Clinical trial results:
A randomized, pilot study to assess the impact of single nucleotide polymorphisms in the ABCB1 and ABCG2 genes on brain and organ distribution of dual Pgp/BCRP substrates in humans.

Summary

EudraCT number	2012-005796-14
Trial protocol	AT
Global end of trial date	05 May 2020

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	1/2013

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Klinische Pharmakologie, Medizinische Universität Wien, 0043 14040029810, klin-pharmakologie@meduniwien.ac.at
Scientific contact	Klinische Pharmakologie, Medizinische Universität Wien, 0043 14040029810, 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	29 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2015
Global end of trial reached?	Yes
Global end of trial date	05 May 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

X To compare 11C-tariquidar and 11C-elacridar brain distribution before and during tariquidar infusion
X To assess the influence of ABCB1 and ABCG2 SNPs on 11C-tariquidar and 11C-elacridar brain distribution before and during tariquidar infusion

Protection of trial subjects:

During the trial subjects were under continous supervision of a physician or experienced nurse.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 2014
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: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Volunteers will be recruited from an existing DNA database available at the Austrian Red Cross, Blood Service for Vienna, Lower Austria and Burgenland. From this database 3 groups of 20 individuals each with the following homozygous genotypes will be selected.

Pre-assignment

Screening details:

Group 1: 11C-Tariquidar
Group 2: 11C-Elacridar
Group 3: (R)-11C-verapamil

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

11C-tariquidar

Arm type	Active comparator
Investigational medicinal product name	11C-tariquidar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Two consecutive i.v. bolus injections of 11C-tariquidar with a maximum activity of 400 MBq. The estimated total effective dose per scan is 2.2 mSv for an i.v. injected activity amount of 400 MBq

Arm title	Group 2

Arm description:

11C-elacridar

Arm type	Experimental
Investigational medicinal product name	11C-elacridar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Two consecutive i.v. bolus injections of (R)-11C-elacridar with a maximum activity of 400 MBq. The estimated total effective dose per scan is 2.2 mSv for an i.v. injected activity amount of 400 MBq

Arm title	Group 3

Arm description:

11C-verapamil

Arm type	Experimental

Investigational medicinal product name	11C-verapamil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Two consecutive i.v. bolus injections of (R)-11C-verapamil with a maximum activity of 400 MBq. The estimated total effective dose per scan is 2.2 mSv for an i.v. injected activity amount of 400 MBq

Investigational medicinal product name	11C-verapamil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Two consecutive i.v. bolus injections of (R)-11C-verapamil with a maximum activity of 400 MBq. The estimated total effective dose per scan is 2.2 mSv for an i.v. injected activity amount of 400 MBq

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	15	7	5
Completed	15	7	5

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	27	27	
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)	0	0	
From 65-84 years	27	27	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	26	26	

End points

End points reporting groups	
Reporting group title	Group 1
Reporting group description: 11C-tariquidar	
Reporting group title	Group 2
Reporting group description: 11C-elacridar	
Reporting group title	Group 3
Reporting group description: 11C-verapamil	

Primary: radioactivity concentration	
End point title	radioactivity concentration
End point description:	
End point type	Primary
End point timeframe: 1 hour	

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	7	5	
Units: kBq/ml				
number (not applicable)	0.72	0.054	0.033	

Statistical analyses

Statistical analysis title	VT
Comparison groups	Group 1 v Group 2 v Group 3
Number of subjects included in analysis	27
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: 30 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0
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 / 27 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 27 (92.59%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	5		
General disorders and administration site conditions			
Phlebitis	Additional description: heat and redness on upper arm		
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	5		
Blood and lymphatic system disorders			

Collapse subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3		
Metabolism and nutrition disorders			
Dysgeusia subjects affected / exposed occurrences (all)	Additional description: metalic taste 15 / 27 (55.56%) 15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2015	Change of PI

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported