Clinical trial results:
A pilot study to assess [11C]elacridar and [11C]tariquidar as two positron emission tomography radiotracers for visualization of P-glycoprotein in humans.

Summary

EudraCT number	2010-020759-30
Trial protocol	AT
Global end of trial date	15 July 2014

Results information

Result version number	v1 (current)
This version publication date	12 July 2019
First version publication date	12 July 2019
Summary attachment (see zip file)	Interaction of C11-tariquidar and C11-elacridar (Publication_ EudraCT 2010-020759-30.pdf)

Trial information

Trial identification

Sponsor protocol code	[11C]inhibitors

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	Währinger Gürtel 18-20, Vienna, Austria, 1090
Public contact	Markus Zeitlinger, MD , Medical University of Vienna, Department of Clinical Pharmacology, 0043 140400 29810, markus.zeitlinger@meduniwien.ac.at
Scientific contact	Markus Zeitlinger, MD , Medical University of Vienna, Department of Clinical Pharmacology, 0043 140 400 29810, markus.zeitlinger@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	16 April 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2013
Global end of trial reached?	Yes
Global end of trial date	15 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Study group 1: To assess the utility of [11C]elacridar and [11C]tariquidar for the visualization of P-gp at the human blood-brain barrier.
Study group 2: To gain data about whole body biodistribution and organ wise radiation dosimetry of [11C]elacridar and [11C]tariquidar in humans.

Protection of trial subjects:

Subjects were during the trial under the supervision of a physician or an experienced nurse.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 2011
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: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited by use of the data base of the Dep. of Clinical Pharmacology, Medical University 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	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	two parallel groups

Arm description:

The study will be performed as a pilot clinical PET-study in two parallel groups.

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

Dosage and administration details:

[11C]tariquidar at a tracer dose of less than 20 µg corresponding to a maximum activity of 400 MBq as an i.v. bolus. Tariquidar at a dose of 4 mg/kg body weight, given once as an i.v. infusion.

Investigational medicinal product name	Elacridar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

[11C]elacridar at a tracer dose of less than 20 µg corresponding to a maximum activity of 400 MBq as an i.v. bolus.

Investigational medicinal product name	Verapamil
Investigational medicinal product code	C08DA01
Other name	Isoptin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

(R)-[11C]verapamil at a tracer dose of less than 20 µg corresponding to a maximum activity of 400 MBq as an i.v. bolus, at an interval of approximately 4 h after the [11C]elacridar or [11C]tariquidar injection.

Number of subjects in period 1	two parallel groups
Started	24
Completed	24

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	24	24	
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)	24	24	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	6	6	
Male	18	18	

End points

End points reporting groups

Reporting group title	two parallel groups

Reporting group description:

The study will be performed as a pilot clinical PET-study in two parallel groups.

Primary: Brain time-activity curves of [11C]elacridar, [11C]tariquidar and (R)-[11C]verapamil before and after infusion of 4 mg/kg body weight tariquidar

End point title	Brain time-activity curves of [11C]elacridar, [11C]tariquidar and (R)-[11C]verapamil before and after infusion of 4 mg/kg body weight tariquidar[1]

End point description:

End point type	Primary

End point timeframe:

0-120 min

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: This study group consists of two radiotracer applications in different subjects, no in between group statistics has been performed

End point values	two parallel groups			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Bq/ml				
number (not applicable)	12			

Statistical analyses

No statistical analyses for this end point

Primary: [11C]elacridar and [11C]tariquidar radiation dose in different organs, normalized to injected dose and expressed as mSv/MBq

End point title	[11C]elacridar and [11C]tariquidar radiation dose in different organs, normalized to injected dose and expressed as mSv/MBq[2]

End point description:

End point type	Primary

End point timeframe:

0-120min

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: This study group comprises radiation dosimetry measurements only, so no statistics was done

End point values	two parallel groups			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Bq/ml				
number (not applicable)	12			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from 11.03.2011 to 26.03.2013	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Serious adverse events	overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 24 (62.50%)		
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
General disorders and administration site conditions			
Hot flush			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Immune system disorders			

Anaphylactic reaction subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Gastrointestinal disorders Dysgeusia subjects affected / exposed occurrences (all)	7 / 24 (29.17%) 7		
Infections and infestations Pharyngitis subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2011	deletion of Exclusion criteria for study Group 2: Study group 2 only - weight: 60 – 85 kg and height: 170 – 185 cm
07 June 2011	One additional PET-Scan on the study day. IMP dose reduction of Tariquidar from 4 mg/kg body weight to 3 mg/kg body weight
10 June 2012	additional genetic Analysis of BCRP (breast cancer resistance Protein)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported