safety analysis set included all participants who received at least 1 dose of the study drug post-randomization.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo matching with PRV-015 SC injection q2w in double-blind treatment period for 24 weeks.

Reporting group title	PRV-015 300 mg

Reporting group description:

Participants received PRV-015 300 mg SC injection q2w in double-blind treatment period for 24 weeks.

Reporting group title	PRV-015 600 mg

Reporting group description:

Participants received PRV-015 600 mg SC injection q2w in double-blind treatment period for 24 weeks.

Reporting group title	PRV-015 100 mg

Reporting group description:

Participants received PRV-015 100 mg SC injection q2w in double-blind treatment period for 24 weeks.

Serious adverse events	Placebo	PRV-015 300 mg	PRV-015 600 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 57 (1.75%)	0 / 57 (0.00%)	1 / 54 (1.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Pelvic Fracture			
subjects affected / exposed	1 / 57 (1.75%)	0 / 57 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Presyncope			

subjects affected / exposed	0 / 57 (0.00%)	0 / 57 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PRV-015 100 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Pelvic Fracture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	PRV-015 300 mg	PRV-015 600 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 57 (38.60%)	22 / 57 (38.60%)	19 / 54 (35.19%)
Nervous system disorders			
Migraine			
subjects affected / exposed	4 / 57 (7.02%)	1 / 57 (1.75%)	1 / 54 (1.85%)
occurrences (all)	4	1	1
Headache			
subjects affected / exposed	1 / 57 (1.75%)	5 / 57 (8.77%)	2 / 54 (3.70%)
occurrences (all)	2	5	2
General disorders and administration site conditions			
Injection Site Bruising			

subjects affected / exposed	0 / 57 (0.00%)	2 / 57 (3.51%)	3 / 54 (5.56%)
occurrences (all)	0	2	3
Injection Site Erythema			
subjects affected / exposed	2 / 57 (3.51%)	3 / 57 (5.26%)	2 / 54 (3.70%)
occurrences (all)	2	6	7
Injection Site Reaction			
subjects affected / exposed	1 / 57 (1.75%)	3 / 57 (5.26%)	3 / 54 (5.56%)
occurrences (all)	2	6	9
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	3 / 57 (5.26%)	0 / 57 (0.00%)	4 / 54 (7.41%)
occurrences (all)	3	0	4
Abdominal Distension			
subjects affected / exposed	1 / 57 (1.75%)	0 / 57 (0.00%)	2 / 54 (3.70%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	1 / 57 (1.75%)	5 / 57 (8.77%)	3 / 54 (5.56%)
occurrences (all)	1	5	3
Diarrhoea			
subjects affected / exposed	6 / 57 (10.53%)	4 / 57 (7.02%)	4 / 54 (7.41%)
occurrences (all)	7	6	4
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 57 (7.02%)	3 / 57 (5.26%)	1 / 54 (1.85%)
occurrences (all)	4	3	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 57 (3.51%)	0 / 57 (0.00%)	2 / 54 (3.70%)
occurrences (all)	2	0	2
Infections and infestations			
Covid-19			
subjects affected / exposed	3 / 57 (5.26%)	8 / 57 (14.04%)	5 / 54 (9.26%)
occurrences (all)	3	8	5
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 57 (8.77%)	4 / 57 (7.02%)	4 / 54 (7.41%)
occurrences (all)	6	4	4

Non-serious adverse events	PRV-015 100 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 56 (32.14%)		
Nervous system disorders			
Migraine			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
General disorders and administration site conditions			
Injection Site Bruising			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Injection Site Erythema			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	8		
Injection Site Reaction			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Abdominal Distension			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 3 / 56 (5.36%) 3		
Infections and infestations Covid-19 subjects affected / exposed occurrences (all) Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	 5 / 56 (8.93%) 5 3 / 56 (5.36%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2021	The antibody tests on the Day -14 visit (Visit -2) were removed to avoid any delay for the Day 0 visit and the start of study treatment. All urine samples were collected at each visit. The maximum levels of tissue transglutaminase and deamidated gluten peptide antibodies for inclusion was revised from 1.5 to 2.0 times the cutoff value for positivity. The Data Monitoring Committee member composition was updated. The window for the baseline endoscopy was increased to 12 days prior to Visit 2 to improve scheduling feasibility. Updated to allow the inclusion of participants with less common human leukocyte antigen types associated with celiac disease. Clarified the consenting procedures for participants undergoing rescreening. Corrected to include hemoglobin A1C at visits designated in the Schedule of Activities. Clarified the procedures for SAE reporting.
24 March 2022	The level of tissue transglutaminase and deamidated gluten peptide antibodies for study inclusion was revised from <2.0 to <3.0 times the cutoff value for positivity. Updated inclusion and exclusion criteria. The planned method for the analysis of delayed TEAEs in participants who discontinued study treatment was removed and deferred to the Statistical Analysis Plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported