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

Published: 04-02-2021
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Primary objective:To assess the efficacy of PRV-015 in attenuating the symptoms of celiac disease in adult patients with NRCD as measured by the Abdominal Symptoms domain of the Celiac Disease Patient- Reported Outcome (CeD PRO)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON52134

Source
ToetsingOnline

Brief title
PROACTIVE (PROvention-Amgen Celiac protecTIVE study)

Condition

- Metabolic and nutritional disorders congenital

Synonym
celiac disease

Research involving

Human

Sponsors and support

Primary sponsor: Provention Bio, Inc.
Source(s) of monetary or material Support: Provention Bio;Inc.

Intervention

Keyword: Celiac Disease

Outcome measures

Primary outcome

Endpoint:

• Absolute change from baseline through Week 24 in abdominal symptoms as measured by the Abdominal Symptoms domain of the CeD PRO questionnaire

Estimand:

• The primary estimand is the difference in the overall mean values (averaged across 24 weeks) of each of the 3 PRV-015 treatment groups compared with placebo of the change from baseline in the Abdominal Symptoms domain of the CeD PRO questionnaire in the target population, regardless of compliance to study treatment or the occurrence of intercurrent events.

Secondary outcome

Secondary efficacy endpoints:

• Absolute change from baseline through Week 24 in the Diarrhea and Loose Stool domain of the CeD PRO

• Absolute change from baseline through Week 24 in gastrointestinal (GI) symptoms as assessed by the Total GI score (comprising the Abdominal Symptoms

domain, the Diarrhea and Loose Stool domain, and the Nausea item) of the CeD PRO

• Absolute change from baseline to Week 24 in small intestinal mucosal inflammation, as measured by intraepithelial lymphocyte (IEL) density using immunohistochemistry (IHC)

Safety endpoints:

• Adverse events (AEs): treatmentemergent adverse events (TEAEs), TEAEs leading to treatment discontinuation, and treatment-emergent serious adverse events (SAEs)

• Treatment-emergent adverse events of special interest (AESIs)

• Potentially clinically important (PCI) changes in clinical laboratory values (hematology, chemistry, and urinalysis), vital signs (blood pressure [BP], heart rate, temperature, respiratory rate), and weight

• Immunogenicity, as assessed by the presence of anti-PRV-015 antibodies

PK endpoint:

• Serum PRV-015 trough concentrations (Cmin)

Study description

Background summary

Celiac disease is a systemic autoimmune disease triggered by gluten consumption in genetically susceptible individuals. Non-responsive celiac disease (NRCD) can be defined as persistent symptoms, signs, or laboratory abnormalities typical of celiac disease despite at least 6-12 months of treatment with a gluten-free diet (GFD). PRV-015 (also known as AMG 714), a monoclonal antibody that blocks interleukin 15 (IL-15), has been shown to reduce intestinal inflammation and improve clinical symptoms induced by gluten consumption in celiac disease. PRV-015 may be effective as an adjunctive treatment to a GFD in

NRCD patients.

Study objective

Primary objective:

To assess the efficacy of PRV-015 in attenuating the symptoms of celiac disease in adult patients with NRCD as measured by the Abdominal Symptoms domain of the Celiac Disease Patient- Reported Outcome (CeD PRO) questionnaire

Secondary objectives:
• To assess the effect of treatment with PRV-015 on other measures of disease activity
• To assess the safety, tolerability, and pharmacokinetics (PK) of PRV-015 when administered to adult patients with NRCD.

Study design

Protocol PRV-015-002b is a Phase 2b, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of PRV-015 in adult patients with NRCD who are on a GFD.

After signing informed consent form (ICF), subjects will undergo screening assessments for the study in a screening period of up to 28 days before Visit 1. The screening assessments will include the collection of demographics, medical history, and past record of the diagnosis of celiac disease if available. Subjects should demonstrate 1) attempted adherence to a GFD, confirmed by a lack of strong serological positivity (<2.0 x cutoff value for positivity), and 2) exposure to gluten contamination by presenting with detectable serology (above the lower limit of quantitation). After initial screening, potentially eligible subjects will enter a single-blind, placebo run-in period for 4 weeks, starting at Visit 1.

Intervention

After the single-blind placebo run-in phase, subjects will be randomized to one of the 4 treatment groups in a ratio of 1:1:1:1 as follows:
• PRV-015 100 mg q2w
• PRV-015 300 mg q2w
• PRV-015 600 mg q2w
• Placebo q2w

At each visit, each subject will receive 4 injections for a total volume of 6 mL

Study burden and risks

Risks which are associated with the study drug and procedures are described in details in the main patient Information sheet and informed consent form. The safety profile to date suggests that the risks associated with PRV-015 are mild and transient, and predominantly injection site reactions.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Adult male or females, 18-70 years of age
• A diagnosis of celiac disease by intestinal biopsy
• Following a GFD for at least 12 consecutive months
• Must have detectable (above the lower limit of detection) serum celiac-related antibodies
• Must have human leukocyte antigen DQ (HLA-DQ) typing consistent with known celiac disease alleles (typically DQ2 and/or DQ8)
• Subjects must have had at least one of the following symptoms at least once per week during the month before screening: diarrhea, loose stools, abdominal pain, abdominal cramping, bloating, or gas.
• Body weight between 35 and 120 kg

Exclusion criteria

• Current diagnosis of any severe complication of celiac disease, such as refractory celiac disease type 1 (RCD-I) or RCD-II, enteropathy-associated T-cell lymphoma (EATL), ulcerative jejunitis, or gastrointestinal (GI) perforation
• Diagnosis of any chronic, active GI disease other than celiac disease
• Presence of any active infection
• Known or suspected exposure to coronavirus disease 2019 (COVID-19) infection in the 4 weeks before screening
• Administration of a live vaccine within 14 days prior to randomization and the first administration of study drug
• History or presence of any clinically significant disease that, in the opinion of the Investigator, may confound the subject's participation and follow-up in the clinical trial or put the subject at unnecessary risk
• Females who are pregnant or planning to become pregnant during the study period, or who are currently breastfeeding

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-02-2022
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ordesekimab
Generic name:	PRV-015

Ethics review

Approved WMO Date:	04-02-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-07-2021
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-000649-16-NL
ClinicalTrials.gov	NCT04424927
CCMO	NL76464.018.21