



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