Clinical trial results:
A Phase II, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Efficacy, and Safety Study of MTAU9937A in Patients With Prodromal to Mild Alzheimer's Disease

Summary

EudraCT number	2017-001800-31
Trial protocol	SE GB DK FI DE PL BE NL ES FR IT
Global end of trial date	15 January 2021

Results information

Result version number	v1
This version publication date	21 January 2022
First version publication date	21 January 2022

Trial information

Trial identification

Sponsor protocol code	GN39763

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03289143
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland,
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	Final
Date of interim/final analysis	15 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of MTAU9937A in participants with prodromal AD (pAD) or mild AD (mAD), ages 50-80, who are amyloid positive by CSF or amyloid PET.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 October 2017
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?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Spain: 43
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Netherlands: 20
Country: Number of subjects enrolled	Poland: 55
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United States: 222
Worldwide total number of subjects	457
EEA total number of subjects	196

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)	110
From 65 to 84 years	347
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consisted of a double-blind treatment period and an optional open-label extension (OLE) period. OLE period was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label semorinemab treatment.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Matching placebo dose of Semorinemab was administered intravenously in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.

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

Dosage and administration details:

Matching placebo doses of Semorinemab was given intravenously (IV).

Arm title	Dose 1 Semorinemab

Arm description:

Semorinemab was administered intravenously at dose 1 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.

Arm type	Experimental
Investigational medicinal product name	Semorinemab
Investigational medicinal product code	
Other name	RG6100, MTAU9937A, RO7105705
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Semorinemab dose 1 was administered intravenously (IV).

Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	RO6880276
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for intravenous (IV) use.

Arm title	Dose 2 Semorinemab

Arm description:

Semorinemab was administered intravenously at dose 2 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.

Arm type	Experimental
Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	RO6880276
Pharmaceutical forms	Infusion, Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for intravenous (IV) use.

Investigational medicinal product name	Semorinemab
Investigational medicinal product code	
Other name	RG6100, MTAU9937A, RO7105705
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Semorinemab dose 2 was administered intravenously (IV).

Arm title	Dose 3 Semorinemab

Arm description:

Semorinemab was administered intravenously at dose 3 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.

Arm type	Experimental
Investigational medicinal product name	Semorinemab
Investigational medicinal product code	
Other name	RG6100, MTAU9937A, RO7105705
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Semorinemab dose 3 was administered intravenously (IV).

Investigational medicinal product name	[18F]GTP1
Investigational medicinal product code	
Other name	RO6880276
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

[18F]GTP1 was administered as a solution for intravenous (IV) use.

Number of subjects in period 1	Placebo	Dose 1 Semorinemab	Dose 2 Semorinemab
Started	135	94	136
Completed	1	0	2
Not completed	134	94	134
Medical Monitor Decision	1	-	-
Caregiver and Participant Withdrew Consent	-	-	1
Physician decision	-	2	2
Withdrawal by Participant	14	6	14
Adverse Event	10	7	6
Protocol Deviation	2	1	3
Drug Interrupted for Too Long	-	-	1
Caregiver Passed Away & Family Moved Out of State	-	-	1
Withdrawal by Caregiver	-	1	-
Absence of Consistent and Reliable Caregiver	-	-	-
Research Department Closure	-	-	1
Participant Non Compliance With Concomitant Meds	-	-	1
Participant Non-Compliance	-	-	1
Caregiver Unavailability	1	1	-
Study Terminated By Sponsor	101	75	100
Death	2	-	2
Caregiver Passed Away	1	-	-
Lost to follow-up	2	1	1
Participant No Longer Has Study Partner	-	-	-

Number of subjects in period 1	Dose 3 Semorinemab
Started	92
Completed	0
Not completed	92
Medical Monitor Decision	-
Caregiver and Participant Withdrew Consent	-
Physician decision	2
Withdrawal by Participant	12
Adverse Event	5
Protocol Deviation	1
Drug Interrupted for Too Long	-
Caregiver Passed Away & Family Moved Out of State	-
Withdrawal by Caregiver	-

Absence of Consistent and Reliable Caregiver	1
Research Department Closure	-
Participant Non Compliance With Concomitant Meds	-
Participant Non-Compliance	-
Caregiver Unavailability	-
Study Terminated By Sponsor	69
Death	1
Caregiver Passed Away	-
Lost to follow-up	-
Participant No Longer Has Study Partner	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo dose of Semorinemab was administered intravenously in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Reporting group title	Dose 1 Semorinemab
Reporting group description:	
Semorinemab was administered intravenously at dose 1 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Reporting group title	Dose 2 Semorinemab
Reporting group description:	
Semorinemab was administered intravenously at dose 2 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Reporting group title	Dose 3 Semorinemab
Reporting group description:	
Semorinemab was administered intravenously at dose 3 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	

Reporting group values	Placebo	Dose 1 Semorinemab	Dose 2 Semorinemab
Number of subjects	135	94	136
Age categorical 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)	29	17	39
From 65-84 years	106	77	97
85 years and over	0	0	0
Age Continuous Units: Year			
arithmetic mean	69.7	70.2	69.3
standard deviation	± 7.3	± 6.7	± 7.1
Sex: Female, Male Units: Participants			
Female	75	51	79
Male	60	43	57
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	1	2

Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	0	2	1
White	129	83	128
More than one race	1	1	0
Unknown or Not Reported	4	6	5
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	4	5
Not Hispanic or Latino	126	80	125
Unknown or Not Reported	8	10	6

Reporting group values	Dose 3 Semorinemab	Total	
Number of subjects	92	457	
Age categorical			
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)	25	110	
From 65-84 years	67	347	
85 years and over	0	0	
Age Continuous			
Units: Year			
arithmetic mean	69.6		
standard deviation	± 6.7	-	
Sex: Female, Male			
Units: Participants			
Female	48	253	
Male	44	204	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	0	3	
Native Hawaiian or Other Pacific Islander	0	1	
Black or African American	1	4	
White	82	422	
More than one race	0	2	
Unknown or Not Reported	9	24	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	3	13	
Not Hispanic or Latino	79	410	
Unknown or Not Reported	10	34	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Matching placebo dose of Semorinemab was administered intravenously in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Reporting group title	Dose 1 Semorinemab
Reporting group description:	
Semorinemab was administered intravenously at dose 1 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Reporting group title	Dose 2 Semorinemab
Reporting group description:	
Semorinemab was administered intravenously at dose 2 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Reporting group title	Dose 3 Semorinemab
Reporting group description:	
Semorinemab was administered intravenously at dose 3 in the double-blind treatment period. Optional Open Label Extension was available to participants who completed the double-blind treatment period and who, in the judgment of the investigator, would potentially benefit from open-label extension.	
Subject analysis set title	Placebo Double Blind
Subject analysis set type	Per protocol
Subject analysis set description:	
Matching placebo dose of Semorinemab was administered intravenously in the double-blind treatment period.	
Subject analysis set title	Dose 1 Semorinemab Double Blind
Subject analysis set type	Per protocol
Subject analysis set description:	
Semorinemab was administered intravenously at dose 1 in the double-blind treatment period.	
Subject analysis set title	Dose 2 Semorinemab Double Blind
Subject analysis set type	Per protocol
Subject analysis set description:	
Semorinemab was administered intravenously at dose 2 in the double-blind treatment period.	
Subject analysis set title	Dose 3 Semorinemab Double Blind
Subject analysis set type	Per protocol
Subject analysis set description:	
Semorinemab was administered intravenously at dose 3 in the double-blind treatment period.	
Subject analysis set title	Dose 2 Semorinemab Open Label Extension Period
Subject analysis set type	Per protocol
Subject analysis set description:	
Semorinemab was administered intravenously at dose 2 in the open-label extension period.	

Primary: Change From Baseline on the CDR-SB

End point title	Change From Baseline on the CDR-SB
End point description:	
The Clinical Dementia Rating-Sum of Boxes (CDR-SB) rates impairment in 6 categories (memory, orientation, judgement and problem solving, community affairs, home and hobbies and personal care) on a 5-point scale in which no impairment = 0, questionable impairment = 0.5 and mild, moderate and severe impairment = 1, 2 and 3 respectively. The score range is from 0 to 18 with a high score indicating a high disease severity. The difference in mean change from Baseline to Week 73 between Semorinemab doses and Placebo treated participants was estimated.	

End point type	Primary

End point timeframe:

Baseline and 73 Weeks

End point values	Placebo Double Blind	Dose 1 Semorinemab Double Blind	Dose 2 Semorinemab Double Blind	Dose 3 Semorinemab Double Blind
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	105	77	113	74
Units: Units on a scale				
arithmetic mean (standard error)	2.19 (± 0.226)	2.36 (± 0.268)	2.36 (± 0.222)	2.41 (± 0.27)

Statistical analyses

Statistical analysis title	Placebo DB (Double Blind), Dose 1 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 1 Semorinemab Double Blind
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6147 [1]
Method	Mixed-effect Model Repeated Measures

Notes:

[1] - Unadjusted

Statistical analysis title	Placebo DB, Dose 3 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 3 Semorinemab Double Blind
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5136 [2]
Method	Mixed-effect Model Repeated Measures

Notes:

[2] - Unadjusted

Statistical analysis title	Placebo DB, Dose 2 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 2 Semorinemab Double Blind
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5778 [3]
Method	Mixed-effect Model Repeated Measures

Notes:

[3] - Unadjusted

Primary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events[4]

End point description:

Percentage of participants with at least one adverse event.

End point type	Primary

End point timeframe:

Up to the data cutoff date 15 January 2021 (up to approximately 39 months)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	Placebo	Dose 1 Semorinemab	Dose 2 Semorinemab	Dose 3 Semorinemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	89	132	90
Units: Percentage of participants				
number (not applicable)	93.1	88.8	94.7	92.2

End point values	Dose 2 Semorinemab Open Label Extension Period			
Subject group type	Subject analysis set			
Number of subjects analysed	360			
Units: Percentage of participants				
number (not applicable)	47.5			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline on the C-SSRS

End point title	Change From Baseline on the C-SSRS[5]

End point description:

Categories are as defined in the Classification Algorithm for Suicide Assessment (CASA) based on the Columbia Suicide Severity Rating Scale (C-SSRS) questionnaire. SI1: Passive category is "Wish to be dead", SI2: Active-Nonspecific (no method, intent or plan), SI3: Active-Method, but no intent or Plan, SI4: Active-Method and intent, but no plan in C-SSRS. The worst post-baseline suicidal ideation is the highest across post-baseline visits, with highest as SI5 and lowest as SI1. Percentages are based on the total number of subjects in a treatment group. Baseline is the last observation prior to initiation of study drug.

End point type	Primary

End point timeframe:

Baseline to data cutoff date 15 January 2021 (up to approximately 39 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	Placebo	Dose 1 Semorinemab	Dose 2 Semorinemab	Dose 3 Semorinemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	89	132	90
Units: Percentage of participants				
number (not applicable)				
Missing/No Event	0.8	0	0	0
Missing/SI1	0	0	0	0
Missing/SI2	0	0	0	0
Missing/SI3	0	0	0	0
Missing/SI4	0	0	0	0
Missing/Missing	0	0	0	0
No Event/No Event	91.5	89.9	93.2	92.2
No Event/SI1	2.3	3.4	0.8	4.4
No Event/ SI2	0	1.1	0	0
No Event/SI3	0	0	0	0
No Event/ SI4	0	0	0	0
No Event/ Missing	0.8	0	0	1.1
SI1/No Event	2.3	3.4	0.8	1.1
SI1/SI1	0	0	0	0
SI1/SI2	0.8	0	0	0
SI1/SI3	0	0	0	0
SI1/SI4	0.8	0	0	0
SI1/Missing	0	0	0	0
SI2/No Event	0	1.1	1.5	0
SI2/SI1	0	0	0.8	0
SI2/SI2	0	0	0	1.1
SI2/SI3	0	0	0	0
SI2/SI4	0	0	0	0
SI2/Missing	0	0	0	0
SI3/No Event	0.8	0	92.2	0
SI3/SI1	0	0	4.4	0
SI3/SI2	0	0	0	0
SI3/SI3	0	0	0	0
SI3/SI4	0	0	0	0
SI3/Missing	0	0	1.1	0
SI4/No Event	0	0	0	0
SI4/SI1	0	0	0	0
SI4/SI2	0	0	0	0
SI4/SI3	0	0	0	0
SI4/Missing	0	0	0	0

End point values	Dose 2 Semorinemab Open Label Extension Period			
Subject group type	Subject analysis set			
Number of subjects analysed	360			
Units: Percentage of participants				
number (not applicable)				

Missing/No Event	0.8			
Missing/SI1	0			
Missing/SI2	0			
Missing/SI3	0			
Missing/SI4	0			
Missing/Missing	0			
No Event/No Event	93.3			
No Event/SI1	1.4			
No Event/ SI2	0.3			
No Event/SI3	0			
No Event/ SI4	0			
No Event/ Missing	0.3			
SI1/No Event	2.2			
SI1/SI1	0.3			
SI1/SI2	0			
SI1/SI3	0			
SI1/SI4	0			
SI1/Missing	0			
SI2/No Event	0.3			
SI2/SI1	0.6			
SI2/SI2	0			
SI2/SI3	0			
SI2/SI4	0			
SI2/Missing	0			
SI3/No Event	0.3			
SI3/SI1	0			
SI3/SI2	0			
SI3/SI3	0			
SI3/SI4	0			
SI3/Missing	0			
SI4/No Event	0			
SI4/SI1	0			
SI4/SI2	0			
SI4/SI3	0.3			
SI4/Missing	0			

Statistical analyses

No statistical analyses for this end point

Primary: Other Abnormal MRI Findings

End point title	Other Abnormal MRI Findings[6]

End point description:

Other abnormal MRI findings by visit. For the Double Blind Period, baseline is defined as last results prior to initiation of study drug. For the Open Label Extension Period, baseline is defined as last results prior to entering the open label period. (Note: SD=Study Treatment; 777777=Not reportable because no participants were analyzed.)

End point type	Primary

End point timeframe:

Baseline, Week 9, Week 49, and Week 73, Study Treatment Discontinuation, and Week 89

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	Placebo	Dose 1 Semorinemab	Dose 2 Semorinemab	Dose 3 Semorinemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	135	94	136	92
Units: Number of participants				
Cerebrovascular Pathology, Baseline	3	0	2	1
CNS Trauma, Baseline	0	0	0	1
Intracranial Tumor, Baseline	0	0	3	2
Lacunar Infarct, Baseline	13	3	11	6
Superficial Hemosiderosis, Baseline	3	0	2	0
Territorial Infarct, Baseline	3	1	0	0
Vasogenic Edema/Sulcal Effusion, Baseline	0	0	0	0
Cerebrovascular Pathology, Week 9	0	1	0	0
CNS Trauma, Week 9	0	0	0	0
Intracranial Tumor, Week 9	0	0	0	0
Lacunar Infarct, Week 9	0	1	0	0
Superficial Hemosiderosis, Week 9	3	0	0	1
Territorial Infarct, Week 9	0	0	0	0
Vasogenic Edema/Sulcal Effusion, Week 9	0	0	1	0
Cerebrovascular Pathology, Week 49	0	0	0	0
CNS Trauma, Week 49	0	0	0	0
Intracranial Tumor, Week 49	0	0	0	0
Lacunar Infarct, Week 49	0	0	0	0
Superficial Hemosiderosis, Week 49	1	1	1	0
Territorial Infarct, Week 49	0	0	0	0
Vasogenic Edema/Sulcal Effusion, Week 49	0	0	0	0
Cerebrovascular Pathology, Week 73	0	0	0	0
CNS Trauma, Week 73	0	0	0	0
Intracranial Tumor, Week 73	1	0	0	0
Lacunar Infarct, Week 73	0	1	0	0
Superficial Hemosiderosis, Week 73	0	1	0	1
Territorial Infarct, Week 73	0	0	0	0
Vasogenic Edema/Sulcal Effusion, Week 73	1	0	0	0
Cerebrovascular Pathology, Study Tx ED	0	0	0	0
CSN Trauma, Study Tx ED	0	0	0	0
Intracranial Tumor, Study Tx ED	0	0	0	0
Lucunar Infarct, Study Tx ED	1	0	0	0
Superficial Hemosiderosis, Study Tx ED	1	0	0	0
Territorial Infarct, Study Tx ED	0	0	0	0
Vasogenic Edema/Sulcal Effusion, Study Tx ED	0	0	0	0
Cerebrovascular Pathology, Week 89 OLE	777777	777777	777777	777777
CNS Trauma, Week 89 OLE	777777	777777	777777	777777
Intracranial Tumor, Week 89 OLE	777777	777777	777777	777777

Lacunar Infarct, Week 89 OLE	777777	777777	777777	777777
Superficial Hemosiderosis, Week 89 OLE	777777	777777	777777	777777
Territorial Infarct, Week 89 OLE	777777	777777	777777	777777
Vasogenic Edema/Sulcal Effusion, Week 89 OLE	777777	777777	777777	777777

End point values	Dose 2 Semorinemab Open Label Extension Period			
Subject group type	Subject analysis set			
Number of subjects analysed	360			
Units: Number of participants				
Cerebrovascular Pathology, Baseline	5			
CNS Trauma, Baseline	1			
Intracranial Tumor, Baseline	4			
Lacunar Infarct, Baseline	23			
Superficial Hemosiderosis, Baseline	7			
Territorial Infarct, Baseline	4			
Vasogenic Edema/Sulcal Effusion, Baseline	0			
Cerebrovascular Pathology, Week 9	777777			
CNS Trauma, Week 9	777777			
Intracranial Tumor, Week 9	777777			
Lacunar Infarct, Week 9	777777			
Superficial Hemosiderosis, Week 9	777777			
Territorial Infarct, Week 9	777777			
Vasogenic Edema/Sulcal Effusion, Week 9	777777			
Cerebrovascular Pathology, Week 49	777777			
CNS Trauma, Week 49	777777			
Intracranial Tumor, Week 49	777777			
Lacunar Infarct, Week 49	777777			
Superficial Hemosiderosis, Week 49	777777			
Territorial Infarct, Week 49	777777			
Vasogenic Edema/Sulcal Effusion, Week 49	777777			
Cerebrovascular Pathology, Week 73	777777			
CNS Trauma, Week 73	777777			
Intracranial Tumor, Week 73	777777			
Lacunar Infarct, Week 73	777777			
Superficial Hemosiderosis, Week 73	777777			
Territorial Infarct, Week 73	777777			
Vasogenic Edema/Sulcal Effusion, Week 73	777777			
Cerebrovascular Pathology, Study Tx ED	777777			
CSN Trauma, Study Tx ED	777777			
Intracranial Tumor, Study Tx ED	777777			
Lucunar Infarct, Study Tx ED	777777			
Superficial Hemosiderosis, Study Tx ED	777777			
Territorial Infarct, Study Tx ED	777777			

Vasogenic Edema/Sulcal Effusion, Study Tx ED	777777			
Cerebrovascular Pathology, Week 89 OLE	0			
CNS Trauma, Week 89 OLE	0			
Intracranial Tumor, Week 89 OLE	1			
Lacunar Infarct, Week 89 OLE	0			
Superficial Hemosiderosis, Week 89 OLE	0			
Territorial Infarct, Week 89 OLE	0			
Vasogenic Edema/Sulcal Effusion, Week 89 OLE	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Repeatable Battery for Assessment of Neuropsychological Status (RBANS)

End point title	Change From Baseline on the Repeatable Battery for Assessment of Neuropsychological Status (RBANS)

End point description:

The RBANS is a validated neuropsychological assessment has been shown to be a useful tool in both clinical and research settings. The RBANS consists of ten subtests that are combined to provide five indices, one for each of the five domains tested (immediate memory, visuospatial/constructional, language, attention, and delayed memory). Scores range from 40 to 160 and a higher score indicates better cognitive functioning. A decrease in the outcome measure from baseline corresponds to disease worsening. The difference in mean change from Baseline to Week 73 between Semorinemab doses and Placebo treated participants was estimated.

End point type	Secondary

End point timeframe:

Baseline and 73 weeks

End point values	Placebo Double Blind	Dose 1 Semorinemab Double Blind	Dose 2 Semorinemab Double Blind	Dose 3 Semorinemab Double Blind
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87	62	93	63
Units: Score on a scale				
arithmetic mean (standard error)	-5.53 (± 0.787)	-5.25 (± 0.93)	-4.62 (± 0.765)	-6.15 (± 0.926)

Statistical analyses

Statistical analysis title	Placebo DB, Dose 1 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 1 Semorinemab Double Blind

Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8198 [7]
Method	Mixed-effect Model Repeated Measures

Notes:

[7] - Unadjusted

Statistical analysis title	Placebo DB, Dose 3 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 3 Semorinemab Double Blind
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6043 [8]
Method	Mixed-effect Model Repeated Measures

Notes:

[8] - Unadjusted

Statistical analysis title	Placebo DB, Dose 2 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 2 Semorinemab Double Blind
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3961 [9]
Method	Mixed-effect Model Repeated Measures

Notes:

[9] - Unadjusted

Secondary: Change from Baseline on the Alzheimer's Disease Assessment Scale−Cognitive Subscale 13 (ADAS-Cog-13) Subscale Score

End point title	Change from Baseline on the Alzheimer's Disease Assessment Scale−Cognitive Subscale 13 (ADAS-Cog-13) Subscale Score

End point description:

The ADAS-Cog-13 assesses multiple cognitive domains including memory, comprehension, praxis, orientation, and spontaneous speech. Most of these are assessed by tests although some are rated by the clinician on a 5-point scale. The ADAS-Cog-13 is the ADAS-Cog-11 with 2 further items: delayed word recall and total digit cancellation. The score range for ADAS-Cog-13 is from 0 to 85 with high scores representing severe dysfunction. The difference in mean change from Baseline to Week 73 between Semorinemab doses and Placebo treated participants was estimated.

End point type	Secondary

End point timeframe:

Baseline and 73 weeks

End point values	Placebo Double Blind	Dose 1 Semorinemab Double Blind	Dose 2 Semorinemab Double Blind	Dose 3 Semorinemab Double Blind
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	94	67	97	66
Units: Score on a scale				
arithmetic mean (standard error)	6.56 (± 0.777)	8.68 (± 0.937)	6 (± 0.769)	7.58 (± 0.932)

Statistical analyses

Statistical analysis title	Placebo DB, Dose 1 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 1 Semorinemab Double Blind
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0783 [10]
Method	Mixed-effect Model Repeated Measures

Notes:

[10] - Unadjusted

Statistical analysis title	Placebo DB, Dose 2 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 2 Semorinemab Double Blind
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.601 [11]
Method	Mixed-effect Model Repeated Measures

Notes:

[11] - Unadjusted

Statistical analysis title	Placebo DB, Dose 3 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 3 Semorinemab Double Blind
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3961 [12]
Method	Mixed-effect Model Repeated Measures

Notes:

[12] - Unadjusted

Secondary: Change from baseline on the Amsterdam Instrumental Activity of Daily Living (iADL) questionnaire

End point title	Change from baseline on the Amsterdam Instrumental Activity of Daily Living (iADL) questionnaire

End point description:

The Amsterdam iADL questionnaire is an informant-based instrument for measuring iADL problems in participants with dementia. This instrument consists of 70 items, scored on a 5-point scale, that uses item response theory for scoring. Items presented to the informant are tailored to responses to earlier items; thus each administration of the Amsterdam iADL may consist of less than the total of 70 items. The resulting score ranges from 20 to 80 with lower scores indicating poorer performance. A decrease in

the outcome measure from baseline corresponds to disease worsening. The difference in mean change from Baseline to Week 73 between Semorinemab doses and Placebo treated participants was estimated.

End point type	Secondary

End point timeframe:

Baseline and 73 weeks

End point values	Placebo Double Blind	Dose 1 Semorinemab Double Blind	Dose 2 Semorinemab Double Blind	Dose 3 Semorinemab Double Blind
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	95	70	109	67
Units: Score on a scale				
arithmetic mean (standard error)	-6.59 (± 0.856)	-6.55 (± 0.999)	-6.92 (± 0.824)	-7.31 (± 1.013)

Statistical analyses

Statistical analysis title	Placebo DB, Dose 1 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 1 Semorinemab Double Blind
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9749 [13]
Method	Mixed-effect Model Repeated Measures

Notes:

[13] - Unadjusted

Statistical analysis title	Placebo DB, Dose 3 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 3 Semorinemab Double Blind
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5789
Method	Mixed-effect Model Repeated Measures

Statistical analysis title	Placebo DB, Dose 2 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 2 Semorinemab Double Blind
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7718 [14]
Method	Mixed-effect Model Repeated Measures

Notes:
[14] - Unadjusted

Secondary: Change from baseline on the Alzheimer’s Disease Cooperative Study Group−Activities of Daily Living Inventory

End point title	Change from baseline on the Alzheimer’s Disease Cooperative Study Group−Activities of Daily Living Inventory

End point description:

The ADCS-ADL (Alzheimer's Disease Cooperative Study-Activities of Daily Living) is the scale most widely used to assess functional outcomes in participants with AD. The ADCS-ADL covers both basic ADL (e.g., eating and toileting) and more complex 'instrumental' ADL or iADL (e.g., using the telephone, managing finances and preparing a meal). The ADCS-ADL consists of 23 questions with a score range of 0 to 78 where a higher score represents better function. The difference in mean change from Baseline to Week 73 between Semorinemab doses and Placebo treated participants was estimated.

End point type	Secondary

End point timeframe:

Baseline and 73 weeks

End point values	Placebo Double Blind	Dose 1 Semorinemab Double Blind	Dose 2 Semorinemab Double Blind	Dose 3 Semorinemab Double Blind
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	104	76	112	74
Units: Score on a scale				
arithmetic mean (standard error)	-8.55 (± 0.996)	-9.52 (± 1.179)	-7.75 (± 0.986)	-7.99 (± 1.183)

Statistical analyses

Statistical analysis title	Placebo DB, Dose 1 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 1 Semorinemab Double Blind
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5235 [15]
Method	Mixed-effect Model Repeated Measures

Notes:
[15] - Unadjusted

Statistical analysis title	Placebo DB, Dose 3 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 3 Semorinemab Double Blind
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.713 [16]
Method	Mixed-effect Model Repeated Measures

Notes:
[16] - Unadjusted

Statistical analysis title	Placebo DB, Dose 2 Semorinemab DB
Comparison groups	Placebo Double Blind v Dose 2 Semorinemab Double Blind
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5612 [17]
Method	Mixed-effect Model Repeated Measures

Notes:
[17] - Unadjusted

Secondary: Serum Concentrations of Semorinemab at Specified Timepoints

End point title	Serum Concentrations of Semorinemab at Specified

End point description:
Serum concentrations of Semorinemab at specified timepoints. Note: 999999=Not reportable. Below the level of detection. 888888=Data not reported because SD was non-estimable since only 1 participant was evaluated for this category. 777777=Not reportable. No participants were analyzed.

End point type	Secondary

End point timeframe:
Up to 109 weeks

Notes:
[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Dose 1 Semorinemab	Dose 2 Semorinemab	Dose 3 Semorinemab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	132	90	
Units: ug/mL				
arithmetic mean (standard deviation)				
Week 1, 0-4 Hours Predose (n=87, n=132, n=90)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
Week 1, 1 Hour Postdose (n=87, n=132,n=90)	472 (± 131)	1580 (± 496)	2690 (± 689)	
Week 1, 2 Hours Postdose (n=86, n=130, n=90)	476 (± 123)	1510 (± 419)	2600 (± 707)	
Week 1, 4 Hours postdose (n=86, n=128, n=89)	463 (± 135)	1370 (± 405)	2570 (± 785)	
Week 3, 0-4 hours Predose (n=89, n=131, n=89)	184 (± 52.7)	601 (± 211)	1100 (± 449)	
Week 3, 30 min Post dose (n=88, n=130, n=88)	718 (± 198)	2320 (± 581)	4190 (± 1010)	
Week 5, 0-4 Hours Predose (n=88, n=131, n=87)	318 (± 81.5)	955 (± 256)	1920 (± 614)	
Week 5, 30 min Postdose (n=86, n=130, n=85)	908 (± 508)	2780 (± 695)	4860 (± 1250)	
Week 9, 0-4 hours Predose (n=88, n=130, n=83)	344 (± 128)	961 (± 288)	1840 (± 513)	
Week 9, 30 Minutes Postdose (n=89, n=129, n=85)	889 (± 321)	2790 (± 757)	4960 (± 1270)	

Week 13, 0-4 Hours Predose (n=87, n=128, n=86)	360 (± 105)	1060 (± 333)	1910 (± 545)	
Week 13, 30 Minutes Postdose (n=86, n=127, n=86)	998 (± 896)	2900 (± 668)	4880 (± 1250)	
Week 17 (n=0, n=0, n=1)	7777777 (± 777777)	777777 (± 777777)	1750 (± 888888)	
Week 17, 0-4 Hours Predose (n=84, n=127,n=83)	386 (± 116)	1040 (± 316)	1890 (± 522)	
Week 17, 30 Minutes Postdose (n=84, n=126, n=86)	819 (± 242)	2930 (± 902)	4770 (± 1270)	
Week 33, 0-4 Hours Predose (n=83, n=126, n=83)	404 (± 134)	960 (± 277)	2050 (± 648)	
Week 33, 30 Minutes Postdose (n=82, n=126, n=80)	801 (± 260)	2540 (± 853)	4800 (± 1200)	
Week 49, 0-4 Hours Predose (n=78, n=119, n=79)	377 (± 105)	1060 (± 332)	2160 (± 605)	
Week 49, 30 Minutes Postdose (n=77, n=117, n=80)	871 (± 260)	2810 (± 967)	4960 (± 1030)	
Week 65 (n=0, n=0, n=1)	777777 (± 777777)	777777 (± 777777)	2100 (± 888888)	
Week 65, 0-4 Hours Predose (n=67, n=101, n=66)	405 (± 127)	1170 (± 276)	2020 (± 681)	
Week 65, 30 Minutes Postdose (n=67, n=100, n=67)	963 (± 401)	2930 (± 830)	4710 (± 1450)	
Week 73, n=71, n=104, n=69)	327 (± 154)	1030 (± 451)	1830 (± 752)	
Week 73, 0-4 Hours Predose (n=0, n=1, n=0)	777777 (± 777777)	382 (± 888888)	777777 (± 777777)	
Week 73, 1 Hour Postdose (n=0, n=1, n=0)	777777 (± 777777)	1910 (± 888888)	777777 (± 777777)	
Week 73, 2 Hours Postdose (n=0, n=1, n=0)	777777 (± 777777)	1740 (± 888888)	777777 (± 777777)	
Week 73, 4 Hours Postdose (n=0, n=1, n=0)	777777 (± 777777)	1710 (± 888888)	777777 (± 777777)	
Week 77 OLE, 0-4 Hours Predose (n=13, n=20, n=13)	180 (± 71.0)	724 (± 167)	1030 (± 345)	
Week 77 OLE, 1 hour Postdose (n=12, n=20, n=12)	1700 (± 523)	2460 (± 868)	2670 (± 707)	
Week 77 OLE, 2 hours Postdose (n=13, n=20, n=13)	1830 (± 552)	2270 (± 442)	2510 (± 579)	
Week 77 OLE, 4 hours Postdose (n=11, n=20, n=12)	1850 (± 516)	2270 (± 480)	2790 (± 558)	
Week 93 OLE, 0-4 Hours Pre-dose (n=2, n=2, n=4)	632 (± 37.5)	1040 (± 113)	1290 (± 3007)	
Week 93 OLE, 30 Minutes Postdose (n=2, n=2, n=4)	1920 (± 431)	2570 (± 91.9)	2880 (± 492)	
Week 109 OLE, 0-4 Hours Predose (n=0, n=1, n=0)	777777 (± 777777)	1270 (± 888888)	777777 (± 777777)	
Week 109 OLE, 30 Minutes Postdose (n=0, n=1, n=0)	777777 (± 777777)	3330 (± 888888)	777777 (± 777777)	

Statistical analyses

No statistical analyses for this end point

Secondary: Presence of anti-drug antibodies during the study relative to their presence at baseline

End point title	Presence of anti-drug antibodies during the study relative to their presence at baseline

End point description:

Presence of anti-drug antibodies during the study relative to their presence at baseline.

End point type	Secondary

End point timeframe:

Up to 109 weeks

End point values	Placebo	Dose 1 Semorinemab	Dose 2 Semorinemab	Dose 3 Semorinemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	89	132	90
Units: Percentage of participants				
Baseline (n=127, n=87, n=132, n=90)	0	0	0	0
Post-baseline (n=0, n=86, n=128, n=88)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug to the data cutoff date: 15 January 2021 (up to 39 months)

Adverse event reporting additional description:

The safety-evaluable population included all participants who were randomly allocated and received at least one dose of study drug (semorinemab or placebo) during the double-blind treatment period with treatment groups defined according to actual treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo Double Blind Period

Reporting group description:

Matching placebo dose of Semorinemab was administered intravenously in the double-blind treatment period.

Reporting group title	Dose 2 Semorinemab Open Label

Reporting group description:

Semorinemab was administered intravenously at dose 2 in the open-label extension period.

Reporting group title	Dose 3 Semorinemab Double Blind Period

Reporting group description:

Semorinemab was administered intravenously at dose 3 in the double-blind treatment period.

Reporting group title	Dose 1 Semorinemab Double Blind Period

Reporting group description:

Semorinemab was administered intravenously at dose 1 in the double-blind treatment period.

Reporting group title	Dose 2 Semorinemab Double Blind Period

Reporting group description:

Semorinemab was administered intravenously at dose 2 in the double-blind treatment period.

Serious adverse events	Placebo Double Blind Period	Dose 2 Semorinemab Open Label	Dose 3 Semorinemab Double Blind Period
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 130 (10.77%)	17 / 360 (4.72%)	16 / 90 (17.78%)
number of deaths (all causes)	2	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Chronic lymphocytic leukaemia			

subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Benign pancreatic neoplasm			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Prostate cancer			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
General disorders and administration site conditions			

Sudden death			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Euthanasia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Tonsillar cyst			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Acute respiratory failure			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Hypoxia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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

Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Agitation			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paranoia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Aggression			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Mental status changes			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Persecutory delusion			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			

subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Spinal fracture			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Craniocerebral injury			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Spinal compression fracture			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Femoral neck fracture			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Fracture displacement			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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

Hip fracture			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Foot fracture			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Femur fracture			
subjects affected / exposed	1 / 130 (0.77%)	1 / 360 (0.28%)	0 / 90 (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
Fall			
subjects affected / exposed	2 / 130 (1.54%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin wound			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Myocardial infarction			

subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Bradycardia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Atrial fibrillation			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Congestive cardiomyopathy			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Cardiac arrest			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Sinus node dysfunction			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Coronary artery disease			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Atrioventricular block			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Ventricular fibrillation			

subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Nervous system disorders			
Coma			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Cluster headache			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Post-traumatic headache			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Syncope			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Encephalopathy			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Amnesia			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Ischaemic stroke			

subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Sciatica			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Gastrointestinal disorders			
Inguinal hernia strangulated			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Rectal polyp			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Pancreatitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Haemorrhoids			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Enteritis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Inguinal hernia			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Cholecystitis			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Cholelithiasis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Calculus urinary			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Urinary bladder polyp			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Fracture pain			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (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
Bursitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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

Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 130 (0.77%)	1 / 360 (0.28%)	3 / 90 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Parainfluenzae virus infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 130 (0.00%)	1 / 360 (0.28%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 130 (0.00%)	0 / 360 (0.00%)	0 / 90 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 130 (0.77%)	0 / 360 (0.00%)	0 / 90 (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

Serious adverse events	Dose 1 Semorinemab Double Blind Period	Dose 2 Semorinemab Double Blind Period	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 89 (19.10%)	17 / 132 (12.88%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			

subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign pancreatic neoplasm			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 89 (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			

Sudden death			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Euthanasia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar cyst			
subjects affected / exposed	0 / 89 (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	
Acute respiratory failure			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 89 (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	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 89 (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	
Agitation			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranoia			
subjects affected / exposed	0 / 89 (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	
Aggression			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 89 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 89 (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	
Confusional state			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Persecutory delusion			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			

subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 89 (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	
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	0 / 89 (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	
Spinal fracture			
subjects affected / exposed	0 / 89 (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	
Craniocerebral injury			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 89 (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	
Femoral neck fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hip fracture			
subjects affected / exposed	1 / 89 (1.12%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 89 (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	
Road traffic accident			
subjects affected / exposed	0 / 89 (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	
Skin wound			
subjects affected / exposed	0 / 89 (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	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 89 (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	
Bradycardia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	0 / 89 (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	
Cardiac arrest			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			

subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Coma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 89 (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	
Cluster headache			
subjects affected / exposed	0 / 89 (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	
Post-traumatic headache			
subjects affected / exposed	0 / 89 (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 / 89 (1.12%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 89 (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	
Amnesia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia strangulated			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Calculus urinary			
subjects affected / exposed	0 / 89 (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	
Urinary bladder polyp			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 89 (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	
Fracture pain			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 89 (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	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 89 (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	0 / 89 (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 / 1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 89 (1.12%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 89 (1.12%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 89 (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	
Parainfluenzae virus infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	1 / 89 (1.12%)	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			
Dehydration			
subjects affected / exposed	1 / 89 (1.12%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 89 (0.00%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo Double Blind Period	Dose 2 Semorinemab Open Label	Dose 3 Semorinemab Double Blind Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 130 (58.46%)	76 / 360 (21.11%)	60 / 90 (66.67%)
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 130 (1.54%)	3 / 360 (0.83%)	2 / 90 (2.22%)
occurrences (all)	2	3	3
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	4 / 130 (3.08%)	5 / 360 (1.39%)	0 / 90 (0.00%)
occurrences (all)	4	5	0

Infusion related reaction			
subjects affected / exposed	6 / 130 (4.62%)	5 / 360 (1.39%)	6 / 90 (6.67%)
occurrences (all)	6	5	11
Fall			
subjects affected / exposed	22 / 130 (16.92%)	18 / 360 (5.00%)	7 / 90 (7.78%)
occurrences (all)	26	21	11
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 130 (5.38%)	4 / 360 (1.11%)	5 / 90 (5.56%)
occurrences (all)	7	5	6
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 130 (9.23%)	4 / 360 (1.11%)	7 / 90 (7.78%)
occurrences (all)	12	4	9
Headache			
subjects affected / exposed	10 / 130 (7.69%)	15 / 360 (4.17%)	6 / 90 (6.67%)
occurrences (all)	13	15	9
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 130 (1.54%)	1 / 360 (0.28%)	5 / 90 (5.56%)
occurrences (all)	2	3	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 130 (3.08%)	5 / 360 (1.39%)	4 / 90 (4.44%)
occurrences (all)	4	6	4
Nausea			
subjects affected / exposed	0 / 130 (0.00%)	3 / 360 (0.83%)	4 / 90 (4.44%)
occurrences (all)	0	4	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 130 (3.08%)	5 / 360 (1.39%)	5 / 90 (5.56%)
occurrences (all)	4	5	8
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 130 (2.31%)	2 / 360 (0.56%)	5 / 90 (5.56%)
occurrences (all)	3	2	5
Depression			

subjects affected / exposed	5 / 130 (3.85%)	3 / 360 (0.83%)	5 / 90 (5.56%)
occurrences (all)	5	3	6
Anxiety			
subjects affected / exposed	3 / 130 (2.31%)	1 / 360 (0.28%)	6 / 90 (6.67%)
occurrences (all)	3	1	6
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 130 (6.15%)	5 / 360 (1.39%)	6 / 90 (6.67%)
occurrences (all)	8	5	7
Arthralgia			
subjects affected / exposed	8 / 130 (6.15%)	8 / 360 (2.22%)	8 / 90 (8.89%)
occurrences (all)	10	8	8
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	10 / 130 (7.69%)	10 / 360 (2.78%)	5 / 90 (5.56%)
occurrences (all)	13	11	8
Upper respiratory tract infection			
subjects affected / exposed	15 / 130 (11.54%)	4 / 360 (1.11%)	5 / 90 (5.56%)
occurrences (all)	21	4	6
Nasopharyngitis			
subjects affected / exposed	11 / 130 (8.46%)	2 / 360 (0.56%)	12 / 90 (13.33%)
occurrences (all)	15	2	14

Non-serious adverse events	Dose 1 Semorinemab Double Blind Period	Dose 2 Semorinemab Double Blind Period	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 89 (64.04%)	88 / 132 (66.67%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 89 (1.12%)	8 / 132 (6.06%)	
occurrences (all)	1	12	
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	6 / 89 (6.74%)	2 / 132 (1.52%)	
occurrences (all)	6	2	
Infusion related reaction			

subjects affected / exposed	10 / 89 (11.24%)	11 / 132 (8.33%)	
occurrences (all)	16	15	
Fall			
subjects affected / exposed	14 / 89 (15.73%)	22 / 132 (16.67%)	
occurrences (all)	15	33	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 89 (4.49%)	14 / 132 (10.61%)	
occurrences (all)	4	14	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 89 (5.62%)	6 / 132 (4.55%)	
occurrences (all)	7	7	
Headache			
subjects affected / exposed	2 / 89 (2.25%)	8 / 132 (6.06%)	
occurrences (all)	2	11	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 89 (1.12%)	4 / 132 (3.03%)	
occurrences (all)	1	5	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 89 (5.62%)	10 / 132 (7.58%)	
occurrences (all)	7	11	
Nausea			
subjects affected / exposed	9 / 89 (10.11%)	8 / 132 (6.06%)	
occurrences (all)	9	9	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 89 (6.74%)	7 / 132 (5.30%)	
occurrences (all)	6	7	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 89 (2.25%)	4 / 132 (3.03%)	
occurrences (all)	2	4	
Depression			

subjects affected / exposed	5 / 89 (5.62%)	7 / 132 (5.30%)	
occurrences (all)	5	8	
Anxiety			
subjects affected / exposed	10 / 89 (11.24%)	6 / 132 (4.55%)	
occurrences (all)	10	7	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 89 (5.62%)	8 / 132 (6.06%)	
occurrences (all)	5	8	
Arthralgia			
subjects affected / exposed	6 / 89 (6.74%)	10 / 132 (7.58%)	
occurrences (all)	7	12	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 89 (4.49%)	10 / 132 (7.58%)	
occurrences (all)	4	11	
Upper respiratory tract infection			
subjects affected / exposed	6 / 89 (6.74%)	7 / 132 (5.30%)	
occurrences (all)	8	8	
Nasopharyngitis			
subjects affected / exposed	5 / 89 (5.62%)	18 / 132 (13.64%)	
occurrences (all)	6	24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2017	Protocol was amended to include extensions to the 8-week screening period and 15-day baseline period on a case-by-case basis. Several exclusion criteria have been modified. Amyloid positron emission tomography (PET) guidance has been clarified. The Caregiver Global Impression of Change Scales have been added to the assessments performed in both the blinded and open-label portions of the study. The requirement that participants with two consecutive Mini-Mental State Examination (MMSE) scores <10 must be discontinued from the study has been removed, as it remains uncertain whether continued efficacy might be observed in participants who progress to that level of AD severity. The primary efficacy analyses were clarified to state that they will include adjustments for baseline clinical status rather than baseline MMSE score.
11 June 2019	Protocol was amended to include modified exclusion criteria: - The exclusion criterion for biologic therapy has been clarified to indicate that any investigational biologic therapy is prohibited at screening and during the study. - The exclusion criterion for systemic immunosuppressive therapy has been revised to indicate that short courses (<=2 weeks) of high-dose corticosteroid therapy are permitted, and that chronic therapy (>2 weeks) is permitted as long as the dose is <7.5 mg/day prednisolone equivalent and the condition being treated is not expected to deteriorate significantly during the study period. The description of the recall time frame for the Caregiver Global Impression of Change Scales has been corrected to align with the time frames used for the assessment. Study visits during the protocol safety follow-up period were clarified to state that patients who discontinue from treatment early will have a treatment discontinuation visit. Adverse event reporting was clarified to include reporting of adverse events that occur after the protocol defined adverse event reporting interval following the last dose of [18F]GTP1 or study drug administration for adverse events leading to discontinuation from the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported