Coeliac Disease Clinical Trial

A Phase IC, Randomised, Double Blind, Placebo Controlled, Multi-Centre Study To Evaluate The Safety, Pharmacokinetics, Immunogenicity, and Biological Effects of DONQ52 in Coeliac Disease Patients with Gluten Challenge.

ABOUT THIS RESEARCH STUDY

This study is designed to investigate the safety and effectiveness of a single subcutaneous (SC) dose of DONQ52 with a 3-day gluten challenge in well-controlled CeD patients. A SC injection is one that is given under the skin. In this study, the injection will be given in the abdomen or thigh. This study includes a 3-day gluten challenge. All participants must maintain a gluten-free diet (GFD) throughout the study (by the study completion/early termination visit) except for the instructed and controlled gluten challenge.

The investigational medicinal product (IMP) for this study is DONQ52 (test product) and the placebo (comparator). The IMP will be administered subcutaneously into the abdomen except for the area directly surrounding, within 5 cm of, the navel, and avoid sites where the skin is
tender, bruised, red, or hard (the anterior thigh may be used as an alternative site if there is sufficient subcutaneous tissue). Preparation and administration of DONQ52/placebo are conducted by unblinded staff. To keep the double-blind nature of the study, the unblinded staff will not be involved with any participant evaluation or care.

A total of 36 male and female well-controlled CeD patients in a 1:1 ratio of active versus placebo will be enrolled across Australia.

Human leukocyte antigen (HLA) genotyping test is a kind of genetic test that may be done if your patient does not have a prior result.

STUDY RATIONALE

DONQ52 is a humanised monoclonal modified immunoglobulin G (IgG) 1 antibody with a bispecific antibody structure that specifically binds to complexes formed by HLA-DQ2.5 and gluten peptides and neutralises gluten peptides dependent CD4+ T cell activation. Although it is known that various gluten peptides are pathogenic, such as α1 gliadin, α2 gliadin, ω1 gliadin, ω2 gliadin, B/C hordein, etc., DONQ52 has a broad spectrum of cross-reactivity against these peptides. On the other hand, DONQ52 has no substantial binding activity against complexes formed by HLA-DQ2.5 and endogenous peptides or pathogen-derived peptides. This binding specificity leads to improved pharmacokinetic (PK) profiles and limited toxicity risk. DONQ52 is therefore expected to specifically block gluten-dependent inflammation.

Though roughly 1 in 70 Australians have Coeliac disease[1], the only way to manage the symptoms of this condition is to follow a strict gluten-free diet. However, cross-contamination in food preparation settings, including restaurants, supermarkets, and healthcare facilities, can increase a person's risk of gluten exposure[2] and complications from untreated Coeliac disease, such as malnutrition, anaemia, and osteoporosis[3]. As such, by striving to develop a standard treatment option for people with Coeliac disease, this study could free them from the daily struggle of self-management and improve their quality of life.

[1] Coeliac disease. Coeliac Australia. Accessed October 26, 2023. https://coeliac.org.au/learn/coeliac-disease/

[2] Silvester JA, Graff LA, Rigaux L, Walker JR, Duerksen DR. Symptomatic suspected gluten exposure is common among patients with coeliac disease on a gluten-free diet. Aliment Pharmacol Ther. 2016 Sep;44(6):612-9. doi: 10.1111/apt.13725. Epub 2016 Jul 22. PMID: 27443825; PMCID: PMC5283559.

[3] Complications: Coeliac disease. NHS. Accessed October 26, 2023. https://www.nhs.uk/conditions/coeliac-disease/complications/

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WHAT IS INVOLVED?

If a participant is deemed eligible for the study, their study participation is expected to last approximately 30 weeks, and they will be required to attend the study site up to 13 times. This includes:

- A screening period of 28 days.
- A randomisation and treatment period of 29 days, including:
  - Day 1: Treatment with the investigational medication DONQ52 OR placebo administered subcutaneously at the study site.
  - Day 9: 10g of vital wheat gluten consumed orally (mixed in water or chocolate milk) and then monitored at the study site for 6 hours.
  - Days 10 and 11: 10g of vital wheat gluten consumed orally (mixed in water or chocolate milk) at home after an 8 hour overnight fasting (during the fasting period, participants are allowed to take only water. Participants will be allowed to eat and drink from 30 minutes after the gluten challenge).
  - Thereafter, they will visit the study site on an outpatient basis until the last observation on Day 29.
- A follow-up period from Day 30 to Day 176, during which they will need to return to the study site 5 more times.

Eligible participants will be randomised in a 1:1 ratio to DONQ52 or placebo treatment groups. The randomisation scheme to active treatment and placebo groups is considered necessary to generate an adequate within-study comparator dataset to allow proper evaluation of the magnitude of any treatment effects.

Participants may withdraw from the study at any time.

By referring potential participants, you could play a pivotal role in advancing research into Coeliac disease treatments, aiming to improve health outcomes that benefit those suffering from Coeliac disease.

This trial has been approved by an independent ethics committee.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Chugai Pharmaceuticals, a Japanese pharmaceutical company headquartered in Tokyo, Japan.

MAJOR INCLUSION CRITERIA

- Aged between 18 and 70.
- Have a history of medically diagnosed Coeliac disease.
- Have a body mass index (BMI) of 18 to 35kg/m2 at screening.
- Be on a gluten-free diet (GFD) for at least 12 months prior to the screening visit.
- Have experienced, at most, mild symptoms of Coeliac disease within a month before the screening visit.
- Willing to consume food containing gluten protein as part of a 3-day gluten challenge

MAJOR EXCLUSION CRITERIA

- Have an allergy to wheat
- Have refractory Coeliac disease defined as persistent or recurrent malabsorptive symptoms and signs with villous atrophy (Marsh grade 3) despite following a strict gluten-free diet for more than 12 months.
- Have any other chronic, active gastrointestinal disease, such as inflammatory bowel disease, microscopic colitis, or irritable bowel syndrome.
- Have used oral or parenteral corticosteroids within 4 weeks prior to the screening visit - though, topical or inhaled corticosteroids are acceptable.
- Are pregnant or breastfeeding, or intend to become pregnant during the study or within 176 days of receiving the investigational medication.

For more information, CLICK THE LINK BELOW.

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