EU Clinical Trials Register

Clinical trial results:
Pilot study to assess P-glycoprotein function at the blood-brain barrier of patients with mild to moderate Alzheimer's disease

Summary

EudraCT number	2013-001724-19
Trial protocol	AT
Global end of trial date	13 May 2016

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	2013/2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria,
Public contact	Klinische Pharmakologie, Medizinische Universität Wien, 0043 1404002981, klin-pharmakologie@meduniwien.ac.at
Scientific contact	Klinische Pharmakologie, Medizinische Universität Wien, 0043 1404002981, klin-pharmakologie@meduniwien.ac.at

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	14 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2016
Global end of trial reached?	Yes
Global end of trial date	13 May 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to examine differences in Pgp function at the BBB between AD patients and age-matched control subjects by performing (R)-11C-verapamil PET scans before, during and after Pgp modulation with tariquidar. Tariquidar will be administered at a dose of 3 mg/kg which corresponds to the half-maximum effect dose for inhibition of Pgp at the BBB. We hypothesize that AD patients will show higher increases in (R)-11C-verapamil brain distribution following tariquidar administration than control subjects due to reduced cerebral Pgp function in AD patients. Furthermore the influence of ABCB1 single nucleotide polymorphisms (SNPs, 3435C>T, 2677G>T, 1236C>T) on (R)-11C-verapamil distribution to the brain before, during and after tariquidar infusion will be assessed.

To compare rate constants of (R)-11C-verapamil transport across the BBB before, during and after tariquidar infusion between AD patients and age-matched control subjects.
Secondary objectives:

Protection of trial subjects:	
Subjects were during the trial under the supervision of an physician or an experienced Nurse.	
Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	16 December 2013
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	Austria: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	13
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited using the data base of the Dep. of Clinical Pharmacology, Medical University of Vienna.

Pre-assignment

Screening details:

Check of the in- and exclusion criteria, physical examination, vital signs, laboratory assessment and ECG recording

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group B: Age-matched controls

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tariquidar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg BW given once as an i.v. infusion over 30 min
(R)-11C-verapamil at a tracer dose of <100 µg corresponding to an activity of approximately 5.5 MBq/kg BW, maximum 400 MBq as an i.v. bolus twice per study day

Arm title	Group C: Young controls

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tariquidar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg BW given once as an i.v. infusion over 30 min
(R)-11C-verapamil at a tracer dose of <100 µg corresponding to an activity of approximately 5.5 MBq/kg BW, maximum 400 MBq as an i.v. bolus twice per study day

Number of subjects in period 1	Group B: Age-matched controls	Group C: Young controls
Started	5	11
Completed	5	11

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	16	16	
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)	13	13	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	14	14	

End points

End points reporting groups

Reporting group title	Group B: Age-matched controls
Reporting group description: -	
Reporting group title	Group C: Young controls
Reporting group description: -	

Primary: Rate constants of (R)-11C-verapamil transport across the BBB before, during and after tariquidar infusion obtained from kinetic modeling of the blood and PET data

End point title	Rate constants of (R)-11C-verapamil transport across the BBB before, during and after tariquidar infusion obtained from kinetic modeling of the blood and PET data

End point description:

End point type	Primary

End point timeframe:

scan 1: 120 min, scan 2: 40 min, for 5 healthy subjects scan 3: 60 min,

End point values	Group B: Age-matched controls	Group C: Young controls		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	11		
Units: kBq/ml	5	11		

Statistical analyses

Statistical analysis title	End point statistic
Comparison groups	Group B: Age-matched controls v Group C: Young controls
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events: 10.09.2014-13.05.2016	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Adverse events overall trail

Reporting group description: -

Serious adverse events	Adverse events overall trail		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adverse events overall trail		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Phlebitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dysgeusia			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			

Nasal congestion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2013	Amendment to study protocol
30 May 2014	Amendment to study protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 May 2016	Unsuccessful recruitment	-

Notes:

Limitations and caveats

 None reported