Clinical trial results:
An Extension Study of ABBV-8E12 in Early Alzheimer's Disease

Summary

EudraCT number	2018-000268-26
Trial protocol	ES FI BE DK NL IT
Global end of trial date	30 September 2021

Results information

Result version number	v1 (current)
This version publication date	10 September 2022
First version publication date	10 September 2022

Trial information

Trial identification

Sponsor protocol code	M15-570

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03712787
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road,, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, AbbVie Deutschland GmbH & Co. KG, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, AbbVie Deutschland GmbH & Co. KG, 001 8006339110, abbvieclinicaltrials@abbvie.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	30 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the long-term safety and tolerability of ABBV-8E12 in participants with early Alzheimer's Disease (AD).

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 26
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	United States: 222
Worldwide total number of subjects	364
EEA total number of subjects	86

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)	43
From 65 to 84 years	308
85 years and over	13

Subject disposition

Recruitment

Recruitment details:

A total of 364 participants who had completed the parent study (Study M15-566; NCT02880956) were enrolled into this extension study from a total of 57 sites in the United States, Australia, Belgium, Canada, Denmark, Finland, Italy, New Zealand, Spain, and Sweden.

Pre-assignment

Screening details:

Prior to enrollment, 87 participants had received tilavonemab 300 mg, 97 participants had received tilavonemab 1000 mg, 88 participants had received tilavonemab 2000 mg, and 92 participants had received placebo in the parent study.

Pre-assignment period milestones

Number of subjects started	364
Number of subjects completed	363

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Enrolled but not treated: 1

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	300 mg/1000 mg Tilavonemab

Arm description:

Participants who received 300 mg tilavonemab in Study M15-566 received 1000 mg tilavonemab in Study M15-570 via intravenous (IV) infusion every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	tilavonemab
Investigational medicinal product code	ABBV-8E12
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were to receive study drug infusion every 4 weeks.

Arm title	1000 mg/1000 mg Tilavonemab

Arm description:

Participants who received 1000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	tilavonemab
Investigational medicinal product code	ABBV-8E12
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Subjects were to receive study drug infusion every 4 weeks.

Arm title	2000 mg/2000 mg Tilavonemab
Arm description: Participants who received 2000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	
Arm type	Experimental
Investigational medicinal product name	tilavonemab
Investigational medicinal product code	ABBV-8E12
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Subjects were to receive study drug infusion every 4 weeks.	

Arm title	PBO/2000 mg Tilavonemab
Arm description: Participants who received placebo (PBO) in Study M15-566 received 2000 mg tilavonemab in Study M15-570 via IV infusion every 4 weeks.	
Arm type	Experimental
Investigational medicinal product name	tilavonemab
Investigational medicinal product code	ABBV-8E12
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Subjects were to receive study drug infusion every 4 weeks.	

Number of subjects in period 1[1]	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab
Started	87	97	88
Completed	0	0	0
Not completed	87	97	88
Consent withdrawn by subject	4	14	12
Adverse Event	2	3	-
COVID-19 Logistical Restrictions	1	1	-
COVID-19 Infection	-	1	-
Lost to follow-up	1	1	2
Other, Not Specified	79	77	74

Number of subjects in period 1[1]	PBO/2000 mg Tilavonemab
Started	91

Completed	0
Not completed	91
Consent withdrawn by subject	8
Adverse Event	4
COVID-19 Logistical Restrictions	-
COVID-19 Infection	-
Lost to follow-up	1
Other, Not Specified	78

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: 1 enrolled subject did not received any treatment, and is accounted for in the Pre-Assignment table.

Baseline characteristics

Reporting groups	
Reporting group title	300 mg/1000 mg Tilavonemab
Reporting group description:	
Participants who received 300 mg tilavonemab in Study M15-566 received 1000 mg tilavonemab in Study M15-570 via intravenous (IV) infusion every 4 weeks.	
Reporting group title	1000 mg/1000 mg Tilavonemab
Reporting group description:	
Participants who received 1000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	2000 mg/2000 mg Tilavonemab
Reporting group description:	
Participants who received 2000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	PBO/2000 mg Tilavonemab
Reporting group description:	
Participants who received placebo (PBO) in Study M15-566 received 2000 mg tilavonemab in Study M15-570 via IV infusion every 4 weeks.	

Reporting group values	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab
Number of subjects	87	97	88
Age categorical Units: Subjects			
< 65 years	8	11	14
>= 65 years	79	86	74
Gender categorical Units: Subjects			
Female	39	48	48
Male	48	49	40
Race Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	1	0
Black or African American	3	1	0
White	81	94	86
More than one race	0	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	5	4	3
None	82	93	85

Reporting group values	PBO/2000 mg Tilavonemab	Total	
Number of subjects	91	363	
Age categorical Units: Subjects			
< 65 years	10	43	
>= 65 years	81	320	

Gender categorical Units: Subjects			
Female	56	191	
Male	35	172	
Race Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	0	2	
Native Hawaiian or Other Pacific Islander	0	1	
Black or African American	2	6	
White	89	350	
More than one race	0	3	
Ethnicity Units: Subjects			
Hispanic or Latino	4	16	
None	87	347	

End points

End points reporting groups

Reporting group title	300 mg/1000 mg Tilavonemab
Reporting group description:	
Participants who received 300 mg tilavonemab in Study M15-566 received 1000 mg tilavonemab in Study M15-570 via intravenous (IV) infusion every 4 weeks.	
Reporting group title	1000 mg/1000 mg Tilavonemab
Reporting group description:	
Participants who received 1000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	2000 mg/2000 mg Tilavonemab
Reporting group description:	
Participants who received 2000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	PBO/2000 mg Tilavonemab
Reporting group description:	
Participants who received placebo (PBO) in Study M15-566 received 2000 mg tilavonemab in Study M15-570 via IV infusion every 4 weeks.	

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs Leading to Discontinuation of Study Drug, and Fatal TEAEs

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs Leading to Discontinuation of Study Drug, and Fatal TEAEs[1]

End point description:

Treatment emergent adverse events (TEAEs) are defined as any adverse event from the time of study drug administration until 20 weeks after discontinuation of study drug. An adverse event (AE) is defined as any untoward medical occurrence, which does not necessarily have a causal relationship with treatment. A serious AE (SAE) is defined as any event that: results in death; is life-threatening; results in hospitalization or prolongation of hospitalization; is a congenital anomaly; results in persistent or significant disability/incapacity; is an important medical event requiring medical or surgical intervention to prevent serious outcome. Severity of AEs was categorized as mild, moderate, or severe. Relationship of the AE to the study treatment was categorized as having a reasonable possibility or no reasonable possibility.

Safety Data Set: All participants who received at least 1 dose of study drug in Study M15-570.

End point type	Primary

End point timeframe:

From first dose of study drug to 20 weeks after last dose of study drug; overall median time on treatment was 279 days.

Notes:

[1] - 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: Descriptive statistics are presented per protocol.

End point values	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	88	91
Units: participants				
Any TEAE	54	66	59	57
Severe TEAE	9	8	10	7

TEAE With a Reasonable Possibility of Relationship	7	10	15	5
Serious TEAE	16	11	12	10
TEAE Leading to Discontinuation of Study Drug	2	4	0	5
Fatal TEAE	1	1	1	0

Statistical analyses

No statistical analyses for this end point

Primary: Hematology: Number of Participants With Postbaseline Potentially Clinically Significant (PCS) Values

End point title	Hematology: Number of Participants With Postbaseline Potentially Clinically Significant (PCS) Values[2]

End point description:

Clinical laboratory PCS criteria were adapted from National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. ULN=upper limit of normal.

Safety Data Set: All participants who received at least 1 dose of study drug in Study M15-570.

End point type	Primary

End point timeframe:

Baseline to 20 weeks after last dose of study drug; overall median time on treatment was 279 days.

Notes:

[2] - 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: Descriptive statistics are presented per protocol.

End point values	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	88	91
Units: participants				
Hemoglobin - Low (< 100 g/L)	1	0	2	1
Hemoglobin - High (> 40 g/L above ULN)	0	0	0	0
Platelets - Low (< 75 × 10^9/L)	0	0	0	0
Leukocytes - Low (< 2 × 10^9/L)	0	0	0	0
Leukocytes - High (> 100 × 10^9/L)	0	0	0	0
Neutrophils - Low (< 1 × 10^9/L)	1	0	0	0
Lymphocytes - Low (< 0.5 × 10^9/L)	0	0	1	0
Lymphocytes - High (> 20 × 10^9/L)	0	0	0	0
Activated Partial Thromboplastin Time (> ULN)	0	0	0	0
Prothrombin International Normalized Ratio (> ULN)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Chemistry: Percentage of Participants With Postbaseline PCS Values

End point title	Clinical Chemistry: Percentage of Participants With Postbaseline PCS Values[3]

End point description:

Clinical laboratory PCS criteria were adapted from NCI CTCAE version 4.03.

Safety Data Set: All participants who received at least 1 dose of study drug in Study M15-570.

End point type	Primary

End point timeframe:

Baseline to 20 weeks after last dose of study drug; overall median time on treatment was 279 days

Notes:

[3] - 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: Descriptive statistics are presented per protocol.

End point values	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	88	91
Units: participants				
Alanine Aminotransferase (> 3 × ULN)	0	0	0	0
Aspartate Aminotransferase (> 3 × ULN)	0	0	0	0
Alkaline Phosphatase (> 2.5 × ULN)	0	0	0	0
Bilirubin (> 1.5 × ULN)	0	0	1	1
Creatinine (> 1.5 × ULN)	0	0	0	0
Calcium - Low (< 1.75 mmol/L)	0	0	0	0
Calcium - High (> 3.1 mmol/L)	0	0	0	0
Sodium - Low (< 130 mmol/L)	0	1	0	1
Sodium - High (> 155 mmol/L)	0	0	0	0
Potassium - Low (< 3 mmol/L)	0	0	0	0
Potassium - High (> 6 mmol/L)	0	0	0	0
Glucose - Low (< 2.2 mmol/L)	0	0	0	0
Glucose - High (> 13.9 mmol/L)	0	0	0	1
Albumin (< 20 g/L)	0	0	0	0
Cholesterol (> 12.92 mmol/L)	0	0	0	0
Triglycerides (> 5.7 mmol/L)	0	0	1	0
Phosphate (< 0.6 mmol/L)	0	0	0	0
Uric acid (> 590 µmol/L)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Columbia-Suicide Severity Rating Scale (C-SSRS) During Double-Blind Treatment Period

End point title	Columbia-Suicide Severity Rating Scale (C-SSRS) During

	Double-Blind Treatment Period[4]

End point description:

The C-SSRS is a systematically administered instrument developed to track suicidal adverse events across a treatment study. The instrument is designed to assess suicidal behavior and ideation, track and assess all suicidal events, as well as the lethality of attempts. Suicidal ideation categories include the following: wish to be dead; nonspecific active suicidal thoughts; active suicidal ideation without intent to act; active suicidal ideation with some intent to act but no plan; active suicidal ideation with plan and intent. Suicidal behavior categories include the following: actual attempt; interrupted attempt; aborted attempt; preparatory acts or behavior; suicidal behavior; completed suicide.

Safety Data Set: All participants who received at least 1 dose of study drug in Study M15-570.

End point type	Primary

End point timeframe:

Baseline to 20 weeks after last dose of study drug; overall median time on treatment was 279 days.

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: Descriptive statistics are presented per protocol.

End point values	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	88	91
Units: participants				
Suicidal behaviors or ideations	4	3	8	4
Suicidal behaviors	0	0	0	0
Suicidal ideations	4	3	8	4
Suicidal ideations only (no suicidal behavior)	4	3	8	4

Statistical analyses

No statistical analyses for this end point

Primary: Brain Magnetic Resonance Imaging (MRI) Results: Number of Participants With Cerebral Edemas, New Microhemorrhage(s), and Severe White Matter Disease

End point title	Brain Magnetic Resonance Imaging (MRI) Results: Number of Participants With Cerebral Edemas, New Microhemorrhage(s), and Severe White Matter Disease[5]

End point description:

Safety Data Set: All participants who received at least 1 dose of study drug in Study M15-570. Participants with postbaseline value for the respective parameter.

End point type	Primary

End point timeframe:

Baseline to 20 weeks after last dose of study drug; overall median time on treatment was 279 days.

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: Descriptive statistics are presented per protocol.

End point values	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	2000 mg/2000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	84	79	78
Units: participants				
Cerebral Edemas	1	1	0	0
Questionable Cerebral Edemas	0	1	0	0
New Microhemorrhage(s)	4	5	11	5
Severe White Matter Disease	9	5	6	5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug to 20 weeks after last dose of study drug; overall median time on treatment was 279 days.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	300 mg/1000 mg Tilavonemab
Reporting group description:	
Participants who received 300 mg tilavonemab in Study M15-566 received 1000 mg tilavonemab in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	1000 mg/1000 mg Tilavonemab
Reporting group description:	
Participants who received 1000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	PBO/2000 mg Tilavonemab
Reporting group description:	
Participants who received PBO in Study M15-566 received 2000 mg tilavonemab in Study M15-570 via IV infusion every 4 weeks.	
Reporting group title	2000 mg/2000 mg Tilavonemab
Reporting group description:	
Participants who received 2000 mg tilavonemab in Study M15-566 were continued on the same dose in Study M15-570 via IV infusion every 4 weeks.	

Serious adverse events	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 87 (18.39%)	11 / 97 (11.34%)	10 / 91 (10.99%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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

COLON CANCER			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
COLORECTAL ADENOCARCINOMA			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	2 / 87 (2.30%)	0 / 97 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC STENOSIS			
subjects affected / exposed	1 / 87 (1.15%)	1 / 97 (1.03%)	0 / 91 (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
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
GAIT DISTURBANCE			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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

Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
Respiratory, thoracic and mediastinal disorders			
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
Psychiatric disorders			
AGGRESSION			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BEHAVIOUR DISORDER			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
CONFUSIONAL STATE			

subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 87 (0.00%)	2 / 97 (2.06%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
PROCEDURAL INTESTINAL PERFORATION			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
SOFT TISSUE INJURY			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
ARRHYTHMIA			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
CARDIOPULMONARY FAILURE			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEMENTIA			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
SEIZURE			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
SYNCOPE			

subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
Ear and labyrinth disorders			
VESTIBULAR DISORDER			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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 ARTERY OCCLUSION			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
Gastrointestinal disorders			
COLITIS ISCHAEMIC			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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			
BILIARY COLIC			

subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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 KIDNEY DISEASE			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 87 (2.30%)	0 / 97 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 PNEUMONIA			
subjects affected / exposed	2 / 87 (2.30%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CYSTITIS ESCHERICHIA			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
DIVERTICULITIS			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOCCAL INFECTION			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
ESCHERICHIA URINARY TRACT			

INFECTION			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
INFLUENZA			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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
PNEUMONIA LEGIONELLA			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (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
PYELONEPHRITIS			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 91 (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	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 91 (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
FAILURE TO THRIVE			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	2000 mg/2000 mg Tilavonemab		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 88 (13.64%)		
number of deaths (all causes)	1		
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLADDER TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COLON CANCER			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COLORECTAL ADENOCARCINOMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PROSTATE CANCER			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
AORTIC STENOSIS			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GAIT DISTURBANCE			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PULMONARY OEDEMA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY FAILURE			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
AGGRESSION			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BEHAVIOUR DISORDER			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CONFUSIONAL STATE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HIP FRACTURE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PROCEDURAL INTESTINAL PERFORATION			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SOFT TISSUE INJURY			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ANGINA UNSTABLE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ARRHYTHMIA			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ATRIAL FLUTTER			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIOPULMONARY FAILURE			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DEMENTIA			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

ENCEPHALOPATHY				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SEIZURE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBARACHNOID HAEMORRHAGE				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SYNCOPE				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRANSIENT ISCHAEMIC ATTACK				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
VESTIBULAR DISORDER				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
RETINAL ARTERY OCCLUSION				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
COLITIS ISCHAEMIC				

subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INGUINAL HERNIA			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
BILIARY COLIC			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

CYSTITIS ESCHERICHIA				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIVERTICULITIS				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ENTEROCOCCAL INFECTION				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ESCHERICHIA URINARY TRACT INFECTION				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFLUENZA				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA LEGIONELLA				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PYELONEPHRITIS				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				

DEHYDRATION			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FAILURE TO THRIVE			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	300 mg/1000 mg Tilavonemab	1000 mg/1000 mg Tilavonemab	PBO/2000 mg Tilavonemab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 87 (29.89%)	37 / 97 (38.14%)	26 / 91 (28.57%)
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	2 / 87 (2.30%)	6 / 97 (6.19%)	0 / 91 (0.00%)
occurrences (all)	2	8	0
FALL			
subjects affected / exposed	10 / 87 (11.49%)	10 / 97 (10.31%)	10 / 91 (10.99%)
occurrences (all)	14	12	13
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 87 (2.30%)	5 / 97 (5.15%)	0 / 91 (0.00%)
occurrences (all)	2	5	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	5 / 87 (5.75%)	2 / 97 (2.06%)	2 / 91 (2.20%)
occurrences (all)	5	2	3
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	5 / 87 (5.75%)	5 / 97 (5.15%)	1 / 91 (1.10%)
occurrences (all)	5	6	1
Psychiatric disorders			
AGITATION			

subjects affected / exposed	1 / 87 (1.15%)	6 / 97 (6.19%)	0 / 91 (0.00%)
occurrences (all)	1	6	0
ANXIETY			
subjects affected / exposed	3 / 87 (3.45%)	1 / 97 (1.03%)	3 / 91 (3.30%)
occurrences (all)	3	1	3
CONFUSIONAL STATE			
subjects affected / exposed	1 / 87 (1.15%)	2 / 97 (2.06%)	5 / 91 (5.49%)
occurrences (all)	1	2	6
DELUSION			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	2 / 91 (2.20%)
occurrences (all)	0	1	2
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 87 (1.15%)	2 / 97 (2.06%)	2 / 91 (2.20%)
occurrences (all)	1	2	2
BACK PAIN			
subjects affected / exposed	5 / 87 (5.75%)	4 / 97 (4.12%)	5 / 91 (5.49%)
occurrences (all)	6	4	7
Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 87 (4.60%)	8 / 97 (8.25%)	1 / 91 (1.10%)
occurrences (all)	10	8	3

Non-serious adverse events	2000 mg/2000 mg Tilavonemab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 88 (37.50%)		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
FALL			
subjects affected / exposed	12 / 88 (13.64%)		
occurrences (all)	16		
Vascular disorders			
HYPERTENSION			

subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 6		
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all)	 2 / 88 (2.27%) 2		
Gastrointestinal disorders DIARRHOEA subjects affected / exposed occurrences (all)	 3 / 88 (3.41%) 3		
Psychiatric disorders AGITATION subjects affected / exposed occurrences (all) ANXIETY subjects affected / exposed occurrences (all) CONFUSIONAL STATE subjects affected / exposed occurrences (all) DELUSION subjects affected / exposed occurrences (all)	 2 / 88 (2.27%) 3 7 / 88 (7.95%) 8 4 / 88 (4.55%) 4 5 / 88 (5.68%) 5		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all)	 6 / 88 (6.82%) 6 3 / 88 (3.41%) 3		
Infections and infestations URINARY TRACT INFECTION subjects affected / exposed occurrences (all)	 0 / 88 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 January 2019	• Update Section 1.0, Title Page, to add sponsor contact. • Update Section 5.3.1.1, Study Procedures, to add instructions for ECG collection and made editorial changes for clarity. • Update Section 5.5.1, Treatments Administered, to add visit window and allow faster rates for infusion. • Update Section 5.5.2.2, Storage and Disposition of Study Drugs, to revise language on storage temperature excursion. • Update Section 7.0, Protocol Deviations, to update the names and information for sponsor clinical personnel. • Update Section 9.3, Subject Information and Consent, to change the location of storage of subject informed consent from medical record to study record. • Update Appendix C, Study Activities, to correct typographical errors, clarify previous text, and clarify retinal imaging scan language. • Added Appendix E, Protocol Amendment: List of Changes, to describe changes made with this amendment.
20 October 2020	• Update Section 3.0 Introduction Clinical Experience to remove studies. • Update Section 3.2 Benefits and Risks to include language for the coronavirus disease-19 (COVID-19) pandemic. • Update Section 5.1 Overall Study Design and Plan: Description to specify timing in schedule of activities. • Update Section 5.2.2 Exclusion Criteria to add a rationale for the exclusion criteria. • Update Section 5.3.1.1 Study Procedures [Physical Examination, Neurological Examination, Vital Signs, 12-Lead Electrocardiogram (ECG), Abnormal Findings, Optional Lumbar Puncture, Magnetic Resonance Imaging (MRI), and Positron Emission Tomography (PET) Tau Imaging] to include language for the COVID-19 pandemic. • Update Section 5.3.1.1 Study Procedures, Table 2 to specify optional tests. • Update Section 5.3.1.1 Study Procedures [Positron Emission Tomography (PET) Tau Imaging] to specify timing in schedule of activities. • Update Section 5.3.1.1 Study Procedures to remove procedures. • Update Section 5.3.1.1 Study Procedures, Table 3 to specify timing of scales. • Update Section 5.3.1.1 Study Procedures, EuroQuality of Life-5-level (EQ-5D5L) to add language describing the scale. • Update Section 5.3.1.2 Collection and Handling of Biomarker and Pharmacogenetic Research Samples (Blood and Optional CSF Biomarker Samples; Optional Pharmacogenetic Research Samples) to include language for the COVID19 pandemic. • Update Section 5.3.2.1 Collection of Samples for Analysis (Optional CSF Samples for ABBV-8E12 Assay) to include language for the COVID-19 pandemic. • Update Section 5.3.6.1 Biomarker Research Variables, Volumetric MRI to include language reflecting analysis. • Update Section 5.3.6.1 Biomarker Research Variables to remove language. • Update Section 5.4.1 Discontinuation of Individual Subjects to include language for the COVID-19 pandemic. • Update Section 5.5.1 Treatments Administered to specify timing of drug administration.

20 October 2020	(continued) Update Section 5.5.2 Identity of Investigational Product, Table 4 to add additional strength of study drug • Update Section 6.1.5 Adverse Event Reporting to include language for the COVID-19 pandemic. • Update Section 8.1.1 Analysis Data Sets, Data Set for Safety Analyses to remove language pertaining to analysis. • Update Section 8.1.1 Analysis Data Sets, Data Set for Biomarkers to include language pertaining to analysis. • Update Section 8.1.4 Safety Analysis to include language pertaining to analyses. • Update Section 8.1.4.2 Analysis of Adverse Events to include language pertaining to analyses. • Update Section 8.1.5 Biomarker Analyses to include language pertaining to analysis. • Update Section 8.1.5 Biomarker Analyses, Volumetric MRI Variables to include language pertaining to analysis. • Update Section 9.2 Ethical Conduct of the Study to include language for the COVID-19 pandemic. • Update Section 9.3 Subject Information and Consent to include language for the COVID-19 pandemic. • Update Section 11.0 Data Quality Assurance to include language for the COVID19 pandemic. • Update Section 15.0 Reference List to replace reference.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported