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A study to learn if ZED1227 can improve continued celiac disease symptoms despite a gluten-free diet

Submission date 09/01/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 12/03/2024	**Overall study status** Ongoing	
Last Edited 11/07/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
This study is investigating if the study drug, ZED1227 (an oral capsule), can help reduce the symptoms and damage to cells in the intestine caused when coeliac disease sufferers eat gluten. ZED1227 will be compared with a 'placebo' which will help better assess its effects and side effects. A 'placebo' looks identical to the ZED1227 capsule but contains no active study drug substance.

Who can participate?
Patients 18-80 years old who have had coeliac disease for at least 12 months and, despite being on a gluten-free diet for at least 12 months, still experience symptoms

What does the study involve?
Participants will be given either ZED1227 or a placebo. A third study group might be opened during the study, where patients receive a reduced ZED1227 dose if data from another ongoing study supports this. Participants will be divided into treatment groups by randomisation. Randomisation is the assignment of a subject to a treatment group by chance (like tossing a coin). Randomisation will be performed electronically, neither the participant nor the study doctor can influence which treatment group is assigned.
Participants take ZED1227 or placebo three times a day with a meal and eat a gluten-containing snack bar three times a week (this mimics unintended gluten exposure). Before randomisation into the study, participants will be asked to eat a gluten-free snack bar to make sure they can tolerate the ingredients other than gluten.
Study participation will last about 23 weeks and will involve seven visits to the study site. At these visits the participant will have procedures performed including collection of blood and urine samples, they will be asked to complete study questionnaires and discuss their medication and health. Two gastrointestinal endoscopies with biopsies will be required; one at the start of the study and another at the end. For the duration of the study the participants will be asked to complete an electronic diary, recording, for example: when they took their medication, their coeliac symptoms and health issues experienced.

What are the possible benefits and risks of participating?
Participants may have an allergic reaction to the snack bar which is eaten as part of the study to provide gluten exposure. Actions to prevent an allergic reaction or mitigate symptoms that may arise include incorporating an exclusion criterion for participants with food allergies to any of the snack bar ingredients, informing the participant in the PIS of the ingredients of the snack bar and having the participant eat a snack bar (minus the gluten) whilst observed in clinic as part of the screening visit to ensure they can tolerate it.
The gluten-containing snack bar may exacerbate the participants' symptoms in response to gluten, this cannot be avoided as the study drug's effect on these symptoms is what is being studied. Upon discontinuation of snack bars, the symptoms will resolve. These symptoms, occurrence and severity are recorded by the subject and reviewed as part of the study. There is also an exclusion criterion for patients who have known hypersensitivity and/or allergy to wheat and/or gluten.
Participants may experience side effects to the study drug, they are questioned at each visit on their health status, and they are instructed in the PIS and at the visits to contact the site should they have any severe reactions/illnesses. Patients with known intolerance/hypersensitivity /resistance to the study drug, its excipients or drugs of a similar chemical structure are excluded from the study.
Upper gastrointestinal endoscopy might cause bleeding that may need medical attention, this is a rare complication. Other severe side effects, such as perforations resulting from the procedure, are reported in 0.04% to 0.01% of endoscopies. Endoscopies are performed as they would be in normal clinical practice with the same safeguards and any necessary follow-up. Participants should contact the site if they feel unwell after their endoscopy. Endoscopies are invasive procedures but are required to see if the study drug has an effect on the gut morphology, this is a study endpoint.
Blood sampling might cause discomfort, bruising, clotting of the vein at the needle insertion site (unusual), venous inflammation (thrombophlebitis) or nerve injury. Site staff will be trained and will endeavour to cause as little pain as possible and to cause no serious injury.
The participants are expected to keep a diary detailing when they take the study medication and any gluten-related symptoms they experience. They also have a number of questionnaires to complete. This can all be a bit onerous, however, the diary can be accessed on the participant's mobile phone or computer and thus is easy to access and the site staff will provide training to the participant on how to use the device. Diary entries mainly require ticking certain boxes. The questionnaires are largely multiple choice and no lengthy text input is required from the participant.
There is a possibility of breach of confidentiality, but as all staff are trained healthcare or allied healthcare professionals, trained in the processes for clinical trials, are aware of GDPR and work to their site’s/company’s SOPs, this risk is minimal.

Where is the study run from?
Dr Falk Pharma (Germany)

When is the study starting and how long is it expected to run for?
January 2024 to August 2027

Who is funding the study?
Dr Falk Pharma (Germany)

Who is the main contact?
Beate Niemeier

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Additional identifiers

Clinical Trials Information System (CTIS)
2023-506150-21

Integrated Research Application System (IRAS)
1008894

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CEC-013/CEL, IRAS 1008894, CPMS 59048

Study information

Scientific Title
A Phase II, double-blind, randomised, placebo-controlled trial to evaluate the efficacy and tolerability of ZED1227 in celiac disease subjects experiencing symptoms despite gluten-free diet

Study objectives
The main objective of this study is to establish how effective ZED1227 is at stopping or reducing the symptoms of coeliac disease.

The secondary objectives are:
1. To assess how effective ZED1227 is at stopping or reducing cell damage in the gut due to eating gluten
2. To assess how effective ZED1227 is at reducing non-stool-related symptoms of coeliac disease such as abdominal pain, bloating and nausea
3. To assess how safe it is to take ZED1227 and if taking it causes any side effects

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 21/02/2024, Seasonal REC 2 (Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)20 7104 8144, +44 (0)20 7104 8129, +44 (0)20 7104 8057; Seasonal.rec@hra.uk), ref: 24/LO/0071

Study design
Randomized placebo-controlled double-blind parallel-group trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Coeliac disease

Interventions
Participants will be divided into two or three treatment groups. During this clinical study, ZED1227 will be compared with a placebo. This comparison is intended to assess better the effects and side effects of ZED1227. A placebo capsule looks identical to a ZED1227 capsule but contains no active study drug substance. Participants will be given either ZED1227 or a placebo. Optionally, a third study arm might be opened during the study, where patients receive a reduced ZED1227 dose. The study drug received will be decided by a predetermined random procedure like tossing a coin; this is called randomisation. The optional third treatment group will be added if data from another ongoing study supports it. If there are only two treatment groups, half of the participants will be given the study drug and the other half of the participants will receive a placebo. If the optional third group is added, two-thirds of the subjects will be given the study drug. Before randomisation into the study, participants will be asked to

eat a gluten-free snack bar to make sure they can tolerate ingredients other than gluten. If the participant is suitable for the study, they will start taking the gluten-containing snack bar three times a week.

The randomisation (i.e., assignment of a subject to one of the treatment groups by chance) will be performed by an electronic procedure. Neither the participant nor the study doctor can influence which treatment group is assigned.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
ZED1227

Primary outcome(s)
Coeliac Disease Symptom Diary (CDSD) GI Specific Symptom Score at Baseline Visit B (V2, week 3) to V5 (week 15). Weekly symptom-specific scores for diarrhoea, abdominal pain, bloating, nausea, and tiredness will be calculated from daily average scores (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe). A weekly GI severity score will include diarrhoea, abdominal pain, bloating, and nausea. The higher the score, the more severe the coeliac disease symptoms.

Key secondary outcome(s))
1. Villous Height to Crypt Depth ratio (VH: CrD) measured using digital morphometry of formalin-fixed samples from Baseline Visit A from Week 0 to Week 15
2. Non-stool GI symptoms measured using the CDSD Non-Stool GI Symptom Score (abdominal pain, bloating, nausea) from Week 3 to Week 15. A weekly Non-Stool GI Severity Score will be calculated for non-stool GI symptoms (i.e., abdominal pain, bloating and nausea) from daily average scores (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe). The higher the score, the more severe the coeliac disease symptoms.
3. Duodenal mucosal inflammation measured as the density of CD3-positive intraepithelial lymphocytes (IELs) from Baseline Visit A (V1, Week 0) to V5 (Week 15)

Completion date
02/08/2027

Eligibility

Key inclusion criteria
1. Signed informed consent
2. Men or women between 18 and 80 years of age, inclusively
3. Documented initial biopsy-proven diagnosis of coeliac disease or, in case of missing histological documentation, TG2-IgA >10 x upper limit of normal (ULN) at diagnosis at least 12 months prior to V0
4. Adherence to a gluten-free diet (GFD) for at least 12 months prior to V0
5. Human leukocyte antigen DQ (HLA-DQ) typing compatible with coeliac disease
6. At least one moderate or severe gastrointestinal symptom (i.e., diarrhoea, abdominal pain, bloating, or nausea) during the last 4 weeks prior to Baseline Visit A and last 3 weeks prior to

Baseline Visit B as a GI total mean symptom score (measured using CDSD) for the worst 25% of the days of ≥ 2 on a 5-point scale
7. Biopsy showing VH:CrD ratio of ≤ 2.5 from distal duodenum biopsies in Trial Period A
8. Negative diagnosis of Helicobacter pylori infection and no history of eradication within the last 2 months before biopsy sampling in Trial Period A
9. BMI between 17.0 and 35 kg/m², inclusively
10. Willingness to follow her/his usual dietary patterns, including eating at restaurants and others' homes during the trial
11. Willingness to maintain current GFD throughout participation in the trial
12. Negative pregnancy test in female subjects under 60 years of age at Screening Visit and Baseline Visit B
13. Women of child-bearing potential should use a highly effective method of birth control which is defined as those which result in a low failure rate (i.e. less than 1% per year) when used consistently and correctly, such as implants, injectables, combined oral contraceptive pills, combined contraceptive patches and vaginal rings, copper-containing intrauterine devices, sexual abstinence or vasectomised partner. The investigator is responsible for determining whether the subject has adequate birth control for trial participation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Presence of hypo- or hyperthyroidism. A patient with a well-controlled thyroid disorder during the previous 3 months can be included.
2. Patients diagnosed with confirmed refractory coeliac disease type I (RCDI) or II (RCDII), with the exception that patients with a diagnosis of RCDI can be included if they don't have clear signs of T cell monoclonality or atypical T cells (e.g., as revealed by CD3/CD8 immunohistochemistry) & if they don't present with very severe symptoms &/or parameters of significant malabsorption & if they haven't received prior treatment with immunosuppressants e. g. budesonide or azathioprine.
3. Severe complications of coeliac disease
4. Concomitant diseases of the intestinal tract, e.g. Crohn's disease, ulcerative colitis, severe irritable bowel syndrome, microscopic colitis, small intestinal bacterial overgrowth, exocrine pancreatic insufficiency
5. History/presence of dermatitis herpetiformis.
6. History/presence of neurological disorders like ataxia or neuropathy

7. Any severe concomitant cardiovascular, renal, endocrine (type 1 diabetes mellitus with HbA1C >8% / 64 mmol/mol or hospitalisation or emergency visit for hyperglycaemia or hypoglycaemia within 12 months of screening), or psychiatric disorder or other disease.
8. Any prior invasive malignancy diagnosed within the last 5 years prior to Screening visit. Patients with basal cell carcinoma of the skin completely resected can be included.
9. Evidence of relevant systemic disease (e.g., active tuberculosis)
10. Abnormal hepatic function [alkaline aminotransferase (ALT) or alkaline phosphatase (ALP) > 2.5 x ULN), liver cirrhosis, or portal hypertension.
11. Glomerular filtration rate ≤ 60 ml/min/1.73 m^2
12. Continuous intake of systemic (oral/intravenous) corticosteroids or immunomodulators (e.g., glucocorticoids, cyclosporine, methotrexate, anti-TNF-α therapy, anti-integrin therapy, Janus kinase inhibitors), high dose inhaled corticosteroids during the past 3 months before V0.
13. Continuous intake of drugs with suspicion of impact on villous atrophy, e.g.
14. Alcohol use > 12 g/d for women, >24 g/d for men within the past 12 months before screening.
15. Dual antiplatelet therapy or oral anticoagulants
16. Unwillingness to undergo gastrointestinal endoscopy with biopsy as required per protocol
17. Unwillingness to ingest SIGE bars
18. Allergies to SIGE bar nongluten ingredients (tapioca syrup, oats, almonds, rice crisp, chocolate, almond butter, cocoa butter, oat flour, glycerine, sunflower lecithin, salt, & natural flavours) or significant symptoms on eating the gluten-free SIGE bar
19. Known hypersensitivity reaction &/or allergy, including anaphylaxis, to wheat &/or gluten
20. If more than 10% of planned enrolled subjects report a greater than 1 point improvement in PGI-S during Trial Period A, further subjects with >1 point improvement in PGI-S will be excluded
21. Known intolerance/hypersensitivity/resistance to the study drug & excipients or drugs of similar chemical structure/pharmacological profile.
22. Doubt about the subject's cooperation, e.g., because of addiction to alcohol or drugs
23. Existing or intended pregnancy or breastfeeding
24. Affiliation with the investigator or persons working at the study sites or subject who is employed by the Sponsor
25. Subjects who are institutionalised because of legal/regulatory order
26. Participation in another trial of a therapeutic who received IMP within the last 30 days prior to V0

Date of first enrolment
31/03/2024

Date of final enrolment
08/01/2025

Locations

Countries of recruitment
United Kingdom

Wales

Australia

Austria

Croatia

Finland

Georgia

Germany

New Zealand

Norway

Poland

Romania

Spain

Sweden

Switzerland

Study participating centre
Royal Hallamshire Hospital
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Sponsor information

Organisation
Dr Falk Pharma (Germany)

ROR
https://ror.org/05sh9vm75

Funder(s)

Funder type
Industry

Funder Name
Dr. Falk Pharma

Alternative Name(s)
Falk Pharma, Dr Falk Pharma, Dr Falk Pharma GmbH, Dr. Falk Pharma GmbH, Dr. Falk Pharma UK Ltd

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data will be stored in a non-publicly available repository at Dr. Falk Pharma, Freiburg, Germany, for 25 years and will then be erased or anonymised. The type of data stored will be Clinical data and diary/questionnaire answers, the data will be stored in a pseudonymized manner. Personal data will stay at the study site of the participant. Data will be published after the appropriate time for review and written agreement by Dr. Falk Pharma GmbH after the end of the trial. The data will be shared in a pseudonymized manner with parties working with the Sponsor, with Ethics Committees and regulatory agencies in Europe, the USA, and other countries where the Sponsor seeks approval of this study or where the study is conducted, as well as to agencies responsible for marketing authorisation within and outside the EU, including the USA and other countries. Participants' consent has been obtained to pass data in a pseudonymized form to the aforementioned parties. The types of analyses and the mechanisms used for the analysis have not yet been defined.

IPD sharing plan summary
Stored in non-publicly available repository