Clinical trial results:
A Randomized, Double-Blind, Placebo-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of TAK-861 for the Treatment of Narcolepsy without Cataplexy (Narcolepsy Type 2)

Summary

EudraCT number	2022-002966-34
Trial protocol	NO SE FR IT ES FI
Global end of trial date	25 December 2023

Results information

Result version number	v1 (current)
This version publication date	29 December 2024
First version publication date	29 December 2024

Trial information

Trial identification

Sponsor protocol code	TAK-861-2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05687916
WHO universal trial number (UTN)	U1111-1282-8382
Other trial identifiers	jRCT: jRCT2031230050

Notes:

Sponsors

Sponsor organisation name	Takeda Development Center Americas, Inc.
Sponsor organisation address	95 Hayden Avenue, Lexington, Massachusetts, 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)	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	25 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the effect of TAK-861 on excessive daytime sleepiness (EDS) as measured by sleep latency from the Maintenance of Wakefulness Test (MWT).

Protection of trial subjects:

All study participants were required to read and sign an informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 January 2023
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	France: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	71
EEA total number of subjects	22

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)	70
From 65 to 84 years	1

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 28 investigative sites globally from 09 January 2023 to 25 December 2023.

Pre-assignment

Screening details:

Participants with a diagnosis of narcolepsy type 2 (NT2) were enrolled in the study to receive either TAK-861 or placebo.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Participants received placebo tablets matching TAK-861, orally, BID, from Days 1 to 56.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were administered TAK-861 matching placebo tablet twice a day 3 hours apart or once a day as required.

Arm title	TAK-861 2 mg BID

Arm description:

Participants received TAK-861 2 mg, orally, BID, from Days 1 to 56.

Arm type	Experimental
Investigational medicinal product name	TAK-861
Investigational medicinal product code	TAK-861
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were administered TAK-861 2 milligrams (mg) tablets twice a day 3 hours apart.

Arm title	TAK-861 2 mg and 5 mg

Arm description:

Participants received TAK-861 2 mg followed by the 5 mg dose, orally, from Days 1 to 56.

Arm type	Experimental

Investigational medicinal product name	TAK-861
Investigational medicinal product code	TAK-861
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were administered TAK-861 2 mg followed by 5 mg 3 hours apart or TAK-861 7mg once daily.

Number of subjects in period 1	Placebo	TAK-861 2 mg BID	TAK-861 2 mg and 5 mg
Started	24	23	24
Completed	21	19	22
Not completed	3	4	2
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	1	2	-
Reason not Specified	1	-	-
Protocol deviation	-	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo tablets matching TAK-861, orally, BID, from Days 1 to 56.	
Reporting group title	TAK-861 2 mg BID
Reporting group description:	
Participants received TAK-861 2 mg, orally, BID, from Days 1 to 56.	
Reporting group title	TAK-861 2 mg and 5 mg
Reporting group description:	
Participants received TAK-861 2 mg followed by the 5 mg dose, orally, from Days 1 to 56.	

Reporting group values	Placebo	TAK-861 2 mg BID	TAK-861 2 mg and 5 mg
Number of subjects	24	23	24
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	37.0	34.9	36.8
standard deviation	± 12.69	± 9.77	± 12.61
Gender categorical Units: Subjects			
Female	18	14	17
Male	6	9	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	5	2
Not Hispanic or Latino	18	18	20
Unknown or Not Reported	0	0	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	3	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	7	1	5
White	13	19	14
More than one race	0	0	0
Unknown or Not Reported	1	0	2
Average Sleep Latency From the Maintenance of Wakefulness Test (MWT)			
The MWT is a validated, objective measure that evaluates a participant's ability to remain awake under soporific conditions for a defined period. During each MWT session (1 session = 40 minutes), participants were instructed to sit quietly and remain awake for as long as possible. Sleep latency in each session was recorded on electroencephalography (EEG). If no sleep was observed according to these rules, then the latency was defined as 40 minutes.			
Units: minutes			
arithmetic mean	10.8	9.9	8.4

standard deviation	± 8.72	± 10.29	± 8.26

Reporting group values	Total		
Number of subjects	71		
Age Categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	49		
Male	22		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13		
Not Hispanic or Latino	56		
Unknown or Not Reported	2		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	9		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	13		
White	46		
More than one race	0		
Unknown or Not Reported	3		
Average Sleep Latency From the Maintenance of Wakefulness Test (MWT)			
The MWT is a validated, objective measure that evaluates a participant's ability to remain awake under soporific conditions for a defined period. During each MWT session (1 session = 40 minutes), participants were instructed to sit quietly and remain awake for as long as possible. Sleep latency in each session was recorded on electroencephalography (EEG). If no sleep was observed according to these rules, then the latency was defined as 40 minutes.			
Units: minutes arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo tablets matching TAK-861, orally, BID, from Days 1 to 56.	
Reporting group title	TAK-861 2 mg BID
Reporting group description:	
Participants received TAK-861 2 mg, orally, BID, from Days 1 to 56.	
Reporting group title	TAK-861 2 mg and 5 mg
Reporting group description:	
Participants received TAK-861 2 mg followed by the 5 mg dose, orally, from Days 1 to 56.	

Primary: Change from Baseline in the Average Sleep Latency as Determined From the MWT at Week 8

End point title	Change from Baseline in the Average Sleep Latency as Determined From the MWT at Week 8
End point description:	
The MWT is a validated, objective measure that evaluates a participant's ability to remain awake under soporific conditions for a defined period. During each MWT session (1 session = 40 minutes), participants were instructed to sit quietly and remain awake for as long as possible. Sleep latency in each session was recorded on EEG. If no sleep was observed according to these rules, then the latency was defined as 40 minutes. The linear mixed effects model for repeated measures (MMRM) was used for analysis. The Full Analysis Set included all participants who were randomized, received at least 1 dose of study drug, and had at least 1 post-dose efficacy measurement. Subjects analysed is the number of participants with data available for analyses.	
End point type	Primary
End point timeframe:	
Baseline, Week 8	

End point values	Placebo	TAK-861 2 mg BID	TAK-861 2 mg and 5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	22	
Units: minutes				
least squares mean (standard error)	2.14 (± 2.246)	1.90 (± 2.384)	4.54 (± 2.300)	

Statistical analyses

Statistical analysis title	Average Sleep Latency
Comparison groups	Placebo v TAK-861 2 mg BID

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.989 [1]
Method	MMRM
Parameter estimate	LS Mean Difference Estimate
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.67
upper limit	6.18
Variability estimate	Standard error of the mean
Dispersion value	3.277

Notes:

[1] - The analysis used a linear MMRM with fixed effects for Baseline, age, prior use of narcolepsy medications, treatment, visit, and treatment-by-visit interaction as covariates. The p-value reported is adjusted for multiplicity.

Statistical analysis title	Average Sleep Latency
Comparison groups	Placebo v TAK-861 2 mg and 5 mg
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.916 [2]
Method	MMRM
Parameter estimate	LS Mean Difference Estimate
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.93
upper limit	8.72
Variability estimate	Standard error of the mean
Dispersion value	3.227

Notes:

[2] - The analysis used a linear MMRM with fixed effects for Baseline, age, prior use of narcolepsy medications, treatment, visit, and treatment-by-visit interaction as covariates. The p-value reported is adjusted for multiplicity.

Secondary: Number of Participants with at Least One Treatment Emergent Adverse Event (TEAE)

End point title	Number of Participants with at Least One Treatment Emergent Adverse Event (TEAE)

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of the study intervention, whether or not the occurrence is considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (example, a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. A TEAE was defined as an AE whose date of onset occurred on or after the first dose of study drug. The Safety Analysis Set included all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

From first dose of the study drug up to end of the study (up to 3 months)

End point values	Placebo	TAK-861 2 mg BID	TAK-861 2 mg and 5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: participants	8	10	18	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Epworth Sleepiness Scale (ESS) Total Score at Week 8

End point title	Change from Baseline in Epworth Sleepiness Scale (ESS) Total Score at Week 8

End point description:

The ESS is a subjective, self-administered, validated scale (scored 0 to 3) to respond to each of the 8 questions of daily life that asks participants how likely they are to fall asleep in those situations. The scores are summed to give an overall score of 0 to 24. Higher scores indicate stronger subjective daytime sleepiness, and scores below 10 are considered to be within the normal range. The MMRM was used for analysis. The Full Analysis Set included all participants who were randomized, received at least 1 dose of study drug, and had at least 1 post-dose efficacy measurement. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Placebo	TAK-861 2 mg BID	TAK-861 2 mg and 5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	19	22	
Units: score on a scale				
least squares mean (standard error)	-3.39 (± 1.140)	-3.71 (± 1.206)	-6.45 (± 1.121)	

Statistical analyses

Statistical analysis title	Epworth Sleepiness Scale (ESS) Total Score
Comparison groups	Placebo v TAK-861 2 mg and 5 mg

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.216 [3]
Method	MMRM
Parameter estimate	LS Mean Difference Estimate
Point estimate	-3.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.18
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	1.59

Notes:

[3] - The analysis used a linear MMRM with fixed effects for Baseline, age, prior use of narcolepsy medications, treatment, visit, and treatment-by-visit interaction as covariates. The p-value reported is adjusted for multiplicity.

Statistical analysis title	Epworth Sleepiness Scale (ESS) Total Score
Comparison groups	Placebo v TAK-861 2 mg BID
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.989 [4]
Method	MMRM
Parameter estimate	LS Mean Difference Estimate
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.57
upper limit	2.92
Variability estimate	Standard error of the mean
Dispersion value	1.656

Notes:

[4] - The analysis used a linear MMRM with fixed effects for Baseline, age, prior use of narcolepsy medications, treatment, visit, and treatment-by-visit interaction as covariates. The p-value reported is adjusted for multiplicity.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of the study drug up to end of the study (up to 3 months)	
Adverse event reporting additional description:	
The Safety Analysis Set included all participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo tablets (]matching TAK-861, orally, twice daily (BID), from Days 1 to 56.	
Reporting group title	TAK-861 2 mg and 5 mg
Reporting group description:	
Participants received TAK-861 2 mg followed by the 5 mg dose, orally, from Days 1 to 56.	
Reporting group title	TAK-861 2 mg BID
Reporting group description:	
Participants received TAK-861 2 milligrams (mg), orally, BID, from Days 1 to 56.	

Serious adverse events	Placebo	TAK-861 2 mg and 5 mg	TAK-861 2 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 23 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Placebo	TAK-861 2 mg and 5 mg	TAK-861 2 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	14 / 24 (58.33%)	7 / 23 (30.43%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			

Urinary incontinence			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Micturition urgency			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
Pollakiuria			
subjects affected / exposed	0 / 24 (0.00%)	8 / 24 (33.33%)	3 / 23 (13.04%)
occurrences (all)	0	9	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 24 (8.33%)	5 / 24 (20.83%)	2 / 23 (8.70%)
occurrences (all)	2	5	2
Infections and infestations			
Pharyngitis streptococcal			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported