

**Clinical trial results:****Phase IIa Biomarker Study to Evaluate the Efficacy, Safety and Tolerability of AT-1 in Patients with Hereditary Cystatin C Amyloid Angiopathy (HCCAA) - the AT1-HCCAA study****Summary**

EudraCT number	2017-004776-56
Trial protocol	IS
Global end of trial date	03 September 2020

**Results information**

Result version number	v1 (current)
This version publication date	13 October 2021
First version publication date	13 October 2021
Summary attachment (see zip file)	AT NAC Phase II Synopsis (AT NAC Phase II Synopsis final.pdf)

**Trial information****Trial identification**

Sponsor protocol code	AT1-2017
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**Additional study identifiers**

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

Notes:

**Sponsors**

Sponsor organisation name	Arctic Therapeutics ehf.
Sponsor organisation address	Sóltún 11, Reykjavík, Iceland, 105
Public contact	Head, Clinical Development, Arctic Therapeutics ehf., + 1 2674554534 , hakon@hakonarson.com
Scientific contact	Head, Clinical Development, Arctic Therapeutics ehf., + 1 2674554534 , hakon@hakonarson.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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	01 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2020
Global end of trial reached?	Yes
Global end of trial date	03 September 2020
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

- Evaluate safety and tolerability of AT-1 administered orally in adults (ages 18 and over) with HCCAA with or without dementia symptoms
- Assess dose-response relationship of AT-1 on HCCAA disease progression, including
- Biomarker response from skin biopsies (reduction in cystatin C stain)
- Assessment of cognitive status using dementia rating scales

Protection of trial subjects:

Independent data monitoring committee (IDMC) was established to review and oversee any issues with trial subjects. Clinical trial protocol was designed to minimize pain and distress of trial subjects.

Background therapy:

None.

Evidence for comparator:

N/A. No comparators used in this study.

Actual start date of recruitment	29 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Iceland: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

Notes:

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**Subjects enrolled per age group**

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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)	14

From 65 to 84 years	3
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Subjects were all recruited from Iceland, starting on July 1, 2019 through November 28, 2019. Adults (18+ years old) who were suspected carriers of the L68Q mutation in Cystatin C were invited to participate.

### Pre-assignment

Screening details:

All adult subjects (18+ years old) were invited to participate in the study. Overall, 22 subjects were screened, and 5 were excluded when confirmation genetic testing revealed they were not carriers or L68Q mutation.

### Pre-assignment period milestones

Number of subjects started	22 <sup>[1]</sup>
Number of subjects completed	17

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not carry L68Q mutation: 5
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 22 subjects screened, of whom 17 were officially enrolled. 5 were excluded since they failed screening due to absence of L68Q mutation.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A. Open label study.

### Arms

Arm title	All subjects
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Arm description:

All enrolled subjects dosed daily with active drug in this open label study.

Arm type	Experimental
Investigational medicinal product name	N-acetyl cystein
Investigational medicinal product code	AT-1
Other name	Mucolysin, acetylcystein
Pharmaceutical forms	Effervescent tablet
Routes of administration	Oral use

Dosage and administration details:

1200mg of AT-1 administered bid (twice daily) per os (orally) via soluble effervescent tablets (600mg each tablet).

<b>Number of subjects in period 1</b>	All subjects
Started	17
Completed	15
Not completed	2
Pregnancy	2

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	17	17	
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)	14	14	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	6	6	

## End points

### End points reporting groups

Reporting group title	All subjects
Reporting group description:	
All enrolled subjects dosed daily with active drug in this open label study.	

### Primary: Dementia rating scale

End point title	Dementia rating scale <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe:	
Baseline and 3, 6, and 9 months after treatment with AT-001.	

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: No notable decline/change in cognitive function throughout study based on physicians' assessments.

End point values	All subjects			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Rating scale score				
arithmetic mean (standard deviation)				
Total score, baseline	135.6 (± 10.72)			
Total score, 3 months	133.93 (± 11.27)			
Total score, 6 months	137.53 (± 12.23)			
Total score, 9 months	133.33 (± 12.51)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline and 3, 6, and 9 months after treatment with AT-001

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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### Reporting groups

Reporting group title	All treated subjects
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Reporting group description: -

Serious adverse events	All treated subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 17 (47.06%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hemorrhage	Additional description: Small intracranial hemorrhage observed upon CT scan, consistent with natural history of HCCAA disease.		
subjects affected / exposed	5 / 17 (29.41%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Migraine	Additional description: Headache/migraine that had worsened after a fall, but then resolved on its own.		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pregnancy	Additional description: Subject became pregnant during course of study, initially detected by urine pregnancy test then confirmed. Withdrew from study.		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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



<b>Non-serious adverse events</b>	All treated subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 17 (88.24%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
General disorders and administration site conditions			
Dry mouth			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	5		
Sleep disturbance			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported