Clinical trial results:
A Phase II, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Efficacy, and Safety Study of MTAU9937a in Patients With Moderate Alzheimer's Disease

Summary

EudraCT number	2018-003398-87
Trial protocol	ES
Global end of trial date	

Results information

Result version number	v1
This version publication date	31 July 2022
First version publication date	31 July 2022

Trial information

Trial identification

Sponsor protocol code	GN40040

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03828747
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	Interim
Date of interim/final analysis	20 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 July 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial was to evaluate the clinical efficacy, safety, pharmacokinetics, and pharmacodynamics of semorinemab in participants with moderate AD.

Protection of trial subjects:

All study subjects were required to read and sign and Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	United States: 171
Worldwide total number of subjects	272
EEA total number of subjects	101

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)	49
From 65 to 84 years	209

85 years and over	14

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 49 centers in 4 countries.

Pre-assignment

Screening details:

A total of 272 participants were enrolled at 49 centers. 5 participants did not receive blinded treatment. These 267 participants represented the Safety Analysis population and data for this population is presented here.

Period 1

Period 1 title	Double-Blind Treatment 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
Arm title	Semorinemab

Arm description:

Semorinemab will be administered intravenously in the double-blind treatment period and will be administered intravenously in the optional open-label extension period.

Arm type	Experimental
Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for intravenous (IV) use, as part of positron emission tomography (PET) imaging.

Investigational medicinal product name	Semorinemab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive semorinemab every 2 weeks (Q2W) for the first three doses of the double-blind treatment period and every 4 weeks (Q4W) thereafter during the double-blind treatment period. Semorinemab will be administered Q4W in the OLE period.

Arm title	Placebo

Arm description:

Placebo was administered intravenously in the double-blind treatment period and semorinemab will be administered intravenously in the optional open-label extension.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo Q2W for the first three doses of the double-blind treatment period and Q4W thereafter during the double-blind treatment period.

Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for IV use, as part of PET imaging.

Number of subjects in period 1[1]	Semorinemab	Placebo
Started	135	132
Completed	104	96
Not completed	31	36
Consent withdrawn by subject	19	21
Physician decision	-	3
Adverse Event	6	6
Death	1	2
Various reasons	5	3
Lost to follow-up	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 5 participants didn't receive blinded treatment.

Period 2

Period 2 title	Open-Label Extension
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Semorinemab

Arm description:

Semorinemab will be administered intravenously in the double-blind treatment period and will be administered intravenously in the optional open-label extension period.

Arm type	Experimental
Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for intravenous (IV) use, as part of positron emission

tomography (PET) imaging.

Investigational medicinal product name	Semorinemab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive semorinemab every 2 weeks (Q2W) for the first three doses of the double-blind treatment period and every 4 weeks (Q4W) thereafter during the double-blind treatment period. Semorinemab will be administered Q4W in the OLE period.

Arm title	Placebo

Arm description:

Placebo was administered intravenously in the double-blind treatment period and semorinemab will be administered intravenously in the optional open-label extension.

Arm type	Placebo
Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for IV use, as part of PET imaging.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo Q2W for the first three doses of the double-blind treatment period and Q4W thereafter during the double-blind treatment period.

Number of subjects in period 2[2]	Semorinemab	Placebo
Started	104	95
Completed	0	0
Not completed	104	95
Consent withdrawn by subject	19	16
Adverse Event	3	4
Death	-	2
Various reasons	1	1
Lost to follow-up	4	-
Continuing on study	77	72

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The number of participants starting this period differs from those that completed the

previous period as this was an optional open-label extension for participants to join.

Baseline characteristics

Reporting groups	
Reporting group title	Semorinemab
Reporting group description:	
Semorinemab will be administered intravenously in the double-blind treatment period and will be administered intravenously in the optional open-label extension period.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered intravenously in the double-blind treatment period and semorinemab will be administered intravenously in the optional open-label extension.	

Reporting group values	Semorinemab	Placebo	Total
Number of subjects	135	132	267
Age Categorical Units: Participants			
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)	30	18	48
From 65-84 years	99	106	205
85 years and over	6	8	14
Age Continuous Units: years			
arithmetic mean	71.6	73.1	
standard deviation	± 8.2	± 8.0	-
Gender Categorical Units: Participants			
Female	93	80	173
Male	42	52	94
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	3	7
Not Hispanic or Latino	116	111	227
Unknown or Not Reported	15	18	33
Race (NIH/OMB) Units: Subjects			
Asian	1	0	1
Black or African American	4	5	9
White	121	115	236
Unknown or Not Reported	9	12	21

Subject analysis sets	
Subject analysis set title	Semorinemab (Modified ITT)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified intent-to-treat population included all randomized participants who received at least one dose of study drug and had at least one baseline and one postbaseline ADAS-Cog11 score. For ADCS-ADL, CDR-SB and MMSE, participants also had the respective score at the given time point.

Subject analysis set title	Placebo (Modified ITT)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified intent-to-treat population included all randomized participants who received at least one dose of study drug and had at least one baseline and one postbaseline ADAS-Cog11 score. For ADCS-ADL, CDR-SB and MMSE, participants also had the respective score at the given time point.

Reporting group values	Semorinemab (Modified ITT)	Placebo (Modified ITT)	
Number of subjects	123	115	
Age Categorical Units: Participants			
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)	29	17	
From 65-84 years	89	92	
85 years and over	5	6	
Age Continuous Units: years			
arithmetic mean	71.2	72.8	
standard deviation	± 8.2	± 8.2	
Gender Categorical Units: Participants			
Female	84	70	
Male	39	45	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	2	
Not Hispanic or Latino	104	97	
Unknown or Not Reported	15	16	
Race (NIH/OMB) Units: Subjects			
Asian	1	0	
Black or African American	4	4	
White	109	101	
Unknown or Not Reported	9	10	

End points

End points reporting groups

Reporting group title	Semorinemab

Reporting group description:

Semorinemab will be administered intravenously in the double-blind treatment period and will be administered intravenously in the optional open-label extension period.

Reporting group title	Placebo

Reporting group description:

Placebo was administered intravenously in the double-blind treatment period and semorinemab will be administered intravenously in the optional open-label extension.

Reporting group title	Semorinemab

Reporting group description:

Semorinemab will be administered intravenously in the double-blind treatment period and will be administered intravenously in the optional open-label extension period.

Reporting group title	Placebo

Reporting group description:

Placebo was administered intravenously in the double-blind treatment period and semorinemab will be administered intravenously in the optional open-label extension.

Subject analysis set title	Semorinemab (Modified ITT)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified intent-to-treat population included all randomized participants who received at least one dose of study drug and had at least one baseline and one postbaseline ADAS-Cog11 score. For ADCS-ADL, CDR-SB and MMSE, participants also had the respective score at the given time point.

Subject analysis set title	Placebo (Modified ITT)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified intent-to-treat population included all randomized participants who received at least one dose of study drug and had at least one baseline and one postbaseline ADAS-Cog11 score. For ADCS-ADL, CDR-SB and MMSE, participants also had the respective score at the given time point.

Primary: Change From Baseline to Last Visit of Double-Blind Treatment Period in Cognitive Function as Measured by the Alzheimer’s Disease Assessment Scale, Cognitive Subscale, 11-Item Version (ADAS-Cog11)

End point title	Change From Baseline to Last Visit of Double-Blind Treatment Period in Cognitive Function as Measured by the Alzheimer’s Disease Assessment Scale, Cognitive Subscale, 11-Item Version (ADAS-Cog11)

End point description:

A 70-point scale used to quantify the areas of cognitive function most often affected in Alzheimer's disease. Lower scores indicate better cognitive function.

End point type	Primary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab (Modified ITT)	Placebo (Modified ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	115		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	23.93 (± 0.533)	24.09 (± 0.589)		
Week 49	3.96 (± 0.658)	6.85 (± 0.643)		
Week 61	5.71 (± 0.907)	8.47 (± 0.965)		

Statistical analyses

Statistical analysis title	Week 49
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-2.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.56
upper limit	-1.21
Variability estimate	Standard error of the mean
Dispersion value	0.849

Statistical analysis title	Week 61
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0351
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-2.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.31
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	1.287

Primary: Change From Baseline to Last Visit of Double-Blind Treatment Period in Functional Capacities as Measured by the Alzheimer's Disease Cooperative Study-Daily Living Inventory (ADCS-ADL)

End point title	Change From Baseline to Last Visit of Double-Blind Treatment Period in Functional Capacities as Measured by the Alzheimer's Disease Cooperative Study-Daily Living Inventory (ADCS-ADL)

End point description:

A scale used to quantify performance of activities of daily living. Scores on the ADCS-ADL range from 0-78, with higher scores indicating better ADL function.

End point type	Primary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab (Modified ITT)	Placebo (Modified ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	115		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	62.03 (± 0.764)	59.74 (± 0.842)		
Week 49	-7.63 (± 1.002)	-6.80 (± 0.974)		
Week 61	-9.29 (± 1.343)	-7.57 (± 1.462)		

Statistical analyses

Statistical analysis title	Week 61
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3704
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	2.07
Variability estimate	Standard error of the mean
Dispersion value	1.911

Statistical analysis title	Week 49
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5207
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.39
upper limit	1.72
Variability estimate	Standard error of the mean
Dispersion value	1.295

Secondary: Change From Baseline to Last Visit of Double-Blind Treatment Period on the Clinical Dementia Rating-Sum of Boxes (CDR-SB)

End point title	Change From Baseline to Last Visit of Double-Blind Treatment Period on the Clinical Dementia Rating-Sum of Boxes (CDR-SB)

End point description:

A scale used to quantify the severity of symptoms of dementia. The CDR-SB is obtained through interviews of patients and informants, and disease severity is rated in 6 domains of functioning: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Each domain is rated on a 5-point scale of functioning as follows: 0, no impairment; 0.5, questionable impairment; 1, mild impairment; 2, moderate impairment; and 3, severe impairment (personal care is scored on a 4-point scale without a 0.5 rating available). The CDR-SB score is obtained by summing each of the domain box scores, with scores ranging from 0 to 18, with the higher values representing more severe impairment.

End point type	Secondary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab (Modified ITT)	Placebo (Modified ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	115		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	6.23 (± 0.156)	6.51 (± 0.182)		
Week 49	1.80 (± 0.217)	1.54 (± 0.214)		
Week 61	2.45 (± 0.367)	2.28 (± 0.393)		

Statistical analyses

Statistical analysis title	Week 49
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3501
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.82
Variability estimate	Standard error of the mean
Dispersion value	0.282

Statistical analysis title	Week 61
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7431
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	1.22
Variability estimate	Standard error of the mean
Dispersion value	0.525

Secondary: Change From Baseline to Last Visit of Double-Blind Treatment Period on the Mini-Mental State Examination (MMSE)

End point title	Change From Baseline to Last Visit of Double-Blind Treatment Period on the Mini-Mental State Examination (MMSE)

End point description:

The Mini Mental State Examination (MMSE) is a brief clinical cognitive examination commonly used to screen for dementia and other cognitive deficits that has a total score of 0-30. Higher scores indicate better cognitive function.

End point type	Secondary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab (Modified ITT)	Placebo (Modified ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	115		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	18.38 (± 0.182)	18.15 (± 0.197)		
Week 49	-2.86 (± 0.330)	-3.12 (± 0.325)		
Week 61	-3.14 (± 0.429)	-4.22 (± 0.466)		

Statistical analyses

Statistical analysis title	Week 49
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5366
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	1.11
Variability estimate	Standard error of the mean
Dispersion value	0.429

Statistical analysis title	Week 61
Comparison groups	Semorinemab (Modified ITT) v Placebo (Modified ITT)

Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0851
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	0.618

Secondary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events

End point description:

An Adverse Event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.

End point type	Secondary

End point timeframe:

Up to CCOD of July 20, 2021 (approximately 2.5 years)

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	132		
Units: Percentage of Participants				
number (not applicable)	83.7	81.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of RO7105705 at Specified Timepoints

End point title	Serum Concentration of RO7105705 at Specified Timepoints

End point description:

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Weeks 1,3,5,9,13,25,37,49, and at treatment discontinuation (up to Week 48) for Cohort 1. Weeks

1,3,5,9,13,25,37,49,61, and at treatment discontinuation (up to Week 60) for Cohort 2.

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: ug/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[1] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[2] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of RO7105705 at specified timepoints

End point title	Serum concentration of RO7105705 at specified timepoints

End point description:

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Weeks 1,3,5,9,13,25,37,49, and at treatment discontinuation (up to Week 48) for Cohort 1. Weeks 1,3,5,9,13,25,37,49,61, and at treatment discontinuation (up to Week 60) for Cohort 2.

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: ug/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[3] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[4] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between ADA Status and Percentage of Participants with Adverse Events

End point title	Relationship between ADA Status and Percentage of Participants with Adverse Events

End point description:

Descriptive statistics will be used for assessment. Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Up to 57 weeks for Cohort 1, and up to 69 weeks for Cohort 2.

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Percentage of Participants				
number (not applicable)				

Notes:

[5] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[6] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-drug antibodies (ADAs) during the study relative to the prevalence of ADAs at baseline

End point title	Incidence of anti-drug antibodies (ADAs) during the study relative to the prevalence of ADAs at baseline

End point description:

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Weeks 1,13,25,37,49, and at treatment discontinuation (up to Week 48) for Cohort 1. Weeks 1,13,25,37,49,61, and at treatment discontinuation (up to Week 60) for Cohort 2.

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	0[8]		
Units: Participants				
number (not applicable)				

Notes:

[7] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[8] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period in Cognitive Function as Measured by the Alzheimer's Disease Assessment Scale, Cognitive Subscale, 11-Item Version (ADAS-Cog11)

End point title	Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period in Cognitive Function as Measured by the Alzheimer's Disease Assessment Scale, Cognitive Subscale, 11-Item Version (ADAS-Cog11)

End point description:

Descriptive statistics will be used for assessment.

A 70-point scale used to quantify the areas of cognitive function most often affected in Alzheimer's disease. Lower scores indicate better cognitive function.

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: Units on a Scale				
least squares mean (standard error)	()	()		

Notes:

[9] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[10] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period in Functional Capacities as Measured by the Alzheimer's Disease Cooperative Study-Daily Living Inventory (ADCS-ADL)

End point title	Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period in Functional Capacities as Measured by the Alzheimer's Disease Cooperative Study-Daily Living Inventory (ADCS-ADL)

End point description:

Descriptive statistics will be used for assessment.

A scale used to quantify performance of activities of daily living. Scores on the ADCS-ADL range from 0-78, with higher scores indicating better ADL function.

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: Units on a scale				
least squares mean (standard error)	()	()		

Notes:

[11] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[12] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period on the Mini-Mental State Examination (MMSE)

End point title	Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period on the Mini-Mental State Examination (MMSE)

End point description:

Descriptive statistics will be used for assessment.

The Mini Mental State Examination (MMSE) is a brief clinical cognitive examination commonly used to screen for dementia and other cognitive deficits that has a total score of 0-30. Higher scores indicate better cognitive function.

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	0[14]		
Units: Units on a scale				
least squares mean (standard error)	()	()		

Notes:

[13] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[14] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period on the Clinical Dementia Rating-Sum of Boxes (CDR-SB)

End point title	Relationship Between ADA Status and Change From Baseline to Last Visit of Double-Blind Treatment Period on the Clinical Dementia Rating-Sum of Boxes (CDR-SB)

End point description:

Descriptive statistics will be used for assessment.

A scale used to quantify the severity of symptoms of dementia. The CDR-SB is obtained through interviews of patients and informants, and disease severity is rated in 6 domains of functioning: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Each domain is rated on a 5-point scale of functioning as follows: 0, no impairment; 0.5, questionable impairment; 1, mild impairment; 2, moderate impairment; and 3, severe impairment (personal care is scored on a 4-point scale without a 0.5 rating available). The CDR-SOB score is obtained by summing each of the domain box scores, with scores ranging from 0 to 18, with the higher values representing more severe impairment.

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Baseline to Week 49 for Cohort 1, and Baseline to Week 61 for Cohort 2

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[15]	0[16]		
Units: Units on a scale				
least squares mean (standard error)	()	()		

Notes:

[15] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[16] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADA Status and Serum Concentration of RO7105705 at Specified Timepoints

End point title	Relationship Between ADA Status and Serum Concentration of RO7105705 at Specified Timepoints

End point description:

Descriptive statistics will be used for assessment.

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Weeks 1,13,25,37,49, and at treatment discontinuation (up to Week 48) for Cohort 1. Weeks 1,13,25,37,49,61, and at treatment discontinuation (up to Week 60) for Cohort 2.

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[17]	0[18]		
Units: ug/ml				
arithmetic mean (standard deviation)	()	()		

Notes:

[17] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[18] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADA Status and Incidence of Anti-Drug Antibodies (ADAs) During the Study Relative to the Prevalence of ADAs at Baseline

End point title	Relationship Between ADA Status and Incidence of Anti-Drug Antibodies (ADAs) During the Study Relative to the Prevalence of ADAs at Baseline

End point description:

Descriptive statistics will be used for assessment.

Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

End point type	Secondary

End point timeframe:

Weeks 1,13,25,37,49, and at treatment discontinuation (up to Week 48) for Cohort 1. Weeks 1,13,25,37,49,61, and at treatment discontinuation (up to Week 60) for Cohort 2.

End point values	Semorinemab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	0[20]		
Units: Percentage of Participants				
number (not applicable)				

Notes:

[19] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[20] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to CCOD of July 20, 2021 (approximately 2.5 years)	
Adverse event reporting additional description:	
The adverse events presented refer to those that occurred in the double-blind period only.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Semorinemab
Reporting group description:	
Semorinemab will be administered intravenously in the double-blind treatment period and will be administered intravenously in the optional open-label extension period.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered intravenously in the double-blind treatment period and semorinemab will be administered intravenously in the optional open-label extension.	

Serious adverse events	Semorinemab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 135 (16.30%)	22 / 132 (16.67%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma recurrent			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Adenocarcinoma metastatic			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 135 (0.74%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 135 (0.00%)	3 / 132 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 135 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Craniocerebral injury			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 135 (0.74%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper motor neurone lesion			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	1 / 135 (0.74%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia strangulated			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 135 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernial eventration			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 135 (0.74%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 135 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	0 / 135 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 135 (0.74%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 135 (0.74%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Semorinemab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 135 (57.04%)	71 / 132 (53.79%)	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	14 / 135 (10.37%)	5 / 132 (3.79%)	
occurrences (all)	30	9	
Fall			
subjects affected / exposed	14 / 135 (10.37%)	19 / 132 (14.39%)	
occurrences (all)	19	28	
Vascular disorders			

Hypertension			
subjects affected / exposed	8 / 135 (5.93%)	5 / 132 (3.79%)	
occurrences (all)	10	5	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 135 (5.93%)	9 / 132 (6.82%)	
occurrences (all)	8	11	
Headache			
subjects affected / exposed	11 / 135 (8.15%)	9 / 132 (6.82%)	
occurrences (all)	14	10	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 135 (5.19%)	5 / 132 (3.79%)	
occurrences (all)	7	6	
Psychiatric disorders			
Agitation			
subjects affected / exposed	8 / 135 (5.93%)	5 / 132 (3.79%)	
occurrences (all)	8	5	
Insomnia			
subjects affected / exposed	7 / 135 (5.19%)	2 / 132 (1.52%)	
occurrences (all)	7	2	
Depression			
subjects affected / exposed	10 / 135 (7.41%)	6 / 132 (4.55%)	
occurrences (all)	10	6	
Anxiety			
subjects affected / exposed	9 / 135 (6.67%)	12 / 132 (9.09%)	
occurrences (all)	11	12	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 135 (5.19%)	4 / 132 (3.03%)	
occurrences (all)	7	4	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	10 / 135 (7.41%)	16 / 132 (12.12%)	
occurrences (all)	14	19	
Nasopharyngitis			

subjects affected / exposed occurrences (all)	9 / 135 (6.67%) 10	3 / 132 (2.27%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 April 2020	The following updates were made: [1] The study design was revised to assign randomized participants to one of up to three cohorts; [2] Endpoints, statistical consideration and analysis plans were updated; [3] For participants in Cohorts 2 and 3, study drug administration was revised for those who missed 2 or more infusions; [4] During the double-blind treatment period, additional clinical outcome assessments (COAs) could be administered remotely due to the COVID-19 pandemic; [5] End of study and length of study were updated; [6] Due to COVID-19 travel restrictions, some study activities could be performed in the participants home or alternate location; [6] Guidance was provided for monitoring participant's signs or symptoms suggestive of new clinically significant neurologic abnormalities; [7] Schedules of activities for the double-blind treatment period and OLE period were added for Cohorts 2 and 3; [8] Mandatory cerebrospinal fluid collection by lumbar puncture was removed.
29 June 2020	The following updates were made; [1] Participants who completed blinded study drug treatment through Week 45 without any missed doses of study drug were eligible to revert to the Cohort 1 Schedule of Activities continue to OLE. Participants who were active in the double-blind treatment period when Protocol Version 4 was implemented who either completed the Cohort 2 Week 49 visit, continued in Cohort 2; [2] Up to 100 participants could be recruited into the study; [3] The option to administer study drug infusion in the participant's home or in an approved alternate location during the COVID-19 pandemic was clarified; [4] Approval by the Medical Monitor for daily treatment with medications from selected drug classes could be permitted during the OLE.
14 December 2021	The following updates were made; [1] Cohort 3 was removed; [2] The option to enroll up to 100 additional participants was removed as it was deemed unnecessary; [3] [18F]GTP1 PET was removed during the OLE at Week 145 for Cohort 1, Week 157 for Cohort 2, and at treatment discontinuation visit (for both cohorts); [4] OLE COAs, with the exception of the Columbia-Suicide Severity Rating Scale, were removed at Week 121 for Cohort 1 and Week 133 for Cohort 2; [5] The collection of serum PK and ADA samples was reduced to only once during the OLE, at Week 97 for Cohort 1 and Week 109 for Cohort 2; [6] The Medical Monitor changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported