Clinical trial results:
A phase IIb, double-blind, randomised, placebo-controlled trial to evaluate the efficacy and tolerability of ZED1227 in celiac disease subjects experiencing symptoms despite gluten-free diet

Summary

EudraCT number	2020-004612-97
Trial protocol	FI LT DE NO EE IE AT FR IT SE ES PL BG HR
Global end of trial date	27 September 2024

Results information

Result version number	v1 (current)
This version publication date	08 November 2025
First version publication date	08 November 2025

Trial information

Trial identification

Sponsor protocol code	CEC-4/CEL

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dr. Falk Pharma GmbH
Sponsor organisation address	Leinenweberstr. 5, Freiburg, Germany, 79108
Public contact	Dept. of Clinical Research & Develo, Dr. Falk Pharma GmbH, +49 7611514156, mohrbacher@drfalkpharma.de
Scientific contact	Dept. of Clinical Research & Develo, Dr. Falk Pharma GmbH, +49 7611514156, mohrbacher@drfalkpharma.de

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	09 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 September 2024
Global end of trial reached?	Yes
Global end of trial date	27 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess 3 different doses and 2 different dosing schedules of ZED1227 capsules for efficacy in improvement of the duodenal mucosal morphology and improvement of celiac disease symptoms assessed by Celiac Disease Symptom Diary (CDSD) in celiac disease subjects experiencing symptoms and having mucosal damage despite gluten-free diet.

Protection of trial subjects:

Close supervision of subjects by implementing interim visits every 14 days first and then 28 days up to week 12 of double-blind treatment and one follow up vist at week 16 to guarantee their safety and wellbeing.
Prior to recruitment of patients, all relevant documents of the clinical study were submitted and approved by the Independent Ethics Committees (IECs) responsible for the participating investigators. Written consent documents embodied the elements of informed consent as described in the Declaration of Helsinki, the ICH Guidelines for Good Clinical Practice (GCP) and were in accordance with all applicable laws and regulations. The informed consent form and patient information sheet described the planned and permitted uses, transfers and disclosures of the patient's personal data and personal health information for purposes of conducting the study. The informed consent form and the patient information sheet further explained the nature of the study, its objectives and potential risks and benefits as well as the date informed consent was given. Before being enrolled in the clinical trial, every patient was informed that participation in this trial was voluntary and that he/she could withdraw from the study at any time without giving a reason and without having to fear any loss in his/her medical care. The patient’s consent was obtained in writing before the start of the study. By signing the informed consent, the patient declared that he/she was participating voluntarily and intended to follow the study protocol instructions and the instructions of the investigator and to answer the questions asked during the course of the trial.

Background therapy:

None.

Evidence for comparator:

As there is no standard therapy, placebo was used as comparator.

Actual start date of recruitment	27 October 2021
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	Norway: 26
Country: Number of subjects enrolled	Poland: 33
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Sweden: 36
Country: Number of subjects enrolled	Croatia: 9
Country: Number of subjects enrolled	Austria: 13

Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Finland: 40
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 118
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	New Zealand: 15
Country: Number of subjects enrolled	Switzerland: 9
Country: Number of subjects enrolled	Bosnia and Herzegovina: 6
Country: Number of subjects enrolled	North Macedonia: 2
Worldwide total number of subjects	397
EEA total number of subjects	325

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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	371
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total 397 patients were included in mentioned countries between October 2021 and September 2024.

Pre-assignment

Screening details:

Screening Criteria: 1. Signed Informed Consent 2. Aged 18 to 80 years 3. Active Celiac Disease. In total, 1001 patients were screened. Thereof 397 patients were randomised.

Period 1

Period 1 title	Treatment Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Placebo three times a day

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Three capsules per day.

Arm title	Arm B

Arm description:

10 mg ZED1227 three times a day.

Arm type	Experimental
Investigational medicinal product name	10 mg ZED 1227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Three 10 mg ZED1227 capsules per day.

Arm title	Arm C

Arm description:

50 mg ZED1227 once daily in the morning.

Arm type	Experimental

Investigational medicinal product name	50 mg ZED1227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 50 mg ZED1227 capsule in the morning. Two placebo ZED1227 capsules at noon and evening each.

Arm title	Arm D

Arm description:

25 mg ZED1227 three times per day.

Arm type	Experimental
Investigational medicinal product name	25 mg ZED1227
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Three 25 mg ZED1227 capsules per day.

Number of subjects in period 1	Arm A	Arm B	Arm C
Started	99	100	99
Completed	91	94	91
Not completed	8	6	8
Consent withdrawn by subject	3	2	6
Inclusion crit. not fulfilled	-	-	-
withdrawal of consent	-	-	-
Adverse event, non-fatal	5	2	-
participant decision/decline in health, unrelated	-	-	1
personal circumstances/relocated	-	1	-
personal circumstances	-	-	1
planned vacation/wish to finish trial	-	1	-
Lack of efficacy	-	-	-
detection of H. pylori	-	-	-

Number of subjects in period 1	Arm D
Started	99
Completed	92
Not completed	7
Consent withdrawn by subject	2
Inclusion crit. not fulfilled	1
withdrawal of consent	1
Adverse event, non-fatal	1

participant decision/decline in health, unrelated	-
personal circumstances/relocated	-
personal circumstances	-
planned vacation/wish to finish trial	-
Lack of efficacy	1
detection of H. pylori	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment Phase

Reporting group description: -

Reporting group values	Treatment Phase	Total	
Number of subjects	397	397	
Age categorical			
397 patients were finally randomised in one of the four treatment groups.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	371	371	
From 65-84 years	26	26	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	40.63		
standard deviation	± 14.35	-	
Gender categorical			
Units: Subjects			
Female	288	288	
Male	109	109	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

includes all randomised participants (as randomised at Baseline Visit B)

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Modified intention-to-treat (mITT) analysis set includes all participants from the intention-to-treat (ITT) analysis set who had acceptable VH:CrD and CDSD results for baseline and end of treatment

Subject analysis set title	SAS
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety analysis set (SAS) includes all randomised participants (as treated) who received at least one dose of the IMP. If there was any uncertainty about whether a participant received any IMP, the participant was included in the SAS.

Reporting group values	ITT	mITT	SAS
Number of subjects	397	338	396
Age categorical			
397 patients were finally randomised in one of the four treatment groups.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	371	314	370
From 65-84 years	26	24	26
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	40.63	41.28	40.64
standard deviation	± 14.35	± 14.42	± 14.36
Gender categorical			
Units: Subjects			
Female	288		
Male	109		

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Placebo three times a day	
Reporting group title	Arm B
Reporting group description:	
10 mg ZED1227 three times a day.	
Reporting group title	Arm C
Reporting group description:	
50 mg ZED1227 once daily in the morning.	
Reporting group title	Arm D
Reporting group description:	
25 mg ZED1227 three times per day.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
includes all randomised participants (as randomised at Baseline Visit B)	
Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Modified intention-to-treat (mITT) analysis set includes all participants from the intention-to-treat (ITT) analysis set who had acceptable VH:CrD and CDSD results for baseline and end of treatment	
Subject analysis set title	SAS
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis set (SAS) includes all randomised participants (as treated) who received at least one dose of the IMP. If there was any uncertainty about whether a participant received any IMP, the participant was included in the SAS.	

Primary: Responder rate (histological and symptom improvement)

End point title	Responder rate (histological and symptom improvement)
End point description:	
Responder rate (histological and symptom improvement)	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	85	87	83
Units: Responder risk estimate				
least squares mean (confidence interval 95%)				
Least square risk estimates	19.3 (12.4 to 30.0)	27.1 (19.1 to 38.4)	25.3 (17.6 to 36.3)	16.9 (10.4 to 27.2)

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	0[1]			
Units: Responder risk estimate				
least squares mean (confidence interval 95%)				
Least square risk estimates	(to)			

Notes:

[1] - Overall analysis does not make sense.

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2377
Method	generalized linear model

Statistical analysis title	Primary analysis
Comparison groups	Arm A v Arm C
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3509
Method	generalized linear model

Statistical analysis title	Primary analysis
Comparison groups	Arm A v Arm D
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6873
Method	generalized linear model

Secondary: Attenuation of gluten-induced mucosal damage

End point title	Attenuation of gluten-induced mucosal damage

End point description:

End point type	Secondary

End point timeframe:

12 weeks

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	85	87	83
Units: Ratio of villus height to crypt depth				
least squares mean (confidence interval 95%)	0.13 (0.03 to 0.22)	0.21 (0.12 to 0.31)	0.26 (0.17 to 0.36)	0.18 (0.08 to 0.27)

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	0[2]			
Units: Ratio of villus height to crypt depth				
least squares mean (confidence interval 95%)	(to)			

Notes:

[2] - Overall analysis does not make sense.

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1903
Method	generalized linear model

Statistical analysis title	Secondary analysis
Comparison groups	Arm A v Arm C
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0375
Method	generalized linear model

Statistical analysis title	Secondary analysis

Comparison groups	Arm A v Arm D
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4454
Method	generalized linear model

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were assessed at all visits.	
Adverse event reporting additional description:	
Treatment-Emergent AEs during Treatment and Follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Placebo	
Reporting group title	Arm B
Reporting group description:	
10 mg three times a day	
Reporting group title	Arm C
Reporting group description:	
50 mg once a day	
Reporting group title	Arm D
Reporting group description:	
25 mg three times a day	

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 99 (2.02%)	4 / 100 (4.00%)	0 / 99 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Maternal exposure during pregnancy			
subjects affected / exposed	1 / 99 (1.01%)	1 / 100 (1.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	1 / 99 (1.01%)	0 / 100 (0.00%)	0 / 99 (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
Tenoplasty			

subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 99 (1.01%)	0 / 100 (0.00%)	0 / 99 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm D		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 98 (1.02%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Maternal exposure during pregnancy			
subjects affected / exposed	0 / 98 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion induced			

subjects affected / exposed	0 / 98 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tenoplasty			
subjects affected / exposed	1 / 98 (1.02%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 98 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 98 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	0 / 98 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 98 (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	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 99 (73.74%)	81 / 100 (81.00%)	80 / 99 (80.81%)
Nervous system disorders			

Headache			
subjects affected / exposed	15 / 99 (15.15%)	15 / 100 (15.00%)	21 / 99 (21.21%)
occurrences (all)	19	31	33
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 99 (3.03%)	4 / 100 (4.00%)	4 / 99 (4.04%)
occurrences (all)	3	6	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 99 (4.04%)	3 / 100 (3.00%)	6 / 99 (6.06%)
occurrences (all)	4	3	6
Diarrhoea			
subjects affected / exposed	6 / 99 (6.06%)	15 / 100 (15.00%)	9 / 99 (9.09%)
occurrences (all)	7	18	9
Abdominal pain			
subjects affected / exposed	4 / 99 (4.04%)	4 / 100 (4.00%)	3 / 99 (3.03%)
occurrences (all)	4	4	3
Abdominal pain upper			
subjects affected / exposed	3 / 99 (3.03%)	4 / 100 (4.00%)	5 / 99 (5.05%)
occurrences (all)	5	4	5
Vomiting			
subjects affected / exposed	3 / 99 (3.03%)	2 / 100 (2.00%)	1 / 99 (1.01%)
occurrences (all)	3	2	3
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 99 (5.05%)	3 / 100 (3.00%)	3 / 99 (3.03%)
occurrences (all)	5	3	3
Psychiatric disorders			
Procedural anxiety			
subjects affected / exposed	2 / 99 (2.02%)	5 / 100 (5.00%)	3 / 99 (3.03%)
occurrences (all)	2	5	3
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 99 (4.04%)	5 / 100 (5.00%)	5 / 99 (5.05%)
occurrences (all)	5	6	5
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	19 / 99 (19.19%)	13 / 100 (13.00%)	18 / 99 (18.18%)
occurrences (all)	23	14	19
COVID-19			
subjects affected / exposed	3 / 99 (3.03%)	6 / 100 (6.00%)	4 / 99 (4.04%)
occurrences (all)	3	6	4
Influenza			
subjects affected / exposed	5 / 99 (5.05%)	2 / 100 (2.00%)	4 / 99 (4.04%)
occurrences (all)	6	2	4
Upper respiratory tract infection			
subjects affected / exposed	2 / 99 (2.02%)	5 / 100 (5.00%)	3 / 99 (3.03%)
occurrences (all)	2	5	3
Urinary tract infection			
subjects affected / exposed	5 / 99 (5.05%)	2 / 100 (2.00%)	3 / 99 (3.03%)
occurrences (all)	6	3	3

Non-serious adverse events	Arm D		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 98 (69.39%)		
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 98 (11.22%)		
occurrences (all)	18		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 98 (5.10%)		
occurrences (all)	5		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	10 / 98 (10.20%)		
occurrences (all)	10		
Diarrhoea			
subjects affected / exposed	8 / 98 (8.16%)		
occurrences (all)	14		
Abdominal pain			
subjects affected / exposed	7 / 98 (7.14%)		
occurrences (all)	7		

Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 98 (5.10%) 6		
Vomiting subjects affected / exposed occurrences (all)	5 / 98 (5.10%) 6		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0		
Psychiatric disorders Procedural anxiety subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	5 / 98 (5.10%) 5		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	12 / 98 (12.24%) 14		
COVID-19 subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 4		
Influenza subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 4		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2022	Amendment 01 forming integrated protocol version 2.0/29.07.2022
14 July 2023	Amendment 02 forming integrated protocol version 3.0/14.07.2023
22 November 2023	Amendment 03 forming integrated protocol version 4.0/22.11.2023

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported