



Clinical trial results: Sunphenon EGCg (Epigallocatechin-Gallat) in the early stage of Alzheimer´s Disease

Summary

EudraCT number	2009-009656-20
Trial protocol	DE
Global end of trial date	13 February 2015

Results information

Result version number	v1 (current)
This version publication date	26 May 2022
First version publication date	26 May 2022
Summary attachment (see zip file)	Consort Flow Diagram_SUN-AK (Consort Flow Diagram_SUN-AK.pdf)

Trial information

Trial identification

Sponsor protocol code	SUN-AK
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité - University Hospital of Berlin
Sponsor organisation address	Charitéplatz 1 , Berlin, Germany, 10117
Public contact	Prof. Dr. Friedmann Paul, NeuroCure Clinical Reaserch Center, +49 30 450 539705, friedemann.paul@charite.de
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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	13 February 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 February 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy and safety of Sunphenon EGCG in early stage Alzheimer 's disease.
Primary outcome: delay of progression of early stage Alzheimer 's Disease (AD), defined by the deterioration in the ADAS-COG 18 months after treatment compared to baseline - in comparison to placebo. A modified version of ADAS-Cog with only 8 subtests was used. The categories linguistic expression, linguistic comprehension and word finding disorders were not scored. The category of orientation was replaced by the sub-category orientation of MMSE. A maximum score of 57 possible points on the ADAS-Cog was achievable in the study.

Protection of trial subjects:

Every 3 months, the participants underwent a total of 6 clinical visits according to a standardized schedule. For each visit medical history, the physical and neurological status, vital sign, the basic laboratory panel and the occurrence of adverse events were assessed. There were also four telephone visits record adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2009
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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	0
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The screening visit include collection of demographic data, review of inclusion and exclusion criteria, the medical history, a physical and neurological examination, vital parameters (hearttrate, blood pressure), weight, a laboratoy screening test with a basic laboratory panel and extended laboratory paramenters, ECG and cerebral MRI.

Pre-assignment

Screening details:

Planned number of cases = 2x25
Subjects assessed for eligibility = 25
Screening failure = 4
Subjects declined to participate = 0
Included subjects = 21

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Verum group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Sunphenon EGCG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Months 1-3: Sunphenon EGCG 1 x daily 1 capsul (corresponding to 1 x 200mg EGCG)
Months 4-6: Sunphenon EGCG 2 x daily 1 capsul (corresponding to 2 x 200mg EGCG)
Months 7-9: Sunphenon EGCG 1 x daily 1 capsul, 1 x daily 2 capsules (corresponding to 3 x 200mg EGCG)
Months 10-18: Sunphenon EGCG 2 x daily 2 capsul (corresponding to 4 x 200mg EGCG)

Arm title	Placebo Group
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Arm description: -

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

Dosage and administration details:

Months 1 to 3: Placebo 1 x daily 1 capsule
Months 4 to 6: Placebo 2 x daily 1 capsule
Months 7 to 9: Placebo 1 x daily 1 capsule, Placebo 1 x daily 2 capsule
Months 10 to 18: Placebo 2 x daily 2 capsule

Number of subjects in period 1	Verum group	Placebo Group
Started	10	10
Completed	8	9
Not completed	2	1
missing data, primary outcome	1	1
Protocol deviation	1	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	Verum group
Reporting group description: -	
Reporting group title	Placebo Group
Reporting group description: -	

Primary: Change of the ADAS-Cog

End point title	Change of the ADAS-Cog
End point description: ADAS-cog, Alzheimer Disease Assessment Scale-Cognitive Subscale; structural cerebral imaging were performed at 6,12 and 18 months	
End point type	Primary
End point timeframe: from baseline to 18 months	

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Score				
arithmetic mean (standard deviation)				
6 months	0 (± 3.8)	-0.9 (± 5.7)		
12 months	2.1 (± 3.8)	0.4 (± 5.6)		
18 months	5 (± 6.14)	5.3 (± 5.4)		

Attachments (see zip file)	ADAS-Cog at different times/ADAS-Cog at different
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Statistical analyses

Statistical analysis title	ADAS-cog from baseline to 18 months
Statistical analysis description: All target variables were evaluated in an exploratory fashion. For the descriptive evaluation, the median with the min and max and the mean with SD were calculated for all continuous parameters of the primary endpoint. Results see attached document ADAS-Cog at different times.	
Comparison groups	Placebo Group v Verum group
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: MMSE

End point title	MMSE
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End point description:

Mini-Mental-State-Examination

End point type	Secondary
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End point timeframe:

18 months

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Score				
number (not applicable)				
median score	21	20.5		

Statistical analyses

No statistical analyses for this end point

Secondary: MMSE change from BL

End point title	MMSE change from BL
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End point description:

End point type	Secondary
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End point timeframe:

18months

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Score				
arithmetic mean (standard deviation)	-3.1 (± 4.3)	-3.3 (± 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: change of the Semantic word fluency

End point title	change of the Semantic word fluency
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End point description:

End point type	Secondary
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End point timeframe:

18 months

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: SCore				
average score	9	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Semantic word fluency change from baseline

End point title	Semantic word fluency change from baseline
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End point description:

End point type	Secondary
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End point timeframe:

18 months

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Score				
arithmetic mean (standard deviation)	-2.6 (\pm 3)	-1.6 (\pm 3.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: MVGT

End point title	MVGT
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End point description:

Munich Verbal Memory Test

End point type	Secondary
End point timeframe:	
18 months	

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Words				
enumerated word count	22	17		
recall task	6	5		
recognition task (false words)	15	17		

Statistical analyses

No statistical analyses for this end point

Secondary: MVGT change to baseline

End point title	MVGT change to baseline
End point description:	

End point type	Secondary
End point timeframe:	
18 months	

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Words				
arithmetic mean (standard deviation)				
enumerated word count	-8.9 (± 8)	-11.4 (± 12.2)		
recall task	-6.3 (± 9.2)	-3.3 (± 6)		
recognition task	4.6 (± 6.5)	3.4 (± 3.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: WHO Quality of Life BREF

End point title	WHO Quality of Life BREF
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End point description:

End point type Secondary

End point timeframe:
18months

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Score				
number (not applicable)	75	62.5		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: TMT

End point title TMT

End point description:
Trail Making Test

End point type Other pre-specified

End point timeframe:
18 months

End point values	Verum group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Score				
arithmetic mean (standard deviation)				
Part A	9.1 (± 59.9)	12.1 (± 40.5)		
Part B	4.0 (± 49.1)	11.1 (± 61.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

18months, overall treatment period

Assessment type	Systematic
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Dictionary used

Dictionary name	own
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Dictionary version	1
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Reporting groups

Reporting group title	Verum Group
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Reporting group description: -

Reporting group title	Placebo Group
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Reporting group description: -

Serious adverse events	Verum Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hospitalization cause of renal insufficiency			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-serious adverse events	Verum Group	Placebo Group	
Total subjects affected by non-serious adverse events subjects affected / exposed	7 / 10 (70.00%)	6 / 10 (60.00%)	
Investigations			
CRP-increase, transient subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Increase of creatine, revisble subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Increase of lipase, asymptomatic subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
delirium	Additional description: pyrexia with delirium		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dizziness subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tingling parästhesia subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anemia subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal fullness subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Epigastric pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Abdominal cramps subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Nausea subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	0 / 10 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	1 / 10 (10.00%) 1	
Emesis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Lower breathing sound subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Skin and subcutaneous tissue disorders Itching with skin rash subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Dermatomycosis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Eczema subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Psychiatric disorders			

Episode of depression subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Musculoskeletal and connective tissue disorders			
Gonarthrosis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
contusion of the shoulder after fall event subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Backache subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 10 (20.00%) 2	
Influenza infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Rhinitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2009	update study protocol Version 1.1, deregistration study centre Münster
15 February 2010	update study protocol Version.1.2, adjustment of inclusion criteria
28 March 2011	update study protocol Version1.3, Change of PI, adjustment inclusion, exclusion and stop criteria, extension of the recruitment period.

Notes:

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.

The aim was to recruit 2x25 subjects and then to recalculate the number of cases. Due to organizational reasons (change of personnel and recruitment problems) only 21 patients were enrolled. This resulted in changes to study protocol.

Notes: