



## Clinical trial results:

### A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of TAK-062 for the Treatment of Active Celiac Disease in Subjects Attempting a Gluten-Free Diet

#### Summary

EudraCT number	2020-005438-14
Trial protocol	FR ES Outside EU/EEA BE PL IT
Global end of trial date	06 November 2024

#### Results information

Result version number	v1 (current)
This version publication date	17 August 2025
First version publication date	17 August 2025

#### Trial information

##### Trial identification

Sponsor protocol code	TAK-062-2001
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05353985
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Ave, Lexington, MA, United States, 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-003116-PIP01-21
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	06 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 November 2024
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The main aim of this trial was to assess the efficacy and safety of TAK-062 for the treatment of symptoms and intestinal damage related to inadvertent gluten exposure in participants with celiac disease.

Protection of trial subjects:

Each participant or their legally authorized representative signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2022
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	Belgium: 6
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 105
Worldwide total number of subjects	153
EEA total number of subjects	38

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)	143
From 65 to 84 years	10
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at various investigative sites globally from 30 June 2022 to 06 November 2024.

### Pre-assignment

Screening details:

Participants with diagnosis of celiac disease were enrolled & randomly assigned to receive either TAK-062 Placebo + SIGE Gluten-Bar or pre-determined amount of TAK-062 + SIGE Gluten-Bar in Cohort 1. 153 participants were enrolled in the trial but 1 participant out of 153 was randomized but not treated. Cohort 2 of trial was not initiated.

### 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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo + SIGE Gluten-Bar

Arm description:

Participants received TAK-062 placebo-matching tablets and SIGE gluten bar, orally for up to 24 weeks.

Arm type	Placebo
Investigational medicinal product name	TAK-062
Investigational medicinal product code	TAK-062
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

TAK-062 placebo-matching tablets and SIGE gluten bar, orally for up to 24 weeks.

<b>Arm title</b>	TAK-062 + SIGE Gluten-Bar
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Arm description:

Participants received pre-determined amount of TAK-062 tablets and SIGE gluten bar, orally, for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	TAK-062
Investigational medicinal product code	TAK-062
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

TAK-062 tablets and SIGE gluten bar, orally, for up to 24 weeks.

<b>Number of subjects in period 1</b>	Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar
Started	76	77
Completed	55	51
Not completed	21	26
Consent withdrawn by subject	13	17
Randomized in Error & Not Treated	-	1
Adverse event, non-fatal	5	7
Reason Not Specified	1	-
Lost to follow-up	1	1
Protocol deviation	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo + SIGE Gluten-Bar
Reporting group description:	
Participants received TAK-062 placebo-matching tablets and SIGE gluten bar, orally for up to 24 weeks.	
Reporting group title	TAK-062 + SIGE Gluten-Bar
Reporting group description:	
Participants received pre-determined amount of TAK-062 tablets and SIGE gluten bar, orally, for up to 24 weeks.	

Reporting group values	Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar	Total
Number of subjects	76	77	153
Age Categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	45.2	46.8	
standard deviation	± 15.35	± 12.95	-
Gender categorical			
Units: Subjects			
Female	57	58	115
Male	19	19	38
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	7	5	12
Not Hispanic or Latino	69	70	139
Unknown or Not Reported	0	2	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	74	71	145
More than one race	0	0	0
Unknown or Not Reported	1	4	5

## End points

### End points reporting groups

Reporting group title	Placebo + SIGE Gluten-Bar
Reporting group description:	
Participants received TAK-062 placebo-matching tablets and SIGE gluten bar, orally for up to 24 weeks.	
Reporting group title	TAK-062 + SIGE Gluten-Bar
Reporting group description:	
Participants received pre-determined amount of TAK-062 tablets and SIGE gluten bar, orally, for up to 24 weeks.	

### Primary: Change in Weekly Celiac Disease Symptom Diary (CDSD) Gastrointestinal (GI) Symptom Severity Score from Baseline to Week 12

End point title	Change in Weekly Celiac Disease Symptom Diary (CDSD) Gastrointestinal (GI) Symptom Severity Score from Baseline to Week 12
End point description:	
CDSD GI symptom severity score is an average of the daily GI symptom severity scores during the week. The daily GI symptom severity score is the average of the severity score for diarrhea, abdominal pain, bloating and nausea, ranging from 0 to 4. Symptom severity is evaluated using 5-point Likert-type scales (none, mild, moderate, severe, and very severe). Higher scores indicate more severe symptoms. Results are reported as least squares (LS) mean change from baseline at Week 12, determined using a mixed-effect model for repeated measures (MMRM). A negative change from baseline indicates improvement. The FAS-SIGE included all randomized participants who were randomized to receive gluten-containing SIGE. Subjects analysed is the number of participants with data available for analysis. Cohort 2 of the trial was not initiated.	
End point type	Primary
End point timeframe:	
Baseline (Week -1) to Week 12	

End point values	Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: score on a scale				
least squares mean (standard error)	-0.128 (± 0.083)	-0.111 (± 0.082)		

### Statistical analyses

Statistical analysis title	Change in Weekly CDSD GI Symptom Severity Score
Comparison groups	Placebo + SIGE Gluten-Bar v TAK-062 + SIGE Gluten-Bar

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.847 <sup>[1]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.162
upper limit	0.197

Notes:

[1] - P-value was based on MMRM analysis with treatment group, week, treatment-by-week interaction, & the randomization stratification factors as fixed effects & baseline CDSD GI symptom severity scores as covariates, and participant as a random effect.

### Secondary: Change in Villous Height to Crypt Depth Ratio (Vh:Cd) from Baseline to Week 24

End point title	Change in Villous Height to Crypt Depth Ratio (Vh:Cd) from Baseline to Week 24
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End point description:

The Vh:Cd ratio represents mucosal architectural changes and a lower Vh:Cd ratio indicates more severe intestinal injury characterized by a flattening of the mucosa. Results are reported as least squares (LS) mean change from baseline at Week 24, determined using an analysis of covariance (ANCOVA) model. A negative change from baseline indicates worsening disease. The FAS-SIGE included all randomized participants who were randomized to receive gluten-containing SIGE. Subjects analyzed is the number of participants with data available for analysis. Cohort 2 of the trial was not initiated.

End point type	Secondary
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End point timeframe:

Baseline (Week -4, Run-in Period) to Week 24

End point values	Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: unitless ratio				
least squares mean (standard error)	-0.006 (± 0.100)	-0.338 (± 0.099)		

### Statistical analyses

Statistical analysis title	Change in Vh:Cd from Baseline to Week 24
Comparison groups	Placebo + SIGE Gluten-Bar v TAK-062 + SIGE Gluten-Bar



Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 <sup>[2]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.331
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.481
upper limit	-0.181

Notes:

[2] - P-value was based on a ANCOVA model with treatment group and randomization stratification factors as fixed effects and baseline Vh: Cd as covariates.

### Secondary: Percentage of Participants Experiencing at Least One Treatment-Emergent Adverse Event (TEAE), Serious Treatment-Emergent Adverse Events (Serious TEAEs) and Treatment-Related TEAEs

End point title	Percentage of Participants Experiencing at Least One Treatment-Emergent Adverse Event (TEAE), Serious Treatment-Emergent Adverse Events (Serious TEAEs) and Treatment-Related TEAEs
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End point description:

Adverse event=any untoward medical occurrence in clinical investigation participant administered a drug;it does not necessarily have to have causal relationship with this treatment.AE can therefore be any unfavorable&unintended sign(e.g.,clinically significant abnormal laboratory value,electrocardiogram[ECG] value,or vital sign measurement),symptom,or disease temporally associated with use of drug whether or not it is considered related to drug.TEAE=new onset or worsening AEs after first dose of study treatment regardless of relationship to study drug.SAE=any untoward medical occurrence at any dose that results in death,is life threatening,requires inpatient hospitalization/prolongation of existing hospitalization,results in persistent/significant disability/incapacity,leads to a congenital anomaly/birth defect/is important medical event.TEAEs considered related to study drug as assessed by investigator were reported.Percentages were rounded

End point type	Secondary
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End point timeframe:

Up to Week 28

End point values	Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	76		
Units: percentage of participants				
number (not applicable)				
TEAEs	64.5	73.7		
Serious TEAEs	5.3	1.3		
Treatment-Related TEAEs	5.3	13.2		

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Positive Antidrug Antibodies (ADA) in Serum for TAK-062

End point title	Number of Participants with Positive Antidrug Antibodies (ADA) in Serum for TAK-062
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End point description:

A positive ADA participant was defined as a participant who had at least 1 positive ADA result during the study and was further categorized as: Transiently positive- defined as participants with confirmed positive ADA in at least 1 sample and no consecutive samples; Persistently positive- defined as participants with confirmed positive ADA in 2 or more consecutive positive ADA samples. Immunogenicity Analysis Set included all randomized participants who received any TAK-062 and had the baseline and at least 1 postbaseline immunogenicity sample assessment.

End point type	Secondary
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End point timeframe:

Up to Week 28

End point values	Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten- Bar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	76		
Units: participants				
At least 1 Positive ADA	27	67		
Transiently Positive	19	8		
Persistently Positive	8	59		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Week 28

Adverse event reporting additional description:

The SAF included all randomized participants who received at least 1 dose of study drug.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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### Reporting groups

Reporting group title	TAK-062 Placebo + SIGE Gluten-Bar
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Reporting group description:

Participants received TAK-062 placebo-matching tablets and SIGE gluten bar, orally for up to 24 weeks.

Reporting group title	TAK-062 + SIGE Gluten-Bar
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Reporting group description:

Participants received pre-determined amount of TAK-062 tablets and SIGE gluten bar, orally, for up to 24 weeks.

Serious adverse events	TAK-062 Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 76 (5.26%)	1 / 76 (1.32%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ANASTOMOTIC COMPLICATION			

subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
GASTROENTERITIS			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	TAK-062 Placebo + SIGE Gluten-Bar	TAK-062 + SIGE Gluten-Bar	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 76 (17.11%)	24 / 76 (31.58%)	
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	3 / 76 (3.95%)	4 / 76 (5.26%)	
occurrences (all)	3	4	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	2 / 76 (2.63%)	4 / 76 (5.26%)	
occurrences (all)	2	4	
ABDOMINAL PAIN			
subjects affected / exposed	3 / 76 (3.95%)	5 / 76 (6.58%)	
occurrences (all)	3	6	
DIARRHOEA			
subjects affected / exposed	2 / 76 (2.63%)	13 / 76 (17.11%)	
occurrences (all)	5	17	
GASTRITIS			

subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	4 / 76 (5.26%) 4	
VOMITING subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 3	4 / 76 (5.26%) 5	
NAUSEA subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 3	4 / 76 (5.26%) 4	
Infections and infestations UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	4 / 76 (5.26%) 4	
PHARYNGITIS STREPTOCOCCAL subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	4 / 76 (5.26%) 4	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 June 2022	The following changes were made as per amendment 1.0: 1. Addition of an exclusion criterion to exclude participants with known hypersensitivity reaction and/or allergy, including anaphylaxis, to wheat and/or gluten.
22 July 2022	The following changes were made as per amendment 2.0: 1. Addition of an exclusion criterion to exclude participants with known history of hypersensitivity, idiosyncratic reaction, or intolerance to any ingredients or excipients in TAK-062 and/or placebo. 2. Addition of the number of TAK-062 and placebo tablets administered for each cohort.
26 October 2022	The following changes were made as per amendment 3.0: 1. Revised the number of study sites. 2. Villous height to crypt depth ratio (Vh:Cd) revised. 3. Removed the internal review committee. 4. Increased the number of participants in the TAK-062 placebo plus SIGE bar treatment group from 30 to 50. 5. Added the TAK-062 treatment group for adolescents and revised the number of participants based on this addition. 5. Revised exclusion criterion to add a maximum of 20% of adult participants without a producible initial biopsy report to be included if they have serology or histology confirmation at screening. 6. Added aspartate aminotransferase (AST) $\geq 3 \times$ upper limit of normal (ULN) as an exclusion criterion. 6. Added region-specific exclusion criteria for participants enrolling in France.
02 June 2023	The following changes were made as per amendment 4.0: 1. Updated the number of sites. 2. Corrected error in the study design diagram. 3. The broad term 'mucosal injury' was replaced with a specific description 'villous atrophy'. 4. Changed simulated inadvertent gluten exposure (SIGE) run-in period to Week -2 through Day -1 instead of Week 2 through Day -1. 5. Revised inclusion and exclusion criteria.
16 November 2023	The following changes were made as per amendment 5.0: 1. Updated the planned approximate sample size from 377 to 357 to account for the combining of participants within the placebo gluten-containing SIGE arms from Cohorts 1 and 2 for analysis. 2. Updated the approximate number of participants to be enrolled in Cohort 2 from 257 to 237. 3. Updated the approximate number of participants to be enrolled to Cohort 2 Group 1 (TAK-062 placebo 3 times a day [TID] + SIGE bar 3 times a week [TIW] from 50 to 30. 3. Added the number of adults and adolescent participants per cohort.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported