



## Clinical trial results:

### A 10-Week, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Donepezil Hydrochloride (Aricept) in the Treatment of the Cognitive Dysfunction Exhibited by Children with Down Syndrome, Aged 6 to 10

#### Summary

EudraCT number	2016-004949-92
Trial protocol	Outside EU/EEA
Global end of trial date	10 December 2008

#### Results information

Result version number	v1 (current)
This version publication date	07 April 2019
First version publication date	07 April 2019

#### Trial information

##### Trial identification

Sponsor protocol code	E2020-A001-336
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00754013
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Eisai Medical Services Inc.
Sponsor organisation address	100 Tice Boulevard, Woodcliff Lake, United States,
Public contact	Eisai Medical Information, Eisai Inc., 011 888247-2378, esi-medinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Inc., 011 888247-2378, esi-medinfo@eisai.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	10 December 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 December 2008
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to determine the efficacy and safety of donepezil hydrochloride (Aricept) in the treatment of cognitive dysfunction shown by children with Down syndrome, aged 6 to 10 years.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following:

- Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008)
- International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
- Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312
- European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states.
- Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan's GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 October 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	9
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	9
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

This study planned to recruit subjects at 26 centers in the United States. However, the study was terminated early and only 5 centers enrolled subjects during the period of 06 Oct 2008 to 10 Dec 2008.

### Pre-assignment

Screening details:

Due to early termination of the study by the Sponsor, only 9 participants were enrolled into the study.

### 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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Donepezil HCl

Arm description:

Donepezil was titrated to a dose of approximately 0.1-0.2 mg/kg/day as liquid containing 1 mg/1 mL of donepezil.

Arm type	Experimental
Investigational medicinal product name	Donepezil HCl
Investigational medicinal product code	
Other name	Aricept
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Blinded oral donepezil hydrochloride (HCl), was started at 1.25 mL daily, followed by 2-week titration intervals over a period of 6 weeks until a maximum dose of 5 mg/kg/day or 10 mg/kg/day was reached. Due to early termination of the study, no participant reached either targeted maximum.

<b>Arm title</b>	Placebo
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Arm description:

Donepezil matched placebo was titrated in the similar way as the donepezil arm.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo in a 1:1:1 ratio.

<b>Number of subjects in period 1</b>	Donepezil HCl	Placebo
Started	4	5
Completed	0	0
Not completed	4	5
didn't return after study terminated	3	4
Lost to follow-up	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	Donepezil HCl
Reporting group description: Donepezil was titrated to a dose of approximately 0.1-0.2 mg/kg/day as liquid containing 1 mg/1 mL of donepezil.	
Reporting group title	Placebo
Reporting group description: Donepezil matched placebo was titrated in the similar way as the donepezil arm.	

Reporting group values	Donepezil HCl	Placebo	Total
Number of subjects	4	5	9
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	9 ± 0.8	8 ± 1.4	-
Gender categorical Units: Subjects			
Female	2	3	5
Male	2	2	4
Race/Ethnicity Units: Subjects			
White (n)	4	5	9

## End points

### End points reporting groups

Reporting group title	Donepezil HCl
Reporting group description: Donepezil was titrated to a dose of approximately 0.1-0.2 mg/kg/day as liquid containing 1 mg/1 mL of donepezil.	
Reporting group title	Placebo
Reporting group description: Donepezil matched placebo was titrated in the similar way as the donepezil arm.	

### Primary: Vineland-II Adaptive Behavior Scales (VABS-II) Parent/Caregiver Rating Form (PCRF) Sum of the 9 Sub-domain V-Scores (3 Scores for Each of the Communication, Daily Living Skills, And Socialization Domains) Using Last Observation Carried Forward

End point title	Vineland-II Adaptive Behavior Scales (VABS-II) Parent/Caregiver Rating Form (PCRF) Sum of the 9 Sub-domain V-Scores (3 Scores for Each of the Communication, Daily Living Skills, And Socialization Domains) Using Last Observation Carried Forward <sup>[1]</sup>
End point description: The primary objective of the study was evaluation of the efficacy and safety of donepezil hydrochloride in the treatment of the cognitive dysfunction exhibited by children with Down syndrome (DS), aged 6 to 10, as assessed by analysis of VABS-II/PCRF in the domains of communication, daily living skills, and socialization, and as assessed by standard safety measurements. The planned efficacy analysis was on the intent-to-treat (ITT) population. This study was terminated early. Primary efficacy data were not analyzed since only 9 of the 140 planned subjects had been enrolled.	
End point type	Primary
End point timeframe: Visit 0 (Screen), Visits 1 (Baseline), 2, and 3 (or Early Termination)	

#### 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: Due to early termination of the study, no analyses were performed.

End point values	Donepezil HCl	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 <sup>[2]</sup>	0 <sup>[3]</sup>		
Units: Units on a scale				
number (not applicable)				

#### Notes:

[2] - This study was terminated early. Analyses were not performed.

[3] - This study was terminated early. Analyses were not performed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change From (Baseline) to Visit 3 (Week 10 or Early Termination) in VABS-II/PCRF Sum of The 9 Sub-domain V-Scores (3 Scores for Each of The Communication, Daily Living Skills, And Socialization Domains) Using Last Observation Carried Forward

End point title	Mean Change From (Baseline) to Visit 3 (Week 10 or Early
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Termination) in VABS-II/PCRF Sum of The 9 Sub-domain V-Scores (3 Scores for Each of The Communication, Daily Living Skills, And Socialization Domains) Using Last Observation Carried Forward

**End point description:**

The planned secondary objectives of the study included further evaluation of efficacy as assessed by additional analyses of the VABS-II/PCRF, by analyses of the Test of Verbal Expression and Reasoning (TOVER), a subject-performance-based measure of expressive language function, and by the Forward Memory and Attention Sustained sub-tests of the Leiter International Performance Scale - Revised (Leiter-R), a cognitive assessment instrument for children and adolescents that is not language dependent. In addition, observed case analyses of these assessments at Week 4 and Week 10 were planned. This study was terminated early. Secondary efficacy data were not analyzed since only 9 of the 140 planned subjects had been enrolled.

End point type Secondary

**End point timeframe:**

Visit 1 (Baseline) to Visit 3 (Week 10 or early termination)

End point values	Donepezil HCl	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 <sup>[4]</sup>	0 <sup>[5]</sup>		
Units: Units on a scale				
number (not applicable)				

**Notes:**

[4] - This study was terminated early. Analyses were not performed.

[5] - This study was terminated early. Analyses were not performed.

**Statistical analyses**

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From date of first dose until 30 days after the last dose of study treatment, up to approximately 3 months.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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### Reporting groups

Reporting group title	Donepezil HCl
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Reporting group description:

Donepezil was titrated to a dose of approximately 0.1-0.2 mg/kg/day as liquid containing 1 mg/1 mL of donepezil.

Reporting group title	Placebo
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Reporting group description:

Donepezil matched placebo was titrated in the similar way as the donepezil arm.

Serious adverse events	Donepezil HCl	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Donepezil HCl	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	3 / 5 (60.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Bruxism			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Tongue disorder			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Psychiatric disorders Abnormal behaviour subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the study terminating early, only 9 subjects were enrolled and these subjects receive only limited exposure to study medications with no subject reaching his/her maximum targeted dose. Therefore, the planned efficacy criteria was not analyzed.
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Notes: